Diseases of the liver, gall-bladder and bile-ducts.

Contributors

Rolleston, Humphry Davy, Sir, 1862-1944.
University of Leeds. Library

Publication/Creation

London : MacMillan & Co., 1912.

Persistent URL

https://wellcomecollection.org/works/nba45qsz

Provider

Leeds University Archive

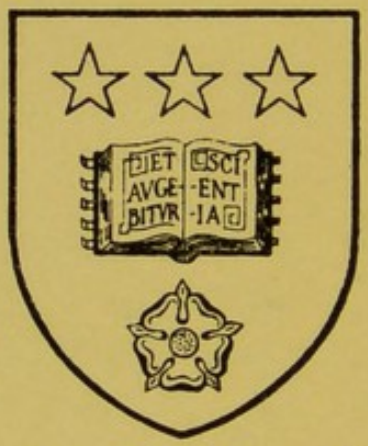
License and attribution

This material has been provided by This material has been provided by The University of Leeds Library. The original may be consulted at The University of Leeds Library. where the originals may be consulted.
Conditions of use: it is possible this item is protected by copyright and/or related rights. You are free to use this item in any way that is permitted by the copyright and related rights legislation that applies to your use. For other uses you need to obtain permission from the rights-holder(s).

wellcome collection

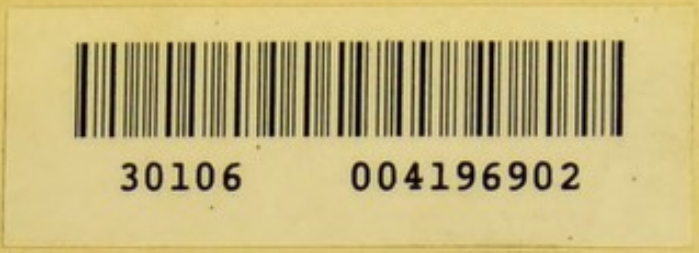
Wellcome Collection
183 Euston Road
London NW1 2BE UK
T +44 (0)20 7611 8722
E library@wellcomecollection.org
https://wellcomecollection.org

Library of the School of Medicine
University of Leeds

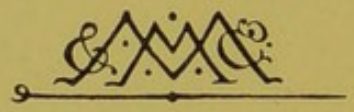


From the library of
The Right Honourable Lord Moynihan
of Leeds
1865 — 1936
Professor of Surgery

STORE
WI 700
ROL


30106 004196902

DISEASES OF THE LIVER, GALL-BLADDER AND BILE-DUCTS



MACMILLAN AND CO., LIMITED
LONDON · BOMBAY · CALCUTTA
MELBOURNE

THE MACMILLAN COMPANY
NEW YORK · BOSTON · CHICAGO
DALLAS · SAN FRANCISCO

THE MACMILLAN CO. OF CANADA, LTD.
TORONTO

PLATE I.

GROWTHS IN LIVER SECONDARY TO CARCINOMA OF THE RECTUM.

DISEASES

OF THE

LIVER, GALL-BLADDER AND BILE-DUCTS

BY

HUMPHRY DAVY ROLLESTON

M.A., M.D. (Cantab.), F.R.C.P.

SENIOR PHYSICIAN, ST. GEORGE'S HOSPITAL
PHYSICIAN, VICTORIA HOSPITAL FOR CHILDREN, CHELSEA
FORMERLY FELLOW OF ST. JOHN'S COLLEGE, CAMBRIDGE

ILLUSTRATED

MACMILLAN AND CO., LIMITED
ST. MARTIN'S STREET, LONDON
1912

COPYRIGHT

First published elsewhere
Second Edition published by Macmillan & Co., Ltd., 1912.

60 2103

3H4H

UNIVERSITY
OF LEEDS
MEDICAL LIBRARY.

PREFACE TO THE SECOND EDITION

THE work has been thoroughly revised; much new matter has been added, many alterations have been made, and condensation has been carried out as far as is compatible with a full consideration of the subject. I am specially indebted to Dr. A. J. Jex-Blake for reading the proofs, and to Dr. R. S. Trevor for generous help in many ways.

H. D. R.

September 1912.

PREFACE TO THE FIRST EDITION

During the past twelve years I have paid special attention to the diseases of the liver, both from the clinical and pathological points of view. Some of my observations have already appeared in various medical journals, Transactions of Medical Societies, and in articles on diseases of the liver in Vols. V and VI of the *Encyclopædia Medica* (in 1900).

Special Treatises often begin by dealing with the normal anatomy and physiology of the part concerned, but to be of any real value or use to the reader the anatomy and physiology of the liver must be dealt with in such detail as would seriously add to the bulk of the work, and I have therefore decided to omit any introductory chapter of this kind. I have done so with less regret as I believe that in most instances readers refer to textbooks or special monographs on the anatomy and physiology of the subject rather than to the introductory remarks at the commencement of a clinical treatise.

In the description of each disease attention is first directed to the underlying morbid changes, as without a grasp of these it is impossible to make a rational diagnosis, to treat the clinical manifestations in a satisfactory manner, or to give a reliable prognosis. Selected cases, for many of which I am indebted to my colleagues at St. George's Hospital, have been embodied in the text, especially in the parts dealing with the symptoms and clinical aspects. These cases and, in most instances, statistical details have been set in

smaller print. The literature of the subject is enormous, and though no trouble has been spared, it is inevitable that omissions must exist. After full consideration I have decided to omit, in almost all cases, the bibliographies which had been prepared, and have only retained the references to authors actually quoted.

The illustrations are nearly all original, and I must cordially acknowledge my gratitude to many past students of St. George's Hospital for their help in this respect, especially to Dr. E. A. Wilson and Mr. Lawrence Jones (coloured plates, etc.), to Dr. H. Spitta and Mr. S. G. Penny (photomicrographs), and to Messrs. P. L. and S. P. Mummery, Dr. G. H. Goldsmith, and Mr. H. G. Drake Brockman. To Dr. H. Morley Fletcher, Professor S. Delépine, and Dr. T. Fisher I am indebted for permission to use or to copy figures which have already appeared elsewhere.

H. D. ROLLESTON.

November 1904.

CONTENTS

DISEASES OF THE LIVER

	PAGE
Anatomical Abnormalities	1
Some Post-mortem Appearances of the Liver	5
Acquired Deformities	8
Displaced Liver	16
Hepatoptosis	22
Functional Disease	36
Diseases of the Hepatic Artery	44
Diseases of the Hepatic Veins	48
Thrombosis of the Portal Vein	53
Suppurative Pylephlebitis	68
Other Affections of the Portal Vein	82
Morbid Conditions of the Lymphatic Vessels and Glands	84
Chronic Venous Engorgement	85
Pericarditic Pseudo-Cirrhosis	96
Infarcts	101
Acute Congestion	107
Acute Hepatitis	111
Abscess	117
Single or Tropical Abscess	117
Multiple Abscesses	154
Perihepatitis	157
Acute	157
Chronic	160
Local	160
Universal	161
Cirrhosis	172

PAGE

Portal Cirrhosis 177
Pigmented Cirrhosis 302
Biliary Cirrhosis 309
Hypertrophic Biliary Cirrhosis 309
Obstructive Biliary Cirrhosis 327
Cirrhosis in Children 333
Tuberculosis of the Liver and Bile-Ducts 336
Tuberculosis and Cirrhosis 345
Syphilis 348
Acquired 348
Secondary Lesions 348
Tertiary Lesions 351
Inherited 370
Actinomycosis 383
Lymphadenoma 388
Hydatid Cysts 391
Alveolar or Multilocular Hydatid 422
Fatty Liver 426
Lardaceous Disease 433
Pigmentation 439
Calcification 440
Leukaemic Infiltration 441
Cysts 444
Cystic Disease 447
Adenoma 455
Angioma 463
Other Innocent Tumours 467
Malignant Tumours 469
Jaundice 531
Jaundice in the Newly Born 568
Icterus Gravis 573
Multiple Non-Inflammatory Necrosis of the Liver 575
Acute Yellow Atrophy 575
Jaundice of Phosphorus Poisoning 592
Infectious Jaundice 596
Weil's Disease 597

DISEASES OF THE GALL-BLADDER

PAGE

Abnormalities 601
Acute Cholecystitis 603
Chronic Cholecystitis 624
Tuberculosis, Etc. 627
Parasitic Affections 628
Innocent Tumours 629
Malignant Tumours 631

DISEASES OF THE BILE-DUCTS

Abnormalities 649
Congenital Obliteration 649
Congenital Syphilitic Stricture 658
Dilatation and Cysts 659
Simple Stricture 661
Catarrhal Jaundice or Acute Catarrhal Cholangitis . . . 663
Suppurative Cholangitis 671
Chronic Catarrhal Cholangitis 678
Pericholangitis 680
Parasitic Affections 682
Innocent Tumours 687
Malignant Tumours of the Larger (Extra-Hepatic) Bile-Ducts . 689
Malignant Tumours of the Ampulla of Vater 702

CHOLELITHIASIS 709

INDEX 783

ILLUSTRATIONS

COLOURED PLATES

No.		
I.	Secondary Carcinoma of the Liver (E. A. Wilson)	*Frontispiece*
II.	Cirrhotic Liver (E. A. Wilson)	*Face page* 198
III.	Tuberculous Cavities in the Liver (L. Jones)	,, 341
IV.	Microscopic appearances of a tuberculous Cavity in the Liver (H. Morley Fletcher)	,, 341
V.	Nodular Cirrhosis or multiple Adenoma (E. A. Wilson)	,, 462
VI.	Gall-stones, spontaneous Fracture (E. A. Wilson)	,, 729
VII.	Cholangitic Suppuration in the Liver (E. A. Wilson)	,, 770

FIGURES

FIG.		PAGE
1-3.	Abnormal Lobulation of the Liver (G. H. Goldsmith)	2
4.	Photomicrograph of foaming Liver (H. Spitta)	7
5.	Constriction Lobe containing secondary Carcinoma (L. Jones)	9
6.	Uniformly cirrhotic tight-laced Liver (P. L. Mummery)	10
7.	Riedel's tongue-like Lobe (T. Fisher)	12
8.	Riedel's Lobe and suppurative Cholangitis (E. A. Wilson)	13
9.	Hepatoptosis (H. B. Roderick)	28
10.	Aneurysm of hepatic Artery (C. K. McKerrow)	44
11.	Thrombosis of portal Vein in Cirrhosis (E. A. Wilson)	55
12.	Temperature Chart in suppurative Pylephlebitis	77
13.	Photomicrograph of Liver in chronic venous Engorgement (S. G. Penny)	90
14, 15.	Microscopic appearances in advanced chronic venous Engorgement	99
16.	Anaemic Infarct of Liver (L. Jones)	102
17.	Photomicrograph of true Infarct of Liver (S. G. Penny)	103
18.	Microscopic appearances in acute Hepatitis	112
19.	Photomicrograph of acute Hepatitis (H. Spitta)	114
20.	Hepatic Abscess rupturing into Inferior Vena Cava (L. Jones)	129
21.	Areolar Abscess of Liver (E. A. Wilson)	129
22.	Acute Perihepatitis and Cirrhosis (S. G. Penny)	158
23.	Microscopic appearances in chronic Perihepatitis	164
24.	Photomicrograph of chronic Perihepatitis (H. Spitta)	168

FIG. PAGE
25. Focal necrosis in enteric Fever 186
26. Cirrhotic Liver with portal Thrombosis (E. A. Wilson) . . . 199
27. Cirrhosis with Enlargement of the Spigelian Lobe 199
28. Section of Liver with multilobular Cirrhosis (E. A. Wilson) . . 200
29, 30. Microscopic appearances of multilobular Cirrhosis . . 201, 202
31. Microscopic appearances of Cirrhosis in Haemochromatosis . . . 203
32. Photomicrograph shewing pseudobile Canaliculi in Cirrhosis (H. Spitta) . 204
33. Microscopic appearances of slight Cirrhosis with fatty Change . . 206
34. Dilated Bile-duct with Pericholangitis in Cirrhosis 209
35. Large parumbilical Vein in Cirrhosis 211
36. Photomicrograph of fibrosis in the Spleen in Cirrhosis (S. G. Penny) . 217
37. Temperature Chart in Cirrhosis 238
38. Microscopic appearances of Cirrhosis in Haemochromatosis . . . 306
39. Microscopic appearances of unilobular Cirrhosis 315
40. Microscopic appearances of focal Necrosis of the Liver in biliary Obstruction 329
41. Large Gumma of the Liver (Delépine and Sisley) 352
42. Microscopic appearances of a recent Gumma 354
43. Photomicrograph of an old Gumma (S. G. Penny) 355
44. Calcification of a Gumma (E. A. Wilson) 356
45. Syphilitic Cicatrices 357
46. Microscopic appearances in intercellular Cirrhosis 372
47. *Treponema pallidum* in intercellular Cirrhosis in congenital Syphilis (E. O. Jordan) 373
48. Fibrosis of the Liver in congenital Syphilis (H. Morley Fletcher) . . 375
49. Clubbing of the Fingers in delayed congenital Syphilis (H. G. Drake Brockman) 380
50. Actinomycosis of the Liver (E. A. Wilson) 385
51. Microscopic appearances of Lymphadenoma of the Liver (H. Spitta) . 389
52. Obsolete hydatid Cyst in the Liver (E. A. Wilson) 396
53. Rupture of hydatid Cyst into common hepatic Duct (E. A. Wilson) . 418
54. Photomicrograph of fatty Change in the Liver (S. G. Penny) . . 430
55. Microscopic appearances in Liver with fatty Change and slight Cirrhosis . 431
56. Photomicrograph of the Liver in Leukaemia (S. G. Penny) . . . 443
57. Cystic Disease of the Liver (H. Morley Fletcher) 450
58. Photomicrograph of congenital cystic Disease of the Liver (H. Spitta) . 451
59. Large single Adenoma of the Liver (I. Strauss) 457
60. Microscopic appearances of Cavernoma of the Liver 465
61. Photomicrograph of primary Carcinoma of the Liver (S. P. Mummery) . 472
62. Pre-cancerous Proliferation of the Bile-ducts in primary Carcinoma of the Liver (L. S. Milne) 475
63. Primary Carcinoma with Cirrhosis (P. L. Mummery) . . . 477
64, 65. Microscopic appearances in primary Carcinoma with Cirrhosis . . 478
66. Photomicrograph of primary Carcinoma with Cirrhosis (H. Spitta) . . 479
67. Multiple primary Sarcoma of the Liver (W. R. Harris) . . . 483

FIG. PAGE
68. Microscopic appearances of a small spindle-celled Sarcoma of the Liver . 484
69. Photomicrograph of a small round-celled Sarcoma of the Liver (S. G. Penny) 485
70. Cystic Change in a secondary carcinomatous Growth in the Liver (L. Jones) 490
71. Photomicrograph of a secondary Perithelioma in the Liver (H. Spitta) . 493
72. Microscopic appearances of a secondary Endothelioma in the Liver . 494
73. Secondary Carcinoma in a Constriction Lobe of the Liver (L. Jones) . 496
74. Minute carcinomatous Emboli in the intrahepatic branches of the portal Vein 497
75. Photomicrograph of secondary melanotic Sarcoma in the Liver (S. G. Penny) 504
76. Multiple primary Sarcoma of the Liver (F. Golla) 508
77. Temperature Chart in secondary Endothelioma of the Liver . . 523
78. Xanthoma multiplex on the Fingers 541
79, 80. Microscopic appearances in acute yellow Atrophy . . 581, 582
81. Temperature Chart in Weil's Disease 599
82. Photomicrograph of the Membrane in membranous Cholecystitis (S. G. Penny) 615
83. Phlegmonous Cholecystitis (E. A. Wilson) 622
84. Chronic Cholecystitis with Calcification (E. A. Wilson) . . . 625
85. Photomicrograph of chronic Cholecystitis (H. Spitta) . . . 626
86. Photomicrograph of columnar-celled Carcinoma of the Gall-bladder (S. G. Penny) 632
87. Squamous-celled Carcinoma of the Gall-bladder (R. S. Trevor) . . 633
88. Carcinoma in the position of the Gall-bladder, containing Calculi . . 634
89. Primary Carcinoma of the Gall-bladder (E. A. Wilson) . . . 636
90. Unilobular Cirrhosis in congenital Obliteration of the Bile-ducts . . 654
91. Microscopic appearances of the common Bile-duct in congenital Obliteration 655
92. Microscopic appearances in congenital syphilitic Stricture of the common Bile-duct 658
93. Photomicrograph of the Liver in suppurative Cholangitis (H. Spitta) . 674
94, 95. Chronic Pericholangitis combined with Pylephlebitis . . . 681
96, 97. Photomicrographs of Psorospermosis of the Bile-ducts in a Rabbit (S. G. Penny) 685, 686
98. Papilloma of the common Bile-duct 688
99. Primary Carcinoma of the common Bile-duct 692
100. Microscopic appearances of primary Carcinoma of the common Bile-duct . 695
101. Diagram of the Ampulla of Vater shewing positions where Carcinoma may arise 704
102. Microscopic appearances of Carcinoma of the Ampulla of Vater . . 706
103. Gall-bladder distended with Calculi (E. A. Wilson) . . . 727
104. Calculus impacted in the Neck of the Gall-bladder (E. A. Wilson) . 728
105. Large intrahepatic Calculi (E. A. Wilson) 729
106. Calculus impacted in the cystic Duct ; Cholecystitis with Distension of the Gall-bladder, Mucocele 746
107. Hour-glass Contraction of the Gall-bladder (G. H. Goldsmith) . . 757
108. Calculus in a Diverticulum of the cystic Duct 759

DISEASES OF THE LIVER

ANATOMICAL ABNORMALITIES

Abnormal Lobulation.—The liver has been found to be devoid of any division into lobes; more often there are many lobes so as to suggest a resemblance to the condition seen in some animals. This lobulation, which is not homologous to fetal lobulation of the kidneys, is more marked on the surface of the right lobe than on the left lobe. As many as 16 lobules have been found (Moser [1]). Whilst these lobules must be distinguished from the irregularities and hobnails of portal cirrhosis and from cicatrices manifestly syphilitic, it is probable that this lobulation is a pathological and not a morphological phenomenon. It may be due to syphilis, fetal peritonitis, or possibly to tuberculosis. Probably congenital syphilis is responsible for the change in many cases, but positive evidence to this effect is very often wanting. When lobulation of the liver is associated with peritoneal adhesions, it is possible that fetal peritonitis has so modified or interfered with the growth of the organ as to lead to fissuring and lobulation of its surface.

The view that lobulation of the liver might be caused by poisons manufactured by the *Bacillus tuberculosis* was put forward by Hanot,[2] who examined seven cases of lobulated livers in patients dying with tuberculosis, and considered that the lobulation was due to a coarse fibrosis induced by the toxins of tuberculosis (*vide* p. 347).

Alteration in the Relative Size of the Right and Left Lobes.—Occasionally the size of the right or of the left lobe is altered, with a corresponding change in the relative and absolute size of the other lobe. In rare instances the liver, though in its normal position, shews the lobulation seen in transposition of the viscera, the right lobe being small and the left large; or transposition of the lobes without *situs transversus*.

J. Davy [3] described a case in which the left lobe was twice the size of the right.

In some instances there is no manifest cause for this reversal of the normal lobulation of the liver, and it may be supposed that it depends on some alteration of the circulation in fetal or early life. In other

[1] Moser. *Med. Rec.*, N.Y., 1898, liii, 671.
[2] Hanot. *Gaz. des hôp.*, Paris, 1893, lxvi, 902.
[3] Davy, J. *Diseases of the Army*, p. 427, 1862.

instances the diminution in size of the right lobe is manifestly due to syphilitic cicatrices.

Penrose[1] recorded this in acquired syphilis, and Lazarus-Barlow[2] in tardive congenital syphilis.

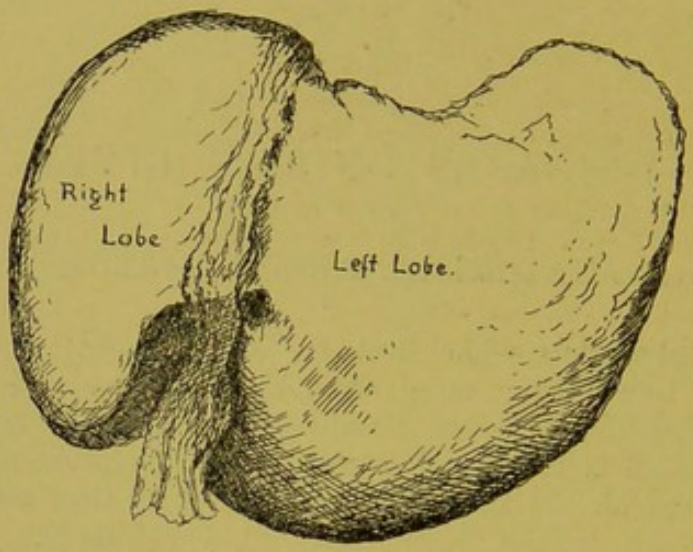
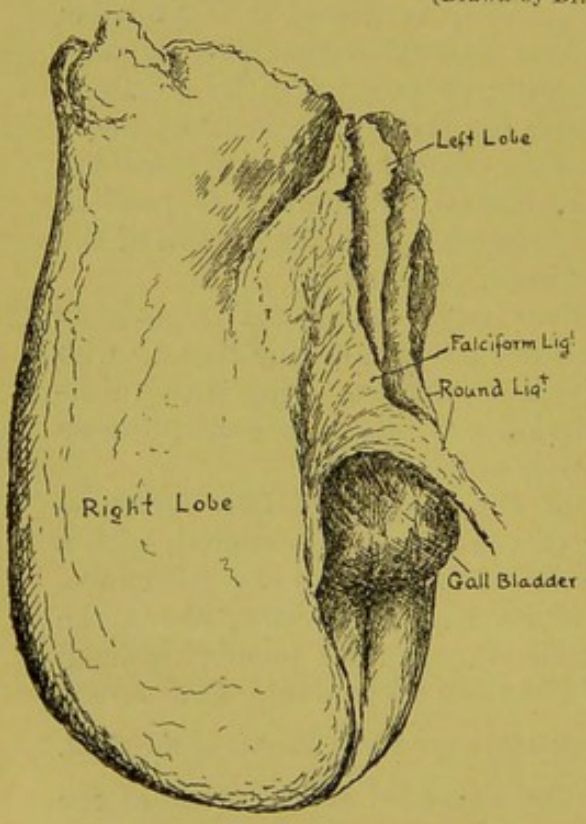


FIG. 1.—Liver with large left lobe and small right lobe; the gall-bladder was on the right lobe. (Drawn by Dr. G. H. Goldsmith.)



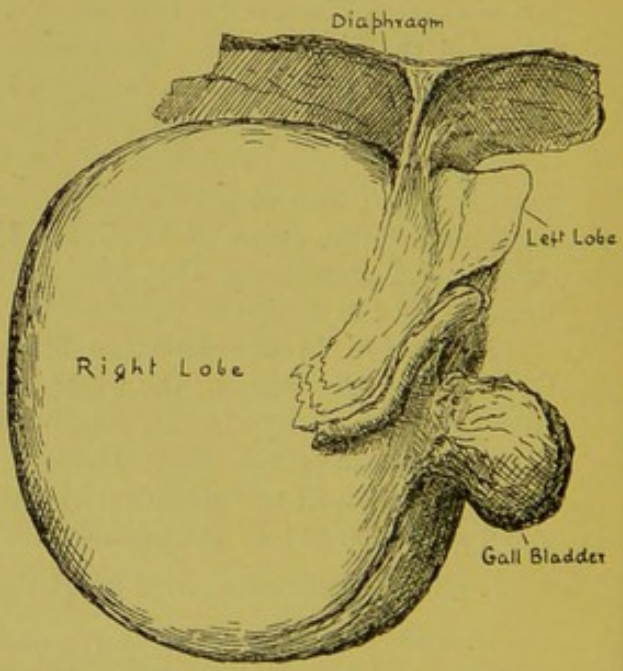


FIG. 2.—Extreme dwarfing of the left lobe of the liver. (Drawn by Dr. G. H. Goldsmith.)
FIG. 3.—Dwarfing of left lobe. The gall-bladder projects from the left margin of the liver and has its long axis in the transverse axis of the body. (Drawn by Dr. G. H. Goldsmith.)

[1] Penrose. *Trans. Path. Soc.*, Lond., 1889, xl, 133.
[2] Lazarus-Barlow. *Ibid.*, 1899, l, 158.

Dwarfing of one of the main lobes is occasionally seen, the other shewing compensatory hypertrophy. The left lobe is the one usually affected, and may be represented by a little flap of hepatic tissue. In these cases the left lateral ligament is correspondingly small and the falciform ligament arises from the left margin of the liver. The stomach is thus abnormally exposed, and the whole of the gall-bladder is visible from the front and projects from the left lateral margin of the liver. Owing to the disturbed relation of the lobes the gall-bladder may be so displaced as to lie with its long axis in the transverse axis of the body (*vide* Fig. 3).

There were 11 cases of dwarfing of one lobe (10 of the left lobe) among about 3000 necropsies at St. Bartholomew's Hospital (Herringham [1]).

There is seldom any very manifest reason why the left lobe should be so atrophied, and it may again be suggested that it is due to some disturbance of the circulation in fetal or early life. The change may be associated with other congenital defects.

Garrod [2] reported extreme dwarfing of the left lobe with lobulation of the right lobe of the liver and the presence of two instead of three aortic valves.

In other instances atrophy of the left lobe may be due to syphilis or to other pathological changes taking place later in life.

I have seen atrophy of the left lobe in a case in which a large intrahepatic calculus pressed upon the vessels entering the left lobe of the liver.

Accessory Lobes.—Small projections of liver substance—about the size of the terminal phalanx of the forefinger—which in miniature imitate the caudate lobe, are quite common and of no pathological significance. Their usual situation is the under surface of the right lobe, near the portal and longitudinal fissures. When markedly pedunculated, they may form "accessory livers." The Spigelian lobe is sometimes curiously pedunculated.

In the Anatomical Museum at Cambridge there is a cast of a pedunculated lobe attached to the left border of the left lobe by a pedicle composed of hepatic tissue. Lawrence and Nabarro [3] described an abnormal process from the left lobe of the liver in association with absence of the inferior vena cava in a female child aged fourteen weeks.

In rare instances large pedunculated tumours, apparently abnormalities and not obviously pathological in origin, may give rise to marked symptoms, such as pyloric obstruction.

An elongated process of the left lobe passed over the stomach and spleen and gave rise to gastric symptoms and signs suggesting a pancreatic cyst in a

[1] Herringham. *St. Barth. Hosp. Rep.*, 1905, xli, 19.
[2] Garrod, A. E. *Trans. Path. Soc.*, Lond., 1897, xlviii, 42.
[3] Lawrence and Nabarro. *Journ. Anat. and Physiol.*, 1901–2, xxxvi, 63.

girl aged 16 years. Removal was followed by relief. Hammond[1] regarded it as congenital. A pedunculated tumour, measuring 3 × 2 inches, which caused pyloric obstruction, was successfully removed by Adams.[2]

Accessory Livers.—Isolated fragments of hepatic tissue or "rests" have been found in the suspensory ligament, but they are very rare, thus contrasting with the frequency of accessory suprarenals and of splenunculi.

Pepere[3] described innumerable small nodules of hepatic tissue or accessory livers scattered over the peritoneum and great omentum. One with a diameter of 7 cm. formed a solitary adenoma in the liver. Thirty-one years previously Wagner[4] recorded a number of nodules composed of liver cells in the falciform ligaments of two infants aged nine days and two months respectively. Chaillous[5] described a large accessory lobe attached to the anterior border of the liver, to the right of and close to the falciform ligament, on a level with the quadrate lobe; it was pear-shaped, like the gall-bladder. It was found in the body of an infant. Davy,[6] in the examination of a man aged twenty-three, dead of dysentery, found a small mass about the size of a hazel-nut, the structure of which appeared to be the same as that of the liver, attached to the concave surface of that organ by a delicate pedicle. Mahomet[7] described an accessory liver attached to the tip of the gall-bladder in a case of cirrhosis; the accessory liver was also cirrhotic. I have seen a somewhat similar condition in a lardaceous liver. Bland-Sutton[8] figures an accessory liver attached to the side of a gall-bladder.

Accessory livers may also be produced by atrophy of the liver cells in the pedicles of the minute accessory lobes so commonly seen on the under surface of the liver, with the result that a small peritoneal ligament unites the accessory liver to the main organ.

It seems possible that some detached lobes seen in adult life may be due to the effects of pressure or to atrophy of some of the liver tissue from interference with the blood-supply. Constriction lobes attached to the lower extremity of the right or more rarely the left lobe are described under the deformities of the liver due to tight lacing (*vide* p. 8). The following may be regarded as examples of atrophy of the intervening liver tissue inducing the appearances of an accessory lobe.

In a specimen in St. George's Hospital Museum the part of the liver representing the left lobe is completely separated for a distance of 3 inches from the rest of the liver; it was also attached by a kind of mesentery to the cardiac end of the stomach.[9] In a man aged twenty-four there was a vestige only of the left lobe, which was not continuous with the right lobe (Davy).

[1] Hammond, L. J. *Ann. Surg.*, 1905, xli, 31.
[2] Adams, J. A. *Glasgow Med. Journ.*, 1906, lxvi, 415.
[3] Pepere. *Arch. per le sc. med.*, 1902, xxvi, 117.
[4] Wagner. *Arch. der Heilk.*, 1861, i, 251.
[5] Chaillous. *Bull. Soc. Anat.*, Paris, 1898, lxvii, 572.
[6] Davy, J. *Diseases of the Army*, p. 428, 1862.
[7] Mahomet. *Trans. Path. Soc.*, Lond., 1877, xxviii, 147.
[8] Bland-Sutton. *Lancet*, Lond., 1907, i, 3.
[9] Series ix. 161A. See also Dickinson, W. H., *Trans. Path. Soc.*, Lond., 1867, xvii, 160.

Atrophy may involve the base of attachment of the Spigelian (Davy [1]) or possibly of the caudate lobe and so lead to a pedunculated lobe.

It may be mentioned that between the peritoneal layers of the left lateral ligament the remains of a rudimentary lobe can be seen in the presence of hepatic and portal vessels, though the liver cells have disappeared. Occasionally small nodules of hepatic tissue are seen in this position (Tarozzi [2]).

Furrows on the surface of the liver not due to cicatrisation, as shewn by the healthy state of the peritoneum and underlying parenchyma, are fairly common, and were divided by Cruveilhier [3] in 1856 into (1) costal and (2) diaphragmatic. The costal grooves are seen on the lateral surface of the right lobe and their direction corresponds with that of the ribs. The diaphragmatic grooves are described on p. 10.

SOME POST-MORTEM APPEARANCES OF THE LIVER

A FEW words may be said about certain common post-mortem appearances of the liver, which will not be described elsewhere in this work.

Post-mortem Discoloration.—The surface of the liver where it has been in contact with the stomach or colon very commonly shews dark purple stains. These stains, which are produced after death and are quite superficial, are due to the action of gases, among them sulphuretted hydrogen, which diffuse through from the colon and stomach and meet with iron in the liver ; as a result, some black compound like sulphide of iron is manufactured.

Irregular white areas on the surface of the liver are seen in cases of fever and various infections, and shew congestion and degenerative changes. This appearance was formerly thought to be merely due to mechanical pressure exerted after death in laying out the body.

Cloudy swelling is a very frequent, if not the commonest, change seen in the liver in routine post-mortem work. The liver is enlarged, heavier than normal, and looks as if it had been boiled, and has a duller, more opaque, and paler aspect than normal. These changes are due to cloudy swelling or parenchymatous inflammation of the liver cells set up by the toxins of numerous diseases. The changes which are shared by other organs, such as the kidneys and myocardium, are especially well seen in pneumonia. In this disease the enlargement of the liver may be very considerable. Long ago Bright [4] thought that the pneumonic lung materially depressed the liver, but it is clear that any increased

[1] Davy, J. *Diseases of the Army*, p. 427, 1862.
[2] Tarozzi. *Sperimentale*, 1904, lviii, 499.
[3] Cruveilhier. *Anatomie pathologique générale*, 1856, iii, 209.
[4] Bright, R. *Abdominal Tumours*, p. 255, 1860. New Sydenham Society.

hepatic dulness below the costal arch is mainly due to cloudy swelling and congestion (*vide* p. 19).

Foaming Liver (*Synonym*: Emphysematous Liver).—The formation of gaseous cysts in the internal organs, formerly put down to putrefaction, was shewn by Welch and Nuttall,[1] in 1892, to be due to the *Bacillus aerogenes capsulatus*. The infection with this micro-organism is generally a secondary and terminal event; in other words, this bacillus follows in the wake of other pathogenetic bacteria and does not appear till the patient is moribund. To these general rules there are exceptions. Pure cultures of the *Bacillus aerogenes capsulatus* have been obtained by Pratt and Fulton,[2] and by Pakes and Bryant;[3] from a case of infective endocarditis, Gwyn[4] repeatedly isolated the micro-organism from the blood during life.

The micro-organism may be present and yet not give rise to any formation of gas (Gwyn, and Pratt and Fulton). Though this infection may occur in the body during life, there is no evidence that it ever produces gas before death. The micro-organism may give rise to necrosis of the cells of the liver and to purulent inflammation, as was shewn in Pratt's and Fulton's case of cholangitis with multiple abscesses in the liver.

The *Bacillus aerogenes capsulatus* is anaerobic, and must be distinguished from the bacillus of malignant oedema. It stains with Gram's method. It is very frequently present in the alimentary canal, and has been found to be widely distributed in nature. Other gas-producing bacteria must be taken into account; thus, the colon bacillus (Kanthack, Pakes and Bryant) and other members of the aerogenes group, such as *B. mucosus capsulatus* (W. T. Howard, Jr.[5]), have been described as giving rise to gaseous cysts. Welch, however, is rather sceptical about their claim to be regarded in this light.

The liver is the organ most frequently affected. In 23 cases tabulated by Pakes and Bryant, this organ was affected in 15.

Etiology.—B. aerogenes capsulatus is often found in association with other micro-organisms, which probably favour the development of *B. aerogenes capsulatus* by diminishing the bactericidal power of the blood, and also by reducing the resistance of the liver. J. H. Drysdale[6] found that hot weather is a factor in the production of foaming liver, but that this condition may occur in the absence of any of the ordinary signs of decomposition. It is found much more frequently when there has been recent loss of blood, which seems to favour the entrance of the micro-organisms into the blood or their development in it. Ulceration and injury of the intestines also favour the entrance of the micro-organisms, which are commonly present in the alimentary canal, into the tissues

[1] Welch and Nuttall. *Bull. Johns Hopkins Hosp.*, Balt., 1892, iii, 81.
[2] Pratt and Fulton. *Boston Med. and Surg. Journ.*, 1900, cxlii, 599.
[3] Pakes and Bryant. *Guy's Hosp. Rep.*, 1900 (1897), liv, 283.
[4] Gwyn. *Bull. Johns Hopkins Hosp.*, 1899, x, 134.
[5] Howard, W. T., Jr. *Journ. Exper. Med.*, 1900–1, v, 139.
[6] Private communication.

of the body. Incubation of livers, taken at random from the post-mortem room, did not give rise to the formation of gaseous cysts, but incubation of livers from cases of haemorrhage gave positive results proving that the micro-organisms had got into the organs.

It is generally recognised that the infection of the liver may take place either by the blood-stream or by the bile-ducts. Infection most commonly arrives by the portal vein, and is due to some lesion, such as ulceration, in the intestinal tract. The inlet of infection may be in other situations, such as the uterus or the urethra. Direct infection of the bile-ducts and gall-bladder from the intestine may occur. In such instances the bile-ducts and gall-bladder may contain gas either in their lumen or in the substance of their walls, especially in the submucous coat. Welch[1] met with five cases of interstitial emphysema of the bile-ducts or gall-bladder.

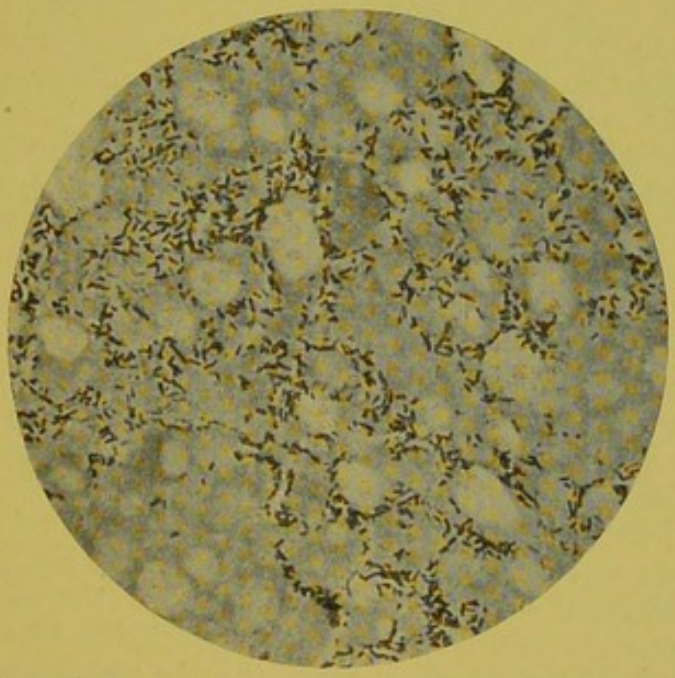


FIG. 4.—Photomicrograph of a foaming liver, shewing minute gaseous spaces lined by the *Bacillus aerogenes capsulatus*. × 1000. (By Dr. H. Spitta.)

Although the gas-producing micro-organisms may give rise to a septicaemia and be isolated from the blood, it is doubtful if formation of gas ever occurs in the living tissues. It may occur very rapidly after death, or, as shewn in emphysematous gangrene, in a part of the body that has lost its vitality. On reviewing the whole subject Welch is inclined to the view that gas is formed in the viscera before death. Clinically it has been thought that tympanites may be due to the formation of gas before death.

[1] For a full résumé of the entire subject the reader should refer to Welch's Shattuck Lecture for 1900, "On Morbid Conditions caused by *Bacillus aerogenes capsulatus*," *Johns Hopkins Hosp. Bull.*, Balt., 1900, xi, 185.

The liver is spongy from the presence of a number of small gas-containing cysts of various sizes, but mostly small. The organ is usually of a somewhat greyish colour from its inflated condition, which must not be mistaken for multiple cystic disease. This change may also be met with in other organs—the kidneys, brain, spleen, intestines, pancreas. Some recorded cases of widespread cystic change in the organs of the body may have been of this nature.

ACQUIRED DEFORMITIES

Tight-laced Liver (*Synonym*: Corset Liver).—Modifications in the shape of the liver due to tight lacing, corsets, and belts are of course common in women, but considerable deformity may be produced in men by the pressure of a tight belt or strap. The effect of tight lacing on the liver varies to a certain extent with fashion, or, in other words, with the position of the waist. Following Hertz,[1] who has studied the changes produced by tight lacing in great detail, the deformities of the liver may be divided into two main types, though mixed or transitional forms may occur.

I. The liver is flattened and elongated from above downwards so that the upper or diaphragmatic surface is diminished while the anterior is increased. From its larger size the right lobe naturally shews the change more than the left. The liver thus forms a flap which covers the abdominal viscera, though occasionally coils of intestine may pass in front of it. Where it passes over the right kidney the elongated right lobe shews atrophy of the hepatic substance and thickening of the capsule, which is opaque and forms a hinge-like ligament between the main part of the right lobe above and the constricted lower portion. This lobe is variously termed partial hepatoptosis, constriction lobe, or the sustentacular formation of the right lobe (Hertz). The constriction furrow is produced by the pressure of the corset in front and the resistance of the kidney behind. The constriction lobe tapers to a point so that the shape of the liver, as seen from the front, is that of a right-angled triangle with the apex downwards. This lobe is often associated with an unduly movable or floating kidney (Keith [2]).

Clinically there is a close resemblance between these constriction lobes of the right lobe and the tongue-shaped or Riedel's lobe, originally described as occurring in special association with gall-stones. The left lobe is prolonged downwards in the same manner, though to a less marked degree, and may even have a constriction lobe attached to it. It has been thought that in the latter event the symptoms were much more marked than in cases in which the ordinary tongue-like lobes from the

[1] Hertz, P. *Abnormitäten in der Lage und Form der Bauchorgane bei dem erwachsenen Weibe*, Berlin, 1894.

[2] Keith, A. *Lancet*, 1903, i, 711.

right lobe were present. A tongue-like lobe arising from the left lobe of the liver would tend to exert pressure on the pylorus, duodenum, pancreas, and nerve plexuses which are supported behind by the spine, while on the right side no important viscera or structures would suffer, though the lobe would probably be in contact with the right kidney.

From impaired nutrition and diminished resistance the constriction lobe may be more markedly affected by morbid changes than the rest of the liver, or may even be the only part affected. Thus, fibrosis or gummatous change may be confined to a constriction lobe, or secondary new-growth may be wholly or chiefly limited to the pendulous lobe.

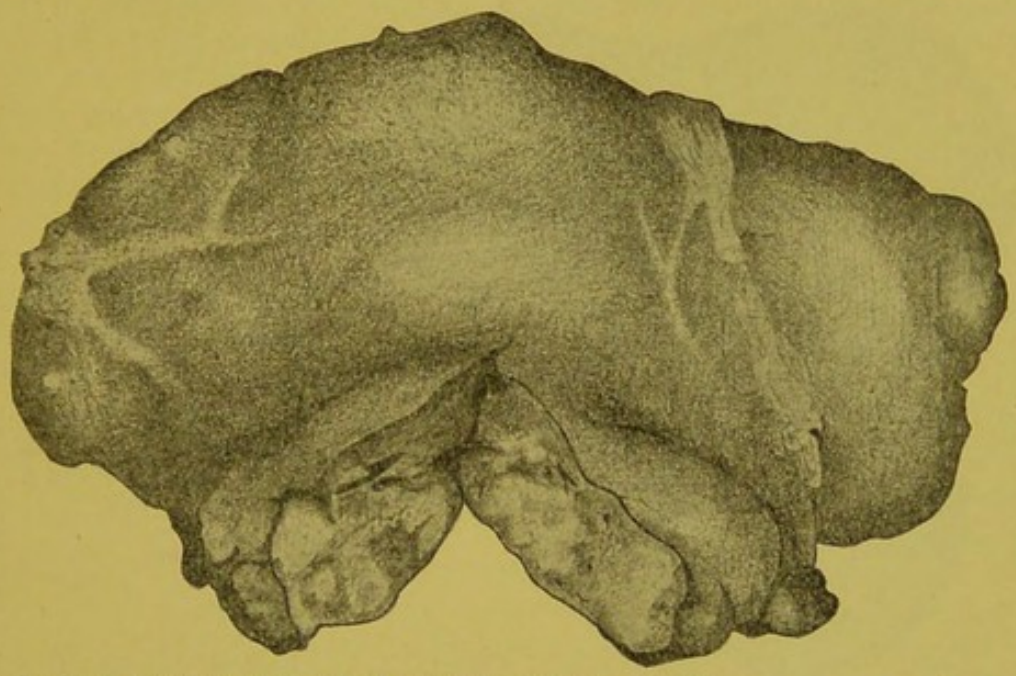


FIG. 5.—Constriction lobe attached to the right lobe of the liver, divided and its halves separated so as to display large secondary carcinomatous nodules in its substance. From case described in the text. (Drawn by L. Jones, M.S.)

In a case of carcinoma of the mamma in a woman who died of diabetes the constriction lobe contained large masses of secondary growth, whilst in the remainder of the liver there were only two small nodules (Fig. 5). Frerichs [1] figures a similar case.

On the other hand, the interference with the blood-supply may to some extent protect the constriction lobe against infection by the blood-stream.

In 1890 I examined after death the body of a man who died with carcinoma of the pylorus; the liver weighed nine pounds and, except the constriction lobe, attached to the right lobe, was full of secondary new-growth.

The whole of the liver, constriction lobe included, may be uniformly affected by cirrhosis (Fig. 6).

[1] Frerichs. *Diseases of the Liver*, ii, 326, Transl. New Sydenham Soc., 1861.

II. In the second variety of tight-laced liver the organ is displaced upwards as a whole and lies high in the abdominal cavity. It is thicker above than below, and is curved and moulded over the spine so that the left lobe may touch or even overlap the spleen. Frerichs [1] figures such a case in which the left lobe of the liver and the spleen were firmly united to each other. The fossa for the inferior vena cava is exaggerated and deepened, while as the result of pressure the right kidney is displaced downwards and its lower end tilted forwards. The lower margin of the right lobe being compressed by the corset or belt, is atrophied in the transverse direction, and shews opacity and thickening of the capsule from local perihepatitis. A triangular constriction lobe may be found attached to the right lobe, but is not such a constant feature as in the previous form, and is never present in connexion with the left lobe. Besides being met with in women, this change in the liver may be met with in men who wear a tight belt.

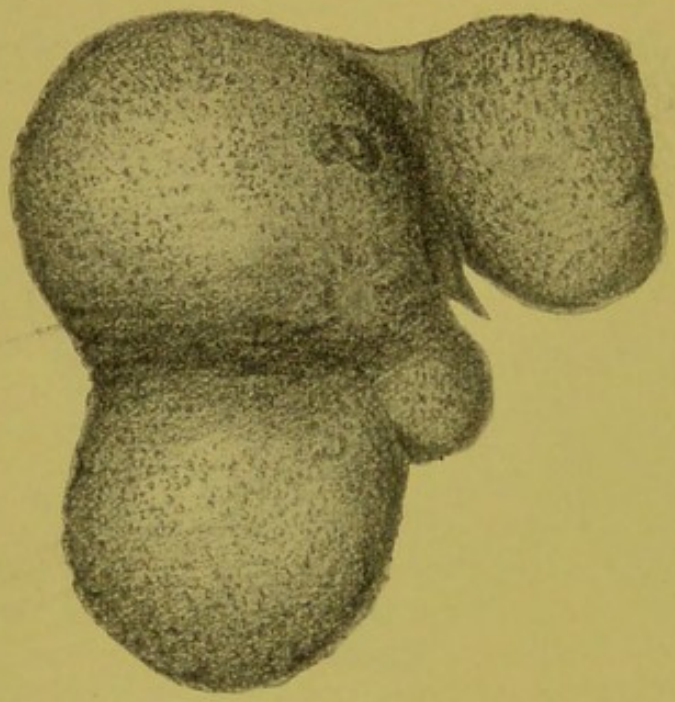


FIG. 6.—Tight-laced liver uniformly cirrhotic. There are two small cysts on the right lobe. From a woman forty-four years old who died with grave anaemia. The liver weighed forty-one ounces. (Drawn by P. L. Mummery, M.B., F.R.C.S.)

Diaphragmatic Sulci. — These are parallel grooves on the convexity of the right lobe, and in rare instances of the left lobe; there may be from one to six of these furrows; Moody [2] mentions a liver with nine. They run antero-posteriorly and are deeper posteriorly. It has been estimated that they occur in 7·3 per cent of all bodies (Adami and Nicholls [3]). They are eight times commoner in women than in men. They are usually associated with emphysema and bronchitis, and with evidence of tight lacing. Various explanations have been given (1) that they are due to circumferential pressure exerted in an upward direction by belts, and in some cases there is a transverse band of thickening near the anterior inferior margin of the liver (Weber [4]); (2) that they are due to the impress left by hypertrophied bundles of the diaphragm and

[1] Frerichs. *Diseases of the Liver*, 1860, i, 41.
[2] Moody, R. O. *Johns Hopkins Hosp. Bull.*, 1905, xvi, 364.
[3] Adami and Nicholls. *Principles of Pathology*, 1911, ii, 460.
[4] Weber, F. P. *Trans. Path. Soc.*, 1897, xlviii, 113; 1900, li, 236.

are not due to pressure (Zahn [1]); the change in the diaphragm being the result of chronic diseases of the respiratory system, with which these furrows are frequently associated. In 58 cases from the Salpêtrière shewing these furrows there were only 5 in which the lungs were healthy (Séglas [2]). Very probably both these factors act together. It is improbable that they are due to pressure exerted by the ribs, inasmuch as the sulci do not correspond to the position of the ribs.

Bacaloglu [3] described a single deep furrow on the upper surface of the liver which had no relation to either the ribs or the diaphragm and was not the result of cicatrisation. He regarded it as directly due to the pressure of the corset.

Furrows of this kind have in rare instances been seen in fetuses, and are possibly due to disproportion between the size of the abdominal cavity and of the liver so that the latter becomes folded in the process of growth (Moody). They must be distinguished from those due to hereditary syphilis. The etiology of these diaphragmatic sulci is discussed in detail by Moody.

Cirrhosis may supervene in a liver the subject of tight lacing, and give rise to a uniform change (*vide* Fig. 6). Local changes, probably due to chronic venous engorgement and resulting in fibrosis, may occur in the portion of the liver below the tight-lacing constriction.

Clinical Features.—Tight-laced livers are often associated with dyspepsia, which may be partly due to the abdominal or gastric embarrassment produced by a tight corset. In other cases the symptoms are due to visceroptosis, which is often associated with tight lacing. Keith [4] has insisted on the importance of tight lacing as a cause of gall-stones, and symptoms of cholelithiasis are not uncommon in patients who have tight-laced livers. But in a very considerable proportion of patients with livers deformed by tight lacing no symptoms referable to that organ are present. A point of considerable interest about tight-laced or corset livers is that the constriction lobe may, when accidentally detected, be easily mistaken for something more important, such as a floating kidney, a tumour of the pylorus or transverse colon, a dilated gall-bladder, cysts of the pancreas or of the mesentery, or in extreme cases for a fibromyoma of the uterus, an ovarian tumour, or appendicitis. The connecting bridge between the constriction lobe and the main part of the liver, as has already been pointed out, is sometimes very thin, and may therefore give a resonant note on percussion, so that its continuity with the remainder of the organ is concealed.

Treatment.—As a rule, no active treatment for the constriction lobe is either required or justifiable; tight lacing should as far as possible be prevented, but this reform requires considerable tact. A straight-fronted

[1] Zahn. *Rev. méd. de la Suisse Romande*, 1882, ii, 19.
[2] Séglas. *Progrès méd.*, Paris, 1886, 2. s., iii, 471.
[3] Bacaloglu. *Bull. Soc. anat.*, Paris, 1899, lxxiv, 67.
[4] Keith, A. *Lancet*, 1903, i, 639.

corset should be substituted for one which tends to constrict the waist and depress the liver. A properly adjusted belt should be fitted to patients with enteroptosis and symptoms due to this cause. Dyspeptic and other associated symptoms should be carefully attended to and constipation prevented. In cases in which the constriction lobe is the seat of much pain it has been removed, but this can seldom be really necessary. In such cases Bötticher[1] considers that hepatopexy, or fixation of the constriction lobe, is a more satisfactory method of surgical treatment.

Tongue-like Lobes (*Synonyms*: Linguiform Lobe, Riedel's Lobe, Partial Hepatoptosis, Floating or Appendicular Lobe).—Although the term partial hepatoptosis has been employed, this condition is quite distinct from complete hepatoptosis or wandering liver, as there is no dropping of the organ as a whole. No doubt confusion between the two conditions has occurred; Glénard considers that the reputed greater incidence of wandering liver in women depends on the fact that some observers have erroneously described tongue-like lobes as wandering livers. These lobes, often spoken of as Riedel's, are really much the same as the constriction lobes just described (*vide* p. 8) in the account of the corset liver. It has been thought, especially by Riedel,[2] that the tongue-shaped lobes depend on disease of the gall-bladder, such as inflammation, gall-stones, distention, traction exerted by pericholecystic adhesions. But this explanation does not apply to all the cases.

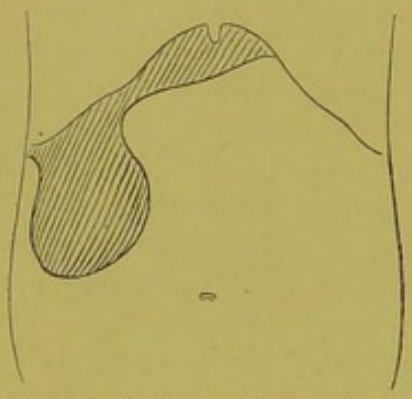


Fig. 7.—Riedel's tongue-like lobe. (After Dr. T. Fisher.)

It is possible that some of the cases of downward projection of the right lobe are connected with or depend on a congenital anatomical variation. This suggestion applies forcibly to cases in which this formation is found in babies or young children. As pointed out by Fisher,[3] there is a considerable amount of variability in the outline of the right lobe, and exaggeration of this might occur as an occasional abnormality without any determining irritation or traction on the part of the underlying gall-bladder. Possibly the formation of Riedel's lobe in some cases of cholelithiasis and its absence in other cases depend on variability in the outline of the right lobe of the liver.

Dr. Fisher has kindly sent me a drawing of a potential Riedel's lobe in a woman aged twenty-five whose gall-bladder was normal; I have observed a similar abnormal lobulation in the body of a man aged fifty-eight. If gall-

[1] Bötticher. *Deutsche Ztschr. f. Chir.*, 1900, lvi, 252.
[2] Riedel. *Berlin. klin. Wchnschr.*, 1881, xxv, 577, 622.
[3] Fisher, T. *Bristol Med.-Chir. Journ.*, 1901, xix, 215.

bladder disease arises in such cases, a Riedel's lobe would probably develop much more readily and rapidly than in a normal liver. McPhedran [1] described seven cases, and regarded the tongue-like lobes as developmental and not artificial. One of his cases was in a baby of eleven months. I have seen an infant four days old with numerous other abdominal malformations in which the gall-bladder lay on a lobe united to the right lobe of the liver by peritoneum and adherent to the umbilicus.

Tight lacing must also be taken into account, especially as, by displacing the fundus of the gall-bladder downwards, it may lead to kinking and occlusion of the cystic duct and so to obstruction to the

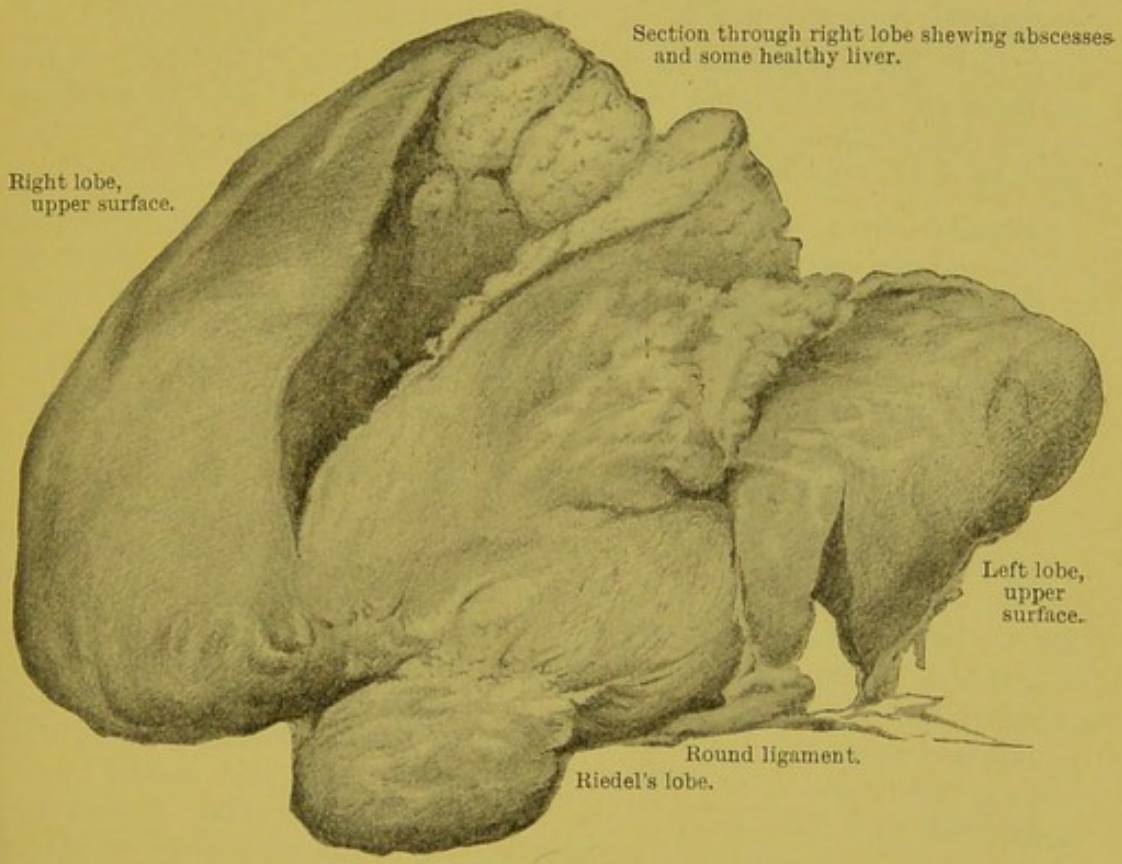


FIG. 8.—The liver with Riedel's tongue-like lobe and areas of suppuration due to suppurative cholangitis. From a case of cholecysto-colic fistula due to gall-stones. (Drawn by Dr. E. A. Wilson.)

outflow of the contents of the gall-bladder—a state of affairs which favours catarrhal inflammation and the production of gall-stones (Keith [2]).

Incidence.—Tongue-shaped lobes are much more frequent in women. This depends on their causation, both tight lacing and cholelithiasis being much commoner in that sex.

Anatomy.—The tongue-shaped lobes may either taper off gradually

[1] McPhedran. *Canadian Practitioner*, 1896, xxi, 401.

[2] Keith, A. "The Anatomy of Glénard's Disease," *London Hosp. Gaz.*, 1902, ix, 55.

into an elongated, thick process from the right lobe, or the connecting pedicle may be reduced to two layers of somewhat thickened peritoneum. In the latter case the tongue-like lobe is freely movable, and during life may appear to be quite distinct from the liver. The gall-bladder may, but need not, be situated on the under surface of the tongue-like lobe, as in two cases excised during life (Martin, Bastianelli); the cystic duct will then run across the pedicle. As a rule, the tongue-like lobe is not perfectly normal in structure; from repeated attacks of congestion it may shew fibrosis, and degeneration, atrophy, and pigmentation of the liver cells, and haemorrhages. It has been found to be gummatous when the remainder of the liver was healthy, and may be the seat of secondary new-growth (compare p. 9).

Roux[1] described primary carcinoma starting in a tongue-like lobe. In his case there was calculous cholecystitis. In similar cases care must be taken to see that the growth does not start in what is a much commoner situation, viz. the walls of the gall-bladder.

Physical Signs.—There is a movable abdominal tumour on the right side of the abdomen, which descends with the diaphragm and the liver on respiration. It is dull on percussion, but this is seldom continuous with the liver dulness, as there is usually a band of resonance between it and the liver. It may be distinctly tender on pressure. It may descend as low as the right iliac region and give rise to difficulty in diagnosis from appendicitis, etc.

Symptoms.—The existence of a tongue-like lobe may be discovered accidentally and may not be accompanied by any bad effects. Usually the symptoms associated with the existence of a tongue-like lobe are due to calculous cholecystitis, which may have played an important part in the production of the deformity. The patient may have been conscious for some time of enlargement and alteration in shape of the abdomen and of a slowly growing tumour, as in Martin's case in which a tumour had existed for twelve years. There are often a feeling of oppression and heaviness in the right hypochondrium and pain in the back. Abdominal pain may be paroxysmal, like gall-stone colic, or may be constant; the pain is usually relieved by rest in the recumbent position. Intense venous engorgement of the lobe may give rise to attacks of palpitation, vomiting, and collapse. Jaundice and ascites are rare and are due to some definite cause, such as gall-stones or chronic peritonitis.

Diagnosis.—Riedel's lobe may appear to have no definite connexion with the liver, and thus appears as a movable abdominal tumour and may easily be mistaken for a floating kidney, as in C. Martin's case.[2]

A woman aged thirty-six had had a lump in her abdomen for twelve years which had recently grown rapidly and become tender and painful. An oval tumour about the size of a six months' pregnancy filled the right half of the

[1] Roux. *Rev. méd. de la Suisse Rom.*, 1897, xvii, 114.
[2] Martin, C. *Birmingham Med. Rev.*, 1898, xliii, 92.

abdomen ; it was tense and very mobile, dull on percussion, and separated from the liver by a band of resonance. It was thought to be an unusually mobile kidney. Laparotomy revealed a pedunculated accessory lobe of the liver bearing the gall-bladder ; it was successfully removed. Its weight was $3\frac{3}{4}$ pounds.

Bastianelli [1] described a case in which a displaced cancerous kidney was diagnosed ; laparotomy revealed a floating lobe of liver, with the gall-bladder on its under surface. This piece, weighing 500 grams (18·75 ounces), was successfully removed ; there were gummas in it, but not in the remainder of the liver.

A tongue-like lobe may be thought to be some other form of abdominal tumour, such as a solid growth in the omentum, a pyloric tumour, a distended gall-bladder, or a cyst of the pancreas or mesentery, or in extreme cases a uterine fibromyoma, ovarian cyst, or appendicitis.

In a case under my care in St. George's Hospital the gall-bladder, greatly thickened from calculous cholecystitis, was adherent to the colon, and was associated with a well-marked tongue-like lobe which before laparotomy was thought by some to be a floating kidney or a growth in the transverse colon. A Riedel's lobe containing two gummas was in one case diagnosed as carcinoma of the caecum (Munro [2]).

Treatment.—In cases in which a tongue-like lobe is diagnosed, treatment is only necessary when pain or discomfort is present. If there is any underlying cholecystitis or cholelithiasis, treatment should be directed to those conditions. In seven cases in which the morbid condition of the gall-bladder was treated, the tongue-like lobe disappeared (Terrier and Auvray [3]). An ill-fitting corset or one which presses on the liver should be replaced by a straight-fronted corset, and tight lacing or constriction of the waist by a belt should be prevented. It is not often that radical treatment, such as stitching the lobe to the abdominal parietes or its complete removal, is necessary.

In three cases the tongue-like lobe has been stitched to the abdominal parietes with success (Billroth,[4] Tscherning,[5] Langenbuch [6]). Removal of the lobe has been carried out by Bastianelli, Martin, and Lockwood.[7]

Effect of Tight Lacing on the Gall-bladder.—The gall-bladder is frequently dilated. Hertz [8] found it so in 24 out of 41 cases. The downward displacement of the duodenum brings tension to bear on the cystic duct, which even under normal conditions requires a spiral valve

[1] Bastianelli. *Policlinico*, April, 1895 ; *Brit. Med. Journ.*, 1895, i, epitome, No. 337.
[2] Munro. *New York State Journ. Med.*, 1908, viii, 183.
[3] Terrier et Auvray. *Rev. de chir.*, 1897, xvii, 735.
[4] Billroth. *Wien. med. Wchnschr.*, 1886, No. 14.
[5] Tscherning. *Centralbl. f. Chir.*, 1888, xv, 426.
[6] Langenbuch. *Ann. Soc. méd.-chir. de Liége*, 1888, xxvii, 414.
[7] Lockwood, C. B. *Lancet*, 1903, ii, 223.
[8] Hertz. *Abnormitäten in der Lage und Form der Bauchorgane*, 1894.

to keep it open (Keith [1]), and thus leads to obstruction. The resulting retention of bile and mucus in the gall-bladder may tend to elongation of the right lobe, and so give rise to, or accentuate, the tongue-like lobe seen in many corset livers. Retention of bile in the gall-bladder disposes to cholecystitis and cholelithiasis, and the predominance of female sufferers from gall-stones is no doubt partly due to the effects of the corset.

When calculi are present in the gall-bladder, the pressure exerted by the corset may, as suggested by Fütterer,[2] increase the friction between the gall-stones and the mucous membrane of the gall-bladder, and thus help to explain the greater frequency of primary carcinoma of the gall-bladder in women. In this connexion it is noteworthy that the larger bile-ducts, which are not affected in the same way by corsets or belts, are the site of primary carcinoma more often in males than in females.

DISPLACED LIVER

Apart from enlargement due to tumours or other causes, the liver may occupy an abnormal position under numerous and very various conditions. A displaced liver which is at the same time freely movable is a wandering liver (*vide* p. 22). Here we are only concerned with displaced livers which are not more movable than normal. Malposition may conveniently be divided in the first instance into (*a*) the congenital and (*b*) the acquired; the latter class is by far the larger.

Congenital Malpositions

Transposition.—In complete transposition of the viscera the liver will be on the left side, but occasionally the heart may be congenitally transposed without the liver sharing in the change. Transposition of the liver without the other viscera being affected is very rare indeed.

Complete transposition of the viscera may lead to an erroneous diagnosis: in a patient with *situs transversus* cholelithiasis was diagnosed as acute yellow atrophy from absence of the hepatic dulness on the right side.[3]

Congenital Ectopia of the Liver (*Synonyms*: Hepatomphalos, Hepatocele).—From congenital defect of the muscles of the abdominal wall the liver may project under the skin either at the umbilicus or in the middle line between the umbilicus and the ensiform cartilage. Congenital hernia or ectopia of the organ at the umbilicus has been called hepatomphalos. The tumour is firm, dull on percussion unless coils of intestine are also present in the sac, and is continuous with the liver dulness. It may be easily reduced, but reappears on removal of the

[1] Keith, A. *Lancet*, 1903, i, 639.
[2] Fütterer, G. Chicago Med. Soc., April 1, 1897.
[3] Billings. *Phila. Med. Journ.*, 1900, vi, 670.

pressure. On the other hand, the liver may become adherent to the walls of the umbilical sac and thus be irreducible. This was the case in a baby aged three weeks.[1] Bullard[2] found the liver herniated into the umbilical cord.

Displacement of the Liver as the Result of Congenital Diaphragmatic Hernia.—Congenital defects of the diaphragm may give rise either to a free communication between the peritoneal and pleural cavities or, from deficiency of the muscular tissue only of the diaphragm, to a membranous pouch which projects up into the thorax. Congenital deficiency of the diaphragm is commoner on the left side (Jaffé[3]) and may allow the left lobe of the liver to enter freely into the thorax.

In a case of Porak and Durante's[4] the peritoneum communicated freely with the left pleura, and the left lobe of the liver was found behind the sternum.

Acquired Displacements

In Diaphragmatic Hernia.—This may occur as part of a severe injury, the diaphragm being torn across, and the stomach, colon, spleen, or part of the liver may pass into the thoracic cavity. Diaphragmatic hernia when found in adult life without any history of injury may of course be congenital in origin, and in cases in which the herniated viscera have been found enclosed in a sac composed of the attenuated remains of the diaphragm or merely of the opposed pleura and peritoneum, this would appear probable. Pouching due to weakness near the oesophagus or xiphoid cartilage may, however, be acquired. In some cases a rent in the diaphragm may have been due to an injury received years before and almost or quite forgotten. The nature of the defect may then be regarded as congenital, whereas it is really acquired. In a considerable number of cases of diaphragmatic hernia the condition is found to have been preceded by trauma years before.

Traumatic diaphragmatic hernia is nearly always on the left side, since the support provided by the liver tends to protect the right leaflet from rupture. The liver is much less often displaced into the cavity of the thorax than the stomach, colon, intestines, or spleen.

In 300 cases the liver was herniated in 60 (Rochard[5]). In one case in which there was a history of a fall fourteen years before, part of a cancerous liver projected into the left pleura (Dietz[6]).

Part of the liver may pass through the rent and become tightly constricted at the margin of the rent like a strangulated hernia.

[1] J. Hutchinson. *Med. Times*, 1870, i, 397.
[2] Bullard. *Am. Med.*, 1902, iv, 742.
[3] Jaffé. *Trans. Path. Soc.*, 1894, xlv, 224.
[4] Porak et Durante. *Bull. Soc. Anat.*, Paris, 1901, lxxvi, 354.
[5] Rochard. *Les Hernies*, p. 382, Paris, 1904.
[6] Quoted by Blum et Ombrédanne. *Arch. gén. de méd.*, 1896, i, 1, 178.

The following case, the necropsy of which I saw, was recorded by C. Ogle.[1] A boy, aged sixteen years, who had had an accident six years before, was admitted with frequent vomiting and signs of a left pleural effusion; aspiration did not remove any fluid. At the necropsy the cardiac end of the stomach and the left lobe of the liver were found in the left pleural cavity, having passed through a rent in the central tendon of the diaphragm, which had a diameter of $1\frac{1}{2}$ inches. The intrathoracic part of the left lobe was connected by a thin atrophied pedicle to the rest of the liver and formed a lump 5 by 4 inches which looked very like a hard, deeply congested spleen. On section it was deep red in parts with white areas, and was mottled. Microscopically there were much haemorrhage, a quantity of blood-pigment, and degeneration of the liver cells.

In Spinal Curvature and in Rickets.—The liver though structurally normal may be very considerably displaced by spinal deformity. Its lower edge may be below the umbilicus and the organ may be unduly movable. In rickets the deformity of the chest to some extent depresses the liver, which is usually somewhat enlarged from the action of intestinal poisons. The view that the liver is enlarged in rickets is true, but the increase in the downward extent of the hepatic dulness is often partly due to displacement by thoracic deformity.

Tight Lacing, etc. — The deformities of the liver resulting from tight lacing and artificial constriction of the lower part of the thorax are described elsewhere (p. 8). In these conditions the liver may be displaced upwards as a whole, or even downwards, according to the position of the "waist," but most commonly the right lobe is elongated downwards and has a constricted area, corresponding to the line of pressure, uniting the floating lobe to the main part of the right lobe.

Thoracic Conditions giving rise to Displacement of the Liver.—*Effusion into the Right Pleural Cavity.* — A large serous effusion or empyema will effect this, but inasmuch as these conditions are usually relieved by paracentesis, the best examples of displacement of the liver due to disease of the pleura are seen in cases of right pneumothorax. A neglected or latent pleural effusion may, however, reach a large size and then produce marked displacement of the liver.

A man aged forty-three years arrived at the hospital in a state of collapse and died in a few minutes. At the autopsy, which I performed, the right pleura contained 10 pints of pus, the liver was greatly depressed, its lower edge being on a level with the anterior superior spines of the ilia. A man sent up to me for a tumour of the liver had 8 pints of blood-stained fluid removed from the right pleura.

Besides being displaced downwards the liver is rotated on its antero-posterior axis. The right leaflet of the diaphragm being depressed or even presenting its convexity downwards, the right lobe is much more depressed than the left, and the left lobe swings upwards, the whole organ being pushed towards the left.

[1] Ogle, C. *Trans. Path. Soc.*, Lond., 1897, xlviii, 114.

A pneumothorax on the right side may in rare cases lead to acute dislocation of the liver when the intrathoracic pressure is raised, as a result of a valvular communication between the lung and the pleural cavity.

Stiller[1] records a case in which a pneumothorax developed as the result of sneezing in a healthy man; the liver was depressed so as to form a large abdominal tumour.

A pleural effusion or pneumothorax on the left side may give rise, if excessive, to downward displacement of the left lobe of the liver.

Malignant Disease of Lung.—Very extensive malignant disease affecting the lung and greatly increasing its volume may displace the liver downwards.

This displacement was extreme in a boy with an enormous calcifying sarcoma in the thorax, secondary to sarcoma of the thigh, who died in St. George's Hospital in 1898. The growth pressed the right leaflet of the diaphragm down so that its under surface was convex, the liver was depressed, and its lower border was on a level with the umbilicus. It was not more freely movable than normal.

In mediastinal growths the liver is not displaced unless, as not infrequently occurs, there is a large pleural effusion.

In *emphysema* the downward displacement of the liver is often easily detected, but the increased downward extent of the liver is not extreme unless there is, in addition, chronic venous engorgement due to failure of the right side of the heart.

Pneumonia.—Bright[2] thought that pneumonia was the direct physical cause of the liver being below the costal arch. But the cloudy swelling of the liver is in part responsible for the projection of the liver downwards. When the whole lung is solid, the diaphragm may be in the position of maximum inspiration, and as a result the liver is somewhat depressed. I have seen downward displacement of the right half of the diaphragm and of the liver at the necropsy of a child with extensive tuberculous pneumonia of the right lung.

Pericardial Effusion.—A large pericardial effusion will depress the diaphragm and with it the liver, usually the left lobe.

In a case figured by Sibson,[3] in which the pericardium contained $3\frac{1}{4}$ pounds of fluid, the right lobe of the liver was displaced and tilted just in the same manner as in a right-sided pleural effusion.

Abdominal Conditions leading to Displacement of the Liver.—Generally speaking, abdominal conditions which displace the liver do so in an upward direction, but occasionally the liver may be depressed, while in other cases it may be pushed, drawn, or rotated laterally. Growths arising from the retroperitoneal space may push the liver for-

[1] Stiller. *Wien. med. Wchnschr.*, 1901, xli.
[2] Bright, R. *Abdominal Tumours*, p. 255, 1860. New Sydenham Soc.
[3] Sibson. Russell Reynolds' *System of Med.*, 1877, iv, 307.

wards, and, conversely, gas free in the peritoneal cavity or under certain conditions tympanitic distension of the intestines may separate the liver from the anterior abdominal wall.

Abdominal Conditions displacing the Liver Downwards.—A subphrenic abscess on the right side may pass between the diaphragm and the convexity of the right lobe and displace the liver downwards. A right-sided subphrenic abscess may be the result of a gastric ulcer situated near the pylorus, of a perforating duodenal ulcer, though the resulting peritonitis unfortunately is rarely localised, and may then contain gas as well as pus, or tract up from perforation of an inflamed appendix, situated in what is not an infrequent abnormal position, viz. running up over the right kidney. Besides these extrinsic origins for a right-sided subphrenic abscess, an abscess in the liver itself, a suppurating hydatid cyst, or the multiple abscesses of pylephlebitis may perforate into the potential space between the liver and diaphragm and give rise to a collection of pus there and so to downward displacement of the liver. In these cases the liver is itself enlarged and the condition is almost the same as hepatic abscess.

A hydatid cyst projecting from the convexity of the liver rather encroaches on the thorax than pushes the liver downwards. Shattuck [1] described a single cystic adenoma of the bile-ducts containing a gallon of clear fluid which pushed the liver downwards (*vide* p. 458).

As the result of peritoneal adhesions due to local peritonitis, *e.g.* from appendicitis or inflamed tuberculous glands (Treves [2]), the liver may be pulled downwards towards the pelvis. In large inguinal or femoral herniae the liver may be drawn down. A liver which in the first instance was freely movable may subsequently become fixed in an abnormal position by local peritonitis or perihepatitis; thus Richelot [3] found the liver fixed in the right iliac fossa close to the caecum.

Upward Displacement of the Liver.—Ascites, flatulent distension of the intestines, excessive dilatation of the colon, or the presence of large abdominal tumours, such as ovarian cysts or uterine fibromyomas, push the liver and diaphragm up and thereby encroach very seriously on the capacity of the thorax. The convexity of the diaphragm may then be on a level with the third rib or even higher.

As an example of extreme displacement of the liver from the pressure exerted by ovarian cysts reference may be made to a remarkable case recorded by F. A. Baldwin [4] in which there were four ovarian cysts, two large and two small, in the abdomen of a woman aged fifty-nine years. The cysts contained 18 gallons of fluid and were estimated to weigh 185½ pounds. The highest point of the liver was on a level with the upper border of the third rib in the nipple line.

[1] Shattuck. *Boston Med. and Surg. Journ.*, 1900, cxlii 427.
[2] Treves, F. *Brit. Med. Journ.*, 1896, i, 1.
[3] Richelot. *France méd.*, Paris, 1893, xl, 449.
[4] Baldwin. *Brit. Med. Journ.*, 1900, ii, 80.

When this upward displacement is very considerable, the liver may largely or even entirely cease to be in contact with the anterior abdominal wall and undergoes a very striking alteration in its relation to other organs. The anterior surface travels backwards and becomes posterior, while the inferior surface looks forwards and upwards instead of downwards and backwards. This is due to the liver moving upwards on a transverse axis running through its connexion with the inferior vena cava, which is relatively a fixed point.

Displacement Forwards.—A retroperitoneal growth or a pancreatic cyst may in rare cases push the liver forwards, a growth of the right suprarenal capsule may displace the right lobe forwards, while a pancreatic cyst will tend to force the left lobe into undue prominence. An aortic aneurysm near the pillars of the diaphragm may so displace the liver forwards as to suggest a new-growth in that organ. In Beatty's[1] case of aortic aneurysm in this situation the liver appeared steadily to increase in size.

Displacement Backwards. — Occasionally coils of intestine or the colon may intervene between the liver and the anterior abdominal wall, thus displacing the liver backwards. This occurs in acute yellow atrophy in which the great diminution or even complete disappearance of the liver dulness is largely due to the flabby liver allowing resonant bowel to come between it and the abdominal parietes. In cases of perforation free gas in the peritoneum may pass between the liver and the anterior abdominal wall and displace the organ backwards. In rare cases a distended piece of small intestine or colon may get between the anterior surface of the liver and the abdominal wall. This accounts in all probability for the occasional absence of liver dulness seen in cases during life for which no definite cause, such as acute yellow atrophy, a subphrenic pyopneumothorax, or perforation, is forthcoming. In these cases, in which there may be no abdominal symptoms, a thickening of the capsule of the liver corresponding to the abnormally situated piece of intestine may sometimes be found after death. Dilatation of the stomach or extreme degrees of dilatation of the descending colon will tend to rotate the liver towards the right.

T. Fisher[2] figures cases of this kind and I have seen several examples of this condition. In one case the colon lay just anterior to the atrophied bridge of liver substance connecting the constriction lobe with the remainder of a tight-laced liver.

A displaced liver is, as a rule, not more movable than one in its normal position. It differs from a wandering liver in this respect, and also in the fact that it cannot be replaced in its normal position, while, in addition, a definite cause for its displacement is often forthcoming. Symptoms which might be referred to a displaced liver, such as weight, pain, and heaviness, are generally thrown into the shade by those of the con-

[1] Beatty. *Dublin Hosp. Rep.*, 1830, v, 166.
[2] Fisher, T. *Bristol Med.-Chir. Journ.*, 1901, xix, 215.

dition responsible for the displacement. The various forms of enlargement of the liver, fatty, lardaceous, leukaemia, new-growth, abscess, cirrhosis, etc., must be differentiated from a displaced liver by a careful physical examination of each individual case.

The **treatment** of a displaced liver is that of the causal condition.

HEPATOPTOSIS

Synonyms: Wandering Liver, Movable Liver, Prolapse or Dislocation of the Liver.

By the term wandering or movable liver is meant one which, being unduly displaceable, leaves its normal position and forms an abdominal tumour.

Historical.—Cantani[1] in 1866 described a clinical case of movable liver, but there was no necropsy. Though Cantani's name is connected with the recognition of its clinical features, the anatomical condition had been described long before.

Heister, as far back as 1754, published the account of an autopsy, with a plate shewing the position of the liver. Gunzius (1744), Buchoby (1768), and Sauvages (1768) also referred to cases. Wickham Legg[2] first drew attention to the subject in this country. In recent times Glénard[3] has done much to direct attention to the subject, and introduced the name hepatoptosis in 1892.

Hepatoptosis is analogous to a wandering spleen. Both these organs are normally "floating" in the abdominal cavity, for while tethered in their normal positions by peritoneal ligaments, they are supported by the mutual pressure of the other abdominal viscera, especially the elastic pad formed by the intestines, and are not fixed and packed round by fat in the way that the kidneys are. The term "floating," which is accurately applied to an unduly movable kidney, is an equally appropriate epithet for a normal liver or spleen, and therefore does not describe an abnormally mobile condition of these viscera. The liver normally moves during respiration, descending with the diaphragm on inspiration half an inch below the costal arch in the right nipple line. A dilated stomach or distension of the colon on the left side will rotate the liver to the right. When this displacement is greatly exaggerated, the state of affairs in wandering liver is imitated.

There is a great difference between an unduly movable liver on the one hand, and one which is merely pushed out of place by a tumour or pleural effusion on the other hand. A displaced liver is not necessarily, or indeed usually, more movable than one in the normal position. Again, the tongue-like and constriction lobes attached to the right lobe of the

[1] Cantani. *Ann. univ. di med.*, Milano, 1866, clxxxviii, 373.
[2] Legg, W. *St. Barth. Hosp. Rep.*, 1877, xiii, 141.
[3] Glénard. *Les Ptoses viscérales*, Paris, 1899.

liver in tight lacing and other conditions must be distinguished from a wandering liver. The wandering liver may be spoken of as total hepatoptosis, while the constriction and tongue-like lobes have been called partial hepatoptosis.

Existence of Total Hepatoptosis.—From the collected cases of Faure, Einhorn, Graham, Bötticher, Glénard, and Telaky, it has been estimated by Dutton Steele [1] that, in all, about 100 cases of undoubted total hepatoptosis are on record, of which 44 have been confirmed by operation or autopsy. Its existence, therefore, admits of no reasonable doubt, but from its intimate attachment to the diaphragm, the liver is not so often affected by visceroptosis as the other abdominal organs.

The existence of movable livers has been doubted from time to time, and the clinical signs of the condition have been explained as due to causes such as floating kidneys, renal or other tumours. This was the view taken by Wickham Legg.[2] In some cases in which a floating liver was diagnosed during life the liver has been found in its natural position after death (P. Müller,[3] Crawfurd). The explanation of this is that after death gaseous distension of the intestines pushes the liver up and the diaphragm ascends.

According to Hertz [4] and Glénard,[5] some at any rate of the cases described as wandering livers were in reality constriction lobes attached to a thinned and elongated right lobe. The part below the corset furrow may thus be mistaken for the whole liver, especially when it is very mobile and the abdomen is lax and pendulous. Glénard, indeed, considers that the predominance of the female sex in the recorded cases of movable liver is thus explained.

Frequency. — Well-marked examples of hepatoptosis with definite symptoms are rare. Minor degrees, however, are fairly often found when looked for; thus Glénard, from researches on a large number (3500) of invalids suffering from various disturbances of nutrition, estimated that 20 per cent of these patients present some degree of it. He put the numbers at 25 per cent for males and 15 per cent for females, thus reversing the usual incidence of really movable livers in the two sexes. For there can be no doubt that cases with characteristic symptoms are usually met with in multiparous women with pendulous abdominal walls. It is noteworthy that Glénard has found some degree of hepatoptosis with greater frequency in his later papers; thus, in 1886, he estimated that it occurred in 2 per cent and in 1892 in 20 per cent of patients with diseases of nutrition. It is fairly safe to assume that many of the latter cases, which would escape observation in less practised hands, do not suffer from the effects of the condition.

Sex.—The female sex provides the vast majority of cases of wandering livers. In 117 cases of hepatoptosis collected from literature by Ssaweljew,[6] 103 were in women, 13 in men, and 1 in a child. In

[1] Dutton Steele. *Univ. Penn. Med. Bull.*, Phila., 1903, xv, 424.
[2] Legg. *St. Barth. Hosp. Rep.*, 1877, xiii, 141.
[3] Müller, P. *Deutsch. Arch. f. klin. Med.*, 1874, xiv, 146.
[4] Hertz. *Abnormitäten in der Lage und Form der Bauchorgane*, 1894.
[5] Glénard. *Les Ptoses viscérales*, Paris, 1899.
[6] Ssaweljew. *Arch. f. klin. Chir.*, Berlin, 1903, lxx, 644.

Graham's[1] 70 cases 56 were in women. Max Einhorn[2] in private practice noted 21 women and 9 men. As already mentioned, Glénard's own observations, which include minor degrees of hepatoptosis, were to the effect that hepatoptosis is really more frequent in men, its apparently greater incidence in females being explained by cases of partial hepatoptosis (Riedel's lobes, constriction lobes) erroneously regarded as complete hepatoptosis.

Age.—The majority of patients with hepatoptosis are over forty years of age. Treves[3] puts the age at between thirty-five and sixty. In exceptional instances it is met with in children.

Freeman,[4] in 496 autopsies on children, met with four examples of hepatoptosis due to relaxation and elongation of the suspensory ligament; the right lobe came down into the pelvis, the left lobe being the only part of the liver touching the diaphragm, while the upper surface was turned to the right.

Factors responsible for the Normal Position of the Liver.—As bearing on the causation of hepatoptosis it will be well to refer to the factors which maintain the liver in its normal position. These are: (1) The healthy tone of the abdominal muscles which keeps up the intra-abdominal pressure and makes the intestines act as an elastic pad or support for the liver. In the rare cases of congenital absence of the muscles of the abdominal wall the liver has been extremely movable (Guthrie[5]). (2) The attachment of the liver by the inferior vena cava to the diaphragm. This, according to Faure,[6] is the most important agent in retaining the liver in its place, and by itself is capable of sustaining weight of 27 kilograms, as against 20 kilograms which the other suspensory ligaments can support. (3) The peritoneal ligaments, the falciform, coronary, and lateral, and the connective tissue uniting the right lobe of the liver to the diaphragm. Graham's[7] observations on the dead body shewed that they can support the liver independently of the abdominal walls, and both he and Dutton Steele[8] found that cutting these ligaments led to a condition which was much the same as that in hepatoptosis. These observations shew that in spite of Symington's[9] statement that under ordinary conditions the suspensory ligaments are not tense, they can, when intact and healthy, prevent any abnormal or excessive descent of the liver.

Intrahepatic blood-pressure may possibly play a part in keeping the liver in its normal position. Injection of water into the vessels of the liver was found by Glénard and Siraud[10] not only to increase its size, but to straighten out its

[1] J. E. Graham. *Canadian Practitioner*, 1895, xx, 399.
[2] Max Einhorn. *Med. Rec.*, N.Y., 1899, lvi, 397.
[3] Treves, F. *Lancet*, 1900, i, 1339. [4] Freeman. *Arch. Pediat.*, 1900, xvii, 81.
[5] Guthrie, L. G. *Trans. Path. Soc.*, 1896, xlvii, 139.
[6] Faure. *Thèse de Paris*, 1892.
[7] Graham, J. E. In Loomis and Thompson's *System of Practical Med.*, iii, 414.
[8] Dutton Steele. *Univ. Penn. Med. Bull.*, 1903, xv, 424.
[9] Symington. *Trans. Med.-Chir. Soc.*, Edin., 1887, vii, 53.
[10] Glénard et Siraud. *Lyon méd.*, 1895, lxxix, 171.

under or concave surface, which became more convex. It is further stated that in chronic engorgement of the liver the organ keeps well in its place even though the abdominal walls are flaccid. Alteration in the intrahepatic blood-pressure may therefore possibly have something to do with dropping of the liver.

Causation of Hepatoptosis.—Undue mobility of the liver might depend on some congenital defect or abnormality of the suspensory apparatus, such as an imperfect development of the falciform or coronary ligaments, or upon elongation, which when extreme might justify the term "mesohepar." There is very little anatomical evidence to support this hypothesis put forward by Meissner,[1] Clarke and Dolley's[2] case of mesohepar being most exceptional. It is quite reasonable to suppose that elongation of the suspensory ligaments may be congenital in the sense that there is an hereditary weakness which, like that underlying hernia and general dropping of the viscera (Glénard's disease), allows elongation of the ligaments to occur later in life under conditions which in ordinary persons would not have this effect. Another equally tenable view is that the tendency to elongation is acquired and depends on degeneration or atrophy of the suspensory ligaments induced by malnutrition and general debility. The associated enteroptosis, pendulous abdominal walls, and lineae albicantes may be regarded as manifestations of the same process, and, as will be seen later, they favour the production of hepatoptosis. Elongation of the suspensory ligaments must occur in order to allow the liver to become movable.

In cases in which the suspensory ligaments are unduly extensible, dragging on the liver by peritoneal adhesions, tumours, cysts, or large accumulations in the gall-bladder may lead to elongation of the ligaments, and so to an excessively movable and displaced liver. This condition resembles a simple displaced liver (*vide* p. 16), but differs from it in excessive mobility. Total hepatoptosis due to traction is a rare event, and must be distinguished from the elongation of the right lobe (Riedel's lobe, partial hepatoptosis) seen in many cases of cholelithiasis (*vide* p. 12).

Thus, in a case of Treves,[3] a young woman aged twenty-two years, the liver descended 2 inches on assuming the erect posture ; there was general visceroptosis due to traction exerted by the great omentum, which was firmly adherent to calcified tuberculous glands in the right iliac fossa.

Tight lacing and corsets are probably extremely important in the production of a freely movable liver. The pressure of the corset and the traction exerted by a heavy skirt at the waist tend to displace the abdominal viscera downwards. The suspensory ligaments of the liver, if degenerate, would thus be easily elongated. Further, tight lacing leads to weakness of the abdominal muscles, and so increases the conditions favourable to hepatoptosis.

[1] Meissner. Schmidt's *Jahrb.*, 1869, cxli, 107.
[2] Clarke, T. W. and Dolley. *Am. Journ. Med. Sc.*, Phila., 1905, cxxx, 969.
[3] Treves. *Brit. Med. Journ.*, 1896, i, 1.

Landau[1] and Hertz, however, who have paid considerable attention to the effects of tight lacing, oppose this view.

Failure of the healthy tone of the abdominal muscles, leading to a pendulous condition of the abdomen with a diminution of intra-abdominal pressure, is an important factor in hepatoptosis. A flaccid abdominal wall removes the support provided to the liver by the intestines, and thus throws the weight of the liver on to the suspensory ligaments, which if not sufficiently strong will stretch and elongate. According to Keith,[2] total hepatoptosis is always part of general visceroptosis. It has, however, been thought that weakness of the abdominal walls alone is not sufficient to cause hepatoptosis, and that, conversely, hepatoptosis may occur when the abdominal walls are healthy.

In 55 cases of hepatoptosis collected by Graham[3] only 19 were definitely stated to have pendulous abdomens.

The causes which lead to weakening of the abdominal parietes are chiefly those producing abdominal distension, such as repeated pregnancy, ascites, intra-abdominal tumours, persistent flatulence, and accumulations of fat. In addition, the wearing of stays and want of exercise diminish the healthy tone of the abdominal muscles, while anaemia, debilitating diseases, and neurasthenia have the same effect. This weakening of the abdominal walls is a most important factor in diminishing the intra-abdominal tension. As these conditions are more frequent in women, abdominal tension is much lower among them than among athletic men. In men who lead a sedentary life, such as tailors and cobblers, however, the intra-abdominal pressure may be low. In women it may even be negative (Bruce Clarke[4]).

Glénard[5] lays stress on "hepatism" as a factor in the production of movable liver. By "hepatism" he means a chronic nutritional change which may be hereditary or acquired, and may be of two kinds, (*a*) cholaemic, (*b*) uricaemic, corresponding to "arthritism" of some French authors, and to Murchison's "lithaemia." (*Vide* p. 39.)

To sum up: The important disposing factors in the production of hepatoptosis are (1) a weak, extensible condition of the suspensory ligaments, and (2) a low intra-abdominal tension due to atony of the abdominal walls. These conditions of impaired nutrition are very prone to go together and to be accompanied by general visceroptosis.

Associated Conditions.—*Visceroptosis.*—Hepatoptosis may be part of this general condition and its most prominent manifestation, or it may occur in cases in which there is no other manifestation of visceroptosis or only a floating kidney. The association of a floating right kidney with hepatoptosis is comparatively frequent.

[1] Landau. *Die Wanderleber und der Hängebauch der Frauen*, Berlin, 1885.
[2] Keith, A. "Hepatoptosis," *System of Medicine* (Allbutt and Rolleston), iv, Part I. 18.
[3] Graham, J. E. Loomis and G. Thompson's *System of Practical Medicine*, iii, 414.
[4] Bruce Clarke, W. *Brit. Med. Journ.*, 1896, ii, 1493.
[5] Glénard. *Les Ptoses viscérales*, p. 736 *et passim*, Paris, 1899.

In 44 cases of hepatoptosis, verified either by laparotomy or necropsy, Dutton Steele found 9 cases of floating right kidney, or 20·4 per cent. In 330 cases of nephroptosis recognised clinically by Glénard [1] in women, there were 70 cases of hepatoptosis.

Neurasthenia, etc.—As already mentioned, neurasthenic conditions and general debility with loss of muscular tone may accompany total hepatoptosis and are probably closely related to the low intra-abdominal pressure. Schwerdt,[2] indeed, regards visceroptosis as primarily dependent on muscular atony of nervous origin.

Exciting Causes.—A wandering liver in the majority of cases develops gradually. But in a certain proportion of the cases—according to Graham, in 5 per cent—there is an acute onset of symptoms suggesting sudden dislocation of the organ. This acute onset may in rare instances be due to severe injuries leading to rupture or laceration of the peritoneal suspensory ligaments, such as the passage of a wheel over the body, falls, or blows. In less extreme cases sudden exertion in lifting heavy weights, violent expiratory efforts, such as sneezing, coughing, vomiting, laughing, or straining, may have the same effect.

Max Einhorn [3] refers to a singer in whom the laborious work of the diaphragm incident to his profession probably led to laceration of the hepatic ligaments.

Forms of Total Hepatoptosis.—In hepatoptosis the liver tends to be rotated in two different directions: (1) On its transverse axis, so that its upper (diaphragmatic) surface comes in contact with the abdominal wall, while the anterior surface points downwards; this is anteversion. (2) On its vertical axis; usually the convexity of the liver is turned to the right and the under surface to the left.

The liver is more commonly displaced downwards and to the right, but it may be displaced downwards and rotated to the left. Thus, the liver may be (1) simply anteverted; (2) anteverted with rotation to the right, the usual form; (3) anteverted with rotation to the left.

Hepatoptosis with Anteversion.—The liver being more fixed posteriorly, where the inferior vena cava runs through it, than elsewhere, movement is least in this situation. The liver moves downwards, the sharp anterior margin sinking down towards the pelvis while the superior or diaphragmatic surface slides forwards and downwards so as to come under the anterior abdominal wall. The inferior surface of the liver at the same time becomes more posterior. The liver becomes much flattened out and elongated (*vide* Fig. 9). As the result of tight lacing, the front of the liver may shew a transverse line of fibrous atrophy. This grooved condition of the liver (*le foie cordé*; *Schnurleber*) when exaggerated has been spoken of as the "pilgrim's bottle liver" ("*le foie en gourde de pèlerin*").

[1] Glénard. *Les Ptoses viscérales*, Paris, p. 503, 1899.
[2] Schwerdt. *Deutsch. med. Wchnschr.*, 1896, xxii, 53.
[3] Max Einhorn. *Med. Rec.*, N.Y., 1899, lvi, 397.

The following case, in which the condition was recognised only on the post-mortem table, is a good example of hepatoptosis with anteversion.

On opening the body of a widow aged fifty who died of bronchitis in St. George's Hospital, I found the liver extremely mobile, and occupying the front of the abdomen like a flattened cake and reaching $1\frac{1}{2}$ inches below the umbilicus; both lobes were much elongated, as shewn in the figure. The coronary ligaments were very much elongated, measuring $2\frac{1}{2}$ inches. There

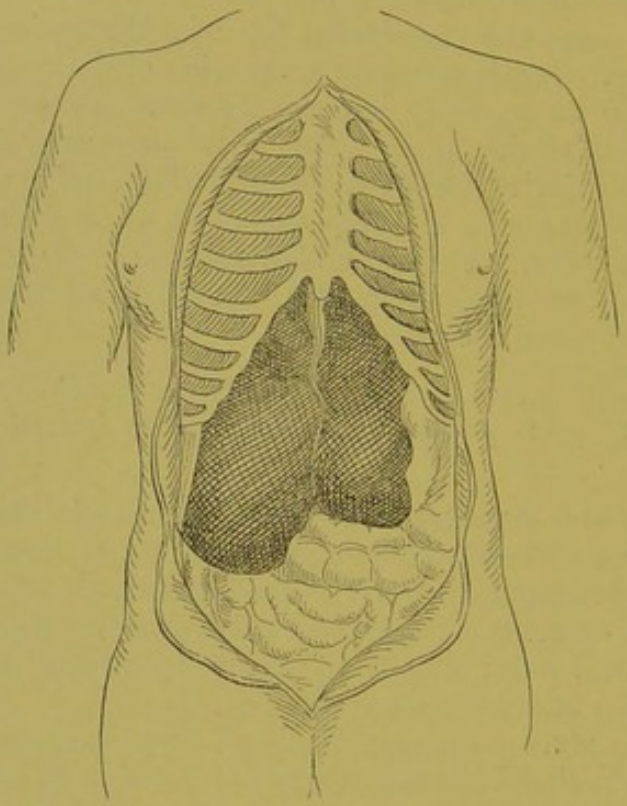


FIG. 9.—Partially anteverted liver with elongation of both lobes. (Drawn by Dr. H. B. Roderick.)

was also evidence of constriction from tight lacing; the lower part of the liver below the constriction could be easily turned up so as to form a double fold of liver substance. The commencement of the cystic duct contained a calculus, and the neck of the gall-bladder was much elongated. The kidneys appeared more movable than natural, and the presence of lineae albicantes on the abdomen as well as the character of the os uteri made it probable that she had had children. This case was evidently one of partially anteverted wandering liver. Somewhat similar cases are described by Crawfurd,[1] Peters,[2] and Griffiths.[3]

Hepatoptosis with Latero-version.—Rotation of the liver on its vertical axis takes place around the round ligament.

The following is a good example of a movable liver with rotation on its vertical axis to the right:—

[1] Crawfurd, R. P. *Lancet*, 1897, ii, 1182.
[2] Peters. *Med. Gaz.*, N.Y., 1882, ix, 412.
[3] Griffiths, T. D. *Brit. Med. Journ.*, 1878, i, 89.

Morestin[1] found the gall-bladder and right lobe of a man's liver in the right iliac fossa. The liver was elongated and rotated so that the convexity pointed to the right and the under surface to the left. The left lobe was reduced in size to a mere tongue of hepatic tissue. There was no morbid change in the liver substance.

In cases of such rotation the right lobe may simulate disease around the appendix.

Complications.—Generally speaking, a movable liver can be replaced in its normal position, but this is not always possible; in 80 cases collected by Glénard this could not be effected in 14, while in 3 more it could only partially be accomplished. A movable liver may contract adhesions when displaced downwards, and so become fixed to the lower part of the abdomen. In these circumstances it readily gives rise to great difficulty in diagnosis and may resemble some abdominal tumour or inflammatory formation.

Richelot,[2] in an exploratory laparotomy for an abdominal tumour of doubtful origin, found the liver rotated and fixed in the right iliac region.

A movable and displaced liver has been found to be cirrhosed, to be associated with calculous cholecystitis,[3] gall-stones, or in exceptional instances to be occupied by malignant disease, gummas (Clarke and Dolley[4]), or a hydatid cyst (Nedwill[5]). A certain amount of atrophy and subsequent fibrous substitution may be due to torsion and twisting of the portal vessels and bile-duct in the lesser omentum.

In 80 cases collected by Glénard[6] the liver was healthy in 50; in 26 it was the subject of disease, usually cirrhosis or gall-stones. In one each cancer and hydatid cyst was present.

Physical Signs.—There is an abdominal tumour which is readily displaceable, and can be put back into the normal position of the liver, to which, indeed, it tends to return when the patient lies down, only to fall when a sitting or erect posture is assumed, the organ dropping two or more inches. The liver still descends on respiration; but the more marked the displacement, the less is this apparent. When the organ is very freely movable, and when presumably the lateral ligaments are greatly stretched or but ill developed, it can be readily rotated on its vertical axis, which passes through the inferior vena cava. This rotation is an exaggeration of that which a dilated stomach or colon may induce in the liver under normal conditions. The freedom of movement may, indeed, be so marked that the liver seems to turn over in its descent. When the patient turns on the left side, it travels in the same direction.

[1] Morestin. *Bull. Soc. anat.*, Paris, 1896, lxxi, 201.
[2] Richelot. *France méd.*, Paris, 1893, xl, 449.
[3] Lennander. *Gaz. d. hôp.*, Paris, 1900, lxxiii, 545.
[4] Clarke, T. W., and Dolley. *Am. Journ. Med. Sc.*, Phila., 1905, cxxx, 969.
[5] Nedwill. *Lancet*, 1901, ii, 914.
[6] Glénard. *Les Ptoses viscérales*, p. 625, Paris, 1899.

The displaced liver is visible under the relaxed abdominal walls as a rounded tumour on the right side about the level of the umbilicus. It is dull on percussion, firm, and smooth. The outline of the liver and perhaps the depression for the fundus of the gall-bladder and the notch between the left and right lobes for the round ligament can also be made out. When the organ has fallen away from the right hypochondrium, the normal liver dulness is replaced by resonance. In such cases the hand may be passed some way over the upper surface of the liver, between it and the diaphragm. There is a sinking or hollow in the right hypochondrium and a compensatory swelling or tumour, formed by the displaced liver, in the right flank or in the abdomen below the umbilicus. The empty state of the upper part of the abdomen below the right costal arch may be very striking.

The abdominal walls may be so lax and thin as to allow peristaltic action to be plainly visible, and divarication of the recti and a pendulous condition of the abdomen may be brought out when the patient rises from the horizontal position. According to Glénard, the lower part of the umbilicus becomes hidden by a fold of skin, upon which tension is brought to bear by the displaced liver through the attachment of the round and falciform ligaments. Other manifestations of visceroptosis, such as a floating kidney, a displaced uterus or stomach, may be present.

Onset.—Generally this is insidious and attracts no attention, but in some instances (Graham[1] says 5 per cent) it may be sudden, and then resembles a traumatic dislocation. There is then a feeling of something giving way, accompanied by sudden, twisting pain, which may be so severe as to make the patient faint, and may then be regarded as biliary colic.

A good case of sudden dislocation of the liver is recorded by Garnett[2] in a woman aged fifty, who, when hurriedly stooping to pick something up from the floor, felt a sudden wrench in the right side of the abdomen. The liver was found reaching to the right iliac crest. Rest in bed and the application of an appropriate bandage were followed by recovery. Graham[3] reported a movable displaced liver due to the wheel of a wagon passing over the abdomen in a boy aged seventeen.

Symptoms.—The symptoms of hepatoptosis may be summed up under different heads; cases may present the features of one or more of the following symptom-groups: (1) Pain, dragging, and heaviness in the hepatic region. (2) Symptoms referable to the intestinal tract, viz. dyspepsia, vomiting, and mucous colitis. (3) Imitating biliary colic, viz. pain and jaundice. (4) Imitating hepatic cirrhosis, viz. ascites, haematemesis, melaena. These symptoms are very rare. (5) Symptoms belonging to the respiratory system, viz. cough, dyspnoea. (6) Hypochondriasis, hysteria. There may, however, be no symptoms at all.

[1] Graham, J. E. Loomis and Thompson's *System of Practical Med.*, iii, 415.
[2] Garnett, A. *Am. Journ. Med. Sc.*, 1881, lxxxi, 110.
[3] Graham, J. E. *Canadian Practitioner*, 1895, xx, 399.

(1) *Hepatic Pain.*—When symptoms are present, the commonest is a feeling of discomfort, weight, or actual pain in the right hypochondrium. The dragging feeling is commonly felt in the right hypochondrium or epigastrium, but it may be more extensive and radiate behind the sternum or even to the base of the neck, the traction exerted on the diaphragm by the liver being perhaps transmitted through the pericardium to the cervical fascia. Dull pain in the region of the right shoulder is common, and has been explained by traction on the diaphragm stimulating the phrenic nerve which communicates with the nerve to the subclavius muscle. The pain and discomfort are usually relieved in the horizontal position, but are aggravated by movement, and may quite prevent the patient from walking or getting about, or even from lying on the right side. The pain, however, may be constant and very distressing, and is then quite probably due to chronic cholecystitis, cholelithiasis, or stretching of adhesions. There are frequently attacks of very severe pain, exactly like biliary colic, but not necessarily accompanied by jaundice (*vide infra*).

In 44 cases of hepatoptosis these colicky attacks occurred in 37, or 84 per cent, and were accompanied by jaundice in 14 only (Dutton Steele [1]).

(2) *Symptoms referable to the Intestinal Tract.*—In other cases the symptoms are mainly dyspeptic. Nausea and vomiting may occur and may be set up by lying on the right side. Intestinal disturbance, such as flatulent distension and constipation, may be present. Glénard [2] considers that the vascular disturbance resulting from a wandering liver is the cause of mucous colitis, which he thinks is often associated with enteroptosis. Probably many symptoms observed in hepatoptosis, such as hysterical mental disturbance and irritability, leucorrhoea, menorrhagia, albuminuria, are rather the results of enteroptosis in general than of hepatoptosis in particular.

(3) *Symptoms imitating Biliary Colic.*—As already mentioned, attacks of pain resembling biliary colic are very frequent in wandering liver.

In 44 cases in which the liver was seen to be displaceable either at a laparotomy or necropsy, attacks of colic occurred in 37, or 84 per cent; in 14 of these 37 there was jaundice and in 10 calculi. In 15 cases attacks of colic and transient jaundice occurred without gall-stones (Dutton Steele).

The colic may be due to at least three causes, viz. calculi, the presence of a floating kidney on the right side,[3] or torsion of one of the bile-ducts. In the absence of gall-stones and a floating kidney on the right side the attacks of colic are probably due to torsion of the cystic duct at its junction with the common bile-duct, which would not necessarily cause jaundice or kinking of the common bile-duct at its commencement.

[1] Dutton Steele. *Univ. Penn. Med. Bull.*, 1903, xv, 424.
[2] Glénard. *Académie de médecine*, April 20, 1897.
[3] Compare J. Hutchinson, Jr. *Practitioner*, 1902, lxviii, 186.

In Crawfurd's[1] case of hepatoptosis with jaundice a twist seemed to have occurred at the commencement of the common bile-duct. In this case I had an opportunity of examining sections of the liver which shewed dilatation of the lymphatics and oedema in the portal spaces, as if the lymphatics had also been twisted and obstructed; but as bile had evidently passed into the general circulation, the obstruction must have been intermittent.

Dutton Steele, in discussing the question why jaundice is not constant, points out that the obstruction is not always in the common bile-duct and that the kinking may be very transitory, the liver returning towards its normal position. His experiments shewed that the further the liver was displaced towards the pelvis, the greater was the pressure required to drive an injection from the biliary papilla into the gall-bladder. A twist in the cystic duct may produce intermitting distension of the gall-bladder and attacks of biliary colic but without jaundice (Villard and Cotte[2]).

In some instances jaundice may occur without pain; Steele refers to two cases. It may be catarrhal (Snowman[3]); a displaced liver may by traction on the ducts lead to stagnation of bile in the ducts, and so favour hydrops of the gall-bladder, cholecystitis, and the production of gall-stones. In Newman's[4] case the gall-bladder contained 30 ounces of straw-coloured fluid and numerous gall-stones.

(4) *Symptoms imitating Hepatic Cirrhosis.*—In very exceptional instances, ascites, probably caused by twisting of the portal vein, and oedema of the legs, probably due to a kink of the inferior vena cava, occur. Twisting of the portal vein, by obstructing the circulation, might be expected to give rise to venous oozing into the stomach and intestines and so to haematemesis and melaena. Haematemesis is, however, extremely rare.

McNaughton Jones[5] described a case of a woman aged thirty-eight, the mother of seven children, who had haematemesis on several occasions, the first at the age of nineteen. The last attack was very severe, and at this time a tumour, thought to be renal, was discovered. At the laparotomy the tumour was found to be liver, which extended into the right iliac fossa.

(5) *Symptoms referable to the Respiratory System.*—In some cases, classed by Max Einhorn[6] as asthmatic, there is dyspnoea in addition to a feeling of fulness and constriction in the upper part of the abdomen.

A dry cough of eighteen years' duration, which, however, disappeared when the patient was in the recumbent posture, was found by L. Vène[7] to be associated with hepatoptosis, and was cured by the application of a flannel bandage. It was

[1] Crawfurd. *Lancet*, 1897, ii, 1182.
[2] Villard et Cotte. *Rev. de chir.*, Paris, 1906, xxxiii, 331.
[3] Snowman. *Lancet*, 1896, i, 1281.
[4] Newman, D. *Brit. Med. Journ.*, 1902, ii, 249.
[5] McNaughton Jones. *Lancet*, 1898, i, 1327.
[6] Max Einhorn. *Med. Rec.*, N.Y., 1899, lvi, 397.
[7] Vène, Louis. *Journ. de méd. interne*, Paris, 1898, ii, 245.

thought that the cough was due to excitation of the diaphragm by traction of the liver on the inferior vena cava.

Some instances of cough usually put down to hysteria may in reality be due to hepatoptosis.

(6) *Hysteria* or *hypochondriasis* is frequently observed to be associated with hepatoptosis; the mental depression may result in the patient acquiring the morphia habit.

Absence of Symptoms.—A freely movable liver may be found accidentally in patients who do not suffer any inconvenience from it. Beddard [1] refers to a case in a placid unmarried lady who lived at her ease and in whom "the tumour" formed by the prolapsed liver merely aroused an "amused curiosity." It is probable that the presence or absence of symptoms largely depends on the life the individual leads and on her temperament. High-strung and nervous women often feel pain and suffer inconvenience from conditions, such as peritoneal adhesions and floating kidneys, of which their more robust sisters are unconscious.

Diagnosis.—The chief points in the diagnosis are the presence of a movable abdominal tumour, resembling the liver, which can be replaced in the position of that organ, and the fact that the hepatic region is sunken and resonant on percussion when the tumour is in the middle of the abdomen. In addition, other conditions, such as a floating kidney, must be excluded.

Differential Diagnosis.—A freely movable or wandering liver must be distinguished from an enlarged liver, from a tongue-like lobe with or without a distended gall-bladder, and from mere downward displacement of the liver such as may result from pleural effusion, pneumothorax, or other causes.

In Packard's [2] case of movable liver the diagnosis during life was subphrenic abscess following enteric fever.

From Floating Kidney.—The most frequent mistake seems to consist in regarding a wandering liver as a floating kidney or as some other form of enlargement of the right kidney. Floating kidneys are much commoner than hepatoptosis, and the general symptoms are so much alike that the condition of the liver may be overlooked, especially when, as is by no means infrequent, there is a floating kidney as well as a wandering liver. Alteration in the position of a movable liver may imitate an intermittent hydronephrosis; concomitant distension of the gall-bladder may have the same effect.

Newman [3] operated on a wandering liver and let out 30 ounces of bile from the gall-bladder. The symptoms had suggested a hydronephrosis.

[1] Beddard, A. P. *Guy's Hosp. Rep.*, 1902, lvii, 179.
[2] Packard. *Trans. Coll. Phys.*, Phila., 1896, xviii, 230.
[3] Newman. *Brit. Med. Journ.*, 1902, ii, 249.

A careful bimanual examination, if necessary under an anaesthetic, should be made; the liver dulness should be percussed, and an attempt to displace the abdominal tumour into the right loin should be made.

From Tumours and Hydatid Cysts in the Liver.—A wandering liver may suggest malignant disease of the organ, especially when, as in rare cases like Crawfurd's,[1] jaundice and ascites are present from torsion of the common bile-duct and portal vein in the lesser omentum. The ease with which the liver is displaced should prevent any mistake of this kind, while, on the other hand, irregularities of the surface of the liver and signs of chronic obstruction of the colon make malignant disease probable.

Hydatid cysts projecting from the upper surface of the liver, or, in rare instances, between the liver and diaphragm, give rise to downward displacement of the organ, but there is no absence of the hepatic dulness below the sixth rib in the right nipple line, as there would be if the liver had dropped away from its normal position. The converse mistake has occurred, and laparotomies undertaken for supposed hydatid cysts have led to the discovery of a wandering liver (Marchant,[2] Areilza[3]).

Gall-stones.—The pain and jaundice may, as in a case of Mathieu's,[4] lead to a diagnosis of biliary colic. Max Einhorn[5] has seen five cases of wandering liver that had previously been erroneously diagnosed as cholelithiasis. The two conditions may both be present.

Tumours and Inflammatory Thickenings of the Omenta, Mesentery, etc.—Tumours and cysts of the omentum and of the mesentery, though movable, cannot be displaced to the same extent from above downwards as a wandering liver; moreover, they are separated by a zone of resonance from the liver dulness. Inflammatory thickenings in the omentum being comparatively fixed, are hardly likely to cause any difficulty in diagnosis. In exceptional cases the question might arise whether a movable tumour is the liver or a mass of growth in the stomach, colon, or inflammation around the appendix; but under ordinary conditions there is little or no resemblance between hepatoptosis and these conditions.

Treatment.—Tight lacing and corsets which constrict the lower part of the thorax and tend to displace the liver downwards must be discontinued. The "straight-fronted" corset should be worn, as it supports the abdomen from below and does not compress the waist unduly. A suitable abdominal belt, binder, strapping, or elastic bandages should be applied so as to support the lower abdomen in an upward direction, and thus, by increasing the intra-abdominal pressure, to support the liver in its proper position. The belt or binder must reach below the hips and should be fixed in position while the patient is still in bed in the morning and before the liver has become prolapsed. This method of replacing

[1] Crawfurd, R. *Lancet*, 1897, ii, 1182.
[2] Marchant, G. *Acad. de méd.*, Paris, Aug. 11, 1891.
[3] Areilza. *Rev. med. y cirug. práct.*, Madrid, 1896, xxxvii.
[4] Mathieu. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1893, 3. s., x, 639.
[5] Max Einhorn. *Med. Rec.*, N.Y., 1899, lvi, 397.

the healthy tone of the abdominal muscles is much more effective than applying a supporting pad to the liver alone. Rest in bed will, for the time being, relieve the pain, and it is advisable to raise the foot of the bed so that the hips are higher than the head. The treatment of movable liver is on the same lines as that of enteroptosis or Glénard's disease.

Diet is a matter of importance, and, as a rule, the patient requires liberal feeding so as to improve the general state of nutrition. The subjects of hepatoptosis are usually weakly, but when there is decided corpulence, the amount and quality of food taken should be supervised by the medical attendant, and any excessive eating interdicted. There will be no difficulty in distinguishing the weakly, flabby patient whose muscles and tissues are in want of better food from the heavy eater whose liver and tissues are congested from the presence of the products of excessive protein metabolism. It is important to keep the bowels freely open, for in this way portal congestion and flatulent distension are relieved and a distended gall-bladder may be emptied, conditions which may conceivably dispose to or exaggerate hepatoptosis.

In order to improve the tone of the abdominal muscles carefully planned gymnastic exercises may be employed. The exercises should be simple and readily carried out. Lea[1] speaks of the following as very efficient: (1) The patient lies on the back without any pillows, the arms being folded in front, and gradually raises herself into the sitting posture without any help from the arms. (2) The patient, being in the same position as before, raises first one lower limb, then both, with the knees extended, to a right angle with the trunk. (3) Deep breathing, especially inspiratory movements with the glottis closed and after a forced expiration. This exercise is useful in drawing up the viscera. Lea directs that each of these exercises should be performed six to twelve times night and morning.

Massage may be used in order to improve the muscular tone.

Electrical stimulation has been applied to the abdominal muscles and has been found to be beneficial. Griffith[2] obtained a good result by stimulating the muscles with an interrupted current daily for three months, but the long duration of the treatment would render it unsuitable in many cases.

If the application of a belt and the other palliative measures mentioned fail to relieve the symptoms, and the pain be so severe as to incapacitate the patient from ordinary life and work, the advisability of surgical interference must be considered. The operation of fixing the liver by sutures or other means in its proper position is known as hepatopexy or hepatorrhaphy. Various methods have been adopted, such as passing sutures through the liver substance and the abdominal wall, tying the round ligament up to the cartilage of the seventh rib and at the same time promoting adhesions between the diaphragm and convexity of the liver by rubbing the peritoneum with aseptic gauze. When the gall-

[1] Lea, A. W. W. *Med. Chronicle*, 1902, xxxvi, 225.
[2] Griffith. *Brit. Med. Journ.*, 1878, i, 89.

bladder contains calculi, the operation for cholecystotomy usually leads to fixation of the liver.

In 1891 Gérard Marchant[1] fixed the anterior margin of the liver to the costal margin by four silk sutures. Treves[2] utilised the round ligament to support the sutures. Lanelongue and Faquet[3] in 1895 sutured the liver to the anterior abdominal wall and roughened the opposed surfaces of the liver and diaphragm so as to get adhesions. Union of the liver to the opposed peritoneal surface of the diaphragm has also been obtained by swabbing the surface of the liver with strong carbolic acid. Péan[4] supported the liver by uniting the peritoneum of the anterior abdominal wall with that of the postero-lateral part of the abdomen below the replaced liver.

In 18 cases of hepatopexy collected by Terrier and Auvray,[5] there were 15 cures; and of 25 collected by Cernezzi,[6] 22 were stated to be cured.

The drawbacks to operative measures are—(1) that the underlying condition disposing to enteroptosis in general and hepatoptosis in particular is not removed; (2) that the incision through the abdominal walls is very prone to become the seat of hernial protrusion, inasmuch as their tone and nutrition are especially defective.

On the other hand, hepatopexy may succeed after all other mechanical and palliative measures have failed, and it does so by compensating for, though not removing, the disposing factors of hepatoptosis. The danger of hernial protrusion in the scar is probably greater in old women with permanently pendulous abdomens than in younger women who are temporarily in a low state of nutrition from several rapidly succeeding pregnancies. In any case an abdominal belt should be worn after the operation.

With regard to *prophylaxis*, tight lacing should be prevented and care should be taken that a pendulous condition of the abdominal wall is not induced or aggravated by getting up too soon after parturition and by neglecting the use of a proper binder.

FUNCTIONAL DISEASE OF THE LIVER

Before entering on the rather difficult subject of functional disease of the liver it will be convenient to enumerate the important functions of the liver.

(1) The secretion of bile.

[1] Marchant. *Acad. de méd.*, Paris, August 11, 1891.
[2] Treves. *Brit. Med. Journ.*, 1896, i.
[3] Lanelongue et Faquet. *Gaz. hebd. d. sc. méd. de Bordeaux*, 1895, xvi, 411.
[4] Péan. *Congrès de chir.*, Paris, 1896. Quoted by Treves, *Lancet*, 1900, i, 1344.
[5] Terrier et Auvray. *Chirurgie du foie et des voies biliaires*, 1901.
[6] Cernezzi. *Rif. med.*, 1910, xxv, 877.

(2) The metabolic processes in connexion with the formation, storage, and hydrolysis of glycogen.

(3) In connexion with protein metabolism. The liver is very largely concerned in the conversion of ammonia into urea, but there is no reason to believe that it is of the same importance in the production of uric acid. In some diseases, in which the liver cells are degenerated, the amount of urea is diminished while the quantity of nitrogen excreted in the urine as ammonia is increased. It has, therefore, naturally been assumed that the fall in the output of urea was due to failure in the functional activity of the liver cells. This, however, is not the true explanation. The real reason is that in these diseases organic acids, of the fatty acid series, are formed and unite with any available bases, among which is ammonia, present in the blood. The ammonia, which under ordinary conditions would be changed by the liver into urea, is now in a form which cannot undergo this transformation, and therefore appears in the urine linked with an organic acid. This occurs in acute yellow atrophy, phosphorus poisoning, and some cases of cirrhosis and fatty liver. In such cases ammonia given by the mouth increases the amount of urea in the urine, thus shewing that the liver cells have not lost their power of transforming ammonia into urea. It is only in the very latest stages of such diseases, shortly before death, that the liver cells appear to lose this power.[1]

(4) Its antitoxic or protective function. Poisons, whether introduced into the alimentary canal or manufactured there as the result of bacterial activity, are normally arrested, or converted into harmless bodies by the liver cells. The detoxicating action of the liver is shewn by the difference in the action of poisons, such as strychnine, conia, snake venom, albumoses, when introduced into the portal circulation, on the one hand, and into the general circulation, on the other hand. It appears from Roger's[2] observations that the antitoxic function of the liver varies with its richness in glycogen and its power of stopping sugar and forming glycogen, and that if the liver loses its power of stopping sugar it is also unable to arrest poisonous bodies brought to it from the portal area. In complete biliary obstruction the antitoxic power of the liver fails, and the grave manifestations seen under these conditions are chiefly due to the poisons which flood the body, and only depend in a minor degree on the presence of the bile in the blood.

From the number and importance of the functions of the liver it is clear that failure in discharge of these duties must be followed by very definite symptoms. Functional disturbance is undoubtedly common in the liver, but the following questions require some consideration :

(1) Are the disorders of hepatic function primary in the liver? and (2) Are they entirely independent of structural change in the organ?

Numerous conditions, many of them in no way connected with the

[1] For a lucid account of this question the reader should refer to Herter's *Lectures on Chemical Pathology*, p. 338, 1902, London.

[2] Roger. *Presse méd.*, Paris, 1897, i, 293.

liver, were formerly described as due to functional disease of that organ. The idea was attractive to the lay mind and is recklessly appealed to in everyday life. Flatulence, dyspepsia, constipation, and the bad effects of overeating and drinking are often euphemistically described as "liver." As a reaction against this inaccurate though comforting doctrine most English medical writers at the present time ignore the subject or deny the existence of primary functional disease of the liver. This swing of the pendulum to the opposite extreme—for it must be admitted that the idea originated with the profession—is due to the knowledge that the symptoms ascribed to functional disease of the liver can in great part be explained as due to other factors, such as indigestion, auto-intoxication, constipation, or to subacute congestion or even inflammation of the organ, often secondary to intestinal disturbance or to absorption of toxic products from the intestine. In other words, the hepatic disturbances formerly regarded as due to primary functional insufficiency are in the vast majority of cases dependent on morbid processes elsewhere, and therefore secondary, or are associated with definite organic change in the liver.

Thus, to consider the symptoms commonly referred to functional disorder of the liver, the distaste for food, dyspepsia, flatulence, constipation or diarrhoea, are due to gastro-intestinal catarrh caused by poisonous or unsuitable food. The icteric tint of the conjunctivae, the muddy skin, and some of the mental depression are either due to the spread of the gastro-duodenal catarrh to the biliary papilla and the slight obstruction to the flow of bile thus induced, or possibly to catarrh of the minute intrahepatic ducts set up by poisons absorbed from the alimentary canal and subsequently excreted into the ducts; and in either case to the passage of bile, which often contains toxic constituents, into the general circulation. The pale colour of the faeces may be due to catarrh of the bile-ducts and a deficient amount of bile, but in cases without any jaundice elsewhere it has sometimes been regarded as due to deficient secretion of bile—acholia. Of this there is no proof; the colourless condition of the faeces may be due to several factors, increase of fat, a colourless form of urobilin, leuco-urobilin, due to over-reduction of urobilin, and often to permeation of the faeces with bubbles of gas from excessive carbohydrate fermentation. This colour of the faeces is often mentioned by the patients as proof that "the liver is not acting" and that there is an imperfect formation of bile. The increased amount of fat may depend on pancreatic rather than on hepatic disease, especially in children.

The headache, giddiness, muscae volitantes, malaise, muscular debility, mental depression, and irritability are due to the local action on the nervous system of poisons absorbed from the alimentary canal. These toxic bodies are either produced in such quantities that the liver fails to stop them, or more probably they act on the liver cells and impair their vitality and function; in either case the general circulation becomes flooded with toxic bodies. The piles, the feeling of weight in the right hypochondrium, and shoulder pain depend on hepatic congestion or

even slight hepatitis brought on by constipation and the advent to the liver of digestive products in excessive amounts and probably of altered (*i.e.* toxic) quality. This state of hepatic congestion is especially apt to be set up in patients who have suffered from malaria in the tropics. (*Vide* Tropical Liver.) Nevertheless there can be no doubt that in some instances morbid results are referred to the functional disturbance of the liver without its being always possible to determine satisfactorily that this disturbance is secondary. Thus, it is possible that in some forms of glycosuria there is an excessive activity of the glycogenic function, and that in alimentary glycosuria the liver fails to discharge efficiently its function of stopping the sugar brought to it by the portal vein. As a rule, in alimentary glycosuria there is some definite underlying cause, such as pancreatic disease, but it cannot be recognised in all cases. These conditions, however, are not ordinarily spoken of as functional disease of the liver.

It has recently been urged that puerperal eclampsia is in many cases due to hepatic insufficiency, and that the renal symptoms are secondary to a primary hepatic toxaemia. During pregnancy toxaemia is favoured by several factors, such as the retention of bodies which are normally removed in the menstrual flow, the passage of toxic bodies, derived from metabolic processes in the fetus, into the maternal circulation, and auto-intoxication from constipation, which is so common during pregnancy. In a woman who inherits a diminished hepatic activity and resistance the liver fails to rise to the occasion and to stop and destroy the poisons which reach it. The blood then becomes flooded with poisons, and symptoms of toxaemia result. These are dyspepsia, severe vomiting, ptyalism, oedema without albuminuria, pruritus, and pigmentation. In more marked instances there are intractable vomiting, jaundice, acute yellow atrophy, mania, and eclampsia. In fatal cases, however, changes are constant in the liver, and consist in focal or more extensive necroses, degeneration of the liver cells, and haemorrhages.

As has already been admitted, functional disorder of the liver is no doubt responsible for many symptoms. The difficulty in regard to the subject is to prove that the functional disturbance is primary in the liver and not secondary to disease or morbid factors elsewhere. The discussion is not a mere academic exercise, but has a practical bearing on the treatment. Thus, if it were thought that there was a primary failure of hepatic activity, as is implied by the common phrase "torpid liver," the rational course would be to stimulate the organ. Whereas, if there was an underlying and primary factor elsewhere, this should be attacked.

The difficulties about the recognition of primary functional disorders of the liver may be best explained by referring to some of the conditions which it has been supposed to cause.

Lithaemia was described by Murchison[1] as a condition of innate defect of power, often hereditary, in the liver, in virtue of which its healthy

[1] Murchison, C. *Croonian Lectures*, Royal College of Physicians, 1874; *Diseases of the Liver*, p. 594, ed. ii, 1877.

functions are liable to be deranged by the most ordinary articles of diet. As a result of this hepatic insufficiency uric acid, instead of urea, was said to be produced in the liver and turned out into the blood. Among the results of lithaemia Murchison enumerates such different conditions as dyspepsia, constipation, gout, urinary calculi, biliary calculi, and acute and chronic renal disease.

This conception has been revived in France under a different name—"hepatism"—by Glénard.[1] It is regarded as a chronic nutritional change which may be hereditary or acquired. It may take (*a*) the cholaemic form; this condition is much the same as the simple family cholaemia described by Gilbert and Lereboullet,[2] in which the blood-serum contains bile-pigment though the urine usually does not. Its primary signs are pigmentation of the skin, which may be of the nature of slight jaundice, or dark and resembling Addison's disease, moles, freckles, or brown areas (the biliary mask) resembling the melasma of pregnancy, and xanthoma of the eyelids. As secondary results such various conditions as the following may arise: dyspepsia, abdominal pain, haematemesis, epistaxis, mucous colitis, migraine, albuminuria, and rheumatic pains, while it is closely related to transient and chronic jaundice, biliary cirrhosis, and similar conditions. (*b*) The uricaemic form, which corresponds to the diathesis termed "arthritism" by some French writers, or to Murchison's lithaemia. Hepatism, according to Glénard, is a functional disturbance of the liver and is the cause of a large number of diseases, including those incriminated by Murchison, and, in addition, neurasthenia, diabetes, chlorosis, and viscero-ptosis. It may be pointed out that the cholaemic form probably depends on slight catarrh of some part of the bile-ducts, either in the liver or close to the lower end of the common bile-duct.

Murchison's conception of lithaemia is very far-reaching, and among other things offers an explanation of gout; in fact, many of the manifestations of lithaemia are those of irregular gout. Among recent writers Yeo[3] and Walker Hall[4] have supported the view that hepatic inadequacy is an underlying factor in the production of gout. The protean manifestations of neurasthenia include many of those formerly ascribed to functional failure of the liver.

This conception of lithaemia depends on the assumption that as the result of imperfect metabolism uric acid, instead of urea, is manufactured by the liver. There are two mistakes here. In the first place, it is now universally agreed that uric acid and urea are the products of entirely distinct metabolic processes, and that there is nothing to support the view that if the formation of urea is left incomplete uric acid results. As Woods Hutchinson[5] graphically expresses it, they are practically as distinct from each other as the urine from faeces. In the second place, it has been proved since Murchison's time that the liver does not play the predominant part in the manufacture of the uric acid. It is true

[1] Glénard. *Les Ptoses viscérales*, Paris, 1899.
[2] Gilbert et Lereboullet. *Gaz. hebd. de méd.*, Paris, 1902, vii, 889.
[3] Yeo. *Brit. Med. Journ.*, 1901, i, 1457.
[4] Walker Hall. *Practitioner*, 1906, lxxvi, 366.
[5] Woods Hutchinson. *Lancet*, 1903, i, 288.

that the liver contains an oxidase which can transform xanthine and hypoxanthine into uric acid. But uric acid is produced in the body generally, and more especially from lymphoid tissue; it is closely associated with leucocytosis, uric acid being derived from the nuclein of the cells. This is well seen in the excessive excretion of uric acid in leukaemia. It is, therefore, too narrow a view of the faulty metabolism of protein material which results in an excessive production of uric acid to say that it depends on functional disorder of the liver to the exclusion of the rest of the body.

Habitual high blood-pressure and its accompaniments, such as migraine, might be thought to depend on a failure of the liver to stop and destroy the poisonous bodies that are continually being carried to it from the intestines. The liver undoubtedly exerts this important function of protecting the body from auto-intoxication, but it is difficult to prove that failure in the discharge of this duty leads to high blood-pressure; since in cases of extensive disorganisation of the liver—for example, in cirrhosis—hepatic insufficiency must exist, but the arterial tension is low and not raised. It is much more likely that high blood-pressure is, like gout, due to some general disorder of metabolism.

In cases popularly described as "biliousness" or "torpid liver" the symptoms are indigestion, some hepatic pain, headache, slight icteric tingeing of the conjunctivae with an apparent or real deficiency of colouring-matter in the faeces. The most probable explanation of these symptoms is gastro-duodenal catarrh with slight catarrhal jaundice and not a primary diminution in the secretion of bile. In these cases it is possible either that there is catarrhal swelling of the biliary papilla in the duodenum, or that, as the result of indigestion, poisonous products are carried to the liver and then, when excreted into the bile-ducts, set up a certain amount of catarrh in the small intrahepatic ducts. This leads to reabsorption of the bile with the poisons contained in it, which pass into the general circulation and act on the body as a whole. According to Sir Lauder Brunton,[1] the proverbial bitter taste of the bile is pathological and due to the presence of poisons absorbed from the bowel and then excreted into the ducts, healthy bile being tasteless.

It must be borne in mind that the liver, like other organs, must vary greatly in different individuals as to its functional activity and reserve power, and that an amount of food-products which can be satisfactorily dealt with by the liver in one individual would in another be entirely beyond his capabilities. This difference in the inherent powers of the liver in different persons is analogous to variations in their muscular and mental powers, and the less powerful should not be described as suffering from functional disease of their muscles or brain because they fail to accomplish the work which their better developed companions have no difficulty with. If, therefore, an individual consumes an amount of food that is excessive for his powers of digestion, fermentation and auto-intoxication will result. These poisons will impair the functional

[1] Brunton, L. *Clin. Journ.*, 1899-1900, xv, 177.

activity of the liver, and as a result the poisonous products of digestion will be allowed to pass into the general circulation and give rise to the various toxic manifestations already referred to. From what has gone before, it is evident that the well-known symptoms ascribed to a "torpid" or "inactive liver" are chiefly due to factors which secondarily interfere with the functional activity of the liver and not to a primary functional failure on the part of that organ. But because the ingenious conception of lithaemia and other views as to primary functional disease of the liver do not commend themselves in the light of later knowledge, it does not follow that hepatic insufficiency or inadequacy is a negligible factor. It is quite possible that primary functional disorder of the liver does occur, but in the present state of our knowledge its existence is almost impossible to recognise with accuracy.

The symptoms of secondary functional disturbance of the liver have already been referred to (p. 38).

Treatment.—The treatment of the symptoms of secondary hepatic inadequacy must therefore be directed to the causes and not to the liver itself. In the first place, the alimentary canal should be cleared out; this is most satisfactorily effected by the use of calomel, grs. iij., or of the old-fashioned blue pill, grs. v., followed by haustus sennae, or saline purgatives, such as sulphate of magnesium or sodium, phosphate of sodium, or some natural mineral water with purgative properties. The mercury drives the bile out of the gall-bladder, unloads the bile-ducts, and by sluicing the common duct tends to remove the causes of catarrh of its lower end. At the same time it acts as an intestinal antiseptic and inhibits excessive fermentation, and thus puts a stop to further auto-intoxication. The saline removes the mercury from the intestinal surface and prevents prolonged irritation, while at the same time it diminishes portal engorgement. The purgative action of these two remedies removes poisons from the alimentary canal. Intestinal fermentation and putrefaction can be most satisfactorily prevented by careful dieting and by the administration of minute doses of calomel ($\frac{1}{40}$ to $\frac{1}{20}$ grain) three times a day, which is preferable to salol, β-naphthol, and other popular drugs employed for this purpose. It is, of course, important that the bowels should be kept properly open. The ordinary purgatives already mentioned may be used for this purpose, or a pill containing euonymin and iridin. These two drugs are often employed and spoken of as if they had some special action other than that of purgatives, but without any satisfactory reason.

Plenty of water should be taken so as to wash out the poisonous products from the circulation and stimulate the functional activity of the kidneys. It is better not to take water in considerable quantities either with or directly after food, but to take it half an hour or so before a meal. Hot water may be sipped first thing in the morning and last thing at night. During the existence of symptoms a liquid diet, of which milk is the staple, should be adopted, and alcohol in any form

should be rigidly avoided. In the second place, the patient should be warned to avoid the forms of food likely to set up intestinal catarrh and fermentation. The articles of food that must be avoided as indigestible will, of course, vary in individual cases, but, generally speaking, the following should be forbidden : Concentrated and highly spiced soups ; rich fish, such as salmon, mullet, eels, kippered fish ; duck, hare, made dishes, entrées, pickles, rich sauces, melted butter, tea cakes, crumpets, sweets, cream, cheese, and much protein food. Alcohol should be avoided or taken in great moderation, well diluted, and with meals. Claret, hock, or whisky are the forms that may be taken if it is thought desirable, but beer, stout, cider, champagne, sherry, Madeira, Port, Burgundy, and liqueurs should be strictly prohibited.

Exercise is important. The form of exercise most suitable to individual requirements varies somewhat, and a stereotyped direction cannot be given to all cases. When the symptoms have existed for a considerable time and when muscular debility is present, active exercise is unsuitable, at any rate at first, and may lead to exhaustion and exaggeration of the symptoms. In such circumstances massage may give very good results and may be followed by carefully regulated exercise, such as Ling's Swedish gymnastics. In ordinary cases, however, massage and gymnastics are hardly necessary. In some persons walking briskly is sufficient, but in many, probably in the majority, a more active form of exertion is more effective, such as horse-riding, bicycling, lawn tennis, or golf. There is the additional advantage that these forms of exercise distract the attention from the individual's private business or worries. Open-air exercise is better than indoor, but when the weather is bad, fencing, racquets, boxing, or gymnastics may be of great use in improving the conditions of health.

It is important to get the skin to act, and for this purpose Turkish baths or hot baths with vigorous friction of the skin by rough towels are useful. When the skin has been acting vigorously after exercise the underclothing should be changed as soon as the individual comes in, so as to avoid chilling the surface of the body. The body should be well but not too warmly clad, and care must be taken to avoid chills to the legs, abdomen, and neck.

A visit to a spa, either in this country, such as Harrogate, Llandrindod Wells, or Strathpeffer, or abroad, Homburg, Ems, Neuenahr, Vichy, Carlsbad, Marienbad, may be followed by improvement or cure. The patient not only undergoes a carefully regulated course of treatment ("the cure"), but gets change, holiday, and rest from the cares of business and other worries.

As to the **prognosis**, the digestive disturbances which give rise to these symptoms are much the same as those leading to cirrhosis, and indeed the symptoms of functional disease of the liver may in some instances be the early manifestations of cirrhosis. As a rule, however, the prognosis is good provided the patient conforms to medical advice.

DISEASES OF THE HEPATIC ARTERY

Aneurysm; Embolism; Thrombosis, Arteriosclerosis, etc.

Aneurysm

Aneurysm of the hepatic artery is rare; Rolland[1] in 1907 referred to 41 instances.

Age and Sex.—In 36 cases in which the ages were given, the average age was thirty-seven years, the extremes being eighty-three and fourteen years. In 40 cases, 10 were females and 30 males. The average age in the women was 10 years higher (45 years) than in the men (35) (Rolland).

Causation. — Some of these aneurysms may be due to embolism, and from the comparatively unsupported condition of the visceral arteries in the abdominal cavity, simple non-infective embolism is more likely to be followed by aneurysm there than in other situations, except, perhaps, in the circle of Willis, where the arteries lie on a yielding water-bed, the subarachnoid space. Trauma has been noted as a cause of hepatic aneurysm; thus, Mester's[2] patient was kicked in the abdomen by a horse. In most cases of hepatic aneurysm there is no evidence of embolism or trauma, and yet these factors seem more probable than mere chronic endarteritis. Perhaps in some instances the cause of the embolism, such as a calcareous plate from the aorta, has naturally been overlooked, or has passed away before the patient's death. Grunert[3] suggests that many cases of hepatic aneurysm are due to some infective disease such as osteomyelitis, enteric, pneumonia. Out of 22 cases analysed by him some acute infection occurred shortly before the aneurysm appeared in 16. Often, however, no antecedent condition, except endarteritis, is recorded.

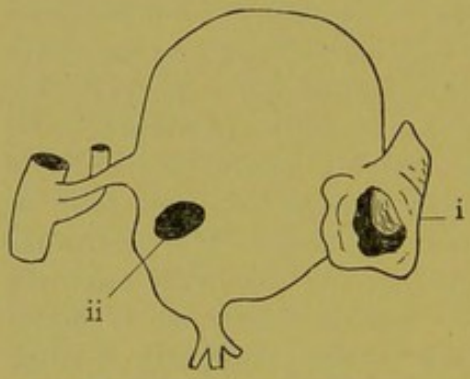


Fig. 10.—Aneurysm of hepatic artery, adherent to small intestine (i.), rupture (ii.) into the abdominal cavity. St. George's Hosp. Museum, Series vi, 86A. (Drawn by Dr. C. K. McKerrow.)

An aneurysm the size of a walnut was found by Pearson Irvine[4] inside an abscess in the left lobe of the liver; here the aneurysm was produced by inflammation and ulceration of the outer coats of the artery in the same way that aneurysms are formed in the vomicae of pulmonary tuberculosis.

[1] Rolland. *Glasgow Med. Journ.*, 1908, lxix, 342.
[2] Mester. *Ztschr. f. klin. Med.*, 1895, xxviii, 93.
[3] Grunert. *Deutsche Ztschr. f. Chir.*, Leipz., 1904, lxxi, 158.
[4] Irvine, Pearson. *Trans. Path. Soc.*, Lond., 1878, xxix, 128.

Aneurysms of the hepatic artery or its branches may be due to ulceration in the gall-bladder or bile-ducts eroding the wall of the artery. At first an aneurysm would result, and later, by extension of the ulceration, the aneurysm would open into the biliary tract.

This ulceration may be due to gall-stones. Naunyn [1] regards Lebert's case of rupture of an hepatic aneurysm into the gall-bladder of a woman aged thirty, with fatal gastro-intestinal haemorrhage, as due to gall-stones, and quotes M. B. Schmidt's [2] case of ulceration of the bile-duct, in connexion with an impacted gall-stone, opening into an aneurysm of the hepatic artery.

In connexion with the production of hepatic aneurysm by ulceration starting in the gall-bladder or bile-ducts and possibly due to cholelithiasis, it is significant that in 40 cases of hepatic aneurysm in which the sex is noted 10 were in women and 30 in men (Rolland). Aneurysm is so rare in women, while gall-stones are so common, that it is probable this proportion of female cases in aneurysm of the hepatic artery may to some extent be due to the mechanism of ulceration of the artery from without. Usually (in 33 out of Rolland's 41 cases) there is a single aneurysm on the trunk or extrahepatic branches of the hepatic artery, but in some instances more than one or even multiple aneurysms have been recorded. Aneurysm of the hepatic artery due to tuberculous infection and possibly the result of erosion by a tuberculous gland was described by Bickhardt and Schümann.[3]

In a boy aged seventeen there were two intrahepatic aneurysms (Borchers [4]), and in a boy aged eighteen Hale White [5] found an aneurysm on each of the main branches of the hepatic artery, one of which was embedded in the substance of the liver. Multiple aneurysms of small size may occur in great profusion in the liver in the rare disease periarteritis nodosa. From an analysis of 19 cases of the allied condition of polyarteritis acuta nodosa, Carnegie Dickson [6] finds that the liver is affected in nearly all the cases. Intrahepatic aneurysms have, however, attracted very little attention, and are very rarely seen.

Symptoms.—Pain is nearly always present, and may be mistaken for that of biliary colic; in fact "pseudo-biliary" colic may be due to the pressure of the aneurysm on the bile-ducts. The attacks may be accompanied by fever. Jaundice is frequently present and is usually due to pressure on the ducts; it may be slight or not appear until late in the course of the disease; when it comes on shortly before death, it may be due to leakage of the aneurysm into the ducts and the formation of a clot (Villandre [7]). Rolland stated that it was present in 16 out of 41

[1] Naunyn. *On Cholelithiasis*, p. 141. Translation, New Sydenham Soc., 1896.
[2] Schmidt. *Deutsch. Arch. f. klin. Med.*, Leipz., 1893–4, lii, 536.
[3] Bickhardt und Schümann. *Ibid.*, 1907, xc, 288.
[4] Borchers. *Aneurysma d. Art. hepat.*, Kiel, 1878.
[5] Hale White. *Brit. Med. Journ.*, 1892, i, 223.
[6] Dickson, Carnegie. *Journ. Path. and Bacteriol.*, Cambridge, 1907, xii, 50.
[7] Villandre. *Arch. gén. de chir.*, Paris, 1909, iii, 111.

cases. Reichmann[1] says it occurred in 64 per cent of 39 collected cases. Aneurysm and new-growth in the portal fissure behave, in a miniature fashion, just as the corresponding lesions in the anterior mediastinum do with regard to the adjacent venous trunks. Aortic aneurysm rarely obstructs the superior vena cava, while mediastinal growth frequently does. In the same way aneurysm of the hepatic artery, though it may push the portal vein aside, does not obliterate it or give rise to ascites.

Hepatic aneurysm may perforate into the peritoneum (17 out of 33 cases (Rolland)), and give rise to fatal collapse. With about equal frequency (13 out of 33 cases) it ruptures into some part of the bile passages, and the blood enters the alimentary canal and may be vomited, or more often passed by the bowel alone; repeated leakage and haemorrhages may occur before a fatal one. The aneurysm may rupture into the hepatic or common bile-ducts, the gall-bladder, portal vein, or stomach. Acute pancreatitis has resulted from regurgitation of bile into Wirsung's duct, the ampulla of Vater being blocked by clot (Dean and Falconer).[2]

A tumour has hardly ever been felt, and pulsation has not been detected.

Hepatic aneurysm, as in a case recorded by Ledieu, may obstruct the circulation in its branches. Reichmann and Dean and Falconer record necrosis of the liver cells with the formation of cysts due to this cause. By experimental ligation of the hepatic artery in dogs Dujarier and Castaigne[3] found that the flow of bile is retarded and that infection of the bile-ducts is thus rendered more easy. This may explain cases in which multiple abscesses in the liver are associated with an aneurysm of the hepatic artery.

Ross and Osler[4] recorded a case in which the sac of an hepatic aneurysm became infective and multiple emboli passed into the liver, leading to numerous abscesses.

Prognosis is very unfavourable.

Diagnosis.—The diagnosis of hepatic aneurysm is very difficult. Most of the recorded cases have been regarded as duodenal ulcer or cholelithiasis. It would be very difficult to distinguish with certainty between an hepatic aneurysm and one of the abdominal aorta in the immediate neighbourhood; especially as the latter may press on the bile-duct and give rise to jaundice.

Treatment is usually merely palliative. Of 6 cases treated surgically, 5 died; in the one which recovered Kehr[5] successfully ligated the hepatic artery and removed the aneurysm.

[1] Reichmann. *Virchows Arch.*, 1908, cxciv, 71.
[2] Dean and Falconer. *Edin. Med. Journ.*, 1912, viii, 124.
[3] Dujarier et Castaigne. *Bull. Soc. anat.*, Paris, 1899, lxxiv, 329.
[4] Ross and Osler. *Canada Med. and Surg. Journ.*, 1877, vi, 1.
[5] Kehr, H. *München. med. Wchnschr.*, 1903, xl, 1861.

Embolism

Embolism of the main trunk of the hepatic artery is very rarely observed; possibly it is sometimes missed, because the artery is not systematically examined. Chiari[1] recorded embolism of the main trunk, and Lancereaux[2] and Ogle,[3] embolism at the bifurcation of the hepatic artery. In Lancereaux's case hepatic pain set in ten hours before death and was referred to the embolism. In Ogle's case there were anaemic infarcts in the liver, but no general necrosis of the liver. Necrosis of the liver has been recorded by Lancereaux and by Chiari in man, and experimentally embolism of the hepatic artery in the hands of Cohnheim and Litten,[4] and of Doyon and Dufourt,[5] has led to the same result. Experimental ligature of the hepatic artery produces necrosis in rabbits but not in dogs; Dujarier and Castaigne found that aseptic ligature in dogs was not followed by necrosis, but that when infection occurred necrosis resulted. Obstruction of the artery may favour portal thrombosis, and by retarding the flow of bile render infection of the bile-ducts easier. In Lancereaux's cases of obstruction of the hepatic artery the liver became greatly engorged from the absence of the driving power or *vis a tergo* normally supplied by the hepatic artery. In rare cases infarction of the liver has followed embolism. (*Vide* p. 105.)

In haemic infections embolism of the small branches of the hepatic artery gives rise to pyaemic abscesses. Embolism also occurs in generalised tuberculosis and sarcomatosis, especially in melanotic sarcoma.

Thrombosis

This is also a pathological curiosity. Lancereaux[6] described a case of a clot in the trunk of an atheromatous hepatic artery in a man aged sixty-five who died with arteriosclerosis and gangrene of the feet which may have been either embolic or thrombotic.

Arteriosclerosis

The trunk of the hepatic artery is sometimes, in common with the rest of the arterial system, found to be atheromatous. When affected, the hepatic artery usually shews endarteritis deformans rather than endarteritis obliterans, or is dilated and varicose from loss of elasticity rather than narrowed. It thus disposes to the rare events, aneurysm and thrombosis of the hepatic artery. It is noticeable that arteriosclerosis does not lead to a fibrotic atrophy of the liver in any way

[1] Chiari. *Ztschr. f. Heilk.*, 1898, xix, 507.
[2] Lancereaux. *Traité des maladies du foie et du pancréas*, p. 541, 1899.
[3] Ogle, C. *Trans. Path. Soc.*, 1895, xlvi, 72.
[4] Cohnheim und Litten. *Virchows Arch.*, 1876, lxvii, 153.
[5] Doyon et Dufourt. *Arch. de physiol.*, 1898, 5. s., x, 522.
[6] Lancereaux. *Loc. cit.*, p. 543.

resembling a granular arteriosclerotic kidney, though senile atrophy of the liver with some fibrous replacement might be thought to depend on a similar process. Inside the liver the branches of the hepatic artery shew endarteritis in the neighbourhood of syphilitic gummas. In haemochromatosis the hepatic artery shews endarteritis; occasionally in ordinary cirrhosis there is endarteritis obliterans. Bonome[1] describes haemorrhagic and necrotic infarcts due to endarteritis obliterans in cirrhosis. In general paralysis of the insane, Angiolella[2] has observed endarteritis of the hepatic artery.

Enlargement of the Hepatic Artery

Enlargement of the hepatic artery is seen in cases of new-growth—though not in all instances—in cases of portal thrombosis of some standing, and in ordinary cirrhosis.

In a case in which the liver weighed 14 pounds from carcinomatous infiltration, secondary to a primary growth in the oesophagus, the hepatic artery was dissected out and was small in size.

DISEASES OF THE HEPATIC VEINS

Occlusion (due to Thrombosis, Stricture); Chronic Periphlebitis and Endophlebitis; Suppurative Phlebitis; Embolism.

Occlusion

Occlusion of the hepatic veins may be due to thrombosis or stricture. The various ways in which occlusion is brought about will be considered first, and then the clinical features.

Thrombosis of the hepatic veins is somewhat rare; it is usually secondary to some other hepatic lesion, but may spread from the inferior vena cava. It may be set up in the following ways:—

(1) New-growth in the liver may extend into the hepatic veins and give rise to thrombosis.

(2) "Adenomas" in nodular hepatitis may rupture into the hepatic veins and thus lead to thrombosis.[3]

(3) In portal cirrhosis thrombosis of the hepatic veins is rare. It may, as has just been pointed out, occur in cases of cirrhosis with multiple adenoma or nodular cirrhosis. Further, thrombosis of the hepatic veins may be due to intercurrent acute or subacute infections

[1] Bonome. *Arch. di biol.*, Firenze, 1899, liii, 319.
[2] Angiolella. *Manicomio mod.*, 1894, 1895.
[3] Compare Delépine. *Trans. Path. Soc.*, Lond., 1890, xli, 362.

falling on a cirrhotic liver and setting up inflammation which involves the thin walls of the hepatic veins. But in some cases of thrombosis of the hepatic veins with a slight degree of cirrhosis, the latter may be merely a secondary fibrous replacement.

(4) Thrombosis may be due to stricture of the hepatic veins. On the other hand, it has been argued that thrombosis may be followed by endophlebitis and stricture (Thompson and Turnbull, Fisher,[1] *vide* p. 51).

(5) Thrombosis may extend from the inferior vena cava.

Thrombosis of the inferior vena cava due to malignant disease of the kidney may spread into the hepatic veins. In a case of thrombosis of the inferior vena cava due to perforation of an amoebic hepatic abscess, the hepatic veins contained thrombi (Winternitz[2]). I have seen a parietal thrombus in the inferior vena cava, where it grooves the liver, associated with thrombosis in the hepatic veins; there was more recent clot in the portal vein. In a case of obliteration of the inferior vena cava recorded by Reynaud the right hepatic vein was thrombosed. In a case of obliteration of the inferior vena cava reported by Dixon Mann and Hall[3] there were thrombi in the hepatic veins. In this case peritonitis was thought to have set up periphlebitis and endophlebitis and the subsequent changes in the inferior vena cava and hepatic veins.

Osler[4] has described considerable stenosis of the orifices of the hepatic veins in a case of obliteration of the inferior vena cava, a condition which would readily dispose to thrombosis.

(6) Thrombosis of the hepatic veins may also occur in association with widespread thrombosis.

Pitt[5] records thrombosis in the aorta, in the splenic, left renal, and right middle cerebral arteries, and in the right hepatic vein. Softened and therefore older thrombi were found in the portal vein.

It appears probable that thrombosis of the hepatic veins may be due to the same causes that set up portal thrombosis, or to an extension of that process.

(7) It may not be possible to assign a definite cause for thrombosis of the hepatic veins in all cases. Possibly toxins or micro-organisms stopped by the liver may be responsible for some cases. Fisher reports a case of hepatic vein thrombosis in a child with bronchopneumonia. Thrombosis of the hepatic veins occurs at an early stage in suppurative inflammation due to hepatic abscess, pylephlebitis, etc.

Stricture of the hepatic veins chiefly occurs at or close to their junction with the inferior vena cava. Pressure from tumours, hydatid cysts, or cicatricial adhesions may obstruct branches of the hepatic veins in the liver and lead to local venous engorgement (*vide* p. 86). Stenosis of the main trunks is rare. It may be due to the following causes:—

[1] Fisher, T. *Bristol Med.-Chir. Journ.*, 1902, xx, 209.
[2] Winternitz. *Johns Hopkins Hosp. Bull.*, Balt., 1911, xxii, 396.
[3] Dixon Mann and W. Hall. *Edin. Med. Journ.*, 1904, N.S., xvi, 56.
[4] Osler. *Journ. Anat. and Phys.*, 1879, xiii, 291.
[5] Pitt, G. N. *Trans. Path. Soc.*, 1895, xlvi, 75.

(1) Cicatricial contraction starting outside the veins, either in the liver or in its neighbourhood. Under the name of phlebitis hepatica adhaesiva, Frerichs [1] described great narrowing of the hepatic veins due to inflammation spreading in from dense adhesions in the neighbourhood. His case was in an alcoholic married man aged forty-five; no mention of syphilis is made. He had ascites and jaundice; there were perihepatitis and probably some cirrhosis as well as a nutmeggy condition of the liver. Kelynack [2] met with a similar condition in a woman aged thirty-two who had probably had syphilis. There were adhesions around the hepatic veins, with marked stenosis and thrombosis; the adhesions were thought to have produced the stenosis.

(2) Gummatous disease or syphilitic fibrosis in the immediate neighbourhood of the main hepatic veins. A gumma may be so situated as to lead to obliteration and thrombosis in one or both of the hepatic veins. Fagge [3] refers to a case in which one of the hepatic veins was so much narrowed by the pressure of a gumma that it only admitted a probe. In rare instances a gumma has involved the inferior vena cava and obliterated the openings of the hepatic veins (Wilks,[4] West [5]).

(3) Extensive hepatic fibrosis and cirrhosis. In some cases the cicatricial formation is very extensive and is associated with general hepatic fibrosis. There is not in all cases a certain syphilitic history, but there is sufficient evidence to suggest that congenital syphilis is a probable factor in the general and extensive fibrosis.

In a man aged twenty-six years under Churton's [6] care ascites suddenly set in, and death occurred nine days later from exhaustion. Well-marked cirrhosis of the liver thought to be due to congenital syphilis with thrombosis and thickening of the walls of the hepatic veins was found at the necropsy; there was no portal thrombosis. Cicatricial contraction causing thrombosis of the hepatic veins was found in a boy aged thirteen who died in St. George's Hospital with well-marked cirrhosis of the liver. The patient had never taken alcohol, but there was reason to believe he was the subject of congenital syphilis, as his mother had three miscarriages after his birth and as there was marked fibrosis in the spleen, which weighed 16 ounces. The liver, 42 ounces, was considerably enlarged and most extensively fibrosed; a large mass of cicatricial tissue involving the hepatic veins suggested early gummatous change; no caseation, however, could be seen microscopically.[7]

The following case is probably a combination of syphilitic cirrhosis with endophlebitis obliterans: Gee [8] described complete obliteration of the orifices of the hepatic veins in a child aged seventeen months. Ascites rapidly appeared

[1] Frerichs. *Diseases of the Liver*, ii, 432-437, New Sydenham Soc., 1861.
[2] Kelynack. *Med. Press and Circ.*, 1897, cxiv, 633.
[3] Fagge. *Principles and Practice of Medicine*, vol. ii, p. 295, 1886.
[4] Wilks, S. *Trans. Path. Soc.*, 1862, xiii, 123.
[5] West, S. *Ibid.*, 1891, xlii, 155.
[6] Churton. *Ibid.*, 1899, l, 145.
[7] Lazarus-Barlow, W. S. *Ibid.*, 1899, l, 147. St. George's Hosp. Museum, Ser. ix, 174 L.
[8] Gee. *St. Barth. Hosp. Rep.*, 1871, vii, 144.

at the age of fourteen months, and paracentesis was twice performed. The liver ($16\frac{3}{4}$ ounces) was cirrhotic. There was considerable perihepatitis around the orifices of the hepatic veins. The hepatic veins ended abruptly, just short of entering the inferior vena cava, being cut off from it by a thin membrane. The lining membrane of the vena cava where the mouths of the hepatic veins should have been shewed dimples which had not at all the look of scars. Gee did not think this was due to a congenital failure of union of the venae revehentes hepaticae with the inferior vena cava, for then the ductus venosus should have remained open. He regarded the primary change as cirrhosis which led to stenosis and obliteration of the hepatic veins. Some of the hepatic veins contained firm clot. The liver was nutmeg. There was a free collateral circulation especially around the left branch of the portal vein. Similar cases have been described by Rosenblatt[1] and Penkert.[2]

(4) To primary obliterative endophlebitis of the hepatic veins. In a few cases there is marked or almost complete stenosis of the openings of the hepatic veins into the inferior vena cava without any evidence that the inflammatory process has spread to the veins from adjacent parts. Craven Moore[3] collected 12 and Hess[4] 23 cases of this primary obliterative inflammation of the hepatic veins. But they both, especially Hess, include cases in which the inflammatory process may have started from without such as Gee's, Rosenblatt's. It may be extremely difficult to decide whether the process started in or outside the veins. The openings into the inferior vena cava may be mere dimples. In some instances, as in two of Chiari's three cases,[5] syphilis was regarded as responsible, but this does not hold good in all cases. The entrance of the ductus venosus into the inferior vena cava in the immediate neighbourhood of the hepatic veins suggests that the process of obliteration of that fetal vessel may spread to the orifices of the hepatic veins and, by excess of the obliterating process, gradually lead to stenosis of the orifices of the hepatic veins, just as stricture of the ileum sometimes occurs at the point where Meckel's diverticulum is normally obliterated, or coarctation of the aorta where the ductus arteriosus joins the aorta. Moore, however, believes that congenital influences may so reduce the resistance of the mouths of the hepatic veins as to enable some haematogenous poison to induce endophlebitis. Kretz[6] suggests that the obliteration is secondary to small tears of the walls of the hepatic veins due to coughing, and that exuberant cicatrisation follows. Thompson and Turnbull[7] argue that the process is not a pure endophlebitis but a thrombophlebitis, and that thrombosis is likely to occur at the junction of the hepatic veins and inferior cava. In their two cases the

[1] Rosenblatt. *Virchows Jahresb. der Med.*, Berlin, 1867, i, 267.
[2] Penkert. *Virchows Arch.*, 1902, clxix, 337.
[3] Craven Moore. *Med. Chron.*, 1902, xxxvi, 240.
[4] Hess. *Am. Journ. Med. Sc.*, Phila., 1905, cxxx, 986.
[5] Chiari. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1899, xxvi, 1.
[6] Kretz. "Pathologie der Leber," *Lubarsch-Ostertag Ergebnisse allg. Path.*, 1904 (1902), viii, Abth., ii, 498.
[7] Thompson and Turnbull. *Quart. Journ. Med.*, Oxford, 1911–12, v, 276.

diaphragmatic closure of the hepatic veins was ascribed to organisation of blood-clot.

Morbid Anatomy.—The liver is in a state of advanced chronic venous engorgement with dilatation of the trunks of the hepatic veins behind the stenosis. The Spigelian lobe may be greatly enlarged (Hess).

Clinical Features.—The symptoms are those of portal obstruction. Ascites is almost constant and pain in the hepatic region common. The veins over the abdomen may be enlarged. Vomiting is common, but haematemesis is rare, and jaundice most exceptional. The liver is usually enlarged and tender; and there may be cyanosis. The disease may either last for several months and imitate cirrhosis or portal thrombosis; or the symptoms may be very acute, beginning with rapid ascites, followed by delirium and coma, and terminating fatally in a few days. The disease may occur at any age, but the average age of Hess' 23 cases was 28·5 years. The sexes are equally affected. A correct diagnosis has never been made. The prognosis is extremely bad.

Chronic Periphlebitis and Endophlebitis of the Hepatic Veins

In adherent pericardium inflammation around the inferior vena cava may spread to the hepatic veins and set up periphlebitis and possibly slight fibrosis in the neighbourhood. In the cases that I have examined, however, there has been no extension of inflammation from the walls of the veins into the surrounding liver substance. In long-standing backward pressure the intima of the hepatic veins may, like that of the inferior vena cava, become somewhat thickened and opaque—a slight degree of chronic endophlebitis due to increased intravascular pressure, and the veins become dilated. Endophlebitis may spread from the inferior vena cava in cases of obliteration of that vessel into the hepatic veins, and may, as in Dixon Mann and Hall's[1] case, give rise to thrombosis of the hepatic veins.

Suppurative Phlebitis of the Hepatic Veins

Suppurative phlebitis is more likely to attack the hepatic veins than the branches of the portal vein in hepatic abscess, since the latter are surrounded by Glisson's capsule, while the hepatic veins and their branches are not protected in this way. When the hepatic veins are thus affected, general pyaemia is more likely to occur than in pylephlebitis, since the emboli can pass more readily into the circulation.

In a case of large hepatic abscess in a man aged thirty-four the abscess set up thrombosis in the right hepatic vein which produced embolism of the right pulmonary artery and suppurating areas in both lungs. In a case of suppuration around a calculous gall-bladder recorded by West[2] the abscess opened into the hepatic veins and produced multiple infarcts in the lungs.

[1] Dixon Mann and W. Hall. *Edin. Med. Journ.*, 1904, N.S., xvi, 56.
[2] West, S. *Trans. Path. Soc.*, Lond., 1886, xxxvii, 281.

In a case of proctitis, due to a bacillus of the influenza group, Ophüls [1] found abscesses in the submucous coat of the rectum, areas of necrosis in the liver, and suppurative thrombosis of the hepatic veins which had produced secondary foci in the right lung. The portal vein was quite healthy. In an areolar abscess of the liver due to *Bacillus mucosus capsulatus* the suppuration started in connexion with the hepatic veins (Hewitt [2]).

Embolism of the Hepatic Veins

Embolism of the hepatic veins can occur only when the embolus travels against the blood-stream and enters the hepatic veins from the inferior vena cava—in other words, retrograde embolism. Retrograde embolism of veins is very rare; when it occurs, it is more frequently seen in the hepatic veins, since they are not protected by valves, and are so close to the heart that fragments of growth or thrombus may drop into their orifices either from the inferior vena cava or from the heart and superior vena cava. Welch [3] quotes examples of fragments of new-growth in the hepatic veins in cases in which the primary growths were in the abdomen and thyroid.

It seems probable that in cases of cranial suppuration with secondary abscesses in the liver, without any abscesses in the lungs, the micro-organisms may drop down the jugular vein, superior vena cava, right auricle, and inferior vena cava into the orifices of the hepatic veins, and so infect the liver. The production of retrograde embolism probably depends on the temporary stagnation or reversal of the direction of the blood-flow. Thus, if a thrombus was passing up the inferior cava and a violent expiratory effort or cough occurred at the moment when it was opposite the openings of the hepatic veins, the embolus might be carried into the liver.

THROMBOSIS OF THE PORTAL VEIN

Synonyms: Pylethrombosis, Pylephlebitis Adhaesiva.

In this condition there is thrombosis of the portal vein which does not go on to suppuration.

Causation.—It will be convenient to deal first with thrombosis depending upon inflammatory and other morbid conditions of the portal vein, and then to consider the influence of hepatic cirrhosis, intra-abdominal malignant disease, tumours, adhesions, and trauma in the production of portal thrombosis.

Inflammatory Conditions causing Portal Thrombosis.—Thrombosis of the portal vein, or, as it may in this particular connexion be more appropriately called, adhesive pylephlebitis, occurs as a preliminary stage in

[1] Ophüls. *Am. Journ. Med. Sc.*, 1901, cxxii, 797.
[2] Hewitt. *Johns Hopkins Hosp. Bull.*, Balt., 1909, xx, 77.
[3] Welch, W. H. Allbutt's *System of Medicine*, 1899, vi. 232.

suppurative pylephlebitis. Whether in a given case the process goes on to suppuration or not probably depends on the nature and virulence of the organisms. In 48 cases analysed by Langdon Brown [1] there was an infective origin in 7, or 14·6 per cent. By extension from adjacent parts inflammation may spread to the walls of the portal vein and set up thrombosis, which does not necessarily go on to suppuration. This may occur in cholangitis, in pancreatitis, in peripancreatitis, in hepatic and subphrenic abscesses, a suppurating mesenteric gland, and in other conditions.

Cholelithiasis, by setting up cholangitis and pericholangitis, may lead to inflammation of the walls of the portal vein and subsequently to thrombosis. In Lissauer's [2] 68 cases of portal thrombosis there were 9 with gall-stones. Kanis [3] described portal thrombosis secondary to an ulcer in the common bile-duct without gall-stones. Extension of inflammation from an hepatic abscess is a rare cause of thrombophlebitis of the portal vein.

A man aged twenty-seven, who had contracted dysentery in the Boer War of 1899–1902, was brought in a moribund state into St. George's Hospital. At the necropsy there was acute peritonitis with several pints of turbid fluid in the abdominal cavity, due to rupture of an abscess in the left lobe of the liver into the peritoneal cavity. There was a firm dry clot in the portal vein, which might have given rise to the ascites. The walls of the portal vein were greatly thickened and the lymphatic glands in the portal fissure much enlarged. It seemed probable that the infection had spread, at any rate partly, by the lymphatic vessels from the abscess to the trunk of the portal vein.

Inflammation, abscess, or infarction of the spleen may set up thrombosis of the splenic vein, which may spread into the portal vein.

Simple ulcer of the stomach must be a very rare cause of portal thrombosis. Wickham Legg [4] mentions two cases; but I have no other references. Thrombosis of the gastric veins may cause ulceration of the gastric mucous membrane. I have seen this in a case of suppurative pylephlebitis due to appendicitis. Indirectly a gastric ulcer may cause portal thrombosis by giving rise to a localised abscess in the neighbourhood. I have seen portal thrombosis in a case of subphrenic abscess due to perforation of a gastric ulcer.

Probably in many of the cases that appear to be primary thrombosis there is in reality microbic infection of a low grade of virulence present which is responsible for the production of a thrombus. The term "adhesive pylephlebitis," formerly used to designate thrombosis of the portal vein, is an expression of the view, originated by Hunter and Cruveilhier, that thrombosis is always the result of phlebitis. Bacteriological examination [5] proves that many thrombi which would

[1] Brown, Langdon. *Brit. Med. Journ.*, 1905, ii, 1393.
[2] Lissauer. *Virchows Arch.*, 1908, cxcii, 278.
[3] Kanis. *Wien. klin. Rundschau*, 1911, xxv, 757.
[4] Legg, Wickham. *St. Barth. Hosp. Rep.*, 1874, x, 236.
[5] Vaquez, *Thèse de Paris*, 1890; Bryant, J. H., *Guy's Hosp. Rep.*, 1902, lvi, 99.

formerly have been regarded as marantic contain micro-organisms, and though the presence of micro-organisms does not necessarily prove that they caused the thrombosis, it justifies the return to the view that most thromboses are secondary to infection of the wall of the vein.

Disease of the Portal Vein.—Chronic phlebosclerosis, which is probably often due to increased blood-pressure in the portal vein, plays an important part in producing portal thrombosis. Though generally associated with cirrhosis, chronic portal phlebitis may be independent of any hepatic disease. It is quite possible that phlebosclerosis may follow thrombosis; but it seems probable that it usually precedes and disposes to portal thrombosis. Borrmann,[1] who insisted on this sequence of events, found phlebosclerosis in 7 out of 20 cases of portal thrombosis.

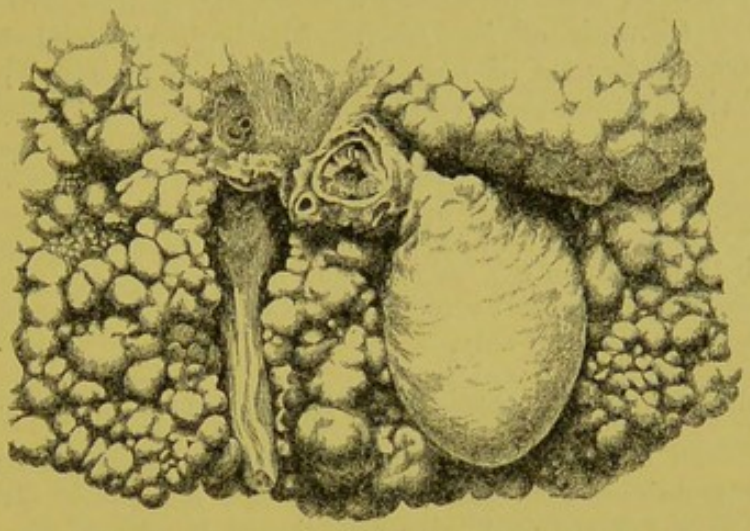


FIG. 11.—The under surface of a cirrhotic liver, shewing thrombosis of the portal vein. (Drawn by Dr. E. A. Wilson.)

When the change is of old standing calcification of the wall of the vein may occur, and calcareous plates or spicules may project into the lumen of the portal vein and induce thrombosis.

In a patient on whom I made a necropsy at St. George's Hospital, the dependence of thrombosis on calcification of the portal vein seemed clear. A man aged sixty-six years, addicted to some alcoholic excess, had been in good health until two months before his death, when ascites appeared. He was thin, but there had been no melaena or haematemesis. Paracentesis was required, but the fluid reaccumulated, diarrhoea set in, and he became delirious and died comatose. At the necropsy there were pigmented scars in the colon as if from old dysentery, but no ulceration. There was localised fibrinous peritonitis around the site of the trocar punctures. The portal vein was much thickened and shewed calcification, and there was a softening thrombus in the right branch of the portal vein. The splenic vein was occluded at its entry into the portal vein and contained a crumbling thrombus in contact with an area of calcification in its wall. The thrombosis did not correspond to the more extensive changes in the walls of the portal vein, and it therefore appeared probable that the thrombosis was secondary to the changes in the portal vein, as presumably the thrombosis had only existed since the ascites developed, viz. two months. The liver was atrophied, weighing 32 ounces, but not

[1] Borrmann. *Deutsch. Arch. f. klin. Med.*, Leipz., 1897, lix, 283.

cirrhotic. The spleen weighed 18 ounces and on section appeared fibrotic, but did not present any infarcts.

Syphilitic inflammation of the portal vein probably gives rise to thrombosis in some cases. This may occur in both the hereditary and the acquired forms of the disease. In 68 cases of portal thrombosis 7, or 10 per cent, were associated with syphilitic disease of the liver (Lissauer).

Cirrhosis of the Liver.—Although cirrhosis is probably the most frequent cause of portal thrombosis it does not appear to be present in half the total cases of that condition.

In 60 cases collected from various sources, including most of Langdon Brown's, there were 22, or 36·7 per cent, due to cirrhosis. These 22 cases do not include those in which cirrhosis and intra-abdominal malignant disease were both present, or the few examples in which the observers believed cirrhosis to be secondary to portal thrombosis. In Lissauer's 68 cases of thrombosis cirrhosis was present in 6 only.

Portal thrombosis is far from common in cirrhosis of the liver.

In a period of thirty-three years Langdon Brown[1] found that in 334 necropsies performed on cases of hepatic cirrhosis at St. Bartholomew's Hospital 10, or 3·3 per cent, were complicated by thrombosis of the portal vein. In 711 cases of cirrhosis Lissauer found pylethrombosis in 6, or ·9 per cent.

In cirrhosis of the liver there are a number of factors favouring portal thrombosis, such as obstruction to the passage of blood through the liver and stagnation of blood in the vein, while the increased venous pressure tends to set up endophlebitis and even secondary calcification of the walls of the vein. Further, the catarrh of the intestinal tract, so common in portal cirrhosis, favours microbic invasion of the walls of the tributaries of the portal vein. In nodular cirrhosis, or cirrhosis with multiple adenoma, thrombosis of the portal vein is relatively common; thus, in 15 cases collected by Ll. Powell[2] there was portal thrombosis in 9. The contents of the adenomas may soften down from necrosis and discharge into the portal vein, thus setting up thrombosis. On the other hand, thrombosis of the portal vein may so impair the nutrition of the adenomas as to set up fatty degeneration and necrosis.

Intra-abdominal Malignant Disease.—After cirrhosis the commonest condition associated with portal thrombosis is malignant disease either in the liver itself or elsewhere in the abdominal cavity. In 60 cases of portal thrombosis 10 were associated with some form of intra-abdominal malignant disease.

Malignant Disease of the Liver.—Carcinoma of the liver may eat its way into the branches of the portal vein and induce thrombosis; this may occur either in primary or secondary malignant disease of the organ, but it is particularly prone to occur when primary carcinoma supervenes

[1] Brown, Langdon. *St. Barth. Hosp. Rep.*, 1901, xxxvii, 62.
[2] Powell, Ll. *Unpublished Thesis for M.B. Cantab.*, 1895.

in a cirrhotic liver. In these cases the contents of the portal vein may be composed of growth as well as of blood-clot.

In other forms of intra-abdominal disease, such as carcinoma of the stomach, pancreas, colon, the growth may involve the tributaries of the portal vein, spread along them, and set up thrombosis.

Carcinoma of the Stomach.—Malignant disease of the stomach occasionally gives rise to portal thrombosis. In Lissauer's 68 cases of portal thrombosis malignant disease of the stomach was present in 7, or 10 per cent. S. and S. Fenwick [1] found it in 3 per cent of their cases of gastric carcinoma. Gastric cancer may set up portal thrombosis in several ways; the growth may enter the gastric veins and extend directly into the portal vein and cause secondary thrombosis; pass up the lesser omentum by continuity and compress and involve the portal vein; or by means of secondary growths in the portal fissure or in the substance of the liver may compress the portal vein.

In the following case there were at least two factors favouring thrombosis of the portal vein. A woman aged sixty-five years died in St. George's Hospital with a small cirrhotic liver weighing 28 ounces and a spheroidal-celled carcinoma near the pylorus. The trunk of the portal vein was thickened and surrounded by adhesions. The right branch of the portal vein was thrombosed and there was an adherent clot at the entrance of the splenic vein. In a case of portal thrombosis secondary to gastric carcinoma Longcope [2] found infarcts in the liver. In a case of carcinoma of the lower end of the oesophagus in a man, examined after death at St. George's Hospital, there was a subphrenic abscess in connexion with breaking down carcinomatous glands, and as a result of the abscess thrombosis of the portal vein.

Malignant Disease of the Pancreas.—In 41 cases of portal thrombosis Langdon Brown found that the condition was associated with malignant disease of the pancreas in three instances. Sometimes when a malignant growth compresses the portal vein, and also infiltrates its walls, a finger-like process of the growth may extend along the lumen of the vein and then set up a secondary thrombosis. This very rarely happens in malignant disease of the pancreas; it is chiefly seen in malignant disease in the liver.

Malignant disease of the glands in the portal fissure secondary to malignant disease of the stomach, pancreas, liver, or gall-bladder might compress the portal vein. Malignant disease of the liver may compress as well as invade branches of the portal vein, and set up thrombosis which travels distally into the main trunk. Portal thrombosis has been recorded in primary carcinoma of the bile-ducts (Bourgeret and Cossy [3]). In Lissauer's 68 cases of portal thrombosis there was primary carcinoma of the gall-bladder in 6, or 9 per cent.

Pressure on the portal vein, by tumours, adhesions, and altered conditions of adjacent viscera, may be, but is not necessarily, accompanied

[1] Fenwick. *Cancer and other Tumours of the Stomach*, 1902, p. 72.
[2] Longcope. *Univ. Penn. Med. Bull.*, Phila., 1901, xiv, 223.
[3] Bourgeret et Cossy. *Bull. Soc. anat.*, Paris, 1873, xlviii, 347.

by thrombosis of the portal vein. By pressure the nutrition of the walls of the vein is impaired, microbic infection is thus favoured, and stagnation of the blood is induced—factors which all dispose to thrombosis. Pressure may be exerted on the portal vein in a number of ways, chiefly by malignant disease involving the adjacent lymphatic glands or the head of the pancreas.

Walker[1] records occlusion and thrombosis of the portal vein by fibrous adhesions due to calculous pericholecystitis.

Chronic Pancreatitis.—The cicatricial contraction of chronic pancreatitis may greatly constrict the superior mesenteric vein or the commencement of the portal vein and lead to thrombosis. Barnard[2] met with a case of this kind. Probably many cases of chronic pancreatitis were formerly spoken of as "scirrhus" of the pancreas.

Chronic peritonitis in rare instances may be the only other morbid lesion forthcoming, and so appear to be the cause, either by extension of inflammation to the walls of the portal vein, or, in very rare instances, by constricting or compressing the vein.

In St. Bartholomew's Hospital Museum there is a specimen [No. 2205 A] of thrombosis associated with chronic peritonitis; the liver was not cirrhotic. Frerichs quotes similar cases.

The traction exerted by adhesions due to gastric or duodenal ulcers (Frerichs[3]) may compress the portal vein and in rare instances induce thrombosis. Similarly adhesions involving the mesenteric veins may start thrombosis which may extend upwards into the trunk of the portal vein (F. Taylor,[4] R. Johnson[5]).

The mechanical pressure exerted by a calculus, in the gall-bladder or more frequently in the ducts, on the portal vein may give rise to simple thrombosis. This is more likely to occur when the calculus is in the common duct, where it is in close contact with the portal vein.

Cases are recorded by Leudet, Geigel, Naunyn,[6] Westenhöffer,[7] Körte.[8] Naunyn also describes a case in which a calculus in the cystic duct compressed and gave rise to portal thrombosis, and refers to a case of Klesser's in which a calculus in the same position compressed one branch of the portal vein. Donkin[9] met with portal thrombosis due to pressure exerted by several calculi in the gall-bladder on the vein.

Gummatous inflammation in the portal fissure is a rare cause. It is possible that *aneurysm* of the abdominal aorta or of the hepatic artery may press on the portal vein and induce thrombosis.

[1] Walker. *Ann. Surgery*, London, 1907, xlv, 27.
[2] Barnard, H. L. *Clin. Journ.*, 1905, xxvi, 133.
[3] Frerichs. *Diseases of the Liver*, i, 272, Transl. New Sydenham Soc., 1860.
[4] Taylor, F. *Trans. Path. Soc.*, 1881, xxxii, 21.
[5] Johnson, R. *Trans. Clin. Soc.*, 1898, xxxi, 212.
[6] Naunyn. *Cholelithiasis*, Transl. New Sydenham Soc., p. 133, 1896.
[7] Westenhöffer. *Semaine méd.*, 1903, xxiii, 32. [8] Körte. *Ibid.*
[9] Donkin. *Med. Press and Circ.*, 1868, ii, 396.

Trauma may be followed by portal thrombosis; cases have been described by Heller,[1] Ponfick, Saxer, Schmorl,[2] Pitt.[3] As an example of post-operative thrombosis Delatour's[4] case of thrombosis of the splenic vein after splenectomy, extending into the portal vein, may be mentioned. Trauma involved in volvulus or in kinking of the mesentery may be the starting-point of thrombosis in the portal area (Langdon Brown).

Thrombosis of the portal vein may be secondary to *thrombosis of the hepatic veins.* The portal thrombosis is probably terminal. Cases have been described by Chiari,[5] Thompson and Turnbull,[6] and myself.[7]

Puerperal eclampsia has been thought by Schmorl[8] to induce portal thrombosis. This may be the result of degenerative changes in the liver giving rise to discharge of necrotic hepatic cells and tissue fibrinogens into the portal vein.

In a number of cases there is no local cause or associated morbid change, such as cirrhosis or inflammation, to account for portal thrombosis. Of this group of *primary portal thrombosis* Lewis and Rosenow[9] have collected 21 cases. In some of these cases it is associated with thrombosis elsewhere in the body, and therefore almost certainly depends on a widespread change in the blood of either a chemical or infective nature. It is analogous to the thrombosis sometimes seen in marasmus. The altered blood condition must favour infection, and the intestinal tract would appear to be so eminently favourable to the passage of micro-organisms into the tributaries of the portal vein that it is surprising that portal thrombosis is so comparatively infrequent. I have on two occasions seen portal thrombosis associated with thrombosis in the iliac veins. Langdon Brown found that 6 of 33 cases were associated with thrombosis elsewhere. Portal thrombosis in a girl aged 18 years was associated with and possibly favoured by an abnormality of the course of the portal vein (Hecht[10]).

It is curious that nothing is known as to the occurrence of portal thrombosis in connexion with diseases such as gout, influenza, pneumonia, and especially typhoid fever, which lead to thrombosis elsewhere in the body.

Sex.—More cases occur in males than in females. In 62 cases, 38 were males and 24 females; the preponderance of males depends on the greater frequency of hepatic cirrhosis in that sex. Cirrhosis of the liver was present in 18 out of the 38 males and in only 4 of the 24 female cases. Intra-abdominal malignant disease accounted for 8, or exactly one-third of the cases of portal thrombosis in women.

[1] Heller. *Verhandl. d. deutsch. path. Gesellsch.*, Jena, 1904, p. 182.
[2] Schmorl. *Ibid.*, Karlsbad, 1902, p. 150.
[3] Pitt, G. N. *Trans. Path. Soc.*, London, 1895, xlvi, 74.
[4] Delatour. *Ann. Surg.*, 1895, xxi, 24.
[5] Chiari. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1899, xxvi, 1.
[6] Thompson and Turnbull. *Quart. Journ. Med.*, Oxford, 1911–12, v, 281.
[7] Rolleston. *Trans. Path. Soc.*, 1899, l, 148.
[8] Schmorl. Quoted by Welch, Allbutt's *System*, 1899, vi, 219.
[9] Lewis and Rosenow. *Arch. Int. Med.*, Chicago, 1909, iii, 233.
[10] Hecht. *Wien. klin. Wchnschr.*, 1908, xxi, 944.

Age.—In 61 cases the average age was forty-four years. The extremes were eighty years in a man and five years in a girl.[1] In the two sexes the average ages were 44·8 years among the males and 41 years among the females. This again corresponds with the slightly earlier age at which cirrhosis is fatal in women. There were ten patients under thirty years of age, equally divided among the two sexes; four were under twenty years of age—three females and one male. The average age of portal thrombosis is thus more than twelve years above the average age (31·6 years) in suppurative pylephlebitis. The explanation of this is that the two conditions—hepatic cirrhosis and intra-abdominal malignant disease—which most frequently cause portal thrombosis are commoner after forty years of age, whereas appendicitis, which is the most prolific source of suppurative pylephlebitis, is essentially a disease of young persons.

The distribution of the thrombosis in the portal vein varies considerably. It may extend throughout the portal vein and its branches. Usually it is more limited; it may occupy the main trunk of the portal vein and one or both of its branches in the liver, or it may obstruct the trunk and one or more of its tributaries, whilst in other instances thrombosis may be confined to one of its intrahepatic branches or one of its tributaries. The clot obstructing a tributary, such as the splenic vein, may just project into, but not obstruct, the blood-flow through the main trunk of the portal vein; in many instances the clot extends from the tributaries upwards into the portal vein. In other instances the clotting may begin in the portal vein and subsequently spread into the peripheral tributaries. Thrombosis may be confined entirely to the tributaries of the portal vein —the splenic, superior and inferior mesenteric veins—or to its intrahepatic branches.

Morbid Anatomy.—The vein is distended with clot, and thus differs from the more or less collapsed condition of the portal vein when containing ordinary post-mortem blood-clot. Distal to the obstructing thrombus the vein may be considerably dilated or even sacculated; this may also occur in the splenic vein. The vein wall is usually thickened, sometimes considerably so, from chronic phlebosclerosis, a condition analogous to arteriosclerosis, which Borrmann considers may be responsible for thrombosis. The wall of the vein sometimes contains calcareous plates, a further stage of chronic phlebosclerosis. In other instances the vein wall is swollen from recent inflammation. If the patient lives for a long time after the onset of thrombosis the portal vein may be reduced to a mere cord of fibrous tissue. In such cases a collateral circulation develops (p. 209), and a plexus of veins may take the place of the portal vein. Dilated veins in the lesser omentum may convey blood to the liver —a hepatopetal collateral circulation (Pick[2]). It is possible that in some cases thickening and calcification of the walls of the portal vein are results of thrombosis with partial canalisation and organisation of the blood-clot.

[1] Taylor, F. *Trans. Path. Soc.*, 1881, xxxii, 61.
[2] Pick, L. *Virchows Arch.*, 1909, cxcvii, 490.

The character of the clot varies according to its age: it may be quite recent and not very firmly adherent to the vein wall, or it may be granular, decolorised, or even laminated. In some instances the lumen of the vein is not obliterated, the clot being only parietal. As has already been mentioned, the thrombosis may be parietal in one part of the portal vein and completely obstruct the lumen in another, or the central part of the clot may be canalised. When the central part of the thrombus softens down, the condition approaches, if it does not merge into, suppurative pylephlebitis. The thrombus may obstruct, without spreading into, the orifice of one of the tributaries of the portal vein; this is not uncommon at the junction of the splenic vein with the trunk of the portal vein.

The *liver* may present conditions that have caused or favoured the occurrence of thrombosis in the portal vein, such as portal cirrhosis, nodular cirrhosis, primary or secondary malignant disease, or abscess. The liver may shew changes secondary to portal thrombosis. Thus, the hepatic artery may be enlarged in order to compensate for obstruction to the advent of blood to the liver by means of the portal vein. Thrombosis of the portal vein may be associated with a fatty or necrotic condition of the "hobnails" of a cirrhotic liver, and it may reasonably be believed that portal thrombosis, by cutting off the blood-supply, has brought about this change. It is, however, possible that the converse occurs, and that a softened hobnail may, by discharging into a branch of the portal vein, start thrombosis.

Infarcts, though rare in the liver, are, when present, associated in a fair percentage of the cases with portal thrombosis. They are, however, very far from being a necessary sequence of that condition. Some other factor, such as thrombosis in the intralobular branches of the portal vein, obstruction of the hepatic artery, or toxaemia, is necessary before infarction occurs in portal thrombosis (*vide* p. 106). The softening and necrosis of cirrhotic hobnails in portal thrombosis might be compared with the production of an anaemic infarct in an otherwise healthy liver under similar conditions. In portal thrombosis the infarcts are usually red or haemorrhagic, and in only a few instances anaemic.

Frerichs[1] described local atrophy and depressions, sometimes leading to a lobulated condition of the liver, as a result of obstruction of individual branches of the portal vein. It is possible that in an early stage of these areas of atrophy there was an infarct.

When portal thrombosis has existed for some considerable time the liver may shew very little change, or may merely be fatty.

In a remarkable case recorded by Langdon Brown[2] symptoms of portal obstruction had existed for twenty years, and indeed this diagnosis had been made early in the patient's illness by the late Sir William Jenner. The portal vein was represented by a fibrous cord with a minute lumen. The liver was

[1] Frerichs. *Diseases of the Liver*, ii, 396. Transl. New Sydenham Soc., 1861.
[2] Brown, Langdon. *St. Barth. Hosp. Rep.*, 1901, xxxvii, 64.

described as natural though pale. Similar cases have been recorded by Cruveilhier,[1] Versé,[2] Winternitz.[3] In other instances the liver is small, atrophied, and shews a little replacement fibrosis. In a case regarded as primary thrombosis of the portal vein by Dickinson[4] in a woman aged twenty-one, the liver, though fatty, presented no signs of cirrhosis and weighed only 28 ounces. A similar case was recorded by Peacock.[5] In a case which I examined after death, the liver weighed 46 ounces and appeared atrophied to the naked eye. Microscopically there was no cirrhosis, though the fibrous tissue around the portal areas was very prominent. I have found exactly the same appearances in two other cases.

It has been thought by West[6] and Goodhart[7] that thrombosis of the portal vein may give rise to portal cirrhosis in a previously healthy liver. There is ample evidence that this need not occur; on the other hand, some atrophy of the liver cells with fibrous replacement is not uncommon, and this relative fibrous increase might have been regarded as cirrhosis of slight degree.

Fibrosis of the liver was produced in dogs by Solowieff[8] as a result of gradual thrombosis of the portal vein. This might possibly have been due to some extension of inflammation into the liver along the portal vein, or have been a replacement fibrosis associated with atrophy of the liver cells from diminished blood-supply. Bermant's[9] experimental researches support Solowieff's views as to the production of cirrhosis by portal obstruction; Bainbridge and Leathes[10] found that ligature of a branch of the portal vein in animals produced atrophy of the liver cells and some replacement fibrosis; Cohnheim and Litten[11] came to a diametrically opposite conclusion.

To sum up the late effects of portal thrombosis on the liver, there may be no alteration except slight fatty change; there may be atrophy of the liver with some fibrous replacement, but there is very little evidence that genuine cirrhosis is produced in this way.

Spleen.—Enlargement of the spleen is almost constant when the trunk of the portal vein is completely occluded by a thrombus. Langdon Brown estimates that it is enlarged in 70 per cent of the cases. Enlargement may be reduced by copious ascites or gastro-intestinal haemorrhages, or prevented by firm perisplenic adhesions or chronic capsulitis. In a case under my care of thrombosis of the portal vein in cirrhosis associated with rapid and excessive ascites the spleen weighed 4 ounces only.

On the other hand, there may be no splenic enlargement with a

[1] Cruveilhier. *Atlas d'Anat. pathol.*, livraison xvi, Pl. 6.
[2] Versé. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1910, xlviii, 520.
[3] Winternitz. *Johns Hopkins Hosp. Bull.*, Balt., 1911, xxii, 396.
[4] Dickinson. *Trans. Path. Soc.*, Lond., 1863, xiv, 63.
[5] Peacock. *Ibid.*, 1873, xxiv, 122.
[6] West, S. *Ibid.*, 1888, xxxix, 106.
[7] Goodhart. *Ibid.*, 1889, xl, 134.
[8] Solowieff. *Virchows Arch.*, 1875, lxii, 195.
[9] Bermant (1897). Quoted by Welch, Allbutt's *System*, 1899, vi, 221.
[10] Bainbridge and Leathes. *Bio-chemical Journ.*, Liverpool, 1906, ii, 25.
[11] Cohnheim und Litten. *Virchows Arch.*, 1876, lxvii, 153.

parietal thrombosis of the portal vein or where the mesenteric veins only are obstructed. Very great enlargement of the spleen follows complete thrombosis of the splenic vein; it may weigh 20 or 30 ounces and may shew infarcts,[1] either anaemic or haemorrhagic. In connexion with the association of infarcts and thrombosis of the splenic vein it should be remembered that an infarct due to arterial embolism may induce thrombosis.

Intestines.—When there is extensive thrombosis of the mesenteric veins there may be haemorrhagic infarction going on to gangrene in part of the small intestine, usually in the middle of the jejunum which is more often affected than the rest of the intestine because it is entirely dependent for its blood-supply on the superior mesenteric artery and does not draw any blood from other sources, such as the parietal veins around the duodenum and caecum. From gangrene of the intestine peritonitis may result.

I have seen *secondary ulceration of the stomach* in portal thrombosis. When the portal vein has been obstructed for some time, an extensive collateral circulation develops, and the small veins in the intestines, oesophagus, lesser omentum, and stomach may be considerably dilated. A varicose vein in the stomach may become eroded and give rise to fatal haemorrhage. In a case of portal thrombosis due to phlebosclerosis, in which the liver was not cirrhotic, fatal haematemesis occurred from an ulcerated oesophageal varix (Curtis[2]).

Clinical Picture.—*Onset.*—In the presence of cirrhosis of the liver or intra-abdominal disease there may be nothing to mark the occurrence of portal thrombosis, especially when ascites is already present. In latent cirrhosis or other cases in which the patient has been in good or in fair health, the onset may be sudden and marked by the rapid development of ascites or by profuse haematemesis. In 34 cases analysed by Langdon Brown the onset was gradual in 14 and acute in 20. Probably the onset is acute when the vein is suddenly occluded and gradual when it occurs slowly.

Symptoms and Signs.—The clinical manifestations of portal thrombosis present a certain amount of variation which may roughly be correlated (1) with the situation and extent of the thrombosis in the portal area, and (2) with the rate at which the lumen of the vein becomes obliterated. Thus, if the portal vein alone is involved, the most prominent symptoms are due to obstruction to the passage of blood through the liver, viz. ascites and haematemesis. If the thrombus occludes the proximal end of the splenic vein where it joins the portal vein, enlargement of the spleen and haematemesis may be expected. When thrombosis of the mesenteric veins occurs acutely it gives rise to haemorrhagic infarction of the mesentery and intestines, and is associated with intestinal obstruction, diarrhoea, melaena, and collapse.

Arranged in the order of their frequency and importance, the chief

[1] Rolleston. *Trans. Path. Soc.*, 1892, xliii, 49.
[2] Curtis. *Proc. Roy. Soc. Med.*, Lond., 1909, ii (Path. Sect.), 159.

clinical features of portal thrombosis are: ascites, enlargement of the spleen, gastro-intestinal haemorrhages, abdominal pain, symptoms of intestinal obstruction, diarrhoea, and manifestations of toxaemia resembling those in the last stages of cirrhosis and not unlike uraemia. It will be seen that thrombosis of the portal vein may present the aspect of cirrhosis of the liver, of a gastro-intestinal disorder, or may combine the features of these two groups.

Ascites is the most frequent clinical manifestation. In 61 collected cases it was present in 40, or 65·6 per cent. It may be absent in acute cases which rapidly prove fatal from gastro-intestinal haemorrhage, or when the mesenteric veins are chiefly involved and the symptoms suggest intestinal obstruction. Copious gastro-intestinal haemorrhage or diarrhoea may prevent the development of ascites. In the rare cases in which life has been prolonged for years there may be no ascites, presumably from compensation brought about by a free collateral anastomosis. Stress was laid by Frerichs on the rapid development of ascites and on its reaccumulating directly after paracentesis as an important diagnostic sign of portal thrombosis, but this is not of much value, as the same phenomena may occur in cirrhosis and occasionally in ascites due to other causes.

Enlargement of the Spleen.—The spleen is very frequently found enlarged after death, but is not palpable in all these cases during life. Since most statistics refer to the size of the spleen as determined after death, a much lower estimate than 70 per cent, the percentage arrived at by Langdon Brown by adding his 41 cases to Frerichs' and to 25 collected by Crofton-Atkins, must be made of the existence of a palpable spleen *intra vitam*. The enlargement may be masked by ascitic or tympanitic distension, and may diminish after copious gastro-intestinal haemorrhage. Very considerable enlargement should suggest the possibility of haematemesis or melaena due to a thrombus obstructing either the splenic vein or its junction with the portal vein. In chronic cases the splenic enlargement may closely imitate chronic splenic anaemia, especially when the splenic vein is thrombosed.

Gastro-intestinal symptoms are somewhat variable and are related to thrombosis involving the trunks or orifices of the gastric and mesenteric veins, rather than to thrombosis of the trunk of the portal vein. Gastro-intestinal haemorrhage was noted in 27 out of 61 collected cases, or in 44·2 per cent. Haematemesis and intestinal haemorrhage may be due to venous oozing or to definite ulceration from necrosis of the mucosa induced by thrombosis of the gastric or mesenteric veins. When the mesenteric veins are thrombosed, haemorrhagic infarction may occur and give rise to paralysis of the bowel with haemorrhagic effusion into its lumen. Gastro-intestinal haemorrhage may be the initial symptom; this was so in 7 out of 20 cases of acute onset collected by Langdon Brown. Haematemesis and melaena may be frequently repeated and rapidly prove fatal. On the other hand, in cases that survive for a number of years haemorrhages may recur from time to time during

the course of the disease in spite of a very considerable collateral circulation.

Diarrhoea.—Frerichs found that diarrhoea was present in 25 out of 28 cases, but in Langdon Brown's 41 cases it was noted in 11 only. The motions are watery and may be mixed with blood. There may be a somewhat sudden onset of acute intestinal symptoms, due to haemorrhagic infarction and paralysis of part of the small intestine.

Dilatation of the Superficial Abdominal Veins.—Enlargement of the subcutaneous veins around the umbilicus, resembling that in ordinary cirrhosis, is noted in less than one-third of the cases of portal thrombosis. It has been thought that its rapid appearance points to portal thrombosis, but no weight can be laid on this, or indeed on the presence or absence of dilated veins around the umbilicus.

Jaundice may be due to the cause responsible for the portal thrombosis; but it does not depend on portal thrombosis, and usually does not occur in uncomplicated cases.

In 41 cases it was present in 13 (Langdon Brown). It may be due to malignant disease, *e.g.* carcinoma of the head of the pancreas, compressing or obstructing both the portal vein and the bile-duct. In only one of Langdon Brown's cases was it thought that the thrombosed vein pressed on the common bile-duct.

The *urine* is diminished in amount. This may be explained as due to the lowered blood-pressure, since experimental ligature of the portal vein is followed by a great fall in arterial pressure. Other causes are loss of blood, diarrhoea, and diminished absorption of fluid. The urine is high coloured and lithatic. Alimentary glycosuria has been thought to be constantly present, and its absence to be good evidence that a suspected case is not one of portal thrombosis. Sugar, if absorbed from the intestinal tract, must pass by collateral channels straight into the general circulation, since it cannot reach the liver by the portal vein. The absorption from the intestines is greatly obstructed, and it is very doubtful if this test is of much value (see p. 234).

It was certainly absent one day before death in a patient with simple portal thrombosis, probably secondary to thrombosis of the hepatic veins; I have never observed it.

In a case of cirrhosis with thrombosis of the portal vein, Boinet[1] observed paralysis of the legs; he also produced paralysis of the hind limbs in animals by aseptic ligature of the portal vein.

In some cases the symptoms are those of toxaemia resembling uraemia, and probably due to hepatic insufficiency. The symptoms are therefore the same as in the terminal stage of portal cirrhosis.

I have seen widespread cutaneous and visceral haemorrhages in portal thrombosis.

Experimentally complete ligature of the portal vein at its entrance to the

[1] Boinet. Quoted by Gorget, *Rev. de méd.*, 1897, xvii, 539.

liver causes death (Bolton [1]); toxic symptoms, such as paraplegia, low temperature, and drowsiness, develop; there is also a marked fall of arterial blood-pressure which may be associated with the great engorgement of the portal system. Castaigne and Bender[2] refer death in experimental ligature of the portal vein to this factor and not to toxaemia. Incomplete obstruction of the lumen may be followed by survival, and if so there is ascites (Bolton).

Diagnosis is very difficult, and a correct opinion is therefore seldom reached during life. The sudden onset of ascites or of haematemesis and their recurrence, accompanied by considerable splenic enlargement, might suggest it. But since these manifestations are much the same as those of *cirrhosis*, with which portal thrombosis is so often associated, it is difficult to differentiate between portal thrombosis and cirrhosis. Cirrhosis is so common, whereas portal thrombosis is so comparatively rare, that in any given case the probabilities are in favour of cirrhosis, even though the onset of symptoms is sudden and severe. The sudden onset of ascites in a case of cirrhosis under my care suggested pylethrombosis, but the cause was *tuberculous peritonitis*.

In some cases of *gastric ulcer* profuse gastro-intestinal haemorrhage with collapse may suggest portal thrombosis. Difficulty is likely to occur only when the gastric ulcer is acute and occurs in an adult male or in a woman who has never had any signs of gastric ulcer and is considerably past the age at which it is commonly seen.

Very profuse haematemesis and melaena in a soldier, aged thirty-five years, coming on suddenly at Pretoria and accompanied by a low temperature, led me to an erroneous diagnosis of portal thrombosis; at the necropsy there was acute "diphtheritic" dysentery with an ulcer of similar nature in the stomach.[3]

In *splenic anaemia* the spleen is very considerably enlarged, there is anaemia of the chlorotic type, with a diminished number of leucocytes, and recurrent gastro-intestinal haemorrhages may occur. The disease is essentially chronic, whereas thrombosis of the portal vein is usually rapid. But in some instances of portal thrombosis, especially when the splenic vein is occluded, the spleen is greatly enlarged, and there may be periodic gastro-intestinal haemorrhages for many years, with fairly good health in the intervals.

Thus, Langdon Brown [4] quoted the case of a woman who had had haematemesis at intervals of ten months for twenty years, and in whom the portal and splenic veins were found occluded. Cases have also been recorded by Dévé,[5] and some have thought that this is the real basis of many cases of chronic splenic anaemia.

Prognosis.—The diagnosis being so beset with difficulties the practical application of prognosis is very limited, but there is no doubt that the

[1] Bolton, C. *Proc. Roy. Soc.*, London, Ser. B, 1907, lxxix, 267.
[2] Castaigne et Bender. *Arch. de méd. expér.*, Par., 1899, ii, 551.
[3] *The Imperial Yeomanry Hospitals in South Africa*, 1902, iii, 193 (Medical and Surgical Reports).
[4] Brown, Langdon. *St. Barth. Hosp. Rep.*, 1901, xxxvii, 155.
[5] Dévé. *Semaine méd.*, Par., 1908, xxviii, 212.

prognosis is infinitely better than in pylephlebitis. It is probable that if the process of portal thrombosis is gradual, so that a compensatory circulation can to some extent be developed before the obstruction becomes absolute, the patient has a much better chance of surviving.

If recovery from the acute symptoms occurs, the patient may live many years, even though the main trunk of the portal vein is obstructed. Thus, Langdon Brown, Osler,[1] Lyons,[2] Rogers,[3] and others have recorded cases in which life was prolonged for many years. In these cases the development of a collateral circulation to some extent compensates for the portal obstruction. There is, however, usually only a partial return to health, as from time to time haematemesis recurs and relieves the engorgement, whilst a very profuse gastro-intestinal haemorrhage or a succession of haemorrhages may prove fatal. It is also possible that thrombosis may occur in the vessels forming the compensatory circulation.

Treatment.—Haematemesis and ascites should be treated on the ordinary lines as in cirrhosis. When portal thrombosis is suspected, the coagulation time and the calcium content of the blood should be determined by A. E. Wright's[4] method, and if the coagulability of the blood and the amount of calcium salts are both found to be increased, citric acid in 30-grain doses may be given three times a day in order to prevent the process of thrombosis extending. The rationale of giving citric acid is to "decalcify" the blood and so reduce its coagulability. It is important that the blood should be tested before giving citric acid, since in some cases of cirrhosis, which is the morbid lesion most frequently associated with portal thrombosis, the alkalinity and coagulating power of the blood are diminished, and no good, and possibly harm, would result from citric acid. In syphilitic subjects iodides and mercury should be given on the chance that there may be a gumma pressing on the portal vein or syphilitic changes in the walls of the vein.

The operation of promoting vascular adhesions around the liver would theoretically be an ideal form of treatment for portal thrombosis, but there would probably be practical difficulties in performing it. Haemorrhage would be likely to occur from the engorged vessels, and there is the further danger that an extension of the thrombotic process might be induced by the necessary manipulation. This operation was performed in one case, but without benefit (Langdon Brown). In recurrent haematemesis thought to be due to portal and splenic thrombosis splenectomy has been suggested (Curtis[5]).

[1] Osler, W. *Journ. Anat. and Physiol.*, 1882, xvi, 208.
[2] Lyons. *Dubl. Journ. Med. Sc.*, 1877, lxiv, 457.
[3] Rogers, B. M. H. *Bristol Med.-Chir. Journ.*, 1899, xvii, 107.
[4] Wright, A. E., and Knapp, H. H. *Lancet*, 1902, ii ; *Med.-Chir. Trans.*, 1903, lxxxvi, 1.
[5] Curtis. *Proc. Roy. Soc. Med.*, Lond., 1909, ii (Path. Sect.), 159.

SUPPURATIVE PYLEPHLEBITIS

Synonyms: Portal Pyaemia, Porto-pyaemic Liver Abscess (Davidson).

SUPPURATIVE inflammation may involve the portal vein together with some of its tributaries and the terminal branches in the liver; thus, in appendicitis there may be continuous suppurative pylephlebitis involving the superior mesenteric vein and the trunk and the intrahepatic branches of the portal vein. Usually it is less extensive and may be limited to the extrahepatic or to the intrahepatic branches. When the branches inside the liver are alone affected, the resulting condition is practically the same as multiple abscesses due to infective embolism of the branches of the portal vein; the only difference is one of degree, viz. more continuous purulent inflammation of the intrahepatic branches of the portal vein in intrahepatic pylephlebitis, while in multiple abscess the branches of the portal vein may be healthy for most of their extent. Since the clinical features of multiple hepatic abscesses due to intestinal infection are much the same as those of pylephlebitis, the description of the latter will cover that of multiple hepatic abscesses. Suppurative pylephlebitis is not common; it is less often seen than multiple liver abscesses due to infective emboli conveyed by the portal vein.

The infrequency of pylephlebitis is shewn by the following statistics. In twenty years 11 cases only were met with at Guy's Hospital (Bryant [1]); and in thirty-three years only 12 were found at St. Bartholomew's Hospital out of 9494 necropsies, or in 0·12 per cent (Langdon Brown [2]).

Etiology.—Suppurative infection of the portal vein is generally secondary to gastro-intestinal lesions, such as ulceration and suppuration.

Thus, in 64 cases of pylephlebitis tabulated by Langdon Brown, 45, or 70·3 per cent, were associated with gastro-intestinal lesions; of the remaining 19, no cause at all was forthcoming in 7; 4 were due to gall-stones; 2 were associated with empyema; and 6 with other forms of intra-abdominal suppuration.

As might naturally be expected from analogy, infection of the portal vein is most readily produced by a collection of pus confined under considerable tension. Thus, a localised abscess in connexion with appendicitis is a relatively frequent cause of suppurative pylephlebitis, while diffuse inflammation of the peritoneum, though it may be a result, is not by itself a causal factor. In some cases pylephlebitis may be secondary to suppuration in the substance of the liver, for example, in single or "tropical" abscess. Suppuration in the gall-bladder and bile-ducts may also cause infective pylephlebitis. A septic wound of the main trunk of the portal vein is hardly likely to cause pylephlebitis, as rapid

[1] Bryant, J. H. *Guy's Hosp. Rep.*, 1900, liv, 77.
[2] Brown, Langdon. *St. Barth. Hosp. Rep.*, 1901, xxxvii, 95.

death from haemorrhage would probably follow. But an exploring syringe might infect some of the intrahepatic branches of the portal vein and so set up pylephlebitis. In a few carefully examined cases no inlet for the infection is found in the area of the portal vein.

In a case of suppurative pylephlebitis in which the primary disease was an empyema rupturing into the lung, Bryant could find no lesion of the alimentary canal, but he considered as possible explanations either that pyogenetic cocci in swallowed pus were absorbed from the stomach and thus reached the portal vein, or that exploratory punctures had passed through the empyema into the liver and thus directly infected it.

Possibly in some of the cases in which no definite source of inlet is found in the intestinal tract the cause may have been pyorrhoea alveolaris and the associated swallowing of pus and micro-organisms. The pyogenetic micro-organisms could pass through microscopic lesions in the stomach into the portal vein.

Appendicitis is the most frequent cause of suppurative pylephlebitis and multiple liver abscesses. This association has been emphasised by the term "appendicular liver" (Dieulafoy [1]). In 64 cases of suppurative pylephlebitis collected by Langdon Brown, the appendix was the source of infection in 27, or 42·2 per cent. But appendicitis is luckily only followed by suppurative pylephlebitis in about 0·5 per cent of the cases.

In 257 cases of perforative appendicitis Fitz [2] found suppurative pylephlebitis in 11 cases, and in 1189 cases of appendicitis operated upon in the Mount Sinai Hospital, New York, there were only 9 cases, or 0·75 per cent (Gerster [3]), whilst in 2714 clinical cases of appendicitis collected from various London hospitals [4] there were 10 cases of suppurative pylephlebitis, or ·4 per cent. In 86 fatal cases of appendicitis collected by Kelly and Hurdon [5] there were 10 cases of pylephlebitis and liver abscess; this high percentage may be due to such cases being published on account of this rare complication.

Infection of the portal vein is more likely to occur when an abscess has formed around the appendix and the pus is under pressure. Pylephlebitis may supervene very rapidly, so that it is well established by the time the appendicular abscess is opened.

In 1908 a man aged 22 was taken ill on June 25, an appendicular abscess was opened on July 4, but the temperature (*vide* Fig. 12) remained raised and he died on July 25 with pylephlebitis.

Sometimes the morbid process in the appendix has begun to subside when the body of a patient with pylephlebitis is examined. Pylephlebitis may occur after the appendix has been removed, infection of the mesenteric veins having already taken place.

[1] Dieulafoy. *Clinique médicale de l'Hôtel-Dieu*, 1898, ii, 167; *Manuel de pathologie interne*, 1901, ii, 785.

[2] Fitz. *Trans. Assoc. Am. Phys.*, 1886, i, 110.

[3] Gerster. *Med. Rec.*, N.Y., 1903, lxiii, 1005.

[4] Statistics of Hawkins, Lett, Lockwood, Jones, and Clogg and Fairbank. *Med.-Chir. Trans.*, Lond., 1905, lxxxviii, 517.

[5] Kelly and Hurdon. *The Vermiform Appendix*, 1905, p. 225.

In a boy under the care of Mr. Pendlebury,[1] in St. George's Hospital, the appendix was removed on May 16 and the temperature remained normal until June 13, 1904, when it rose and a rigor occurred. The temperature continued raised until death, on July 8. There was extensive suppurative pylephlebitis.

Impaction of a pin in the vermiform appendix is rare, but when it does occur there is a great likelihood of intrahepatic suppuration; in 8 out of Mitchell's[2] 33 cases of impacted pins in the appendix there was some form of intrahepatic suppuration, in most instances multiple or pylephlebitic abscesses.

Gastric ulcer is very rarely the starting-point of suppurative pylephlebitis. Cases have been recorded by Carrington,[3] Bristowe,[4] Hart,[5] West,[6] Hawkins and Nitch[7] (3 cases), and others.

In several of the cases pylephlebitis was associated with, and probably the result of, localised suppuration set up by the gastric ulcer. Hart's case was complicated by a left pyopneumothorax. In Carrington's case a gastric ulcer had eroded the substance of the liver and set up local suppuration.

Gastric Carcinoma.—Suppurative pylephlebitis very seldom follows cancer of the stomach; it is even rarer than in simple ulcer. It may in rare instances be due to infection from a sloughing carcinoma. Legg[8] reported a case in carcinoma of the pylorus.

Disease of the Oesophagus hardly ever gives rise to pylephlebitis. Edwards[9] records suppurative pylephlebitis secondary to carcinoma 3 inches from the cardiac orifice.

Duodenal ulcer is a most exceptional cause of suppurative pylephlebitis; Warfvinge[10] and Bryant[11] have reported cases.

Intestinal Ulceration.—The two common forms of ulceration of the small intestine, typhoid and tuberculous, very seldom set up pylephlebitis. Possibly this is accounted for by the open condition of the ulcers, which allow free drainage and discharge into the bowel. When the inflammatory process is more circumscribed in the walls of the bowel, the radicles of the portal vein are in greater danger of infection. It is even rarer then than solitary hepatic abscess after typhoid fever.

Keen[12] refers to 5 cases only of pylephlebitis, Osler[13] has seen one case only, and no case has occurred either at St. Bartholomew's or Guy's Hospitals (Langdon Brown[14]) after typhoid fever.

---

1 Pendlebury. *Lancet*, 1904, ii, 1712.
2 Mitchell. *Johns Hopkins Hosp. Bull.*, 1899, x, 35.
3 Carrington. *Guy's Hosp. Rep.*, 1882, xli, 375.
4 Bristowe, J. S. *Trans. Path. Soc.*, 1858, ix, 279.
5 Hart, S. *Med. and Surg. Rep. Presbyterian Hosp.*, 1900, p. 150.
6 West, S. *Trans. Path. Soc.*, 1890, xli, 146.
7 Hawkins and Nitch, *Med.-Chir. Trans.*, 1907, xc, 339.
8 Legg, W. *St. Barth. Hosp. Rep.*, 1874, x, 239; *Trans. Path. Soc.*, 1874, xxv, 123.
9 Edwards. *Brit. Med. Journ.*, 1910, i, 199.
10 Warfvinge. *Schmidt's Jahrb.*, 1882, cxcv, 130.
11 Bryant. *Guy's Hosp. Rep.*, 1900, liv, 77.
12 Keen, W. W. *Surgical Complications and Sequels of Typhoid Fever*, 1898, p. 247.
13 Osler, W. "Studies in Typhoid Fever," *Johns Hopkins Hosp. Rep.*, No. 3, p. 381.
14 Brown, Langdon. *Brit. Med. Journ.*, 1905, ii, 1393.

Dysentery very seldom gives rise to suppurative pylephlebitis. Bryant records one case. Infective emboli, however, may cause multiple hepatic abscess both in amoebic and in bacillary dysentery.

Penetration of the mesenteric veins by infecting foreign bodies is extremely rare; though a closely allied condition, pins perforating the vermiform appendix, is a less infrequent antecedent of suppurative pylephlebitis.

Lambron [1] published a case in which a fish-bone passed from the stomach into the superior mesenteric vein and set up pylephlebitis. Winge [2] recorded another instance, and Carlson [3] a case in which a fish-bone was supposed to have been carried from the vermiform appendix into the left lobe of the liver where it set up pylephlebitis.

S. Phillips [4] has described suppuration in the spleen and pylephlebitis due to bristles in the inferior mesenteric vein.

The following *pelvic conditions* occasionally give rise to suppurative pylephlebitis: operations on the rectum for piles, fissure, and stricture; carcinomatous and other forms of rectal ulceration; suppuration in connexion with the female genital organs, such as suppurating ovarian cysts, pyosalpinx (De Silva,[5] Bryant).

Suppuration of the umbilical vein in the newly born may extend into the liver and give rise to pylephlebitis (*vide* p. 571). Cantlie [6] states that this condition is extremely common in Hong-Kong.

Suppurative and gangrenous pancreatitis may be associated with suppurative pylephlebitis. Étienne [7] has insisted on the spread of inflammation from the pancreas to the portal vein and the production of suppurative pylephlebitis.

A man aged forty was in St. George's Hospital under the care of Mr. Turner, in 1899, with whom I often saw the patient. On admission there was a fluctuating abscess in the epigastrium which was at once opened, and found to come from the region of the pancreas. The patient improved for a time, but fever and rigors occurred; empyema on the left side and slight jaundice followed. At the necropsy the pancreas was gangrenous, there was pylephlebitis, and pus was found in the intrahepatic branches of the portal vein.

It may, however, be very difficult to decide whether the suppuration in the pancreas is the cause or the result of pylephlebitis. When there is some other available cause for pylephlebitis, such as appendicitis, suppuration in the pancreas must be regarded as secondary.

Suppurating Mesenteric Glands, Suppuration between the Layers of the Mesentery, etc.—Frerichs [8] describes cases, but the glandular affection

[1] Lambron. *Arch. gén. de méd.*, Par., 1842, xiv, 129.
[2] Winge. *Schmidt's Jahrb.*, 1882, cxcv, 131.
[3] Carlson. *Hygiea*, 1907, 2. f., vii, 822.
[4] Phillips, S. *Trans. Clin. Soc.*, Lond., 1895, xxviii, 222.
[5] De Silva. *Ceylon Med. Journ.*, July 1890.
[6] Cantlie, J. *Encyclopaedia Medica*, 1901, vii, 41.
[7] Étienne. *Arch. de méd. expér. et d'anat. path.*, 1898, x, 177.
[8] Frerichs. *Diseases of the Liver*, New Sydenham Soc., 1861, ii, 421.

may, at least in some instances, have been secondary to the suppurative pylephlebitis. In other cases the suppuration in the portal vein and in the mesenteric glands may be both concomitant results of some intestinal or appendicular ulcer that has been overlooked or has healed. J. W. Ogle[1] reported pylephlebitis secondary to suppuration in a collection of hydatid cysts connected with the omenta.

Abscess of the Spleen.—Cases have been recorded by Frerichs,[2] Law,[3] and Langdon Brown. It is probable that in some instances the splenic abscess is in reality secondary to pylephlebitis and not the primary cause. It seems more probable that perisplenic or subdiaphragmatic abscess on the left side may be a primary source of infection for pylephlebitis, as the pus is then under some pressure. It is possible that infective endocarditis by embolism of the branches of the splenic artery may lead to sloughing infarcts of the organ, and so to suppurative thrombosis of the splenic vein and pylephlebitis.

Suppuration in the Liver.—As a result of infection spreading from a solitary abscess or from a suppurating hydatid cyst secondary pylephlebitis may be set up. A suppurating hydatid is, however, much more often the cause of suppurative inflammation of the bile-ducts than of the portal vein, but may give rise to both. Suppurative cholangitis is frequently complicated by an extension of the inflammatory process to the intrahepatic branches of the portal vein, and it is highly probable that the infection may spread by the lymphatics. In most cases in which suppurative pylephlebitis complicates suppurative cholangitis it is evidently secondary and not nearly so widespread. But this tendency to pylephlebitis in suppurative cholangitis makes the latter disease even more formidable.

Gall-stones.—The usual mechanism by which cholelithiasis sets up multiple liver abscesses is by suppurative cholangitis; the multiple abscesses are then in connexion with the bile-ducts. Gall-stones in the ducts may, however, induce pylephlebitis, either by direct spread of inflammation from the ducts to the walls of the veins or through the lymphatic or blood-vessels. In rare cases a fistulous passage between a suppurating bile-duct and the portal vein, or one of its branches, may be the method by which gall-stones in the ducts may set up pylephlebitis; in exceptional instances the gall-stone may pass into the portal vein. It is often stated that three calculi were found in the portal vein of Ignatius Loyola, but this historically interesting case has been disputed by Thudichum[4] and Galliard,[5] the former asserting that they were phleboliths.

The lymphatics may become inflamed in cases of cholangitis, and in this way suppuration may extend along the portal spaces. The suppuration

[1] Ogle, J. W. *St. George's Hosp. Rep.*, 1867, ii, 347.
[2] Frerichs. *Diseases of the Liver*, 1861, ii, 418, New Sydenham Soc.
[3] Law. *Dublin Quart. Journ.*, 1851, xi, 237.
[4] Thudichum. *A Treatise on Gall-stones*, p. 11, 1863.
[5] Galliard. *Méd. mod.*, Paris, 1895, vi, 113.

may then extend to the portal vein, and the pylephlebitis may supervene on cholangitis. This sequence of events probably occurred in a man aged forty-four whose case was described by Strangeways Pigg and myself.[1] In this case there was no evidence of gall-stones; but if it occurs in non-calculous cholangitis, it may presumably occur also in the calculous form. The infection may pass from the ducts by the small veins of the bile-ducts, which open into the branches of the portal vein. Bright[2] recorded a case of calculous cholangitis in which pylephlebitis was probably produced in this way. An abscess due to cholecystitis may erode the portal vein, discharge into it, and set up pylephlebitis and multiple suppurating foci in the liver (Bristowe[3]).

In some instances it is very difficult to make out how cholelithiasis gives rise to suppurative pylephlebitis. A calculus may give rise to cholangitis and infection may spread to the portal vein and so set up pylephlebitis, but the calculus in the meanwhile may be passed and the cholangitis may disappear.

The following case illustrates the difficulties that may arise: a man aged fifty-one was admitted to St. George's Hospital with a history of recent gall-stone colic; he was apparently going on fairly well until he was suddenly seized with abdominal pain and collapse. I saw him when *in extremis* and thought that probably perforation of an abdominal viscus had taken place. At the necropsy there was no perforation of the viscera or peritonitis, but there was suppurative pylephlebitis without any definite cause. The larger bile-ducts were carefully examined and no ulceration or calculi were found in them; the gall-bladder contained two calculi.

Sex.—The condition is commoner in males than in females, probably in accordance with the greater frequency of appendicitis in the male sex. In 76 cases, 52 were males and 24 females.

Age.—The disease usually occurs earlier in life than portal thrombosis; this may be correlated with the fact that it is most frequently secondary to appendicitis. When it occurs later in life it may be due to gall-stones or to malignant or other forms of ulceration of the colon.

In 60 cases the average age was 30 years; being the same in the 40 males and the 20 females. Langdon Brown found that half the cases occur between the ages of twenty and twenty-nine.

Morbid Anatomy.—The portal vein or its branches contain pus and broken-down blood-clot; sometimes there is merely pus, in other instances there is much blood-clot and but little pus, the infection and softening of the thrombus being only in an early stage. The vein walls are swollen, acutely inflamed, and from the resulting softening the vessels dilate, there are endo-, meso-, and periphlebitis; the walls may thus melt away in the suppurative process. As a result of the inflammation of the wall

[1] Rolleston and Strangeways Pigg. *Journ. Path. and Bacteriol.*, 1898, v, 221.
[2] Bright, R. *Guy's Hosp. Rep.*, 1836, i, 632.
[3] Bristowe, J. S. *Trans. Path. Soc.*, 1858, ix, 285.

of the vein, blood-clot forms and becomes adherent to the intima. The clot softens down and a mixture of pus, clot, and blood results. This sanious pus may be of a reddish tint, but from changes in the haemoglobin to something like haematin, the pus frequently has a dirty brown colour. The suppuration may extend through the walls of the vein and lead to an abscess outside the vein; and the mesentery may thus contain an elongated abscess many times larger than the superior mesenteric vein. Thus, in some cases of pylephlebitis there is an abscess behind the pancreas.

As a very rare accident in pylephlebitis Hodenpyl's [1] case may be referred to. A young man aged twenty-five died from rupture of the portal vein, the abdominal cavity being filled with pus. The pylephlebitis was due to streptococcic infection.

The extent of the vein affected may vary very greatly; a localised part of the portal vein or one of its branches may be found full of pus and shut off from the remainder of the vein by a partition of firm clot. Thus, when the trunk of the portal vein is suppurating the splenic vein is sometimes cut off from the infective process by a firm clot at its junction with the portal vein. Occasionally there are two foci of suppuration, one near the periphery, the other in the intrahepatic branches of the portal vein, while the intervening parts of the vein are healthy. In such cases the intrahepatic focus is due to emboli derived from the other focus of suppuration.

The *liver* is nearly always involved, either by an extension to it of the suppurative inflammation of the portal vein, or by secondary abscesses due to emboli from the portal vein. In very rare cases, of which I have examined one, the liver may be free from all signs of acute inflammation; in this case, however, suppurative inflammation had only recently supervened on thrombosis of the vein.

The liver is nearly always enlarged and may be double its natural weight. There is usually perihepatitis due to extension of inflammation to the capsule, which commonly leads to adhesions to the diaphragm. The surface of the organ is generally smooth, but abscesses may project somewhat from the surface and, if seen during an operation, may suggest multiple new-growth. Over these abscesses there may be a thin layer of recent lymph. The liver has a mottled appearance; the abscesses, or the areas where suppuration is about to take place, are of a palish-yellow colour. Before abscess formation occurs, coagulation necrosis of the liver cells may render parts of the liver firm and like nodules of secondary carcinoma. On section multitudes of small abscesses, varying in size from a millet-seed to a walnut, may be seen, due to the transverse section of the suppurating portal canals. By following the course of the portal canals the suppuration can be seen to spread out from the portal fissure into the liver like the branches of a tree. There is often dark-green staining of the portal canals from decomposition. One lobe, or only a

[1] Hodenpyl. *Med. Rec.*, N.Y., 1898, liv, 133.

limited part of a lobe, or again the whole liver, may shew abscesses. The left lobe escapes more often than the right. From the coalescence of a number of originally separate abscesses a large (areolar) abscess may be formed. In other instances the abscesses are so close to each other that a honeycombed condition of part of a lobe results.

The abscesses due to pylephlebitis may resemble at first sight some cases of suppurative cholangitis with abscesses in the liver. A careful examination of the bile-ducts and portal vein and their branches inside the liver should therefore always be made in any case of doubt. Similarly any difficulty in differentiating between tuberculous abscesses in connexion with the bile-ducts and pylephlebitis can, if necessary, be settled by microscopic examination. Multiple pyaemic abscesses, due to emboli conveyed by the hepatic artery, are small and hardly ever resemble pylephlebitis. The condition of multiple abscesses, due to embolism of the portal vein from some focus in its tributaries, only differs from pylephlebitis in the absence of phlebitis of the portal vein; in other respects the two conditions are practically identical.

Leakage or rupture of the small abscesses on the surface of the liver will set up peritonitis, either general or local, such as a subphrenic abscess. When the diaphragm is previously adherent to the liver, extension of infection may set up pleurisy, empyema, or suppuration in the lower lobe of the lung, usually on the right side. Abscesses on the under surface of the liver may give rise to perihepatic or subhepatic collections of pus.

Histology.—Microscopically the portal vein is filled with fibrin and leucocytes, its walls are infiltrated with small round cells, and may be destroyed. In the liver the portal spaces are similarly affected and small-celled infiltration extends between the lobules and around the intralobular branches of the vein. The liver cells at the periphery of the lobules are compressed and become elongated and look somewhat like oval connective-tissue cells; the small-celled infiltration spreads between the liver cells, which undergo degenerative changes. Micro-organisms are seen in the vessels and between the cells.

Bacteriology.—Streptococci, staphylococci, diplococci, and *Bacillus coli* in pure culture have been met with. In dysenteric cases the *Entamoeba histolytica* and other micro-organisms, and in cases after typhoid fever the *Bacillus typhosus*, have been found. Foulerton [1] has described streptotrichial pylephlebitis. Mixed infections are not uncommon.

In Norris's [2] case two anaerobic micro-organisms, a streptococcus resembling the *Micrococcus foetidus* and a new bacillus, were regarded as the cause of suppuration.

The Spleen.—There is usually some enlargement, which may be explained as due to the general infective or toxic condition. In cases in which the splenic vein is occupied by suppurating clot or in which the junction of that vein with the trunk of the portal vein is excluded, the spleen may

[1] Foulerton. *System of Medicine* (Allbutt and Rolleston), 1906, ii, part i, 312.
[2] Norris. *Journ. Med. Res.*, 1901–5, vi, 97.

be very large from venous obstruction. Abscesses are sometimes found in the spleen, and may either be part of suppurative pylephlebitis or its starting-point.

Peritonitis is common; according to Bryant, it occurs in 50 per cent of the cases. It may be due to rupture of the pylephlebitic abscesses on the surface of the liver; it may be general or localised, as a subphrenic abscess usually on the right side. Peritonitis is also frequent around the primary lesion, such as appendicitis.

The pancreas is usually healthy; occasionally it contains abscesses, probably as a result of suppurative phlebitis of the splenic vein spreading into its pancreatic tributaries. An abscess behind the pancreas and around the portal vein sometimes results from suppurative pylephlebitis. An abscess due to suppurative pancreatitis may cause suppurative inflammation of the portal vein.

Pleura.—The right pleura is seldom healthy; there may be recent pleurisy, with or without a serous or purulent effusion. Inflammation readily spreads through the diaphragm from the liver. Rupture of a pyaemic abscess in the lung may set up an empyema or even a pyopneumothorax.

Lungs.—The right lung may shew collapse and hypostatic congestion of the base; abscesses with surrounding pneumonic consolidation may be due to direct extension through the diaphragm, or in rare instances to general pyaemia, some pylephlebitic abscesses having discharged into the hepatic veins.

Pylephlebitis with multiple small abscesses in the liver may give rise to general haemic infection and secondary abscesses in other organs. According to Langdon Brown, this occurs in 40 per cent of the cases.

In a case of pylephlebitis due to appendicitis, there were numerous small abscesses in the brain (Norman Moore [1]), and in Cassirer's [2] case the symptoms were those of a cerebral lesion, the cause—a fish-bone in the appendix—being only found at the necropsy.

Clinical Picture.—The *onset* of symptoms is more often sudden than gradual. In 42 cases analysed by Langdon Brown the onset was acute in 27, gradual in 15. It may be ushered in by rigors, but usually abdominal pain is the earliest symptom. The initial symptoms may be those of the disease—most often appendicitis—causing the pylephlebitis. Thus, pain, vomiting, and abdominal distension may be the first indications that anything is amiss. In a characteristic case there should be, first, evidence of the primary cause, such as appendicitis; secondly, the development of a septicaemic state; and, thirdly, evidence that the liver is involved (Taylor [3]).

Course.—After the onset the patient passes into a state resembling pyaemia; rigors may be present at first, but usually disappear later. After a time evidence of hepatic disease, such as pain, enlargement, and

[1] Norman Moore. *Trans. Path. Soc.*, Lond., 1882, xxxiii, 186.
[2] Cassirer. *Med. Press and Circ.*, 1901, cxxiii, 466.
[3] Taylor, F. *Guy's Hosp. Rep.*, 1902, lvi, 109.

tenderness, is forthcoming in the majority of cases; and signs suggesting empyema, pneumonia of the right lung, or peritonitis may appear. Gradually increasing weakness, often passing into coma, precedes death.

Duration.—There is considerable variation in the duration of the disease. The average of the cases collected by Langdon Brown[1] was forty-seven days, the shortest being three days. In an exceptional case of Goodhart's,[2] in which partial recovery occurred, the duration was two hundred and ninety-six days.

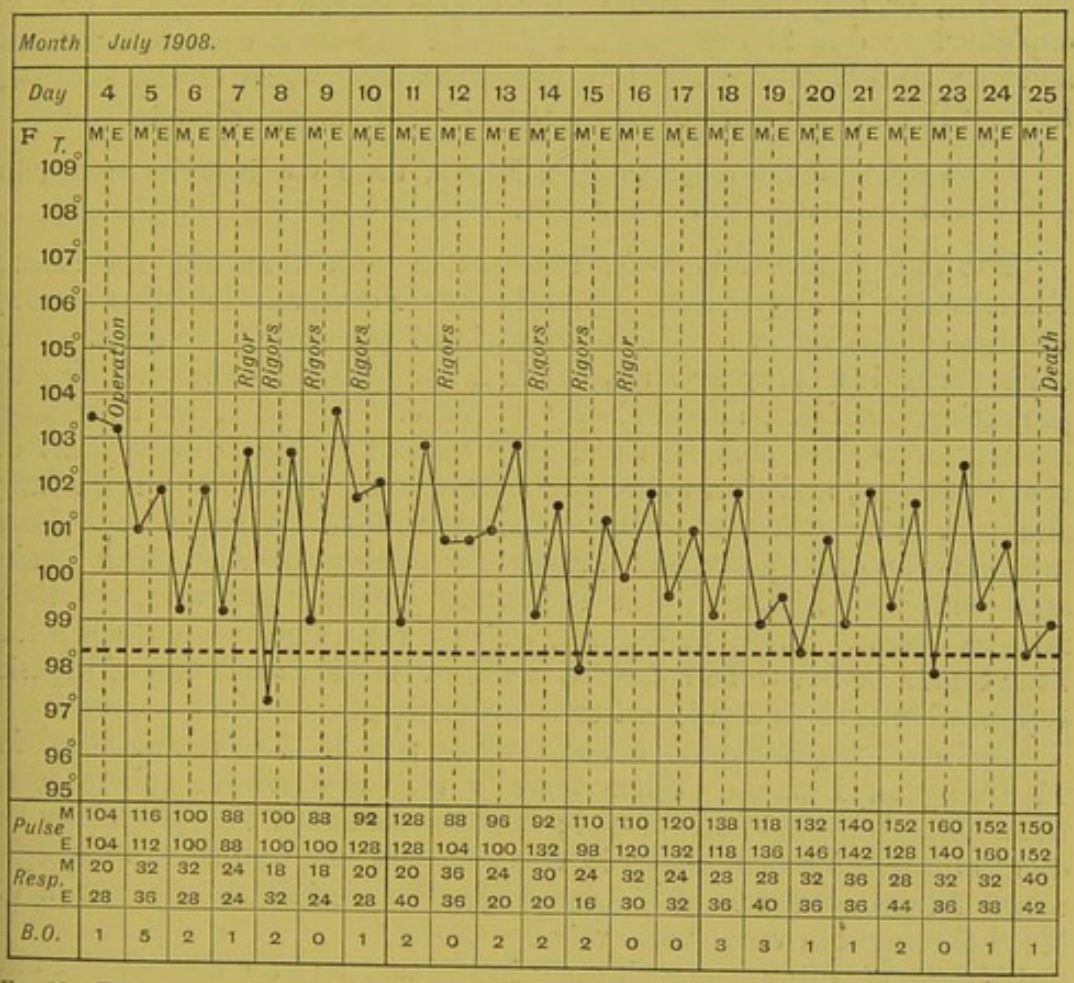


FIG. 12.—Temperature chart of man, aged 22, who was attacked with appendicitis on June 25, had a retrocaecal abscess opened on July 4, and died with pylephlebitis on July 25.

Signs.—The patient has an abdominal facies, looks sallow, ill, and anxious, and has a raised temperature. The type of fever varies very widely; it may be continuous, intermittent, or remittent, and towards the close, subnormal. The pulse is soft, compressible, and rapid (100 to 140). The respirations are quickened. When the disease has lasted some time wasting and prostration appear. Signs of portal obstruction, which are the rule in pylethrombosis, are exceptional in suppurative pylephlebitis.

[1] Brown, Langdon. *St. Barth. Hosp. Rep.*, 1901, xxxvii, 128.
[2] Goodhart. *Trans. Path. Soc.*, Lond., 1882, xxxii, 137.

Rigors are seen in a majority of the cases.

In 42 cases Langdon Brown found them in 29, or 69 per cent; in Bryant's series they were present in half the cases.

The rigors occur during the earlier part of the illness and tend to disappear in the later stages. They are followed by profuse sweating, and are uncontrolled by quinine.

Jaundice occurs in less than half the cases and is often quite slight, transient, or only noted late in the course of the disease, and can be explained as due to the general toxaemia. In some cases it is marked and may be due to cholangitis, concomitant obstruction of the bile-duct by calculi, or to pressure of an abscess on the common bile-duct.

In 44 cases, tabulated by Langdon Brown, there was jaundice in 19; in 4 of these it was very slight or transient, while in 5 it was an initial sign.

The *liver* can be felt to be enlarged in more than half the cases; Frerichs says in 75 per cent, Bryant in 60 per cent, and Langdon Brown, who collected a larger number of cases, in 57 per cent of the cases. The enlargement is usually uniform, but in a few instances elevations, due to projecting abscesses, are distinctly palpable. The enlarged liver may reach down to the umbilicus and may lead to upward displacement of the diaphragm, and thus to collapse of the lower lobe of the right lung and even to displacement of the apex of the heart. A friction rub from inflammation of its peritoneal surface may be heard over the liver. Pain and tenderness in the hepatic region are generally met with, but they may be absent. Local tenderness, which is sometimes present when the liver cannot be felt to be enlarged, is more valuable as evidence of hepatic suppuration than pain referred to the right hypochondrium.

Enlargement of the spleen is not common; in 53 cases it was noted in 11 (Langdon Brown). When there is very considerable enlargement, haematemesis should be expected; because the size of the spleen may be due to obstruction of the splenic vein, which would also lead to engorgement of the cardiac end of the stomach by interfering with the return of blood through the vasa brevia veins.

Vomiting is often met with early in the course of the disease. It was present in 24 out of 42 cases collected by Langdon Brown, being an initial symptom in 11. It is not so much a sign of pylephlebitis as of the disease, such as appendicitis, responsible for it.

In rare instances a *gastric ulcer* may be secondary to pylephlebitis and even go on to perforation.

In a man aged fifty-four examined by me in 1897, with suppurative pylephlebitis secondary to appendicitis, there was perforative peritonitis due to rupture of a gastric ulcer, which, in its turn, was evidently due to thrombosis of a gastric vein.

Diarrhoea occurs in about half the cases. Blood is occasionally seen in the stools. *Constipation* is rarely noticed. *Hiccup* may be troublesome.

Tympanitic distension of the abdomen may occur from peritonitis and will obscure enlargement of the liver and spleen.

Ascites is rare. It was met with in 6 out of 53 cases (Langdon Brown [1]). It is more likely to occur in cases that last a considerable time, and when suppuration supervenes on thrombosis of the portal vein. Although clinically ascites is seldom seen, there may be a small amount of ascitic effusion, due to local acute peritonitis over the abscesses in the liver.

Thoracic Signs.—A friction rub may be audible over the right side of the chest from extension of inflammation through the diaphragm to the pleura. The pressure exerted by the enlarged liver may cause bulging of the chest wall and collapse of the lung, imitating pleurisy with effusion. In some cases there may actually be a purulent effusion into the pleura or the lung may contain abscesses. Such cases may be diagnosed as empyema or septic pneumonia.

Blood.—There is some secondary anaemia, especially in prolonged cases. Leucocytosis, which would naturally be expected, was present in 3 out of 4 cases referred to by Langdon Brown; and in 4 cases, associated with appendicitis, French [2] found marked leucocytosis (24,000) in one and in the others counts of 18,000, 12,000, and 10,500. In 15 cases, investigated by Libman,[3] blood-cultures were sterile in 14; in one accompanied by calculous cholangitis the blood contained pneumococci.

Urine.—Albuminuria is sometimes found and is due to toxic absorption. When there is jaundice bile-pigment will be found in the urine. Indicanuria may be present, and excessive urobilin has been observed (Goodfellow [4]).

Termination.—Towards the end the patient passes into a condition of stupor. Death may occur from peritonitis, from coma and increasing weakness, suddenly, or in rare instances from collapse after haematemesis or melaena.

Diagnosis.—A septicaemic or pyaemic state with evidence that the liver is affected, in a patient who has had appendicitis or some other intra-abdominal condition known to cause pylephlebitis, forms the broad outline of the disease. Enlargement and tenderness of the liver, with pain, fever, and a pyaemic state, not due to any other cause, should suggest suppurative pylephlebitis. Pyaemia from bone and ear disease and infective endocarditis must be excluded. But a diagnosis is not always possible, and since hepatic enlargement is absent or is not detected in a certain proportion of cases of pylephlebitis, there may be nothing to direct attention to the liver. The difficulty of diagnosis is shewn by the fact that in 20 cases examined after death in Guy's Hospital a correct diagnosis during life was only arrived at in two instances during life (Bryant [5]).

[1] Brown, Langdon. *Brit. Med. Journ.*, 1905, ii, 1393.
[2] French, H. S. *Med.-Chir. Trans.*, 1904, lxxxvii, 485.
[3] Libman. *Am. Journ. Med. Sc.*, Phila., 1908, cxxxvi, 548.
[4] Goodfellow. *Med. Chron.*, 1903, xxxvii, 288.
[5] Bryant, J. H. *Guy's Hosp. Rep.*, 1900, liv, 77.

Differential Diagnosis.—In *tropical abscess* there is not such rapid emaciation and prostration as in pylephlebitis, fluctuation may be felt, a history of past dysentery rather than of appendicitis should be forthcoming, and the spleen is not enlarged, as it may be in pylephlebitis. In many cases it is impossible to be certain whether there is a single abscess deeply situated in the liver or pylephlebitis with multiple hepatic abscesses. As mentioned above, the history of pre-existing dysentery is generally in favour of a single abscess, but it must be remembered that dysentery may be followed by multiple abscesses in the liver like those of pylephlebitis; this was the case in the dysentery seen in the South African War of 1899–1902 (*vide* p. 118).

In *hepatic suppuration* secondary to appendicitis multiple foci of suppuration are the rule, but in exceptional instances a large areolar abscess, probably due to the union of originally independent abscesses, results. In a given case with hepatic enlargement, fever, rigors, and pain, the diagnosis between multiple abscesses, pylephlebitis, and a single abscess is very difficult, and probably the patient should be given the benefit of the doubt and abdominal exploration be undertaken. Oedema of the chest wall or definite fluctuation justifies a diagnosis of a large and probably single abscess.

In *suppurative cholangitis* jaundice is commoner, appears earlier, and is more prominent than in pylephlebitis. Splenic enlargement may occur in both, but is more likely to be marked in pylephlebitis. A history of cholelithiasis and biliary colic is in favour of suppurative cholangitis. There may, however, be very slight or no jaundice in suppurative cholangitis and no history of gall-stones, and the diagnosis from pylephlebitis may be impossible, as in case recorded on p. 675.

Syphilitic disease of the liver with fever (*vide* p. 364) may closely simulate suppurative pylephlebitis (Edwards[1]).

Subphrenic abscess may be due to rupture of a pylephlebitic abscess, and may be opened or drained, and the underlying condition be unsuspected unless the liver is much enlarged. In cases of pylephlebitis supervening after appendicitis, but without any manifest hepatic enlargement, there may be a very close resemblance to subphrenic abscess in the right kidney pouch.

Enteric Fever.—In enteric fever the agglutination (Widal's) reaction with typhoid bacilli should be present, while rigors and jaundice, though not unknown, are decidedly rare. A positive agglutination reaction may occur in pylephlebitis when the patient has had enteric fever some time previously.

In a woman aged twenty-eight, who died of pylephlebitis under Dr. F. Taylor's[2] care, there was a positive agglutination reaction with typhoid bacilli although she had not had enteric fever.

Pylephlebitis may closely resemble enteric fever, especially when there

[1] Edwards. *Amer. Journ. Med. Sc.*, Phila., 1910, cxl, 527.
[2] Taylor, F. *Guy's Hosp. Rep.*, 1902, lvi, 109.

is blood in the stools. Bryant lays stress on the difference between the pulse, temperature, and respiration rates; the pulse rate is low (80) in enteric, high (140) in pylephlebitis.

In *infective endocarditis* murmurs are occasionally absent and the aspect of the case is one of pyaemia of obscure origin; in such cases, when accompanied by enlargement of the liver and spleen, the resemblance to pylephlebitis may be considerable. In such cases the discovery of micro-organisms in the blood by means of blood-cultures points to infective endocarditis. A negative result is in favour of pylephlebitis (Libman).

In chronic cases of *malarial infection* the enlarged and sometimes very tender liver and the raised temperature associated with shivering and sweating may lead to considerable difficulty in diagnosis. Malaria should be recognised by the presence of the parasite in the blood and improvement under quinine; further, the patient's condition is not so grave as in pylephlebitis.

Intra-thoracic conditions, such as pleural effusion, empyema, pulmonary abscess or pneumonia, may be diagnosed as the sole condition, from physical signs depending on the spread of inflammation from the liver in pylephlebitis.

Malignant disease of the liver may imitate pylephlebitis when fever and rigors accompany rapid increase of the malignant growth. A case of secondary endothelioma of the liver resembling pylephlebitis is described on p. 522.

In *acute cirrhosis* the enlarged and tender liver and the presence of fever may imitate pylephlebitis (Carrington [1]).

Prognosis.—Since diagnosis is difficult, more cases are recognised on the post-mortem table than during life, and grave doubt must exist as to the nature of cases regarded as suppurative pylephlebitis which have recovered without laparotomy and examination of the liver. It is in the highest degree improbable that widespread suppuration of the portal vein would be followed by recovery, and the general consensus of opinion is that the disease is uniformly fatal. Conceivably this verdict may require some modification in the light of more frequent observations of the state of the liver as seen in the course of exploratory laparotomies. In isolated cases recovery has occurred in which multiple abscesses were thought to exist, but some question must arise if suppurative inflammation of the portal vein was present.

Quénu and Mathieu [2] collected 13 cases of recovery after operation on liver abscesses due to appendicitis; Treves [3] and West [4] recorded two similar cases. Cases presenting appearances at the necropsies of healed suppurative pylephlebitis have been recorded by Goodhart [5] and Moschcowitz.[6]

[1] Carrington. *Guy's Hosp. Rep.*, 1883–4, xlii, 337.
[2] Quénu et Mathieu. *Rev. de chir.*, Par., 1911, xliv, 519.
[3] Treves. Allbutt's *System*, 1897, iii, 927; *Lancet*, 1894, i, 662.
[4] West, S. *Trans. Clin. Soc.*, 1884, xvii, 126.
[5] Goodhart. *Trans. Path. Soc.*, 1882, xxxii, 137.
[6] Moschcowitz. *Ann. Surg.*, 1911, liii, 551.

When the disease is recognised, **treatment** is usually confined to relieving pain and other symptoms. Langdon Brown and Gerster [1] employed antistreptococcic serum without any good results. A trial of such a serum or vaccine should be made on the chance that the infection of the portal vein is a pure streptococcic one, but in most cases there is a mixed infection. Treatment with polyvalent serums, viz. from animals immune against various strains of micro-organisms of the same and of different species (streptococci, *Bacillus coli*), should be employed. Since it is difficult or impossible to be sure that symptoms of pyaemia with hepatic enlargement after appendicitis are not due to a single abscess, operative interference gives the patient a chance of recovery. Further, it is possible that success might follow the opening and draining of several abscesses. When operation is undertaken, the liver should be freely exposed. Aspiration through the abdominal wall is not only fallacious, but dangerous.

Prophylactic treatment is most important, and consists in the early and radical removal of conditions, such as appendicitis, likely to induce suppurative pylephlebitis. During such operations removal of any suppurating veins in the immediate neighbourhood is an important step in preventing the spread of infection from the intestinal branches to the trunk of the portal vein. This was carried out in two cases of appendicitis which recovered (Gerster). It is also important not to disturb the parts unnecessarily, so as to avoid detaching a thrombus and producing embolism of the intrahepatic branches of the portal vein.

OTHER AFFECTIONS OF THE PORTAL VEIN

Embolism ; Endophlebitis ; Calcification ; Parasites ; Angioma.

Embolism of the intrahepatic branches of the portal vein is frequent in suppurative inflammation of the intestinal tributaries of the portal vein and accounts for multiple abscesses in the liver after appendicitis, etc. In most cases the emboli are small and do not themselves attract attention. Similarly embolism plays an important part in the production of secondary growths in the liver in carcinoma of the stomach and intestine. Sometimes large embolic masses of clot may be found in the main intrahepatic branches of the portal vein.

In 17 cases of infarcts in the liver Chiari [2] found that 15 were due to embolism of the portal vein, the emboli being derived from thrombosis in its peripheral tributaries, such as the haemorrhoidal, gastric, splenic and mesenteric veins.

[1] Gerster. *Med. Rec.*, N.Y., 1903, lxiii, 1005.
[2] Chiari. *Ztschr. f. Heilk.*, 1898, xix, 475.

Endophlebitis.—Acute inflammation of the portal vein is practically the same as pylephlebitis. *Chronic endophlebitis* of the portal vein is not uncommonly associated with hepatic cirrhosis, and may be explained as the result of increased blood-pressure in the vein, combined perhaps with degenerative and hyperplastic changes due to the action of toxic bodies. There is a certain amount of chronic endophlebitis of the portal vein in long-standing backward pressure from tricuspid regurgitation, in mitral disease, and in obstructive pulmonary diseases, such as emphysema. According to Borrmann,[1] syphilitic disease of the liver may extend into the portal vein and set up endophlebitis of its walls. But in a certain number of cases the endophlebitis is primary and the liver merely shews a secondary atrophy. The cause of the chronic inflammatory change in the vein is somewhat obscure, and has been referred to various factors. Inflammation may also spread into the vein walls from chronic peritonitis. In splenic anaemia endothelial hyperplasia may spread from the blood sinuses in the spleen into the splenic and portal veins; the terminal cirrhosis of the liver in splenic anaemia (Banti's disease) has been thus explained. Chronic endophlebitis may lead to calcification and to thrombosis; the latter result is of practical importance.

Calcification is a sequel of long-standing endophlebitis and is analogous to secondary calcification in endarteritis. It is probably much commoner than is usually thought; it is not infrequent in chronic splenic anaemia and Banti's disease. I have seen it microscopically in cases in which there was not sufficient infiltration to attract attention in the post-mortem room. It has long been recognised; Frerichs[2] gives references to "ossification" or calcification of the portal vein. The calcareous plates or spicules may project into the lumen of the portal vein and set up thrombosis. But calcification may be very extensive without any trace of thrombosis, and it must not be assumed, as Lancereaux[3] did, that calcification of the wall of the portal vein is merely the result of thrombosis.

A high grade of chronic endophlebitis with calcification of the splenic and portal veins occurred in a man aged fifty-three who died in St. George's Hospital after an operation for hydrocele. The splenic vein was greatly dilated and the splenic artery was very calcareous and had three aneurysms on it. The spleen was much enlarged (42 ounces) and fibrotic. The liver (37 ounces) was scarred, and to the naked eye suggested syphilis, but microscopically it shewed multilobular cirrhosis of old standing and no evidence of syphilis. The colon shewed extensive ulceration, possibly of vascular origin, but there was no thrombosis in the mesenteric arteries or in any part of the portal vein or its branches.[4]

Parasites in the Portal Vein.—*Schistosomum haematobium*, endemic in Egypt, Natal, Mauritius, and Syria, may be found in the trunk of the portal vein or in its haemorrhoidal tributaries, while the walls may

[1] Borrmann. *Deutsches Arch. f. klin. Med.*, 1897, lix, 283.
[2] Frerichs. *Diseases of the Liver*, 1861, ii, 402. Transl. New Sydenham Soc.
[3] Lancereaux. *Traité des maladies du foie et du pancréas*, 1899, p. 571.
[4] Trevor, R. S. *Trans. Path. Soc.*, Lond., 1903, liv, 302.

contain the ova. The liver may shew slight cirrhosis,[1] but there are no symptoms associated with the presence of the worms or their ova in the portal vein. The liver fluke (*Fasciola hepatica*) was described in a case quoted by Budd[2] as being found in the portal vein, but it is conceivable that a dilated bile-duct was mistaken for the vein.

A **haemangioma** may arise in its wall and occlude the portal vein.[3]

MORBID CONDITIONS OF LYMPHATIC VESSELS AND GLANDS

Morbid Conditions of the Lymphatic Vessels.—Comparatively little is known on this subject, and primary affections of the lymphatics of the liver are not recognised. The two main sets of lymphatics, (*a*) those which run along the portal spaces, and (*b*) those which supply the capsule or are superficial, may be separately affected. The lymphatics frequently suffer when the portal spaces are affected by morbid processes such as inflammation and tuberculosis, as shewn by the enlargement of the lymphatic glands in the portal fissure. Inflammation may thus spread from the liver to the pancreas. If from acute inflammation the lymphatics are obstructed, resolution and absorption of inflammatory products in the liver are prevented and cirrhosis may result (Oertel[4]). In chronic perihepatitis the superficial lymphatics are exclusively affected.

Pericholangitis is very closely connected with lymphangitis of the portal spaces. Thus, the glands in the portal fissure are enlarged in hypertrophic biliary cirrhosis, tuberculous cavities in the liver, cholangitis, and pylephlebitis, all of which are inflammatory lesions involving the tissues and the portal canals around the bile-duct and portal vein. In a case of splenic anaemia of the Gaucher type endothelial proliferation in the lymphatic vessels of the portal spaces is figured by Bovaird.[5]

New-growth may sometimes be seen working its way into the liver, against the lymph-stream, along the lymphatics of the portal fissure; more commonly the glands in the portal fissure become infected secondarily to a growth in the liver, the infecting cells travelling in the normal direction along the lymphatic vessels. Distension of the lymphatic vessels in the portal spaces is occasionally due to obstruction; it has also occurred from torsion of the bile-duct in hepatoptosis (*vide* p. 32). In diabetic lipaemia I have seen the lymphatics of the portal spaces graphically mapped out by the contained fat. Maresch[6] described

[1] Symmers. *Journ. Path. and Bacteriol.*, 1904, ix, 237.
[2] Budd. *Diseases of the Liver*, p. 485, 1852, ed. ii.
[3] Pick, L., *Virchows Arch.*, 1909, cxcvii, 490; Emmerich, *Frankfurter Ztschr. f. Path.*, 1912, x, 362.
[4] Oertel, H. *Arch. Int. Med.*, Chicago, 1908, i, 385.
[5] Bovaird. *Am. Journ. Med. Sc.*, Phila., 1900, cxx, 391.
[6] Maresch. *Ztschr. f. Heilk.*, 1903, xxiv, 39.

a pedunculated lymphangioma removed from the right lobe of the liver of a girl aged five years.

The Lymphatic Glands in the Portal Fissure.—Any enlargement of these glands is important inasmuch as pressure may thus be exerted on the bile-ducts and jaundice set up. It has been suggested that the jaundice occasionally seen in the roseolous stage of syphilis may be due to swelling of the glands in the portal fissure. Enlargement of the portal glands may occur in lardaceous disease and leukaemia, but cannot be credited with producing jaundice or ascites by compression of the bile-duct or portal vein.

Enlargement of the portal lymphatic glands may be due to various conditions, chiefly inflammatory, inside the liver, such as abscess, pylephlebitis, suppurative cholangitis, tuberculosis, hypertrophic biliary cirrhosis, and primary carcinoma. As already mentioned, new-growth may extend into the portal fissure along the lymphatic vessels against the flow of lymph, and occasionally infiltration of the portal lymphatic glands may be secondary to carcinoma in the peritoneal cavity, and may give rise to jaundice.

CHRONIC VENOUS ENGORGEMENT OF THE LIVER

Synonyms: Nutmeg Liver, Cardiac Liver, Cyanotic Atrophy, Hepatic Asystole.

THE term red atrophy has been applied to the small nutmeg liver seen in cases of long-standing backward pressure, but unfortunately it may lead to confusion with an entirely different condition, viz. the red atrophy seen in acute (yellow) atrophy. An old and now forgotten name for the condition of the liver was hypertrophy of the white substance.[1] Hanot[2] suggested the term hepatic asystole for those cases in which the hepatic symptoms are more prominent than those of the primary cardiac disease.

Etiology.—Chronic venous engorgement of the liver is practically always secondary to obstructive heart or lung disease. *Cardiac Lesions.*—Mitral obstruction or regurgitation, and some diseases of the myocardium, such as alcoholic dilatation, give rise to backward pressure, tricuspid regurgitation, and chronic hepatic engorgement. Tricuspid stenosis, which is practically always secondary to mitral stenosis, causes a high grade of hepatic engorgement. Mitral stenosis is the most effective cause of chronic venous engorgement of the liver. Acute dilatation of the heart, as in pneumonia or diphtheria, produces an engorged liver.

Lung Lesions.—Obstruction to the passage of blood through the pulmonary artery and its branches in the lungs first causes hypertrophy

[1] Compare Hope. *Principles and Illustrations of Morbid Anatomy*, 1834, p. 102.
[2] Hanot. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1895, xii, 409.

of the right ventricle, but eventually this compensation becomes strained, the right ventricle dilates, and tricuspid incompetence results. This train of events most often follows chronic bronchitis and emphysema, the pneumoconioses, and sometimes chronic interstitial pneumonia. It is remarkable that chronic venous engorgement is not more frequent in ordinary pulmonary tuberculosis. In my experience it is rare in chronic pulmonary tuberculosis, but Gilbert and Weil,[1] in a study of 25 livers, found that in 6 the naked-eye appearances were those of a typical nutmeg liver, and that in 5 more the microscopical appearances were undoubted. Possibly the cases in which it occurs are complicated by alcoholic dilatation of the heart.

Other Factors.—A tumour or aneurysm might press on the small segment of the inferior vena cava between the entrance of the hepatic veins and its termination in the right auricle; but it is extremely rare for an intra-thoracic growth to obstruct the inferior cava. I have seen nodules of secondary growth on the diaphragm in close contact with the inferior cava. A high grade of chronic venous engorgement of the liver is produced by occlusion of the hepatic veins (*vide* p. 48); but in a case of obstruction of the inferior vena cava involving their orifices the liver was cirrhotic rather than nutmeggy (Osler[2]).

Inside the liver the pressure of malignant growths or hydatid cysts may cause areas of chronic venous engorgement. It is possible that marked displacement of the heart in pleural or pericardial effusion, by producing kinking of the inferior vena cava, might lead to venous stasis in the hepatic veins of the liver as well as in the other tributaries of the inferior cava. It has been suggested that pericardial adhesions and chronic mediastinitis may lead to torsion or compression of the inferior vena cava and so to chronic venous engorgement. It has been thought that any pre-existing morbid condition of the liver, such as may result from alcoholism, biliary calculi, or malaria, renders the organ more prone to suffer from the effects of backward pressure in any given case of tricuspid incompetence.

Morbid Anatomy.—Adhesions between the upper surface of the liver and the diaphragm are common. They are the legacies of past attacks of acute perihepatitis which may be due to the spread of inflammation through the diaphragm from acute pleurisy or pericarditis. The upper surface of the right and left lobes often shews a depression corresponding to a hypertrophied and dilated heart; and the peritoneum in this area is often thickened and opaque as the result of increased and long-continued friction. In universal chronic perihepatitis or "iced liver" (*vide* p. 167) there is usually chronic venous engorgement; the stasis is not the cause of the capsular change but is due to cardiac failure, adherent pericardium, or possibly to narrowing of the orifices of the hepatic veins by the thickened capsule.

Size.—After death the liver is sometimes larger than natural, but

[1] Gilbert et Weil. *Arch. de méd. expér. et d'anat. path.*, 1902, xiv, 729.
[2] Osler. *Journ. Anat. and Physiol.*, 1879, xiii, 291.

is smaller than in life. During life the liver is distensible and may vary in size very considerably within short periods as the result of alterations in the amount of backward pressure. After death, and the onset of rigor mortis, coagulation of the protoplasm of the liver cells gives a firmness to the organ which is not present in life.

Sir Lauder Brunton [1] found that if artificial circulation be kept up through the portal vein of an animal just killed, the liver will enlarge and diminish in response to variations in the pressure exerted, almost as if it were a sponge, and much in the same way as it does in cases of pulsating livers.

In the later stages the liver becomes smaller; this is most probably due to atrophy of the liver cells and not to fibrosis. The specific gravity of the liver is increased (Olsho [2]). The liver is of a darkish purple colour externally and is rather firmer than natural. Dilated veins may be seen on the surface, and no doubt their prominence is largely due to atrophy of the surrounding liver tissue. As a rule, the surface shews depressed lines of atrophy, and may thus become slightly uneven, suggesting to the naked eye early cirrhosis. The characteristic mottling is generally not well seen externally. In long-standing ascites, the serous covering of the liver is thickened or opaque.

On section the organ contains an unusual amount of blood and presents the characteristic "nutmeggy" appearance, which depends on the fact that the sublobular and intralobular veins are dilated and appear as dark purple spots or streaks according as they are cut transversely or longitudinally, while the other parts of the lobules, being stained with bile or infiltrated with fat, are paler than natural. This contrast between the dark and the pale areas resembles the section of a nutmeg. In a typical case the centre of the lobule appears as a dark spot; this is surrounded by a whitish-yellow margin due to fatty and slightly bile-stained liver cells. In other cases there is a coarse nutmeg appearance. Some white areas, though to the naked eye resembling fatty change, are nodules of regenerating liver cells without any fatty change or venous engorgement. The hepatic veins are dilated and their walls thicker and more opaque than natural; this phlebosclerosis is accompanied by atrophy and condensation of the hepatic tissue immediately around the vein walls.

Opponet,[3] in a thesis on hepatic asystole, puts forward the view that the incidence of hepatic manifestations in a case of heart disease is determined by a peculiar arrangement of the hepatic veins at their entry into the inferior vena cava; this anatomical disposition he regards as congenital and as fairly common. It seems, however, more natural to regard the size and manner of the openings of the hepatic veins into the inferior vena cava as the results of backward pressure.

In backward pressure in the inferior vena cava the main stress usually

[1] Lauder Brunton in Murchison's *Diseases of the Liver*, p. 134, 3rd ed., 1885.
[2] Olsho. *Arch. Int. Med.*, Chicago, 1909, ii, 171.
[3] Opponet. *Thèse de Paris*, 1895.

falls on the legs; occasionally, however, the renal veins are chiefly involved, as shewn by persistent albuminuria without any corresponding nephritis on histological examination, whilst in cases of hepatic asystole the hepatic veins suffer chiefly.

Occasionally a liver shewing chronic venous engorgement is also distinctly cirrhotic. Thus, a patient with cirrhosis may die with alcoholic dilatation of the heart or with backward pressure from cardiac failure due to other causes. Chronic venous engorgement and cirrhosis are both common and sometimes coincide, but chronic venous engorgement alone does not cause real cirrhosis. This is my firm conviction from an examination of a large number of livers microscopically.

The Question of "Cardiac Cirrhosis."—For a full account of the question whether or not chronic venous engorgement *per se* leads to cirrhosis of the liver the reader should consult Piery's thesis.[1] In 1840 Becquerel[2] stated that chronic venous engorgement was the cause of half the cases of cirrhosis examined by him; his view was supported by Rokitansky,[3] Henle,[4] and others. Possibly, as suggested by Budd, cirrhotic and nutmeg livers were not always differentiated from each other at this time. In 1845 Budd[5] and in 1848 Handfield Jones, who definitely recognised that these two conditions were distinct, stated that chronic venous engorgement did not give rise to cirrhosis.

There has been some discussion as to the situation of the fibrosis in cardiac cirrhosis. Rokitansky and Sabourin[6] described it as centrilobular, whilst English observers—Handfield Jones,[7] Green,[8] and Legg[9]—considered that it was perilobular but not genuine multilobular cirrhosis. Numerous observations prove that chronic venous engorgement of the liver may exist for prolonged periods without producing any fibrosis at all, or only a slight fibrosis, as seen microscopically, which can be satisfactorily accounted for by atrophy of the liver cells and secondary fibrous replacement. The firm appearance of many nutmeg livers often suggests a fibrosis which can only be disproved by microscopic examination. The belief that chronic venous engorgement induces cirrhosis is probably based on naked-eye observation uncorrected by a further microscopic examination. Parmentier[10] experimentally produced chronic venous engorgement of the liver in animals by setting up tricuspid regurgitation, and found that fibrosis did not follow.

In the rather exceptional instances presenting more fibrosis, some

Piery. *Arch. gén. de méd.*, Par., 1900, clxxxvi, 582.
[2] Becquerel. *Ibid.*, 1840, 3. s., vii, 397.
[3] Rokitansky. *Handb. der path. Anat.*, 1842, iii, 347.
[4] Henle. *Ztschr. f. inn. Med.*, 1844.
[5] Budd. *Diseases of the Liver*, 1845, p. 118.
[6] Sabourin. *Rev. de méd.*, 1883, iii, 523.
[7] Handfield Jones. *Med. Gaz.*, 1848, vii, 1033.
[8] Green. *Introduction to Pathology*, 1871, p. 244.
[9] Legg, Wickham. *Med.-Chir. Trans.*, 1875, lviii, 345.
[10] Parmentier. *Études cliniques et anatomo-pathologiques sur la foie cardiaque*, p. 29, Paris, 1890.

other factor, such as prolonged gastro-intestinal catarrh or considerable alcoholic stimulation during the course of chronic valvular disease, may be invoked. In chronic venous engorgement the resistance of the liver is necessarily reduced, and the organ is therefore more likely to be affected by poisons than in health. It would thus be reasonable to expect to find cirrhosis secondary, not to chronic venous engorgement pure and simple, but to factors such as alcoholism, auto-intoxication from intestinal fermentation (dyspeptic or Budd's cirrhosis), or bacterial infection. Piery believes that tuberculosis and acute rheumatism may also be responsible for hepatic cirrhosis in patients with heart disease.

Salaman [1] describes the cirrhotic nutmeg liver as due to repeated attacks of severe cardiac failure which have led to destruction of hepatic cells and subsequent scarring, the ordinary nutmeg liver being due to steady backward pressure. The livers are small, the capsule thickened and irregular, and on section are generally pale and shew a confused "nutmeggy" aspect.

Still, with all these different ways in which cirrhosis may become implanted on a nutmeg liver, the association of well-marked cirrhosis with chronic venous engorgement is infrequent.

Comparison of Chronic Venous Engorgement in the Liver and Lung.—Both these organs have a double blood-supply, the portal vein and the hepatic artery in the one case, and the pulmonary and bronchial arteries in the other. While pulmonary apoplexies are frequent, the structure of the liver does not allow extensive extravasation of blood into the bile-ducts, for haemorrhage into the bile-capillaries and ducts would constitute the exact counterpart of pulmonary apoplexies. Comparatively large areas of haemorrhage into the liver substance occur, however, in chronic venous engorgement. Bonome [2] described haemorrhagic infarcts in nutmeg liver.

Microscopic Appearances.—The conditions vary in different stages of the disease and in different parts of the same liver. The intralobular veins and their capillaries (blood-spaces or sinusoids of Minot) are first dilated. This dilatation is at first limited to the central zone, but in the more advanced stages spreads into the intermediate zone. Eventually large areas composed of blood corpuscles with some fibrin result.

In 35 cases of advanced chronic venous engorgement Hart [3] found capillary thrombosis near the centre of the lobules constantly.

The liver cells are compressed, present varying degrees of distortion, and may undergo necrosis and so leave spaces filled with blood which resemble, but are not, sinusoids; this extreme change is said not to be due to uncomplicated chronic engorgement, but to depend on toxins (Mallory,[4]

[1] Salaman. *Lancet*, 1907, i, 4.
[2] Bonome. *Arch. di biol.*, Firenze, 1899, liii, 319.
[3] Hart. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1904, xxxv, 303.
[4] Mallory. *Journ. Med. Res.*, 1901–5, vi, 264.

Frothingham [1]). Oertel,[2] however, regards it as due to cytolytic ferments derived from the atrophied liver cells. The liver cells contain an iron-free pigment—haematoidin—derived from haemoglobin, which differs from the iron-containing pigment (haemosiderin) deposited in the peripheral zone of the lobule in pernicious anaemia in not striking a blue colour with dilute hydrochloric acid and ferrocyanide of potassium (Perl's test).

The liver cells tend to shew varying degrees of fatty change, and in long-standing cases may contain large globules of fat. This fatty change is not, however, universally met with. It is usually stated that this fatty change is mainly in the peripheral zone of the hepatic lobule; Salaman, however, insists that it is situated in the central zone. The cells near the area of engorgement sometimes shew coagulation-necrosis

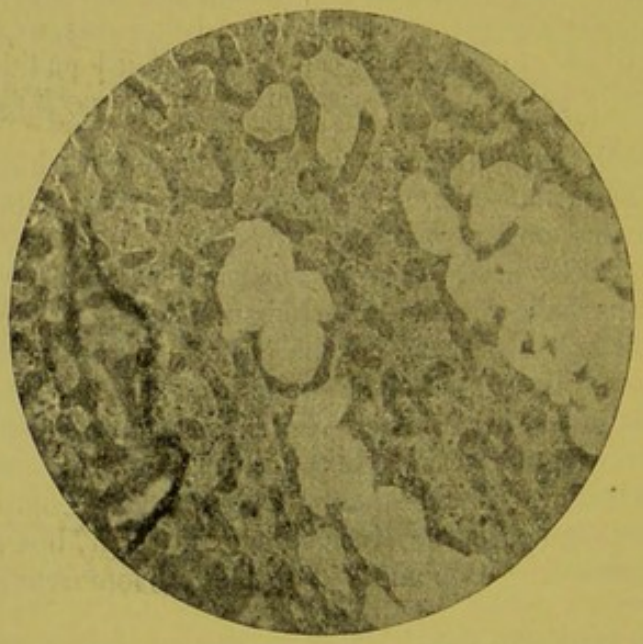


Fig. 13.—Photomicrograph of chronic venous engorgement. Shews extravasated blood and distorted liver cells (Dr. S. G. Penny).

(Opie [3]). In some parts of the liver the central zones may become compressed by compensatory hyperplasia of the persistent peripheral zones of adjacent lobules which may coalesce (Géraudel [4]); the appearances may thus be confusing, as the portal canals appear to be in the centre of the lobules. Compensatory hyperplasia of the liver cells giving rise to the formation of regeneration nodules, which are free from chronic venous engorgement, is common. This process, first described by Letulle [5] and by Jacobi,[6] resembles that seen in nodular cirrhosis.

[1] Frothingham. *Arch. Int. Med.*, Chicago, 1910, v, 1.
[2] Oertel. *Ibid.*, 1910, vi, 293.
[3] Opie. *Trans. Assoc. Amer. Phys.*, 1904, xix, 132.
[4] Géraudel. *Arch. de méd. expér. et d'anat. path.*, 1906, xviii, 514.
[5] Letulle. *Anatomie pathologique*, 1897, i.
[6] Jacobi, A. *Trans. Assoc. Am. Phys.*, 1897, xii, 500.

I have seen two well-marked examples of this condition, which at first sight resembles multiple caseous tubercles.

The fibrous trabeculae contract and become more prominent. This is seen around the portal spaces and the subhepatic and intralobular veins (centrilobular cirrhosis). Its characters are sporadic or irregular distribution and absence of active hyperplasia. It is, therefore, mainly a fibrous replacement and not an active proliferation. As mentioned above, nutmeg livers not infrequently have a naked-eye appearance that suggests cirrhosis, but microscopic examination shews little fibrosis, and that of a sporadic character in no way comparable to cirrhosis. Atrophy of the liver cells and replacement fibrosis are most advanced under the capsule of the liver; macroscopically this subcapsular fibrosis closely resembles chronic perihepatitis. Microscopically, however, the capsule is seen to be unaffected (*vide* Fig. 15).

The morbid anatomy of the other abdominal organs is that seen in the backward pressure of mitral or obstructive lung disease and need not be described in detail. The *spleen* is firm, deeply engorged, but not increased in weight. This is shewn by Kelynack's [1] statistics of the weight of the spleen in 56 cases of nutmeg liver due to cardiac disease and uncomplicated by any infective process, in which the average weight of the spleen was 7·3 ounces, or just about the normal. The *pancreas* may be enlarged from fibrosis and even palpable during life.[2] It may, however, be of normal size.[3]

Clinical Picture.—*Symptoms.*—There is a feeling of tightness, heaviness, and discomfort in the right hypochondrium, which is markedly tender on pressure. It may be noted in passing that the tenderness of an enlarged liver in alcoholic cirrhosis, which is usually explained as being due to active fibrous hyperplasia, may be due to chronic venous engorgement, the result of alcoholic dilatation of the heart. The tenderness may be of three kinds: (i) Superficial, and referred from the distended liver to the 7th to the 10th dorsal skin areas. (ii) Tenderness of the liver itself, which probably depends on the distension and stretching of the capsule of the organ. (iii) Great tenderness accompanied by pain, which is independent of palpation, is due to concomitant perihepatitis and may be accompanied by friction. Mackenzie [4] points out that the tenderness which is usually assumed to be in the liver is often in the abdominal walls, for the area of tenderness is generally more extensive than would correspond to the liver, and the abdominal wall is tender when it is carefully lifted up.

Chronic portal engorgement gives rise to impairment or loss of appetite, dyspepsia, flatulence, tympanites, and favours gastro-intestinal

[1] Kelynack. *Birmingham Med. Rev.*, 1897, xli, 86.
[2] Hale White. *Internat. Clin.*, 1896–97, Series 6, ii, 90.
[3] Lefas. *Arch. gén. de méd.*, 1900, clxxxv, 539.
[4] Mackenzie, J. *The Study of the Pulse*, p. 221, 1902, and *Brit. Med. Journ.*, 1906, i, 1525.

catarrh, constipation, and irregularity of the bowels with perhaps diarrhoea; together they lead to considerable distension of the abdomen. Assimilation is interfered with, and the patients are thin, though this may be somewhat masked by oedema; in children growth is stunted, and there may be very considerable wasting. Haematemesis is usually said to occur, but I have not seen it in uncomplicated cases.

In a case of mitral stenosis[1] with thrombosis of the splenic vein haematemesis occurred, but was evidently due to the extreme venous engorgement of the vasa brevia of the stomach which open into the splenic vein.

Dyspnoea on exertion and in advanced cases orthopnoea, due to the primary cardiac lesion or to concomitant ascites, are common. It is possible that dyspnoea in some instances may be due to hepatic insufficiency, and, like the uraemic form, toxaemic.

Physical Signs.—The skin over the malar bones is much congested and of a high colour. The lips, ears, and skin elsewhere may be cyanosed. The forehead and especially the temples have a slightly icteric tint. The contrast between these two tints of the skin produces a facial aspect which is very characteristic of advanced mitral disease. The slight icteric tinge is probably due to a low grade of catarrhal inflammation of some of the small intrahepatic bile-ducts, but it may be due to oedematous swelling of the mucous membrane of the bile-ducts. Ordinary catarrhal jaundice depending on the spread of gastro-duodenal inflammation to the biliary papilla sometimes supervenes. As a rule the subcutaneous abdominal veins are not dilated, but I have published a drawing of a child shewing considerable enlargement of the veins communicating between the superior and inferior venae cavae.[2]

The *liver* is nearly always enlarged, and can be felt two or three fingers' breadths below the costal arch in the right nipple line. Its size varies with, and is a fair indication of, the condition of the right side of the heart. It diminishes when backward pressure is relieved and is affected in a similar manner by free purgation. The surface of the liver is smooth to the touch and firm. When the engorgement is marked, the liver is tender from distension; the tenderness, like the increased size, is a good index of increased backward pressure. In a small percentage of cases the liver can be felt by the hand to pulsate with each beat of the heart.

In 235 cases of tricuspid regurgitation analysed by Pitt[3] pulsation was present in 15, and in 87 cases of tricuspid stenosis in 8.

With one hand over the liver and the other pressed into the right loin, the liver can be felt to expand and diminish like an accordion. This proves that the pulsation is not a transmitted impulse, but is due to injection of the liver with blood at each beat of the heart. The left lobe pulsates more than the right, as the blood regurgitates into it more readily.

[1] Green, T. H. *Brit. Med. Journ.*, 1899, ii, 1415.
[2] Rolleston. *Trans. Med. Soc. Lond.*, 1909, xxxii, 19.
[3] Pitt, G. N. *System of Medicine* (Allbutt and Rolleston), 1909, vi, 325.

Pulsation may also be communicated to the liver from a hypertrophied and labouring right ventricle, the liver receiving a jog with each beat of the heart, the left lobe being chiefly affected ; in rare instances pulsation is transmitted from an abdominal or even an hepatic aneurysm.

The following are some of J. Mackenzie's [1] conclusions : Pulsation of the liver occurs only in valvular disease, but is very commonly detected by the polygraph, though not by the hands. When once the liver has begun to pulsate, it probably always continues to do so till death. Pulsation of the liver may be synchronous with the systole of the ventricles or of the auricles, and corresponds with the rhythm of venous pulsation in the neck. Pulsation of the liver synchronous with contraction of the auricle is generally associated with tricuspid stenosis and may be confused with pulsation communicated to the liver from a vigorously contracting heart.

If pressure in an upward direction is made on the liver, the jugular veins in the neck may swell up. The incompetency of the valves at the origin of the jugular veins allows the column of blood in the inferior vena cava, right auricle, and superior vena cava to be displaced upwards.

The enlarged liver may push the diaphragm up and by encroaching on the thorax lead to some collapse of the base of the right lung. Dulness, absence of breath-sounds and of vocal vibrations at the right base behind are not uncommon in advanced mitral disease, and may be due to collapse of the lower lobe of the lung or to a pleural effusion.

Chronic venous engorgement of the liver necessitates chronic portal obstruction ; ascites may thus be set up, and if of long duration is associated with some chronic peritonitis. Whether the latter is set up by the ascites or whether the ascites is the result of the chronic peritonitis brought about by chronic portal and peritoneal engorgement is open to discussion. Probably the general opinion is that chronic peritonitis is the primary and important factor. It must be remembered that in the backward pressure of heart disease not only is the venous pressure in the liver increased, but from obstruction to the passage of lymph out of the thoracic duct into the veins the pressure of lymph in the lymphatics is raised. Further, from stagnation the nutrition of the lymphatics and blood-vessels is apt to become impaired. As a result of these factors ascites might occur in the absence of chronic peritonitis. Ascites occurs in more than half the cases of tricuspid regurgitation, but is less frequent than oedema of the feet.

Thus, in 235 cases of tricuspid reflux collected by Pitt, oedema was noted in 200 and ascites in 140 ; oedema and ascites occurred together in 124 cases, oedema alone in 76, ascites alone in only 14, and neither in 21. This tends to support the view that the ascites of nutmeg liver is part of a general oedema.

This form of ascites resembles that of chronic peritonitis in persisting and recurring, and in not being, like the ascites of cirrhosis, a close forerunner of death. The fluid is usually straw-coloured, but it may be

[1] Mackenzie. *A Study of the Pulse*, 1902, p. 220, Edin. and London.

chylous or pseudo-chylous; out of 14 collected cases of milky effusion in heart disease 8 were chylous and 6 were pseudo-chylous (Wallis and Schölberg [1]).

Dry pleurisy may occur or signs of pleural effusion at the right base; these may be explained as the result of pulmonary apoplexy, which is commoner in the lower lobe of the right lung. On the other hand, the upward projection of the enlarged liver may simulate a small effusion.

The *urine* is diminished in amount, and in advanced cases is concentrated, of a high specific gravity, high coloured, and uratic. It contains urobilin and in some instances haematoporphyrin,[2] but unless there is definite jaundice bile-pigment is absent. In some instances there is albuminuria; its occurrence is variable and does not necessarily depend on gross structural change. When backward pressure falls on the renal veins in a marked degree the nutrition of the renal epithelium may be sufficiently impaired to allow of albuminuria. Alimentary glycosuria is quite exceptional and probably depends on concomitant pancreatic change rather than on hepatic insufficiency. The excretion of urea varies with the amount of urine; diminution in its amount has been correlated with hepatic insufficiency. Leucine and tyrosine have exceptionally been found in the urine, but may be transitory (Dixon Mann [3]). Their appearance can be explained either by autolysis of the liver or by failure of the liver to deal with the amino acids absorbed from the alimentary canal. In an advanced case under my care leucine and tyrosine were absent; the examination was kindly made by Dr. Leathes.

There is delay in absorption of liquid from the intestines, and accordingly the amount of urine excreted during digestion, instead of being larger than that excreted during fasting, the normal relationship, is less (Gilbert and Lereboullet [4]). This has been tested by giving meals with eight-hour intervals and collecting the urine every four hours. The term *opsiuria* has been applied to this condition (Lecerf [5]).

Complications.—Well-marked jaundice may be produced by extension of catarrhal gastritis to the duodenum, and so to the biliary papilla and lower end of the common bile-duct. In rare instances jaundice may be a terminal event due to acute infection falling on the liver. In a case under my care in which jaundice appeared three days before death there were enormous masses of streptococci in the sinusoids of the liver [6]; but it is not necessarily infective, for Oertel [7] describes deep jaundice, due to multiple aseptic necrosis of the cells in the centre of the hepatic lobules, as a terminal incident accompanied by stupor, delirium, and coma (*vide* p. 575).

In chronic venous engorgement of the liver there are several factors

[1] Wallis and Schölberg. *Quart. Journ. Med.*, Oxford, 1910–11, iv, 170.
[2] Garrod, A. E. *Lancet*, 1900, ii, 1327.
[3] Dixon Mann. *Quart. Journ. Med.*, Oxford, 1907–8, i, 25.
[4] Gilbert et Lereboullet. *Compt. rend. Soc. Biol.*, Paris, 1901, liii, 276.
[5] Lecerf. *Thèse de Paris*, 1901.
[6] Rolleston. *Trans. Med. Soc. Lond.*, 1909, xxxii, 19.
[7] Oertel. *Arch. Int. Med.*, Chicago, 1910–11, vi, 293.

favouring auto-intoxication. (i) In the liver itself. Owing to malnutrition the antitoxic function of the liver cells is impaired or arrested. Toxic bodies derived from the alimentary canal therefore tend to pass into the general circulation and affect the nervous centres. (ii) Owing to portal stagnation digestion is interfered with and more toxic material is carried to the liver, which is, as has already been said, unable to cope with even the normal amount. (iii) Chronic venous engorgement of the renal veins leads to diminished urinary excretion.

Course.—The course of the disease depends on the condition of the heart, and may, like it, improve periodically only to relapse again. The hepatic enlargement tends to increase during each recurrence, though, as already pointed out, the liver gets somewhat atrophied towards the end of a case. According to Mackenzie, pulsation once it appears remains to the end.

Termination.—Death is commonly due to gradually increasing cardiac failure or to some terminal infection, usually of other parts of the body, such as pneumonia or pleurisy. Infection, however, may attack the liver itself, and thus give rise to icterus gravis. In such cases diarrhoea and vomiting are the early symptoms ; jaundice, haemorrhages, and dry tongue develop, and finally delirium, stupor, and coma precede death. A slighter terminal affection may shew itself by acute perihepatitis.

Diagnosis.—In manifest heart disease there will be no difficulty ; but in the class of cases termed by Hanot hepatic asystole, in which attention is focussed on the liver, the condition may appear to be primarily hepatic and be thought to be cirrhosis, or, when the liver is large and very tender, malignant disease.

The abdominal wall rarely shews the dilated veins seen in many cases of hepatic cirrhosis, and there is no enlargement of the spleen apart from embolism, and the symptoms improve on cardiac tonics. In any case of cirrhosis definite signs of mitral disease should lead to revision of the diagnosis ; but an apical systolic murmur is not infrequent in cirrhosis, though it is seldom persistent. In cases of hepatic asystole the history, the smooth surface of the liver, the comparatively smaller amount of enlargement, and diminution in size following cardiac tonics, together with absence of severe pain and of cachexia, should enable the observer to eliminate malignant disease. Two cases simulating malignant disease have been under my care (*vide* p. 523).

Treatment may be divided into two heads, which, however, overlap to a certain extent. The first and most important is that of the primary heart disease or of the combined lung and heart affections. Digitalis is the most efficacious drug and may be given as the tincture in x. to xx. minim doses four to six times a day, or the fresh infusion in corresponding doses. Digitalin is not so efficacious as the tincture or infusion. The pill containing digitalis, squill, and mercury (Addison's pill at Guy's Hospital, Baillie's pill at St. George's) is often very successful. Digitalis with citrate of caffeine may also be given. Strophanthus, though well adapted for mitral stenosis, and convallaria are not so powerful for good

in tricuspid reflux as digitalis. If there be emphysema and bronchitis, iodide of potassium, carbonate of ammonia, ipecacuanha, may be given in addition. Rest in bed, and if necessary paracentesis of the abdomen or tapping of the legs, are essential parts of the treatment.

In the second place, the engorgement of the liver and its results may be further treated by purgatives, diuretics, and local applications. As purgatives, magnesium sulphate or sodium sulphate should be employed to run off the excess of fluid from the intestinal vessels; mercury in the form of blue pill or calomel is a valuable remedy. Aloes or eau de vie allemande may also be given with advantage. As diuretics the cardiac tonics already mentioned and apocynum may be employed.

The administration of liver substance by the mouth is said[1] to act as a diuretic when the lesion is not too advanced, and to increase the amount of urea and diminish the abnormal constituents, such as urobilin and albumin, present in the urine.

If there be much pain and perihepatitis is present, poultices, hot applications, leeches over the liver, or bleeding may be employed. The diet should be simple, nutritious, and not mainly liquid, as this tends to aggravate the already waterlogged condition of the patient. For sleeplessness morphine is the most satisfactory drug; sulphonal, or preferably trional or veronal, which act more rapidly, chloralamide, or paraldehyde may also be tried, but should not be given constantly; if a sleeping draught is frequently needed, its composition should be changed. Spa treatment at Vichy, Neuenahr, Nauheim, Pougues, etc., may be tried when the patient is sufficiently well to bear the journey.

PERICARDITIC PSEUDO-CIRRHOSIS OF THE LIVER

This condition, which for practical purposes may be regarded as an extreme grade of chronic venous engorgement of the liver in cardiac patients with adherent pericardium, was described by Pick[2] in 1896. The clinical features—recurrent ascites, an enlarged firm liver, absent or slight jaundice, and no oedema of the legs—may suggest cirrhosis, inasmuch as during life adherent pericardium may be latent or overlooked. The liver is in an extreme stage of chronic venous engorgement and shews fibrous hyperplasia. Any peritoneal adhesions or thickening that may be present were regarded by Pick as accidental or secondary either to chronic venous engorgement of the peritoneum or to ascites. The patients are chiefly young subjects with a history of rheumatic endocarditis and pericarditis, and without any of the usual antecedents of hepatic cirrhosis.

[1] Spillmann et Dernang. *Congrès de méd. int.*, Lille, 1899.
[2] Pick. *Ztschr. f. klin. Med.*, 1896, xxix, 385.

This condition merges, on the one hand, into chronic venous engorgement of the liver, with which it is, to my mind, most closely allied ; and, on the other, into cases of universal perihepatitis associated with adherent pericardium (*vide* p. 162). Some few adhesions or slight peritoneal thickenings are comparatively frequent in the cases belonging to the group described by Pick ; when these peritoneal changes are advanced, the condition ceases to be Pick's pseudo-cirrhosis of pericarditic origin and belongs to that of chronic universal perihepatitis associated with adherent pericardium (multiple serositis). Kelly [1] grouped together under the heading of multiple serositis these cases of Pick's pseudo-cirrhosis and the cases of "iced liver," or, as they are usually called in England, "chronic universal perihepatitis." To quote his own words : "Some distinction—anatomically at least—may be drawn between cases in which the lesions are confined to the peritoneum and cases in which lesions are more widespread. The cases in which the pericardium is unaffected reveal no congestive alterations in the liver. Clinically, however, the two classes of cases are very much alike, and the 'Zuckergussleber' may occur in both."

The following case, in which there was some chronic peritonitis, otherwise exactly resembled Pick's pseudo-cirrhosis, but from the presence of peritoneal change it must be regarded as occupying a position midway between pseudo-cirrhosis and chronic peritonitis associated with adherent pericardium (multiple serositis).

A girl aged four was under my care in St. George's Hospital with recurrent ascites, chronic jaundice of slight degree, a large pulsating liver, and pulsating jugular veins more marked on the right side of the neck. The heart was much enlarged, there were systolic and diastolic apical murmurs, and an accentuated pulmonary second sound. At the necropsy the pericardium was universally adherent, the left ventricle was dilated, greatly hypertrophied, and shewed much chronic endocarditis of the musculi papillares. The mitral valve segments were much thickened and the orifice was somewhat dilated. The left auricle was also dilated. The right side of the heart, contrary to what was expected, was not dilated. The heart and pericardium weighed 17 ounces. The hepatic veins were enormously dilated and were each of them as large as the inferior vena cava. The liver was nutmeggy and adherent to the diaphragm. Microscopically the appearances were those in figures 14, 15, namely, sporadic and subcapsular fibrosis and extreme chronic venous engorgement. There were a few adhesions and a few ounces of fluid in each of the pleurae, and general opacity of the peritoneum.

Eisenmenger,[2] who among others disputes the existence of the condition as a distinct morbid entity, believes that in children the vessels of the general systemic circulation have a better tone and are less disposed to allow transudation to occur than in older people, and that the more marked hepatic manifestations are thus accounted for. He further suggests that adhesions in connexion with the adherent pericardium or a concomitant pleural effusion may lead to torsion

[1] Kelly, A. O. J. *Am. Journ. Med. Sc.*, 1903, cxxv, 116.
[2] V. Eisenmenger. *Wien. klin. Wchnschr.*, 1900, xiii, 249.

of the inferior vena cava close to the diaphragm and so set up ascites; and that in other instances local peritonitis in the portal fissure may be the real cause of ascites.

Morbid Anatomy.—The liver is often united to the diaphragm by scattered adhesions. Its general appearance is that of advanced chronic venous engorgement. There is no general chronic peritonitis or universal perihepatitis, but the surface of the liver is usually somewhat irregular, as in ordinary chronic venous engorgement, and often opaque. This opacity is due to fibrosis under the capsule, and on superficial examination resembles chronic perihepatitis, for which it has probably often been taken. On section the liver shews advanced chronic venous engorgement.

The *microscopic appearances* of the liver are those of advanced chronic venous engorgement with very irregularly scattered islands of fibrosis, in which there may be elastic tissue (Carnot and Amet [1]). Much of this apparent fibrosis is due to atrophy of the liver cells, which allows the existing fibrous tissue to come into prominence. There is perhaps a little active fibrous hyperplasia, and, by careful selection, areas resembling multilobular cirrhosis with the addition of chronic venous engorgement can be found. Taken as a whole, however, the amount of fibrosis is scanty, and may be absent in considerable areas. Under the capsule there are extensive atrophy of the liver cells and fibrous replacement. If microscopic examination be limited to a section from this part of the liver, there would appear to be well-marked cirrhosis. But the extent of the fibrous change is confined to a small area under the capsule. It is, however, enough to produce very definite opacity, and, as has already been pointed out, imitates universal chronic perihepatitis. The two conditions are entirely different: in chronic universal perihepatitis (*Zuckergussleber*, "iced liver") the fibrosis is on the outer surface of the capsule. The appearances in subcapsular fibrosis are well shewn in Fig. 15.

Although there is no genuine cirrhosis comparable to portal cirrhosis in cases of ordinary adherent pericardium, well-marked hepatic cirrhosis is found in the majority of cases of calcified adherent pericardium (Diemar,[2] Wells,[3] Mitchell [4]). What relation, if any, exists between calcified pericardium and hepatic cirrhosis is unknown. This condition occurs in adults, while the patients with Pick's pseudo-cirrhosis are usually children. I have examined some of the latter cases, expecting to find an extension of fibrosis from the adherent pericardium along the hepatic veins into the substance of the liver, but have never found any fibrosis, though the inner walls of the hepatic veins and inferior vena cava are opaque and thickened, as is commonly seen in cases of backward pressure. The pericardium is firmly adherent to the heart, and usually to the chest wall as well. These adhesions are usually due to past

[1] Carnot et Amet. *Arch. de méd. expér. et d'anat. path.*, 1906, xviii, 767.
[2] Diemar. *Ztschr. f. Heilk.*, 1899, xx, 257.
[3] Wells, H. G. *Am. Journ. Med. Sc.*, 1902, cxxiii, 259.
[4] Mitchell. *Trans. Chicago Path. Soc.*, 1911, viii, 109.

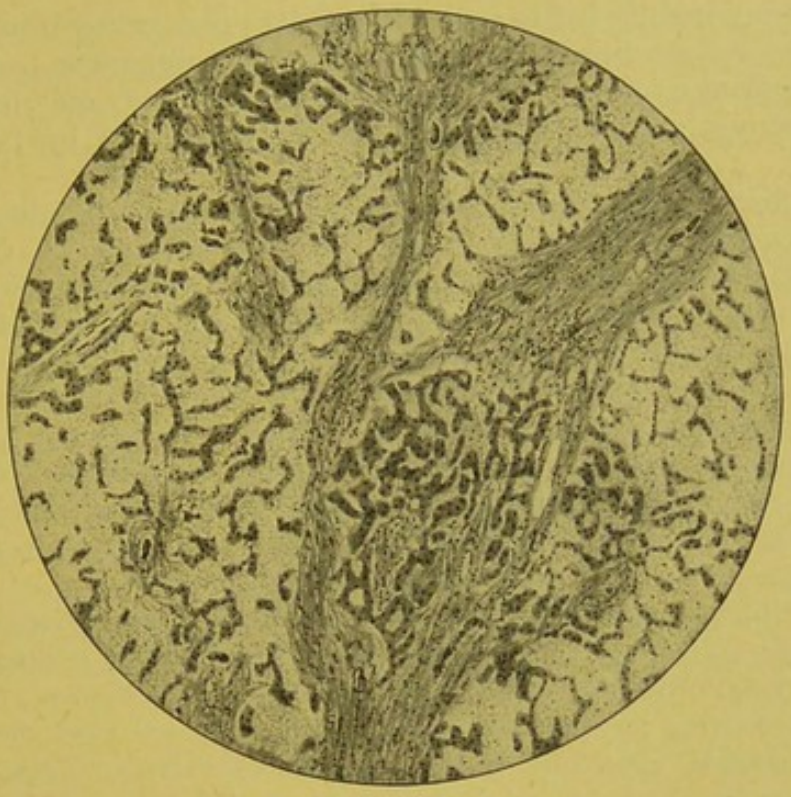


FIG. 14. — Microscopic section from an advanced case of nutmeg liver associated with adherent pericardium (case on p. 97). The liver cells are separated by extravasated blood and compressed and distorted, and there is sporadic fibrosis. This section was specially chosen so as to shew "cardiac fibrosis." × 60.

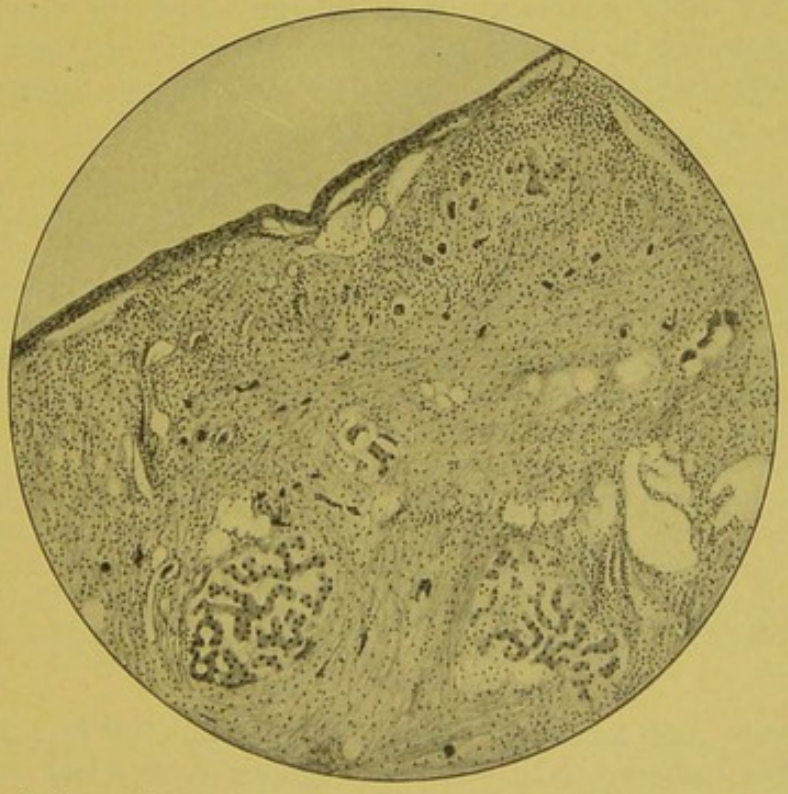


FIG. 15.—Drawing from a microscopic section shewing marked subcapsular fibrosis. The real capsule is seen on the free surface. (From the same case as figure 14.)

rheumatic pericarditis, but in some instances the pericarditis is tuberculous, and under these conditions the liver may also be tuberculous (*vide* p. 101). The tuberculous nature of the adherent pericardium may only be manifest on microscopic examination, as in two cases recorded by Sappington and Rau.[1]

Mechanism of the Morbid Processes.—The pericardial adhesions by contracting lead to dilatation of the right auricle, inferior vena cava, and hepatic veins, and by this means the free regurgitation of blood into the liver is rendered permanent. It is possible that at the time of the primary pericarditis inflammation spreads to the mouths of the hepatic veins, and by weakening their walls leads to dilatation and so to a freer entry of blood into them. When once brought about, this dilatation of the hepatic veins probably becomes permanent. The brunt of backward pressure thus falls on the liver, while the other branches of the inferior vena cava—the renal and iliac veins—suffer less than in ordinary cases of chronic engorgement of cardiac origin.

The **clinical aspect** of the cases has already been referred to, and the absence of oedema of the legs, which may tend to differentiate the condition from ordinary backward pressure of heart disease, mentioned on p. 96. During life the liver may be firm and enlarged, and so may suggest cirrhosis, especially if the presence of valvular disease and an adherent pericardium be overlooked. In most instances the associated cardiac and pericardial disease will be easily detected, and doubt will not arise. It may be necessary to tap the abdomen many times, but the intervals are often prolonged, thus differing from the frequent paracenteses necessary in chronic peritonitis. Jaundice is either absent or slight. The following case illustrates the general features of the condition:

A girl, aged eleven years, was under the care of my colleague, Dr. Penrose, for three years with morbus cordis and ascites, for which tapping had been required about fifteen times. At the necropsy there was mitral and tricuspid incompetence with an adherent pericardium; the liver—3 pounds 6 ounces—was enlarged and shewed some thickening of its capsule with a few adhesions. The hepatic veins were very prominent but there was no fibrosis around them. The surface of the liver was irregular from depressed lines due to atrophy and fibrous increase around the subcapsular veins. On section the liver was nutmeggy and gave the impression of some fibrous increase. Microscopically there was sporadic fibrosis, but no genuine multilobular cirrhosis, the branches of the hepatic veins and intralobular venules were greatly dilated, and the liver cells atrophied. The appearances were those of advanced chronic venous engorgement with more fibrosis than usual. There was no chronic peritonitis; there were old adhesions in the left pleura and recent ones in the right pleura.

Prognosis and Results.—When the condition of hepatic pseudo-cirrhosis has become established the prognosis is very bad, though life

[1] Sappington and Rau. *Arch. Pediat.*, N.Y., 1906, xxiii, 814.

may be prolonged for a considerable time. Tuberculous peritonitis may supervene as a secondary result; this was proved to be the sequence of events in a case recorded by Nachod,[1] in which laparotomy a year before death proved the absence of tuberculosis at that time. Secondary tuberculous infiltration of the portal spaces may occur. The term cardio-tuberculous cirrhosis has been applied to advanced chronic venous engorgement of the liver complicated in this way by tuberculous infection.[2] These cases, which are chiefly met with in children, are associated with tuberculous adherent pericardium and more advanced tuberculous disease elsewhere, especially in the peritoneum and pleura.

These conditions of "hepatic pseudo-cirrhosis" and cardio-tuberculous cirrhosis are closely allied both to nutmeg liver and to the cases of general perihepatitis secondary to adherent pericardium. Clinically the chief difference from nutmeg liver is the absence of any signs of cardiac valvular disease. The proper treatment, however, is that of chronic venous engorgement of the liver, viz. cardiac tonics and diuretics. The treatment suitable for cirrhosis is of no use in these conditions.

INFARCTS

CONTRARY to what might be supposed from the double blood-supply of the liver, from the hepatic artery and portal vein, and their free communication, appearances resembling infarcts in other organs occur in the liver.

There may be (i) true infarcts with necrosis of the liver cells; these are usually anaemic, but in rare instances, as in Versé's and Winternitz's[3] cases, haemorrhagic; or (ii) pseudo-infarcts or sub-infarcts (Adami) in which there is no necrosis of the liver cells. These are much less rare than true infarcts. They are usually haemorrhagic, and are really localised areas of venous engorgement; but in some instances there are anaemic areas without necrosis of the liver cells. To the naked eye true infarcts and pseudo-infarcts resemble each other; the distinction between them is the presence or absence of necrosis of the liver cells. The important factor in causing a true infarct appears to be obstruction or thrombosis of the intralobular branches of the portal vein.

Infarcts and pseudo-infarcts in the liver may be either haemorrhagic or anaemic. The haemorrhagic form is more frequent.

[1] Nachod. *Prag. med. Wchnschr.*, 1898, xxiii, 330.

[2] *Vide* Moizard et Phulpin, *Arch. de méd. des infants*, 1899; Cousin, *Gaz. hebd. de méd.*, Jan. 14, 1900; Wells, H. G., *Am. Journ. Med. Sc.*, 1902, cxxiii, 299; Grancher, *Journ. de méd. et de chir. prat.*, 1904, lxxiv, 412; Monnier, *Gaz. méd. de Nantes*, 1905, 2. s., xxiii.

[3] Winternitz. *Johns Hopkins Hosp. Bull.*, Balt., 1911, xxii, 396.

In 32 cases collected by Lazarus-Barlow,[1] including Chiari's[2] 17 cases, 28 were haemorrhagic and four anaemic. In 50 cases, including most of Lazarus-Barlow's, 36 were haemorrhagic, 12 were anaemic, and in two cases (Pitt,[3] M'Weeney[4]) haemorrhagic and anaemic infarcts were both present.

Morbid Anatomy.—*Haemorrhagic infarcts and pseudo-infarcts* in the liver are well-defined areas, sometimes square or pyramidal. They are not raised above the surrounding surface of the liver; in fact, Zahn spoke of them as atrophic red infarcts. Histologically the liver cells are atrophied, granular, and may contain fat globules, while the nuclei do not stain well. There is, however, no coagulation-necrosis. The capillaries are engorged with blood. There may be considerable leucocytic infiltration of the affected area.

Fig. 16.—Anaemic infarct in the liver from a case with thrombosis of the intrahepatic branches of the portal vein and an empyema. St. George's Hospital Museum, Series ix, 165c. (Drawn by L. Jones, M.S.)

In *anaemic infarcts and pseudo-infarcts* the affected area is of a whitish-yellow colour and is sharply marked off from the surrounding healthy liver substance. There may be, but is not necessarily, a zone of congestion immediately at its junction with the healthy liver tissue. The area has much the same appearance, only it is larger and more prominent, as the white patches seen on the surface of the liver in many infectious diseases, which on microscopic examination shew local fatty change. At the margin of the infarct there are leucocytes, red blood-corpuscles, and altered blood-pigment.

As a result of infarction a slight amount of localised replacement fibrosis may result, but probably not enough to give rise to a cicatrix. Frerichs[5] described depressed areas of atrophy on the surface of the

[1] Lazarus-Barlow, W. S. *Brit. Med. Journ.*, 1899, ii, 1342.
[2] Chiari. *Ztschr. f. Heilk.*, 1898, xix, 475.
[3] Pitt, G. N. *Trans. Path. Soc.*, Lond., 1895, xlvi, 75.
[4] M'Weeney. *Journ. Path. and Bacteriol.*, Cambridge, 1912, xvi, 403.
[5] Frerichs. *Diseases of the Liver*, ii, 396. Transl. New Sydenham Soc., 1861.

liver, producing lobulation, as due to thrombosis of branches of the portal vein; it is conceivable that in their earliest stages these areas were infarcts. Infarct of the liver cannot be recognised clinically and is only of pathological interest.

Etiology.—The conditions which have been thought to play a part in producing true and false infarction of the liver are: (1) Obstruction of the branches of the portal vein, either by embolism or thrombosis; (2) obstruction of the branches of the portal or hepatic veins by new-growth; (3) obstruction of both the portal and hepatic veins at the same time; (4) embolism of the hepatic artery; (5) endarteritis of the

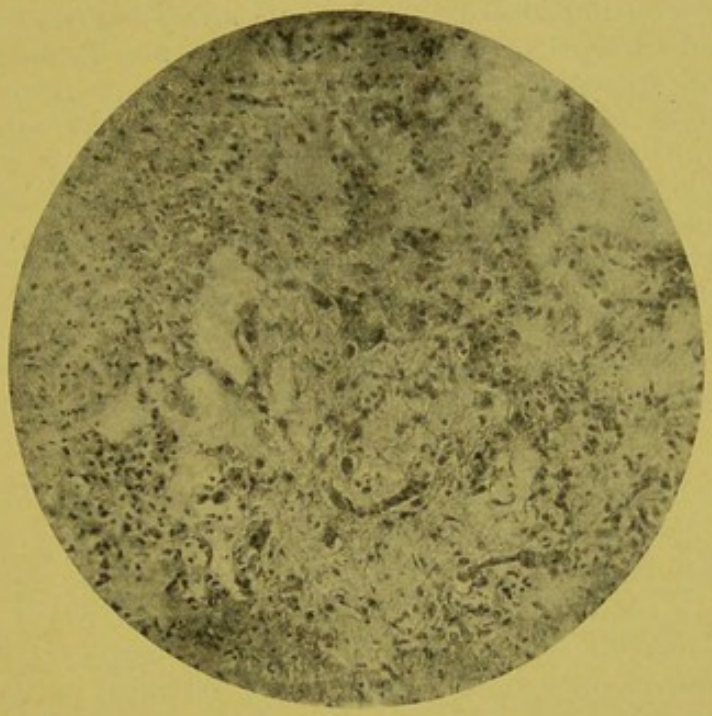


FIG. 17.—Photomicrograph of a true infarct in the liver. In part of the section the liver cells have lost their outline and their nuclei only remain. (Dr. S. G. Penny.)

hepatic artery; (6) retrograde embolism of the hepatic veins; (7) severe trauma.

(1) *Embolism and Thrombosis of the Branches of the Portal Vein.*—The most frequent vascular lesion found in cases of infarcts in the liver is ante-mortem blood-clot in the intrahepatic branches of the portal vein, either embolic and conveyed from thrombosis in its tributaries, or formed *in situ*.

Embolism.—Chiari records 15 cases of haemorrhagic areas in the liver due to embolism. This number is comparatively large and rather contrasts with the isolated observations of others, which, though less numerous, point to thrombosis of the vein as a more frequent antecedent. Chiari's cases, however, include embolism with fragments of new-growth as well as with detached blood-clot.

Thrombosis.—Thrombosis of branches of the portal vein, without any other vascular obstruction, such as embolism of the hepatic artery or thrombosis of the hepatic veins, has been found in cases of hepatic infarction by Osler,[1] Pitt,[2] Chiari,[3] and others. I have seen this association on several occasions.

A man, aged forty-six, died on May 3, 1902, in St. George's Hospital with a right-sided empyema and a dilated heart; there had been no abdominal symptoms and no ascites. The main trunk of the portal vein had an adherent parietal thrombus, and some of the branches of the portal vein in the right lobe of the liver were occluded with firm clots. There were two anaemic infarcts, one as large as one's hand (*vide* Fig. 16), the other a quarter of that size. The veins going to these areas were thrombosed. The hepatic artery was free from embolism, thrombosis, and arteriosclerosis. The infarcted areas were distinctly raised above the level of the surrounding liver substance. Although the macroscopic appearances were those of an anaemic infarct, the microscopic were those of a haemorrhagic infarct, the capillaries being full of blood. It is possible that in this case backward pressure from the dilated heart and infection played some part, in addition to portal thrombosis, in inducing the infarctions.

A man, aged forty-eight, under the care of Sir W. Bennett and myself, was operated upon for a localised subphrenic abscess due to a perforated gastric ulcer. Thrombosis of the right popliteal vein appeared before death, and at the necropsy thrombosis of a branch of the right division of the portal vein with a sharply marked haemorrhagic area was found in the corresponding part of the liver.

(2) *Obstruction of Branches of the Portal or Hepatic Veins in the Substance of the Liver by New-growth.*—Both these conditions may be associated with infarction of the liver. When the intrahepatic branches of the portal vein are obstructed by growth the process is usually embolic and due to small emboli of infective cells derived from a carcinoma in the stomach, colon, or other organ within the territory of its tributaries. When the hepatic veins are occluded, the growth may invade them from without, spread through the capillaries from embolic growths in the portal vein, or in rare cases be due to retrograde embolism (*vide* p. 53).

In a woman, aged forty, who died in St. George's Hospital with a spindle-celled sarcoma surrounding the pancreas, there were secondary growths in the liver which blocked up some branches of the hepatic veins and gave rise to haemorrhagic infarcts in the corresponding areas. There were anaemic infarcts in the spleen due to blocking of the splenic vein. There was no evidence of arterial embolism. Longcope[4] describes an anaemic infarct associated with thrombosis of the hepatic vein, and a haemorrhagic infarct associated with thrombosis of the portal vein; in both Longcope's cases the thromboses were secondary to gastric carcinoma.

[1] Osler. *Trans. Assoc. Am. Phys.*, 1887, ii, 136.
[2] Pitt. *Trans. Path. Soc.*, 1895, xlvi, 75.
[3] Chiari. *Ztschr. f. Heilk.*, 1898, xix, 475.
[4] Longcope, W. T. *Univ. Penn. Med. Bull.*, 1901, xiv, 223.

(3) *Combined Portal and Hepatic Vein Thrombosis.*—Thrombosis of the portal vein may, when combined with thrombosis of the hepatic veins, give rise to infarction of the liver. Thus, Pitt[1] records a case of very widespread thrombosis in the abdominal aorta, splenic, left renal, and right middle cerebral arteries, in the right hepatic and the branches of the portal veins. In Pitt's and in M'Weeney's cases, in which the portal and hepatic veins were thrombosed, there were both anaemic and haemorrhagic infarcts in the liver. But in a case of combined hepatic and portal vein thrombosis that I examined there was no appearance of infarction in the liver.[2]

(4) *Embolism of the hepatic artery* is very rare. It has been found both in man and experimentally to lead to necrosis of the liver (*vide* p. 47). Embolism of its branches may give rise to anaemic infarcts.

In a case of embolism of the bifurcation of the hepatic artery by a vegetation derived from the aortic valves C. Ogle[3] found anaemic infarcts in the liver. In a case of aortic and mitral disease Baldwin[4] found between 20 and 30 anaemic infarcts in the liver which were genuinely necrotic. The corresponding branches of the hepatic artery contained old thrombi. There were infarcts in the spleen, kidneys, brain; so there is little doubt that the infarcts in the liver were embolic.

(5) *Endarteritis obliterans* of the branches of the hepatic artery has been described by Bonome[5] as the cause of haemorrhagic and of necrotic infarcts in the liver in cirrhosis. In an extensive anaemic infarct in a case of eclampsia O'Sullivan found hyaline degeneration of the walls of the capillaries of the hepatic artery.

(6) *Retrograde Embolism.*—Embolism of one of the hepatic veins by a clot derived from the heart which had worked its way against the flow of blood—or retrograde embolism—has been observed to be associated with an hepatic infarct (Arnold[6]).

(7) *Trauma* may lead to the production of appearances resembling infarcts in the liver.

Traumatic Haemorrhagic Infarcts.—In rare instances trauma may lead to the passage of part of the liver through a hole or rupture in the diaphragm. If the piece of liver becomes strangulated, haemorrhage takes place into its substance and the appearance resembles that of a haemorrhagic infarct.

In a case recorded by C. Ogle,[7] part of the left lobe of the liver, measuring 5 by 4 inches, was herniated through the diaphragm, and to the naked eye resembled the section of a "cardiac" spleen. Microscopically the liver tissue was disorganised and contained much blood pigment, red blood-corpuscles, and

[1] Pitt. *Trans. Path. Soc.*, 1895, xlvi, 75.
[2] Rolleston. *Ibid.*, 1899, l, 148.
[3] Ogle, C. *Ibid.*, 1895, xlvi, 73.
[4] Baldwin, F. A. *Journ. Med. Res.*, 1904, viii, 431.
[5] Bonome. *Arch. di biol.*, Firenze, 1899, liii, 319.
[6] Arnold. *Virchows Arch.*, 1891, cxxiv, 388.
[7] Ogle, C. *Trans. Path. Soc.*, Lond., 1897, xlviii, 114.

the remains of liver cells, but differed considerably from the appearances in a haemorrhagic pseudo-infarct of the organ.

Traumatic Anaemic Infarcts.—Severe trauma may cut off the vascular supply to a part or parts of the liver. If life is prolonged for some days, the areas of the liver thus deprived of their blood-supply present to the naked eye an appearance resembling an anaemic infarct. The areas are firm and white in colour and have been regarded as infarcts by Klebs,[1] Lubarsch,[2] Lazarus-Barlow, Gruber,[3] Heile.[4] Microscopic examination shews that there is undoubted necrosis in these areas and that they correspond to true infarcts in the kidney and spleen.

(8) There may be no manifest vascular obstruction. In such cases a septicaemic or toxaemic condition is possibly responsible for the lesion. I have seen an infarct in the liver without any evidence of portal thrombosis or embolism of the hepatic artery. The patient, a man aged twenty-five, died with a localised peritonitis in the lesser sac due to acute pancreatitis.

Pathogeny.—Cohnheim and Litten[5] injected coarsely powdered chromate of lead and wax into the portal vein and produced portal thrombosis but no infarcts. Zahn,[6] however, found that sterilised mercury injected into the mesenteric veins was followed after an interval of eight days by haemorrhagic infarcts. But in actual practice thrombosis of the portal vein or its branches is so frequently seen without hepatic infarction that some other factor would appear to be necessary. Rattone suggested that the additional factor is blocking of the hepatic artery, but this is hardly ever found to be the case; Chiari and Steinhaus[7] argued in favour of a feeble circulation and low blood-pressure in the hepatic artery associated with venous congestion. Kohler[8] thought that backward pressure in the hepatic veins was a necessary adjunct, but this, again, is not borne out by the facts of morbid anatomy. It is probable, therefore, that infarction of the liver is not solely a mechanical process.

By the injection of tissue fibrinogen Wooldridge[9] produced portal thrombosis with haemorrhages and necrotic areas in the liver. Wooldridge's results suggest that, in addition to vascular disturbances, such as thrombosis or embolism of the blood-vessels of the liver, a toxaemic or septicaemic condition is necessary or at least very favourable to the production of infarction in the liver. Possibly a low arterial blood-pressure, which is favoured by septicaemia, may, when combined with an infective or toxic blood state, be sufficient to produce hepatic infarction.

[1] Klebs. Virchows *Festschrift*, 1891, S. 8.
[2] Lubarsch. *Fortschr. d. Med.*, Berl., 1893, xi, 805.
[3] Gruber. *Frankfurter Ztschr. f. Path.*, 1912, x, 442.
[4] Heile. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1900, xxviii, 443.
[5] Cohnheim und Litten. *Virchows Arch.*, 1876, lxvii, 153.
[6] Zahn. *Centralbl. f. allg. Path.*, 1897, viii, 860.
[7] Steinhaus. *Deutsch. Arch. f. klin. Med.*, 1904, lxxx, 364.
[8] Kohler. Quoted by Welch, Allbutt's *System*, 1899, vi, 280.
[9] Wooldridge, L. C. *Trans. Path. Soc.*, Lond., 1888, xxxix, 421.

The importance of an infective condition is supported by the fact that Apert[1] produced multiple anaemic infarcts, resembling the early stage of abscess formation, in the liver, heart, and kidneys of a rabbit by injecting pus containing colon bacilli and numerous anaerobic micro-organisms into the vein of the ear.

ACUTE CONGESTION OF THE LIVER

ACTIVE acute congestion of the liver is, of course, the first stage of acute hepatitis, which may, like similar processes elsewhere, abort and be followed by a rapid return to the normal condition. It is therefore impossible to draw a hard and fast line between the clinical manifestations of active congestion and of acute hepatitis in an early stage. Acute congestion of the liver is both more frequent and of more importance in warm countries, where malaria and dysentery are rife, than in temperate countries.

From a systematic standpoint the **causes** of active congestion of the liver may be first divided into:

(I) Active vaso-dilatation of the capillaries of the hepatic artery; this may be reflex and due to the effects of cold applied to the surface of the body. This is the mechanism by which chills produce active congestion of the liver. In England cold does not act in this way to anything like the same extent that it does in tropical climates, where the resistance of the liver is often much diminished from past attacks of congestion or inflammation in connexion with malaria and dysentery. In persons who have had dysentery or repeated attacks of malaria exposure to cold readily produces active congestion of the liver; this is sometimes spoken of as "a chill on the liver." But all cases described in these words are not thus explained; the effects of excessive eating and drinking, dyspepsia, gastro-intestinal catarrh, and constipation are sometimes described in these euphemistic terms. Exposure to high temperature in the tropics is, especially if followed by an accidental chill, a cause of acute congestion of the liver. Direct nervous stimulation has been suggested to explain active congestion of the liver in diabetes, but the voracious appetite of diabetic patients probably accounts for any active hepatic congestion. Experimentally, however, irritation of the "diabetic centre," as by Bernard's puncture experiment, gives rise to intense hyperaemia of the liver.

(II) The more reasonable and by far the commonest cause of active hepatic congestion is to be found in the toxic bodies reaching the organ through the blood-stream. This may occur (*a*) through the hepatic artery, as in fevers, especially malaria, and various infective conditions,

[1] Apert. *Bull. Soc. Anat.*, Paris, 1900, lxxv, 204.

though in the latter the process may pass on into inflammation or suppuration. It probably occurs in the early stages of icterus gravis, and no doubt is partly responsible for the enlargement of the liver seen in that disease and in the early stage of acute yellow atrophy.

Experimentally it has been shewn that subcutaneous or intravenous injection of the extract obtained from muscular tissue gave rise to intense congestion of the liver in animals (Richet [1]).

(*b*) But generally the poison is derived from the gastro-intestinal tract and reaches the liver by the portal vein. It therefore follows over-eating, and especially alcoholic excess, gout, gastritis, indigestion, dysentery. Physiologically active congestion of the liver occurs in digestion and is heightened by spices, pepper, mustard, and curries; in great excess such condiments may no doubt in a suitable subject set up acute and active hepatic congestion. Alcohol is an important factor, especially in hot climates, in producing acute congestion; this probably explains why hepatitis is seventeen times commoner in Europeans than among the natives of India (Davidson [2]). Other toxins may be carried by the portal vein, as in constipation, or, to take a more extreme case, in phosphorus poisoning. The suppression of menstruation (Senator [3]) or of habitual haemorrhages from piles, and the climacteric, have been thought to give rise to active hyperaemia of the liver, but the evidence is somewhat slender.

Morbid Anatomy.—The liver is enlarged, dark in colour, the uniform congestion contrasting with the partial engorgement seen in the chronic venous stagnation of mitral disease. The liver cells shew cloudy swelling, and may be fatty and pigmented, and the capillaries are dilated and full of red blood-corpuscles. The small bile-ducts may shew proliferation of their lining epithelium (cholangitis), which accounts for jaundice when present.

Clinical Picture.—The symptoms vary. Sometimes the patient is so ill that he must remain in bed; in other cases exercise can quite well be taken. There is malaise, with headache, giddiness, mental depression, irritability, insomnia, and gastro-intestinal symptoms, such as loss of appetite, a foul tongue, a bad taste in the mouth, sometimes nausea, flatulence, and constipation. There is a feeling of discomfort and weight in the hepatic region, and pain in the right shoulder. The conjunctivae become muddy and slightly icteric, the face is often congested, and the skin shares in these changes and may be irritable. The bowels are irregular; there may be diarrhoea or constipation. Epistaxis sometimes occurs.

The symptoms of acute congestion of the liver are much the same as some of those described by Murchison as lithaemia and regarded by him

[1] Richet, C. *Acad. des sciences*, Paris, Dec. 31, 1900; *Progrès méd.*, 1901, p. 23.
[2] Davidson. Article "Tropical Liver," in *System of Medicine* (Allbutt and Rolleston), 1907, ii, part 2, 574.
[3] Senator. *Berlin. klin. Wchnschr.*, 1872, ix, 615.

as due to functional inadequacy of the liver. The liver is usually enlarged and may project two or three fingers' breadths below the costal arch in the nipple line. It is decidedly tender on palpation. As a result of repeated attacks of hepatic congestion piles may be produced. Some writers describe oedema of the feet in acute hepatic congestion.

The urine is high coloured, uratic, concentrated, and of high specific gravity. The amount of urobilin is increased. The amount of ammonia in the urine is little, if at all, above the normal, and thus contrasts with the increase of ammonia found in the urine of patients with cirrhosis (Bain [1]). If there is jaundice, bile-pigment will be found in the urine. Albuminuria only occasionally occurs; it is transitory and can be explained as the result of poisons passing from the bowel and failing to be stopped by the liver; the kidneys are thus affected, and toxic albuminuria results.

The term *tropical liver* describes the more or less chronic condition found in persons who have had many attacks of acute congestion in hot climates. According to Cantlie, there is usually a history of malaria, diarrhoea, dysentery, or long-standing indigestion. Anaemia, weakness, nervous irritability, and irregularity of the bowels are essential features. The spleen is generally enlarged in addition to the liver. Probably some of these cases are in the early or pre-ascitic stage of cirrhosis.

Duration.—Acute congestion when treated usually lasts about a week, but may, if neglected, become chronic, and may then be a preliminary stage to cirrhosis.

Treatment.—In marked cases the patient should be confined to bed and kept on a milk diet. If, as sometimes happens, ordinary milk cannot be borne, skimmed milk, junket, milk jelly, or whey should be tried, and, if necessary, chicken broth or the juice of raw meat should be given. Plenty of water should be allowed, but alcohol must be strictly prohibited. Intestinal antiseptics, such as fractional doses of calomel, perchloride of mercury, guaiacol, or salol, should be given and the bowels kept freely open by calomel and salines, such as Carlsbad or Epsom salts and mineral waters. By free purgation the congestion is greatly relieved, as shewn by diminution in the size and disappearance of tenderness of the liver. Chloride of ammonium in xx.-grain doses has been credited with the power of reducing the congestion and preventing inflammation and suppuration. At the outset, if there are symptoms of gastritis, a soothing mixture containing bismuth and bicarbonate of sodium should be given.

Local Applications, etc.—For the pain in the hepatic region a large linseed poultice may be applied, and if it gives relief, be changed every three hours. Turpentine stupes, cold compresses, or dry cupping may be employed if poultices fail. If there is pain on respiration, resembling that of pleurisy and due to perihepatitis, the side should be strapped as for fractured ribs. Leeches applied over the hepatic region or at the margin of the anus have been employed to deplete the congested liver. Pain is

[1] Bain. *Brit. Med. Journ.*, 1898, ii, 941.

undoubtedly relieved by leeching the skin over the liver, although it is hardly probable that much blood is withdrawn from the liver through dilated venous anastomoses between the veins of the abdominal wall and the parumbilical vein of the falciform ligament. Neither is it likely that leeches applied to the anus draw off much blood from the portal vein. Venesection from the veins of the elbow was formerly much in vogue in hepatic congestion, but has almost completely gone out for many years. Direct aspiration of the liver and abstraction of blood is highly spoken of by many. In performing this risky operation the puncture of the liver may have to be performed several times before a vessel of sufficient size to bleed freely is struck. This withdrawal of blood from the liver is by no means a harmless proceeding. If a large branch of the portal vein or the inferior vena cava is wounded, fatal haemorrhage may take place into the peritoneal cavity. Indian surgeons, such as Hatch[1] and Maitland,[2] who have had fatal experience of aspirating the liver, condemn the procedure. Cantlie,[3] by limiting the length of the aspirating needle to $3\frac{1}{2}$ inches or so, considers that the danger of wounding the inferior vena cava is obviated.

When the more acute symptoms have passed off, the patient's diet should be improved, and tonics, such as strychnine in an acid mixture, should be given. When convalescent, the patient will be benefited by change of air. A cool, somewhat high, inland resort is usually most suitable. The seaside, especially when the patient lives near the shore, is often harmful and gives rise to constipation and so to a return of hepatic congestion.

In the slighter forms of active congestion of the liver due to overeating, drinking, and aggravated by constipation and a sedentary life, free purgation with blue pill and haustus sennae, followed by a simple diet and exercise, should be enjoined. Exercise on horseback or on a bicycle will in many cases act like a charm.

Treatment at a spa, such as Vichy, Ems, Neuenahr, Carlsbad, Marienbad, Harrogate, Leamington, Llandrindod Wells, has a beneficial effect both by reducing congestion of the liver through purgation and by preventing indiscretions in diet, while the freedom from business worries has a good influence on the mental condition.

Prophylaxis.—In gouty patients care as to diet should be taken to prevent undue hepatic congestion; but it is chiefly in persons who are, or have lived, in the tropics and have suffered from malaria that active congestion of the liver is likely to occur, and in whom, therefore, special care should be taken to avoid causes, such as chills and alcoholic or dietetic excess, which bring on this condition.

Exposure to east wind, sudden changes of temperature, cold draughts, and the risk of chills should be avoided by a malarial patient. The parts of the body exposure of which to cold is most liable to give rise to

[1] Hatch, W. K. *Ind. Med. Gaz.*, 1898, xxxiii, 137.
[2] Maitland. *Brit. Med. Journ.*, 1902, i, 458.
[3] Cantlie, J. *Ibid.*, 1903, ii, 656.

hepatic congestion are the abdomen, the back of the neck, and the legs and feet (Brunton). These parts should be suitably protected; a good plan is to wear a knitted cholera belt over the abdomen, which should always be changed after free action of the skin. Alcohol is best avoided, and if taken at all should be in small quantities well diluted at meal times. Made dishes, much meat, pastry, and sauces should be avoided.

Constipation should be guarded against by diet, viz. fruit and vegetables, porridge, and a sufficiency of water. If necessary, small doses of calomel or blue pill followed by a saline should be given. Active exercise, not merely walking, but riding, climbing, and other forms of exertion, such as rowing, skipping, which lead to compression of the liver between the diaphragm and the abdominal wall, a kind of natural massage, should be taken by persons whose strength and physique are suitable.

ACUTE HEPATITIS

THERE are a large number of different conditions in which the liver is acutely inflamed. At the outset a division into suppurative and non-suppurative hepatitis may conveniently be made. The suppurative forms of hepatitis are described elsewhere under other headings, such as abscess, pylephlebitis, cholangitis. Acute non-suppurative hepatitis may chiefly attack the liver cells, as in icterus gravis and in acute yellow atrophy, or the brunt of the change may fall on the connective-tissue framework, as in the hepatitis seen after scarlet fever (Klein[1]). (*Vide* also p. 191.) In malaria the liver cells are affected, but not in the same degree as in icterus gravis. The focal necroses seen in typhoid fever, puerperal eclampsia, and in some other infections and intoxications are allied to acute parenchymatous hepatitis, and represent a patchy or localised distribution of the process, which when diffuse gives rise to acute yellow atrophy. Hepatitis may also be due to influenza.

Acute active congestion of the liver and non-suppurative hepatitis are often two stages of the same process, and any attempt to distinguish sharply between them clinically is difficult or impossible.

Morbid Anatomy.—So many different forms of pathological change are included under the title of "acute hepatitis" that no one description can possibly be inclusive. The appearance of the liver varies according to the nature and intensity of the inflammation. In the more acute changes affecting the cells of the liver the condition will resemble that seen in icterus gravis or in acute yellow atrophy, while in less severe types of inflammation the aspect of the liver will resemble that in active congestion (*vide* p. 108). In acute hepatitis as seen in pyaemia the lobules of the liver may be very sharply marked out as bile-stained areas surrounded by greyish-white rings.

[1] Klein. *Trans. Path. Soc.*, 1877, xxviii, 439.

In a patient who had had a prolonged attack of dysentery the liver was deeply congested, oedematous, and almost fluctuating when it was seen during an operation undertaken by Bérard [1] under the idea that there was an abscess. The liver was explored in four places; blood alone came out and the patient rapidly recovered.

The liver of severe malarial infection, which is a definite form of acute inflammation, is usually swollen, enlarged, and more or less pigmented, from a brownish to a slaty black tint. The outline of the lobules is indistinct. In more chronic malarial infection two forms of hepatitis, described by Kelsch and Kiener,[2] should be mentioned here: (i) Hyperémie phlegmasique, in which the enlarged and soft liver shews perihepa-

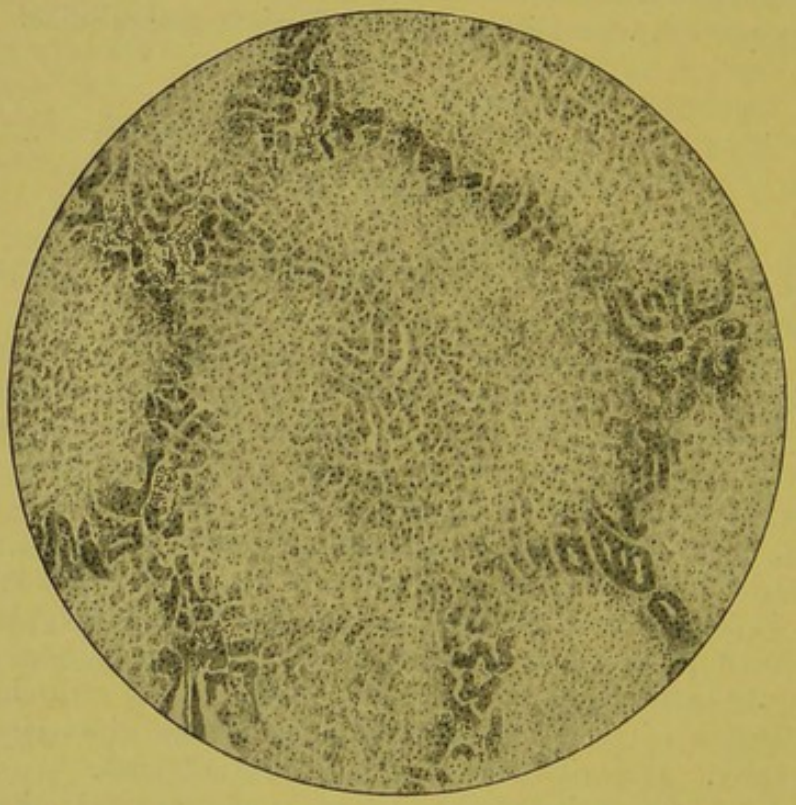


FIG. 18.—Drawing from a microscopic section from a case of pyaemia due to acute necrosis of both fibulae. Shews cloudy swelling and necrosis of the liver cells in the intermediate zone of the liver, and small-celled infiltration at the margin of the lobule.

titis, cloudy swelling, and karyokinesis of the liver cells with small-celled infiltration of the portal spaces; (ii) nodular parenchymatous hepatitis, in which there is hyperplasia of the liver cells forming small nodules on the surface of the organ, which may resemble multiple adenomas or even masses of secondary new-growth, though they are not umbilicated.

Attention may also be drawn to a rare form of *acute parenchymatous hepatitis* which shews in a marked degree compensatory hyperplasia of the liver cells. The condition is very closely allied to the nodular

[1] Bérard. *Lyon méd.*, 1902, xcviii, 752.

[2] Kelsch et Kiener. *Arch. de physiol. norm. et path.*, 1878, 571; 1879, 354.

parenchymatous hepatitis just described, but is not confined to malarial infection, and resembles the condition of the liver in subacute atrophy (*vide* p. 583).

I described a case of this kind in 1892,[1] but the Morbid Growths Committee of the Pathological Society regarded the condition as allied to cirrhosis. Prof. S. Delépine communicated to me full details of a case of acute interstitial and parenchymatous inflammation with imperfect regeneration of the liver cells, forming tubules containing plugs of bile, and giving rise to hyperplastic nodules. The patient, aged eleven years, was under Sir Lauder Brunton's care in 1887 for jaundice after one of the acute specific fevers ; from this recovery occurred, but six months later the jaundice recurred and proved fatal. The liver, 44 oz., shewed yellow areas of nodular hyperplasia in which the cells had undergone fatty degeneration and so led to the fatal result.

In this condition of acute parenchymatous hyperplasia of the liver cells with symptoms of subacute atrophy there may either be complete jaundice, no bile passing into the intestine (Widal and Abrami [2]), or the stools may be coloured. The larger bile-ducts are healthy, and jaundice has been thought to be due to pressure on the minute bile channels exerted by the enlarged liver cells (Ramond and Géraudel [3]).

The *histological appearances* in acute hepatitis also necessarily vary in the different forms. They may be those already described in acute congestion of the liver, viz. dilatation of the capillaries, acute lymphangitis, cloudy swelling, fatty degeneration and pigmentation of the liver cells, and catarrhal inflammation of the small bile-ducts. In addition the liver cells may shew focal necroses, with thrombosis of small vessels, and in some instances a varying degree of small-celled infiltration. The small cells are partly polymorphonuclear and other leucocytes, and partly young connective-tissue cells, and are found in the areas of focal necrosis and at the periphery of the lobules.

In some cases there is a diffuse small-celled infiltration, which is, like the hepatitis of congenital syphilis, unicellular. Figure 19 from a case of acute hepatitis accompanied by fever and jaundice and without any suppuration of the liver illustrates this condition. Cases of *subacute diffuse hepatitis* are sometimes seen, and may be regarded in the light of a very acute form of cirrhosis or midway between portal cirrhosis and acute yellow atrophy (Symmers [4]).

In the liver of severe malaria there are, in addition, many large phagocytes containing the parasites and pigment. As well as leucocytes, the endothelial cells of the vessels and Kupffer's star-like cells act as phagocytes.[5] The liver cells undergo degeneration and contain pigment, granules of bile and of haemosiderin. There is little fatty change in the

[1] Rolleston. *Trans. Path. Soc.*, Lond., 1892, xliii, 81.
[2] Widal et Abrami. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1905, 3. s., xxv, 523.
[3] Ramond et Géraudel. *Ibid.*, 1905, 3. s., xxv, 600.
[4] Symmers, D. *Am. Journ. Med. Sc.*, Phila., 1908, cxxxv, 251.
[5] See Barker. *Johns Hopkins Hosp. Rep.*, Balt., 1895, v, 221.

cells. Dilatation of the capillaries may lead to the production of areas resembling cavernous tissue (Ewing [1]).

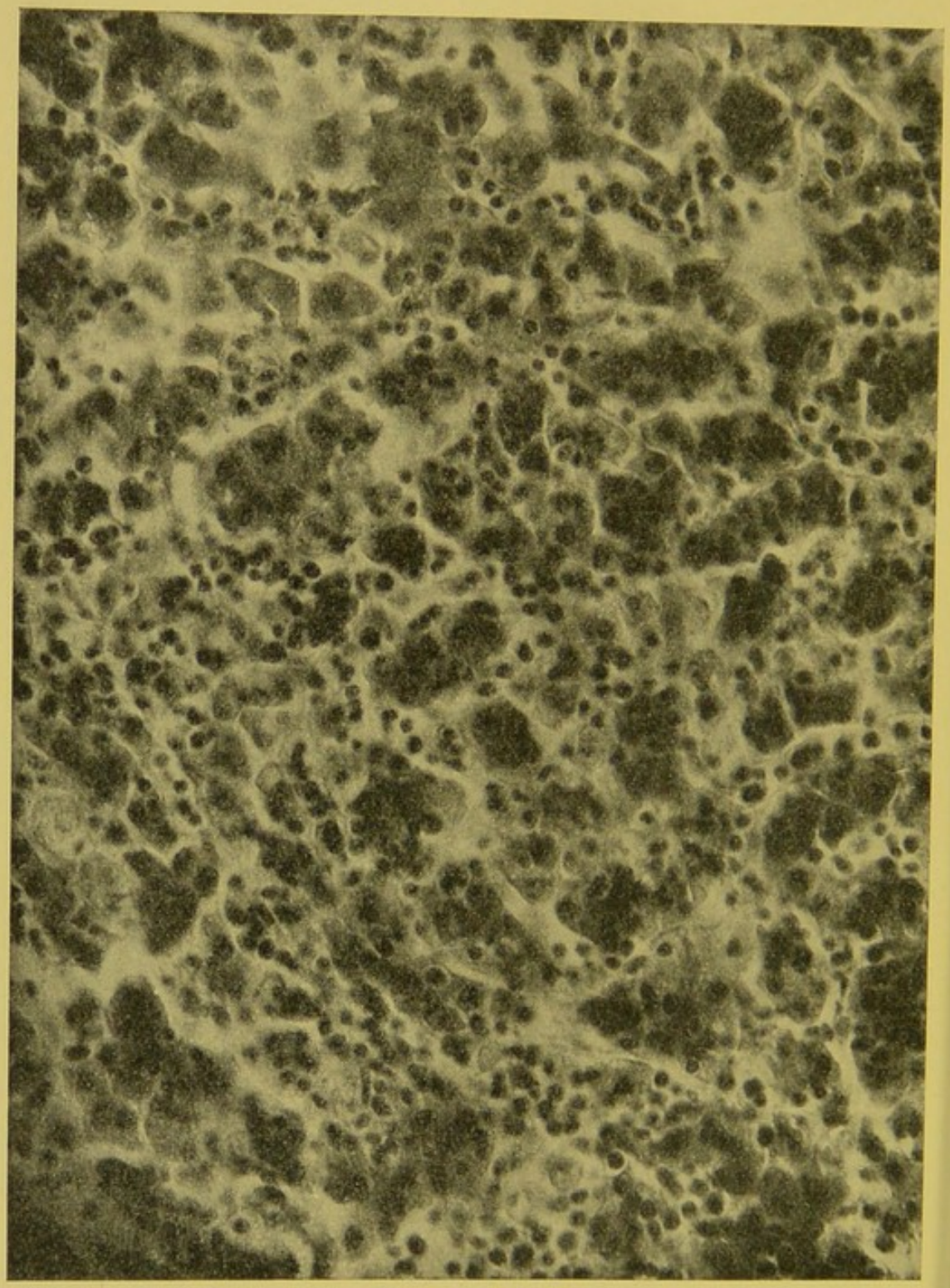


FIG. 19.—Photomicrograph of acute hepatitis. The liver cells are separated from each other by small round-celled infiltration. From a section prepared by Dr. Bolam. (Photomicrograph by Dr. H. Spitta.)

[1] Ewing. *Journ. Exper. Med.*, N.Y., 1901–5, vi, 154.

Clinical Picture.—Acute non-suppurative hepatitis due to a general infection or toxaemia may shew itself by jaundice. If the constitutional symptoms accompanying the jaundice are severe, the condition resembles that described under icterus gravis. With a milder grade of clinical manifestations, the jaundice is spoken of as being infectious or toxaemic, or may conform to the type of Weil's disease. When hepatitis due to a general infection is not accompanied by jaundice, there may be little to attract attention to the liver, though on examination it may be found to be somewhat enlarged and tender. The condition, which in this country is, perhaps rather vaguely, usually spoken of as acute hepatitis, occurs in patients who have suffered from frequent attacks of malaria, from dysentery, or from both diseases. As the result of exposure to cold or of excess in eating or drinking they suffer from the train of symptoms described later on.

Clinically acute hepatitis is seldom seen in England except in persons who have returned from the tropics. It is an acute form of the reaction to irritants which in temperate climates is chronic and eventually gives rise to cirrhosis. The irritant causing hepatitis is in many instances derived from the gastro-intestinal tract. The symptoms are the same as those of active congestion of the liver, to which reference should be made, but are more marked. The temperature in hepatitis is raised, and on the degree of fever a clinical distinction has been drawn between active congestion and hepatitis; Cantlie [1] considers that a temperature above 100° shews that the condition is inflammatory, and one below this point, active congestion. Davidson,[2] however, fixes the dividing line at 102° F. The gastro-intestinal symptoms described in acute congestion are accentuated and vomiting is more frequent. The bowels may be constipated, or there may be diarrhoea; in both cases the motions are very offensive. The pain in the shoulder is more marked than in simple congestion, and from extension of hepatitis to the capsule of the liver the case may become complicated by perihepatitis. This makes the descent of the diaphragm painful and leads to shallow respirations. The diminished movement of the diaphragm can be seen by *x*-rays. The patient is irritable, low-spirited, and sits up in bed. The abdomen is rigid and the liver is uniformly enlarged and tender. When there is concomitant malaria, the spleen is also enlarged. Toxic albuminuria, which has been spoken of as hepatogenic (Teissier [3]), is occasionally present.

Diagnosis.—When there is distinct jaundice, a diagnosis must be made in the most severe cases from acute yellow atrophy and from phosphorus poisoning. In acute yellow atrophy the rapid course, the presence of nervous symptoms, and the fact that the liver, if at first increased in size, soon diminishes, are characteristic. In phosphorus

[1] Cantlie. *Encyclopaedia Medica*, Edin., 1901, vii, 10.

[2] Davidson. Article "Tropical Liver," *System of Medicine* (Allbutt and Rolleston), 1907, ii, part ii, 576.

[3] Teissier, J. *Les Albuminuries curables*, p. 34, 1900, Paris.

poisoning the history and the haemorrhagic condition of the vomit and stools are points of importance. In acute atrophy and phosphorus poisoning the constitutional symptoms are far more severe than in acute hepatitis. But the distinction between acute hepatitis with jaundice and subacute atrophy of the liver may be very difficult. When the jaundice is slight, infectious jaundice should be thought of.

In some cases in which the liver is very considerably enlarged and the other symptoms severe it may be very difficult or impossible to be sure that there is not suppuration in the liver, especially as acute hepatitis may be the first stage of a tropical abscess. This difficulty not uncommonly occurs in malarial patients. According to Rogers,[1] leucocytosis occurs in amoebic hepatitis but differs from that in ordinary suppuration in not shewing any relative increase in the polymorphonuclears; it then resembles amoebic abscess (*vide* p. 137). In 5 out of 15 cases of amoebic hepatitis recorded by Rogers, exploration for abscess gave negative results.

Bérard's case, already referred to, is an example of the difficulty in making a diagnosis between acute hepatitis and hepatic abscess. Remlinger,[2] Bozzolo,[3] and others describe a form of acute hepatitis under the name of "the infective liver" which clinically imitates hepatic abscess.

The same difficulty may arise in differentiating the condition from more diffuse forms of hepatic suppuration, such as suppurative pylephlebitis and cholangitis. In these cases some time may be required before an accurate differential diagnosis can be made.

The cases of subacute diffuse hepatitis described by Symmers merge clinically into the conditions of acute cirrhosis and of subacute atrophy of the liver.

The **treatment** is on the same general lines as in simple congestion, but is rather more active. The patient should be kept in bed on a low diet, and the local pain and tenderness over the liver relieved by cold applications, poultices, scarifying the skin, leeching, dry cupping, or by strapping the hepatic region with narrow strips of plaster as if for fractured ribs. Milk, or the modifications of it mentioned on page 297, is the staple diet, but if it disagrees, raw meat-juice, chicken broth, jelly, or other similar preparations should be substituted. Plenty of water should be given or its equivalent, such as soda water or lemonade. Alcoholic drinks of all kinds should be strictly tabooed.

The bowels should be kept freely open by salines, such as sulphate of sodium or of magnesium, or calomel may be given with advantage. Vomiting and signs of gastritis should be allayed by bismuth, hydrocyanic acid, bicarbonate of sodium, etc. Diarrhoea, unless excessive, should not be checked. Large doses of ipecacuanha, 20 to 40 grs. once or twice a day after a dose of tincture of opium, are invaluable in amoebic hepatitis,

[1] Rogers, L. *Med.-Chir. Trans.*, Lond., 1907, xc, 163.
[2] Remlinger. *Presse méd.*, 1903, i, 86.
[3] Bozzolo. *Riv. crit. di clin. med.*, 1902, iii, 169.

whether there be dysentery or not, as a means of preventing suppuration (Rogers [1]). Chloride of ammonium in twenty-grain doses should be given three times a day during the acute stage, and may be combined with dilute hydrochloric acid and a few minims of liquor strychninae. If there is a history or evidence of malaria, quinine should be given as soon as the gastro-intestinal symptoms have subsided.

The abstraction of 10 to 15 ounces of blood from the substance of the liver by means of an aspirator is much advocated and has been thought to prevent the further development of suppuration. It is, however, not entirely without risk, as fatal haemorrhage into the peritoneal cavity has been known to follow [2] (*vide* p. 110). When convalescent, the patient should go to a cool, fairly bracing climate, and will get benefit from treatment at a spa, such as Harrogate, Carlsbad, Marienbad, Neuenahr, Ems, Vichy. The prophylactic treatment is that of acute congestion (*vide* p. 110).

HEPATIC ABSCESS

INTRAHEPATIC suppuration may be conveniently divided into two main groups: (I) The large, single, or "tropical" abscess, and (II) multiple abscesses. Strictly speaking, this classification is not entirely satisfactory; for occasionally there may be two large abscesses in the liver, and a single abscess may infect the remainder of the liver and give rise to several secondary abscesses; while, on the other hand, multiple abscesses may unite and eventually form a large areolar abscess. It has, however, a practical advantage, for cases of large single or tropical abscess are accompanied by more characteristic signs and are in general curable by operation, whereas multiple abscesses are less easy to diagnose and cannot be benefited by surgical treatment.

SINGLE OR TROPICAL ABSCESS

Etiology.—*Dysentery.*—The causation of tropical abscess is more closely related to dysentery than to any other condition. In some statistics there is a close association between the diseases termed dysentery and the subsequent development of hepatic abscess. Azevedo Sodré,[3]

[1] Rogers. *Med.-Chir. Trans.*, Lond., 1907, xc, 145.
[2] Hatch, *Ind. Med. Gaz.*, 1898, xxxiii, 137; Maitland, *Brit. Med. Journ.*, 1902, i, 458.
[3] Azevedo Sodré. *XXth Century Practice of Medicine*, 1899, xvi, 253.

adding together the statistics of Moore, Macpherson, Marshall, Morehead, and Dutrouleau, found that in 1997 necropsies on dysentery there were 407 hepatic abscesses, or 20 per cent. In 314 selected cases of hepatic abscess taken by Kelsch and Kiener,[1] 268, or 75 per cent, had had dysentery. In a later analysis by Kelsch[2] of 500 cases of hepatic abscess dysentery was present in 85 per cent. On the other hand, E. J. Waring's[3] statistics from India do not shew such a close relation; thus, in 2758 cases of dysentery treated in the Madras Presidency between the years 1826 and 1843 there were 68 cases of abscess, or 2·5 per cent; whereas in his 300 fatal cases of abscess, only 82, or 27 per cent, were admitted for dysentery. Buchanan's[4] figures also shew a want of parallelism between the curves of the incidence of dysentery and of hepatic abscess in India. Thus, the natives suffer more severely from dysentery and less from hepatic abscess, while the converse holds good among European soldiers.

In 79,723 cases of dysentery among the natives there were 127 cases of hepatic abscess, or 1 in 628; while in the European army during four years (1893–96) there were 7972 cases of dysentery and 441 cases of abscess, or 1 in 18.

The following arguments have also been urged against the too exclusive view of the dysenteric origin of hepatic abscess:—

(i) That hepatic abscess is much commoner among English soldiers in India than in other tropical countries, such as Jamaica, where dysentery is as frequent as it is in India.

(ii) That an increase in the curve of dysentery—for example, in war-time—is not accompanied or followed by any increase in the liver abscess curve.[5]

In the bacillary dysentery of Japan Shiga has never seen hepatic abscess as a complication, and in the dysentery seen in the South African War, 1899–1902, which was not amoebic, hepatic abscess was very rare. In 250 cases observed by Washbourn and Richards[6] at the Imperial Yeomanry Hospital, Deelfontein, there was only one hepatic abscess; out of 466 cases of dysentery treated at the Imperial Yeomanry Hospital, Pretoria, there were two fatal cases of pylephlebitis, and another case, in which after an operation for piles performed some six months after an attack of dysentery, a single hepatic abscess developed and was successfully operated upon. While in South Africa (1901) I made enquiry from medical officers, who all agreed that single hepatic abscess as a sequel of South African dysentery was extremely rare. In 1906 a man who was in South Africa in 1901, but had not been in any other foreign country,

[1] Kelsch et Kiener. *Traité des maladies des pays chauds*, Paris, 1889.
[2] Kelsch. *Sem. méd.*, 1900, xx, 80.
[3] E. J. Waring. *Abscess in the Liver in the East Indies*, p. 123, 1854.
[4] Buchanan, W. J. *Journ. Trop. Med.*, 1899, i, 173.
[5] Editorial, *Ind. Med. Gaz.*, 1902, xxxvii, 193.
[6] Washbourn and Richards. *Brit. Med. Journ.*, 1900, ii, 668.

came under my care with a single hepatic abscess. In 422 cases of dysentery in Rhodesia there were 11 cases of hepatic abscess (Curtis [1]).

Dysentery in temperate climates occurs sporadically as "ulcerative colitis" and in epidemics in asylums. Vedder and Duval [2] have shewn that asylum or institution dysentery is due to a bacillus identical with that described by Shiga and Flexner as the cause of acute epidemic dysentery. Liver abscess is very rare after asylum dysentery. In Gemmel's [3] 80 cases examined after death at the Lancaster Asylum there were two cases; in the epidemics of dysentery at Millbank, 1840–47, W. Baly [4] did not find any case of abscess.

(iii) That in some cases of hepatic abscess there is no history of dysentery, and that after death the colon may appear quite healthy.

In 456 cases of fatal hepatic abscess recorded in the annual reports of the sanitary commissioner of India during the five years 1896 to 1900 the intestines were free from ulceration in 47 per cent. Charles [5] quotes similar statistics.

In the cases of amoebic abscess in which the colon is normal at the necropsy [6] it is possible that the amoebae gain entrance to the portal system by some minute lesion which subsequently heals over.

The absence of any history of dysentery in some cases of hepatic abscess may be explained by its having remained latent. In cases in which evidence of dysentery is found at the necropsy, and in which no history has been forthcoming, the original attack may have been forgotten, since an abscess may occur years, even ten,[7] after dysentery, or may be remembered and described as diarrhoea.

(iv) It has been thought that the dysenteric ulceration of the colon is secondary to the abscess. The older observers believed that pus passed down the bile-ducts into the intestine and set up diarrhoea and ulceration. This explanation is no longer accepted. But that absorption from the abscess may set up diarrhoea and intestinal ulceration is shewn by some cases of fatal hepatic abscess in which a recurrence of dysentery or recent ulceration is seen in a colon with evidences of old dysentery. Flexner,[8] indeed, considers that even in amoebic dysentery the intestinal lesions may be secondary to the amoebic hepatic abscess.

(v) Another view is that the two diseases are both independent results of the same infection. In favour of this it has been urged that when dysentery breaks out, patients may develop hepatic abscess who have not shewn any signs of dysentery, while those who contract dysentery do not necessarily become the subjects of hepatic abscess.

[1] Curtis, H. *Clin. Journ.*, Lond., 1907, xxxi, 57.
[2] Vedder and Duval. *Journ. Exper. Med.*, 1901–5, vi, 181.
[3] Gemmel. *Idiopathic Ulcerative Colitis*, p. 29, 1898, Lond.
[4] Baly, W. *Lond. Med. Gaz.*, 1847, xxxix, 441.
[5] Charles. *Brit. Med. Journ.*, 1908, ii, 1235.
[6] Buxton, J. T., *Proc. Phila. Path. Soc.*, 1899, ii, 49; Flexner, S., *Am. Journ. Med. Sc.*, 1897, cxiii, 553; Thompson, *Manchester Med. Students' Gaz.*, 1903, p. 146; Futcher, *Journ. Am. Med. Assoc.*, 1903, xli, 480.
[7] Josserand. *Lyon méd.*, 1897, lxxxvi, 421.
[8] Flexner. *Amer. Journ. Med. Sc.*, 1897, cxiii, 553.

The, at first sight, puzzling difference in various parts of the world between the relation of the disease called dysentery and the subsequent development of a single hepatic abscess, may be explained in the following way: Under the heading dysentery at least two distinct forms of colitis have been included in the past: (*a*) amoebic dysentery of a chronic type, which is followed by single or tropical hepatic abscess, and (*b*) acute bacillary dysentery, which is not followed by single hepatic abscess. Bacillary dysentery was described in Japan by Shiga,[1] where it was extremely severe, by Flexner[2] in Manila, by Castellani[3] in Ceylon, by Duval and Vedder[4] in America, and by Kruse[5] in Germany. Amoebic and bacillary dysentery may occur side by side; and a patient with acute bacillary dysentery may contract amoebic dysentery. The two diseases were studied and could be distinguished from each other in Manila during the Spanish-American War. This is well shewn by Craig's[6] contrast of 60 cases of amoebic dysentery with hepatic abscess in 22, or 36·6 per cent, and 60 cases of bacillary dysentery, with multiple abscesses in 2 cases.

Tropical dysentery is more often followed by abscess than the dysentery seen in temperate countries, because it is more often amoebic. In 2590 cases of tropical dysentery hepatic abscess occurred in 507 (Councilman and Lafleur[7]). Few statistics are available to determine the incidence of hepatic abscess in amoebic dysentery. Davidson[8] says one-twelfth of those suffering from amoebic dysentery develop abscess. In 119 cases of amoebic dysentery treated in the Johns Hopkins Hospital 27, or 22·6 per cent, had hepatic abscess (Futcher[9]); in Strong's 79 necropsies on cases of amoebic dysentery 14 had liver abscess.

Other Causes of Single or Tropical Abscess.—Apart from dysentery the factors which can be regarded as having a causal relationship to hepatic abscess are comparatively insignificant.

Trauma may give rise to hepatic abscess either (i) directly—for example, when a penetrating wound introduces micro-organisms into the liver substance—or (ii) indirectly, by so reducing the resistance of the liver that any pus-producing micro-organisms which happen to reach the liver either from the general circulation by means of the hepatic artery, or from the alimentary canal, are then enabled to grow and multiply. Thus a blow on the liver may produce a small rupture inside the liver without damaging the capsule; recovery should then occur, but if micro-organisms have previously gained access to the damaged part of the liver, an abscess may follow.

(i) Penetrating wounds with a dagger, knife, or bullet may introduce

[1] Shiga. *Centralbl. f. Bakteriol. u. Parasit.*, 1898, xxiii, 549; xxiv, 817, 870, 913.
[2] Flexner. *Johns Hopkins Hosp. Bull.*, 1900, xi, 37; *Brit. Med. Journ.*, 1900, ii, 20; *Univ. Penn. Med. Bull.*, 1901.
[3] Castellani. *Journ. Hyg.*, Camb., 1904, iv, 495.
[4] Duval and Vedder. *Journ. Exper. Med.*, 1901–5, vi, 181.
[5] Kruse. *Deutsche med. Wchnschr.*, 1900, xxvi, 637.
[6] Craig. *Amer. Journ. Med. Sc.*, Phila., 1904, cxxviii, 145.
[7] Councilman and Lafleur. *Johns Hopkins Hosp. Rep.*, 1891, ii, 67.
[8] Davidson. *System of Medicine* (Allbutt and Rolleston), 1907, ii, part ii, 598.
[9] Futcher. *Journ. Am. Med. Assoc.*, 1903, xli, 480.

micro-organisms, or infection may occur later. A bullet may carry some of the patient's clothing, and thus micro-organisms, into the wound. Infection may also supervene either from the wound or from the blood-stream.

It appears probable that a foreign body may remain encysted in the liver for a considerable time and that suppuration may eventually supervene around it. In such cases it is probable that this part of the liver, having its resistance diminished, becomes infected more easily by the blood-stream. It is hardly likely that micro-organisms introduced at the same time as the foreign body—a bullet, for example—have remained latent. In rare instances, a pin, needle, or fish-bone may penetrate the alimentary canal and enter the liver substance, thus giving rise to hepatic abscess.

(ii) Trauma without any penetrating wound may be followed by hepatic abscess. This is not common. F. C. Turner [1] in 1882 was only able to refer to 12 cases, but this estimate must not be taken as actually representing its incidence. On the other hand, it may be merely that after trauma a latent abscess increases in size or by leakage sets up a perihepatic or subphrenic abscess.

Extension of Inflammation from Adjacent Parts.—This method of formation of a single hepatic abscess is very rare, and not of much importance. Calculi in the gall-bladder may, by giving rise to ulcerative cholecystitis and perforation, set up suppuration in the adherent liver (*vide* p. 619).

Perforation of a simple or of a malignant gastric ulcer into the liver may set up suppuration in a comparatively limited area. In these cases the abscess cavity may shew necrotic changes which, according to Gilbert and Lippmann,[2] depend chiefly on anaerobic micro-organisms.

I have seen 4 cases in which malignant disease of the cardiac end of the stomach grew directly into the left lobe of the liver and gave rise to somewhat diffuse suppuration in its substance. In one of these cases death was caused by peritonitis due to leaking from the abscess. In a man aged forty-nine years, who died in St. George's Hospital in 1906, and whose chief symptom was grave anaemia, there was an abscess the size of a tangerine orange in the left lobe of the liver; this communicated by a large opening, with thickened edges, with the pylorus and the first part of the duodenum. Microscopically the growth was a columnar-celled carcinoma. The abscess cavity contained blood-clot.

An empyema or an abscess in the base of the right lung, suppuration in or around the right kidney, or a localised subphrenic abscess have also been described as extending into and giving rise to suppuration inside the liver. But in such cases it is not always certain whether the suppuration began in the organ named and extended into the liver, or whether it originated in the liver.

Enteric fever in very rare instances is followed by a solitary hepatic

[1] Turner, F. C. *Trans. Path. Soc.*, 1882, xxxiii, 177.

[2] Gilbert et Lippmann. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1903, 3. s., xx, 871.

abscess. It is said to be less rare in the tropics than in temperate countries (Bertrand and Fontan [1]), and possibly this is due to the influence of dysentery or to the diminished resistance of the liver induced by dysentery, malaria, and alcoholism. A solitary abscess following enteric fever may be due to infection from an abscess elsewhere, such as suppuration of the parotid, and is rare in uncomplicated enteric fever.

In 2000 fatal cases of enteric fever examined at Munich Hölscher [2] found 12 cases of solitary hepatic abscess. W. W. Keen [3] collected 16 additional cases, some of which were secondary to abscesses elsewhere ; Louis's case—one of the earliest on record—and Osler's [4] had parotitis, and Chvostek's perichondritis of the larynx. In 1911 von Eberts [5] collected 30 cases in association with enteric fever ; in 9 cases the typhoid bacillus was isolated from the abscess, in the remaining 21 it was not proved to have a causal relation.

Typhoid bacilli can give rise to a solitary hepatic abscess, but, as a rule, there is a mixed infection.

In two cases of solitary abscess following typhoid fever bacteriological examination gave a pure culture of typhoid bacilli in one ; in the other typhoid bacilli and staphylococci were present (Cassuto [6]).

I have seen one case of a single hepatic abscess after enteric fever.

An Imperial Yeomanry trooper, aged thirty years, who had never had dysentery or been previously out of England, was inoculated against enteric fever in 1900 when on his way to South Africa. He had two attacks of enteric fever in the next twelve months in Africa ; when convalescent from the second attack he had acute pneumonia on the right side, followed by signs suggesting empyema. The chest was aspirated and 12 ounces of sanious pus containing liver cells, but perfectly sterile, were evacuated. Mr. D. Drew excised part of the sixth rib and freely opened an abscess in the anterior part of the right lobe of the liver. The patient was invalided home, and was seen in December 1901 in perfect health.

Influenza.—Tédenat [7] recorded 4 cases of single hepatic abscess arising about twenty-five to thirty days after influenza ; there was no other cause forthcoming. The pus was sterile. Influenza may light up a latent abscess.

Suppurating Hydatid Cyst, etc.—When a hydatid cyst suppurates the conditions are for all practical purposes the same as a single hepatic abscess. In rare instances a round worm in the intrahepatic bile-ducts may give rise to a single small abscess, but, as a rule, there is suppurative cholangitis with multiple suppurating foci.

Infective Granulomas.—Suppuration commonly occurs in actinomycosis

[1] Bertrand et Fontan. *L'Hépatite suppurée*, Paris, 1895.
[2] Hölscher. *München. med. Wchnschr.*, 1891, xxxviii, 43.
[3] Keen, W. W. *Surgical Complications and Sequels of Typhoid Fever*, p. 246, 1898.
[4] Osler. *Studies in Typhoid Fever, Johns Hopkins Hospital*, p. 380, 1895.
[5] Von Eberts. *Amer. Journ. Med. Sc.*, Phila., 1911, cxli, 803.
[6] Cassuto. *Thèse de Paris*, 1900.
[7] Tédenat. *Gaz. hebd. d. méd.*, Paris, 1902, vii, 1073.

(*vide* p. 383), and in rare instances supervenes in gummas (*vide* p. 356) and in tuberculomas (*vide* p. 345).

Single Pyaemic Abscess.—A single hepatic abscess is sometimes due to causes, such as general haemic infection, or infection of the portal system, which, as a rule, give rise to multiple abscesses. In exceptional instances suppuration or infection elsewhere in the body is the only cause to account for a single hepatic abscess. Thus, it has followed cutaneous abscesses, whitlow, suppuration of the parotid, bronchiectasis (Muir [1]), parametritis and pyosalpinx (Roughton [2]), prostatic abscess (Lancereaux [3]), scarlet fever.[4]

A single hepatic abscess may also occur as the result of emboli derived from the portal vein or its tributaries. Thus, in exceptional instances it may follow gastric ulcer (Dalton [5]), appendicitis, ulcers in the colon, or ligature of piles.

A single loculated or areolar abscess may be the late stage of a number of neighbouring areas of multiple diffuse suppuration, due to pylephlebitis or suppurative cholangitis affecting a comparatively large intrahepatic branch of the portal vein or bile-duct. What appears to be a single hepatic abscess may therefore occur as the result of portal infections which usually produce multiple hepatic abscesses.

In appendicitis, a single hepatic abscess is very rare indeed; Elsberg [6] in 1906 collected 15 undoubted cases, and in 1911 Quénu and Mathieu [7] accepted 14 only. It sometimes happens that a single abscess is diagnosed and operated upon, but the patient dies, and in the absence of a necropsy the actual condition remains doubtful; when a necropsy is made, multiple abscesses are usually found.

A man had an appendicular abscess, and the appendix was removed; thirteen days later an amoebic abscess of the liver, which was probably present at the time of the first operation, was opened, and after an interval of twenty-eight days more pus was evacuated through the wound of the second operation. Curtis [8] inclined to the view that the appendicitis was subsequent to the hepatic suppuration, and compared the sequence of events to that of appendicitis secondary to gall-bladder infection (Dieulafoy.[9] *Vide* also p. 604).

In the following case a large abscess due to the union of originally separate abscesses was due to infection from the appendix:

A girl aged seven years who, except for a stitch in the right side of the abdomen for more than a year, had never had any signs of appendicitis, came under observation with signs of right-sided pleurisy. Subsequently hepatic

[1] Muir. *Edin. Hosp. Rep.*, 1894, ii, 100.
[2] Roughton. *St. Barth. Hosp. Rep.*, 1885, xxi, 173.
[3] Lancereaux. *Traité des maladies du foie et du pancréas*, 1899.
[4] Guy's Hospital Museum, No. 1294.
[5] Dalton, N. *King's Coll. Hosp. Rep.*, 1896, ii, 25.
[6] Elsberg. *Ann. Surg.*, 1906, xliv, 220.
[7] Quénu et Mathieu. *Rev. de chir.*, Paris, 1911, xxxi, 519.
[8] Curtis. *Trans. Med. Soc. Lond.*, 1906, xxix, 353.
[9] Dieulafoy. *Presse méd.*, Paris, 1903, p. 448.

abscess was diagnosed, and several operations with the evacuation of pus from the liver were performed. At the necropsy the vermiform appendix was surrounded by old adhesions and recent lymph, and was perforated by a pin. The portal vein was healthy. The liver, greatly enlarged, contained a loculated area of suppuration as large as one's fist in the upper and back part of the right lobe. In the immediate neighbourhood there were spreading foci of suppuration. The rest of the liver was of a bright yellow colour resembling that seen in phosphorus poisoning.[1]

Disposing Factors.—*Geographical Distribution.*—Large hepatic abscess is a disease of tropical climates, and cases seen in this country are usually in persons who have been in hot climates and suffered from dysentery, or even from a previous hepatic abscess abroad. Although a tropical disease, hepatic abscess is not met with uniformly in different parts of the tropics; thus, while it is frequent in India, Senegal, Mauritius, Algiers, Egypt, Java, Sumatra, Mexico, Peru, Chile, it is much less common in the West Indies, China, Brazil, Guiana, Ceylon.

Altitude.—In parts of the tropics where the elevation is sufficiently high to reduce the mean temperature to that of a temperate climate, hepatic abscess does not occur.

Climate.—A high mean temperature very decidedly favours the production of hepatic abscess; but an important factor is the occurrence of sudden variations. From the incidence of chills, the commencement of the cold season has been said to be a favourite time for the development of hepatic abscess. But from an analysis of the 236 cases of hepatic abscess in Calcutta Rogers[2] found that there was no special seasonal prevalence.

Acclimatisation.—It would appear that persons who have recently become resident in tropical climates are more likely to suffer from hepatic abscess than those who have been there some time.

In 114 cases E. J. Waring[3] found that 22 per cent of cases of abscess occurred in India in soldiers who had been less than one year in the country, 10·5 per cent in the second year, and 10·5 per cent in the third year. Figures quoted by Davidson,[4] however, shew that, although the mortality is very high in the first year, long residence increases the liability of Europeans in India to abscess.

Race.—Europeans are much more liable to hepatic abscess in the tropics than the natives.

In 79,723 cases of dysentery among the natives of India collected by W. J. Buchanan[5] there were only 127 cases of hepatic abscess, or 1 in 628 cases, whereas in 7972 cases of dysentery among Europeans in India there were 441 cases of hepatic abscess, or 1 in 18.

[1] Rolleston. *Trans. Path. Soc.*, Lond., 1898, xlix, 106.
[2] Rogers, L. *Brit. Med. Journ.*, 1902, ii, 844.
[3] Waring, E. J. *Hepatic Abscess*, p. 113, 1854.
[4] Davidson. *System of Medicine* (Allbutt and Rolleston), 1907, ii, part ii, 591.
[5] Buchanan, W. J. *Journ. Trop. Med.*, 1899, i, 173.

But when natives give way to alcohol they are more likely to be attacked by abscess. It is said to be commoner in the rich than in the poor natives of India.

The greater susceptibility of the European male to hepatic abscess does not depend, at any rate entirely, on the fact that he is not acclimatised to tropical climates, for hepatic abscess is very rare in European women and children in the tropics, though they are equally subject to dysentery; further, it does not depend on a special liability to dysentery, for in India the natives are more subject to dysentery and less to hepatic abscess than Europeans. The factors which account for the greater liability of European males to hepatic abscess will be referred to again on p. 126.

Occurrence in England.—As already mentioned, most of the cases observed in England have come from tropical climates, but in a certain number of instances the patient has never left this country. An amoebic liver abscess has been recorded in a patient who had never been out of England (Saundby and Miller[1]). The cases seen in ordinary hospital practice are few, probably not more than two or three a year for each of the large London hospitals.

In sixteen years there were 13 fatal cases of single hepatic abscess at St. George's Hospital; in 3 of these the fatal abscess was a recurrence, the patients having been previously successfully operated upon. Ten of the cases, all men, had been abroad, 8 in India, 1 in China, and 1 in South Africa. In 15 fatal cases at Guy's Hospital in twenty years, 5 had been in China, India, or in the West Coast of Africa, but in 10 there was no such history, and several patients had never been out of England (Hilton Fagge[2]).

Alcoholism, by depressing the resistance of the liver, disposes to hepatic abscess. Abscess is rare in total abstainers, and, conversely, natives who drink may suffer from liver abscess while their fellows who are teetotallers escape.

According to Sandwith,[3] hepatic abscess is met with only in those natives of Egypt who are addicted to alcohol. In 40 cases tabulated by E. J. Waring[4] only 13, or 32·5 per cent, were sober and temperate; the remainder, 67·5 per cent, were intemperate. In 170 cases investigated by Megaw[5] 119, or 70 per cent, habitually took alcohol, whilst 51, or 30 per cent, did not.

A stimulating and excessive *diet*, by giving rise to considerable physiological congestion, which under the influence of the tropical climate and a sedentary life may become pathological, prepares the way for hepatitis and so for abscess. As a disposing factor errors of diet are far inferior to alcoholic excess.

Malaria, by diminishing the resistance of the liver and producing a

[1] Saundby and Miller. *Brit. Med. Journ.*, 1909, i, 771.
[2] Hilton Fagge's *Textbook*, edited by Pye-Smith, ii, 525, 4th ed.
[3] Sandwith. Quoted by Davidson, *System of Medicine* (Allbutt and Rolleston), 1907, ii, part ii, 591.
[4] Waring, E. J. *Hepatic Abscess*, p. 114, 1854.
[5] Megaw. *Ind. Med. Gaz.*, 1905, xl, 81.

certain amount of hepatitis, disposes to hepatic abscess, and in a minor degree plays much the same part as alcoholism. Hepatic abscess, however, occurs in places where malaria is unknown. Malaria and dysentery occur so frequently in the same districts that malaria is often an antecedent condition of hepatic abscess. It is not, however, a true cause of hepatic suppuration.

Malta fever may precede, and dispose in a similar way to, hepatic abscess (Gabbi [1]).

Yellow fever may precede the development of an hepatic abscess, but this is probably merely accidental, and there is no reason to think that there is any direct relation between them; though no doubt after yellow fever the resistance of the liver is weakened and the organ more liable to infection.

Sex.—Single tropical abscess is much commoner in males than in females. This applies to adults, for in children the incidence is about equal in the two sexes.

In E. J. Waring's 300 Indian cases 291 were males and 9 females, or 30 to 1; Davidson gives a lower ratio of 7 to 1. In 13 fatal cases at St. George's Hospital 11 were males; in one of the females the abscess was probably connected with cholelithiasis.

The greater predominance of the male sex is due to various factors. First, the larger number of male Europeans resident in tropical climates must be taken into account, for Europeans are much more subject to abscess than natives. But even after allowing for this, males are more subject to abscess than women; for though dysentery affects European men and women equally, abscess seldom occurs in women. The factors which have been thought to increase the tendency of European males to abscess are: (i) Alcoholism, which disposes to hepatitis and favours infection by reducing the resistance of the organ; (ii) greater exposure to chills; and (iii) greater liability to blows in the hepatic region.

Age.—Hepatic abscess is a disease of adult life, and is rare in children and in old persons.

In 227 fatal cases tabulated by Waring,[2] 112, or 49·3 per cent, were between the ages of twenty and thirty. It must be remembered, however, that the cases were from the Indian army, which contained a very large number of men about this age. The oldest case met with by Waring was a pensioner aged seventy-two years, and the youngest in a girl aged fifteen years.

In young children large hepatic abscesses are rare; they may be due to dysentery, to worms in the bile-ducts, to trauma, or to appendicitis.

Legrand [3] collected 31 cases in children due to dysentery. Of Amberg's [4] 12 cases in children due to dysentery, only one (Slaughter's [5]) shewed motile

[1] Gabbi. *Lavori dell' Istituto*, Messina, 1906, Fasc. i, 23.
[2] Waring, E. J. *Loc. cit.*, p. 112.
[3] Legrand. *Arch. de méd. des enfants*, Paris, 1906, ix, 129.
[4] Amberg. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 355.
[5] Slaughter. *Virginia Med. Monthly*, 1895–96, xxii, 722.

amoebae in the pus, though dead amoebae were seen in the pus of Gneftos's[1] case. Amoebic abscess is therefore very rare in children.

Niblock[2] records the case of a child aged eleven months who recovered after 18 oz. of pus had been removed from the abscess. Finizio[3] reports a fatal case of hepatic abscess subsequent to dysentery in a boy aged six years. In a boy aged nine years the abdomen was so distended that the condition was thought to be ascites (Hatch[4]).

Morbid Anatomy.—*Situation.*—Between 60 and 80 per cent of large single abscesses are in the right lobe of the liver. Occasionally a large abscess may occupy parts of both the right and left lobes.

Of E. J. Waring's cases, 67 per cent were in the right lobe; 6·6 per cent in the left lobe; and 14·5 per cent in both the right and the left lobe. In Rouis's[5] series 78·6 per cent were in the right lobe, 16·8 per cent in the left, and 4·6 per cent in the Spigelian lobe. From injection with methylene-blue, Sérégé[6] states that the blood from the stomach and spleen is carried into the left lobe, and that from the pancreas and intestines into the right lobe. This serves in part to explain the greater frequency of abscess in the right lobe. In addition, the right lobe being six times the size of the left naturally receives the larger share of blood. Rogers[7] suggests that the frequency of dysenteric ulceration in the ascending colon and hepatic flexure, which would favour the passage of amoebae across the peritoneum to the surface of the liver, may also account for the preponderance of abscess in the right lobe.

The abscess is often deeply embedded in the right lobe towards its posterior and upper border. When in this situation it may work its way forward and present anteriorly, but more often it projects upwards under the diaphragm. In the latter site the existence of an abscess is often very difficult to determine with certainty by percussion, as it may carry the diaphragm upwards, and if the lung is adherent to the chest wall there will be comparatively little dulness. In such cases skiagraphy is of great service, by shewing the position and amount of movement of the right leaflet of the diaphragm. The under surface of the right lobe of the liver close to the hepatic flexure of the colon is another favourite site of abscess. According to Lafleur[8] and Rogers, it is probable that amoebae may pass through the walls of the colon and infect the surface of the liver at this point.

When an abscess is near the surface of the liver and close to the suspensory ligament, it may rupture into the space between the two layers of that peritoneal ligament and form an abscess between the liver and diaphragm. This has been spoken of as a suprahepatic abscess by

[1] Gneftos. *Deutsche med. Wchnschr.*, 1891, xvii, 853.
[2] Niblock. *Ind. Med. Gaz.*, 1911, xlvi, 137.
[3] Finizio. *Pediatria*, Napoli, 1896, iv, 340.
[4] Hatch. *Ind. Med. Gaz.*, 1898, xxxiii, 285.
[5] Rouis. *Recherches sur les suppurations endémiques*, 1860, Paris.
[6] Sérégé. Vide *Bull. et mém. Soc. méd. des hôp. de Paris*, 1901, 3. s., xviii, 393; *Journ. de méd. de Bordeaux*, May 25, June 1 and 8, 1902.
[7] Rogers, L. *Brit. Med. Journ.*, 1902, ii, 850.
[8] Lafleur. Allbutt's *System of Medicine*, 1897, iv, 156.

Cantlie,[1] who, however, considers that this form of abscess begins in the lymphatics in the ligament and not in the liver.

Number.—A large abscess may be the only focus of suppuration in the liver or it may be associated with one or more abscesses, usually smaller.

In E. J. Waring's 288 fatal cases 177, or 61·4 per cent, were solitary abscesses, and in 33, or 11 per cent, there were two abscesses. Davidson[2] gives 75 per cent as solitary, thus agreeing with Rouis, 11 per cent with two abscesses, and 14 per cent with more than two. In 509 necropsies tabulated by the Sanitary Commissioner with the Government of India there were 34 per cent of single and 66 per cent of multiple abscesses.[3] In 13 fatal cases at St. George's Hospital there was a single abscess in ten.

The smaller abscesses may be secondary and due to infection from the originally single abscess, or they may belong to a series of small abscesses which have united to form an areolar abscess. Two or even three large abscesses may be independent in origin. Godlee[4] believes that many of the cases of a second abscess following a previous one are due to the drainage-tube having been removed too soon, or to some diverticulum of the original abscess having been imperfectly explored and drained.

The *shape* of an abscess varies considerably; usually it is round, but it may be oval or irregular, and when due to the union of previously separate abscesses, may be branching or areolar.

The *size* of a single abscess varies greatly. Not uncommonly it contains three-quarters of a pint of pus, but as much as 16 or even 19 pints have been recorded.

Morbid Appearances of the Liver.—The surface may shew recent inflammation and adherent fibrin over the abscess, or, when the process is of some duration, fibrous adhesions uniting it to the diaphragm, abdominal wall, or adjacent viscera. These are most frequent between the convexity of the right lobe and the diaphragm; the abscess may then project upwards under the dome of the diaphragm and give rise to comparatively little enlargement of the liver in a downward direction.

In its earliest stage a liver abscess appears as a pale, softened area, sometimes irregular in shape from the union of two or more such foci. This condition of commencing suppuration if aspirated may be recognised by finding cylinders of liver cells in the blood-stained material withdrawn, which, however, has no naked-eye resemblance to pus. The softened areas break down into recent abscess cavities which have ragged walls lined by necrosing liver tissue. Immediately around the spreading abscess the liver substance is softened, buff-coloured from swelling, degeneration, and necrosis of the liver cells and infiltration with polymorphonuclear leucocytes. The vessels may contain emboli of pyogenic cocci. As the

[1] Cantlie, J. *Brit. Med. Journ.*, 1899, ii, 646.
[2] Davidson. *System of Medicine*, 1907, ii, part ii, 592.
[3] Report Sanitary Commissioner with Govern. of India, 1901.
[4] Godlee, R. J. *Med.-Chir. Trans.*, Lond., 1902, lxxxv, 119.

inflammatory change spreads outwards it may set up suppurative thrombosis in the portal spaces and thus give rise to foci of suppuration in the neighbourhood, which may eventually open into the original abscess.

In an abscess of some standing there is lining of granulation tissue, which is ragged at first, and later becomes smooth. Outside this there is a fibrous capsule which runs into and invades the surrounding liver substance for a short distance. The internal lining of granulation tissue may have debris and fibrin adherent to it, and is often necrotic on the surface. The granulation tissue contains newly-formed vessels, and in its deeper layers developing fibrous tissue. In this way a capsule is formed, which in old abscesses is of considerable extent, and is formed of dense, well-formed fibrous tissue. This fibrous tissue invades the liver for a short distance and passes between the liver cells, which are flattened and often spindle-shaped, so as to suggest the erroneous view that they become transformed into fibrous tissue. The liver cells proliferate and give rise to columns of small cubical cells—the so-called new bile-ducts—and as a result the developing fibrous capsule around an abscess of some duration contains altered liver cells and pseudobile canaliculi. The capsule of old abscesses is often pigmented, and may be calcified. Occasionally suppurating foci are found outside the comparatively well-formed wall of a single abscess.

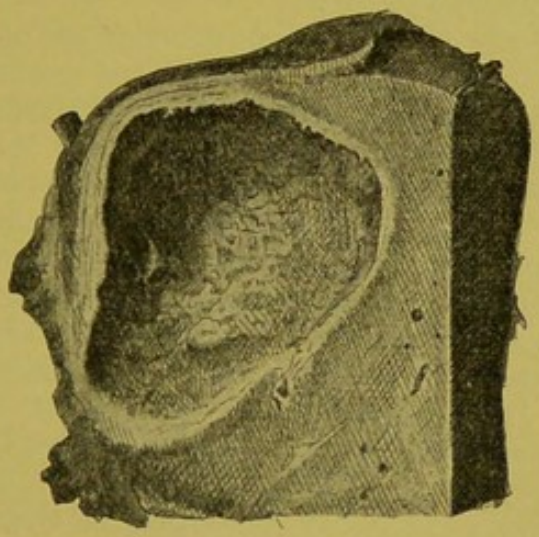


FIG. 20.—Single abscess with a definite capsule. A glass rod shews where it ruptured into the inferior vena cava. From a specimen (series ix, 171M) in St. George's Hospital Museum. (Drawn by L. Jones, M.S.)

FIG. 21.—Section of the right lobe of the liver, shewing the union of a number of separate abscesses into an areolar abscess cavity. From a specimen (series ix, 171C) in St. George's Hospital. (Drawn by Dr. E. A. Wilson.)

The *rest of the liver* is usually enlarged, and after evacuation of the abscess heavier than in health. In 132 cases tabulated by Waring this was the condition of the organ in 113. The large size is chiefly due to parenchymatous inflammation and cloudy swelling, but, in addition, compensatory hypertrophy of the remainder of the liver occurs. In chronic cases in which there has been a fistula, increase in size of the liver may be due to lardaceous disease. There may, in addition, be pylephlebitic abscesses in the liver. In rare instances the liver substance may be bright yellow in colour and firm in consistence, resembling the appearances in phosphorus poisoning.

I met with this appearance in a case of a loculated liver abscess due to infection derived from the appendix which contained a pin.[1] In St. Bartholomew's Hospital Museum there is a specimen (2196D) of multiple abscesses with this appearance. E. J. Waring[2] in 113 fatal cases mentions one in which the liver had this aspect.

The scars of former abscesses that have been opened are sometimes seen. Abscess is very rare in a genuinely cirrhotic liver; in Waring's 113 cases the rest of the liver was cirrhotic in two.

In *amoebic abscesses* of the liver the histological appearances are so peculiar that special reference must be made to them. In small and recent abscesses there is a glairy, translucent fluid, which when removed leaves a shreddy, spongy wall. The wall is irregular from the remains of the portal canals, which are left by the necrosis and disintegration of the surrounding liver cells. The liver cells necrose probably as the result of the action of toxic substances manufactured by the amoebae, and then liquefy and disintegrate. Amoebae are found in the capillaries in the immediate neighbourhood of the abscess. There is a remarkable absence of leucocytic massing in the neighbourhood of the small abscesses which is quite characteristic (Lafleur[3]). The process is one of colliquative necrosis rather than of inflammation. Rogers,[4] however, who regards the small multiple amoebic abscesses as due to a mixed infection of amoebae and pyogenic cocci, figures small-celled infiltration in these minute abscesses.

Large chronic amoebic abscesses differ little from the appearances in other chronic hepatic abscesses. Amoebae are much less numerous than in the recent small amoebic abscesses, but are found in the same situation, viz. in the wall of the abscess cavity.

Contents of the Abscesses.—In large abscesses the character of the pus may vary very considerably; it may be white and creamy, yellow, brownish-red or chocolate colour, green; thick, mucoid, or even serous. The red colour is due to admixture with blood and the remains of the liver tissue. In amoebic abscess the contents of the smaller abscesses are

[1] Rolleston. *Trans. Path. Soc.*, 1898, xlix, 106.
[2] Waring, E. J. *Abscess of the Liver*, p. 137, 1854.
[3] Lafleur. Allbutt's *System of Medicine*, 1897, iv, 158.
[4] Rogers, L. *Brit. Med. Journ.*, 1903, i, 1318.

translucent, glairy, and do not flow easily. In larger amoebic abscesses the fluid is very viscid and does not resemble ordinary pus.

Microscopically the amoebic abscesses contain amoebae, which are naturally more numerous in the recent abscesses, necrosing liver cells, and red blood-corpuscles. Very few leucocytes are present, and the contents thus differ markedly from ordinary pus. Charcot-Leyden crystals have been found (Kruse and Pasquale[1]). Amoebic abscesses may be free from any pus-producing bacteria; Rogers says this is so in 80 per cent of the cases; they may contain various micro-organisms, such as streptococci, staphylococci, *Bacillus coli*. The pus is said to have a mawkish taste, and is not, as a rule, offensive. In abscesses on the under surface of the liver in contact with the bowel the contents may have a very faecal odour, due probably to secondary infection with members of the colon group. Da Costa[2] mentions an abscess of the liver secondary to appendicitis, which contained gas produced by bacteria.

Bacteriology.—Hepatic abscesses may be divided into (i) those which contain amoebae—called dysenteric by Kartulis; and (ii) the non-amoebic, due to micro-organisms, usually absorbed from the alimentary tract, and termed by Kartulis idiopathic.

Amoebae.—Since the discovery of amoebae in dysentery and in hepatic abscesses, some uncertainty has naturally arisen as to what proportion of the cases of tropical liver abscesses are due to this cause and to what extent amoebae are concerned in the production of suppuration.

Three species of amoebae occur as internal parasites of man; it is usually stated that the *Amoeba buccalis*, met with in patients with carious teeth, and the *Amoeba coli* Lösch occurring in the colon are harmless, and that the *Entamoeba histolytica* Schaudinn is the only one concerned in amoebic dysentery; but recent observations shew that this view is too sweeping (Greig and Wells[3]).

The causal relation of amoebae to the amoebic abscesses of the liver has given rise to a considerable amount of discussion, and the question is very far from being settled. The following views have been held.

(1) Kartulis,[4] who first recognised amoebae in the pus of liver abscesses, believed that they played an important accessory part in the production of abscesses, by conveying pus-producing micro-organisms to the liver and by rupturing the hepatic capillaries by their active movements; the production of pus not being due to amoebae, but to the pyogenetic micro-organisms.

(2) Kruse and Pasquale regarded the disintegration of the liver and abscess formation as due to a direct co-operation of the amoebae with micro-organisms.

(3) It has been suggested that the presence of amoebae in liver

[1] Kruse und Pasquale. *Ztschr. f. Hyg.*, 1894, xvi, 1.
[2] Da Costa. *Modern Surgery*, p. 875, 1907.
[3] Greig and Wells. *Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Government of India*, 1911, N.S., No. 47.
[4] Kartulis. *Centralbl. f. Bakt.*, 1887, ii, 745; *Virchows Arch.*, 1889, cxviii, 97.

abscesses is a secondary infection, and that they gain a footing in the liver only when it has been damaged by bacterial invasion (Sheldon Amos [1]). This view is supported by the absence of amoebae from some cerebral abscesses in cases in which they are found in the pus from the liver. Kelsch and Nimier [2] deny that amoebae are responsible for the production of liver abscess.

(4) Councilman and Lafleur [3] believe that the amoebae alone are responsible for the abscess, since in the smallest abscesses bacteria are absent while amoebae are plentiful. In larger abscesses bacteria are not numerous, and the lesions are not like those produced by bacteria. These lesions are largely necrotic, and are thought to be due to a soluble toxin manufactured by the amoebae. L. Rogers [4] endorsed Councilman and Lafleur's view that amoebae alone give rise to large hepatic abscesses, as he finds that at least two-thirds of amoebic abscesses are quite free from ordinary pyogenetic organisms, and in the view that amoebae may work their way from the bowel across the peritoneum to infect the surface of the liver.

When an abscess is opened, amoebae usually do not appear in the pus until some days have elapsed; the explanation of this is that amoebae are chiefly found in the walls of the abscess and not in its contents. By scraping the wall of the abscess amoebae may be found, though absent from the pus (Rogers [5]). In hepatic abscesses examined in England, Manson [6] found amoebae in considerably over 50 per cent.

Bacteria.—In non-amoebic cases bacteriological examination of the pus has given discordant results. In some instances the pus is sterile; this has been explained by supposing that in chronic cases the micro-organisms originally present have died out. Pus-producing micro-organisms have frequently been found, such as the *Staphylococcus pyogenes aureus, albus, citreus*, and streptococci. Typhoid bacilli have been found in pure culture (Cassuto [7]) or in combination with other micro-organisms. Ordinary pneumococci, Friedländer's pneumobacillus, *Bacillus pyocyaneus*, and the colon bacillus are also sometimes present. Eyre and Fawcett [8] described a case in which there was a pure culture of *Micrococcus melitensis*. Diplococci resembling gonococci were obtained from an hepatic abscess of a native Egyptian who denied gonorrhoea (Bousfield [9]). In an areolar abscess Hewitt [10] found *Bacillus mucosus capsulatus*.

Inflammation of the *pleura* is a very common occurrence in hepatic abscess; it may be due to a spread of infection along the lymphatics and may be dry, serous, or purulent. Pleurisy may give rise to universal

[1] Sheldon Amos. *Journ. Path. and Bacteriol.*, 1902, viii, 346.
[2] Kelsch et Nimier. *Bull. Acad. de méd.*, Paris, 1900, xliii, 237.
[3] Councilman and Lafleur. *Johns Hopkins Hosp. Rep.*, 1891, ii, 395.
[4] Rogers, L. *Brit. Med. Journ.*, 1902, ii, 844; 1903, i, 1315; 1906, i, 1397.
[5] *Idem. Ibid.*, 1905, ii, 1291.
[6] Manson. *Tropical Diseases*, p. 456, 1903.
[7] Cassuto. *Thèse de Paris*, 1900.
[8] Eyre and Fawcett. *Guy's Hosp. Rep.*, 1905, lix, 206.
[9] Bousfield. *Journ. Roy. Army Med. Corps*, 1908, x, 80.
[10] Hewitt. *Johns Hopkins Hosp. Bull.*, Balt., 1909, xx, 77.

adhesions and so prevent the abscess rupturing into the pleura, but thus favour its rupture into the lung. An empyema due to this course may, as in Duplant's case, be encysted between the lobes of the lung. Rupture or direct leakage of an abscess into the pleura will give rise to a large empyema.

Lungs.—The lower lobe of the right lung may be compressed by the upward pressure of the liver and diaphragm, or by a pleural effusion; or if it is adherent to the diaphragm it may become inflamed from direct extension of inflammation from the abscess through the diaphragm, or the abscess may burst into the lung. In cases in which the abscess has leaked into the hepatic veins or into the inferior vena cava there may be pyaemic abscesses in the lungs. The rupture of an hepatic abscess into the lung will be referred to on p. 141.

Clinical Picture.—*Symptoms.*—Latency; onset; fever; sweating; rigors; pain; shoulder pain; tenderness; cough; digestive disturbances; arthritis; nervous disorders.

There is very great variation both in the individual symptoms and also in their association; this is shewn by the number of conditions for which hepatic abscess has been mistaken (*vide* p. 146). Very frequently the symptoms suggest rather than definitely point to hepatic abscess.

Latency.—An abscess may remain perfectly latent and only be found at death; according to Rouis, this occurs in 13 per cent. In some cases there are no definite symptoms or signs until the abscess ruptures and rapidly brings about a fatal result.

The onset of symptoms is gradual, as a rule, and is ushered in by malaise, languor, general debility, and the signs and symptoms of acute congestion of the liver and acute hepatitis (*vide* p. 115). Indefinite malaise may precede by many weeks any definite evidence of abscess. In some instances there is an acute onset with shivering or a rigor, so as to imitate pneumonia of the right lower lobe.

Fever is perhaps the most constant sign of hepatic abscess. The temperature varies; it may be continuous at first, then remittent, and in the later stages intermittent. It may closely imitate malaria, or be extremely irregular. In chronic cases the temperature may be normal, and in severe and advanced cases it may be low and even subnormal.[1] In exceptional instances there may be little or no fever, even with a large and recent abscess. There may be practically no pyrexia from start to finish.

Moir[2] records an abscess containing 70 ounces of pus, in which the temperature ranged between subnormal and 99° F.

Sweating.—Nocturnal sweats may be very profuse. Perspiration often occurs during the day when the patient drops off to sleep. In fact, the sweating is more related to sleep than to the night hours, and is chiefly nocturnal because sleep is more general then.

[1] Smith, Johnson. *Brit. Med. Journ.*, 1900, ii, 550.
[2] Moir, D. M. *Ind. Med. Gaz.*, 1897, xxxii, 218.

Rigors are often met with in the course of the disease. In some cases there is a single rigor at the onset or early in the course of the disease; in others there are frequent rigors; in some instances they do not appear until near the end of the case. A feeling of chilliness often accompanies the evening rise of temperature.

Pain over the liver and a sense of fulness in the right hypochondrium are very commonly present. Though pain may be present from the start of suppuration, it is much more in evidence when the abscess is large and approaching the capsule of the liver, than early in the process or when the abscess is deeply situated. The pain may be constant and dull, probably from increased tension inside the liver; this is usually early in the disease; or intermittent and sharp and stabbing, and, like pleuritic pain, brought on by respiratory movements. It may be actually due to pleurisy or to inflammation of the capsule of the liver, and is then rather a late symptom. Pain on swallowing, due to disturbance of the liver by food entering the stomach, is mentioned by Manson.[1]

Shoulder Pain.—In abscess, as in some other affections of the liver, pain may be referred to the shoulder, and may be felt over the scapula or at the tip of the acromion process. According to Manson, it occurs in about one-sixth of the cases. It has been suggested that this localisation may depend on the communication between the nerve to the subclavius muscle and the phrenic nerve. It is most frequently present when the abscess is in the upper part of the right lobe. In abscesses in the left lobe the pain may be referred to the left shoulder. Very rarely the pain is bilateral (E. J. Waring[2]).

Tenderness.—On deep palpation or percussion tenderness of the liver is generally elicited, and is perhaps the least unsatisfactory sign of hepatic abscess.[3] This localised tender spot is a useful guide to the position of the abscess. Occasionally vomiting is constantly induced by pressure on one spot (Smits[4]).

Cough.—In hepatic abscess there is often a spasmodic hacking cough, which is usually worse at night, and may be ineffectual or unaccompanied by sputum. It may be due to irritation of the pleura over the diaphragm, to actual pleurisy, or possibly merely to reflex irritation from the liver. It is not peculiar to liver abscess. When the abscess discharges through the lung, severe cough comes on and expectoration may be copious. As much as 4 pounds of pus has been brought up in twenty-four hours (Waring[5]). The colour of the expectorated matters differs greatly in different cases; it may be mixed with bile. In amoebic abscesses amoebae may be found in the sputum before the abscess has burst into the lung.

Digestive Symptoms.—Vomiting appears to be more frequent when the

[1] Manson, P. *Tropical Diseases*, p. 353, ed. i, 1898, London.
[2] Waring, E. J. *Abscess of the Liver*, p. 147, 1854.
[3] Smith, Johnson. *Brit. Med. Journ.*, 1900, ii, 550.
[4] Smits. *Arch. f. klin. Chir.*, 1900, lxi, 173.
[5] Waring. *Loc. cit.*, p. 153.

abscess is in the left lobe or when there is an abscess in the left lobe together with one in the right. In very rare instances vomiting may be due to the abscess pressing on the pylorus and leading to pyloric obstruction. Maclean[1] described pyloric obstruction due to hepatic abscess. Appetite is poor or completely lost, as a rule, but sometimes it is well preserved. Flatulence may be troublesome.

There may be constipation, diarrhoea, or the two may alternate. Absorption from the abscess may give rise to ulceration of the intestine and diarrhoea. A recrudescence of a former dysentery is not uncommonly described. When the abscess bursts into the alimentary tract, large quantities of pus may appear in the stools. In rare cases there may be considerable haemorrhage from the bowel.[2]

Captain Weston, R.A.M.C., has told me of a case in which there were profuse haemorrhages from the bowel apparently due to an abscess in the quadrate lobe of the liver pressing on the portal vein.

Arthritis, etc.—Swelling and painful enlargement of the joints may occur, just as in dysentery. They may be pyaemic, but are probably usually toxic; at any rate, they tend to disappear when the abscess is opened or discharges. Girard[3] observed clubbing of the fingers in a case of hepatic abscess free from pulmonary lesions. Possibly this change was toxic.

Nervous Symptoms.—As in most hepatic diseases, there is a good deal of irritability or mental depression, which may even become so marked as to pass into melancholia. Insomnia is very common. The mental disturbance may be referred to the action on the cerebral cortex of poisons absorbed from the liver abscess or from the alimentary tract, the liver being unable to deal with them. Cerebral symptoms in rare instances depend on pyaemic abscesses in the brain or on meningitis. In the terminal stages delirium or, in rare instances, convulsions may occur.

Physical Signs. — Wasting; decubitus; facial aspect; jaundice; pulse; blood; respiratory system; abdominal signs—painful succussion, skiagraphy, rigidity of right rectus muscle, ballottement, hepatic dulness, friction; oedema of feet; urine.

Wasting is progressive and may be very considerable; its degree necessarily depends on the duration and intensity of the disease and the size of the abscess. In rare instances weight may actually be put on while an abscess is maturing (Osler[4]).

Decubitus, or the position assumed by the patient, is generally dorsal or right-sided, as being that in which there is greatest freedom from pain. When the patient lies on his back, the chest is raised and the knees are somewhat flexed. When he turns on to the left side, the liver tends to fall away from the wall of the abdomen on the right side, and

[1] Maclean. *Brit. Med. Journ.*, 1874, ii, 138.
[2] Hassler. *Deutsche med. Wchnschr.*, 1902, xxviii, 47.
[3] Girard. *Compt. rend. Soc. Biol.*, Paris, 1903, liv, 106.
[4] Osler. *Med. News*, N.Y., 1902, lxxx, 673.

pain is frequently felt. This is probably due to stretching of adhesions or to the separation of the inflamed capsule of the liver from the parietal peritoneum. On the other hand, the patient is sometimes more comfortable on the left side. The differences in the position assumed by the patient may depend on the increased size of the liver and on the presence of adhesions. Thus, when the liver is greatly enlarged the right-sided position is most comfortable; but with peritoneal adhesions in certain situations, the right-sided position may give rise to tension on them and so to pain.

Facial Aspect.—The complexion is pale or sallow with a muddy tint, and often slightly icteric. The conjunctivae if not jaundiced are often of a waxy, white colour. The expression is anxious and worried, the eyes are often sunken, and the general aspect, which is more easily recognised than described, may be peculiarly suggestive of the disease. The skin in the early stages may be hot and dry, but later it becomes moist and clammy.

A remarkable diffuse cyanosis, for which there was no satisfactory explanation, was noticed by Osler in one case.

The tongue is usually furred along the centre with a red tip. A smooth red tongue with fissures running in all directions is not uncommon. Brun,[1] indeed, considers a bright red and absolutely dry tongue to be pathognomonic. A strong hepatic odour from the patient is described by Hatch[2]; probably it is present only when the abscess is of considerable size.

Jaundice is very rarely deep; a slight degree, probably due to local catarrh of intrahepatic ducts near the abscess, and tingeing the conjunctivae, are sometimes present. In exceptional cases an abscess may press on the extrahepatic ducts in the portal fissure (Moir[3]).

Definite jaundice was seen in 58 out of 375 cases, or in 16 per cent (Thierfelder[4]).

The pulse is of low tension, full, and somewhat quickened—80 to 100. Exceptionally it is slow.

The blood may shew leucocytosis; and this, when present, is of great service in distinguishing hepatic abscess from malaria or typhoid fever. The existence of considerable leucocytosis—30,000 to 50,000 per cubic millimeter—has led to the detection of abscess in patients formerly the subjects of dysentery (Boinet[5]) or thought to have malaria (Rogers[6]). When leucocytosis is present, it is said to be constant (Boinet), and not to appear and disappear as it does in intermittent hepatic fever. The

[1] Brun. *Rev. de méd.*, Paris, 1904, xxiv, 396.
[2] Hatch. *Brit. Med. Journ.*, 1900, ii, 1374.
[3] Moir. *Ind. Med. Gaz.*, 1902, xxxvii, 391.
[4] v. Ziemssen's *Cyclopaedia of Practical Medicine*, 1880, ix, 126.
[5] Boinet. *Compt. rend. Soc. Biol.*, Paris, 1900, lii, 1089.
[6] Rogers, L. *Brit. Med. Journ.*, 1902, i, 831; ii, 844; 1905, ii, 1291.

differential count is usually said to give a high percentage (75 to 80) of polymorphonuclears; according to Marchoux[1] and Rogers[2] this is true of abscesses due to bacterial infection, but not of amoebic abscesses in which there is increase of the mononuclears. Leucocytosis, though highly suggestive, is not constantly found in abscess. When absorption is prevented by a thick capsule there may be no leucocytosis. It has been thought that leucocytosis is most marked in small, deeply seated abscesses, and less in large abscesses bulging on the surface of the liver (Rogers).

It was absent in 3 out of 5 cases recorded by Osler,[3] and in 6 cases mentioned by Charles[4]; Rispal[5] failed to find more than a slight leucocytosis (15,000 per cubic millimeter) in 3 cases.

Iodophilia, or the iodine reaction in the polymorphonuclears, occurs unless the abscess is so thick-walled as to prevent absorption (Da Costa[6]). Blood-cultures are said to be negative by Libman[7]; but in bacterial cases the blood may shew the corresponding micro-organism (Simon[8]).

Respiration is shallow and chiefly thoracic, since movement of the abdomen may cause pain. The rhythm is more rapid than normal, both because of the fever and on account of the shallow respirations. In cases of amoebic abscess the organisms may be found in the expectoration.

Lung Signs.—Compression of the lower lobe of the right lung, as shewn by crepitations and dulness, is common. When inflammation has spread through the diaphragm to the pleura, friction may be heard. Hepatic abscess may therefore imitate pneumonia or empyema at the right base; right-sided pleurisy in a patient who has had dysentery should always suggest the possibility of an abscess of the liver. The appearance of pleuritic friction in a case of suspected hepatic abscess is a sign that the inflammatory process is spreading to the thorax, and is therefore a signal for operative interference, so as to prevent rupture of the abscess into the pleura or into the lung. But in some cases of acute hepatitis which have been fruitlessly explored and have recovered, friction at the base of the right lung has been present.

Hepatic abscess may cause an empyema in several ways. The abscess may burst directly into the pleura, or the infection may spread through the diaphragm, or pus may pass into the pulmonary artery and set up abscess formation in the lung with the secondary production of an empyema. An empyema may form between the lobes of the lung and be very difficult to evacuate.

Rupture of an hepatic abscess into the lung may give rise to the

[1] Marchoux. *Brit. Med. Journ.*, 1908, ii, 1252.
[2] Rogers, L. *Med.-Chir. Trans.*, London, 1907, xc, 163.
[3] Osler. *Med. News*, N.Y., 1902, lxxx, 673.
[4] Charles. *Brit. Med. Journ.*, 1908, ii, 1235.
[5] Rispal. *Compt. rend. Soc. Biol.*, Paris, 1901, liii, 862.
[6] Da Costa. *Therap. Gaz.*, Detroit, 1906, xxii, 676.
[7] Libman. *Am. Journ. Med. Sc.*, Phila., 1908, cxxxvi, 518.
[8] Simon. *Clinical Diagnosis*, p. 641, 1911.

signs of a cavity in the lower lobe, which, according to Godlee,[1] are usually below and to the inner side of the right nipple, but may be present posteriorly.

The heart's apex may be displaced upwards, into the fourth space, especially when the abscess is in the left lobe of the liver.

The abdomen is full and somewhat distended; sometimes the distension is general, as if from tympanites. There is often definite fulness or bulging in the right hypochondrium or epigastrium, and sometimes a rounded projection in the position of, or in connexion with, the liver may be seen to move with respiration. In some cases fluctuation can be made out over the tumour. An abscess near the middle line of the body may shew transmitted impulsation from the aorta.

Carpenter[2] describes a painful swelling the size of a fetal head pulsating visibly, but not expansile; operation proved that it was an hepatic abscess containing two pints of pus.

Bulging of the chest on the right side as compared with the left, and in some cases protrusion and widening of the intercostal spaces, may be seen. Redness of the skin or localised oedema indicates that an abscess is in close contact with the affected cutaneous area. Though a very valuable sign, oedema over the abscess is only present in about 5 per cent of the cases (Stevenson[3]). A very large abscess may fill the greater part of the abdomen, and has given rise to a diagnosis of ascites. Much ascites is extremely rare. Bradshaw[4] records a case in which ascites appeared to be due to the pressure exerted on the portal vein by an abscess in the Spigelian lobe. It is possible that it may be induced by puncture of the liver with subsequent escape of blood into the peritoneal cavity; I have seen one case suggesting this sequence of events.

Painful Succussion.—If the patient is shaken, much in the same manner as in obtaining "Hippocratic succussion" in pyopneumothorax, pain is felt in the liver and may spread to the right shoulder, the pit of the stomach, across the abdomen, or to the right iliac fossa, according to the situation of the abscess. Malbot[5] considers this a certain sign of abscess.

Skiagraphy.—In health the shadow cast on the screen shews that the right leaflet of the diaphragm is 1½ inches above the level of the left leaflet, and moves with respiration. In cases of abscess it is displaced upwards and does not move. Dr. Herringham has told me of a large hepatic abscess which displaced the diaphragm upwards, but did not prevent it from moving freely with respiration. The position of the abscess may be shewn by increased density of the shadow.

Rigidity of the upper part of the right rectus muscle may certainly occur when an abscess is present, but it is far from constant; moreover, it is

[1] Godlee. *Med.-Chir. Trans.*, Lond., 1902, lxxxv, 119.
[2] Carpenter. *Brit. Med. Journ.*, 1899, ii, 208.
[3] Stevenson. *Lancet*, 1898, i, 1428.
[4] Bradshaw. *Ibid.*, 1908, i, 146.
[5] Malbot. *Arch. gén. de méd.*, 1899, clxxxiv, 172.

met with in other conditions, such as inflammation of the gall-bladder, disease of the pylorus, duodenal ulcer, or inflammation of the muscle itself, and therefore is not a sign of any very special value. The rigidity of the rectus may considerably interfere with the examination of the liver. Dalton [1] refers to a case in which the rigidity did not relax under an anaesthetic.

Percussion, besides eliciting tenderness and causing pain, may convey to the examiner a sensation of *ballottement*, as if he were percussing a thick-walled elastic bag filled with air.[2]

Hepatic Dulness.—The area of hepatic dulness is increased both in an upward and in a downward direction. Though this is the rule, it is not without exception, and in some instances the underlying colon may mask the dulness which a collection of pus would naturally give rise to. The dulness in extreme cases may reach as high as the second rib (Waring [3]). As the abscess is usually in the right lobe, the enlargement is mainly on that side, and since the abscess is most frequently near the convexity of the liver, the enlargement is chiefly in an upward direction and not downwards, as in cirrhosis and in lardaceous and malignant disease. When an abscess is in the posterior and upper part of the right lobe there may be no hepatic enlargement below the costal arch. When the abscess is deeply situated, the whole lobe is expanded and enlarged, but later, when the abscess reaches the surface, it may give rise to a definite projection from the outline of the organ.

Friction due to perihepatitis, set up by the approach of the abscess to the surface of the organ, may be heard or sometimes even felt by the hand. There is commonly friction over the base of the right lung, due to pleurisy set up by the spread of infection along the lymphatics of the diaphragm.

Fine crepitation, like that obtained by pressing on frozen snow, may be heard over the liver; it occurs with inspiration and expiration. Bertrand regarded it as due to perihepatitis, but Hassler and Boisson have heard it in cases in which laparotomy shewed that there was no perihepatitis, and believe that it is produced in the softened and oedematous liver substance around the abscess.

The *spleen* is rarely enlarged. This is of importance in distinguishing abscess from malaria.

Oedema of the feet often occurs late in the course of the disease.

The urine is high-coloured and may be of a high specific gravity, and loaded with urates. When considerable destruction of the hepatic substance has taken place, the amount of urea may be diminished and the ammonia increased. According to Axisa [4] the diminution on the amount of urea runs parallel with the size of the abscess. Indican may occur. Albuminuria is sometimes present. From absorption of pus albumose

[1] Dalton, N. *King's Coll. Hosp. Rep.*, 1896, ii, 25.
[2] Hassler et Boisson. *Rev. de méd.*, Paris, 1896, xvi, 785.
[3] Waring, E. J. *Abscess of the Liver*, p. 149, 1854.
[4] Axisa. *Zentralbl. f. inn. Med.*, 1905, xxvi, 929.

may be found in the urine; but it has been absent in the cases I have seen.

In a case of abscess following dysentery crystals of leucine, tyrosine, and cholesterol were present in the urine for ten weeks; on opening the abscess the urine became normal.[1] Crystals resembling tyrosine, but really composed of a soap of lime and magnesium, were found in one case by Pfahler.[2]

Course and Duration.—The abscess may remain latent until it ruptures and gives rise to acute symptoms or is revealed by a discharge of pus from the alimentary or respiratory tract. It is difficult to say when hepatitis passes into suppuration, and therefore to estimate precisely the duration of an abscess in the liver. An abscess may run its course in three weeks, or if it gives rise to a fistula, especially in connexion with the lungs, may drag on for many months.

Termination.—If not operated upon, an hepatic abscess may either remain intact or may rupture into some neighbouring cavity or viscus. An abscess which remains intact may in rare instances tend to dry up and become shut off and encysted, giving rise to a caseous mass surrounded by a fibrous capsule. How often this actually occurs it is difficult to say, inasmuch as an abscess cannot be certainly diagnosed until it has reached a considerable size, and would then be operated upon.

In 25 cases in which recovery took place, there were fair grounds for believing that the abscess underwent this spontaneous cure in two (E. J. Waring[3]).

Possibly this spontaneous cure is even less frequent than is sometimes thought, since some so-called "receding" abscesses found post-mortem may in reality have been gummas. If the abscess remains intact and does not discharge its contents spontaneously, it usually leads to death.

In 300 fatal cases tabulated by E. J. Waring, 48, or 16 per cent, were operated upon, while 169, or 56 per cent, died with the abscess intact.

Though the abscess practically remains intact, it may give rise to secondary abscesses in the lungs and to general pyaemia. Death may be due to detachment of a thrombus formed in one of the hepatic veins and pulmonary embolism. In some cases the destructive suppurative change in the lungs may cause fatal haemoptysis. As a rule, the fatal result is due to septicaemia and exhaustion. Diarrhoea or an apparent recurrence of dysentery may carry the patient off. In rare cases death may be directly due to intestinal haemorrhage (Hassler,[4] Duplant[5]).

Rupture.—If undetected or not operated upon, an hepatic abscess may rupture internally, or in very rare instances on the surface of the body.

[1] *Lancet*, 1909, ii, 1729.
[2] Pfahler. *New York Med. Journ.*, 1902, lxxv, 270.
[3] Waring, E. J. *Abscess of the Liver*, p. 195, 1854.
[4] Hassler. *Deutsche med. Wchnschr.*, 1902, xxviii, 47.
[5] Duplant. *Lyon méd.*, 1902, xcviii, 109.

The percentage of cases in which rupture occurs depends on the diagnosis and on the frequency with which operative measures are undertaken. In 563 cases of hepatic abscess collected by Cyr, 83, or 15 per cent, were operated upon, and rupture occurred in 159, or 28·6 per cent. But interesting examples of perforation of hepatic abscess are more likely to be put on record than more commonplace cases. More than half the cases of perforation, as will be seen from Cyr's and Thierfelder's tables, were in an upward direction—through the diaphragm.

	Cyr,[1] 159 Cases.		Thierfelder,[2] 170 Cases.	
Lung	59	57 per cent.	74	59 per cent.
Pleura	31		26	
Pericardium	1		4	
Peritoneum	39		23	
Stomach	8		13	
Intestines	13		32	
Kidney	2		1	
Inferior vena cava	3			
Bile passages	4			
Externally	2			

In both these series perforation occurred in two positions in three cases, so that the numbers of the perforations exceed the number of cases.

The various situations in which rupture occurs may conveniently be considered seriatim under the following heads : rupture into—(1) Lung, (2) Pleura, (3) Pericardium, (4) Peritoneum, (5) Stomach and duodenum, (6) Intestines, (7) Gall-bladder and bile-ducts, (8) Kidney, (9) Hepatic veins and Inferior Vena Cava, (10) Portal Vein, (11) On the surface of the body.

(1) *Rupture into the Lung.*—This is the most frequent method by which an hepatic abscess spontaneously discharges. In an overwhelming majority of cases it is the right lung into which the abscess opens. Before the abscess can extend into the lung the liver must become adherent to the diaphragm, and the diaphragm to the base of the lung. The inflammatory processes necessarily cause pain and usually signs of basal pleurisy and cough. Inflammation spreads into the lung and consolidation with suppuration ensues ; the communication between the abscess in the liver and that in the lower lobe of the right lung is usually somewhat small, like a shirt-stud abscess, and may be missed ; in some instances no naked-eye perforation of the diaphragm is forthcoming. In rare cases there may be a small collection of pus between the diaphragm and lung as well as an abscess in the lower lobe of the lung. The formation of an abscess in the lower lobe is, according to Lafleur, due to an extension of inflammation and infection by continuity from the liver, and not haematogenous and due to embolism through the pulmonary artery. On the other hand, amoebae have been found in the small branches of the pulmonary

[1] Cyr. *Traité pratique des maladies du foie*, 1887.

[2] Thierfelder. *Cyclopaedia of the Practice of Medicine*, v. Ziemssen, 1880, ix, 138.

artery, so that haematogenous infection is quite conceivable. The suppurative process in the lower lobe spreads into the surrounding pulmonary tissue and tends to produce fistulous passages in the lung which as a result becomes much disorganised. The abscess discharges into one of the bronchi in the lower lobe of the lung and characteristic sputum mixed with blood is coughed up. The sputum contains pus, blood, and often fragments of hepatic and pulmonary tissue, fat globules, micro-organisms, and amoebae. Occasionally a fistulous communication between the bronchi and a bile-duct in the liver may be established and bile may be brought up from the lungs.

The pulmonary abscess may progress, and, indeed, prove fatal from exhaustion or haemoptysis, when the original hepatic abscess has undergone complete cure. Since the pus is like that brought up from the liver and may contain amoebae, the expectoration of chocolate-coloured pus does not prove that the original liver abscess has not healed (Godlee [1]). Lafleur [2] gives a very unfavorable prognosis in rupture of amoebic abscess of the liver into the lung. Other writers take a very different view; Decastro,[3] for example, estimating that recovery occurs in 76 per cent of the cases.

(2) *Rupture into the pleura*, though much the same process, is less frequent than rupture into the lung. This depends on the fact that the abscess as it advances through the diaphragm tends to set up adhesive pleurisy and so glues the lower lobe of the lung to the diaphragm. When the abscess opens into the pleura, the signs are those of an empyema. The effusion may reach a very large size with great rapidity and seriously endanger life.

(3) *Rupture into the Pericardium.*—Rupture into the pericardium is very rare, since this is likely to occur only when the abscess is in the left lobe of the liver—a rare situation.

Waring [4] quotes 6 recorded cases and I have notes of 13 others, making 19 in all. In Bentley's [5] case there were four pints of sero-purulent fluid in the pericardium which communicated with an abscess in the left lobe of the liver. Rupture of an hepatic abscess which also communicated with the intestine has been known to set up a gaseous purulent pericarditis (Wilks [6]).

An abscess in the left lobe may leak on to the surface of the liver and set up a subphrenic abscess which may subsequently perforate into the pericardium (Tolot [7]). The clinical evidence of rupture into the pericardium is severe pain, dyspnoea, and the rapid development of a pericardial effusion. Death usually, but not invariably, follows very soon after this accident.

1 Godlee. *Med.-Chir. Trans.*, Lond., 1902, lxxx, 119.
2 Lafleur. Allbutt's *System of Medicine*, 1897, iv, 168.
3 Decastro. *Des abcès du foie des pays chauds*, Paris, 1870.
4 Waring, E. J. *Abscess of the Liver in the East Indies*, p. 133, 1854.
5 Bentley. *Trans. Path. Soc.*, 1850, ii, 70.
6 Wilks. *Lectures on Pathological Anatomy*, p. 108, ed. iii, 1889.
7 Tolot. *Lyon méd.*, 1902, xcviii, 51.

(4) *Rupture into the Peritoneum.*—This is comparatively common. It may occur into the general peritoneal cavity, or may give rise to a localised intraperitoneal abscess which may subsequently burst into the general cavity of the peritoneum, or may discharge into the bowel or even externally. Rupture into the general peritoneum may be due to trauma or to muscular exertion, and the danger of leakage must always be borne in mind when aspiration with a trocar through the abdominal wall is contemplated. Perforation into the general peritoneal cavity is more likely to follow sudden exertion or trauma than to occur spontaneously, as an abscess pointing on the surface of the liver tends to set up local peritonitis and adhesions before actually rupturing. Rupture into the general cavity of the peritoneum causes severe collapse, and if the patient survives long enough, acute peritonitis, which is nearly always fatal. In cases in which the existence of an hepatic abscess has not been recognised, the sudden onset of acute symptoms may imitate perforation of an intestinal ulcer in ambulatory typhoid fever.

A soldier, aged twenty-seven, who had contracted dysentery in the Transvaal War of 1900, was admitted moribund into St. George's Hospital. The necropsy disclosed several pints of turbid fluid in the peritoneal cavity and general peritonitis due to leakage from an abscess in the left lobe of the liver. The ruptured abscess was thin-walled and quite small, it communicated with a large abscess the size of a fetus' head, which occupied the whole of the left lobe of the liver, and had walls composed of glistening fibrous tissue about $\frac{1}{2}$ inch thick. The right lobe of the liver was greatly scarred from cicatrices, but did not contain any gumma ; it shewed early lardaceous change. The portal vein was thrombosed ; there had probably been ascites before the onset of acute peritonitis.

Hulke [1] recorded recovery from rupture of an hepatic abscess into the general peritoneal cavity which was flushed out some twenty-four hours after rupture occurred. In this patient an hepatic abscess had previously ruptured through the lung, and rather more than a year after recovery from the operation for rupture into the peritoneum, a third abscess in the liver was successfully operated upon.

(5) When rupture occurs into the *stomach or duodenum* pus is vomited, sometimes in very considerable quantities, and is passed by the bowel, but from the distance which it has to travel the pus may not be detected in the faeces. After rupture the size of the liver may perceptibly diminish, and in some instances a tympanitic note has resulted from entrance of air into the abscess cavity. Rupture into the stomach is preceded by dyspepsia and discomfort, and accompanied by vomiting and severe epigastric pain.

(6) *Rupture into the Intestines.*—An hepatic abscess very seldom opens into any part of the small intestine except the duodenum. Rupture into the colon is not uncommon ; it is accompanied by colicky pain and collapse, and is followed by the passage of pus by the bowel.

(7) *Rupture into the gall-bladder or bile-ducts* is very rare. The pus may pass down the common bile-duct into the duodenum and so imitate

[1] Hulke. *Med.-Chir. Trans.*, 1893, lxxvi, 81.

rupture of an abscess into the bowel. Symptoms of biliary colic have been noted.

(8) *Rupture into the pelvis of the right kidney* is very rare. H. J. Waring[1] estimates the recorded cases at about 10.

(9) *Rupture into the Hepatic Veins and Inferior Vena Cava.*—Since the hepatic veins are not surrounded by any fibrous sheath at all comparable to Glisson's capsule around the portal canals, an hepatic abscess is more likely to leak or rupture into them than into the branches of the portal vein. The abscess may burst into one of the hepatic veins quite close to the inferior vena cava. In a few cases hepatic abscess has perforated directly into the inferior vena cava and not into the hepatic veins.

Cyr's list contains 3 cases. Flexner[2] (1897) described 2 cases and Novis 1.[3] In a case in St. George's Hospital (Fig. 20) the abscess occupied a third of the liver and had set up parietal thrombosis in the inferior vena cava. The pulmonary artery contained firm thrombi and there was pneumonic consolidation of the right lower lobe.

When the abscess begins to penetrate the wall of the hepatic veins or inferior vena cava parietal thrombosis may be set up, and thus for a time prevent the free entry of pus into the circulation, but eventually pus passes into the blood-stream and may give rise to secondary abscesses in the lungs. Detachment of a clot may cause pulmonary embolism.

(10) *Rupture into the portal vein* is extremely rare. Occasionally the abscess is in contact with the wall of the vein and sets up thrombosis in the vein which would prevent the contents of the abscess from passing into the vein.

(11) *Rupture Externally on to the Surface of the Body.*—A liver abscess is very seldom allowed to rupture spontaneously on the surface of the body. Most frequently the abscess points anteriorly, but occasionally it presents in the loin.

Complications.—Apart from manifest rupture hepatic abscess may give rise to secondary inflammation and suppuration, especially in the thorax. The spread of inflammation through the diaphragm may cause a serous pleurisy on the right side. Infection may travel through the diaphragm and set up an empyema on the right side, which may be encysted between the lobes of the lung, as in Duplant's[4] case. Infection may spread through the diaphragm, produce pleurisy and adhesions between the base of the lung and the diaphragm, and then extend into the substance of the lower lobe, setting up pneumonic consolidation, in the middle of which an irregular abscess may develop. Rupture into the lung and pleura and broncho-biliary fistula have already been described.

Cerebral Abscess.—Jacob[5] collected 15 cases; in one group the cerebral abscess contained amoebae, in the other this was not decided.

1 Waring, H. J. *Diseases of the Liver*, p. 98, 1897, Edin. and London.
2 Flexner. *Amer. Journ. Med. Sc.*, 1897, cxiii, 553.
3 Novis. *Brit. Med. Journ.*, 1911, ii, 1408.
4 Duplant. *Lyon méd.*, 1902, xcviii, 109.
5 Jacob. *Rev. de chir.*, Paris, 1911, xliv, 549

Novis[1] refers to 5 cases seen at Bombay within 6 months. The cerebral abscess may be derived from an abscess in the lungs; in Godlee's[2] case the hepatic abscess had healed, but there were abscesses in the lungs.

As a result of firm adhesions, associated with an old amoebic abscess in the left lobe of the liver, fatal *strangulation of the small intestine* has been recorded (Rogers[3]). Adhesions about the portal fissure, in cases in which an abscess has been successfully operated upon, may compress and exert traction on the bile-ducts giving rise to jaundice, or on the colon or pylorus, producing kinking and dilatation of the stomach (Godlee[4]).

Thrombosis of the inferior vena cava is a very rare complication; a parietal thrombus may form when an abscess bursts into the inferior vena cava, which also is very rare.

Pheasants[5] has collected 8 cases of thrombosis, and Rixford[6] has recorded obliteration of the inferior vena cava. In a case of hepatic abscess with extreme marasmus under the care of my colleague, Dr. Ewart, there was extensive thrombosis of the inferior vena cava, which appeared to have spread from the iliac veins, though there was no focus of suppuration in the pelvis. There was some oedema of the feet and legs.

Escape of bile from the fistula of the operation wound is not very uncommon, but it is rare for all the bile to pass in this way, as in three cases mentioned by Godlee.

Lardaceous disease may supervene as the result of long-continued discharge of pus.

Diagnosis.—There is no one sign or symptom which may not be absent in tropical abscess. The most frequent indications are pain in the region of the liver, progressive enlargement of the organ, and fever; but these may be present in congestion, acute hepatitis, and other conditions. The presence of a fluctuating swelling or oedema of the abdominal wall over the liver makes the diagnosis almost certain, but unfortunately they are often, and in the case of oedema generally, absent. The history of dysentery or of residence in tropical countries, manifest illness, and the presence of some of the commoner signs and symptoms of abscess, such as hepatic pain, enlargement, and tenderness, and continued fever in the absence of any evidence of malaria or other sufficient cause, are strong grounds for suspecting a tropical abscess.

A considerable leucocytosis is of value in cases in which there is no other proof of abscess (Boinet,[7] Rogers[8]), but the leucocytosis may be comparatively slight or absent (Osler[9]). In a doubtful case leucocytosis is in favour of abscess, but its absence does not exclude abscess.

[1] Novis. *Brit. Med. Journ.*, 1911, ii, 1408.
[2] Godlee. *Med.-Chir. Trans.*, 1902, lxxxv, 119.
[3] Rogers, L. *Brit. Med. Journ.*, 1903, i, 1316.
[4] Godlee. *Med.-Chir. Trans.*, 1902, lxxxv, 121.
[5] Pheasants. *Johns Hopkins Hosp. Bull.*, 1909, xx, 292.
[6] Rixford. *Occid. Med. Times*, 1895, ix, 415.
[7] Boinet. *Compt. rend. Soc. Biol.*, Paris, 1900, 11. s., ii, 1089.
[8] Rogers, L. *Brit. Med. Journ.*, 1905, ii, 1291.
[9] Osler. *Med. News*, N.Y., 1902, lxxx, 673.

Puncture of the liver with a trocar in order to determine if pus is present, is often employed to settle the diagnosis. It is not, however, in spite of statements to the contrary, free either from fallacy or from danger, especially from haemorrhage in malarial cases. The trocar may, of course, miss the abscess or may pass through it, or may get blocked and not bring any pus away. Death has followed exploratory puncture from haemorrhage (Hatch,[1] Maitland[2]); in order to diminish this risk, Maitland urges that when a fruitless puncture has been made, a second puncture in another direction should not be made while the end of the trocar is still in the liver, since this manoeuvre tends to enlarge the orifice and so favours haemorrhage; if necessary, an entirely fresh puncture should be made. Cantlie,[3] who strongly advocates the use of the aspirating syringe, considers that the inferior vena cava is the only vessel likely to be wounded, and that if the needle is not introduced for more than $3\frac{1}{2}$ inches, this danger can be eliminated. The risk from haemorrhage is said to be greatest in cases in which there is no abscess. Further, a puncture may lead to peritonitis or may be the means of spreading infection in the liver by passing through the abscess and carrying the pus into other parts of the organ. When performed, aspiration should be employed as a means of localising the position of an abscess immediately before operation, and not merely for diagnosis.

Differential Diagnosis.—Suppurating Hydatid; Subdiaphragmatic Abscess; Pylephlebitis and Multiple Abscess; Suppurative Cholangitis; Intermittent Hepatic Fever; Pancreatic Cyst, Acute Pancreatitis; Suppuration in Rectus Muscle; Acute Hepatitis; Enteric Fever; Malaria; New Growth; Lymphadenoma; Acute Leukaemia; Gumma; Ascites; Dilated Gall-Bladder; Right Pleural Effusion and Empyema; Tuberculosis.

Suppurating Hydatid Cysts.—In simple hydatid disease the liver is enlarged but the general health and nutrition are good, there is no fever; and the general absence of symptoms, especially of pain, forms a striking contrast to the prominent local physical signs. No difficulty is therefore likely to arise in distinguishing between an ordinary hydatid cyst and abscess of the liver. When, however, a hydatid cyst suppurates, the condition of affairs is exactly the same as an abscess. In such cases the history that there had been a quiescent tumour in the position of the liver for a considerable time before the onset of symptoms would suggest the true state of affairs; otherwise it will be impossible to make an accurate diagnosis before operation. Difficulty might conceivably arise in diagnosing a simple hydatid complicated by fever from an abscess of the liver.

A *subphrenic abscess* may be due to various causes, such as leakage of an hepatic abscess or suppurating hydatid cyst, suppurative cholecystitis, perforation of a gastric or duodenal ulcer, appendicitis, calculous or tuberculous disease of the kidney, and in rare cases from suppuration in

[1] Hatch. *Ind. Med. Gaz.*, 1898, xxxiii.
[2] Maitland. *Brit. Med. Journ.*, 1902, i, 458.
[3] Cantlie, J. *Ibid.*, 1903, ii, 656.

the spleen or in connexion with malignant disease of the large intestine. When an abscess, either tropical or one of the multiple abscesses seen in suppurative pylephlebitis or cholangitis, leaks on to the convexity of the liver and gives rise to a localised abscess between the diaphragm and the liver, the condition of affairs is for all practical purposes much the same as the original intrahepatic disease. When a localised peritoneal abscess is due to perforation of a gastric or duodenal ulcer, the cavity contains air and is often termed a subphrenic pyopneumothorax. The physical signs—resonance on percussion, a bell note, and succussion—distinguish it from hepatic abscess. A non-gaseous subphrenic abscess may be extremely difficult to differentiate from an abscess in the liver. Thus, in neglected appendicitis a large abscess may pass upwards from the right iliac fossa, displace the right lobe of the liver forwards, and cause increase in the hepatic dulness and apparent enlargement of the liver. It should be differentiated from an hepatic abscess by the history, the signs of appendicular mischief in the right iliac fossa, and by its tendency to bulge more into the right loin. The history or evidence of recent appendicitis is of some importance, for subphrenic abscess is commoner than hepatic abscess as a result of appendicitis (Elsberg [1]).

Suppurative Pylephlebitis and Multiple Abscesses.—The general resemblance of single and of multiple abscesses is often very close and an absolute diagnosis between them is not always justified. The points on which a distinction can be based are (i) local signs of abscess, such as fluctuation over a prominent swelling, or oedema of the body wall over the liver; (ii) the history of dysentery in the case of single abscess, or of appendicitis in multiple pylephlebitic abscesses. Bacillary dysentery, however, may be followed by multiple abscesses. In a patient who has had dysentery, agglutination of the Shiga-Flexner bacillus would point to bacillary dysentery and to multiple rather than single intrahepatic suppuration.

In a case, seen on March 22, 1903, at Coltishall, multiple abscesses, secondary to appendicitis, very closely resembled a single abscess. A man aged forty-eight was seized seven weeks before with pain at the umbilicus which lasted for one day; since that date there had been continued fever. There were dulness, friction, and distant bronchial breathing at the right base, but no enlargement of the liver in front. His temperature had fallen that morning to 96·4°, he was collapsed, looked almost moribund, and had a pulse of 140. A transpleural operation let out serous fluid from the pleura, and opened an abscess about the size of a teacup in the back of the right lobe of the liver; no other abscesses could be seen. The man seemed much better and the temperature remained below normal for four days; it then became hectic and he died on April 2. At the necropsy the vermiform appendix was gangrenous and the right lobe of the liver riddled with abscesses.

Intermittent Hepatic Fever.—In intermittent hepatic fever, depending on infective cholangitis due to calculi in the ducts, periodical attacks of

[1] Elsberg. *Ann. Surg.*, 1901, xxxiv, 729.

fever, jaundice, pain, and hepatic enlargement occur. The history in such cases would probably point to cholelithiasis, and the variation in the size of the liver or absence of enlargement, the periodicity of the jaundice, and the intervals of fair health, would eliminate hepatic abscess. Infective cholangitis may, however, go on to suppuration and the temperature is then continuously raised.

A *pancreatic cyst* lifting up the left, or less often the right, lobe of the liver may imitate an abscess in the substance of that viscus, but it is not necessarily accompanied by fever and often appears after a blow. But in very exceptional instances an abscess in the liver is not accompanied by pyrexia and may of course supervene after trauma. As a rule, a pancreatic cyst forms a definite tumour in the left hypochondrium of large size, and, as shewn by inflation of the stomach, lies behind that viscus.

Acute pancreatitis with the production of an abscess limited to the lesser sac of the peritoneum may, as shewn in the following case, resemble an abscess in the left lobe of the liver.

A man aged forty came into St. George's Hospital on September 15, 1899, having been ill sixteen days, with a fluctuating tumour in the epigastrium which had been noticed four days before. It was in the position of the left lobe, but the rest of the liver shewed no enlargement and the patient had never been out of England. A tentative diagnosis of suppurating hydatid cyst or of a pancreatic cyst was made. Mr. G. R. Turner operated the same day and opened a large abscess which was not in the liver but occupied the lesser sac of the peritoneum and went back to the spine. The patient did well for a time, but in October fever returned, he had rigors, and eventually died on November 8. The necropsy shewed an abscess cavity in the lesser sac of the peritoneum, gangrene of the tail of the pancreas, suppurative pylephlebitis, multiple abscesses in the liver, and a left-sided empyema.

Suppuration in the rectus muscle is rare, and when it does occur, as it has been known to do after typhoid fever, is usually below the umbilicus. An abscess in the rectus muscle above the umbilicus might imitate a pointing hepatic abscess, but there is not complete dulness over the swelling and the liver is not enlarged. A needle introduced into an abscess in the abdominal wall remains stationary, whereas a needle projecting into an abscess in the liver should move with respiration (Middeldorff's method). This test may fail when the liver is firmly adherent to the abdominal wall (Osler[1]), and is not devoid of danger, since leakage may take place from the puncture in the liver.

A *phantom tumour* is likely to be mistaken for an abscess only when the patient has been in the tropics or has been exposed to dysentery. The gradual disappearance of a phantom tumour under a general anaesthetic is important in the diagnosis from hepatic abscess. Bennett[2] has described, in a man who had had dysentery, a phantom tumour which was operated upon.

[1] Osler. *Practice of Medicine*, p. 516, 6th ed., 1905.
[2] Bennett, W. H. *Lancet*, 1902, i, 3.

Since *acute hepatitis* precedes and may be considered an early stage of abscess, the question often arises whether suppuration has actually developed or not in a patient who has had dysentery and presents symptoms suggesting suppuration in the liver (*vide* p. 116).

In obscure forms of septicaemia the association of fever and enlargement of the liver from cloudy swelling may easily lead to a diagnosis of abscess. Remlinger[1] and Bozzolo described a form of acute hepatitis as the infectious liver which imitates abscess very closely.

In *enteric fever* considerable hepatic enlargement sometimes occurs and may give rise to a diagnosis of hepatic abscess.[2] This difficulty is more likely to arise in warm climates, where the two diseases are both prevalent. The presence or absence of the agglutination reaction should be of very great assistance, but it might be present in a patient with hepatic abscess who had previously had enteric fever. An examination of the blood should always be made, since there is no leucocytosis in uncomplicated enteric fever, whereas in abscess it may be present and be very considerable.

From *malaria* hepatic abscess may be diagnosed by examination of the blood for the parasite. In malarial cases treated with quinine the blood does not shew the parasite; in such cases leucopenia points to malaria, whereas in hepatic abscess there may be a high leucocytosis. Cases of hepatic abscess with little enlargement of the liver may easily be regarded as malarial in the absence of a blood examination; conversely, chronic malaria with hepatitis may imitate hepatic abscess, in the enlargement, pain both in the liver and the right shoulder, and the general ill-health. In malaria the hepatic enlargement is more uniform and is accompanied by enlargement of the spleen.

Influenza is sometimes accompanied or followed by hepatic enlargement and a continued temperature strongly suggesting suppuration; Goodhart[3] refers to such cases and I have had a similar experience.

New Growth.—Confusion sometimes arises when rapidly growing malignant disease in the liver is associated with a raised temperature. A soft growth, especially when in the left lobe, may cause a bulging of the abdominal wall and give rise to a sense of fluctuation more or less obscure. In such cases (*vide* p. 522) exploration is the only sure means of diagnosis. It is very rare indeed for the converse to occur, viz. for an abscess to be regarded as a new growth. It is more likely to occur in cases in which the patient is extremely cachectic and deeply jaundiced.

In a case of Osler's[4] the probable diagnosis was gall-stones with cancer. Woman, sixty-four years, dyspepsia for two years, loss of weight, pain in right side at intervals for three months, attacks of vomiting, slight jaundice, pro-

[1] Remlinger. *Presse méd.*, 1903, p. 86.
[2] Bozzolo, *Riv. crit. di clin. med.*, 1902, iii, 169; H. Jones, *Brit. Med. Journ.* 1897, ii, 1581.
[3] Goodhart. *System of Medicine* (Allbutt and Rolleston), 1905, i, 964.
[4] Osler. *Med. News*, N.Y. 1902, lxxx, 673.

gressive weakness, no rigors, no leucocytosis, increase in size of liver, slight fever. Death. Amoebic abscess in the right lobe of liver. No ulceration of intestines.

In generalised *lymphadenoma* the temperature may closely resemble that of suppuration, and in rare instances there is very considerable enlargement of the liver.

Some years ago a man was under my care with a pedunculated mass in the left groin of many years' standing, which turned out to be lymphadenoma ; he developed a hectic temperature and considerable enlargement of the liver. The condition was not unlike hepatic abscess and the question of operation was raised during life. At the necropsy the liver shewed lymphadenoma. I have seen a case in which lymphadenoma of the liver and mesenteric glands with very slight enlargement of the superficial lymphatic glands had been operated upon for hepatic abscess.

As a rule, there is not much enlargement of the liver in generalised lymphadenoma. In lymphadenoma there is usually no leucocytosis, whereas in abscess there may be a polymorphonuclear leucocytosis. Further, in lymphadenoma the superficial glands are usually affected.

Acute leukaemia, especially in the absence of glandular enlargement, may imitate hepatic abscess unless a blood examination is available (Emerson,[1] Kelly [2]).

In some cases of *syphilis* there is continued fever (*vide* p. 364) and very considerable hepatic enlargement; in patients who have been in countries where hepatic abscess is common these manifestations may easily lead to an erroneous diagnosis.[3] Cases of hepatic gumma have been operated upon for abscess.

Ascites.—In a few cases an abscess has been so large as to imitate ascites, and the abdomen has been tapped on this assumption. This is more likely to occur in young subjects. Cases have been recorded by Hatch [4] and Powell.[5]

Though it seems unlikely, a greatly *dilated gall-bladder* has been tapped under the idea that it was an hepatic abscess (*vide* specimen (No. 1381) in St. Thomas's Hospital Museum).

Right-sided Pleural Effusion.—There may be a very close resemblance between hepatic abscess and a right-sided pleural effusion. An abscess in the upper and back part of the right lobe of the liver will push the diaphragm up and give rise to dulness at the base of the lung. The dulness is said to be curved and to be higher in front and in the axilla than behind, but this is not constant, as there may be a small concomitant pleural effusion in the right pleura due to the spread of inflammation through the diaphragm. In a right-sided pleural effusion Grocco's paravertebral triangle of dulness is present on the left side; in 32 cases

[1] Emerson. *Johns Hopkins Hosp. Bull.*, 1907, xviii, 80.
[2] Kelly, A. O. J. *Trans. Assoc. Amer. Phys.*, 1903, xviii, 481.
[3] Compare Barry, C. *Ind. Med. Gaz.*, 1904, xxxix, 298.
[4] Hatch. *Ibid.*, 1898, xxxiii, 285.
[5] Powell. *Ibid.*, 1898, xxxiii, 41.

of hepatic abscess Castellani[1] found that Grocco's triangle was absent. The upward displacement of the diaphragm does not displace the heart to the left in the same way that a large pleural effusion does, but this is not of much use, as hepatic abscess rarely imitates a large pleural effusion. In hepatic abscess the patient's general condition is worse than it would be in a comparatively small empyema or pleural effusion; further, the liver is usually enlarged downwards in abscess, whereas a pleural effusion of the size which hepatic abscess imitates would not displace the liver downwards. As has been pointed out, hepatic abscess often gives rise to pleurisy and pleuritic pain, so that the question to be decided is whether there is an abscess in the liver or whether the whole disease is intrapleural. In a case of tropical abscess following enteric fever (*vide* p. 122) the resemblance to an empyema was considerable.

Cases of *pulmonary tuberculosis* with hectic temperature and with an enlarged fatty liver, in which the physical signs of pulmonary disease are not prominent or have not been detected, have been diagnosed as hepatic abscess.[2] In hepatic abscess without any hepatic enlargement in patients who have never been out of England the continued temperature may, in the absence of any other signs, suggest generalised tuberculosis.

The **prognosis** of hepatic abscess, though always serious, and specially severe in the presence of complications, which will be referred to later, is by no means necessarily bad.

In a collection of 1094 cases the mortality was 30 per cent (Solonoff[3]).

Lafleur[4] considers the prognosis more unfavourable in amoebic than in other forms of hepatic abscess, but Manson[5] joins issue on this point. The prognosis is considerably modified by the period at which operative interference takes place. In cases operated upon early, the outlook is favourable. This probably explains why operation in private practice in India is much more successful than in hospital.

According to Moorhead[6] 75 per cent of private cases and 50 per cent of hospital cases recover. Hatch[7] found that in some years 90 per cent of the hospital cases terminated fatally, while in private practice the mortality was about 20 per cent.

When operation is undertaken late, the prognosis is bad, inasmuch as extensive destruction of the liver substance has taken place, the patient's strength is exhausted by the continued fever, and secondary results, such as pyaemia and emaciation, have had time to develop.

Rupture of the abscess externally is favourable; rupture into the lung is generally regarded as fairly favourable, though convalescence

[1] Castellani. *Riv. crit. di clin. med.*, Firenze, 1908, ix, 375.
[2] Josserand. *Lyon méd.*, 1897, lxxxvi, 421.
[3] Solonoff. *Brit. Med. Journ.*, 1903, i, 262.
[4] Lafleur. Allbutt's *System of Med.*, 1897, iv, 168.
[5] Manson, P. *Tropical Diseases*, p. 457, 1903.
[6] Moorhead. *Brit. Med. Journ.*, 1899, i, 1032.
[7] Hatch. *Lancet*, 1902, ii, 1543.

may be tedious; thus, De Castro[1] estimates that 76 per cent recover, and Manson[2] that spontaneous recovery occurs in 50 per cent; but Lafleur and Godlee take an unfavourable view of this complication. Rupture into the colon is usually followed by recovery. On the other hand, rupture into the general peritoneal cavity and into the pericardium are nearly always fatal. The presence of active dysentery or diarrhoea is unfavourable. The existence of more than one abscess makes the prognosis bad; this is difficult to diagnose, but it should be suspected if the temperature remains raised when an abscess has been opened and is discharging quite freely. When the abscess continues to discharge for a long time and signs of lardaceous disease—albuminuria, oedema of the feet, and diarrhoea—appear, the outlook becomes grave.

After apparent recovery from hepatic abscess there is a danger of recurrence, more especially if the patient remains in a tropical country or returns to it too soon after recovery.

Treatment.—*Prophylaxis* of hepatic abscess is in the first instance the treatment of acute hepatitis (*vide* p. 116). Alcohol should be tabooed and care taken by the subjects of past dysentery to avoid chills and recurrences of diarrhoea. Large doses, 20-40 grains daily, of ipecacuanha are invaluable in amoebic hepatitis as a means of preventing suppuration (Rogers,[3] Pilgrim,[4] Greig and Wells[5]). The dose should be taken at night on an empty stomach; to prevent vomiting chloral or chloretone should be given before the ipecacuanha, or the latter may be taken in keratin-coated pills. The patient should be kept in bed on a low diet. Dysentery should of course be avoided by attention to the drinking-water. The bowels should be kept open by mild laxatives, and local pain relieved by leeches, cupping, the application of an ice-bag, and other methods mentioned in the treatment of acute hepatitis. Chloride of ammonium in xx.-grain doses three times a day has been recommended, but its value is somewhat problematical. Removal of blood from the congested organ by aspiration has been thought to be of use in preventing suppuration, but, as already pointed out, it is not entirely free from risk (*vide* p. 146).

The *treatment* of hepatic abscess is essentially surgical and consists in removal of the pus and free drainage of the abscess cavity at the earliest opportunity. Medical treatment is only justifiable when it is doubtful if an abscess has formed, and during the period when acute hepatitis will explain the symptoms; and, apart from symptomatic remedies, has been dealt with under "prophylaxis."

Aspiration.—Tapping the liver through the abdominal walls with a Dieulafoy's aspirator has been commonly advocated and is often successful. It is, however, dangerous, and should not be attempted. The

[1] De Castro. *Les Maladies du foie dans les pays chauds*, Paris, 1870.
[2] Manson. *The Lane Lectures on Tropical Diseases*, p. 192, 1905.
[3] Rogers. *Med.-Chir. Trans.*, Lond., 1907, xc, 145.
[4] Pilgrim. *Ind. Med. Gaz.*, 1910, xlv, 332; *Brit. Med. Journ.*, 1910, ii, 2039.
[5] Greig and Wells. *Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Government of India*, 1911, N.S., No. 47.

abscess may leak into the general peritoneal cavity and set up general peritonitis; severe haemorrhage may occur if the aspirator wounds a large branch of the hepatic artery, or possibly the aspirator may perforate one of the hollow abdominal viscera, such as the stomach or intestines.

In England Manson and Cantlie[1] have enthusiastically advocated drainage of the abscess by means of a trocar and cannula, and establishing a syphon drainage. This method has not found favour with Indian surgeons. It is urged that this method does not provide thorough drainage, that if the tube becomes displaced there is great difficulty in replacing it, and that if the tube gets out the pus may escape into the peritoneal cavity.

In amoebic abscesses containing no pyogenetic organisms cure has followed aspiration and injection of a solution containing 30 grains of the acid bihydrochloride of quinine into the abscess cavity (Rogers and Wilson[2]).

The most satisfactory treatment of an abscess is free opening and drainage. For the surgical procedure the reader should refer to surgical textbooks. The position of the abscess must be first determined, and though it is not a harmless procedure, this must often be done by exploration with an aspirator under an anaesthetic. The abscess should be freely opened so as to allow of its interior being explored and any adjacent abscess opened. It is essential that adequate provision for free drainage should be made.

When an abscess bursts into the pleura or peritoneum operation should be undertaken, and in the case of the peritoneum of course without delay (*vide* p. 143). The treatment of rupture into the lung requires consideration; some authorities urge immediate operation in order to prevent further destruction of the lung. Others advise that the case should be treated with vaccins and an open-air life, and that if improvement is steady no surgical steps are needed, but if the symptoms persist operation should be advised. Drainage of an abscess through the lung has been satisfactorily treated by placing the patient in the upside-down position so as to facilitate drainage (M'Kechnie[3]). In rupture into the colon no operation is necessary unless there are signs of peritonitis. Operation should be undertaken in the rare cases in which rupture occurs into the pericardium or pelvis of the kidney, but in the former event death may be very rapid.

During *convalescence* tonics, fresh air, and nourishing food are necessary. Change of air to the seaside should be recommended. The patient should not remain in a tropical climate, or return until two years have elapsed since the abscess was opened, and if possible should remain permanently in England or a temperate climate.

[1] Cantlie, J. *Brit. Med. Journ.*, 1903, ii, 656.
[2] Rogers and Wilson. *Ibid.*, 1906, i, 1397.
[3] M'Kechnie. *Lancet*, Lond., 1912, i, 865.

MULTIPLE ABSCESSES IN THE LIVER

The infection leading to multiple abscesses in the liver may reach the organ in several ways. The method of production provides a means of classifying multiple hepatic abscess.

(1) Ordinary pyaemic abscesses, in which the infection arrives by the hepatic artery.

(2) Abscess due to portal vein infection. (*a*) Multiple abscesses in bacillary and amoebic dysentery, in appendicitis, etc., due to infective emboli. (*b*) Suppurative pylephlebitis (*vide* p. 68).

(3) Suppuration in and spreading from the bile-ducts. This is described under "Suppurative Cholangitis," and includes verminous abscesses due to worms which have travelled up the common bile-duct.

(4) Secondary abscesses due to the spread of infection from a large single abscess.

Pyaemic Abscesses.—In general pyaemia numerous minute abscesses may be found in the liver.

In 24 cases of general pyaemia that were examined in the post-mortem room of St. George's Hospital, 1890–1896, abscesses were found in the liver in 4 cases, multiple in 3, in the remaining case there were two abscesses.

In infective endocarditis secondary abscesses in the liver are rare; thus, in 65 fatal cases of infective endocarditis collected by Kelynack[1] there was only one case in which the liver was affected. In 10 cases of systemic blastomycosis examined after death the liver shewed small suppurating foci in 4 (Montgomery and Ormsby[2]).

An hepatic abscess may be secondary to suppuration anywhere in the body, even when there is no pyaemia. In such cases the liver is probably in a state of diminished resistance, so that micro-organisms which would be destroyed elsewhere are able to flourish there. Percival Pott long ago stated that multiple abscesses in the liver were especially apt to follow injuries and suppuration in the head.

The commonest causes of pyaemia, which is a comparatively infrequent disease, are acute infective periostitis and middle-ear disease. In cases of middle-ear disease multiple hepatic abscesses may be merely pyaemic. But it is noticeable that sometimes abscesses are not found in any other organ. This is difficult to explain. It might be said that the micro-organisms manage to get through the lungs without being arrested there and that the liver is the place of least resistance, the other organs in the body destroying the micro-organisms. Another conceivable explanation is that the micro-organisms pass down from the head and drop,

[1] Kelynack. *Encyclopaedia Medica*, 1900, iv, 365.
[2] Montgomery and Ormsby. *Arch. Int. Med.*, Chicago, 1909, ii, 12.

so to speak, through the right auricle into the hepatic veins. This passage of micro-organisms against the current of blood or retrograde embolism is rare, but it undoubtedly occurs.[1] It is possible that in the pre-anaesthetic days of Pott, retrograde infection of the liver from suppuration about the head was commoner than at the present time, when operations are quietly performed under an anaesthetic. Thus retrograde embolism is favoured by violent expiratory efforts which may result in blood, and the pus or micro-organisms in it, being driven out of the right auricle into the hepatic veins. Such expiratory efforts would be likely to occur at the time of any operation in the pre-anaesthetic days.

Multiple Abscesses due to Portal Vein Infection.—Multiple abscesses may be due to widespread embolism of the intrahepatic branches of the portal vein. When this occurs without any pylephlebitis of the extrahepatic parts of the portal vein, the process in the liver may be regarded as due to "portal pyaemia." In reality no hard-and-fast line can be drawn between such cases and ordinary pylephlebitis with multiple foci of suppuration in the liver.

Multiple abscess may occur in dysentery. It is rare in amoebic, rather less so in bacillary, dysentery. In both these forms of dysentery there may be a number of small abscesses all of about the same size and due to multiple embolism of the intrahepatic branches of the portal vein. There may be a single large abscess which has, by infection of the branches of the portal vein, given rise to secondary and multiple foci of suppuration.

In amoebic dysentery the contents of the small multiple abscesses are barely liquid. The walls are formed of necrotic liver tissue and the abscesses have evidently originated in a portal space. There is usually absence of the ordinary small-celled infiltration seen in other forms of suppuration (Lafleur[2]). According to Rogers,[3] the small multiple abscesses are due to a mixed infection of amoebae and pyogenetic cocci, while the large abscesses are solely due to amoebae. Rogers figures small-celled infiltration in the small multiple abscesses. Multiple abscesses containing amoebae have been found in cases in which the intestines appeared normal (Buxton[4]).

In bacillary dysentery the multiple abscesses are like those in pylephlebitis. In the dysentery seen in South Africa in the war of 1899–1902 hepatic suppuration, when it occurred, was usually in the form of multiple liver abscesses without pylephlebitis.

Multiple abscesses from portal vein infection are most commonly secondary to appendicitis. The abscesses may be due to multiple infective emboli which have passed up from a small abscess in connexion with the appendix, the intervening part of the portal and superior mesenteric veins being normal; there may be as many as 200 abscesses.

[1] For examples *vide* Welch, Allbutt's *System of Medicine*, 1899, vi, 233; Risel, *Virchows Arch.*, 1905, clxxxii, 258.

[2] Lafleur. Allbutt's *System*, 1897, iv, 158.

[3] Rogers, L. *Brit. Med. Journ.*, 1903, i, 1317.

[4] Buxton. *Proc. Phila. Path. Soc.*, 1899, ii, 49.

In some instances there is a large abscess with smaller ones around it; the large abscess may be due to originally separate abscesses running together. Leakage or rupture of a small abscess causes general or localised peritonitis; in the latter event there may be an abscess between the convex surface of the liver and the diaphragm. Either an empyema on the right side or merely pleurisy with effusion is a frequent complication. Luckily hepatic suppuration is not a common complication of appendicitis; it is more likely to occur with a small abscess under considerable tension (*vide* also p. 69).

In 112 cases of appendicitis examined after death there were 2 cases of abscess of liver, 2 cases of suppurative hepatitis, and 2 of perihepatitis (Langheld[1]).

The following is a good example of Dieulafoy's "appendicular liver":—

A woman aged twenty-four with a history of appendicitis presented signs of a local abscess in the right iliac fossa; the appendix, which was thickened, and an ounce of pus in its neighbourhood were removed. The patient went on well for a week, when the discharge from the wound became very profuse; exploration shewed that there was a suppurating cavity lined by coils of intestines. Her condition became one of chronic pyaemia, and in the last seven weeks of life the temperature was only normal on four occasions. At the necropsy the right lobe was riddled with abscesses; there was no general pylephlebitis or thrombosis of the portal vein, but a few intrahepatic branches of the portal vein in the right lobe were thrombosed.

Sometimes the existence of the primary source of infection in the appendix is entirely latent and the patient comes under observation with a hectic temperature, rigors, and an enlarged liver.

Multiple abscesses of the liver are very seldom secondary to gastric ulcer; Murchison[2] recorded two cases. Suppurative pylephlebitis is also extremely rare after gastric ulcer. In Lambert's[3] curious case a pin passed from the stomach into the right lobe of the liver and set up multiple abscesses. In very rare instances, of which Gibbon[4] has collected nine examples, multiple abscesses occur in the liver after typhoid fever; they may be secondary to intercurrent appendicitis and pylephlebitis (Osler[5]) due to embolism of the small branches of the portal vein, or to infection through the hepatic artery and secondary to an abscess elsewhere in the body.

In a case reported by Mackie Whyte[6] multiple hepatic abscesses without any pylephlebitis were due to infection derived from a false diverticulum of the sigmoid flexure. In a case of primary ulceration of the lower part of the

[1] Langheld. Quoted by Loison, *Rev. de chir.*, Paris, 1900, xxi, 522.
[2] Murchison. *Trans. Path. Soc.*, 1866, xvii, 145.
[3] Lambert. *New York Med. Journ.*, 1898, lxvii, 177.
[4] Gibbon, J. H. *Am. Journ. Med. Sc.*, 1903, cxxv, 592.
[5] Osler. *Trans. Assoc. Am. Physicians*, 1897, xii, 382.
[6] Mackie Whyte. *Scot. Med. and Surg. Journ.*, 1906, xviii. 120.

rectum multiple abscesses in the liver, containing *Bacillus influenzae similis*, were found by Ophüls.[1] There was no thrombosis in the haemorrhoidal or portal veins.

Multiple abscesses in the liver may be due to suppuration in the pelvis, the portal vein being infected through the communications between the superior haemorrhoidal branch of the inferior mesenteric vein and the branches (middle and inferior haemorrhoidal) of the internal iliac veins.

Thus, a prostatic abscess (Lancereaux[2]), gonorrhoeal salpingitis (Handford[3]), perimetric abscess (Roughton[4]), and a suppurating submucous fibromyoma (Delestre[5]) have been known to cause multiple abscesses in the liver.

Secondary Abscesses due to the Spread of Infection from a Large Single Abscess.—Small abscesses are often found associated with a large single abscess cavity. In some instances the large abscess is due to confluence of small abscesses; in other instances the small abscesses are secondary to infection from the originally single abscess, and are usually found in its neighbourhood. They were described by Davidson[6] under the name of "secondary pyo-septicaemic abscess."

The clinical features, diagnosis, and prognosis in cases with the larger multiple abscesses in the liver are practically the same as in suppurative pylephlebitis, to which the reader should refer. The miliary abscesses in the liver in general pyaemia do not give rise to any special symptoms.

PERIHEPATITIS

PERIHEPATITIS, or inflammation of the peritoneal capsule of the liver, may be acute or chronic.

ACUTE PERIHEPATITIS

Causation.—In temperate climates acute inflammation of the peritoneum covering the liver and the underlying capsule is not a primary and independent condition, in the same way that pericarditis and pleurisy often are, but is secondary to disease in the liver or in the neighbourhood, and is usually quite subordinate to the primary affection. The only exception to this is the occurrence of traumatic perihepatitis such as follows fracture of the ribs on the right side; in such cases acute inflammation of the peritoneum covering the bruised or wounded areas of the

[1] Ophüls. *Am. Journ. Med. Sc.*, 1901, cxxii, 797.
[2] Lancereaux. *Traité des maladies du foie et du pancréas*, p. 231, 1899.
[3] Handford. *Trans. Path. Soc.*, 1886, xxxvii, 267.
[4] Roughton. *St. Barth. Hosp. Rep.*, 1885, xxi, 173.
[5] Delestre. *Bull. Soc. anat.*, Paris, 1898, lxxiii, 219.
[6] Davidson. Allbutt's *System of Med.*, 1897, iv, 133.

liver may be found if there is a fatal termination. It has been thought (Cantlie[1]) that in the tropics it may be a primary affection like acute pleurisy; but it is reasonable to believe that its frequency in hot climates depends on the fact that active congestion of the liver and acute hepatitis, which are common, often extend to the surface of the liver and thus set up perihepatitis.

Acute perihepatitis may be secondary to acute hepatitis, gummas, suppuration inside the liver, such as abscess, suppurating hydatid cyst, pylephlebitis, and cholangitis. It may also be seen over nodules of new growth involving the surface of the liver.

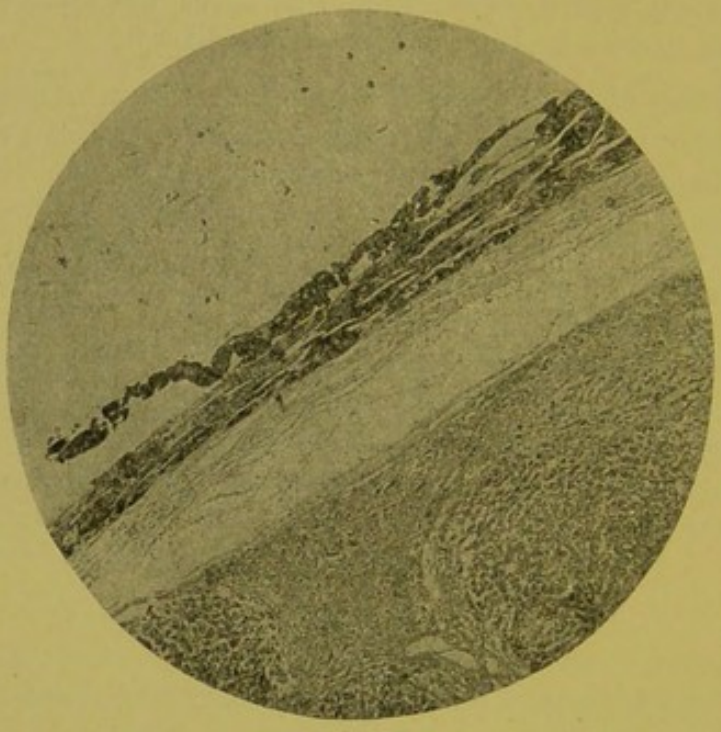


FIG. 22.—Lymph in acute perihepatitis on the surface of a cirrhotic liver which shews some thickening of the capsule. The lymph appears opaque. Some separation has taken place between the layers of the thickened capsule. (Photomicrograph by Dr. S. G. Penny.)

Acute inflammation of the peritoneal surface of the liver necessarily occurs in general peritonitis and in some forms of localised peritonitis due to inflammation, ulceration, and perforation of adjacent viscera; for example, in pancreatitis and inflammation localised to the lesser sac of the peritoneum, in cholecystitis, and in subphrenic abscess. In such conditions in which the surface of the liver happens to form the wall of an abscess cavity there is really no need to speak of pyoperihepatitis or pyopneumo-perihepatitis.[2] The first symptoms of a subphrenic abscess due to appendicitis may be those of acute perihepatitis.

In acute pleurisy, pneumonia, and pericarditis, inflammation may spread through the diaphragm and set up local peritonitis over the convexity of the liver. Occasionally it develops in the course of chronic venous engorgement of the liver, either as part of a passing, or of a terminal, infection of the liver. Acute perihepatitis is more often partial than universal.

Morbid Anatomy.—The surface of the liver in the affected area shews the dulling, loss of gloss, and slight granular appearance seen in acute peritonitis elsewhere. The vessels of the capsule are injected with blood

[1] Cantlie, J. *Encyclopaedia Medica*, 1901, vii, 2.

[2] *Vide* Chauffard, in *Traité de médecine* (Bouchard-Brissaud), 1902, v, 154.

and the cells of the liver immediately under the capsule may shew cloudy swelling. At a later date organisation of the fibrinous lymph takes place and filamentous adhesions unite the liver to the diaphragm, abdominal wall, and the adjacent viscera. These adhesions are not progressive and must not be considered as evidence of chronic perihepatitis. Such adhesions are very common in the post-mortem room, and in the great majority of instances have not given rise to any symptoms during life. Exceptionally they induce pain and a sense of dragging in the right hypochondrium. If the adhesions involve the stomach, its movements may be so interfered with that dyspepsia of a very obstinate nature adhesion dyspepsia) may be produced.

The late Mr. Allingham performed laparotomy on a patient with very severe dyspepsia, under the care of Dr. Vernon Jones, and found firm adhesions between the stomach and liver; these were divided and the symptoms were relieved. There was a history of acute perihepatitis twelve years before in India.

As an example of perihepatitis due in all probability to a terminal infection the following case is of interest:—

A boy aged ten years died in St. George's Hospital with adherent pericardium, a dilated and hypertrophied left ventricle, and signs of backward pressure. In the last few days of life he had pain over the liver and a raised temperature, but no jaundice. At the necropsy there was recent lymph on the surface of the liver, which weighed 29 ounces. On section the liver was swollen, of a mottled yellow colour, not nutmeggy.

Signs and Symptoms.—There is pain over the liver, which is made worse on respiration and is accompanied by a friction rub. The right side of the chest moves little and the liver is tender to the touch, and when an attempt to examine it is made, the overlying abdominal muscles at once become rigid. If the liver is grasped between the two hands, placed in front and behind, and moved backwards and forwards, acute pain is elicited, which may run up to an area between the clavicle and the acromion process of the scapula on the front of the chest (Cantlie), thus differing from the shoulder pain of intrahepatic disease. Dry cough may occur and be readily induced by examination of the liver. Fever, sense of weight in the hypochondrium, and other symptoms may be due to accompanying and underlying hepatitis and active congestion. Hiccup is not uncommon, and nausea and vomiting may occur. Occasionally there is ascites, but very rarely a sufficient amount to be detected clinically (compare p. 245).

Diagnosis.—Perihepatitis is practically always due to some underlying condition, and search must always be made for the primary disease, such as abscess and other forms of intrahepatic suppuration, hepatitis, new growth, chronic venous engorgement. Acute perihepatitis is very likely to be confused with acute pleurisy on the right side; indeed, in many cases the two conditions coexist, the inflammation spreading from one

serous surface to the other. In differentiating these two conditions Cantlie lays stress on grasping the liver between the hands and moving it; pain running up into the supraclavicular fossa is regarded as diagnostic of perihepatitis.

Treatment.—Rest and warmth in bed are important, while the underlying cause is sought for and treated. Treatment of the inflamed capsule of the liver will consist chiefly in the relief of pain. If severe, six or more leeches may be applied and be followed by a poultice; in slighter cases hot fomentations over the liver, or counter-irritation in the form of a mustard poultice or leaf, will be sufficient. Dry cupping often gives considerable relief. Strapping the side, as in the method employed for fractured ribs, will minimise movement and pain. A light milk diet should be given at first until the patient feels able to take solid food.

Chronic Perihepatitis

Under this heading two conditions of very different importance are included—(i) local and (ii) universal perihepatitis.

Local Chronic Perihepatitis

This condition may be due to various causes. In its slighter degrees it is seen as the result of pressure in tight-laced livers, when a belt has been worn, or may result from the communicated pulsations of a large heart. The thickening of the capsule, often associated with some atrophy of the liver substance immediately subjacent, is analogous to the milk spots so commonly seen on the surface of the heart. In many cases this local thickening of the capsule is associated with backward pressure due to obstructive heart or lung disease; in such cases the distension, and perhaps pulsation, of the liver, by giving rise to increased friction and attrition, help to call forth the capsulitis. In 18 cases of Hale White's[1] backward pressure was present in 10. In 87 cases of tricuspid stenosis recorded by Pitt[2] perihepatitis was present in 11. The local perihepatitis is occasionally part of malignant or tuberculous peritonitis, or may be found over a gumma or hydatid cyst embedded in the liver; it may also be due to the irritation of a calculous gall-bladder or of a gastric ulcer. Capsulitis of the spleen is frequently associated with it (in 9 out of 18 of Hale White's cases).

Local perihepatitis very seldom goes on, so far as is known, to the diffuse or universal form. Nicholls[3] records a case of local perihepatitis due to cholecystitis in which this transformation was in progress. The thickened portion of the capsule of the liver does not peel off, but is firmly adherent; it thus contrasts with the "false membranes" seen in universal perihepatitis, which lie on the surface of, and not in the sub-

[1] Hale White. *Trans. Clin. Soc.*, Lond., 1888, xxi, 219.
[2] Pitt. Allbutt's *System*, 1899, vi, 23.
[3] Nicholls, A. G. *Studies from the Royal Victoria Hosp., Montreal*, 1902, i, 41.

stance of, the capsule of the liver. The local thickenings on the liver resemble anatomically the milk spots on the heart and the corneal fibromas on the capsule of the spleen. Microscopically they shew parallel strands of hyaline fibrous tissue with cells between them, but do not contain blood-vessels. These local areas of chronic capsulitis may be adherent to adjacent parts, but usually they are free.

Local chronic perihepatitis may account for some pain and tenderness over the liver and may possibly give rise to a friction rub over the organ. Strictly localised perihepatitis does not give rise to ascites; but in some cases in which areas of chronic perihepatitis are scattered over the surface of the liver so as to produce a transition between local and universal chronic perihepatitis, ascites may possibly be due to this cause. The cases of cirrhosis of the liver with ascites requiring frequent tappings may be due to this form of chronic peritonitis. Strictly localised chronic perihepatitis is of little or no clinical importance apart from the associated morbid conditions of the liver.

Treatment.—If the condition is suspected and there is pain, it may be treated by local applications, such as poultices, hot compresses, or belladonna plasters, but usually no special treatment is required.

Universal Chronic Perihepatitis

Synonyms: Diffuse Chronic Hyperplastic Perihepatitis, Chronic Hyaline Perihepatitis, Chronic Deforming Perihepatitis, Sugar-iced Liver (*Zuckergussleber*).

History, etc.—The condition was observed by Budd[1] in 1852. Curschmann[2] in 1884 described the morbid changes in detail and invented the graphic name of sugar-iced liver (*Zuckergussleber*). The writings of Hilton Fagge[3] and Hale White[4] have been of great value in distinguishing the clinical aspects of perihepatitis from those of cirrhosis, and in drawing attention to the relationship between chronic interstitial nephritis and chronic perihepatitis. Nicholls[5] (1902) published a monograph of 80 pages, and Kelly[6] wrote an exhaustive paper on this subject.

This condition has received a number of rather cumbrous names, but is usually only a local manifestation of diffuse chronic peritonitis. It is in fact artificial to separate chronic universal perihepatitis from diffuse chronic peritonitis. The chronic inflammatory change may begin in the peritoneal coat of the liver and subsequently involve the adjacent peritoneum, or it may extend to the serous covering of the organ in cases of more or less general chronic peritonitis. The name chronic perihepatitis

[1] Budd. *Diseases of the Liver*, p. 139.
[2] Curschmann. *Deutsche med. Wchnschr.*, 1884, x, 564.
[3] Hilton Fagge. *Principles and Practice of Med.*, 1886, ii, 294.
[4] Hale White. *Trans. Clin. Soc.*, 1888, xxi, 219; *Guy's Hosp. Rep.*, 1893, xlix, 1.
[5] Nicholls, A. G. *Studies from the Royal Victoria Hospital, Montreal*, i, No. 3, 1902.
[6] Kelly, A. O. J. *Amer. Jour. Med. Sc.*, 1903, cxxv, 116.

thus suggests a more intimate relationship to the liver than actually exists. A more accurate though longer descriptive title would be chronic peritonitis with perihepatitis, or chronic peritonitis involving the liver.

Pathogeny.—The chronic peritonitis, of which chronic perihepatitis is part, is usually that form spoken of as simple, since it is not manifestly due to tuberculosis or to new-growth. It is characterised by a widespread fibrosis with cicatricial contraction, so that the mesentery and omenta are shortened and the viscera become inclosed in a firm casing which contracts upon and compresses them. In considering the question of causation, it will be convenient to divide cases of chronic perihepatitis and peritonitis into three groups:—

(I) When associated with varying degrees of chronic inflammation of the pericardium and pleurae (multiple serositis).

(II) When associated with arteriosclerosis and granular kidneys.

(III) When associated with other conditions.

(I) *When associated with Varying Degrees of Chronic Inflammation of the Pericardium and Pleurae* (*Multiple Serositis*).—Chronic peritonitis and chronic universal perihepatitis may be associated with varying degrees of the same change in, or in connexion with, the serous membranes in the thorax—the pericardium and pleurae. The combined changes in more than one serous membrane are spoken of as multiple progressive hyaloserositis, polyorrhymenitis, or Concato's disease. There may be a descending scale in the extent of the associated intrathoracic changes. Thus, there may be extensive fibrosis of the mediastina with adherent pericardium and pleurae (indurative mediastino-pericarditis), adherent pericardium with thickening and obliteration, partial or complete, of both or of only one pleura, or only a calcified and adherent or an adherent pericardium. In this class the inflammatory change is most intense on each side of the diaphragm, and fades off in the more distant parts of the peritoneum and pleurae; probably the constant movement of the diaphragm assists in keeping up the morbid process when once it has been started. The inflammatory change beginning on one side of the diaphragm readily spreads through the lymphatics to the neighbouring serous membrane. In most cases the inflammatory change is primary in the pericardium or pleura and spreads to the convexity of the liver, but in some it is probable that it begins as an acute inflammation close to the convexity of the liver and subsequently becomes chronic and extends to the right pleura and pericardium. In chronic perihepatitis associated with intrathoracic changes of the same kind the kidneys are, as a rule, healthy, or merely shew chronic venous engorgement. But in some instances they are granular and thus merge into the next group.

A well-marked example of chronic proliferative peritonitis and perihepatitis associated with chronic indurative mediastino-pericarditis was seen in a man aged fifty-five years, in St. George's Hospital, in 1896. He presented ascites, which required tapping 26 times, and oedema of the legs; during life mediastinal growth appeared probable from the existence of post-sternal dulness.

At the necropsy the pericardium was firmly adherent to the heart and to all the surrounding parts, especially in the region of the thymus, which was occupied by very dense firm fibrous tissue (microscopically only fibrosis). There were very dense pleural adhesions, ½ an inch thick on the left side, and universal chronic peritonitis and perihepatitis. The liver, 72 ounces, microscopically shewed early cirrhosis, though to the naked eye it appeared normal. The kidneys, 8 ounces each, were healthy.

A number of cases of universal chronic perihepatitis associated with adherent pericardium have been recorded and the condition is not in reality rare.

Gilbert and Garnier[1] described 11 cases under the name of *symphyse péricardio-périhépatique.* Heidemann,[2] in a paper on the results of adherent pericardium, collected 7 fresh cases. Kelly referred to 27 cases of universal perihepatitis associated with adherent pericardium. I have seen 2 cases in which chronic perihepatitis was associated with, and probably due to, extension of inflammation through the diaphragm, from an adherent pericardium that had undergone calcification.

A condition closely allied to universal chronic perihepatitis associated with adherent pericardium was described by Pick[3] as pericarditic pseudo-cirrhosis of the liver, in which together with latent adherent pericardium there was ascites due to fibrous hyperplasia and circulatory disturbance in the liver. Any evidences of chronic inflammation of the peritoneum were regarded by Pick as accidental or secondary to ascites and chronic venous engorgement. Cases of this kind without chronic universal perihepatitis or chronic peritonitis certainly occur, and have already been described as exaggerated cases of chronic venous engorgement of the liver (*vide* p. 96). Kelly, on the other hand, groups together under the heading of "multiple serositis" these cases of pericarditic pseudo-cirrhosis and the cases of "iced liver," or chronic universal perihepatitis, and while admitting some anatomical distinctions, regards them as very much alike clinically.

(II) *Chronic Perihepatitis associated with Arteriosclerosis and Granular Kidneys.*—Chronic perihepatitis is frequently associated with arteriosclerosis and granular kidneys; this was so in 19 out of Hale White's[4] 22 cases. In this group there is not the same intimate relationship between chronic perihepatitis and thoracic lesions as in the previous category, though the two conditions may be found together.

There appears to be some connexion between arteriosclerosis and fibrosis of the serous membranes (perivisceritis[5]). It is conceivable that arteriosclerotic change in the kidneys is a disposing cause of chronic inflammation in the body generally. As Flexner[6] has shewn, the bactericidal power of the blood is reduced in chronic renal disease and so

[1] Gilbert et Garnier. *Compt. rend. Soc. Biol.*, Paris, 1898, l, 48.
[2] Heidemann. *Berlin. klin. Wchnschr.*, 1897, xxxiv, 92.
[3] Pick. *Ztschr. f. klin. Med.*, Berlin, 1896, xxix, 385.
[4] Hale White. *Trans. Clin. Soc.*, Lond., 1888, xxi, 221.
[5] Labadie-Lagrave et Deguy. *Arch. gén. de méd.*, 1898, ii, 411 (Perivisceritis).
[6] Flexner. *Journ. Exper. Med.*, N.Y., 1896, i, 559.

allows microbic infections to occur. It is reasonable to believe that chronic perihepatitis and peritonitis might be produced by micro-organisms of no great virulence but capable of inducing considerable fibrosis. It is more probable that the process is microbic than that it is purely toxic and due to an altered (uraemic) condition of the blood. In either case the influence of arteriosclerosis and granular kidneys should lead to a similar change in the other serous cavities, the pleurae and pericardium. This condition of combined inflammation of several serous membranes—polyorrhymenitis [1] or multiple serositis—sometimes occurs in cases of granular (arteriosclerotic) kidneys, but it is by no means constant

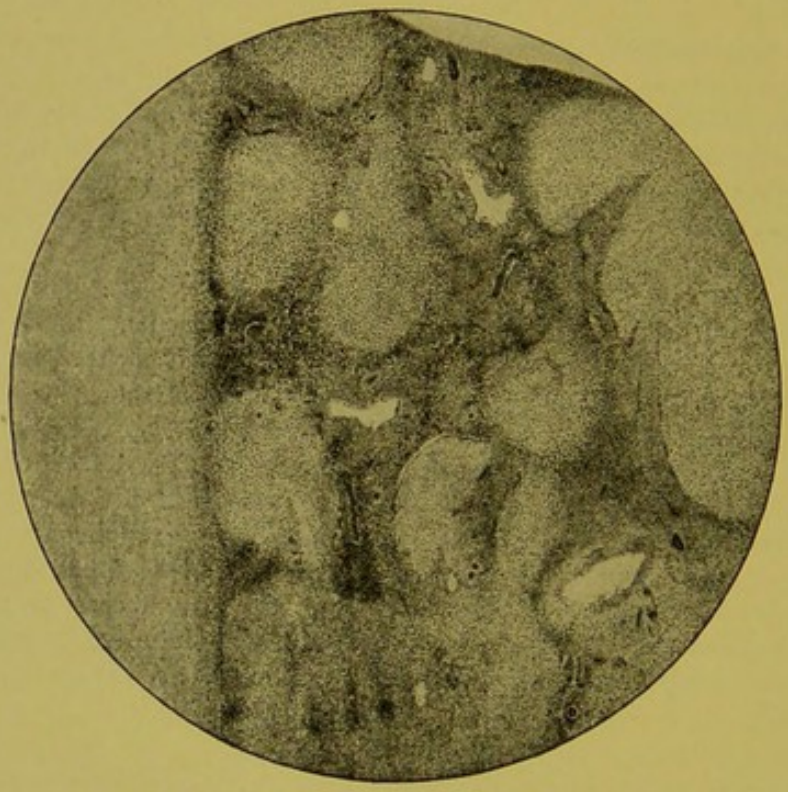


FIG. 23.—Microscopic section shewing homogeneous hyaline membrane on the surface of the liver with a similar hyaline change in the fibrous tissue of the portal spaces in the underlying liver substance. From a case of myxoedema.

to find another serous membrane involved as well as the peritoneum. In order to explain cases in which the peritoneum alone is attacked or is much more affected than any of the other serous membranes, it may be suggested that the facilities for infection are greater in the abdomen and that the resistance of the peritoneum has been specially lowered in these cases. It has been thought that arteriosclerosis of the small vessels of the peritoneum may produce chronic peritonitis—a fibrosis due to impaired nutrition.

As an example of this form the following case may be quoted: A woman aged sixty-nine years had ascites requiring paracentesis; eventually she died in

[1] For an account of this condition see Taylor, F., *Brit. Med. Journ.*, 1900, ii, 1698; Kelly, A. O. J., *Am. Journ. Med. Sc.*, 1903, cxxv, 116.

an extremely thin and cachectic state. The necropsy revealed granular kidneys, universal chronic peritonitis, a liver which weighed only 23 ounces, and on section looked cirrhotic, but not in the least nutmeggy. Microscopically the liver was nutmeggy and shewed only slight replacement fibrosis. The heart, 8 ounces, was devoid of epicardial fat; on section it shewed brown atrophy of the myocardium.

A well-marked example of chronic universal perihepatitis with similar changes in the pleurae and pericardium, and granular kidneys, occurred in a woman who died in St. George's Hospital in coma in 1898. She had often been treated for myxoedema. She had ascites, universal chronic perihepatitis, perisplenitis, and peritonitis with a number of fibrous nodules in the peritoneum near the umbilicus (peritonitis fibrosa). Both layers of the pericardium were much thickened, and the cavity contained excess of fluid. The pleurae were both thickened, shewed adhesions, and contained about 8 ounces each of clear fluid. The liver (60 ounces) was nutmeggy and free from cirrhosis. Microscopically there was a dense layer of fibrous tissue on the surface of the liver replacing the capsule. There was subcapsular atrophy of the liver cells, while the branches of the hepatic artery and portal vein appeared as prominent objects from a very peculiar swelling of their coats (*vide* Fig. 23). This change seemed to be due to myxomatous degeneration and to be connected with the primary disease—myxoedema. The kidneys (right, 3½ ounces; left, 3½ ounces) were red and granular. The heart weighed 14 ounces. The thymus could not be found, and the pituitary was not enlarged. The thyroid was atrophied and pale yellow in colour. There was obsolete tubercle in the lungs.

(III) *Universal Chronic Perihepatitis due to other or Obscure Causes.*—In a few instances perihepatitis may be associated with syphilitic lesions of the liver, but, as a rule, hepatic gummas only give rise to a local thickening of the capsule of the liver.

Cheadle[1] believed that perihepatitis is more marked and frequent in association with syphilitic disease of the liver than in any other condition. In 22 cases of universal perihepatitis collected by Hale White[2] there were 3 in which syphilis was the apparent factor. Numerous small syphilitic gummas may so extensively involve the capsule as to set up universal perihepatitis (Sharkey,[3] N. Moore[4]).

In the following case universal perihepatitis and chronic peritonitis were associated with the presence of three old and several recent gummas in the liver. The patient, a man aged thirty-seven years, who denied syphilis, but drank 3 pints of beer daily, had been well until three and a half months before his death, when he began to suffer from morning sickness and abdominal pain. A month later he became jaundiced, ascitic, oedematous as to his legs, and vomited a little blood. He was tapped twice, 40 pints being removed. The urine was free from albumin. After death universal chronic perihepatitis and a moderate degree of general chronic peritonitis were found; the

[1] Cheadle, W. B. *Some Cirrhoses of the Liver*, pp. 41, 43, 1900.
[2] Hale White. *Trans. Clin. Soc.*, Lond., 1888, xxi, 219.
[3] Sharkey, S. J. *Trans. Path. Soc.*, Lond., 1883, xxxiv, 118.
[4] Moore, N. *Ibid.*, 133.

liver weighed 56 ounces and contained three gummas in the right lobe and several scars and recent gummas in the left lobe; there was no general fibrosis of the liver. There appeared to be kinking of the portal vein and bile-duct in the portal fissure, but on cutting away the adhesions around them the vein and duct were found to be unobstructed. The kidneys weighed 6 ounces each and were healthy and free from lardaceous change. The heart weighed 8 ounces and was healthy.

In rare instances universal chronic perihepatitis may be associated with intra-abdominal malignant disease or be due to tuberculosis. In the latter case the lesions are those of chronic fibrosis and are very different from those of ordinary tuberculous peritonitis.

Chronic peritonitis and perihepatitis may be associated with and possibly due to the condition sometimes called "cirrhosis of the stomach," though really diffuse carcinoma of the organ. I have seen two cases of universal perihepatitis associated with this condition.

It has been thought to be due to traumatic peritonitis, for example as the result of the kick of a horse (Gazzotti [1]). It may also be found in cases of backward pressure without any adherent pericardium.

A woman, aged thirty-two at the time of her death, was very frequently under my care with chronic bronchitis, cyanosis, and recurring ascites, for which she was tapped forty-one times, over five hundred pints of fluid being removed. At the necropsy the kidneys, pericardium, and left side of the heart were normal; the lungs shewed chronic bronchitis and some emphysema, and the right side of the heart was dilated. There was marked chronic peritonitis in the upper part of the abdomen involving the capsules of the liver and spleen.

In other instances alcoholism has been thought to be the only antecedent condition, while sometimes, as in the very extreme condition—systematic hypertrophic cirrhosis of the peritoneum described by Du Pacquier [2]—no cause is forthcoming.

It is conceivable that in some instances chronic perihepatitis and peritonitis may start from foci of local irritation which usually only give rise to circumscribed perihepatitis. In such cases the widespread effect is analogous to the development of a cheloid in the skin after a slight injury.

Nicholls recorded in full detail a case of widespread chronic hyperplastic inflammation of the serous membranes (including perihepatitis) in a woman aged forty-eight with a chronic duodenal ulcer and slight chronic interstitial nephritis. The changes in the serous membranes were referred to irritation and possibly infection from the duodenal ulcer.

Finally, since the process is evidently a chronic and progressive inflammation, it is reasonable to imagine that it is due to infection with micro-organisms of a somewhat attenuated virulence. Nicholls suggests *Bacillus tuberculosis*, *B. coli*, and *B. typhosus* as probable organisms; this

[1] Gazzotti. *Policlin.*, Roma, 1909, xvi (Sez. med.), 381.
[2] Du Pacquier. *Arch. gén. de méd.*, 1897, clxxx, 651.

suggestion is extremely attractive, but proof is wanted. The occurrence of a special form of reaction to the tubercle bacillus in the intestines—chronic hyperplastic tuberculosis—makes it tempting to suppose that attenuated human tubercle bacilli or possibly bovine bacilli (M'Weeney[1]) may be the cause of at least some cases of chronic perihepatitis and peritonitis.

Morbid Anatomy.—The surface of the liver is covered over by a crust or coating of fibrous tissue of cartilaginous consistence. It is glistening and white, resembles the icing of confectioners, and thus accounts for the name "sugar-iced liver" (*Zuckergussleber*) which has been applied to this condition by Curschmann. The surface of this casing is pitted or fenestrated, probably as a result of rupture during its spontaneous shrinking and contraction. This coat can be peeled off, leaving the peritoneal surface in a fairly healthy state. The liver is compressed and deformed by the constant traction which the cicatricial tissue exerts upon it. Thus the anterior margin may be bent upwards and over so as to touch the convex surface. The convexity of the liver is usually much more affected than the under surface, and of course the portions uncovered by peritoneum are free from the change. In uncomplicated cases the gall-bladder is nearly always collapsed and buried under thick membrane and is with difficulty discovered, its position being sometimes merely indicated by a depression.

In the one instance in which I have seen it dilated there was malignant disease of the peritoneum in addition to chronic perihepatitis and peritonitis.

Even when the portal fissure is invaded by the perihepatitis the portal vein hardly ever becomes compressed as might be expected. Hale White[2] points out that if the portal vein were compressed or kinked the bile-duct would also be affected, and that this must be very rare from the clinical absence of jaundice. His point is that ascites is due to the chronic peritonitis and not to mechanical interference with the portal vein, for in two cases—very exceptional ones—of universal chronic perihepatitis without any chronic peritonitis there was no ascites. In the case given on pages 165, 166, however, there appeared to be kinking of the portal vein and bile-duct. There may be adhesions between the surface of the liver and the diaphragm, abdominal walls, and adjacent organs.

The *liver* is usually soft, fatty, and shews chronic venous engorgement with general atrophy. Multilobular cirrhosis is very rarely combined with well-marked perihepatitis of the kind now under discussion. It is true that adhesions and opacity with thickening of the capsule are often seen in advanced cirrhosis, but the combination of the "iced liver" and cirrhosis is so rare that in Nicholls' monograph one example only is admitted. Superficial fibrosis spreading in from the surface (Glissonian cirrhosis) is not uncommon, but it does not extend for any distance.

[1] M'Weeney. *Trans. Roy. Acad. Med. Ireland*, 1906, xxiv, 402.
[2] Hale White. Allbutt's *System of Medicine*, 1897, iv, 120.

Microscopically the thickened membrane is seen to lie on Glisson's capsule, which is thrown into wavy folds. This "icing" membrane is composed of well-formed fibrous tissue arranged in horizontal laminae with a few nuclei between them. Oertel[1] describes extensive involvement of the superficial lymphatics. The structure is like that of a lamellar fibroma of the spleen. The fibrous tissue has undergone hyaline degeneration. From the presence of this change Nicholls speaks of the condition as hyaloserositis. The membrane does not contain blood-vessels and there is usually a distinct line of separation between the membrane and the underlying capsule of the liver. In the deeper layers there are collections of leucocytes and mast-cells; there is no reaction for fibrin (Nicholls). Carnot and Amet[2] describe a thin wavy layer of elastic tissue, containing numerous small blood-vessels.

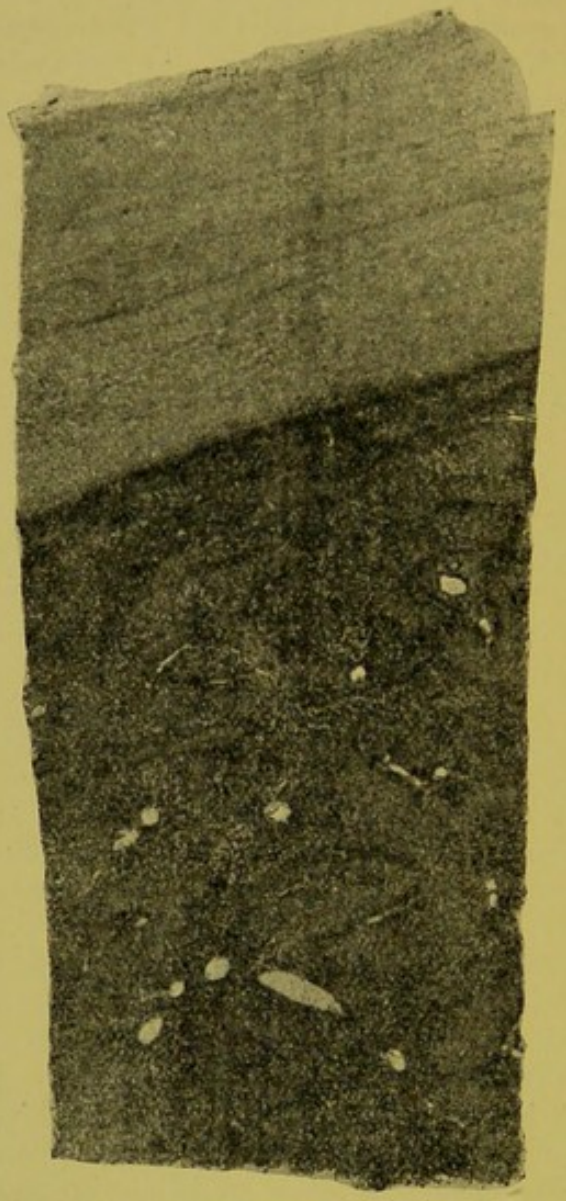


Fig. 24.—The thick "icing" in chronic universal perihepatitis. The line of distinction between it and the liver is well seen. The liver shewed some fibrosis and chronic venous engorgement. (Photomicrograph by Dr. H. Spitta.)

The condition of the underlying liver varies a little; it is rarely absolutely normal, being generally atrophied, with fatty and pigmentary changes in the liver cells; chronic venous engorgement is very common. Not very rarely there is slight Glissonian cirrhosis or fibrosis spreading a short way into the substance of the liver. The underlying liver tissue may shew a similar hyaline change in the fibrous septa (Fig. 23).

In cases of calcified adherent pericardium cirrhosis of the liver has been described (*vide* p. 98; Diemar,[3] Wells[4]).

[1] Oertel. *Arch. Int. Med.*, Chicago, 1908, i, 385.
[2] Carnot et Amet. *Arch. de méd. expér. et d'anat. path.*, Paris, 1906, xviii, 758.
[3] Diemar. *Ztschr. f. Heilk.*, 1899, xx, 257.
[4] Wells. *Am. Journ. Med. Sc.*, Phila., 1902, cxxiii, 259.

The *spleen* is usually rather larger than natural, its capsule shares in the chronic thickening of the peritoneum, and is often firmly adherent to the diaphragm and abdominal wall.

The *kidneys* in cases associated with indurative mediastino-pericarditis, adherent pericardium, and chronic pleurisy may shew little change except chronic venous engorgement. When chronic perihepatitis is associated with arteriosclerosis, the kidneys usually share in the change and are red and granular.

The *peritoneum* shews the same fibroid and hyaline change as the capsule of the liver, and undergoes the same cicatricial contraction and puckering. The great omentum is rolled up and transformed into a hard cord, the mesentery is thickened, and by its retraction tethers the intestines, which are much shortened, to the spine, so that they cannot reach to the front of the abdominal wall. As a result of this the abdomen may be uniformly dull in front. The right pleura is more often affected by the chronic fibroid change than the left. The body as a whole is thin and may be extensively oedematous.

Clinical Picture.—*Sex.*—The sexes are about equally affected, thus contrasting with cirrhosis, in which the male sex predominates.

In Hale White's[1] 21 cases there were 13 males and 8 females. In 20 cases that I have tabulated the sexes were equally affected.

Age.—The age varies considerably, but is generally about the same as in cirrhosis.

In Hale White's cases the average age was forty-seven and a half years, the youngest being twenty-nine and the oldest sixty-eight years. In my 20 cases the average age was 42·6 years, being practically the same in the two sexes ; the extremes were fourteen and sixty-eight years.

Heredity does not appear to have any influence in the development of the disease.

The *onset* of ascites is usually gradual, but in some instances is acute ; this was so in 6 out of 14 cases selected by Nicholls. The condition has been thought to date back to, and be started by, an acute inflammatory change involving the pericardium or liver.

The *course* of the disease is slow and extends over years. Nicholls finds that the duration of the disease is from two to sixteen years. Ascites, which constantly recurs, is the main symptom, but the general health and strength are fairly maintained for a long time. Emaciation gradually appears and death occurs from some intercurrent disease or infection, such as acute peritonitis or pneumonia.

In one case under my care death was due to influenza, and at the necropsy there were two small recent ulcers in the first part of the duodenum with acute inflammation of the duodenum.

[1] Hale White. Allbutt's *System of Medicine*, 1897, iv, 121.

Signs and Symptoms.—The condition is practically always accompanied by ascites, and thus contrasts with cirrhosis which may be quite latent. Ascites must be due to chronic inflammation where the process is spreading, for it is difficult to imagine that any exudation could occur from the extremely thickened membrane seen in the oldest parts of the change. Ascites is the chief physical sign and requires frequent tapping. Thus, Osler[1] refers to a child in whom this operation was performed 121 times. Tapping becomes necessary at shorter intervals and may be called for every fortnight or even sooner. Ascites is compatible with fair health and strength during the earlier part of the disease, and in the intervals between the tappings the patient may be up and about.

A woman with universal chronic perihepatitis, secondary to calcification of the pericardium, who died after her fifty-second tapping, was married after being tapped twenty times. She was under the care of Dr. Ewart, in St. George's Hospital.

The recurrence of ascites combined with fair health, or at any rate freedom from toxaemia, are important points in the diagnosis from cirrhosis. The ascitic fluid is clear and straw-coloured, but contains a high percentage of albumin (3 per cent), which allies it with inflammatory exudations rather than with passive transudations. If allowed to stand, threads of fibrin may form. Occasionally the ascites is encysted by adhesions. The liver may be enlarged and palpable in the earlier stages, but becomes smaller as time goes on. Ascitic distension of the abdomen may interfere with the estimation of the size of the liver and spleen. Some enlargement of the spleen is usual in young subjects.

The omentum may be felt as a transverse band passing across the abdomen, and must not be regarded as the lower border of the liver. The subcutaneous abdominal veins (superior and inferior epigastric veins) are sometimes enlarged and are seen to form a collateral circulation between the superior and inferior venae cavae. These veins do not converge towards the umbilicus, as is the case in the collateral circulation of portal obstruction. Jaundice is almost always absent; it was present in only one of Hale White's 22 cases, and when it occurs is probably due to some independent factor. In a case of ascites and intense jaundice examined by Bryant[2] the ascites was due to perihepatitis, and the jaundice to acute yellow atrophy. The *urine* is diminished in amount and may contain albumin, either from chronic venous engorgement or from arteriosclerotic change in the kidneys.

In addition to ascites there may be signs of the conditions specially associated with chronic perihepatitis: viz. (i) adherent pericardium, chronic mediastinitis, dense pleural adhesions, or (ii) arteriosclerosis and granular kidney. Oedema of the legs is common late in the disease and may extend to the trunk and upper extremities.

[1] Osler. *Practice of Medicine*, p. 576, 4th ed., 1901.
[2] Bryant, J. H. *Guy's Hosp. Gaz.*, 1900, xiv, 141.

Since the liver substance is well preserved, there is little constitutional disturbance and no tendency to hepatic inadequacy or to haemorrhages, drowsiness, and the other toxaemic manifestations seen in cirrhosis. If such symptoms do develop, they are to be referred to concomitant renal disease. In many cases which clinically present themselves as failing heart from granular kidneys, with ascites and general dropsy, there is universal perihepatitis. There may be loss of appetite and dyspepsia, and the relaxed and flabby condition of the abdominal walls favours constipation. Gastro-intestinal haemorrhage does not occur unless there is some complication, such as gastric or duodenal ulcer or, in rare instances, cirrhosis.

Diagnosis.—The presence of long-continued ascites not manifestly due to obstructive heart or lung disease, or to chronic nephritis, points very strongly to universal chronic perihepatitis and peritonitis.

Differential Diagnosis.—*From Cirrhosis of the Liver.*—When ascites occurs in cirrhosis the end is usually near and paracentesis is not likely to be often required unless the ascites is due to associated chronic peritonitis. Repeated tappings are therefore strongly in favour of chronic peritonitis and perihepatitis; evidence of arteriosclerotic kidney disease would also strengthen this view. Jaundice, grave constitutional and toxaemic symptoms, haematemesis, melaena, haemorrhages, and an enlarged liver and spleen point to cirrhosis.

From the effects of backward pressure due to dilatation of the right side of the heart, mitral disease, etc., the diagnosis depends on the recognition of the underlying cause and on the good effects of treatment by cardiac tonics. In cases of adherent pericardium and advanced nutmeg liver (compare p. 96) the resemblance to chronic perihepatitis associated with adherent pericardium is very close, but cardiac treatment is much more effective in the former condition, which occurs mainly in the young, while universal chronic perihepatitis is little affected by this treatment and usually occurs in adults.

In malignant disease of the liver with ascites there is progressive enlargement of the liver, with perhaps some palpable nodules of new-growth, and the course of the disease is much more rapid.

Syphilitic gummas in the liver may closely imitate perihepatitis by giving rise to recurrent ascites, and the distinction between them is often very difficult. Outward signs of syphilis may be entirely absent, even when there are numerous gummas in the liver. The Wassermann test should be tried; the best means of making a diagnosis is vigorous anti-syphilitic treatment.

Chronic Tuberculous Peritonitis.—In this condition the effusion is seldom very large and lumps may be felt in the abdomen. Induration around the umbilicus, concomitant pleurisy, and fever are points in favour of tuberculous peritonitis. In cases of doubt the tuberculin tests can be employed.

Prognosis.—The prognosis is most unfavourable: death always occurs eventually, though it may be postponed for a long period. According to

Kelly[1] 50 per cent of the patients live four years or more, and 70 per cent two years or more. Thus a patient may live to be tapped 60 or even 100 times. But the tappings become necessary at shorter intervals, and the patient gradually gets weaker. The disease has been said to be more rapidly fatal in cases associated with adherent pericardium.

Treatment.—Treatment is only palliative. Dry diet, viz. limiting the intake of fluid, and diuretics, such as citrate of caffeine, diuretin, strophanthus, digitalis, apocynum, may be tried. Iodide of potassium is usually given a trial, but it is very doubtful if it has any effect except when there is syphilitic disease of the liver. However, as the diagnosis between gummas involving the portal vein and universal perihepatitis may be difficult, it is well to give iodides on the chance of an error in diagnosis. Paracentesis should be performed when necessary; a permanent drain externally is dangerous from the risk of infection and subsequent peritonitis, and it should therefore not be employed; but the peritoneum may be drained into the subcutaneous tissues as in the ascites of cirrhosis (*vide* p. 260).

Removal of a small piece of the membrane covering the liver and union of the liver with the abdominal wall, as in the Talma-Morison operation for cirrhosis, tried in one case of Dr. Ewart's[2] in St. George's Hospital, and I believe by others, failed to give any permanent benefit.

CIRRHOSIS OF THE LIVER

Classification of the Various Forms of Cirrhosis

Cirrhosis of the liver has been classified in various ways, according to its causes, according to the methods by which the cirrhosis is brought about, according to the anatomical changes and lesions, and according to the distinctive clinical features. Some writers, such as Lancereaux,[3] consider cirrhosis under the headings of alcoholic, malarial, and syphilitic. But as other factors may lead to cirrhosis, this classification is not sufficiently broad.

Classification according to the Methods by which Cirrhosis is Induced.—The following is Chauffard's[4] classification:—

I. Vascular. (*a*) Toxic.
- (i) Poisons taken by the mouth.
- (ii) Poisons manufactured in the intestinal tract.

(*b*) Infective.
- (i) The direct action of micro-organisms.

[1] Kelly, A. O. J. *System of Medicine* (Osler and M'Crae), 1908, v, 742.
[2] Ewart. *Brit. Med. Journ.*, 1899, i, 908.
[3] Lancereaux. *Traité des maladies du foie et du pancréas*, 1899.
[4] Chauffard, A. *Traité de médecine* (Bouchard, Brissaud), 1902, v, 172.

(ii) The action of bacterial toxins, either produced by bacteria in the liver itself or manufactured elsewhere in the body and carried to the liver.

(*c*) Dystrophic.

(i) Due to arteriosclerosis; this form of cirrhosis would be homologous to a granular arteriosclerotic kidney, the fibrosis being a replacement fibrosis.

(ii) Due to chronic venous engorgement, the fibrosis of a nutmeg liver.

II. Biliary. (*a*) Secondary to obstruction of the larger bile-ducts.

(*b*) Primarily an inflammation of the smallest bile-ducts, leading to a unilobular cirrhosis. Hanot's hypertrophic cirrhosis with chronic jaundice.

III. Capsular cirrhosis or perihepatitis.

(*a*) Chronic localised.

(*b*) Chronic universal.

This classification is too elaborate, for the toxic and infective forms overlap, and from a clinical standpoint some of these subdivisions are too minute to be of practical value.

Anatomical Classifications.—Adami[1] has proposed a division of cirrhosis on anatomical grounds.

(I) Portal cirrhosis, (*a*) with enlargement, (*b*) with contraction.

(II) True biliary cirrhosis.

(III) Obstructive biliary cirrhosis, (*a*) with enlargement, (*b*) with contraction.

(IV) Pericellular or diffuse cirrhosis.

(V) Capsular cirrhosis (cirrhosis with perihepatitis).

A certain amount of fibrosis may spread into the liver substance from the capsule, but the most marked perihepatitis may exist without any trace of hepatic fibrosis; when an extension inwards does occur, the sequence of events is analogous to what occurs in interstitial pneumonia secondary to chronic pleurisy (pleurogenous pneumonia). It has been suggested that toxic bodies manufactured in the process of perihepatitis may be absorbed by the lymphatics, pass into the liver, and set up fibrosis.

(VI) Senile atrophy and arteriosclerosis.

Arteriosclerotic fibrosis of the liver might naturally be expected in the aged, and a statement to this effect is sometimes made. Personally, from a microscopic examination of a large number of livers I consider it to be very rare, and when present of very slight degree. I have often seen considerable atrophy of the liver cells without any replacement fibrosis. Barbacci,[2] by means of

[1] Adami, J. G. *Principles of Pathology*, 1911, ii, 471.

[2] Barbacci. *Sperimentale*, Firenze, 1910, lxiv, 31.

Bielschowski's silver nitrate method, has found a diffuse fibrosis which is not shewn by ordinary staining methods.

(VII) Cirrhosis from chronic venous engorgement. This question is discussed on p. 88.

The Author's Anatomical Classification.—A purely structural classification may be drawn up from the microscopic appearances as follows:—

(I) *Multilobular cirrhosis* in which a varying number of lobules are enclosed in a fibrous ring; the following sub-varieties may be recognised:—

(*a*) With fatty change in the liver cells.

(*b*) With hyperplasia of the liver cells to such an extent that nodular cirrhosis, or cirrhosis with adenoma, results.

(*c*) With pigmentation of the liver cells and also of the fibrous tissues (haemochromatosis).

(*d*) Mixed, with intercellular infiltration of the hepatic lobules. This is sometimes seen in rapidly advancing cirrhosis.

Multilobular cirrhosis is almost always due to poisons brought by the portal vein, and is therefore spoken of as periportal or venous cirrhosis, but it may, in exceptional instances, be associated with changes in the larger bile-ducts.

(II) *Unilobular cirrhosis*; each lobule is separated from its fellows by a delicate fibrosis. The arrangement thus far imitates that normally seen in the pig's liver. Unilobular cirrhosis is specially related to inflammation of the minute bile-ducts, but is sometimes described as a result of cholangitis of the larger ducts. Unilobular cirrhosis is often complicated by multilobular cirrhosis and is frequently associated with intercellular cirrhosis, so that a mixed form of cirrhosis results.

(III) *Intercellular cirrhosis*; each hepatic cell is separated by young connective tissue from its fellows.

(IV) *Mixed cirrhosis*; in which there are various combinations of the three preceding main types, the multilobular, unilobular, and intercellular. This is met with in many cases of portal cirrhosis, especially when the course of the disease has been rapid, and is also seen at the termination of long-standing cases of hypertrophic biliary cirrhosis. Mixed cirrhosis is a common anatomical form, but has no claims to be considered as a clinical type of cirrhosis.

(V) *Sporadic fibrosis*, in which there are isolated patches of fibrosis not corresponding with any of the preceding categories. Under this heading come local fibrosis around parasites, cysts, granulomas, the results of small areas of focal necrosis, and the replacement fibrosis seen in chronic venous engorgement.

In the foregoing anatomical classifications the portal and biliary forms of cirrhosis are of great clinical importance, the others, with the exception of the intercellular cirrhosis of congenital syphilis and the cirrhosis

of haemochromatosis (p. 303), are chiefly of pathological interest. Oertel [1] considers that a classification of cirrhosis is not possible on anatomical grounds, because all cirrhosis is intralobular and the described forms merge freely into one another.

Clinical Classifications.—If any formal classification be adopted, it should be one that can be used at the bedside. A large number of different varieties of hepatic cirrhosis have been described, and in many cases the probable causes, or associated conditions, of the cirrhosis, such as alcohol, malaria, syphilis, tuberculosis, diabetes, dyspepsia, biliary obstruction, have been taken as grounds for establishing different types of the disease. Again, cirrhosis has been classified according to the size of the liver or of the spleen. A large (hypertrophic) cirrhotic liver and a small (atrophic) cirrhotic liver are often spoken of; while the French school has distinguished different types of biliary cirrhosis not only according to the relation in size between the liver and spleen, but also according to the time incidence of enlargement of the two organs. Thus, the liver may be much larger (hepatomegalic), of relatively much the same size (splenomegalic), or even smaller (hypersplenomegalic biliary cirrhosis) than the spleen; or the liver may be enlarged before (presplenomegalic), at the same time (splenomegalic), or after (metasplenomegalic hypertrophic biliary cirrhosis) the enlargement of the spleen is detected. These titles serve to shew the minute and elaborate character of the classification attempted.

Senator's classification can to some extent be utilised in clinical practice.

I. Portal Cirrhosis.
   (*a*) The hobnailed liver, diminished in size.
   (*b*) With jaundice, which is either due to gastro-intestinal catarrh obstructing the common bile-duct, or to pressure exerted on the intrahepatic radicles of the bile-ducts.
   (*c*) With increased size of the liver, which may subsequently be followed by a diminution in bulk.

II. Biliary Cirrhosis.
   (*a*) Due to calculous obstruction of the ducts. No splenic enlargement, no ascites.
   (*b*) With an enlarged spleen. This is a transitional form to the next.

III. Hypertrophic biliary cirrhosis with chronic jaundice.

From a practical point of view it seems to me to be best to make, in the first instance, a broad division of cirrhosis into two principal types as shewn by their clinical features:—

(*a*) Ordinary or common cirrhosis (portal),
in which haematemesis is an early symptom and ascites a terminal incident. Jaundice is not prominent; death may be preceded by a toxaemic state without much or any ascites.

[1] Oertel. *Arch. Int. Med.*, Chicago, 1908, i, 390.

The liver may be either large or small, but shews multilobular fibrosis; the spleen is enlarged, but not so constantly or markedly as in the second category.

(*b*) The biliary type. Jaundice is the most prominent feature and may be constant for long periods; haematemesis and ascites are only met with exceptionally. A little ascites may develop as a terminal phenomenon shortly before death. The liver is enlarged, sometimes to an extreme degree. The surface is smooth and the fibrosis of a mixed, diffuse, or unilobular type. The spleen is enlarged, sometimes greatly.

In this work these two main types of cirrhosis will be adhered to, but short sections on the sub-varieties of cirrhosis, included under these two main types, will be added.

Portal Cirrhosis.

Variety: Pigmentary Cirrhosis.

Biliary Cirrhosis.

(i) Hypertrophic Biliary Cirrhosis.

(ii) Obstructive Biliary Cirrhosis.

Comparison of the Main Forms of Cirrhosis with some Forms of Kidney Disease.—Portal cirrhosis may be compared to granular kidney. Hypertrophic biliary cirrhosis may be likened to chronic parenchymatous nephritis, the changes being due to poisons reaching the organs by the arterial blood-stream. The terminal production of multilobular cirrhosis in long-standing hypertrophic biliary cirrhosis corresponds to the evolution of a contracting or small white kidney, due to the addition of the changes of a granular or arteriosclerotic kidney to chronic parenchymatous nephritis (large white kidney). Lastly, obstructive biliary cirrhosis is comparable to consecutive nephritis.

PORTAL CIRRHOSIS

Synonyms: Common, Alcoholic, or Atrophic Cirrhosis; Multilobular, Annular, or Venous Cirrhosis; Laennec's Cirrhosis; Hobnailed, Gin- or Whisky-drinker's Liver; Chronic Interstitial Hepatitis.

THE term atrophic cirrhosis, though commonly used as synonymous with portal cirrhosis, is unsuitable, inasmuch as the liver is often larger than natural. The adjectives portal, multilobular, and common are more accurate. Old names, now forgotten, for the condition are granulated, tuberculated, lobulated liver.

Definition.—The disease is characterised anatomically by fibrosis spreading from the portal spaces and enclosing varying numbers of lobules, in which the cells tend to shew degenerative changes. Clinically dyspepsia, haematemesis, splenic enlargement, terminal ascites, and oedema of the feet are the essential features, while jaundice is either absent or transient and slight. The disease is commonest about the age of fifty and is frequently related to chronic alcoholism.

History.—The hardened condition of the liver was described by Vesalius, Harvey, Morgagni, and others. Payne[1] in reviewing the history of cirrhosis reproduced the drawing of a cirrhotic liver described in the *Philosophical Transactions* of 1685 by John Browne, surgeon to St. Thomas's Hospital. The ascites in this case, as in others before this date, was thought to be the result of drinking too much water, "a fault which," according to Payne, "the bold spirits of the time were much on their guard against." Matthew Baillie[2] gave a good naked-eye description of the disease under the name of "common tubercle of the liver"; he was really the first to separate it from "scirrhous tumours," and he regarded it as a disease peculiar to the liver and more apt to occur in those accustomed to drink spirituous liquors. The word "cirrhosis" was invented in 1819 by Laennec,[3] who regarded the bile-stained "hobnails" as masses of yellow (κιρρός) new-growth, invading the liver, hence cirrhosis. Hanot dutifully proposed that portal cirrhosis should be spoken of as Laennec's cirrhosis.

Carswell[4] in 1838 was the first to point out the presence and importance of fibrosis in cirrhosis, and was confirmed by Kiernan's histological researches. For further details as to the history of cirrhosis the reader is referred to Wickham Legg's[5] essay.

Etiology.—*Age.*—Portal cirrhosis is a disease of late middle life, and usually proves fatal about fifty years of age.

[1] Payne, J. F. *Trans. Path. Soc.*, Lond., 1889, xl, 310.
[2] Baillie, M. *Morbid Anatomy*, p. 141, 1793.
[3] Laennec. *Traité de l'auscultation méd.*, 1819, tome i, p. 368 (*note*).
[4] Carswell. *Illustrations of Elementary Forms of Disease.*
[5] Legg, W. *St. Barth. Hosp. Rep.*, 1872, vii, 74.

In 165 adults whose livers were cirrhotic the average age was 48·7 years; of these, 121 were males (average age, 49·4 years) and 44 females (average age, 47 years). In Yeld's[1] 128 cases the average age was 47·5 years.

There is a definite group of cases of genuine portal cirrhosis in young children, which will be specially referred to elsewhere (*vide* p. 334).

Hilton Fagge[2] found that the average age of persons in whose bodies cirrhosis of the liver was discovered without any marked symptoms during life was five years higher than that of persons dying of the disease. This would suggest that the compensatory processes had been very successful; but in my own figures there is very little difference between these two classes.

In 78 patients dying from cirrhosis the average age was 48·3 years, whereas in 87 patients who died from independent causes but whose livers were cirrhotic the average age was 49·1 years.

There is reason to think that cases of cirrhosis with a very distinct alcoholic history are fatal at an earlier age than cases of cirrhosis in which alcoholic excess either did not exist or is not a prominent recent feature in the history. This is especially marked in the case of women.

In 114 cases tabulated by Fenton and myself the average age of all the alcoholic cases of cirrhosis was 46·6 years, as against 49·9 years for the non-alcoholic cases. Taking the ages of the sexes separately, the figures read as follows—alcoholic males, 47·8 years; non-alcoholic males, 49·3; alcoholic females, 42·8; non-alcoholic females, 51·5.

Sex.—Portal cirrhosis is commoner in men than in women; probably in the proportion of about 3 to 1.

Among 645 cases in which cirrhosis of the liver was found after death, obtained by adding together the statistics of Price (Guy's Hospital), Kelynack (Manchester), Yeld (St. Bartholomew's), Candler[3] (Charing Cross), and St. George's, there were 479, or 74·3 per cent, males, and 166, or 25·7 per cent, females. From the bills of mortality of New York for the years 1889–1899, Crook[4] found that of 4737 deaths from cirrhosis 2980, or 62·3 per cent, were males, and 1757, or 37·7 per cent, females. The Registrar-General's returns for England and Wales shew much less difference; in the ten years ended 1904 there were certified as dying of cirrhosis 41,085 persons, of which 22,830, or 55·6 per cent, were males, and 18,255, or 44·4 per cent, females.

From statistics of St. George's Hospital it appears that cirrhosis is more often latent in men than in women (*vide* p. 227).

In children the incidence of portal cirrhosis is a little higher in the male sex; in 90 cases under twenty-one years of age there were 48

[1] Yeld. *St. Barth. Hosp. Rep.*, 1898, xxxiv, 215.
[2] Hilton Fagge. *Guy's Hosp. Rep.*, 1874–5, xx, 193.
[3] Candler. *Arch. Neurol. Claybury Asylum*, 1907, iii, 439.
[4] Crook. *Med. News*, N.Y., 1902, lxxx, 246.

males and 42 females (Woolley[1]); in 67 cases of alcoholic cirrhosis in children 39 were in boys and 28 in girls (E. Jones[2]).

Occupation, etc.—Cirrhosis is more frequent in those who are brought in contact with alcoholic drinks, especially publicans, commercial travellers, and others who have occasion frequently to drink over business.

In 149 persons connected with the liquor traffic, Dickinson[3] found that post-mortem examination shewed cirrhosis to occur in 22, while in 149 other persons not brought specially into contact with alcohol it was present in 8 only.

Cirrhosis is more often seen in those whose life is sedentary than in persons leading an active outdoor life. Sir D. Duckworth[4] in 1874 quoted the experience of Sir W. Gull and Sir G. Burrows to the effect that cirrhosis was rare in the upper and well-to-do classes.

Geographical Distribution.—The distribution of cirrhosis does not run hand in hand with that of alcoholism. The abuse of alcoholic drinks is very widespread, but the distribution of cirrhosis does not by any means correspond. Thus, in hot countries alcoholic excess more often tends to produce a rapid reaction in the liver, such as hepatitis, while in cold climates cirrhosis is a more frequent result. But in temperate climates the incidence of cirrhosis varies very considerably; thus, cirrhosis is common in London, but comparatively rare in Scotland. There are also curious differences as to the distribution of cirrhosis in France which cannot be correlated with that of temperance and intemperance. It is an interesting question whether the incidence of cirrhosis has undergone any marked change in the course of years. In 1857 Budd[5] wrote that "cirrhosis is more common in England and Scotland than in France"; at the present day cirrhosis is probably quite as frequent in France as in England, and much more so than in Scotland. In this connexion it is significant that alcoholism has enormously increased in France of late years. In India cirrhosis is much commoner in natives than in Europeans; the reverse holds good as regards hepatic abscess. In England and Wales the death-rate from cirrhosis per million living has greatly increased since the Registrar-General reports were instituted; in the quinquennium 1866–70 it was 42, and there was an almost uniform increase up to 134·6 per million living in the quinquennium 1896–1900; in the quinquennium 1901–5 there was a fall to 121. As already mentioned, the death-rate from cirrhosis fluctuates with that of alcoholism in England and Wales.

Heredity.—Multilobular cirrhosis is not a "family" disease or one that tends to recur in members of the same family; in this way it contrasts with hypertrophic biliary cirrhosis, which may attack several members

[1] Woolley. Unpublished thesis for M.D. Cantab., 1906.
[2] Jones, E. *Brit. Journ. Children's Diseases*, 1907, iv, 6.
[3] Dickinson, W. H. *Med.-Chir. Trans.*, 1873, lvi, 34.
[4] Duckworth. *St. Barth. Hosp. Rep.*, 1874, x, 56.
[5] Budd. *Diseases of the Liver*, p. 150, 3rd ed., 1857.

of the same family. In a few instances several adults may die of alcoholic cirrhosis, probably from a family failing towards alcoholism. In children the death of two or more members of the same family from multilobular cirrhosis is less rare. This may depend on hereditary influences, syphilis disposing the organ to the incidence of ordinary cirrhosis—parasyphilitic cirrhosis (*vide* p. 381). An important factor in the development of cirrhosis is the vitality of the liver; if its resistance is congenitally feeble, factors otherwise harmless, such as the specific fevers and indiscretions in diet, may induce cirrhosis. It is conceivable that alcoholism in the mother may so influence the livers of her offspring that cirrhosis develops in them more readily than it otherwise would. Precocious alcoholism or peculiarly unsuitable food, such as pickles or fish soaked in vinegar, may cause cirrhosis in two or more members of the same family. Jollye[1] described cirrhosis in a brother and sister accustomed to take vinegar.

Two sisters, aged nine years and ten years, died in St. George's Hospital in 1899 and 1901 with hobnailed livers weighing 20 and 12 ounces respectively. In both of them laparotomy was performed: in the younger because tuberculous peritonitis was suspected; in the older, who had a temperature of 104° and diarrhoea, because perforation of a typhoid ulcer appeared probable. The mother was extremely alcoholic, but persisted that she had not given alcohol to the children. A brother aged sixteen years had laparotomy performed for supposed tuberculous peritonitis in St. Thomas's Hospital in 1901; no evidence of perihepatitis or peritonitis, but a hobnailed liver was found. All three cases died shortly after laparotomy and were examined after death. No abdominal lesion except hepatic cirrhosis and no evidence of syphilis was found in any of them.

Pathogeny.—Cirrhosis of the liver is the result of some poison, or possibly of poison-producing bodies such as micro-organisms, reaching the liver. These agents may reach the liver either (1) by the portal vein, or (2) by the hepatic artery; in other words, they may be derived from the alimentary canal or from the general circulation. When the active agent travels by the portal vein, the resulting cirrhosis is usually of the ordinary portal type; when the liver is affected secondarily to an arterial infection or toxaemia, the cirrhosis is often of a more mixed type, and may then resemble that of biliary cirrhosis. In some instances, however, in which the poison arrives by the hepatic artery, the cirrhosis is of the portal type.

In reviewing the etiology of cirrhosis it will be convenient, first of all, to consider the poisons and micro-organisms which reach the organ by the portal vein, and then those conveyed by the hepatic artery.

[1] Jollye. *Brit. Med. Journ.*, 1892, ii, 858.

SYNOPSIS

I.—Poisons conveyed to the Liver by the Portal Vein.
(*a*) Ingested poisons: (1) alcohol; (2) other poisons.
(*b*) Poisons manufactured in the alimentary canal. Dyspeptic cirrhosis.
(*c*) Umbilical vein cirrhosis and congenital syphilis.
(*d*) Poisons manufactured in the spleen.
II.—Micro-organisms conveyed to the Liver by the Portal Vein.
III.—Poisons conveyed to the Liver by the Hepatic Artery.
IV.—Micro-organisms conveyed to the Liver by the Hepatic Artery.
Conclusion.

I. The Poisons conveyed to the Liver by the Portal Vein may be divided into the following categories:—

(*a*) The poisons introduced into the intestinal tract from without: (1) alcohol, and (2) other bodies.

(*b*) Those manufactured in the alimentary canal as the result of faulty digestion, fermentation, and putrefaction.

(*c*) The poison of congenital syphilis, conveyed by the umbilical vein.

(*d*) Poisons manufactured in the spleen.

(*a*) Ingested Poisons.—Of these, alcohol requires much the most consideration and discussion.

(1) *Alcohol and Alcoholic Drinks.*—With regard to the question whether or not *alcohol* is the cause of cirrhosis, clinical and experimental evidence are opposed. In practice there are few points more certain than that the abuse of alcoholic drinks is a frequent precursor of hepatic cirrhosis, while from experiments on animals the bulk of the evidence is in a contrary direction. The deaths from cirrhosis and from alcoholism, as shewn by the Registrar-General statistics,[1] correspond in a striking manner. Thus, in the quinquennium 1871–75 there were 72 deaths from cirrhosis and 37 from alcoholism per million living; in the quinquennium 1901–5 the corresponding numbers were 121 and 78.

Among drunkards, however, cirrhosis is not so frequent as is usually assumed. Thus in 250 necropsies on confirmed drunkards who died suddenly from the effects of alcohol, Formad[2] found cirrhosis in six only. The reason why alcoholics frequently escape cirrhosis is probably either that they have considerable resistance or that some other and necessary factor, which usually accompanies alcoholism, such as intestinal auto-intoxication, is wanting. Cirrhosis appears to be rare among the insane, and yet alcoholism is the cause of insanity in at least 10 per cent of the inmates of asylums (Sullivan); probably the explanation of the

[1] *Sixty-Eighth Annual Report of the Registrar-General for 1905*, p. 19.
[2] Formad. *Trans. Assoc. Amer. Phys.*, 1886, i, 225.

rarity of cirrhosis in alcoholic insanity is that only persons with an inherently stable nervous system can drink long enough to acquire advanced cirrhosis (Mott [1]).

There are, of course, many cases of ordinary cirrhosis, especially in children, in which alcoholism can be excluded as an antecedent factor in the production of cirrhosis.

Experimentally the introduction of alcohol into the stomach or portal vein of animals has usually given rise to fatty change and sometimes to some necrosis of the liver cells with a little small-celled infiltration around, but in only a few instances has cirrhosis resulted.

Numerous observers, Strassmann,[2] Afanasieff,[3] von Kahlden,[4] Sabourin,[5] Lafitte,[6] Pohl,[7] Scagliosi,[8] perseveringly administered alcohol in considerable quantities to animals over a fairly prolonged period, and entirely failed to detect any evidence of cirrhosis in the liver. Straus and Blocq [9] introduced a tube into the stomach of rabbits, and by this means gave 10 grams of alcohol daily ; after three or four months a small-celled proliferation was found at the periphery of the lobules. This is hardly comparable to genuine cirrhosis, and, moreover, the introduction of the tube into the stomach complicates matters, inasmuch as it may have led to catarrh, and thus to the manufacture and subsequent absorption of other irritating bodies. De Rechter [10] has seen cirrhosis follow the continued administration of alcohol in dogs and rabbits. Out of 120 rabbits given alcohol experimentally for prolonged periods 4 shewed cirrhosis (Friedenwald [11]).

Since alcohol alone is not sufficient to account for cirrhosis either in man or animals, the undoubted association between alcoholism and cirrhosis must be explained in some other way. Two possibilities may be referred to : (i) That though ordinary ethylic alcohol itself does not produce cirrhosis, alcoholic drinks in virtue of other bodies contained in them are responsible for cirrhosis. It has been suggested that amylic alcohol is the important factor, but this requires definite proof. Lancereaux [12] believed that sulphate and bisulphate of potassium, which are added to wines and beers, are the causal factor in the production of cirrhosis, and supports his contention by the production of cirrhosis in rabbits, guinea-pigs, and dogs fed on sulphate of potassium. The amount of the salt given to these animals was very large, corresponding for an adult man, according to Vallin,[13] to a quantity of 60 to 350 grams per

[1] Mott. *Arch. Neurol. Claybury*, 1907, iii, 439.
[2] Strassmann. *Vrtljhr. f. gericht. Med.*, 1888, xlix, 232.
[3] Afanasieff. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1890, viii, 443.
[4] v. Kahlden. *Ibid.*, 1891, ix, 349.
[5] Sabourin. *La Gland biliaire d'Homme*, 1888.
[6] Lafitte, *Thèse de Paris*, 1892.
[7] Pohl. *Arch. f. exper. Path. u. Pharmak.*, 1893, xxxi, 281.
[8] Scagliosi. *Virchows Arch.*, 1896, cxlv, 546.
[9] Straus et Blocq. *Arch. de physiol. norm. et path.*, 1887, 3. s., x, 409.
[10] De Rechter. *Bull. Acad. Méd. de Belg.*, 1892, 4. s., vi, 425.
[11] Friedenwald. *Journ. Amer. Med. Assoc.*, 1905, xlv, 780.
[12] Lancereaux. *Bull. Acad. de Méd.*, Paris, 1897, xxxviii, 202 ; 1910, lxiii, 15.
[13] Vallin. *Ibid.*, 1897, xxxviii, 285, 343 ; 1898, xxxix, 257.

diem. Viola's[1] observations on cirrhosis in Venice lent support to Lancereaux's theory.

(ii) That alcohol and alcoholic drinks act indirectly, and either (*a*) set up gastro-intestinal catarrh and thus lead to the production of poisonous bodies which when carried to the liver cause cirrhosis, or (*b*) when acting on the liver simultaneously with bacterial poisons so lower its resistance that cirrhosis results from the effects of the latter.

(*a*) Boix described "dyspeptic cirrhosis," which is not necessarily alcoholic, but is due to the action of fatty acids, such as butyric, lactic, acetic, and valerianic; this he supports by experimental results. Clinically the frequent existence of long-continued dyspepsia is quite in accord with this hypothesis (*vide* p. 185).

(*b*) Scagliosi concludes that, though alcohol or bacterial poisons alone do not permanently damage the liver, alcohol may render persistent the lesions induced temporarily in the liver by the poisons of the specific fevers and other infections, and so induce cirrhosis. Ramond[2] adopted much the same view. He produced cirrhosis by giving alternate doses of bacterial toxins and alcohol by the mouth to animals. He found, by examination of the toxicity of the faeces in man, that alcohol does not necessarily increase the poisonous bodies in the alimentary canal; he was therefore not inclined to support the first view. He believes that alcohol acts as a cellular poison on the liver cells and thus inhibits their special function of destroying poisons; these poisons are then free to induce cirrhosis. There is not much to choose between these two views; and it is neither necessary nor possible to adopt one exclusively. It is, indeed, not improbable that both of them may be true.

To conclude: with regard to the rôle of alcohol in the production of cirrhosis, it may safely be held that alcoholism is frequently an antecedent condition, but that *per se* alcohol has no specific action on the liver except fatty degeneration. It gives rise to cirrhosis in a secondary manner, either by leading to the production of sclerogenic poisons or by enabling such poisons to have full sway on the liver. The importance of alcoholism has been rather exaggerated, and it is not sufficiently recognised that other factors may cause cirrhosis, and that a congenital or acquired want of resistance on the part of the liver itself is, though hard to estimate, probably of great importance.

(2) *Cirrhosis due to Ingested Poisons other than Alcohol.*—There are numerous cases of undoubtedly non-alcoholic cirrhosis, especially in children. In some of these there has been a definite history of high living, and occasionally two or even more members of a family have early in life become affected with hepatic cirrhosis. Cases are on record in which fish pickled in vinegar had been largely taken; and spices, curries, and highly flavoured food have long been thought to account for some cases of cirrhosis. But here it at once becomes evident that it is difficult to draw a hard-and-fast line between poisons which are ingested and

[1] Viola. *Arch. gén. de méd.*, 1898, i, 1, 164, 318.
[2] Ramond. *Presse méd.*, 1897, p. 178.

give rise to cirrhosis by virtue of their own inherent irritating properties, and those factors which set up gastro-intestinal catarrh and by the manufacture of fermentation products inside the alimentary canal lead to what has been termed dyspeptic cirrhosis. Experimentally, it is true, Boix [1] produced some cirrhosis in rabbits by feeding them on acetic, butyric, valerianic, and lactic acids, but these acids are, on the whole, more likely to be produced by fermentation in the human alimentary canal than to be swallowed as such in food. A good example of cirrhosis due to poisonous food is reported by Segers [2] among the Fuegians, who eat large quantities of mussels daily. At a certain stage of their development the mussels are toxic from the presence of mytilotoxin. As a result of this poison the livers of the Fuegians become enlarged and subsequently cirrhotic and small.

In rare instances cirrhosis has been found to be associated with the presence in the liver, or possibly to be caused by the irritation, of particles of carbon absorbed from the alimentary canal. This form of cirrhosis—cirrhosis anthracotica—has been seen in connexion with pulmonary anthracosis, and Adami [3] refers to an analogous form associated with stonemason's lung—silicosis. Lancereaux [4] says it occurs in workers in copper and in coal-miners, and that the intestinal walls are pigmented from the presence of the carbon, this shewing the route taken in its absorption. The lymphatic glands in the abdomen are also crowded with particles of carbon. Welch [5] also described a case (*vide* p. 302).

Arsenic appears to be capable of setting up cirrhosis of the liver. In the epidemic of arsenical peripheral neuritis due to poisoned beer in the north of England in 1900–1901 an unusual number of cases of cirrhosis of the liver and ascites were seen (Reynolds,[6] Sturrock [7]). Hutchinson [8] and Hamburger [9] reported ascites in patients who had long been addicted to the medicinal use of arsenic; but in both these instances recovery followed suspension of the drug, so that the existence of cirrhosis was not proved. It has even been suggested that Banti's disease, or the terminal cirrhosis which supervenes in some cases of chronic splenic anaemia, is due to the arsenic given medicinally (W. Broadbent [10]). Experimentally cirrhosis has been produced by chronic arsenical and by chronic aluminium poisoning, but cirrhosis in man has not been traced to the latter metal.

In a case of argyria, in which nitrate of silver had been taken for four months for epilepsy, Frommann [11] found early hepatic cirrhosis with deposit of silver.

[1] Boix. *Arch. gén. de méd.*, Paris, 1899, clxxxiv, 210.
[2] Segers. *Sem. méd.*, 1891, xi, 448.
[3] Adami. *Sajous' Annual*, 1898, ii, 313.
[4] Lancereaux. *Traité des maladies du foie et du pancréas*, p. 340, 1899.
[5] Welch. *Johns Hopkins Hosp. Bull.*, 1891, ii, 32.
[6] Reynolds, E. S. *Med.-Chir. Trans.*, 1901, lxxxiv, 425.
[7] Sturrock. *Brit. Med. Journ.*, 1900, ii, 1815.
[8] Hutchinson, J. *Arch. Clin. Surg.*, 1895, vi, 389.
[9] Hamburger. *Johns Hopkins Hosp. Bull.*, 1900, xi, 87.
[10] Broadbent, W. *Brit. Med. Journ.*, 1903, i, 1140.
[11] Frommann. *Virchows Arch.*, 1859, xvii, 135.

Lead.—Experimentally some slight degree of hepatic fibrosis has resulted from feeding animals with lead (Lafitte[1]), but clinically lead has no claim to be considered a cause of cirrhosis; Lavrand,[2] indeed, states that the liver is generally unaffected in chronic plumbism. There is, moreover, some doubt as to the mechanism by which lead would produce cirrhosis; perhaps the more probable view is that it leads to arteriosclerosis of the branches of the hepatic artery, and so to slight dystrophic fibrosis.

Chloroform.—Experimentally chloroform usually produces fatty change, but Opie[3] found that when given interruptedly over a period of sixty days cirrhosis resulted. When chloroform was given by the mouth, and bacteria injected into the blood, cirrhosis was readily produced.

Naphthol.—By injecting small quantities of naphthol into the portal vein Bouchard[4] produced some fibrosis in the liver.

Bacterial Toxins.—Experimentally Charrin[5] injected boiled cultures of the *Bacillus pyocyaneus* into the portal vein, and produced extensive small-celled infiltration in the portal canals. Krawkow[6] obtained cirrhosis in birds in similar experiments when prolonged, but Ramond failed to induce cirrhosis in animals by the administration of toxins by the mouth alone, though he obtained positive results when alcohol was given as well.

Krawkow, by introducing cultures of *Staphylococcus pyogenes aureus* and of other micro-organisms into the alimentary canal produced experimental cirrhosis. The micro-organisms may have merely manufactured a poison, which passed into the portal vein and so to the liver, and set up a purely toxic cirrhosis, but, on the other hand, the micro-organisms may themselves have reached the liver either by the portal vein or by ascending the bile-duct. These points will be referred to later.

(*b*) Cirrhosis due to the Action of Poisons manufactured in the Intestine.—This hypothesis has already been referred to (*vide* p. 183), in order to explain cirrhosis supervening in alcoholic subjects, where it was suggested that alcohol sets up gastro-enteritis, and thus leads to the formation of poisons which are the direct causes of cirrhosis. Boix[7] and Hanot[8] have described non-alcoholic cirrhosis due to dyspepsia. The liver is first enlarged and tender, and later cirrhosis and jaundice may supervene. The cirrhosis ascribed to gout may be of this nature, while the non-alcoholic cirrhosis in Mohammedans and the natives of India and Egypt, a form long ago referred by Budd[9] to the action of spices, curries, and other stimulating articles of food, such as ginger, may be explained as depending on the irritating effects of acetic, butyric, lactic, or other

[1] Lafitte. *Thèse de Paris*, 1892.
[2] Lavrand. *Le Néphrite des saturnines*, p. 12, 1899.
[3] Opie. *Journ. Exper. Med.*, N.Y., 1910, xii, 367.
[4] Bouchard. *Thérapeutique des maladies infectieuses*, p. 313, 1889.
[5] Charrin. *Arch. de physiol. norm. et path.*, 1893, xxv, 554.
[6] Krawkow. *Arch. de méd. expér. et d'anat. path.*, 1896, viii, 268.
[7] Boix. "La Foie des dyspeptiques," *Thèse de Paris*, 1894; *Arch. gén. de méd.*, 1899, clxxxiv, 210.
[8] Hanot et Boix. *Congrès de méd.*, Rome, 1894.
[9] Budd. *Diseases of the Liver*, p. 151, 1857.

acids manufactured as the result of intestinal fermentation. Cirrhosis of this kind is sometimes described as due to auto-intoxication or as autochthonous, and in a posthumous article by Hanot[1] was called "Budd's cirrhosis." D'Amato[2] gave butyric acid daily for six months to animals and found parenchymatous, but no interstitial, changes in the liver. By the administration of paracresol, phenol, and indol, which are produced by the colon group, Metchnikoff[3] produced early cirrhosis in animals. In order to meet the obvious objection that dyspepsia is comparatively seldom followed by cirrhosis, Boix argues that the resistance of the liver is an important factor, and that where this is congenitally feeble continued dyspepsia will lead to cirrhosis. This idiosyncrasy or predisposition is included under the French term "arthritism."

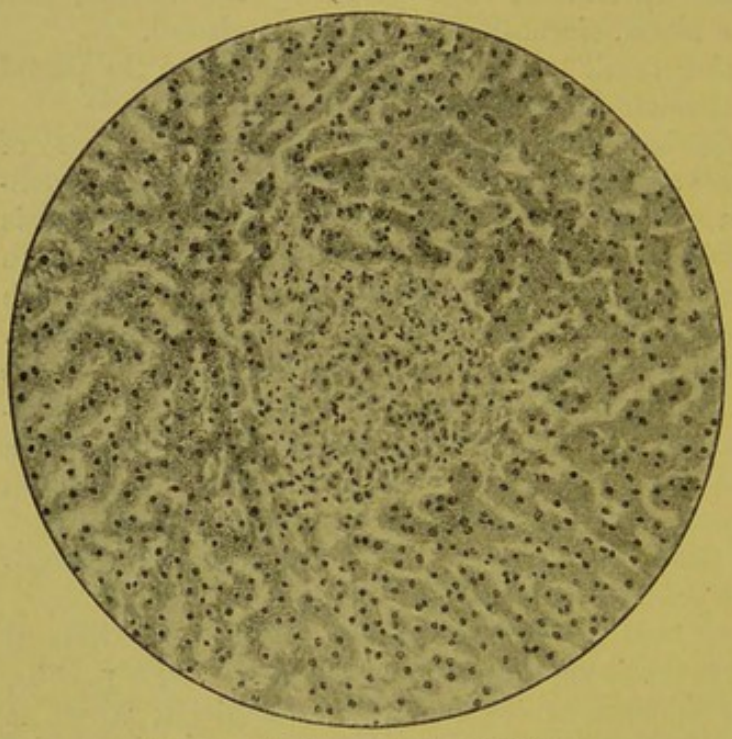


Fig. 25.—Focal necrosis in enteric fever.

In long-standing mitral disease hepatic fibrosis may be due to several causes. A certain degree of fibrous replacement may result from atrophy of the liver cells; and gastro-intestinal catarrh may give rise to the formation of irritating bodies which, when absorbed, find the liver in a condition of diminished resistance and are thus able to set up changes. The fibrosis secondary to chronic venous engorgement, however produced, is slight and of no clinical importance (*vide* p. 88).

Among Brahmins and other high-class Hindus who, as a rule, never touch alcohol, cirrhosis is frequent (Young[4]). Out of 163 cases of cirrhosis in natives of India, 138 had never touched alcohol (Sutherland[5]). Ginger-eating is prevalent with them and they are addicted to cardamoms, red pepper, and other hot spices. The cirrhosis may well be secondary to dyspeptic changes thus induced. In Egypt cirrhosis is found among Mohammedans, who take no alcohol, and may possibly be due to ankylostomiasis and the production of toxins in the intestine.

[1] Hanot. "La Cirrhose de Budd," *Arch. gén. de méd.*, 1899, clxxxiii, 3.
[2] d'Amato. *Giorn. internaz. d. sc. med.*, Napoli, 1907, N.S., xxix, 337.
[3] Metchnikoff. *Ann. de l'inst. Pasteur*, Paris, 1910, xxiv, 755.
[4] Young, L. T. *The Carlsbad Treatment*, p. 129, 2nd ed., 1899 ("Ginger Liver").
[5] Sutherland, D. W. *Ind. Med. Gaz.*, 1905, xl, 120.

In enteric fever[1] necrotic areas of small size, focal necroses, "lymphomata," or "lymphoid nodules," as they have been variously called, are often met with. The liver cells first degenerate and subsequently a certain amount of small-round-celled infiltration surrounds the necrotic areas. It is conceivable, therefore, that under favourable conditions a sporadic multiple fibrosis may result throughout the liver; usually these lesions are recovered from. Some observers have regarded enteric fever as a starting-point for cirrhosis. It is possible that if alcohol is taken and the resistance of the liver thus further diminished, this change may be rendered permanent. From Reed's and M'Crae and Klotz's[2] observations it appears probable that these focal necroses are due to toxins conveyed to the liver and possibly to thrombosis, and that these areas do not contain typhoid bacilli. Hanot found similar nodules in the liver in tuberculous enteritis. According to Mallory,[3] two distinct lesions have been described as lymphoid nodules: (1) a focus of lymphoid and plasma-cells confined to the connective tissue around the portal vessels and independent of the liver cells; (2) focal necrosis of cells in hepatic lobules due to blocking of capillaries by proliferated and phagocytic cells.

Pearce[4] has shewn experimentally that focal necroses can be directly caused by hyaline thrombosis (fused red blood-corpuscles) in the vessels, produced by intravenous injection of haemagglutinative serum, and that as the result of reparative processes around these focal necroses well-marked cirrhosis occurs in dogs.

Cirrhosis has been regarded as a late result of cholera; and it seems reasonable to believe that the slightly increased fibrosis around the portal spaces sometimes seen in rickets is due to gastro-enteritis. On the other hand, prolonged diarrhoea and gastro-enteritis in children do not play any part in the etiology of cirrhosis. It is conceivable that toxins absorbed in the course of appendicitis[5] may initiate cirrhotic changes in the liver.

By intraperitoneal injection of a micro-organism of the colon group Weaver[6] obtained cirrhosis in guinea-pigs, but the micro-organism was not found in the liver, hence the change in the liver may be regarded as due to the toxins absorbed by the portal vein.

(*c*) Umbilical Vein Cirrhosis.—In *congenital syphilis*, the blood containing the pathogenetic spirochaete arrives by the umbilical vein and thus passes into the branches of the portal vein in the liver. The resulting lesion is a diffuse unicellular cirrhosis. In exceptional instances a similar change is found in acquired syphilis; but otherwise syphilis does not directly produce hepatic cirrhosis, though it may lead to local

[1] Friedreich, *Virchows Arch.*, 1857, xii, 53; Reed, *Johns Hopkins Hosp. Rep.*, v, 379; Handford, *Trans. Path. Soc.*, 1889, xl, 129; Hanot, *Compt. rend. Soc. Biol.*, 1893, xlv, 856; Siredey, *Rev. de méd.*, 1886, vi, 465; Legrey, *Thèse de Paris*, 1892.

[2] M'Crae and Klotz. *Journ. Path. and Bacteriol.*, Cambridge, 1908, xii, 279.

[3] Mallory. *Journ. Exper. Med.*, N.Y., 1898, iii, 622.

[4] Pearce, R. M. *Ibid.*, 1906, viii, 64.

[5] Tuffier et Mauté. *Presse méd.*, 1904, p. 408.

[6] Weaver. *Johns Hopkins Hosp. Rep.*, 1900, ix, 543.

fibrosis, gummas, and cicatrices. Though this is undoubtedly true, it appears that unicellular cirrhosis, which is a secondary lesion of syphilis and therefore curable, often leaves behind a deficient resistance on the part of the liver and thus disposes it to become cirrhotic in the ordinary way. I have seen several cases of multilobular cirrhosis in the subjects of congenital syphilis. In other words, congenital syphilis so prepares the soil that ordinary cirrhosis may supervene. In these conditions the cirrhosis may be regarded as a parasyphilitic lesion.

Other poisons may travel from the mother to the fetus by the umbilical vein and give rise to changes in the liver. Our knowledge of umbilical vein cirrhosis is extremely meagre, but it is possible that the disease known as congenital obliteration of the bile-ducts may start in the liver and be due to toxins conveyed by the umbilical vein, and that the subsequent obliteration of the ducts is a later change due to a descending cholangitis (*vide* p. 651).

(*d*) Poisons manufactured in the Spleen.—In haemic infections micro-organisms tend to accumulate in the spleen, and, if not rapidly destroyed, produce toxins which travel to the liver and may there produce changes analogous to cirrhosis. Chauffard[1] has argued that cirrhosis is in some cases secondary to morbid processes originating, or at any rate most marked, in the spleen. Thus, in malaria the spleen is greatly enlarged and cirrhosis of the liver in malarial subjects may in part be due to poisons manufactured in the spleen. In chronic splenic anaemia a terminal cirrhosis of the liver with jaundice sometimes occurs (Banti[2]); this has been termed Banti's disease. The conception of Banti's disease has been much criticised; Gilbert and Lereboullet[3] insist that the splenic enlargement is due to passive engorgement produced by latent hepatic lesions.

As will be seen in the description of hypertrophic biliary cirrhosis, the typical unilobular cirrhosis is very frequently obscured by the addition of multilobular cirrhosis. This latter change may be explained as due to the infective agent, which primarily reached the liver by the hepatic artery and sets up unilobular cirrhosis, settling down in the spleen and producing toxins which, when conveyed by the splenic vein to the liver, induce multilobular cirrhosis. In support of the hypothesis that poisons are manufactured in the spleen and conveyed to the liver is the fact that endophlebitis of the splenic vein has been described in malaria by Kelsch and Kiener,[4] in enteric fever by Bezançon[5] and in splenic anaemia (Oettinger and Fiessinger[6]).

The portal vein may indeed be regarded as having two main sources in adult life—(*a*) the gastro-intestinal veins, by which poisons commonly travel to the liver, and (*b*) the splenic vein. In fetal life the umbilical vein is a third tributary and may also convey poisons to the liver.

[1] Chauffard. *Semaine méd.*, Par., 1899, xix, 177.
[2] Banti, G. *Ibid.*, 1894, xiv, 318.
[3] Gilbert et Lereboullet. *Rev. de méd.*, Par., 1904, xxiv, 893.
[4] Kelsch et Kiener. *Traité des maladies des pays chaudes*, p. 405, 1889.
[5] Bezançon, F. *Thèse de Paris*, 1895.
[6] Oettinger et Fiessinger. *Rev. de méd.*, Par., 1907, xxvii, 1109.

Sérégé,[1] from injection experiments with methylene-blue, concludes that the blood from the spleen goes exclusively to the left lobe of the liver. If this is true, cirrhosis due to poisons produced in the spleen should be confined to, or chiefly in, the left lobe of the liver. I am not aware that there is any evidence in support of this.

At present the existence of hepatic cirrhosis as a sole result of poisons manufactured in the spleen requires further investigation, but it is an attractive idea and is compatible with the fact that in one variety of hypertrophic biliary cirrhosis, the so-called metasplenomegalic, the spleen is enlarged before there is any manifest change in the liver.

II. Micro-organisms conveyed to the Liver by the Portal Vein

Cirrhosis thus produced would be described as infective in contradistinction to toxic cirrhosis, which is due to the action of poisons without the presence of microbes in the liver. This view is highly probable, but cannot be accepted at present. Hamilton[2] suggested that micro-organisms passing into the mesenteric veins undergo bacteriolysis in the portal blood, and that their toxins are carried to the liver and set up cirrhosis, bacterial cirrhosis. Adami,[3] in the Pictou cattle disease, found unicellular cirrhosis accompanied by swelling of the peri-portal and retroperitoneal lymphatic glands, and oedema of parts of the intestine. These lesions were associated with a minute bacillus belonging to the colon group. Adami has found the colon bacillus almost constantly in human livers; when the livers are healthy, the bacilli appear to have been killed by the liver cells. In progressive cirrhosis there are, in addition to dead bacilli, some areas where they appear active. This suggests the possibility that virulent colon bacilli may under conditions of diminished resistance of the liver cells, such as may be induced by alcohol, lead to cirrhosis. Adami[4] considered that a primary inflammation of the alimentary canal favoured invasion of the liver by the bacilli which set up cirrhotic changes in that organ.

It is, a priori, extremely probable that an acute hepatitis due to the brunt of a haemic infection falling on the liver would, if not fatal, leave behind it hepatic cirrhosis. Cases in human beings occur in which a febrile condition, accompanied by enlargement and tenderness of the spleen and liver, ushers in and precedes an illness which eventually is seen to have for its chief anatomical lesion a cirrhotic liver. Oertel[5] points out that if in acute hepatitis the lymphatics become obstructed from lymphangitis and perilymphangitis, resolution is prevented and cirrhosis results.

[1] Sérégé, H. *Journ. de méd. de Bordeaux*, 1902, xxxii, 357.

[2] Hamilton. "The Alimentary Canal as a Source of Contagion," p. 37, *Studies in Pathology*, Aberdeen Quater-Centenary, 1906.

[3] Adami. *Brit. Med. Journ.*, 1898, ii, 1215.

[4] *Idem. Report of Minister of Agriculture for the Dominion of Canada for the Year 1901*, p. 135.

[5] Oertel. *Arch. Int. Med.*, Chicago, 1908, i, 385.

In a boy, aged sixteen years, death occurred fourteen days after the onset of measles. Roger and Conte [1] found that an acute localised enteritis in the ileum had given rise to hepatitis, inflammation between the liver and diaphragm, an acute rapid putrid effusion into the right pleura, and, finally, gangrene of the lung. The bacillus resembled the *B. coli*. The liver shewed masses of round-celled infiltration in the portal spaces, degeneration of the liver cells, cholangitis, and endarteritis. The process was very acute, but it makes it easy to understand that a slighter degree of the same process, if recovered from, might be the starting-point of cirrhosis.

Some fibrosis is seen in prolonged cases of acute yellow atrophy. By intraperitoneal injections of cultures of a bacillus belonging to the pseudo-diphtheria group Hektoen [2] produced cirrhosis of the liver in animals. The bacilli were found in the capillaries of the liver.

By introducing cultures of micro-organisms into the intestines of birds Krawkow sometimes produced cirrhosis ; but the result may have been merely due to their toxins, for there is no evidence that the micro-organisms reached the liver.

It is possible that in exceptional instances tubercle bacilli carried from the intestines to the liver may set up some cirrhosis. Hanot and Gilbert's [3] experiments shew that avian tubercle bacilli may induce cirrhosis in guinea-pigs, and they believe that this sclerogenic result depends either on relatively high resistance on the part of the liver or on a slight degree of virulence on the part of the bacilli. As a rule, of course, tubercle bacilli give rise either to tubercles or to degeneration in the liver cells (*vide* p. 345). The ova of bilharzia may cause cirrhosis.[4] Kartulis [5] states that the liver is usually enlarged and that symptoms of cirrhosis are absent, but according to Phillips [6] it may cause ascites. Cirrhosis may also be set up by *Schistosomum japonicum* (Catto [7]). Michelazzi [8] described cirrhosis due to ankylostomiasis. Day [9] considers that in native Egyptians cirrhosis is probably due to some specific protozoan infection.

III. Cirrhosis due to Poisons conveyed to the Liver by the Hepatic Artery

This cirrhosis may be spoken of as toxic and due to the action of poisons on the liver. It has been suggested that cirrhosis may be set up by the specific fevers, typhoid fever, scarlet fever, measles, small-pox,

[1] Roger et Conte. *Presse méd.*, 1897.
[2] Hektoen. *Journ. Path. and Bacteriol.*, Edin. and London, 1901, vii, 214.
[3] Hanot et Gilbert. *Compt. rend. Soc. Biol.*, Paris, 1892, xliv, 72.
[4] Symmers. *Journ. Path. and Bacteriol.*, 1904, ix, 237.
[5] Kartulis. *Sem. méd.*, 1894, xiv, 415.
[6] Phillips. *Rec. Egyptian Government School of Medicine*, 1904, ii, 49.
[7] Catto. *Brit. Med. Journ.*, 1905, i, 11.
[8] Michelazzi. *Giorn. internat. d. sc. med.*, Naples, 1907, xxix, 241.
[9] Day. *Lancet*, Lond., 1909, i, 258. See also Ferguson and Day. *Ann. Trop. Med.*, Liverpool, 1909, iii, 379.

and pneumonia. Theoretically, the toxins of these diseases may, when absorbed into the general circulation, set up focal necrosis of the liver cells, and under certain conditions fibrosis might develop around these areas of necrosis.

Focal necrosis may occur in typhoid, scarlet fever, measles, small-pox, diphtheria, malaria, and other acute infections. In typhoid fever the poison might reach the liver by the hepatic artery and give rise to focal necrosis. Klein[1] and Crooke[2] described acute interstitial hepatitis in scarlet fever, and more recently Pearce[3] has met with focal necroses of the liver cells; this is analogous to scarlatinal nephritis, but it probably is a transient condition and clinically there is little relation between scarlet fever and hepatic cirrhosis. Focal necroses in measles have been described and figured by Freeman.[4] Small-cell accumulations, like those produced in typhoid fever, have been described in the liver in variola by Roger and Weil.[5] Arnaud,[6] who describes in addition small-celled infiltration near the portal spaces, suggests that cirrhosis may subsequently follow.

In diphtheria focal necroses occur round the intralobular vein (Councilman, Mallory, and Pearce[7]), with some proliferation of the endothelium. These changes are due to the action of poisons and not to the presence of diphtheria bacilli in the liver. Weaver[8] injected a micro-organism allied to the colon group into the abdominal wall of guinea-pigs and produced local abscesses in which the bacilli were found, none being present in the liver, which shewed focal necroses and cirrhosis. It is reasonable to believe that as the result of other local infections focal necroses in the liver may be produced, and that under favourable conditions some sporadic fibrosis might develop around these foci. The question whether absorption from tuberculous pulmonary vomicae which are secondarily infected with streptococci can induce cirrhosis is referred to elsewhere (p. 347).

The conditions favouring the development of permanent cirrhosis after infections are congenital susceptibility, want of resistance on the part of the liver, and the presence of other factors, such as alcoholism.

Experimentally, a certain amount of hepatic fibrosis has followed prolonged poisoning with vegetable, mineral, and bacterial poisons. The intoxication must be induced gradually and continued for a considerable period. If the poison is employed in too large amounts, the results are those of acute poisoning, viz. degeneration and necrosis of the liver cells, focal or diffused, as in phosphorus poisoning. In the same way, the injection of bacterial poisons into the circulation, when

[1] Klein. *Trans. Path. Soc.*, 1877, xxviii, 439.
[2] Crooke. *Birmingham Med. Rev.*, xx, xxi.
[3] Pearce. *Boston (U.S.A.) City Hosp. Rep.*, 1899, p. 74.
[4] Freeman. *Arch. Pediat.*, 1900, xvii, 81.
[5] Roger et Weil. *Compt. rend. Soc. Biol.*, 1900, lii, 911.
[6] Arnaud. *Marseille méd.*, 1899, p. 39.
[7] Councilman, Mallory, and Pearce. *Diphtheria, a Study of 220 Fatal Cases*, Boston, U.S.A., 1901.
[8] Weaver. *Johns Hopkins Hosp. Rep.*, Balt., 1900, ix, 543.

carried on rapidly, gives rise to necrotic changes in the liver cells around the intralobular veins; when the process is less intense and more prolonged a certain amount of cirrhosis results. Krawkow[1] obtained positive results with sterilised cultures of *Bacillus pyocyaneus*, and Claude[2] with diphtheritic toxin. But it is probable that these effects are transitory, and do not, when uncomplicated (*vide* p. 183) by alcoholism, induce cirrhosis in man. Flexner,[3] in a careful study of chronic intoxication by ricin and abrin—vegetable alkaloids or phytalbumoses—produced a form of cirrhosis. As a result of injection of phosphorated oil into the subcutaneous tissues of rabbits, Aufrecht[4] found that the liver cells shewed degeneration, and that later some small-celled infiltration took place around the lobules. Other poisons, when injected into the circulation, such as carbonate of ammonia, indol, skatol, phenol, sulphonal, have also led to a slight degree of microscopic fibrosis.

IV. Cirrhosis due to Micro-organisms conveyed to the Liver by the Hepatic Artery

In haemic infection the liver changes are often extremely acute and give rise either to suppuration or to widespread degenerative changes allied to acute yellow atrophy. In less acute haemic infections the supporting fibrous tissues shew proliferation and accumulation of leucocytes in the portal canals and in the peripheral parts of the lobules of the liver. These changes are the same as those seen in the acute specific fevers, such as scarlet fever (*vide* p. 191). Occasionally in pyaemia and septicaemia, due to streptococci, staphylococci, etc., as in acute necrosis, infective endocarditis, puerperal septicaemia, and erysipelas,[5] considerable small-celled infiltration of the liver is met with.

In the hepatitis due to repeated malaria there is considerable damage done to the liver cells, as shewn by focal necroses (Barker[6]), and fibrous hyperplasia is sometimes seen. The importance of malaria as a cause of cirrhosis appears to be surprisingly small (*vide* p. 308). Rogers[7] describes cirrhosis due to the Leishman-Donovan parasite of kala azar.

Enteric fever has already been referred to as leading to small necrotic areas in the liver (p. 191). In ordinary enteric fever these nodules appear to be due to the action of toxins conveyed from the alimentary canal, and not to bacilli. But infection of the liver by the hepatic artery may also occur. The changes in the liver due to general haemic infections are probably usually recovered from if the patient lives, but should conditions arise which depress the resistance of the liver, such as alcoholism, cirrhosis might conceivably result. This is supported by Opie's[8]

[1] Krawkow. *Arch. de méd. expér. et d'anat. path.*, 1896, viii, 269.
[2] Claude. *Thèse de Paris*, 1897.
[3] Flexner. *Journ. Exper. Med.*, N.Y., 1897, ii, 19.
[4] Aufrecht. *Deutsch. Arch. f. klin. Med.*, 1897, lviii, 302.
[5] Roger et Garnier. *Rev. de méd.*, 1901, xxi, 97.
[6] Barker. *Johns Hopkins Hosp. Rep.*, 1895, v, 241.
[7] Rogers. *Ann. Trop. Med. and Parasit.*, 1908, ii, 417.
[8] Opie. *Journ. Exper. Med.*, N.Y., 1910, xii, 367.

observation that administration of chloroform accompanied by intravenous injection of *B. coli* readily sets up cirrhosis.

Experimentally there is some evidence that haemic infections may induce hepatic cirrhosis. Krawkow [1] injected cultures of various micro-organisms into the muscles of fowls and pigeons, and found that after a considerable interval hepatic cirrhosis developed. This was especially well marked when the *Bacillus pyocyaneus* and the *Staphylococcus pyogenes aureus* were employed. By subcutaneous injection of cultures of a bacillus belonging to the pseudo-diphtheria group, Hektoen [2] obtained well-marked portal cirrhosis in animals.

It must, however, be remembered that in chronic haemic infections the spleen becomes crowded with micro-organisms, and that if they multiply there, toxins may be manufactured in considerable quantities and carried by the splenic and portal veins to the liver, and there set up a cirrhosis of splenic origin (*vide* p. 188).

Conclusion.—Experiment shews that numerous poisons are capable of giving rise to hepatic changes comparable to those of cirrhosis. Often, it is true, these lesions are early, or, at the best, not well marked. But the facts are of value as indicating that cirrhosis in man may reasonably be considered to be the result of a toxic process. These poisons may be absorbed either from the alimentary canal, and then reach the liver in a comparatively concentrated form, or they may travel to the liver by the hepatic artery, and are then comparatively dilute. Ordinary cirrhosis in man is generally due to poisons travelling by the portal vein. Alcoholism is rather an antecedent condition than a true cause, and acts indirectly or in an accessory manner. The possibility that cirrhosis is definitely due to micro-organisms must be faced; from analogy it is most probable, but at present it has not been certainly established. It is also highly probable that poisons, or perhaps micro-organisms, reaching the liver by the hepatic artery, may give rise to cirrhotic changes. The mechanism of this change will be further referred to in the section on "Hypertrophic Biliary Cirrhosis." As a result of destruction of the hepatic cells and absorption of their proteins into the circulation, hepatic anti-bodies or cytolysins are produced. These destroy the liver cells and thus a vicious circle is produced (Fiessinger [3]).

Nature of the Fibrosis of Cirrhosis. — It was formerly held that cirrhosis is primarily and essentially a chronic inflammation or hyperplasia of the connective tissue in the portal areas, and that the atrophic and degenerative changes in the liver cells are either (i) entirely secondary and due to pressure exerted by the contracting fibrous tissue, or to impaired nutrition from curtailed blood supply, or (ii) unimportant and almost accidental concomitant phenomena.

Subsequently it was thought that cirrhosis is essentially a replacement

[1] Krawkow. *Arch. de méd. expér. et d'anat. path.*, 1896, viii, 268.
[2] Hektoen. *Journ. Path. and Bacteriol.*, Edin. and Lond., 1901, vii, 214.
[3] Fiessinger. *Journ. physiol. et path. gén.*, Paris, 1908, x, 671.

fibrosis and is secondary to a primary degeneration and atrophy of the liver cells (Payne,[1] L. Beale). The changes in cirrhosis of the liver would thus be regarded as analogous to those in systemic scleroses of the spinal cord or to those in an arteriosclerotic kidney. Against this it may be urged—

1. That extensive atrophy or degeneration may occur without any fibrosis resulting. Thus, in old age there may, as I have seen, be marked atrophy of the cells in the peripheral zone of the hepatic lobule, with little or no fibrosis. In extensive central necrosis of the hepatic lobules the fibroblasts do not proliferate when the liver cells alone are destroyed (Mallory[2]). In lardaceous disease and in universal fatty change there may be complete freedom from fibrosis. In reply, it may be said that in such cases there is a general debility of the whole organ, and that the fibrous tissues share in it, and are therefore unable to proliferate (Kanthack[3]). MacCallum[4] has reported marked local fibrosis around an extensive area of degeneration set up during acute illness.

2. That, microscopically, the proliferation of the connective tissue is so exuberant, so like that of active inflammation elsewhere, and the degenerative changes in the cells so slight in comparison, that it is difficult to believe that the latter changes can be primary. In such cases there may well be two factors at work, namely, proliferation of the connective tissues and degenerative changes in the liver cells, and both may be due to the simultaneous action of the toxin. But, while bearing this explanation in mind, it must be remembered that a replacement fibrosis shews itself, not only as a passive overgrowth, but as a proliferation, for, both in degenerative "neuritis" and in granular kidney (arteriosclerotic in origin), much small-celled proliferation may sometimes be seen. Again, the absence of any extensive degeneration of the liver cells in cirrhosis must not be allowed to weigh too heavily, for the foci of degenerated cells may have disappeared. Kretz,[5] MacCallum,[6] and Milne[7] regard cirrhosis as a process of repair and as the result of successive regenerations of repeated focal lesions of the liver cells at the peripheries of the lobules. The frequent degenerations and subsequent regenerations of the hepatic cells lead to a progressive fibrosis which subsequently contracts. This view is supported by Pearce's[8] observations that cirrhosis follows focal necroses set up by hyaline thrombosis of the vessels.

3. That inasmuch as cirrhosis is, in ordinary conditions, due to the action of a poison, it is reasonable to believe that the effects will be no more limited to the hepatic cells than to the fibrous tissues, as was formerly

[1] Payne, J. F. *Trans. Path. Soc.*, Lond., 1889, xl, 321.
[2] Mallory. *Johns Hopkins Hosp. Bull.*, Balt., 1911, xxii, 69.
[3] Kanthack. *St. Barth. Hosp. Journ.*, Lond., 1896, iv, 22.
[4] MacCallum. *Journ. Amer. Med. Assoc.*, 1906, xlvii, 984.
[5] Kretz. *Wien. klin. Wchnschr.*, 1900, xiii, 271.
[6] MacCallum. *Journ. Amer. Med. Assoc.*, 1904, xliii, 649.
[7] Milne. *Journ. Path. and Bacteriol.*, Cambridge, 1909, xiii, 127.
[8] Pearce, R. M. *Journ. Exper. Med.*, 1906, viii, 64.

supposed to be the case. In other words, that the parenchymatous and interstitial changes are both, in the first instance, due to the same cause, and therefore vary directly in intensity. If this be so, it is easy to understand that the hepatic cells, being more sensitive, will react before the more resistant connective tissue, and that degenerative changes in them will generally, for this is their usual method of reacting, precede hyperplasia of the connective tissues. There are further grounds supporting the view of a simultaneous reaction on the part of the liver cells and framework as the starting-point, or first stage at any rate, in some cases of cirrhosis. In early cirrhosis the liver cells may shew evidence of active proliferation in the nuclear mitoses, while at the same time there is fibrosis. This process might perhaps be regarded as a general hyperplasia, and many cirrhoses, such as the nodular cirrhosis sometimes seen in malaria or tuberculosis, might be spoken of as hypertrophies that failed.

But it is important to bear in mind that there are possibly, if not probably, different ways in which the fibrosis of cirrhosis is brought about, and that the causative factors may vary during the course of an individual case. Thus, while both the changes may at the outset be the result of the toxin, irritative hyperplasia in one case, degeneration in the other, subsequently one of these changes may react on the other process.

In conclusion, it is, in the present state of our knowledge, safest not to regard the cirrhotic process as exclusively due either to irritative hyperplasia of the connective tissues, the hepatic cells being quite passive, on the one hand, or to primary degenerative or atrophic changes in the hepatic cells with a resulting replacement fibrosis on the other, but to steer a middle course, and to take the view that the irritating poisons leading to cirrhosis affect both elements in different ways, and that the resulting changes in one tissue may further initiate fresh changes in the other tissue, or modify those already existing.

Morbid Anatomy.—*Size and Weight.*—The size of the liver in ordinary cirrhosis varies very greatly; it may be smaller than natural, and is then often spoken of as "atrophic," and in extreme instances may not weigh more than 30 ounces; or, on the other hand, it may be very large and weigh as much as 150 or 200 ounces. A cirrhotic liver which is actually smaller than natural often weighs as much as a healthy liver or even more, its specific gravity being much increased. There are transitions between a small and a large multilobular cirrhotic liver, but they all belong to the same category of disease. It is undesirable to speak of the small ones as "atrophic" and the large ones as "hypertrophic" cirrhosis, since the practice of calling a large multilobular cirrhotic liver "hypertrophic" has caused much confusion with hypertrophic biliary cirrhosis.

The large size of some cirrhotic livers may be due to considerable fatty change in the liver cells. It has been assumed, I believe incorrectly, that increased size and fatty change in cirrhosis are specially connected with over-indulgence in malt liquors rather than in spirits.

These points were considered in the course of an analysis of 114 cases of cirrhosis undertaken by Fenton and myself.[1] Taking an equal number of alcoholic cirrhotic livers from cases in which malt liquors on the one hand and spirits on the other had been chiefly drunk, there was found to be very little difference between the average weights of the livers in the two series. The number of cases available was very small, since in most of the 114 cases in which the form of stimulant taken is mentioned, both beer and spirits were taken. In 10 beer livers the average was 69 ounces, and in 10 spirit livers 67 ounces. The spirit livers appeared to be more frequently fatty. Analysis of Foxwell's cases points to the same conclusion.[2] A series of microscopic examinations shewed that fatty change occurred in an equal proportion in large and in small cirrhotic livers, and that half the large livers examined did not shew fatty change.

In cirrhosis complicating pulmonary tuberculosis the liver is usually somewhat enlarged from fatty change. As will be shewn later (p. 197), the liver is larger in cases of cirrhosis in which the disease is latent, and death occurs from some independent cause, than in those cases that die directly from cirrhosis. The enlargement is chiefly due to compensatory hyperplasia of the liver cells, but there may be considerable fatty change in the hepatic cells, as in the form specially described by Hanot and Gilbert[3] as "hypertrophic alcoholic cirrhosis." In other instances the large size of the liver is due to the fibrosis having a smaller mesh and approaching a unilobular type or shewing that arrangement in parts. Enlargement of a cirrhotic liver is often temporary and due to congestion, either active, when the cirrhotic process is progressing, or passive and due to backward pressure from dilatation of the heart.

In cases dying from the effects of cirrhosis the liver is larger in younger subjects than in those of more advanced years. There are some grounds for thinking that in patients dying from cirrhosis in whom no alcoholic history is forthcoming, the liver is smaller than in the more familiar type of alcoholic patients dying from cirrhosis.

In 6 cases in which cirrhosis was fatal and in which there was no evidence of alcoholic excess the average weight of the liver was 41 ounces, whereas in 36 fatal cases of alcoholic cirrhosis the average weight was 67·7 ounces.

In latent cirrhosis the liver is a little larger in patients addicted to alcoholic excess than in the non-alcoholic, but the difference is very small as compared with that mentioned above in patients dying from the effects of cirrhosis.

In 29 cases in which death was due to some other cause and evidence of alcoholic excess was forthcoming, the average weight of the cirrhotic liver was 62·2 ounces, whilst in 26 cases in which alcoholic cirrhosis was latent the average weight of the liver was 67·9 ounces.

[1] Rolleston and Fenton, W. J. *Birmingham Med. Rev.*, 1896, xl, 198.
[2] Foxwell, A. *Ibid.*, 1896, xxxix, 221.
[3] Hanot et Gilbert. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1890, 3. s., vii, 492.

Sex does not exert any very special influence on the weight of the cirrhotic liver.

In 116 men the average weight of the cirrhotic liver was 61·5 ounces, or $8\frac{1}{2}$ ounces in excess of 53 ounces, the normal weight, while in 41 females the average weight was 55·5 ounces, or 10 ounces in excess of the normal weight, 45 ounces.

The large cirrhotic livers are less knobby than the smaller examples which especially merit the title "hobnailed." When both the liver and the spleen are much enlarged, the left lobe of the liver may touch or overlap the spleen.

The weight of the liver in portal cirrhosis may be diminished, normal, or increased, but it is less often below than above or of the normal weight.

In 142 cases tabulated by Price[1] the liver weighed less than normal in 27 per cent.

My own statistics shew a very considerable increase in the weight of the cirrhotic liver, but in 100 cases collected by Hawkins[2] the average weight was 52 ounces, and in 93 tabulated by Kelynack[3] 53 ounces, which is very close to Reid's average weight for the normal liver (53 ounces for males, 45 ounces for females). The average weight of the liver in cases dying from the effects of cirrhosis appears to be less than that of patients with latent cirrhosis who die from independent causes.

In 155 consecutive necropsies on patients with cirrhotic livers at St. George's Hospital the average weight was 63·6 ounces. Of these, 75 died from the effects of cirrhosis, the average weight of the liver being 60 ounces; the average weight of the liver in the remaining 80 patients who had cirrhotic livers but died from other causes was 67 ounces. In 11 of the 142 cases tabulated by Price death was due to accident, and the average weight of these cirrhotic livers was 76 ounces.

In latent cirrhosis the weight of the liver diminishes as age advances; this is probably a senile atrophic change. In this connexion it is interesting to note that in cases of latent cirrhosis in fatal granular kidney, which is perhaps a premature senile change, the weight of the liver is not increased.

In 8 cases of combined hepatic and renal cirrhosis examined at St. George's Hospital the average weight of the liver was 56·5 ounces, the average age of the patients being 52·25 years, or 3·5 years above the average age at death in cirrhosis. Pitt's[4] figures pointed to the same conclusion, but Price's figures, also from Guy's, tended to shew that granular kidney was associated more often with a large than with a small cirrhotic liver.

[1] Price. *Guy's Hosp. Rep.*, 1884, 3. s., xxvii, 295.
[2] Hawkins. *System of Medicine*, 1908, iv, Part i, 173.
[3] Kelynack. *Birmingham Med. Rev.*, 1897, xli, 86.
[4] Pitt, G. N. *Trans. Path. Soc.*, Lond., 1889, xl, 348.

In cases dying from cirrhosis the weight of the liver becomes less as age advances; this, again, may be partly due to the advance of years.

Morbid Appearances in the Liver.—The peritoneal surface of the liver is opaque; this may be due to chronic peritonitis, which is sometimes (*vide* p. 223) associated with cirrhosis. Not uncommonly there is more thickening of the peritoneum over the liver than elsewhere. The opacity of the capsule is, however, largely due to subcapsular fibrosis and atrophy of the liver cells, which, though it gives somewhat the same naked-eye appearance, is essentially different from genuine perihepatitis. It is probable that chronic perihepatitis is often described when subcapsular fibrosis is the actual condition present. This opacity is not uniform; it is more marked between the projections or hobnails, where there is underlying fibrous tissue.

General perihepatitis occurred in 15 out of 53 cases of cirrhosis recorded by Cheadle,[1] or 28 per cent, and in 13 out of 78 necropsies tabulated by Sears and Lord,[2] or 16·6 per cent.

There may be adhesions between the liver and adjacent parts, especially the diaphragm. These adhesions may be dense, but are often comparatively delicate. They may be remarkably vascular. The surface of the organ is irregular; the projections vary in size from a pea to that of a pigeon's egg. When they are small, the surface of the organ somewhat resembles that of a granular kidney, and the term "granular liver" is applicable. When, as more rarely occurs, the hobnails are large, the organ may look as if it were occupied by numerous secondary growths, especially when the projections shew marked fatty change and appear white, but the hobnails never shew the umbilication usually present in secondary carcinoma. When the projections are exceptionally large, the condition is sometimes spoken of as nodular cirrhosis or cirrhosis with multiple adenoma (*vide* p. 459).

Occasionally in an otherwise uniformly cirrhotic liver there is one large prominent hobnail; this has been described as solitary adenoma with cirrhosis. It is probable that this condition is of the same nature as multiple adenoma in cirrhosis, but differs in there being one area only of marked hyperplasia. Caminiti[3] collected four examples of solitary adenoma with cirrhosis.

The hobnails are tawny yellow or brown in colour, being often stained by bile; the peritoneum over them sometimes shews dilated vessels. During life the liver looked uniformly red in the laparotomies on cases of cirrhosis I have seen. The capsule, which is not much thickened as a rule, is more opaque in the depressions between the nodules. Usually the liver is uniformly affected, especially when it is enlarged and the nodules are small, but the change may be irregular and the left lobe is

[1] Cheadle, W. B. *Lancet*, 1900, i.
[2] Sears and Lord. *Boston Med. and Surg. Journ.*, 1902, cxlvii, 285.
[3] Caminiti. *Arch. f. klin. Chir.*, 1903, lxix, 630.

PLATE II.

Portion of a Finely Granular Cirrhotic Liver Shewing the Surface and the Section.
Dr. E. A. Wilson.

often in a more advanced condition and may be very small. It is possible that the resistance of the left lobe is less than that of the right, for it is not infrequently more affected in acute yellow atrophy than the right. Sometimes, on the other hand, one of the smaller lobes, such as the Spigelian or caudate, may be enlarged out of proportion to the others, even when the organ as a whole is little, if at all, bigger than normal. The process is one of compensatory hypertrophy. The enlarged Spigelian lobe may be so blended with the right lobe as to form a complete tunnel for the inferior vena cava (Fig. 27). During the course of a Talma-Morison operation on a patient of mine the enlarged Spigelian lobe was regarded as evidence of malignant disease.

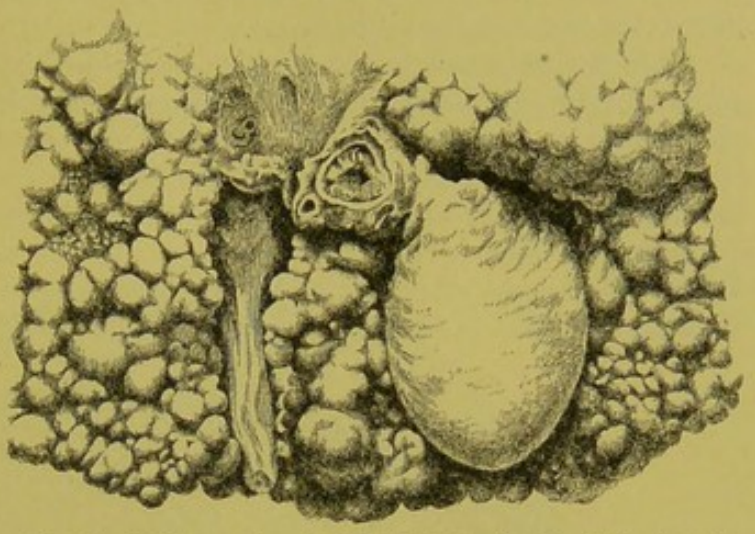


FIG. 26.—Under surface of cirrhotic liver shewing hobnails and thrombosis of the portal vein. (Drawn by Dr. E. A. Wilson.)

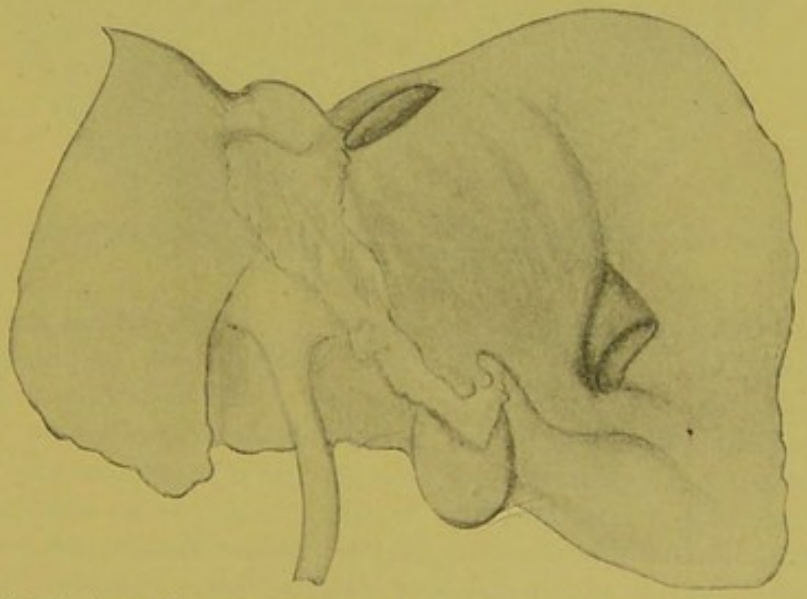


FIG. 27.—Cirrhotic liver with such enlargement of the Spigelian lobe as to form a complete tunnel for the inferior vena cava.

On section the liver is tough and, like a piece of conglomerate stone, is divided into areas of irregular size by grey, slightly gelatinous-looking, fibrous tissue. In extreme cirrhosis the interlobular tissue may have a red, somewhat spongy appearance and be rather depressed, as

compared with the masses of liver tissue that are embedded in it and stand up on section on a higher level. This fibrous tissue is continuous with the depressed, more opaque areas in the capsule, and by its contraction has squeezed into prominence the more healthy parts of the liver, which thus form the nodules or hobnails.

This fibrosis spreads out from the medium-sized portal canals. The areas of liver substance thus enclosed vary in size, being usually from $\frac{1}{6}$ to $\frac{1}{4}$ inch in diameter, and contain six to ten lobules, each of which normally measures $\frac{1}{20}$ to $\frac{1}{16}$ inch in diameter. The liver substance is much paler than in health and has a yellowish-brown colour either from staining with bile or from fatty change. In the same liver the colour of different hobnails often varies, some being yellow, others brownish-red. This may be due to irregularity in the amount of fatty change.

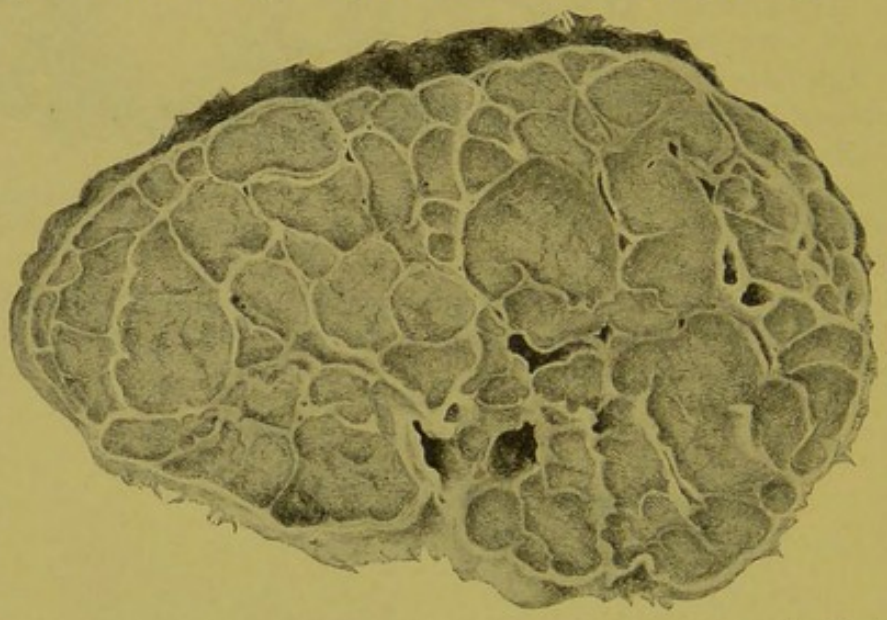


FIG. 28.—Section of multilobular cirrhotic liver shewing irregularity in the mesh of the fibrous trabeculae. (Drawn by Dr. E. A. Wilson.)

In rare instances haemorrhages are found in the interstitial tissue, in the hobnails, or in both. The liver cells may be compressed by the extravasated blood and sometimes shew necrosis. When the haemorrhage is widespread in the interlobular tissue and the hobnails have undergone fatty change, an appearance exactly like new-growth may be produced. The haemorrhages may possibly be due to the toxic condition of the blood, but this is unlikely, since hepatic haemorrhages are rare in fatal cases of cirrhosis, in which death is usually due to toxaemia. In some instances it is due to fatty change in the cells in the hobnails removing the support of the contained vessels; Bonome[1] has suggested that end-arteritis of the hepatic artery may produce necrosis of the liver cells and haemorrhages. As a coincidence I have seen numerous haemorrhages into the cirrhotic liver of a man who died from haematemesis. Occasion-

[1] Bonome. *Arch. di biol.*, Firenze, 1899, liii, 319.

ally small thrombosed veins may be seen in the liver without any similar change in the portal vein or its larger branches. It has been suggested that thrombosis of the terminal branches of the portal vein may determine ascites, but this is seldom observed.

Histology.—In the early and more progressive stages there is small-celled infiltration in and around the portal spaces; these cells are due to hyperplasia of the existing connective tissues of Glisson's capsule and to some leucocytic invasion. In a well-marked case there is an irregular meshwork of connective tissue extending throughout the liver and dividing it up into variously sized islands of liver tissue. Inasmuch

FIG. 29.—Multilobular cirrhosis. Well-formed fibrous tissue separating off masses of liver cells of various sizes. The normal arrangement of the liver cells is lost. In the fibrous tissue there are a few "newly-formed bile-ducts."

as several lobules are enclosed within the same fence of connective tissue, the term multilobular cirrhosis is applied. The number of lobules enclosed in these compartments varies; in some parts there are many, in other areas a single lobule or half a lobule is separated off from the rest.

The French school considers that the fibrosis is not only portal, but also around the sublobular veins or bivenous (Sabourin[1]). It does not appear, at any rate to me, that there is fibrosis around the intralobular veins. At the margin of the lobules the fibrous tissue can be seen to surround bits of the lobule and thus to shave off groups of cells from the edge of the lobule. In some large cirrhotic livers, in which the mesh-

[1] Sabourin. *Rev. de méd.*, Paris, 1882, ii, 465.

work is still multilobular as a whole, there are parts where it is more diffuse and approaches the unilobular type; this mixed cirrhosis is, from an anatomical point of view, a transitional stage to hypertrophic biliary cirrhosis; but it is common in ordinary portal cirrhosis when the disease is rapidly advancing.

When the morbid process is progressing rapidly the lobules are often actually invaded, so that a certain amount of intercellular fibrosis is superadded; Oertel [1] insists that the fibrosis is always intralobular as well as interlobular, and that what are described as lobules are not intact hepatic lobules. There are often areas of unilobular and intercellular

FIG. 30.—Multilobular cirrhosis. Shews invasion of a lobule by young connective tissue, so that there is local intercellular cirrhosis. Some of the liver cells thus isolated are hypertrophied and beginning to divide. The older connective tissue has some so-called new bile-ducts in its meshes. ×140.

cirrhosis in addition to the prevailing multilobular type. It is not justifiable or necessary, however, to construct a special clinical type of mixed cirrhosis to correspond to these microscopic appearances. The nature of the fibrous tissue varies according to its age, and whether the process is progressive or stationary. There is nearly always some well-formed fibrous tissue containing small round and spindle cells. In cases running a rapid course the amount of small round cells is increased, while in latent or stationary cases there may only be old fibrous tissue. The interstitial tissue contains numerous newly formed vessels derived from the hepatic artery, which are sometimes much dilated. The

[1] Oertel. *Arch. Int. Med.*, Chicago, 1908, i, 385.

lymphatics undergo obliteration from endothelial proliferation, and to compensate for this fresh channels are formed (Oertel).

The increase in connective tissue, formerly assumed to consist solely of white fibrous tissue, has been shewn by modern histological methods to be partly due to an increase in the amount of elastic tissue.

Hohenemser[1] demonstrated elastic fibres in the connective tissue of portal cirrhosis ; this has been confirmed by Melnikow-Raswedenkow,[2] Flexner,[3] and Fenzi.[4] The elastic tissue spreads out from the sheaths of the hepatic artery, portal vein, and bile-duct, and is also found in the capsule. More elastic

FIG. 31.—Cirrhosis in haemochromatosis. Section at margin of lobule. Shews haemosiderin as dark granules in the liver cells and also in the fibrous tissue surrounding the lobules. Prepared from Dr. Maude Abbott's case. (*Vide Trans. Path. Soc.*, Lond., 1900, li, 56.) ×220.

tissue is found in portal than in biliary and mixed forms of cirrhosis. According to Carnot and Amet[5] there is considerable variation in the amount of elastic tissue present, but generally speaking there is more in old than in early cases of cirrhosis.

In pigmentary cirrhosis (*vide* p. 302), which may be due to more than one cause, the fibrous tissue may become occupied by opaque masses of pigment. In the cirrhosis of haemochromatosis the pigment is eventually liberated from the liver cells and passes into the connective tissues.

[1] Hohenemser. *Virchows Arch.*, 1895, cxl, 192.
[2] Melnikow-Raswedenkow. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1899, xxvi, 526.
[3] Flexner. *Univ. Med. Mag.*, Phila., 1900–1901, xiii, 613.
[4] Fenzi. *Sperimentale*, 1904, lviii, 403.
[5] Carnot et Amet. *Arch. de méd. expér. et d'anat. path.*, Paris, 1906, xviii, 752.

FIG. 32.—Photomicrograph shewing deeply stained pseudobile canaliculi branching and twisting in the fibrous tissue. The margin of a lobule is also shewn. From a case of multilobular cirrhosis. (Dr. H. Spitta.)

Pigmentation of the fibrous tissue in cirrhosis is also seen in malaria and in the extremely rare condition of cirrhosis anthracotica (*vide* p. 302).

Newly Formed Bile-ducts—Pseudobile Canaliculi—Bile-duct-like Structures.—In active cirrhosis the interstitial tissue shews as a prominent feature double columns of small cells which stain deeply and may shew mitotic figures. The cells are small and may be cubical, but are often elongated so as to lie in the long axis of the column; they are arranged, on much the same pattern as in a small bile-duct, around a potential lumen. Histologically they differ from normal interlobular bile-ducts in having either no elastic fibres, or a very imperfect development of them only (Flexner [1]). It is indeed open to doubt if similar structures containing a dilated lumen or masses of inspissated bile are exactly the same as these so-called new bile-ducts. The so-called new bile-ducts twist and branch in the interlobular connective tissue and form a rough network. The individual columns catch the eye as minute worm-like bodies under a low power. They often end in contact with liver cells, and it has therefore been thought that they (i) are derived from proliferation of liver cells, or (ii) that though derived from bile-ducts they form liver cells.

Special importance was formerly attached to the presence of these so-called new bile-ducts in hypertrophic biliary cirrhosis, but they may be just as prominent in common cirrhosis, and indeed are present in a number of conditions, such as local fibrosis around a hydatid cyst, gumma, tubercle, lymphadenoma, acute yellow atrophy, and other lesions which have in common destruction of the liver cells.

A considerable amount of discussion has arisen as to their nature. It has been thought that they are the normal bile-conducting channels running between the liver cells and the interlobular bile-ducts, which are left in a conspicuous position by the atrophy and recession of the liver cells; the brilliant staining of the cells has been explained by supposing that some proliferation of the cells normally lining the ducts in the interlobular tissues around the portal canals extends into the flat-walled ducts between the liver cells. Milne [2] argues that when these bile-duct structures are exposed in granulation tissue, their lining cells swell up in the same way that the lining cells of the air alveoli in chronic interstitial pneumonia do. In this way ducts lined with cubical epithelium are produced. Against the view that they are pre-existing bile channels is the fact that in senile or other forms of simple atrophy of the liver cells the appearance of so-called new bile-ducts is not seen. From their resemblance to small bile-ducts it has been widely thought that they are due to proliferation of pre-existing bile-ducts (Muir [3]). Another suggestion is that the liver cells become surrounded by the advancing fibrous tissue, which, so to speak, slices off columns of hepatic cells from the periphery of the lobules (*vide* Fig. 30). The liver cells then atrophy, become compressed, and are said to revert to the type of a tubular liver. This view as to the nature of the change is supported by some appearances, but is opposed to the facts that they stain deeply and are evidently

[1] Flexner. *Univ. Med. Mag.*, Phila., 1900, xiii, 617.
[2] Milne. *Journ. Path. and Bacteriol.*, Cambridge, 1909, xiii, 127.
[3] Muir. *Brit. Med. Journ.*, 1908, ii, 1169.

proliferating actively. It has also been argued by Dreschfeld[1] and others that they are the result of active proliferation of the liver cells, and, as Hanot[2] believed, an attempt at compensatory hyperplasia. The healthy liver cells proliferate in order to compensate for the destruction of the hepatic tissues. Appearances strongly suggesting hyperplasia of the cells may be seen at the periphery of the lobules, and the columns of small cells may in fortunate sections be traced into continuity with a liver cell. Craven Moore[3] suggests that the bile-duct structures are derived from cells transitional between the liver cells and the bile-ducts.

FIG. 33.—Slight multilobular cirrhosis with extensive fatty change in the liver cells. The vacuolation of the liver cells is irregular. Some groups of cells are unaffected, whilst others have hardly any protoplasm left. × 72.

Since some doubt at any rate exists as to their being bile-ducts, it is more convenient to speak of them as the so-called new bile-ducts or pseudobile canaliculi.

The *liver cells* in the early stages shew degenerative changes which precede any interstitial reaction (Fiessinger[4]). There is a peculiar hyaline change which goes on to necrosis. These cells become surrounded by polymorphonuclear or endothelial leucocytes which absorb them (Mallory[5]). Active mitoses may be seen in the neighbouring cells,

[1] Dreschfeld. *Journ. Anat. and Physiol.*, 1881, xv, 69.
[2] Hanot, V. *Gaz. des hôp.*, Paris, 1896, lxix, 897.
[3] Moore, F. C. *Brit. Med. Journ.*, 1908, ii, 1168.
[4] Fiessinger. *Arch. de méd. expér. et d'anat. path.*, Paris, 1908, xx, 313.
[5] Mallory. *Johns Hopkins Hosp. Bull.*, Balt., 1911, xxii, 73.

a sign of regeneration on which Kretz [1] and MacCallum [2] lay stress. The normal trabecular arrangement in the lobule becomes disturbed and disappears. The intralobular vein may be absent or at one side of the enclosed mass of cells. In some cases, owing to backward venous pressure from cardiac failure, the capillaries between the columns of liver cells become dilated and separate single columns of cells from each other. In other cases the lymphatic capillaries are dilated and the lobule becomes oedematous. Fatty change is often present in a greater or lesser degree, and is the effect of the action of alcohol or some other toxic substance. It has been thought that fatty change is specially related to excess in beer and other sugar-containing beverages, but this assumption has not been proved (*vide* p. 195).

The degenerative changes are extremely prominent in cases which run a rapid or an acute course. The protoplasm may shew cloudy swelling and become granular, while the nucleus may stain badly or be obscured. The presence of granules of bile is seen in cases in which jaundice has existed, while in malaria, haemochromatosis, and in other examples of pigmented cirrhosis (*vide* p. 302) the liver cells are crowded with pigment and are markedly degenerated. The liver cells may shew siderosis quite apart from the existence of general haemochromatosis.

In 16 cases of cirrhosis Abbott [3] found pigment in the liver cells in 6 cases, and in 26 cases examined by Kretz [4] pigmentation existed in 14. Since this pigment is probably due to the haemolytic action of intestinal bacteria, it is curious that it is not more constant in cirrhosis.

In the early stages of cirrhosis a majority of the liver cells, even those embedded in fibrous tissue, contain glycogen. This observation of Brault's [5] helps to explain the absence of glycosuria in cirrhosis. He suggests that in cirrhosis there may be excessive glycogen storage in the liver cells in order to compensate for the cell destruction.

Compensatory hyperplasia of the liver cells occurs in cirrhosis. The proliferation of the liver cells begins at the margin of the lobule, probably because the blood-supply is more copious there. The liver cells become larger, divide usually by direct nuclear division, but sometimes by karyokinesis, and by multiplying lead to deformity and to an increase in the size of the lobules and to the formation of actively growing masses of liver tissue. Turnbull and Worthington [6] describe two stages, (*a*) the regeneration-nodule, and (*b*) adenoma in which the cells are further removed from the normal hepatic cells. Many of the "hobnails" in a cirrhotic liver are of this nature. When the process is well marked, the condition is called nodular cirrhosis, or cirrhosis with adenoma. This

[1] Kretz. *Wien. klin. Wchnschr.*, 1900, xiii, 271.
[2] MacCallum. *Journ. Amer. Med. Assoc.*, 1904, xliii, 649.
[3] Abbott, M. *Trans. Path. Soc.*, Lond., 1900, li, 79.
[4] Kretz. *Beitr. z. klin. Med. u. Chir.*, Wien, 1896, Heft 15.
[5] Brault. *Arch. de méd. expér. et d'anat. path.*, 1902, xiv, 453; *Bull. Soc. anat.*, Paris, 1901, lxxvi, 334.
[6] Turnbull and Worthington. *Arch. Path. Inst. London Hosp.*, 1908, ii, 63.

process is important in compensating for the destruction of the liver cells and allowing the disease to become latent (Hanot and Gilbert [1]). As already pointed out, it has been thought that regeneration of liver tissue may be due to proliferation of the liver cells to form pseudobile-canaliculi (Dreschfeld, Hanot). Milne has recently denied that these "pseudobile canaliculi" are derived from hepatic cells or form them.

Gall-bladder and Bile-ducts.—The gall-bladder and larger bile-ducts do not shew any constant change to the naked eye. In some instances the walls of the gall-bladder are thickened from past or from chronic cholecystitis, and occasionally there is inflammation of the larger ducts. I have seen acute pneumococcic cholecystitis in latent cirrhosis (*vide* p. 613). In ascites the serous coat of the gall-bladder may be oedematous.

Gall-stones occur slightly more often in cirrhosis than in ordinary cases. Thus in 157 cases of cirrhosis examined after death at St. George's Hospital gall-stones were found in 23 or 14·6 per cent. In 209 male cases of cirrhosis gall-stones were found in 8 per cent, and in 41 females in 17 per cent (Klopstock [2]).

The small intrahepatic bile-ducts are usually healthy or shew little change. In some instances there is concomitant catarrhal cholangitis.

A young man, aged twenty-six years, with slight jaundice died from fatal haematemesis on Feb. 22, 1905. Eleven months previously he had had jaundice, from which he had completely recovered. The liver (72 oz.) was cirrhotic, the bile-ducts contained turbid milky bile, and microscopically (*vide* Fig. 34) there was pericholangitis and the formation of minute calculi in the intrahepatic bile-ducts. The spleen weighed 34 oz. The lymphatic glands in the portal fissure and around the pancreas were swollen, oedematous, and black from altered blood pigment.

In one case microscopic sections of a cirrhotic liver with some perihepatitis shewed cystic dilatation of the bile-ducts in a few of the portal spaces. It is indeed remarkable how extremely rare any dilatation of the small ducts is in cirrhosis, especially in view of the frequency of cysts in a granular kidney, which may be considered as homologous to hepatic cirrhosis (*vide* p. 444).

Portal Vein.—The intrahepatic branches of the portal vein are compressed, some are obliterated, and occasionally some are thrombosed. The trunk of the portal vein and its branches are dilated, and very occasionally varicosities are seen on its mesenteric radicles. The walls of the vein are thickened by periphlebitis and there is opacity of the intima from endophlebitis; in extreme instances secondary calcification may occur in the intima. These changes are comparable to arterio-sclerosis and are connected with increased pressure in the portal vein, or possibly with the presence of poisons in the blood. Thrombosis of the trunk of the portal vein is probably more often associated with hepatic cirrhosis than with any other condition, but it is a rare complication; it occurred in 6 out of 711 cases tabulated by Lissauer,[3] or 0·9 per cent,

[1] Hanot et Gilbert. *Bull. Soc. méd. des hôp. de Paris*, 1890, 3. s., vii, 492.
[2] Klopstock. *Virchows Arch.*, 1907, clxxxvii, 111.
[3] Lissauer. *Ibid.*, 1908, cxcii, 278.

and in 10, or 3·3 per cent, of Langdon Brown's 334 cases of cirrhosis.[1]

Dilatation of the Communications between the Portal Vein and the General Systemic Veins.—This is important as providing a collateral circulation for venous blood which would otherwise have to force its way against the obstruction offered by the cirrhotic liver. This compensatory anastomosis is one of the factors which enable cases of multilobular cirrhosis to become latent or to appear cured. The normal communications between the portal vein radicles and the general systemic veins have

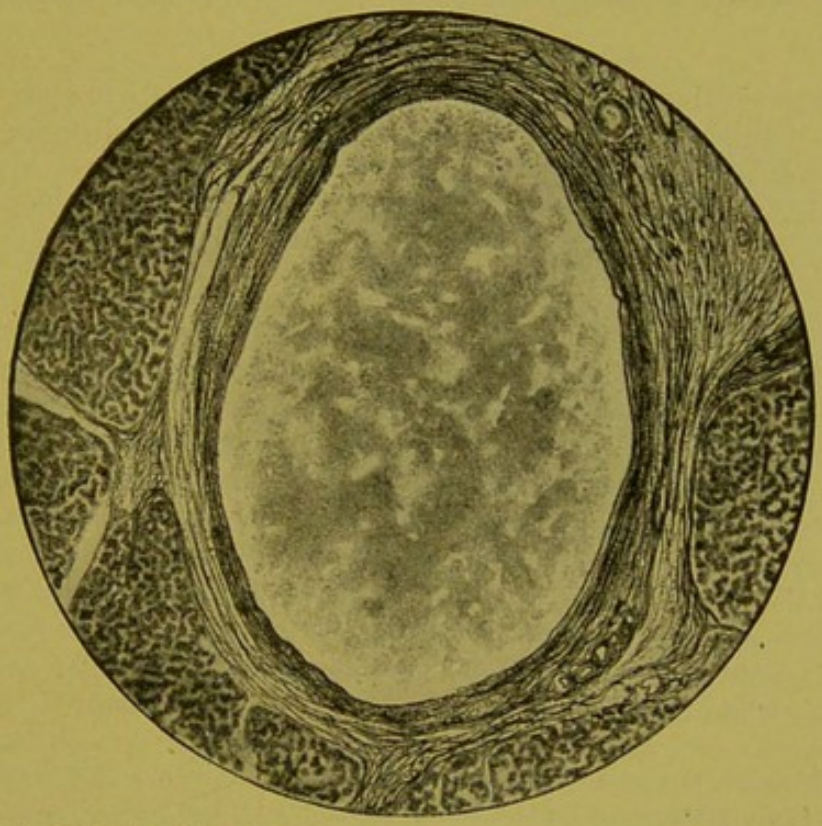


Fig. 34.—Dilatation of small bile-duct with pericholangitis in portal cirrhosis. × 24.

been tabulated by Thomas[2] as (i) between the portal vein and the superior vena cava, (*a*) superficial, and (*b*) deep communications; and (ii) between the portal vein and the inferior vena cava, (*a*) superficial, and (*b*) deep. In both cases the deep communications are the more important. It is sufficient to consider them as (i) general and (ii) local.

(i) *General Communications* between the retroperitoneal veins, opening into the lumbar and azygos veins, and the veins of the peritoneum and of the intestines occur especially where, as in the case of the duodenum, pancreas, ascending and descending colon, areas drained by the portal vein are bound down to the abdominal parietes. The veins in the

[1] Brown, Langdon. *St. Barth. Hosp. Rep.*, 1901, xxxvii, 62.

[2] Thomas. "Beiträge zur Differentialdiagnose zwischen Verschluss der Pfortader und der unteren Hohlader." *Bibliotheca Medica*, 1895.

capsule and perirenal fat of the left kidney anastomose to some extent with the veins of the descending colon (Tuffier and Lejars [1]), and venous trunks may put the renal vein itself into communication with the colica sinistra vein. The veins of the descending colon may communicate with the spermatic plexus, and this has been thought to favour the development of varicocele on the left side (Bennett [2]). Compensatory dilatation of this anastomosis has been recorded, especially in Livierato's [3] case, in which the left spermatic vein was 30 inches long, tortuous, and greatly dilated; but in general it is of little or no importance. It has not appeared to me that varicocele is specially common or marked in cirrhosis.

A communicating branch between the splenic and the left renal veins has been seen, and in Jacobson's [4] case of compensated hepatic cirrhosis, in which death occurred from uraemia due to granular kidneys, a vein as large as the thumb ran from the left renal vein into the trunk of the portal vein. Virchow [5] observed a somewhat similar anastomosis between the splenic and the azygos veins.

In some cases of cirrhosis the greater part of the parietal peritoneum, more especially on the posterior wall and upper part of the abdomen, is markedly injected and in some areas resembles a "claret stain" on the skin. The significance of this, and also the fact that it is not due to a terminal peritonitis, are shewn by the absence of this injection from the peritoneum covering the free coils of the small intestine. This subperitoneal plexus of anastomoses between the branches of the portal vein and the inferior vena cava was specially described by Retzius,[6] after whom it is sometimes called. Peritoneal adhesions around the liver, stomach, omentum, or spleen may become markedly vascular and thereby assist the collateral circulation.

This hint on the part of nature has been taken in a surgical sense in the operation (Talma-Morison) for the relief of ascites by the production of artificial peritoneal adhesions (*vide* p. 260).

(ii) *Local.*—(*a*) Around or in connexion with the liver: An internal porto-caval anastomosis develops in the lobules of the liver between the branches of the portal vein and the intralobular vein. Communications may develop between the veins in the substance and capsule of the liver and the phrenic and intercostal veins, where the liver and diaphragm are uncovered by peritoneum, *i.e.* between the layers of the coronary ligament and its lateral fringes, the lateral ligaments.

[1] Tuffier et Lejars. *Arch. de physiol.*, Paris, 1891, xxiii, 41.
[2] Bennett, W. H. *On Varicocele*, p. 43, 1891.
[3] Livierato. *Riforma med.*, Napoli, 1911, xxvii, 505.
[4] Jacobson, G. *Arch. gén. de méd.*, 1893, i, 353.
[5] Virchow. Quoted in Frerichs' *Diseases of the Liver*, vol. ii, p. 41. Transl. New Syd. Soc., 1861.
[6] Retzius. *Ztschr. f. Physiol.*, 1833, v, 105.

In a man aged fifty-eight years, who died under the care of Dr. C. Ogle in St. George's Hospital, the left internal mammary vein shewed a local varicose dilatation behind the sternum, where during life a loud murmur had been heard, and then turned inwards into the falciform ligament and ran into the left lobe of the liver and communicated with the left branch of the portal vein. The liver was small and cirrhotic (28 oz.).

The falciform ligament of the liver may contain a large vein which runs to the umbilicus and may communicate there with the veins of the abdominal wall, and so establish a communication between the portal vein in the transverse fissure of the liver and the deep epigastric and external iliac veins. This vein is comparable with the epigastric vein of cold-blooded air-breathing vertebrates, such as the frog. This vessel may be a greatly dilated parumbilical vein, which, according to Luschka, normally puts the portal and epigastric veins into communication, and runs alongside of the obliterated umbilical vein. It was originally stated by Rokitansky and Bamberger that this vein was the umbilical vein, which had become pervious again and, so to speak, had reverted to its fetal function of carrying blood, with the difference that the blood runs away from, instead of to, the liver. Sappey [1] insisted that the large vein found in the falciform ligament in some cases of cirrhosis was always independent of the umbilical vein; but this is not in accord with cases quoted by Champneys.[2] This vein may be extremely large; Wilks [3] mentions a case in which it was as big as the portal vein, and in Sappey's case and the one figured here it admitted the little finger. This big vein is probably not so infrequent as would appear from the recorded cases, for the vein collapses after death and is not seen unless the falciform ligament is specially examined. I have seen it full of carcinoma in a case of carcinoma with cirrhosis.

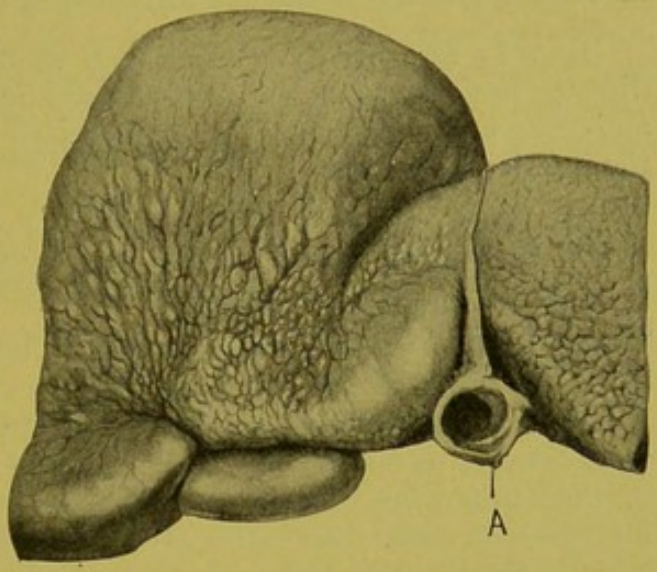


FIG. 35.—A cirrhotic liver with a large parumbilical vein (A) in the falciform ligament. (St. George's Hosp. Museum, Series ix, 174M.)

As a result of the anastomosis thus opened up the veins of the abdominal wall, especially around the umbilicus, may become dilated and prominent. When marked, this condition is spoken of as a "caput

[1] Sappey. *Bull. Acad. de méd.*, 1859, xxiv, 270.
[2] Champneys. *Journ. Anat. and Physiol.*, 1872, vi, 417.
[3] Wilks. *Pathological Anatomy*, p. 467, 1889.

Medusae," but is hardly ever so well developed as the caput Medusae produced by mechanical obstruction of the inferior vena cava. There is a difference in the situation of these two collateral venous circulations in the abdominal wall; that due to portal obstruction is most marked around the umbilicus, while that seen in the obstruction of the inferior vena cava runs from the middle of the groins to the costal arches and avoids the umbilicus (*vide* p. 249).

It may be pointed out that in healthy subjects the round ligament at its junction with the right branch of the portal vein is pervious for a distance of $\frac{1}{2}$ to $1\frac{1}{2}$ inches and then becomes occluded. This channel is no doubt utilised in the formation of a collateral and compensatory circulation.

In very rare instances the ductus venosus, which in the fetus runs directly from the umbilical vein into the inferior vena cava, is persistent, and thus provides a direct communication between the portal vein and the inferior vena cava.

In an interesting case of hepatic cirrhosis with obstruction of the superior vena cava described by Duckworth and Garrod [1] there were greatly dilated veins under the skin of the abdomen, the blood running into them in both directions, but it is noteworthy that there was an absence of these veins around the umbilicus.

In ordinary cirrhosis extensive ascites may so compress the inferior vena cava as to lead to the development of a caput Medusae comparable to that seen when there is obstruction to the blood flow through the inferior vena cava. An extremely rare complication of cirrhosis is thrombosis of the inferior vena cava, which would produce the same conditions.

Pheasants [2] collected 8 cases. Councilman [3] met with a terminal streptococcic infection in cirrhosis in which the retroperitoneal glands and tissues were suppurating and had thus caused thrombosis of the inferior vena cava.

Occasionally there may be a kind of belt of dilated cutaneous venules over the line of attachment of the diaphragm. This, however, is not pathognomonic of portal obstruction, as has sometimes been thought; for it occurs in emphysema, bronchitis, and sometimes in elderly men without at any rate any manifest morbid lesion (*vide* p. 229).

(*b*) At the terminations of the intra-abdominal parts of the alimentary canal: The veins of the oesophagus, which open into the azygos veins, communicate at the cardiac orifice with the gastric veins and so with the portal vein. This communication may become so developed as to produce varicosities at the lower end of the oesophagus, or "oesophageal piles," and from ulceration or rupture may be the source of severe haemorrhage. Though usually developed to a certain degree, it is only occasionally that there are large varicosities. This may be explained on

[1] Duckworth and Garrod. *St. Barth. Hosp. Rep.*, 1896, xxxii, 71.
[2] Pheasants. *Bull. Johns Hopkins Hosp.*, 1909, xx, 292.
[3] Councilman, W. T. *Trans. Assoc. Am. Phys.*, 1896, xi, 213.

the ground that there are valves guarding the entrance of the gastric vein (Macalister[1]), which would tend to prevent reflux of blood from the portal into the gastric veins.

It should be noted that oesophageal varix may occur without cirrhosis of the liver ; cases of fatal haemorrhage have occurred from this cause in a child and in a boy of seventeen.[2]

The coronary vein of the stomach communicates with the phrenic vein, and it would be natural to anticipate that the branches of the gastric veins would be often dilated. This is very seldom observed, though it is possible that it is overlooked. The walls of the vein may undergo chronic inflammation, and from fibrotic atrophy shew local dilatations. These become adherent to the mucosa, and the raised area may, as the result of trauma, toxic irritation, or infection, become ulcerated. The resulting haemorrhage may, as in two cases of cirrhosis recorded by Letulle,[3] be fatal.

Varicosity of the gastric veins and fatal haematemesis may occur in the absence of any hepatic disease (Barr,[4] Lancaster[5]).

Dilatation of the anastomosis between the superior haemorrhoidal vein opening into the inferior mesenteric, on the one hand, and the middle and inferior haemorrhoidal, which pour their blood into the internal iliac vein, on the other hand, may also occur. It would if excessively developed lead to piles, and it has been assumed that piles are common in cirrhosis. This, however, is not the case, and constipation is a far more frequent and important factor than cirrhosis in the production of piles.

It is possible that the compensatory effects of these anastomotic channels have been somewhat overestimated. Thus the dilated venous channels may be absent in latent cirrhosis fatal from other causes, and may be well developed in cases dying with ascites. In the latter instance the compensatory process, though considerable, cannot be regarded as having been successful.

In an examination of 78 autopsies of cases with cirrhosis, Sears and Lord[6] found this dilated anastomosis in 29 cases, being most often present when the cirrhotic process was most advanced. But in 22 out of the 29 cases there was ascites.

Bad Effects and Results which may depend on Excessive Development of this Venous Anastomosis.—The development of a free communication between the portal and general systemic veins, while it relieves portal

[1] Macalister's *Anatomy*, p. 431, 1889.
[2] Graham. *Trans. Assoc. Am. Phys.*, 1896, xi, 215.
[3] Letulle. *Presse méd.*, Paris, 1898, ii, 313.
[4] Barr. *Lancet*, 1889, ii, 1226.
[5] Lancaster. *Trans. Clin. Soc.*, Lond., 1897, xxx, 32.
[6] Sears and Lord. *Boston Med. and Surg. Journ.*, 1902, cxlvii, 285.

engorgement, may lead to bad effects. In the first place, if the communications are extensive, it necessarily follows that a considerable quantity of blood carrying the products of digestion, instead of going to the liver, will pass directly into the general circulation and set up toxaemia. If the anastomosis is very free, the condition would resemble that in Eck's fistula, or the experimental communication between the inferior vena cava and the portal vein, in which all the portal blood passes into the inferior vena cava. A most elaborate and interesting series of experiments on these lines was carried out by Hahn, Massen, Nencki, and Pawlow.[1] In animals thus treated, effects equivalent to those of hepatic insufficiency naturally resulted, and when a protein diet was adopted, symptoms comparable to those of uraemia developed, which were regarded as due to the presence of carbamic acid in the blood. In man excessive development of the collateral circulation may lead to a toxaemic condition verging on uraemia. This has been insisted on by Stockton,[2] and it is interesting to note that one of Morison's[3] patients, after the operation for the surgical relief of ascites, was alternately excited and depressed for three weeks after the operation. Possibly a very free collateral anastomosis between the portal and general venous systems, while relieving portal engorgement, may lead to arteriosclerosis and granular kidneys. In cases in which the two conditions of renal and hepatic fibrosis are combined the patients usually die from renal disease with latency of the hepatic cirrhosis. This was the termination of Jacobson's[4] remarkable case, in which a vein as large as a thumb ran between the portal vein and the left renal vein.

In the second place, haemorrhage may occur from rupture of the dilated venous anastomoses. This generally occurs into the gastro-intestinal tract, but in very rare instances, of which examples will be given, haemorrhage may take place into the abdominal wall or into the peritoneal cavity. Haematemesis not very infrequently results from rupture of an ulcerated varicose vein in the oesophagus, while slight bleeding from piles may go on for a considerable time.

The occurrence of a haematoma in the anterior abdominal wall close to the round ligament, though rare, is another illustration of a pathological event in the course of this compensatory mechanism, and is analogous to haematemesis from dilated oesophageal veins.

A case is recorded by Lefas[5] of a haematoma the size of a tangerine orange to the left of the middle line in a man, aged fifty-five, with cirrhosis. There is an interesting specimen (380·8) in the Museum of the College of Medicine, Newcastle-upon-Tyne, shewing a large haematoma in the abdominal wall close to the round ligament, which contains a number of dilated veins. The liver

[1] *Arch. f. exper. Path. u. Pharmak.*, 1893, xxxii, 161.
[2] Stockton. *Journ. Am. Med. Assoc.*, 1889, xiii, 267 ; 1901, xxxvii, 817.
[3] Morison. *Lancet*, 1899, i, 1426.
[4] Jacobson, G. *Arch. gén. de méd.*, 1893, i, 353.
[5] Lefas. *Bull. Soc. anat.*, Paris, 1902, lxxvii, 586.

shewed ordinary portal cirrhosis. Thomas[1] records a similar haematoma in the abdominal wall in the middle line, but below the umbilicus.

In extremely rare instances trauma may lead to rupture of dilated veins in peritoneal adhesions and so to extensive haemorrhage into the peritoneum.

A man, aged forty-five, received a blow on the abdomen, and died in St. George's Hospital after being in a condition of collapse for eleven hours. The necropsy shewed cirrhosis of the liver (78 ounces) with marked engorgement of the veins in the substance of the liver, so that the organ had a naevoid appearance. The abdominal cavity was full of blood. The spleen was enlarged, and had haemorrhage into its substance, but there was no rupture of its capsule. There was laceration of some vascular adhesions, from which the blood probably came. Microscopically the liver shewed latent multilobular cirrhosis of old date with hardly any recent proliferation of the connective tissues.

From the anastomoses between the veins of the capsule of the left kidney and the branches of the portal vein in the mesocolon congestion of the vessels of the left kidney has been described (Gilbert and Villaret[2]) and may thus account for haematuria.

Hepatic Artery.—The hepatic artery is usually considerably enlarged, as it is thought to supply the added fibrous tissue with blood. Chronic endarteritis is not a special feature of ordinary cirrhosis, but it is seen in cirrhosis due to haemochromatosis and sometimes in cirrhosis in syphilitic patients and in parasyphilitic cirrhosis.

The *portal lymphatic glands* are not enlarged in uncomplicated cases. I have seen them swollen, oedematous, and black from blood pigment in fatal haematemesis (*vide* p. 208), and on several occasions pigmented by carbon.

The Spleen is enlarged in portal cirrhosis, though not so markedly as in hypertrophic biliary cirrhosis. According to Klopstock[3] it is enlarged in 80 per cent of the cases.

In Kelynack's series of 84 cases of cirrhosis the average weight of the spleen was 12·9 ounces. In 147 cases of cirrhosis examined at St. George's Hospital the average weight of the spleen was 10 ounces. So that if the weight of the normal spleen be taken at 7 ounces, there is seen to be a very definite increase in cirrhosis. The weight of the spleen varied between the two extremes of 2 ounces, in a case of latent cirrhosis, and 48 ounces, in a man who survived thirty months after the operation for producing artificial peritoneal adhesions had been performed. This weight is very exceptional in portal cirrhosis, though not in hypertrophic biliary cirrhosis.

In cases in which there has been fatal and very profuse haematemesis or very rapid ascites, the spleen may be small.

In latent cirrhosis the enlargement and increase in the weight of the spleen are much less than in cases in which death has been directly due to cirrhosis.

[1] Thomas, Pierre. *Lyon méd.*, 1901, xcvii, 289.
[2] Gilbert et Villaret. *Arch. gén. de méd.*, 1906, xviii, 422.
[3] Klopstock. *Virchows Arch.*, 1907, clxxxvii, 111.

In 74 cases in which cirrhosis, though present, was not the cause of death, the average weight of the spleen was 9 ounces; while in 73 cases in which death was referred to the effects of cirrhosis, the average weight of the spleen was 11·5 ounces.

The fact that the spleen is bigger and heavier in cases dying from the effects of cirrhosis than in latent cirrhosis may be explained as depending on two factors which come into play in progressive cirrhosis—viz. (1) general toxaemia, and (2) increased pressure in the portal vein—but are either absent or largely obviated in latent compensated cirrhosis.

In very exceptional cases, of which I have seen two, the spleen is greatly enlarged and the liver shews slight and very old fibrosis. One of these cases was published by R. S. Trevor,[1] the other was a case of chronic splenic anaemia. This combination is not Banti's disease, in which cirrhosis supervenes as a terminal phenomenon of chronic splenic anaemia. It appears indeed to be the reverse of Banti's disease, and to be a continuation and exaggeration of morbid changes in the spleen in latent or practically cured cirrhosis.

Morbid Appearances of the Spleen.—The capsule of the spleen is often thickened and shews perisplenitis. This may be local, the thickened area being a lamellar fibroma, a condition frequently seen in splenic enlargement from any cause, or it may be general, and then usually forms part of a general chronic peritonitis.

Perisplenitis was present in 43, or 33 per cent, of 131 cases of cirrhosis analysed by Yeld;[2] and in 23, or 29·5 per cent, of the 78 cases recorded by Sears and Lord.[3]

The spleen is frequently adherent to the peritoneum covering the diaphragm, abdominal wall, and stomach. When the spleen and liver are both considerably enlarged, the left lobe of the liver may overlap the spleen. Though this is more likely to occur in hypertrophic biliary cirrhosis, it may occasionally be seen in multilobular cirrhosis.

On section the organ is sometimes firmer than natural and fibrosed; in other cases, probably as the result of terminal infections, it is soft or even diffluent. Occasionally areas of extravasation of blood are seen.

In a case of cirrhosis which survived the Talma-Morison operation for two and one-half years, the spleen was greatly enlarged, weighing 48 ounces, and contained numerous gritty spots. Microscopically these areas shewed fibrosis surrounding calcareous granules and particles which turned blue on being treated with ferrocyanide of potassium and hydrochloric acid (*vide* Fig. 36). There was also considerable hyperplasia of the endothelial cells lining the sinuses.

Microscopic Appearances.—There is dilatation of the blood-vessels generally, which spreads to the capillaries in the Malpighian bodies and

[1] Trevor, R. S. *Trans. Path. Soc.*, 1903, liv, 302.
[2] Yeld, R. A. *St. Barth. Hosp. Rep.*, 1898, xxxiv, 215.
[3] Sears and Lord. *Boston Med. and Surg. Journ.*, 1902, cxlvii, 285.

is followed by secondary atrophy of the lymphoid tissue in the Malpighian bodies. Some difference of opinion exists as to proliferation of the splenic pulp. Oestreich[1] described it in early cases, but neither Sieveking[2] nor Azzurrini[3] confirmed this. From examination of 38 cases Christian[4] found increase of connective tissue due to proliferation of the reticular tissue of the pulp, but little or no increase in the white fibrous and elastic tissues. Fibrosis of the spleen due to increase in the trabeculae occurs in cases of some standing.

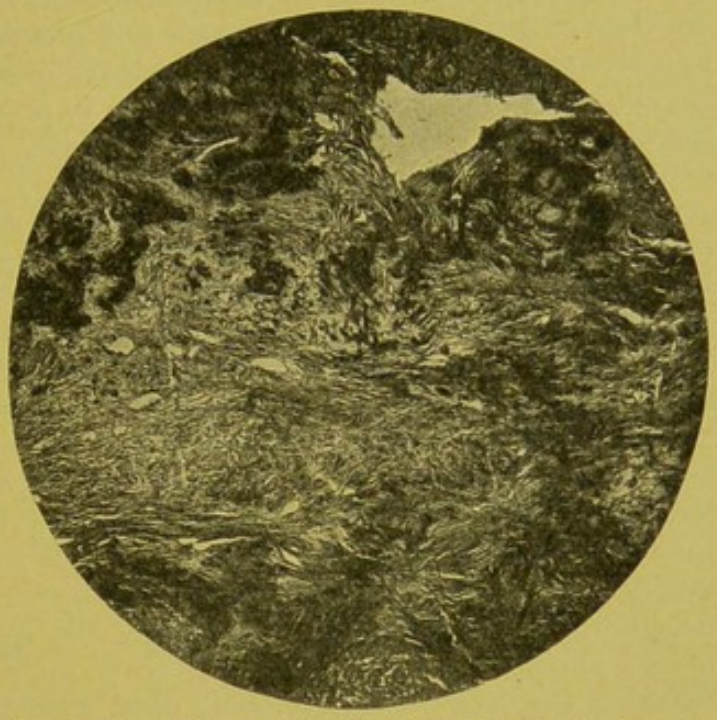


Fig. 36.—Photomicrograph shewing fibrous area in the spleen. Around it are dark masses which stained blue with ferrocyanide of potassium and hydrochloric acid. (By Dr. S. G. Penny.)

The Cause of Splenic Enlargement in Hepatic Cirrhosis.—There are two views as to the causation of the splenic enlargement.

(I) The mechanical view: that it is due to backward pressure and chronic venous engorgement of the organ brought about by the portal obstruction existing in the liver. In favour of this is the fact that the enlargement may diminish after profuse gastro-intestinal haemorrhage or diarrhoea. The manifest objection to this view is that in the chronic venous engorgement of heart disease the spleen, though firmer than natural, is not increased in weight. This is well brought out in a comparison drawn up by Kelynack[5] between the weights of the spleen (i) in 84 cases of cirrhosis and (ii) in 56 cases of nutmeg liver, in cases of heart disease uncomplicated by any febrile or other condition likely to affect the size of the organ.

	Average Weight.		
	Males.	Females.	Both Sexes.
"Hepatic" spleen	14·25	11·62	12·93
"Cardiac" spleen	7·32	7·32	7·32

Some explanation of this difference might be found in the fact that the liver would act as a kind of buffer when the backward pressure is

[1] Oestreich. *Virchows Arch.*, 1895, cxlii, 285.
[2] Sieveking. *Centralbl. f. allg. Path. u. path. Anat.*, Jena, 1894, v, 1017.
[3] Azzurrini. *Arch. di biol.*, Firenze, 1902, lvi, 597.
[4] Christian. *Journ. Am. Med. Assoc.*, 1905, xlv, 1615.
[5] Kelynack. *Birmingham Med. Rev.*, 1897, xli, 86.

due to heart or lung disease, and so protect the spleen from excessive venous engorgement, whereas in cirrhosis the spleen is nearer to the venous obstruction. In support of this argument of Foxwell's[1] it may be added that in thrombosis of the splenic vein the spleen is very markedly enlarged. But, on the other hand, the splenic enlargement is much more marked and may precede any manifest change in the liver in hypertrophic biliary cirrhosis,[2] in which the obstruction to the passage of blood through the liver is much less than in portal cirrhosis. It appears, therefore, that backward pressure does not, at any rate completely, explain the splenic enlargement.

(II) The toxaemic view: that the spleen is enlarged as a result of poisons circulating in the blood and reaching it through the splenic artery, and that there is an active inflammatory swelling of the spleen like that seen in bacterial and some toxic conditions. In favour of this view is the absence of splenic enlargement in latent cirrhosis, in which the disease is arrested or compensated for. The toxaemia responsible for the enlargement might be either the same as that producing hepatic cirrhosis or it might be secondary to hepatic insufficiency, the cirrhotic liver allowing poisons, which should normally be arrested by it, to pass into the general circulation. This question is a difficult one. The spleen and liver react in different degrees to haemic intoxication, the spleen usually to a greater extent. Probably the spleen may suffer to some extent at the same time as the liver in early cirrhosis, if the poison, reaching the liver, as it generally does, from the portal system escapes into the general circulation. But when the liver becomes unable to stop poisons and general toxaemia supervenes, the conditions favourable for splenic enlargement are greatly increased.

Histologically Oestreich[3] found proliferation of the splenic pulp and concluded that it was due to toxins reaching the organ by the splenic artery.

To sum up: Splenic enlargement in cirrhosis probably depends primarily on poisons setting up hyperplasia and inflammatory softening of the organ so that it is readily overdistended with blood. Though chronic venous engorgement alone is not enough to cause enlargement of the spleen, it favours the stagnation of poisons and irritating bodies, and, further, it supplies blood to distend the softened splenic blood sinuses. Hence it may be concluded that the enlargement of the spleen is primarily due to toxic action and is aided by increased venous pressure in the portal system.

Relation between the Size of the Liver and that of the Spleen.—It might be surmised that in portal cirrhosis there would be a general relation between the size of the liver and that of the spleen. Examination of cases and statistics shews that this is a complicated question. Thus, in some cases, especially those running a rapid course and those

[1] Foxwell, A. *The Enlarged Cirrhotic Liver*, p. 6, 1896.
[2] Compare F. P. Weber. *Edin. Med. Journ.*, 1897, N.S. ii, 579.
[3] Oestreich. *Virchows Arch.*, 1895, cxlii, 285.

presenting a mixture of portal and biliary cirrhosis, the liver and spleen are both enlarged. On the other hand, in latent or compensated cirrhosis the liver is considerably increased in size, being bigger than in cases fatal from the effects of cirrhosis, whilst the spleen is either of normal size or but slightly heavier than normal. Again, in cases fatal from cirrhosis the liver is sometimes smaller than natural, while the spleen is almost constantly larger and heavier than normal.

In order to see if any relation exists between the weight of the liver and of the spleen in cirrhosis the following percentages were extracted from a number of cases examined at St. George's Hospital.

In 43 male cases in which the liver weighed over 60 oz. (averaging 79·6 oz.), the spleen averaged 11 oz. ; while in 7 males in which the liver weighed under 50 oz. (averaging 39·4 oz.), the spleen weighed 9·4 oz. In 11 female cases in which the liver weighed over 55 oz. (averaging 73·5 oz.), the spleen weighed 7·6 oz. ; while in 9 cases in which the liver weighed less than 45 oz. (averaging 35·4 oz.), the spleen weighed as much as 9·8 oz. Therefore, in male cases of cirrhosis, whether fatal from the disease or from other causes, large livers were associated with a more considerable enlargement of the spleen than is seen when the livers are small. But in a corresponding collection of female cases the spleen was heavier in the series of small livers than in the large liver series.

A consideration of the whole subject shews that the weight of the spleen has no constant relation to that of the liver, and that it depends on other factors, which may or may not be associated with increased weight and size of the liver.

Morbid Appearances in other Viscera.—Some writers regard hepatic cirrhosis as a disease which is not strictly limited to the liver, but as part of a general change, and in this respect comparable to the condition of red granular kidneys which is a local manifestation of a general vascular change—arteriosclerosis. Portal cirrhosis might in the same way be considered to be part of a general change in the alimentary system, in which the spleen, the intestines, and the pancreas share. Klippel and Lefas[1] have pointed out that in some instances of cirrhosis the changes may be more advanced in the pancreas than in the liver. This relation of cirrhosis to a general cause is also seen in haemochromatosis, in which, as a secondary result, cirrhosis of the liver and pancreatic fibrosis may occur (*vide* p. 303).

The Oesophagus.—There may be chronic oesophagitis with general thickening of the mucous membrane, which in places shews localised elevations due to hyperplasia of the epithelium—small corns. The longitudinal veins running in the submucosa of the oesophagus in its lower 3 or 4 inches are often dilated and varicose (*vide* p. 212). Inflammatory changes in the varicose veins lead to adhesions between the veins and the mucous membrane, and elevations on the surface of the oesophagus thus result. Ulceration may then occur and give rise to very profuse haemorrhage.

[1] Klippel et Lefas. *Rev. de méd.*, Paris, 1903, xxiii, 23.

Stomach.—Portal obstruction induces chronic venous engorgement of the stomach which nearly always shews chronic gastritis, mammillation of the mucous membrane and pigmentation, especially near the pylorus. There is occasionally dilatation of the gastric veins close to the cardiac orifice, but a varicose condition of the veins of the stomach is very rare. Cases of haematemesis depending on ruptured varicose gastric veins have been described (*vide* p. 271). Acute gastritis sometimes supervenes on the chronic gastritis, and small multiple ulcers which are quite superficial may then occur. A single chronic gastric ulcer is, however, rare in cirrhosis of the liver.

The Intestines. — There may be signs of chronic enteritis, such as thickening of the mucous membrane with tenacious mucus on its surface. Mere engorgement is not of very much importance after death, inasmuch as it may be largely due to stagnation of venous blood, from a dependent position of the intestinal coils. The mucous membrane may be pigmented from chronic catarrhal enteritis and venous engorgement. This is often more marked in the duodenum and the upper part of the jejunum than elsewhere. Occasionally the mucous membrane is oedematous. The subperitoneal tissues of the intestine may also be oedematous, either with or without oedema of the mucous membrane. Dilated venules and submucous haemorrhages are sometimes seen.

The small and large intestines become diminished in length in severe cases of portal cirrhosis; instead of 25 feet, the small intestine may only measure 15 feet, while the colon may be shortened in a corresponding or even in a greater degree. This fact, originally observed by Bright, has been explained as due to chronic enteritis, to concomitant chronic peritonitis, or to chronic inflammation of the radicles of the portal vein. It is important in that it diminishes the area of the mucous membrane from which absorption can take place. In rare instances the colon may be oedematous.

A little girl aged ten years was admitted to St. George's Hospital with a temperature of 104°, diarrhoea, and a swollen abdomen; the next day the abdomen was more distended and it was thought that perforation of a typhoid ulcer might have occurred. Laparotomy revealed a clear ascites and a cirrhotic liver. The patient died the next day. At the necropsy the liver (12 oz.) shewed extreme portal cirrhosis; there was no portal thrombosis. The mucous membrane of the colon was enormously swollen from oedema, and shewed a little follicular ulceration. There was no haemorrhage into the mucosa. There was no tubercle. An acute infection probably accounted for the high temperature and the oedema of the colon (*vide* also p. 180).

The rectum occasionally shews dilated veins, but, contrary to what might be expected, piles are rare (*vide* p. 213). Occasionally there is intense congestion of the rectum with small ulcers which may give rise to considerable haemorrhage.

Changes in the *pancreas* are extremely frequent.

Lando found some fibrosis, either inter- or intra-lobular, in every pancreas in 23 cases of cirrhosis. Steinhaus [1] found chronic interstitial pancreatitis in 11 out of 12 cases; Klippel and Lefas found it constantly in 8 cases of cirrhosis. I have seen extreme fibrosis and a calculus in the pancreas in fatal cirrhosis.

The pancreas is usually enlarged as a whole, but the tail is relatively more affected than the body and head of the gland. In his first series Lefas [2] found the weight increased by a third. Microscopically there is chronic interstitial pancreatitis, the fibrosis being either perilobular, intralobular, or partly periacinous but chiefly intralobular. There are scattered areas of small-celled infiltration. Occasionally there is intralobular oedema. The gland cells undergo fatty and pigmentary change; but the islands of Langerhans remain intact. In the cirrhosis of haemochromatosis, however, there is such extensive interstitial pancreatitis, the islands of Langerhans being destroyed, that eventually diabetes (*diabète bronzé*) results. According to Klippel and Lefas there is no relation between the size and consistency of the pancreas and these changes in the liver, and in some instances the pancreas shews more advanced change than the liver. The change in the pancreas may be due to the same factors that set up cirrhosis of the liver (Klippel and Lefas), or in some cases it may be secondary to hepatic cirrhosis and the result of chronic venous engorgement (Lando [3]).

Kidneys.—In the great majority of cases of portal cirrhosis the kidneys are free from any gross old-standing change, but are enlarged in about 50 per cent of the cases.

In 89 cases of fatal cirrhosis collected by Milian and Bassuet,[4] the kidneys were perfectly normal in 19; in 53, or 59·5 per cent, they were healthy or more or less hypertrophied. Pitt [5] found that when otherwise healthy the kidneys were enlarged in 50 per cent of the cases of cirrhosis.

This hypertrophy of the renal substance is a point of some interest as regards its explanation. In some instances the hypertrophy may merely be due to overwork from excessive drinking. It has been suggested that the hypertrophy is a compensatory process with the object of removing the toxic bodies which, owing to hepatic inadequacy, have flooded the circulation (Mollard [6]). In some instances enlarged kidneys are fatty or shew cloudy swelling. The kidneys are arteriosclerotic (granular) in about 25 per cent of cases dying with cirrhotic livers; and in about 5 per cent of the cases there is tubal nephritis. The relation of renal disease to cirrhosis is referred to again under the heading of associated morbid lesions (*vide* p. 224).

Diaphragm.—In cases in which the abdomen has been distended for a

[1] Steinhaus. *Deutsch. Arch. f. klin. Med.*, 1902, lxxiv, 537.
[2] Lefas. *Arch. gén. de méd.*, Paris, 1900, clxxxv, 538.
[3] Lando. *Ztschr. f. Heilk.*, 1906 (*Abt. path. Anat.*), xxvii, 1.
[4] Milian et Bassuet. *Bull. Soc. anat.*, Paris, 1903, lxxviii, 337.
[5] Pitt. *Trans. Path. Soc.*, Lond., 1889, xl, 349.
[6] Mollard. *Lyon méd.*, 1902, xcix, 665.

considerable time, the diaphragm may shew marked muscular hypertrophy from overwork. It is, however, very seldom noticed.

There was great hypertrophy of the diaphragm in a patient who survived the Morison-Talma operation, for 2½ years.

Associated Lesions.—*Tuberculosis.*—Tuberculosis is met with in the bodies of patients with cirrhosis more often than in other non-tuberculous diseases.

Thus in 706 fatal cases of cirrhosis obtained by combining the statistics given by Lancereaux,[1] Pitt,[2] St. George's, Kelynack,[3] and Yeld,[4] 209, or 29·6 per cent, presented some evidence of tubercle. Taking the general incidence of tuberculosis in routine post-mortem work as 27·5 per cent (Osler[5]), and deducting the large number of cases dying directly from tuberculosis—about 14 per cent—it is evident that tubercle is more frequent in cirrhosis than in ordinary non-tuberculous diseases.

Alcohol and the other poisons which induce cirrhosis diminish the resistance of the body and so dispose to tuberculosis. Although a tuberculous cirrhosis (*vide* p. 346) has been described (Hanot and Gilbert[6]), there is no reason to think that ordinary cirrhosis is ever due to tuberculosis or to tuberculous peritonitis; when tuberculosis and cirrhosis are associated, the cirrhosis is, as a rule, the older condition.

Age plays some part in influencing the incidence of tuberculosis in patients with cirrhosis. Thus, while it is rare in the somewhat infrequent cases of hepatic cirrhosis in childhood, Pitt's statistics shew that alcoholic cirrhosis in patients under forty is accompanied by tuberculosis in two-thirds of the cases. The lungs and the peritoneum are the most frequent sites of tuberculosis in the subjects of cirrhosis. The tuberculosis may be old, acute, chronic or recrudescent, and not infrequently escapes detection during life.

Pulmonary Tuberculosis.—In patients with cirrhosis pulmonary tuberculosis is the direct cause of death in from 12 (Kelynack) to 14·5 per cent (Rolleston and Fenton). In cases of cirrhosis, whether fatal from the disease itself or from other diseases (excluding tuberculosis), the lungs are the most frequent site of tuberculous lesions.

In 584 cases of cirrhosis obtained by combining the statistics of Lancereaux, St. George's, Kelynack, and Yeld, tuberculous lesions were found in the lungs in 132, or 22·6 per cent. On the basis of Heitler's[7] estimate that tuberculosis is present in the lungs of 5 per cent of patients dying from diseases other than pulmonary tuberculosis—a low estimate—there is a marked increase in the incidence of tubercle in the lungs.

---

[1] Lancereaux. *Traité des maladies du foie et du pancréas*, p. 302, 1899.
[2] Pitt. *Trans. Path. Soc.*, Lond., 1889, xl, 350.
[3] Kelynack. *Med. Chronicle*, 1897, vi, 262.
[4] Yeld. *St. Barth. Hosp. Rep.*, 1898, xxxiv, 215.
[5] Osler. *Practice of Medicine*, p. 295, 6th ed., 1905.
[6] Hanot et Gilbert. *Arch. gén. de méd.*, 1889, clxiv, 513.
[7] Quoted by Hilton Fagge. *Practice of Medicine*, vol. i, p. 953, 1886.

Pulmonary tuberculosis is more often found in patients who die from the effects of cirrhosis than in patients who have cirrhosis but die from other causes (excluding tuberculosis).

In 97 cases of cirrhosis in which death was not due to pulmonary tuberculosis tubercles were found in the lungs in 17. Of these 97 cases, 47 were fatal from the direct effects of cirrhosis, and pulmonary tuberculosis was found in 10, or 21·2 per cent; while in the remaining 50 cases in which cirrhosis was latent and death was due to some independent cause, pulmonary tuberculosis being of course excluded, tubercle was present in 7, or 14 per cent.[1]

Tuberculous Peritonitis.—Next to the lungs, the peritoneum is the most frequent situation of tuberculous infection in cirrhosis. In 584 cases of cirrhosis obtained by combining the statistics of Lancereaux, Fenton and myself, Kelynack, and Yeld there were 53 cases of peritoneal tubercle, or 9 per cent. In a large number of cases of peritoneal tubercle the lungs are previously infected. Tuberculous peritonitis is rare in adult males, and when it does occur is most often associated with hepatic cirrhosis. In 121 cases of cirrhosis Kelynack found active tuberculosis of the peritoneum in 12, in 4 of whom the peritoneum was alone affected. This suggests that cirrhosis of the liver disposes to the local invasion of the peritoneum by tubercle.

A certain degree of *simple chronic peritonitis* is often seen in the bodies of those who have died from cirrhosis of the liver, but a high degree of chronic peritonitis is comparatively rare in association with well-marked cirrhosis.

In Yeld's 131 cases of cirrhosis simple chronic peritonitis was present in 10·7 per cent, and in Sears and Lord's[2] 78 cases in 19 per cent.

The relation between cirrhosis and chronic peritonitis is probably not always the same; possibly in some cases the chronic peritonitis is secondary to the ascites induced by cirrhosis, the toxic bodies or bacteria in the ascitic fluid irritating the peritoneum; and it is conceivable that occasionally they are both related to alcoholism. In many instances the two processes are probably independent; thus, simple chronic peritonitis may be associated with and due to arteriosclerosis. As has just been pointed out, tuberculosis may supervene in the peritoneum.

Arteriosclerosis.—Since cirrhosis and arteriosclerosis occur about the same time of life, it is natural to find arterial degeneration of a greater or lesser degree in the bodies of patients dying from cirrhosis. There is, however, no direct relation between these two conditions; cirrhosis is accompanied by a low blood-pressure, and thus does not tend to set up arterial degeneration, while endarteritis is not a cause of genuine hepatic cirrhosis. In some exceptional instances syphilitic endarteritis is associated with hepatic cirrhosis (probably parasyphilitic) in children, and in the rare disease haemochromatosis, cirrhosis of the liver and endarteritis of

[1] Rolleston and Fenton. *Birmingham Med. Rev.*, 1896, xl, 193.
[2] Sears and Lord. *Boston Med. and Surg. Journ.*, 1902, cxlvii, 285.

the hepatic artery may occur. From the statistical point of view, arteriosclerosis is the commonest, and one of the least essential, morbid changes found in the bodies of patients with hepatic cirrhosis.

In 78 cases of cirrhosis tabulated by Sears and Lord, arteriosclerosis was noted in 49 instances; often, however, there was only a small patch in the aorta.

The *heart* is frequently flabby and dilated, and the muscular tissue often shews cloudy swelling or fatty degeneration, due to toxaemia or alcoholism. In uncomplicated cirrhosis the heart may be smaller than natural (Carnot[1]); this is associated with the habitually low blood-pressure in cirrhosis.

In 114 cases of cirrhosis, obtained by uniting Cheadle's[2] and Sears and Lord's statistics, there was fatty degeneration in 33, or 28·9 per cent, and myocarditis in 3.

In rare instances infective endocarditis may occur as a complication. Chronic valvulitis, like arteriosclerosis, is frequently associated with cirrhosis. Although adherent pericardium does not induce genuine hepatic cirrhosis, calcification of the pericardium is said to be associated in the majority of cases with definite cirrhosis (*vide* p. 98).

Renal Disease.—The kidneys in fatal cases of cirrhosis are, generally speaking, free from any marked structural change; they often shew enlargement from overwork (drinking), chronic venous engorgement from cardiac failure, or some degree of tubal changes, such as fatty degeneration or cloudy swelling, from toxaemia or alcohol. When definite structural change is present, it is usual to find that the kidney is granular from the effects of arteriosclerosis; definite lardaceous disease and tubal nephritis are quite rare. The association of granular kidney with hepatic cirrhosis is intelligibly explained by the fact that the two diseases are common at the same time of life, and are therefore met with together in a certain number of cases. But though both the liver and kidney are very liable to fibrosis, this change in the two organs respectively is due to different morbid agencies (Dickinson[3]).

In an analysis of 78 fatal cases of cirrhosis, Sears and Lord[4] found chronic nephritis (interstitial or tubular) in 23, or 29·4 per cent, fatty change in 15, and lardaceous change in 2. In 440 cases of cirrhosis of the liver obtained by combining the statistics of Pitt,[5] Kelynack,[6] Yeld,[7] Cheadle, and myself[8] there were 110 with distinct fibrosis of the kidneys, or 25 per cent. In some of the cases the renal change was not very marked, and as the average age for death

[1] Carnot. *Progrès méd.*, Paris, 1909, v, 61.
[2] Cheadle, W. B. *Some Cirrhoses of the Liver*, Lond., 1900, p. 47.
[3] Dickinson, W. H. *Med.-Chir. Trans.*, 1873, lvi, 34.
[4] Sears and Lord. *Boston Med. and Surg. Journ.*, 1902, cxlvii, 285.
[5] Pitt, G. N. *Trans. Path. Soc.*, Lond., 1889, xl, 348.
[6] Kelynack, T. N. *Birmingham Med. Rev.*, 1897, xli, 86.
[7] Yeld, R. A. *St. Barth. Hosp. Rep.*, 1898, xxxiv, 215.
[8] Rolleston and Fenton. *Birmingham Med. Rev.*, 1896, xl, 193.

in cirrhosis is over forty-five years, it is probable that in some instances the change in the kidney was senile. Dickinson estimated that well-marked granular kidneys occurred in 15 per cent of the cases of cirrhosis.

As would be naturally expected from the greater frequency of both hepatic cirrhosis and arteriosclerosis in men, the two conditions are more often seen associated in the male than in the female sex.

The question whether a granular kidney is more often associated with a large or with a small cirrhotic liver has been referred to already (p. 197). Pitt's and my own observations point to a small cirrhotic liver as more frequently associated with a granular kidney; Price's statistics were to the opposite effect.

Cirrhosis complicated with Carcinoma, etc.—The form of primary carcinoma of the liver described by Hanot and Gilbert as cancer with cirrhosis is essentially cirrhosis first with a secondary hyperplasia of the liver cells. At first this hyperplasia is compensatory and gives rise to cirrhosis with adenoma; subsequently the cellular proliferation becomes so riotous as to be malignant and constitutes carcinoma. It is very hard to draw the line between the different stages of cirrhosis, cirrhosis with adenoma, and carcinoma with cirrhosis (*vide* p. 474).

Secondary Carcinoma in a Cirrhotic Liver.—Cirrhosis of the liver and carcinoma elsewhere in the body are both so common that it is remarkable that secondary growths are so rare in cirrhotic livers. In a case in St. George's Hospital there was a secondary growth in a cirrhotic liver, the primary growth being a carcinoma of the pylorus. In 608 cases of secondary malignant disease of the liver the organ was cirrhotic in two (Colwell [1]). Hale White [2] refers to a case of sarcoma of bone with a secondary growth in a cirrhotic liver, and Poulain [3] and Achard and Laubray [4] to cases secondary to carcinoma of the colon and stomach. The coexistence of a cirrhotic liver (without any secondary growths) and malignant disease in some other part of the body is also rare; in 2634 necropsies at the Middlesex Hospital on cases of malignant disease hepatic cirrhosis was present in 27 only (Colwell).

Other Accidental Lesions in the Liver.—In a few cases a hydatid cyst has been found embedded in a cirrhotic liver (*vide* p. 397). Among 174 cases of hepatic gumma, obtained by combining J. L. Allen and Flexner's [5] cases, universal cirrhosis was present in 13, or 7·5 per cent. Tubercles are sometimes implanted in a cirrhotic liver. It is rare to find cirrhosis and lardaceous disease combined. A tight-laced liver may be cirrhotic (*vide* Fig. 6).

[1] Colwell. *Arch. Middlesex Hosp.*, 1905, v, 135.
[2] Hale White. Allbutt's *System*, 1897, iv, 208.
[3] Poulain. *Bull. Soc. anat.*, Paris, 1899, 6. s., i, 1089.
[4] Achard et Laubray. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1902, 3. s., xix, 335.
[5] Flexner. *New York Med. Journ.*, 1902, lxxv, 101.

Clinical Features

The course of ordinary cirrhosis may be divided into: (1) The early or pre-ascitic stage, which is often divided into two by early haematemesis. (2) The late or ascitic stage.

Cases may die from intercurrent diseases during the course of cirrhosis or may be cut off by a very profuse gastro-intestinal haemorrhage long before the onset of ascites. Again, complications, such as tuberculosis, cardiac failure, peripheral neuritis, or other manifestations of alcoholism, may supervene and prove fatal or mask the symptoms of cirrhosis.

The *early stage* begins gradually and vaguely; though in some cases it may be dated back to some acute illness or to a passing attack of gastro-enteritis. The symptoms are mainly those of dyspepsia, often of an alcoholic nature, with loss of appetite, occasional nausea and vomiting, especially in the morning, flatulence, abdominal pain or unrest, and looseness or irregularity of the bowels. Sometimes symptoms are absent; at other times they are those of chronic alcoholism. Bodily strength, vigour, and energy may be seriously impaired, and the condition resembles neurasthenia; or, on the other hand, there may be little or no complaint of altered health.

There may be some heaviness or tenderness in the epigastrium and hypochondrium, especially after meals, which is partly due to dyspepsia and perhaps partly to hepatic enlargement. The liver is generally somewhat enlarged and may be slightly tender. The enlargement may vary considerably within short intervals, and is perhaps due to engorgement. The spleen is usually not enlarged, but it may be palpably so, especially shortly before haematemesis supervenes.

Epistaxis may occur now and then, but the most important event in the early stage is the occurrence of haematemesis. This may come on after some premonitory discomfort and fever, or may occur with little or no warning, except perhaps slight faintness immediately before a large quantity of blood is brought up. It is very rarely fatal, and is very seldom repeated within a short interval. After it the patient is blanched and anaemic for a time, but soon recovers.

Usually some months or even years elapse after haematemesis before ascites develops, especially if the patient has taken warning and altered his manner of life. The disease may then become latent from the development of compensatory processes. But in cases of acute cirrhosis, in which there is fever, the effects of haematemesis are hardly recovered from before ascites begins.

The Late or Ascitic Stage.—The onset of ascites is somewhat sudden; when it occurs quite suddenly and with great rapidity it may be due to another factor, viz. thrombosis of the portal vein. The onset of ascites may be preceded by gaseous distension of the intestines, which for a time

may mask the ascites. Oedema of the feet may also precede instead of follow the appearance of ascites.

When ascites occurs, the patient has undergone a considerable amount of wasting, shews marked muscular debility, and is unfit to be out of bed. The wasting of the temporal and facial regions gives a characteristic appearance to the patient. The atrophy of the thoracic muscles shews up the bony skeleton, and contrasts with the swollen abdomen. The skin becomes dry, harsh, and loses its elasticity, and may shew petechiae, while there may be haemorrhages from the various mucous membranes and oozing from the gums. The ascites may require tapping once, twice, or even oftener, but in cases of cirrhosis uncomplicated by chronic peritonitis paracentesis is seldom required more than twice. The patient emaciates rapidly, loses strength, becomes stupid, drowsy, or even delirious, and dies, sinking down in the bed without any great reaccumulation of fluid in the peritoneal cavity. A patient often goes downhill very rapidly after paracentesis, not because of the tapping, but from the advanced stage of the disease. Sometimes, in fact, ascites disappears, while the patient becomes more drowsy and uraemic, and passes into what may be spoken of as a post-ascitic stage. The patient may then linger on in a semi-comatose condition for some weeks, and die from an acute and terminal infection or gradually from mere weakness.

Latency.—Cirrhosis of the liver is not uncommonly latent and gives rise to no symptoms. It may be found in the bodies of persons who have died as the result of accidents or from other diseases. Of 82 cases in which cirrhosis was found after death at Charing Cross Hospital, 12 were in fatal street accidents (Mott and Candler[1]). It would be incorrect to say that when a patient dies from some other disease the cirrhosis has necessarily been entirely latent, since patients with cirrhosis rapidly die with pulmonary tuberculosis and are very bad subjects for pneumonia, erysipelas, and other acute infections. The fact, however, that out of 167 consecutive necropsies at St. George's Hospital in which the liver was cirrhotic, 86, or just over half, died from other diseases and not directly from cirrhosis, shews how frequently cirrhosis remains latent. It thus differs from universal chronic perihepatitis, which is practically always accompanied by ascites. The latency of portal cirrhosis depends on the compensatory processes, *i.e.* the collateral circulation between the branches of the portal and general systemic veins, and hyperplasia of the liver cells. These two compensatory mechanisms are further discussed on p. 291.

When cirrhosis becomes latent, the liver is enlarged as the result of compensatory hyperplasia of the liver cells. Hanot and Gilbert[2] insisted on the enlarged liver of latent cirrhosis, and spoke of it under the title of hypertrophic alcoholic cirrhosis. Cirrhosis is more often latent in men than in women. This is not merely because cirrhosis is commoner

[1] Mott and Candler. *Arch. Neur. Path. Lab., Lond. County Asyl., Claybury*, 1907, iii, 439.

[2] Hanot et Gilbert. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1890, 3. s., vii, 493.

in men than in women, for the ratio of women to men is lower among the cases dying independently of cirrhosis than among the cases fatal from the direct effects of cirrhosis.

In 167 cases in which the liver was cirrhotic at the necropsy at St. George's Hospital, 121 were males and 46 females, or a ratio of 5 to 2. Of these, 80 died from the direct effects of cirrhosis, 50 being males and 30 females, a ratio of 5 to 3 ; while of the 87 who died from other factors independent of cirrhosis, 71 were males and 16 females, a ratio of $4\frac{1}{2}$ to 1.

Minor Signs and Symptoms.—*Facial Aspect.*—The face may be bloated and shew rosacea due to dyspepsia, either induced by, or independent of, alcoholism ; the area of skin affected involves the nose and the cheeks and roughly corresponds with the common site of lupus erythematosus, the so-called "flush area." Galloway [1] recorded a case with subsequent atrophy of the skin. The condition of the skin of the face varies ; in early cases it may be pale and clear, but often it is sallow, muddy, and dirty-looking. This pigmentation is sometimes so accentuated as to suggest that the cirrhosis may be a terminal stage of haemochromatosis. In the more advanced stages the face is drawn and thin, the eyes deeply set, and the conjunctivae congested and muddy, or slightly icteric. The wasting in the temporal regions is often very manifest. The skin of the face may present clusters of dilated vessels or stigmata ; these may be capillary or in some instances arterial, as shewn by pulsation and by the character of their bleeding, which may occur on slight provocation. It is an interesting question why these stigmata should develop in cirrhosis ; they cannot be due to increased pressure in the portal system. It has been thought that they depend on alcoholism ; Bouchard [2] has suggested that, owing to altered internal secretion of the liver, the arteries all over the body undergo a special change resulting in local dilatations. The lips are usually dry and apt to be fissured ; the tongue flabby, furred, or dry, and sometimes tremulous. The gums are apt to become spongy and, when hepatic insufficiency has become established, to bleed. The throat is often chronically congested, and pharyngitis and laryngitis are frequent.

The *skin* of the body is often dry and harsh with loss of elasticity. Probably from failure of the antitoxic function of the liver eruptions such as erythema exudativum may occur. Angioneurotic oedema has been observed (Corner [3]). Local haemorrhages may occur as the result of slight or unnoticed traumatism. When cirrhosis is advancing, small angiomas may crop up all over the surface of the body, and in exceptional instances may unite to form areas of considerable extent. A remarkable case of multiple haemangiomas, many of which were solid, has been recorded by Winternitz and Boggs.[4] Bouchard records a case

[1] Galloway. *Brit. Med. Journ.*, 1908, i, 665.
[2] Bouchard. *Rev. de méd.*, 1902, xxii, 837.
[3] Corner. *Lancet*, Lond., 1909, ii, 295.
[4] Winternitz and Boggs. *Johns Hopkins Hosp. Bull.*, 1910, xxi, 203.

in which angiomas appeared when the disease was advancing and receded when improvement took place. According to Gilbert and Herscher,[1] capillary angiomas are commoner on the trunk, and arterial on the hands and face. A zone of dilated capillaries on the chest about the attachment of the diaphragm has no real significance, since it is seen in many men of middle age, especially those with emphysema, who have nothing wrong with their livers.[2] Dilatation of the subcutaneous veins around the umbilicus (cirsomphalos) points to portal obstruction; when well marked, this is spoken of as a "caput Medusae." Trousseau[3] described a palpable thrill as well as a bruit in these veins. The collateral circulation around the umbilicus, due to portal obstruction, must be distinguished from dilatation and varicosity of the superior and inferior epigastric veins in obstruction of the inferior vena cava. This latter anastomosis is often developed in a minor degree as the result of ascites pressing on the inferior vena cava. In pure portal obstruction the visible dilated veins are mainly around and above the umbilicus; the dilated veins due to obstruction of the inferior vena cava are first seen below the umbilicus (*vide* p. 249).

Jaundice is not a prominent feature in portal cirrhosis, but it is met with at some time in the course of the disease, as shewn by statistics, in more than one-third of the cases.

Thus, in 293 cases, obtained by combining the statistics of Fagge,[4] Yeld,[5] and Sears and Lord,[6] jaundice was recorded in 107, or 36·5 per cent.

The jaundice is usually slight and often transient. It may be merely an incident in the course of the disease, and have passed away before the patient comes under observation with indubitable cirrhosis. Not uncommonly there is slight jaundice with staining of the skin and blood serum, but no bile pigment in the urine, or "acholuric jaundice" (Gilbert and Herscher[7]).

Definite, well-marked jaundice may be catarrhal and due to gastro-duodenal inflammation — an exceedingly common event in alcoholic subjects. It is not infrequent in cases of acute cirrhosis, and is then probably due to inflammation of the small intrahepatic bile-ducts. In rare instances it is dependent on a gall-stone in the common duct, or terminal and the result of acute and widespread degenerative changes in the liver cells (icterus gravis).

Clubbing of the fingers, also spoken of as "Hippocratic fingers," which is sometimes seen in long-standing cases of hypertrophic biliary cirrhosis, is extremely rare in portal cirrhosis.

[1] Gilbert et Herscher. *Compt. rend. Soc. Biol.*, 1903, lv, 167.

[2] For further information about this "costal fringe" see Solis-Cohen (*Am. Journ. Med. Sc.*, 1894, cviii, 135), F. P. Weber (*Edin. Med. Journ.*, 1904, N.S., xv, 346), and Haeberlin (*Deutsch. Arch. f. klin. Med.*, Leipz., 1908, xciii, 43).

[3] Trousseau. *Lectures on Clinical Medicine*, v, 131, Transl. New Syd. Soc., 1872.

[4] C. Hilton Fagge and Pye-Smith. *Practice of Medicine*, ii, 270, 1886.

[5] Yeld. *St. Barth. Hosp. Rep.*, 1898, xxxiv, 215.

[6] Sears and Lord. *Boston Med. and Surg. Journ.*, 1902, cxlvii, 285.

[7] Gilbert et Herscher. *Presse méd.*, Paris, 1903, p. 541.

Flückiger[1] in 1884 and Bouchard[2] in 1890 described cases. I watched it develop in a patient in whom, two and a half years before, Morison's operation for the relief of ascites had been successfully performed. There was no other obvious cause, such as pulmonary or heart disease. Obermayer[3] reported a case of portal cirrhosis with hypertrophic osteo-arthropathy.

Debility.—Marked weakness and languor out of proportion to the physical signs are not uncommon, and may be the first symptoms calling for treatment, before there are sufficient data for diagnosing cirrhosis. Muscular weakness and asthenia are usually constant in the late stages of the disease, and are only natural when the poor state of general nutrition is taken into account. The debility is partly due to the toxaemia of hepatic inadequacy.

Wasting in advanced cirrhosis is usually very considerable; the muscles of the trunk, extremities, and face become flabby and atrophied. The limbs become like spindles. The face gets sharpened, the fat disappears from the buccal pads, and the temporal fossae fall in, so that the face often has the aspect of a case of advanced pulmonary tuberculosis or of malignant disease. In latent cirrhosis, however, bodily nutrition may be very good, and there may be a thick layer of fat over the body.

I have several times seen somewhat fat patients with latent hepatic cirrhosis die from rapid or generalised tuberculosis. In such cases the existence of cirrhosis is very likely to be overlooked. The large size of the liver is, however, fairly constant.

Offensive Breath.—In some, but certainly not in all, patients with cirrhosis the breath is very offensive without any local cause, such as decayed teeth, chronic follicular tonsillitis, or ozaena. The odour is often peculiar, and is described as cadaveric or earthy. It resembles the smell of dried and decomposing blood, and is sometimes associated with oozing from the gums or epistaxis. It is probably due to failure of the antitoxic function of the liver and to the passage into the general circulation of poisons manufactured in the alimentary canal. In other words it depends on hepatic inadequacy, and is therefore of bad omen.

Experimentally Roger and Garnier[4] find that in healthy rabbits a hypodermic injection of sulphuretted hydrogen is followed by excretion of the gas by the lungs, but that about double the quantity must be injected into the rectum before it passes through the lungs. When the functional activity of the rabbit's liver has been reduced by the subcutaneous injection of phosphorated oil, a much smaller rectal injection of sulphuretted hydrogen was followed by the excretion of the gas by the lungs.

The amylolytic power of the *saliva* is not necessarily reduced; it may even be increased (Robertson[5]). If there is ascites or diarrhoea, the amount of saliva will tend to be diminished.

[1] Flückiger. *Wien. med. Wchnschr.*, 1884, xxxiv, 1457.
[2] Bouchard. Quoted by Klippel et Vigouroux. *Presse méd.*, 1903, i, 245.
[3] Obermayer. *Wien. klin. Rundschau*, 1897, xi, 625.
[4] Roger et Garnier. *Compt. rend. Soc. Biol.*, Paris, 1898, l, 714.
[5] Robertson, W. G. A. *Journ. Path. and Bacteriol.*, 1901, vii, 118.

V. Leube[1] mentions a case of excessive salivation in which 3 litres were secreted in one twenty-four hours, and as a result ascites, which was present, disappeared. Cirrhosis of the liver was found after death.

Dyspepsia is almost constant in portal cirrhosis, and usually precedes, often for some years, the first striking manifestation of the disease, namely, haematemesis. It may be irritative and intermittent, or flatulent and very persistent. In the early stages it is due to gastritis—often of alcoholic origin—and has a causal relation to dyspeptic cirrhosis, inasmuch as the chronic gastric catarrh manufactures the toxins which are carried to the liver and induce cirrhosis. Later, when portal obstruction and engorgement of the stomach and intestines have supervened, gastritis and indigestion are aggravated. The portal obstruction favours infection and at the same time interferes with the digestion and absorption of food. Absorption is also impaired as the result of the curtailed length of the intestinal tract; the process of digestion is interfered with from a deficiency in the secretion of hydrochloric acid. Exceptionally hyperchlorhydria is present. Hewes[2] has recorded two cases of gastrosuccorrhoea associated with cirrhosis. There is loss of appetite for solid food, especially for meat. Morning vomiting may be present, and is naturally more often seen in alcoholic subjects. Occasionally acute or subacute attacks of gastritis may supervene, and if seen for the first time in one of these exacerbations, the underlying condition of cirrhosis may not at first be manifest.

Tympanites may come on acutely or subacutely in the late stage of cirrhosis. It is probably toxic (Wilkinson[3]).

Diarrhoea.—Comparatively early in the disease diarrhoea or excessive looseness of the bowels may be due to a general catarrh of the intestinal tract in alcoholic subjects, and to diminished and delayed absorption. In other cases diarrhoea may alternate with the more usual state of constipation. Diarrhoea is more often met with in multilobular cirrhosis in children.

In the last stage of the disease, when the patient is in a toxaemic state, diarrhoea may set in and be very rebellious. It may continue until the patient dies of exhaustion. It is, however, possible that the diarrhoea is, like that of renal disease, of use in getting rid of toxic substances.

Constipation is often present. Chronic catarrh of a certain degree may cause it instead of diarrhoea, by impairing the peristaltic powers of the intestine; chronic portal engorgement impairs both the muscular and nervous activity of the bowel. In the later stages ascites helps to produce constipation, both by weakening the muscular walls of the abdomen and by withdrawing water from the bowel. Thus a patient with ascites may chiefly complain of constipation. Moreover, milk diet leaves little

[1] v. Leube. *Deutsches Arch. f. klin. Med.*, 1899, lxvi.
[2] Hewes. *Boston Med. and Surg. Journ.*, 1906, clv, 163.
[3] Wilkinson. *Med. Chron.*, Manchester, 1910, li, 212.

residue for the faeces and may thus accentuate this tendency. Constipation leads to putrefaction and fermentation and so to auto-intoxication.

The *urine* is usually diminished in amount in the late stages of cirrhosis. The smaller quantity is closely associated with, in fact mainly depends on, low arterial pressure, which in turn is correlated with increased blood-pressure in the portal vein. Normally more water passes through the kidneys during digestion, owing to increased absorption from the alimentary canal; in cirrhosis, absorption is delayed on account of the increased pressure in the portal vein, and, as a result, the normal relation between the amount of urine excreted during digestion and in the intervals is reversed, more urine being excreted during fasting. This phenomenon, described by Gilbert and Lereboullet,[1] has been termed "opsiuria."

Another abnormal feature in the excretion of urine in cirrhosis, described by Chauffard and Castaigne,[2] is that methylene-blue when taken by the mouth is excreted intermittently, and not continuously as in health.

The urine is strongly acid, usually of a high specific gravity, high coloured, often reddish orange, from the presence of uroerythrin, and, like the urine of cardiac disease, commonly precipitates urates on standing.

The amount of urobilin is increased in cirrhosis,[3] while the pigment described as urohaematoporphyrin, which is in reality not a definite chemical compound, but a mixture of a large quantity of haematoporphyrin with a small quantity of urobilin, has been said to occur in the urine of some cases of cirrhosis (McMunn[4]). Indican may also appear in the urine without any special evidence of intestinal disturbance.

Since jaundice is somewhat uncommon in portal cirrhosis, bile pigment is not often found in the urine, but it may be present without any manifest staining of the skin. I have seen this during the comatose condition preceding death. The converse is more often seen, viz. slight icteric coloration of the skin, due to small quantities of bile pigment in the blood serum, without any bile pigment in the urine (acholuric jaundice), though the amount of urobilin in the urine is increased. Gilbert and Herscher[5] believe that bilirubin is transformed by the kidneys into urobilin; this condition was formerly called "urobilin jaundice" (*vide* p. 534). Strauss[6] found the fatty acids increased.

In cases of advanced cirrhosis a port-wine coloration is, in rare instances, obtained when liquor ferri perchloridi is added to the urine; in the absence of drugs, such as salicylates, aspirin, salol, diuretin, which give a similar colour reaction, this is due to the presence of diacetic acid (Gerhardt's reaction).

[1] Gilbert et Lereboullet. *Compt. rend. Soc. Biol.*, Paris, 1901, liii, 276.
[2] Chauffard et Castaigne. *Ibid.*, 1898, l, 359.
[3] Garrod, *Lancet*, 1900, ii, 1323 (Bradshaw lecture); Durandeau, *Thèse de Paris*, 1900, No. 346.
[4] McMunn. *Journ. Physiol.*, 1889, x, 71.
[5] Gilbert et Herscher. *Presse méd.*, Dec. 27, 1902; 1903, p. 541.
[6] Strauss. *Deutsche med. Wchnschr.*, 1901, xxvii, 759.

If the urine is previously heated, the coloration is less marked; this is due to the transformation of diacetic acid into acetone, which does not give this coloration with ferric chloride. The presence of diacetic acid points to the presence in the blood of organic acids, such as β-oxybutyric acid, or to acidosis. This condition is one of great gravity, inasmuch as it may pass into coma. When the urine gives the reaction for diacetic acid, bicarbonate of sodium should be given in large doses, and if coma begins to appear, transfusion of saline solution with bicarbonate of sodium (2 drams to the pint) should be performed. As is well known, starvation, especially in women with gastric ulcer, may induce diaceturia without any other sign of acid intoxication.[1]

When the disease is well established, the amount of *urea* excreted is diminished, while that of uric acid is increased. The diminution in the output of urea accompanies, but is not a direct result of, destruction of the liver cells; it is correlated with an increase in the nitrogen excreted in the form of ammonia in the urine. The nitrogen in the form of ammonia may be present in the urine in the normal amount (2 to 5 per cent of the total nitrogen), but when destructive changes in the liver cells are active it may rise to as much as 20 per cent of the total nitrogen. This increase in ammonia is correlated with a diminished formation of urea. According to Herter,[2] the increase in ammonia is not due to inability of the liver cells to form urea—for, as shewn by Weintraud, if ammonia is given to such patients it appears in the urine as urea—but to the fact that the ammonia is seized upon by organic acids before it can be transformed into urea. The ammonia neutralises the organic acid and so tends to prevent acidosis. In advanced cases with extensive destruction of the liver cells leucine and tyrosine may be found in the urine.

The *chlorides* are diminished when there is ascites.

Albuminuria is comparatively rare. When it does occur, it is usually due to some concomitant organic renal disease, such as granular kidney, tubal nephritis, or lardaceous change. In 89 cases tabulated by Milian and Bassuet[3] albuminuria occurred in three.

As a result of hepatic insufficiency toxaemia commonly occurs in the late stages of cirrhosis, and sometimes so affects the renal tubules as to give rise to albuminuria and casts. Albuminuria is sometimes associated with cardiac failure, and probably toxaemia combined with chronic venous engorgement of the kidney is the most favourable condition for the production of albuminuria. In rare cases albuminuria may be mechanical and due to the pressure of a considerably enlarged spleen on the left renal vein and possibly on the left kidney. Falkenheim[4] in 1884, and in 1902 the writer,[5] observed intermittent albuminuria due to this cause in cirrhosis. In these cases there is considerable albuminuria with high-

[1] *Vide* Rolleston and Tebbs. *Brit. Med. Journ.*, 1904, ii, 114.
[2] Herter, C. A. *Lectures on Chemical Pathology*, p. 347, 1902.
[3] Milian et Bassuet. *Bull. Soc. anat.*, Paris, 1903, lxxviii, 337.
[4] Falkenheim. *Deutsch. Arch. f. klin. Med.*, 1884, xxxv, 446.
[5] Rolleston. *Lancet*, 1902, i, 585.

coloured and uratic urine, thus resembling that of chronic venous engorgement, when the patient lies on the left side or on his back; when the patient is in the erect position, lies on the right side or on his face, the urine is free from albumin (Falkenheim).

Albumose is very occasionally observed in the urine when hepatic inadequacy has supervened, and may be associated with albuminuria (Teissier [1]).

Haematuria is distinctly rare; it may be due to concomitant subacute nephritis in a previously damaged kidney, or to toxaemia and occur at the same time as epistaxis and oozing from the gums.

Glycosuria is rare in ordinary cirrhosis. Glycosuria occurs in a high proportion of the cases of pigmented cirrhosis from haemochromatosis (*diabète bronzé*; *vide* p. 303), but it is then due to a concomitant fibrosis of a very intimate nature in the pancreas—a change which is not present in ordinary cirrhosis. The great rarity of glycosuria in cirrhosis is certainly curious, since the liver is usually regarded as stopping sugar reaching it from the alimentary canal. It might naturally be expected that sugar would pass through the cirrhotic liver, or that by means of the compensatory venous anastomoses some sugar would avoid the liver and pass into the general circulation, and so appear in the urine. Brault's [2] histological examinations of cirrhotic livers shew that the glycogenic function of the liver is well maintained, and agree with the great rarity of glycosuria. It has sometimes been observed that if an excessive amount of sugar in the form of syrup is given to a patient with cirrhosis, alimentary glycosuria is produced when it would not occur in a healthy person.

In a normal person 3½ ounces (100 grams) of sugar given in half a pint of water or tea on an empty stomach will not produce alimentary glycosuria. To test for alimentary glycosuria this quantity of sugar should be given before food and the urine should be obtained after six hours and tested for sugar (Strauss [3]).

Alimentary glycosuria is by no means constant in cirrhosis; in 95 collected cases it was positive in 42 (Simon [4]); even if it were more frequent it would not prove that the liver was at fault, for it appears that it is to be correlated with changes in the pancreas (Steinhaus [5]). According to most observers, such as Kraus and Ludwig,[6] Bloch,[7] Colasanti,[8] Linoissier and Roque,[9] Gorget,[10] Ingelnans and Dehon,[11] and

[1] Teissier. *Semaine méd.*, Paris, 1899, xix, 282.
[2] Brault. *Arch. de méd. expér. et d'anat. path.*, 1902, xiv, 453.
[3] Strauss. *Deutsche med. Wchnschr.*, 1901, xxvii, 757.
[4] Simon. *Clinical Diagnosis*, p. 569, 1911.
[5] Steinhaus. *Deutsch. Arch. f. klin. Med.*, 1902, lxxiv, 537.
[6] Kraus und Ludwig. *Wien. klin. Wchnschr.*, 1891, iv, 855, 897.
[7] Bloch. *Ztschr. f. klin. Med.*, 1893, xxii, 525.
[8] Colasanti. *Arch. ital. de biol.*, 1892, xvii, 335.
[9] Linoissier et Roque. *Arch. de méd. expér. et d'anat. path.*, 1895, vii, 228.
[10] Gorget. *Rev. de méd.*, 1897, xvii, 537.
[11] Ingelnans et Dehon. *Arch. de méd. expér. et d'anat. path.*, 1903, xv, 189.

Churchman,[1] alimentary glycosuria is a most unreliable sign of hepatic insufficiency. Alimentary laevulosuria, however, has been thought to be of some value as an indication of hepatic inadequacy (Naunyn,[2] Halász[3]), and is said to be almost constant in cirrhosis (Goodman[4]). The glycogenic function may be retained while other functions have failed, as is commonly seen in cirrhosis; again, sugar taken into the alimentary canal may be delayed in absorption and undergo fermentation, thus vitiating the test. Cammidge[5] obtained a positive pancreatic reaction in 14 out of 21 cases. Chyluria has been observed in exceptional cases.[6]

Urotoxic Coefficient.—In cases with hepatic insufficiency, due to destructive changes in the liver cells, the toxicity of the urine has been found to be increased (Surmont,[7] Gorget), as shewn by the fact that when injected into dogs it appeared to be decidedly more toxic than healthy urine (Roger[8]).

Symptoms connected with the Vascular System.—From a flabby, possibly fatty, condition of the myocardium the left ventricle may be dilated and a systolic apex murmur and accentuated second sound over the pulmonary artery, due to mitral regurgitation, may be present. When the heart is displaced upwards by ascites, the apex-beat may be in the left fourth or even in the third intercostal space, and from slight kinking of the pulmonary artery a systolic murmur may be produced in that area. The murmurs at the apex and over the pulmonary artery may disappear after paracentesis of the abdomen. The impulse is, as a rule, feeble. The second sound over the aorta is rather less distinct than in health, and is correlated with the low arterial blood-pressure.

Fatty degeneration of the heart may account for sudden death in cases of cirrhosis.

The following is a good example of gradual cardiac failure occurring in the course of cirrhosis.

A man aged fifty-six who died under my care in St. George's Hospital had general oedema, slight jaundice, albuminuria, a low-tension pulse, and wandering delirium. He had in previous years had jaundice and haematemesis. His respirations were very rapid (56); he had signs of a small pleural effusion on the right side and haemoptysis. The necropsy shewed marked multilobular cirrhosis, kidneys free from old disease, right pleural effusion, collapse of lower lobe of right lung, but no pulmonary apoplexy or tubercle. The heart, 21 ounces, was dilated and hypertrophied, and shewed fatty degeneration in both ventricles. The valves were healthy.

The pulse-rate is usually slightly quickened; in the late stages when there is general toxaemia the pulse may be rapid and in coma there may

[1] Churchman. *Johns Hopkins Hosp. Bull.*, 1912, xxiii, 10.
[2] Naunyn. *Diabetes Mellitus*, 1900.
[3] Halász. *Wien. klin. Wchnschr.*, 1908, xxi, 44.
[4] Goodman. *Journ. Am. Med. Assoc.*, Chicago, 1909, liii, 2054.
[5] Cammidge. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Med. Sect.), 174.
[6] *Boston City Hosp. Rep.*, U.S.A., 1911, 27.
[7] Surmont. *Arch. gén. de méd.*, 1892, i, 162.
[8] Roger. *Presse méd.*, 1897, i, 293.

be tachycardia. The blood-pressure is rather low when the disease is active or producing symptoms and falls after paracentesis, but when it is latent or compensated for it may be normal. According to Gilbert and his pupils,[1] the low blood-pressure is a mechanical effect due to the increased portal engorgement. Herrick's[2] view that in portal cirrhosis there is a freer communication between the hepatic artery and the portal vein, which accounts for the increased pressure in the portal vein, would also to some extent explain the fall of arterial pressure. It would, however, appear highly probable that the low tension is a toxic effect. The low blood-pressure is associated with an increased rate of the pulse and with a small output of urine. Capillary pulsation with healthy aortic valves has been observed (Bouchard[3]); and pulsation of the veins of the forearm (Hitschmann[4]) has been recorded.

The Blood.—In early or latent cases when the general health is well maintained the blood is practically normal. When definite symptoms appear there is usually a secondary anaemia which becomes more marked as the disease progresses. In Emerson's[5] 32 cases the red blood-corpuscles varied from 3,100,000 to 5,000,000, with a mean of 4,500,000; the average haemoglobin percentage was 68. From repeated haemorrhages a grave secondary anaemia with normoblasts may be produced. Occasionally a grave anaemia develops in patients with cirrhosis without any manifest cause, such as haemorrhage.

In a case quoted by Cabot[6] the blood count was as low as 1,300,000 reds and 22 per cent of haemoglobin. Von Limbeck[7] refers to a case in which the red blood-corpuscles were reduced to 1,500,000.

A distinction should be drawn between (*a*) secondary and other forms of anaemia in patients with cirrhosis, and (*b*) cases of Banti's disease or chronic splenic anaemia in which a terminal cirrhosis develops.

Secondary anaemia may be modified by cyanosis which leads to an increase in the number of red cells, hence if cyanosis is due to ascites the blood count may be lowered by tapping; on the other hand, rapid ascitic exudation may by concentration increase the blood count; thus tapping, by favouring the recurrence of ascites, has been observed to be followed by a higher blood count. Hence a patient who is manifestly pale and anaemic may have a relatively high count. Leucocytosis does not occur except from some complication, such as haemorrhage or inflammation. The mean of 22 cases was 6623 (Hanot and Meunier[8]). In Calcutta Rogers[9] finds that leuco-

[1] Gilbert et Garnier, *Compt. rend. Soc. Biol.*, 1899, li, 59; Gilbert et Weil, *ibid*, 1899, li, 511; De Brynine, *Thèse de Paris*, 1900.
[2] Herrick, F. C. *Journ. Exper. Med.*, N.Y., 1907, ix, 93.
[3] Bouchard. *Rev. de méd.*, 1902, xxii, 837.
[4] Hitschmann. *Centralbl. f. inn. Med.*, 1904, xxv, 42.
[5] Emerson. *Clinical Diagnosis*, p. 586, 1906.
[6] Cabot. *Examination of the Blood*, p. 248, 1897.
[7] v. Limbeck. *Pathology of the Blood*, p. 318. Transl. New Sydenham Soc., 1901.
[8] Hanot et Meunier. *Compt. rend. Soc. Biol.*, Paris, 1895, xlvii, 49.
[9] Rogers. *Lancet*, Lond., 1912, ii, 355.

cytosis is common and that a high degree is a bad prognostic. The blood serum, as shewn by Garrod's test, may appear to contain uric acid. In advanced cases the alkalinity may be diminished from acidosis. Fiessinger[1] has found that the blood may contain anti-bodies which destroy hepatic cells. Their presence is not constant, but coincides with periods when the cirrhotic process (and the destruction of liver cells which initiates the formation of anti-bodies) is progressing. Welch[2] has noticed marked auto-agglutination of the red blood-corpuscles in some cases.

Respiration.—When there is abdominal distension from ascites or flatulence, the upward displacement of the diaphragm causes shallow and more rapid respirations. Apart from this there is nothing noticeable about respiration, as a rule. The respiration rate may be slowed from a toxaemic state of the nerve centres.

Temperature.—As a general rule, the temperature is not raised; fever is much less frequent in multilobular cirrhosis than in hypertrophic biliary cirrhosis, and should at once suggest the presence of some complication, such as tuberculosis, pleural effusion especially on the right side, malaria, infective endocarditis, or other infections. In 44 cases tabulated by Carrington[3] the temperature was irregular in 18.

Fever is usually associated with hepatic enlargement and sometimes with diarrhoea. It may, in fact, depend on gastro-enteritis, and may then simulate enteric fever or hepatic suppuration (*vide* case on p. 220). A case of cirrhosis with a tongue-shaped lobe and fever has been operated upon for cholecystitis (Henderson[4]).

Apart from manifest secondary infections a febrile temperature is more often seen early in the disease, when its progress is somewhat rapid. Fever is seen in the acute forms of multilobular cirrhosis, and therefore makes the prognosis worse. It may be difficult to decide whether fever in any given case is due to some undetected complication, such as tuberculosis, or to acute progressive changes in the liver.

In a man aged forty-one, whose chart is attached (Fig. 37), admitted for haematemesis, the temperature was almost constantly raised, and in a few weeks ascites developed. Mr. G. R. Turner performed the operation of fixing the omentum between the diaphragm and the liver, and the man greatly improved, and the temperature fell.[5] He died from cirrhosis in a uraemic state about two and a half years later.

Liver.—Clinically the liver is more often enlarged than diminished in size. Foxwell[6] considered that "in the large majority of cases of hepatic cirrhosis at all stages of the disease the liver is felt below the ribs." It has often been assumed that enlargement of a cirrhotic liver depends largely on fat, and that this is more likely to occur in beer

[1] Fiessinger. *Journ. de physiol. et path. gén.*, Paris, 1908, x, 671.
[2] Welch. *Brit. Med. Journ.*, 1902, ii, 1112.
[3] Carrington. *Guy's Hosp. Rep.*, 1883–4, xlii, 337.
[4] Henderson. *Practitioner*, Lond., 1907, lxxix, 686.
[5] *Vide* Rolleston and Turner. *Lancet*, 1899, ii, 1660.
[6] Foxwell, A. *The Enlarged Cirrhotic Liver*, p. 20, 1896.

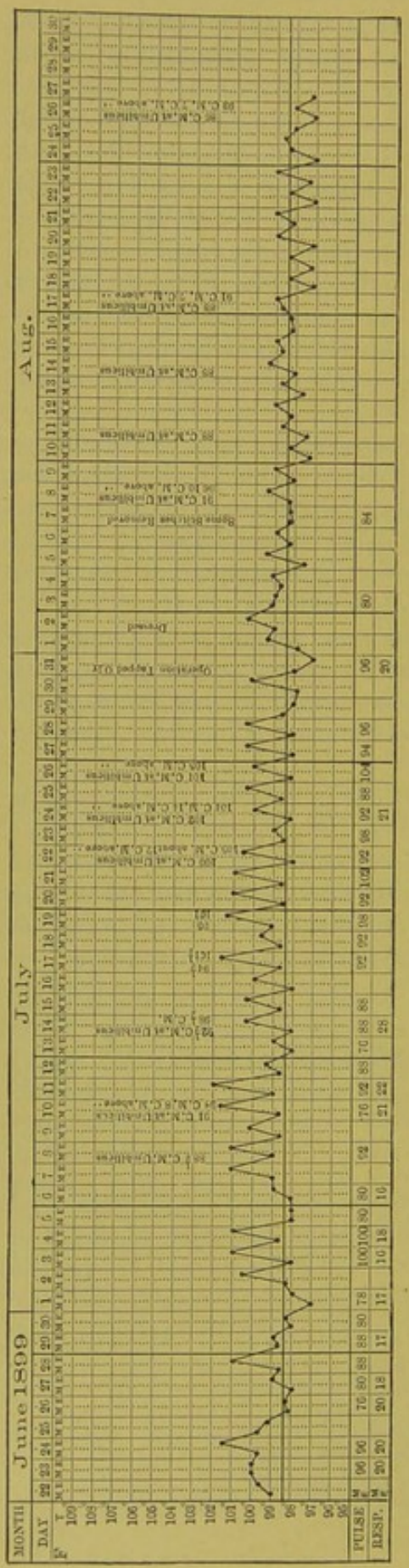


FIG. 37.—Temperature chart from a case of cirrhosis with fever. (*Vide* p. 237.)

drinkers than in spirit consumers. But Foxwell's and my own statistics do not bear out the suggestion that cirrhotic livers of beer drinkers are usually larger than those of spirit drinkers. Further, it is far from universally true that large cirrhotic livers are fatty (*vide* p. 196).

In a decided minority of cases, chiefly, I believe, in persons whose history shews no alcoholic excess, the liver is considerably smaller than natural. From ascites, flatulent distension, or from obesity it may be impossible to make out the enlargement. Tympanites often precedes and masks the onset of ascites and prevents an accurate estimation of the size of the liver. Before ascites has appeared the liver may usually be felt, sometimes several finger-breadths, beyond the costal margin in the right nipple line, its surface being firm, slightly irregular, and often tender. In other instances its rough and hard margin can be reached by pushing the fingers under the costal margin, while in other cases, although conditions are favourable, the liver cannot be felt on deep inspiration, and percussion may shew that there is definite diminution in the liver dulness. It should be remembered that percussion is subject to the fallacy that a resonant note may be obtained over the edge of the liver from distended bowel immediately behind. In rare cases the colon may pass in front of the liver and lead to great diminution in the apparent size of the organ. Palpation is therefore more reliable than percussion.

It has been widely assumed that the liver is enlarged in the early

stages of the disease and that subsequently it becomes smaller from shrinking and contraction of the fibrous tissue inside it. This sequence of events is sometimes noted (Taylor[1]); thus a considerable time before death the organ has been found to be large, and at the necropsy some months later it has receded behind the costal arch. This may be due to atrophy of areas of compensatory hyperplasia of the lower cells, and not solely to cicatricial contraction. Alterations in the size of the organ may be due to other factors; thus, in the early stage, the enlargement may vary within a comparatively short space of time, thus shewing that the increase in size is due to engorgement. Thus, in alcoholic subjects a drinking bout may lead to rapid increase in size of a cirrhotic liver, the organ feeling firm and being tender, while low diet, total abstinence, and judicious purgation are followed by a return to its former size. Dilatation of the heart due to alcoholic excess, or cardiac failure induced in other ways, may give rise to considerable increase in the size of a cirrhotic liver.

It has been noticed by many observers that the cirrhotic livers of people dying from accident and other causes unconnected with the disease are larger than those of patients dying from the disease.[2] This might be thought to support the view that the liver is enlarged in the early stage from proliferation of the interstitial connective tissue and that later it becomes smaller from cicatricial contraction. But it is more probable that these cases of cirrhosis were latent and that the large size of the livers depended on compensatory hyperplasia of the liver cells, than that the cases were in an early stage of progressive cirrhosis. The surface of the liver may be fairly smooth, especially when it is considerably enlarged, but in other cases its surface is irregular, and sometimes the knobby feel of the "hobnails" is perceptible. These hobnails are not depressed in the centre or umbilicated, but the depressed area of liver substance between two adjacent elevations may imitate the umbilications of multiple carcinomatous nodules.

Hepatic Pain.—Some discomfort and a sense of uneasiness in the region of the liver are very common. Pain is very seldom prominent, but it is present from time to time in a considerable number of the cases, and may be due to transient attacks of perihepatitis, as shewn by the frequency of adhesions between the liver and the diaphragm. Pain of a somewhat severe character over the liver may be due to right-sided pleurisy. Hepatic tenderness is by no means constant; it is often present over large cirrhotic livers after bouts of alcoholic excess, and may be an expression of passive engorgement from failing heart.

Venous Bruits.—In rare instances a venous hum accompanied by a thrill may be heard over the epigastrium; the hum is louder on inspiration. The murmur and thrill may diminish or disappear spon-

[1] Taylor, F. *Guy's Hosp. Rep.*, 1888, xlv, 310.

[2] Fagge, C. Hilton, *ibid.*, 1875, Ser. iii, xx, 155; Price, J. A. P., *ibid.*, 1883–84, Ser. iii, xxvii, 295.

taneously or as the result of tapping, and reappear when the ascites re-collects. There may or may not be enlarged veins visible in the epigastrium. The murmur may be best heard near the umbilicus, and is then thought to arise in a large vein in the falciform ligament. When the hum is loudest over the lower end of the sternum, above the lower margin of the liver, it is probably produced in a dilated coronary vein or in a dilated communication between the internal mammary vein and branches joining the portal vein (*vide* p. 211). The thin-walled and dilated veins may readily be kinked as the result of adhesions or temporarily distorted by the descent of the diaphragm or even by the pressure of a stethoscope. Martini [1] described a soft murmur over the hepatic region, especially in the right axilla, which he regarded to be due to constriction of the inferior vena cava where it passes behind the liver.

In a man aged forty-three who was under my care in St. George's Hospital there was a continuous bruit in the epigastrium resembling the *bruit de diable* in the neck. At the necropsy the liver was markedly cirrhotic and the falciform ligament contained a thin-walled vein as large as the little finger (*vide* Fig. 35).

It has also been thought to be due to pressure on the portal vein by enlarged glands, or even to narrowing of the inferior vena cava where it lies in contact with the posterior border of the liver (v. Gambarati [2]).

Spleen.—Enlargement of the spleen is an important feature in portal cirrhosis. It is almost constantly present in fatal cases of progressive cirrhosis, though not so markedly as in hypertrophic biliary cirrhosis. The amount of splenic enlargement has been regarded as an index of the severity of the cirrhosis, and enlargement in cases in which cirrhosis appears to be latent or compensated for should always be an indication for treatment and a cautious prognosis. Considerable enlargement may precede haematemesis, and may therefore be regarded as a danger-signal and call for free purgation. After haematemesis, melaena, or bleeding from piles the spleen may diminish in size. Gilbert and Lereboullet [3] mention cases in which the spleen diminished to one-half or even one-quarter of its previous size after copious haematemesis. In some cases of portal cirrhosis enlargement of the spleen is easily made out, and the organ can be felt to be firm and resistant. In other instances the splenic dulness is increased, though the organ cannot be felt, and in a number of cases the enlargement of the spleen is obscured by tympanites or ascites. Slight pain or discomfort is sometimes experienced in the splenic region, and, apart from the referred pain of flatulence, may be due to inflammation of the capsule, to tension and engorgement of the

[1] Martini. *Riforma med.*, Napoli, 1894, x, 663.
[2] Gambarati, v. *Ibid.*, 1903, xix, 153.
[3] Gilbert et Lereboullet. *Compt. rend. Soc. Biol.*, Paris, 1904, lvi, 370.

spleen, or to dragging on adhesions between the spleen and neighbouring parts.

Venous Bruits.—As in splenic enlargement from other causes, such as malaria and splenic anaemia, a venous bruit, like the well-known *bruit de diable* in the neck of chlorotic patients, is occasionally heard over the spleen in cirrhosis; according to Catti[1] in one-fifth or one-sixth of all cases of cirrhosis. It has also been compared to the uterine souffle. It may be continuous and increased during inspiration, or may only be heard during inspiration; there may be a palpable thrill. Its position varies, but is generally in the anterior axillary line. It may be due to temporary or prolonged kinking of the dilated splenic vein or of its branches in the hilum of the spleen. Thayer[2] has given a full account of venous murmurs in cirrhosis.

Oedema of the feet usually occurs after, but it may be quite independent of, the onset of ascites; it may even come on in the latest stages, when ascites has passed away and the patient is in a toxaemic state. On the other hand, oedema may begin in the feet before the appearance of ascites. The amount of oedema is usually small; sometimes it is very soft, probably from laxity of the skin and underlying tissues from wasting of the subcutaneous fat and of the muscles. Pre-ascitic oedema of the feet is generally considered to be rather unusual; Silvestri,[3] however, estimates that it occurs in 75 per cent of the cases.

Oedema of the feet is often referred to the ascites mechanically impeding the return of blood through the inferior vena cava. But this explanation will not fit all cases; for example, those in which oedema comes on before the advent of ascites, or when there is so little peritoneal effusion that there can be no increase in the intra-abdominal pressure. In such cases the toxic origin of oedema may be invoked.

It has been thought that the pressure of a firm cirrhotic liver on the inferior vena cava just before it passes through the diaphragm may be sufficient to cause oedema of the feet. This is conceivable, but if it is a factor of any importance, much more oedema of the legs than actually occurs would be expected in cases of malignant disease involving the liver, while a dilated venous plexus, like that seen in mechanical obstruction of the inferior vena cava, should also be present under the skin of the abdominal wall to provide for the return of blood from the lower limbs. Silvestri indeed believes that pre-ascitic oedema of the feet is due to increased pressure in the inferior vena cava brought about by this collateral circulation. As a matter of fact, dilatation of the epigastric and mammary veins may occur when there is ascites, but hardly ever when oedema of the feet is present in the absence of ascites.

[1] Catti. *Ztschr. f. klin. Med.*, 1907, lxi, 269.
[2] Thayer. *Am. Journ. Med. Sc.*, Phila., 1911, cxli, 313.
[3] Silvestri, T. *Riforma med.*, 1905, xxi, 1101.

In some cases of cirrhosis oedema of the feet may be the outcome of complications, such as the backward pressure of cardiac failure, alcoholism, or valvular disease. Again, it may be due to alcoholic neuritis; in the latter contingency there will be muscular tenderness and absence of the Achillis- and knee-jerks. It is probable that a slight degree of peripheral neuritis is more frequent in the course of cirrhosis than is generally recognised, and that it is specially likely to accompany an aggravation of the liver symptoms with abdominal pain, tympanites, and dyspepsia. When oedema of the feet is associated with considerable ascites, it may be brought about by the pressure of the fluid on the inferior vena cava and the lymphatic vessels going to the thoracic duct.

General oedema is very rare, but the dropsy of the legs and thighs may spread to the abdomen and appear as a lumbar cushion on the back.

McCall Anderson[1] recorded a case of recurrent attacks of universal dropsy in a boy aged eighteen who had no renal disease and whose liver (4 pounds) shewed changes compatible with the view that there was subacute cirrhosis.

ASCITES.—*Derivation.*—ἀσκός, the belly, ὁ ἀσκίτης ὕδρωψ, the abdominal dropsy.

The words "ascites" and "tympanites" have a masculine adjectival termination -ιτης, like the feminine adjectival termination -ιτις in neur*itis* and peritoni*tis*, which agrees with the feminine word νόσος, disease, understood. In the case of *-itis* an entirely secondary meaning, viz. "inflammation," has been evolved.[2]

Definition.—Free fluid in the peritoneal cavity.

Incidence.—Ascites, the association of which with hepatic disease was recognised by Erasistratus (304 B.C.), occurs in 50 per cent of all patients dying with cirrhotic livers. Since it is a late event in the course of the disease it naturally occurs far more frequently in cases fatal from the effects of cirrhosis than in patients who, having cirrhotic livers, die from independent disease, such as pneumonia, tuberculosis, or erysipelas. Ascites occurs in the vast majority of the cases of cirrhosis which run their full course, but a certain number of cases who die, so to speak, prematurely from the direct effects of cirrhosis, such as haematemesis or melaena, do not present ascites.

In Price's[3] 142 cases ascites occurred in 72. In 121 cases of cirrhosis taken from the post-mortem records of the Manchester Royal Infirmary, Kelynack[4] found ascites in 56 per cent. In 166 cases of cirrhosis examined after death at St. George's Hospital ascites was or had been present in 84, or 50·6 per cent. In 80 of these cases death was directly due to cirrhosis, and in 68 of them, or 85 per cent, ascites was present. In the 86 cases fatal from other factors, 16, or 18·6 per cent, had ascites.

[1] McCall Anderson. *Contributions to Clinical Medicine*, p. 345, 1898, Edin.
[2] Compare Buzzard, T. *Trans. Path. Soc.*, 1889, xl, 347.
[3] Price, J. A. P. *Guy's Hosp. Rep.*, 1883–4, 3. s., xxvii, 295.
[4] Kelynack, T. N. *Birmingham Med. Rev.*, 1897, xli, 86.

Relation between the Weight of the Liver and the Incidence of Ascites.—Ascites is much more often found in association with a comparatively small than with a large cirrhotic liver. This is due to two factors: (*a*) because in an early stage the liver may be larger than it is later in the disease, and (*b*) because when cirrhosis becomes latent from compensatory hyperplasia of the liver cells the organ is considerably increased in size.

Causes of Ascites.—The factors which give rise to the peritoneal effusion in cirrhosis require some discussion. It will be most convenient to refer to them in order and then briefly to summarise their claims.

(I) Mechanical factors: (*a*) Obstruction to the passage of portal blood through the liver. (*b*) Thrombosis of the radicles of the portal vein in the liver. (*c*) Thrombosis of the trunk of the portal vein.

(II) Toxaemia.

(III) Concomitant inflammation of the peritoneum and perihepatitis.

(IV) Associated cardiac failure.

(I) (*a*) *Obstruction to the passage of portal blood through the cirrhotic liver* is undoubtedly present, and appears from Herrick's [1] investigations to depend on the direct communication of arterial pressure to the portal vessels through dilated capillaries, and to the larger volume-flow of the hepatic artery in proportion to the portal flow, as compared to that in the normal liver. It leads to chronic engorgement of the portal vein area, as shewn by the development of a collateral circulation, dilatation, and thickening of the intima of the portal vein, and to some extent clinically also by haematemesis and melaena. The predominance of endothelial cells in the ascitic fluid of uncomplicated cirrhosis is in favour of the view that the ascites is mechanical (Gilbert and Villaret,[2] Ross [3]). But that increased pressure in the portal vein alone does not necessarily produce ascites is suggested by the absence of ascites in cirrhosis at a time when the venous pressure in the portal vein appears to be high, as shewn by haematemesis and melaena. Further, the extreme rapidity with which the effusion may be poured out—a pint a day in some instances—is hardly compatible with the view that it is solely due to increased venous pressure. If the peritoneal effusion was due to the fibrosis in the liver, it would come on gradually, *pari passu* with the morbid changes in the liver, whereas ascites often develops suddenly and rapidly.

Since the collateral circulation is a compensatory means of carrying on the circulation, great importance has been attached to it as preventing ascites. But ascites is often present in spite of considerable collateral circulation, and conversely both ascites and evidence of any portal anastomosis may be absent (Hanot [4]).

[1] Herrick, F. C. *Journ. Exper. Med.*, N.Y., 1907, ix, 93.
[2] Gilbert et Villaret. *Compt. rend. Soc. Biol.*, Paris, 1906, lix, 820.
[3] Ross. *Trans. Path. Soc.*, Lond., 1906, lvii, 435.
[4] Hanot. *Arch. gén. de méd.*, 1886, clxxvii, 603.

In Lévi's [1] case of cirrhosis with terminal delirium there were no ascites and no collateral circulation. It is remarkable that there was peritoneal tuberculosis in addition, which in itself is a sufficient cause of ascites.

For these reasons increased venous pressure due to hepatic obstruction, though very frequently associated with ascites, does not entirely account for the peritoneal effusion.

(*b*) It has been suggested that the additional factor required to bring about ascites is thrombosis or obliterating endophlebitis of the terminal branches of the portal vein, either in the liver or where the portal tributaries anastomose with the adjacent systemic veins. There is, however, at present little proof of this.

(*c*) Thrombosis of the portal vein may give rise to ascites, but it is so rare in cirrhosis that it has no claim to be considered among the important causes of ascites.

In 334 cases of cirrhosis examined after death portal thrombosis was present in 10, or 3·3 per cent (Langdon Brown [2]); and in Lissauer's [3] 711 cases in 6, or 0·8 per cent.

(II) *The Toxic Nature of Ascites.*—As a result of hepatic inadequacy poisons absorbed from the alimentary canal or possibly produced elsewhere are no longer stopped and destroyed by the liver, but pass into the general circulation, and a condition of hepatic toxaemia, analogous to that of renal toxaemia, results; the patients become drowsy and may have numerous haemorrhages in various parts of the body. The poisons may either damage the vessels so as to allow increased transudation, or exert a lymphagogue action. It is significant that oedema of the feet may occur before the onset of ascites, inasmuch as this shews that the oedema of the feet is not necessarily a mechanical effect due to the pressure of ascitic fluid on the inferior vena cava. The absence of ascites in biliary cirrhosis, in which there is some reason to believe that the blood is toxic, viz. the considerable splenic enlargement, is perhaps due to the liver cells remaining in a better state of nutrition than in portal cirrhosis, and possibly to the poisons, if present, not being of the same nature as in ordinary cirrhosis.

(III) *Ascites due to Concomitant Inflammation of the Peritoneum.*—In many cases of cirrhosis there is in addition chronic peritonitis, which accounts for the ascites, and especially for ascites which continues for a considerable time or recurs again and again after tapping. Bright, indeed, considered the ascites of cirrhosis to be the result of portal obstruction and of an extension of chronic inflammation from the liver along the portal vein and its branches to the peritoneum. This in a modified form is the opinion held by many authorities, and there is no doubt that ascites is very often satisfactorily explained on this hypothesis. But chronic peritonitis does not account for the onset of ascites in all

[1] Lévi. *Arch. gén. de méd.*, 1886, clxxvii, 221.
[2] Brown, Langdon. *St. Barth. Hosp. Rep.*, 1901, xxxvii, 62.
[3] Lissauer. *Virchows Arch.*, 1908, cxcii, 278.

cases of ordinary cirrhosis, for it is often absent when there is marked ascites. In some cases ascites passes away when the patient is in a semi-comatose condition; now, since chronic peritonitis would give rise to persistent ascites, such cases may be expected to be free from chronic peritoneal inflammation.

The possibility that ascites is due to a low form of microbic infection will require consideration when more is known about the bacteriology of hepatic cirrhosis. This suggestion is attractive from the fact that bacterial infections may occur in other parts of the body in the later stages of cirrhosis. From analogy it appears probable that the peritoneum would suffer similarly, since infection from the intestinal tract, which is often in a condition of chronic catarrh, might easily occur. Again, ascites may supervene after infective processes have occurred elsewhere in the body, thus suggesting that the ascites is in some way secondary.

Although as seen in laparotomies on cases with ascites the peritoneum is highly injected, there is no inflammation or acute peritonitis. So if there be a microbic origin for ascites, the micro-organisms are of a low degree of virulence. Tuberculosis of the pleura and peritoneum may give rise to almost pure serous effusions; and in these cases the fluid withdrawn may appear to be almost, if not quite, free from bacilli until inoculated into guinea-pigs. Possibly the same may hold for ascites of cirrhosis, viz. that it is due to a micro-organism which does not appear in the fluid withdrawn by paracentesis.

Ascites due to Concomitant Perihepatitis.—Some thickening of the capsule of the liver is frequent in cirrhosis, and in some instances satisfactorily explains ascites. But it is not a constant cause, for ascites may occur when there is little or no perihepatitis, and it may be absent when there is as much perihepatitis as there is in cases in which the peritoneal effusion is thus explained. Parkes Weber[1] suggested that effusion resulting from localised areas of inflammation may possess sufficiently irritating properties to lead to a copious exudation of normal or nearly normal fluid from the non-inflamed surfaces. On this view quite local perihepatitis might account for ascites. Against this view is the occurrence of foci of perihepatitis in the absence of ascites, both in cirrhosis and in other conditions. Weber[2] has also suggested that transient ascites in cirrhosis may be due to local peritonitis which is temporary.

(IV) *Ascites from Cardiac Failure.* — In cases of latent cirrhosis dilatation of the heart from valvular disease, from affections of the myocardium, whether chronic or acute, or from obstructive lung disease may develop and give rise to ascites. The cirrhosis and ascites are therefore associated, but the ascites is not necessarily dependent on the cirrhosis. On the other hand, backward pressure very probably favours the onset of ascites in patients with cirrhosis; in other words, an amount of backward pressure which in an ordinary case would not produce ascites may be the cause of ascites in a patient with progressive

[1] Weber, F. P. *Brain*, 1902, xxv, 150.
[2] *Idem*. *Edin. Med. Journ.*, 1903, N.S., xiii, p. 322.

cirrhosis. Heart disease may therefore induce ascites in cirrhosis in two ways: (i) Merely by backward pressure, as in some cases of tricuspid regurgitation; (ii) by bringing about conditions, such as venous engorgement, the stagnation of toxins, or damage to the endothelial cells of the peritoneum, which precipitate ascites due to cirrhosis.[1]

In conclusion, ascites may be merely associated with cirrhosis and directly due to chronic or possibly to subacute peritonitis and perihepatitis, or to cardiac failure; in rare cases it may be due to a direct complication of cirrhosis, *i.e.* thrombosis of the portal vein, or, on the other hand, it may be due to cirrhosis alone. In the latter case it may be explained as being partly due to portal obstruction which provides the vascular conditions favourable to transudation, and partly to the presence of toxins in the blood which damage the vessel walls or act as lymphagogues and so induce an exaggerated flow of fluid into the peritoneal cavity. It is probable that this form of ascites may be brought about prematurely by cardiac failure.

The **onset of ascites** may follow so soon after some event, such as a blow, fall, or exposure to cold, that there would appear to be a definite connexion between them. It is possible that by a blow the resistance of the peritoneum may be so reduced that the real responsible cause of ascites is enabled to produce its effect sooner than it otherwise would.

In a boy aged twelve years a radical cure for hernia was rapidly followed by ascites; this was tapped eight times; at the necropsy the liver (27 ounces) was extremely cirrhotic; there was no chronic peritonitis, but there were some adhesions from a past attack of acute peritonitis.

As the result of a chill, vasomotor paralysis of the splanchnic vessels results, and might thus precipitate ascites, so to speak. These cases have been spoken of as acute ascites.[2] It must be remembered that what appears to be acute ascites may prove to be acute peritonitis. Ascites may come on after various infections, such as suppuration, erysipelas, influenza, or typhoid.

Though it may be sudden, the onset of ascites is usually gradual, and is often masked by flatulent distension of the abdomen. It thus contrasts with the sudden and rapid development of ascites in thrombosis of the trunk of the portal vein. Ascites occurs late in the course of uncomplicated cirrhosis, that is, in cases in which there is no concomitant chronic peritonitis. The onset of ascites in such cases is a grave event, as the patient seldom survives long enough to require tapping more than two or three times; Hale White says the patients do not live long enough to require more than one tapping, but in my experience this view is too extreme.

Characters of Ascitic Fluid.—The ascitic fluid is clear, greenish or

[1] Compare Cheadle, W. B. *Some Cirrhoses of the Liver*, p. 103, Lond., 1900.

[2] B. Weil (Acute Ascites), *Thèse de Paris*, 1899, No. 278; Potain, 'Ascites a frigore," *Sem. méd.*, 1888, viii, 9.

yellow in tint, and sometimes slightly bile-stained. Its reaction is alkaline and its specific gravity between 1008 and 1015. It contains more albumin than ascitic fluid of renal disease and less than that of cardiac ascites (Dickinson[1]). If there is any added peritonitis, its specific gravity and the proportion of albuminous matter increase and flakes of coagulated fibrin may form on standing. It contains from 0·5 to 4·4 per cent of albuminous material and occasionally a trace of sugar, urea, urobilin. The large amount of chlorides in ascitic fluid is associated with the diminished output in the urine. If the specific gravity is above 1015, contains more albumin, and microscopically shews polymorphonuclear leucocytes, there is some inflammatory change in the peritoneum.

Character of the Cells in the Ascitic Fluid.—In uncomplicated cirrhosis the endothelial cells are present in predominating numbers (Cade,[2] Ross,[3] Gilbert and Villaret[4]) and may constitute 95 per cent of the cells. As the result of several punctures the percentage of endothelial cells may fall owing to infection (Gilbert and Villaret). In cases with an equal percentage of endothelial cells and lymphocytes tuberculous infection should be suspected. A predominance of lymphocytes points to tuberculous peritonitis. Grenet and Vitry[5] found endothelial cells and a few lymphocytes. Souques,[6] and Achard and Laubry,[7] in two cases of lactescent ascites in cirrhosis, found lymphocytes chiefly represented.

Chylous ascites due to an admixture of chyle may occur in cirrhosis.

Wallis and Schölberg[8] collected 13 cases in which cirrhosis was associated with chylous ascites; in Merklen's[9] case chylous ascites followed a fall, and thus suggests laceration of lymphatic vessels, though this was not made out at the necropsy. In Nichols'[10] case the receptaculum chyli was thrombosed.

Resembling true chylous ascites in appearance, but differing from it chemically, are the two following forms: (*a*) the chyliform or fatty, and (*b*) the milky non-fatty ascites.

In chyliform or fatty (adipose) ascites the fat, which is present in larger globules than in the chylous ascites, is probably the outcome of degenerative changes in cells suspended in the ascitic fluid. In cases of fatty ascites in cirrhosis, Souques and Achard and Laubry found both fat and a nucleo-albumin; the latter gave rise to an opalescent solution. Fatty ascites would thus differ from the next form only in the presence of fat, since in both there may be a nucleo-albumin capable of rendering ascitic

[1] Dickinson, W. H. Allbutt's *System of Med.*, 1898, v, 668.
[2] Cade. *Arch. de méd. expér. et d'anat. path.*, Paris, 1906, xviii, 769.
[3] Ross, E. A. *Trans. Path. Soc.*, Lond., 1906, lvii, 435.
[4] Gilbert et Villaret. *Compt. rend. Soc. Biol.*, Paris, 1906, lix, 820.
[5] Grenet et Vitry. *Sem. méd.*, 1903, xxiii, 235.
[6] Souques. *Bull. Soc. méd. d. hôp. de Paris*, 1902, 3. s. xix, 290.
[7] Achard et Laubry. *Ibid.*, 295.
[8] Wallis and Schölberg. *Quart. Journ. Med.*, Oxford, 1910–11, iv, 170.
[9] Merklen. *Sem. méd.*, 1897, xvii, 181.
[10] Nichols, H. J. *Med. News*, N.Y., 1905, lxxxvii, 925.

fluid milky. Fatty ascites has been thought to be due to lipaemia, and in a case of cirrhosis the fibrotic changes in the pancreas were suggested as the underlying factor (Gaultier[1]).

In opalescent, milky (non-fatty) ascites, of which Jousset[2] has collected 14 cases in portal cirrhosis, there are a large number of mononuclear leucocytes which probably give rise, as the outcome of degeneration, to some body, such as nucleo-albumin or globulin, which is responsible for the lactescent appearance of the fluid. It has, however, been suggested that lecithin may cause the milky character. No fat can be extracted by ether from the ascitic fluid in this form. In both the fatty and the non-fatty forms of milky ascites the change may appear on the second tapping, in cases in which the fluid withdrawn on the first occasion was clear.

Haemorrhagic ascites is very rare in cirrhosis. It is not due to hepatic insufficiency, like the oozing from the gums and epistaxis. Neither is it usually due to concomitant tuberculosis of the peritoneum. It may be the result of previous tapping; thus, in cases in which the fluid is serous at the first paracentesis and sanguineous at subsequent tappings, it is probable that the trocar wounded some of the vascular adhesions or dilated veins in the peritoneum (Barjon and Henry[3]). In some instances of cirrhosis chronic haemorrhagic peritonitis occurs and possibly may be due to, at any rate is associated with, alcoholism (Fernet[4]). Acute infection, for example with streptococci, as in a case recorded by Bauer,[5] may render haemorrhagic the ascites of chronic peritonitis associated with cirrhosis.

Bacteriology of Ascitic Fluid.—More observations are required as to the bacteria present in the ascites of cirrhosis, and very probably may be obtained by the method of inoscopy. It consists in taking the coagulum of the fluid; or, if there is no spontaneous one, producing one, dissolving it with aseptic gastric juice, and examining for micro-organisms; this method depends on the fact that the clot filters off the micro-organisms from the fluid. By this method Jousset[6] found tubercle bacilli in many cases thought to be cirrhosis, which is quite in accord with the comparative frequency of tuberculous peritonitis in cirrhosis.

M. Abbott[7] found a colon bacillus, of the same type as Adami's minute diplococcus, in the ascitic fluid of three cases of cirrhosis. In one instance, in which there was chronic peritonitis as well as hepatic cirrhosis, this micro-organism was isolated from three tappings during life.

Tension of Ascitic Fluid.—There may be a positive pressure inside the abdomen in ascites, as shewn by the upward displacement of the diaphragm.

[1] Gaultier. *Compt. rend. Soc. Biol.*, Paris, 1906, lix, 429.
[2] Jousset. Quoted by Souques.
[3] Barjon et Henry. *Lyon méd.*, 1898, lxxxviii, 258.
[4] Fernet. *Bull. Soc. méd. d. hôp. de Paris*, 1900, 3. s., xvii, 781.
[5] Bauer. *Arch. gén. de méd.*, 1905, cxcv, 1351.
[6] Jousset. *Arch. de méd. expér. et d'anat. path.*, 1903, xv, 289.
[7] Abbott, Maude. *Journ. Path. and Bacteriol.*, 1900, vi, 315.

Pitres[1] found that it may vary between 30 and 6 millimetres of mercury, the average positive pressure being about 12 millimetres.

This positive intra-abdominal pressure varies with respiration and is associated with increased pressure in the portal vein and low arterial pressure (Gilbert and Weil[2]).

Physical Signs.—The abdomen is greatly enlarged; its girth may be 50 inches or even more. The enlargement, which is fairly uniform, is more marked antero-posteriorly at first; when it has lasted for some time there is bulging in the flanks. The parietes are stretched and the skin often shews the effects of distension in lineae albicantes, which are especially visible after paracentesis. The abdominal muscles become lax and atrophied and the umbilicus may be everted and project like a tense thin-walled bladder; it may ulcerate, and has been known to burst. In a man under my care who had been tapped several times the thin-walled bulla at the umbilicus became the site of a Littré's hernia. The veins over the umbilicus are sometimes very prominent. The loss of tone in the abdominal parietes favours flatulent distension, especially after the intra-abdominal pressure has been reduced by paracentesis. The costal margins are pushed forwards and the ensiform cartilage may be carried upwards and forwards. The subcutaneous veins of the abdominal walls become prominent and enlarged. There are two sets of veins: (*a*) Those around and above the umbilicus, which form part of the compensatory anastomosis between the veins of the abdominal wall and the parumbilical veins in the falciform ligament. A dilated and varicose condition of the veins around the umbilicus has been called cirsomphalos. (*b*) The veins running up from the middle of the groin (the superficial and deep epigastric veins) towards the middle of the costal arch (superior epigastric and long thoracic veins). Dilatation of these veins points to obstruction to the passage of blood through the inferior vena cava. A large ascitic effusion may, by increasing the intra-abdominal pressure, seriously interfere with the return of blood from the lower extremities, and so lead to opening up of this anastomotic channel. Hence in considerable ascites both these sets of veins are manifestly enlarged; removal of the ascitic fluid is followed by disappearance of the "caval," while the "portal" veins remain (Gilbert and Villaret[3]).

The ascitic fluid presses the diaphragm up and diminishes the capacity of the thorax. The heart may thus be so displaced upwards that the apex beat is in the third interspace. This displacement may be associated with a systolic murmur over the pulmonary artery, due to twisting or kinking of its trunk. When the displacement is corrected by tapping this murmur disappears.

The liver dulness is displaced upwards, and anteriorly may reach to the fourth, third, or even second rib, while posteriorly the resonance over

[1] Pitres. *Compt. rend. Soc. Biol.*, Paris, 1899, li, 674.
[2] Gilbert et Weil. *Ibid.*, 1899, li, 511.
[3] Gilbert et Villaret. *Rev. de méd.*, Paris, 1907, xxvii, 334.

the bases of both lungs is also encroached upon. If there is dulness over the lower lobe of the right lung alone, the question arises whether this is due solely to upward displacement of the liver and collapse of the lung or whether there is, as often occurs (*vide* p. 285), an effusion into the right pleural cavity. When the patient takes a deep breath, the dulness is unaltered if there is an effusion, but will diminish somewhat if due solely to the liver; in pleural effusion the dulness is higher in the axilla, while the dulness due to the liver is more marked behind; when the patient lies on his face dulness due to the liver diminishes or disappears.

In women, the uterus is pressed forwards by the fluid in Douglas' pouch, and depressed, and may thus become prolapsed.

The fluid collects in the flanks, which are dull on percussion. In order to distinguish ascites from faecal distension of the colon the patient should be turned over, when the note will become resonant; this shifting dulness is proof of free fluid in the peritoneal cavity. It should be pointed out that in a certain proportion of cases of ascites there is resonance in one or both flanks, due to gaseous distension of the colon. The absence of dulness in the flanks, therefore, must not be taken as absolute proof against ascites and in favour of an ovarian cyst. After collecting in the flanks the fluid rises out of the pelvis and gives rise to a dull note on percussion. This dull area gradually increases in extent and approaches the umbilicus. The stomach and intestines are floated upwards against the abdominal parietes in the middle line between the umbilicus and the ensiform cartilage. The area of resonance eventually roughly corresponds with that of the epigastric region. Chronic peritonitis may be combined with cirrhosis, and if well marked may lead to such retraction of the mesentery that the intestines, being more or less tethered to the spine, are unable to reach the anterior abdominal wall; in such cases there may be complete absence of resonance over the front of the abdomen.

In definite ascites a thrill is readily produced by flipping the abdominal wall in one flank with the finger; a distinct impulse is then felt by the other hand laid flat on the opposite side. In order to prevent the impulse from being transmitted through the abdominal walls, an assistant should place his hand or a piece of cardboard on the linea alba in the long axis of the body. When the abdominal wall is laden with fat or swollen from subcutaneous oedema, the precaution is especially necessary. In the presence of old peritoneal adhesions, the ascitic effusion will very probably become encysted. The physical signs may then resemble those of a fixed cyst, and are very difficult to interpret correctly. Encysted ascites is, however, rare in connexion with hepatic cirrhosis.

When there is free fluid in the peritoneal cavity, it is found under certain conditions that if the hand is placed flat over the liver and a sudden sharp flexion of the fingers made, a sensation of displacement of fluid is produced and the finger-tips come in contact with the firm liver. This sign—"dipping for the liver"—cannot always be obtained. It depends on the presence of fluid between the liver and the abdominal wall. Hence adhesions between the liver and the parietes, or the fact

that the liver is in immediate contact with the abdominal wall, prevent this manifestation of ascites.

Symptoms and Effects of Ascites.—There is a feeling of tightness and discomfort in the tense and stretched abdominal walls. The upward displacement of the diaphragm causes collapse of the lower lobes of the lungs, and so dyspnoea, and even orthopnoea. There is often some bronchitis, and in rare instances haemoptysis may result from the engorged and collapsed lung. When, with increasing ascites, signs of oedema of the lower lobes of the lungs appear, the abdomen should be tapped without delay.

The upward displacement of the heart may be accompanied by irregularity, palpitation, or faintness. The pressure of ascites on the kidneys and their vessels may help to curtail the excretion of urine and possibly to produce albuminuria, but the diminished amount of urine is chiefly due to the low arterial pressure. Oedema of the legs may be accelerated by the pressure of the peritoneal effusion on the inferior vena cava, but it is not solely due to this mechanical cause, inasmuch as oedema of the feet may precede the appearance of ascites, or indeed occur independently. As is pointed out elsewhere, toxaemia plays an important part in the production of oedema of the feet (*vide* p. 241).

If ascites becomes excessive, the umbilicus, which has become everted and thin, may burst; this spontaneous discharge has also been known to take place through the cicatrix of an umbilical hernia (Merklen and Gougelet [1]). Such an event should never be allowed to occur; not only is the extreme distension very harmful, but the rupture of the abdominal wall may introduce infection, and so set up fatal peritonitis. Most of the recorded cases occurred years ago, when paracentesis was postponed as long as possible.

Differentiation of Ascites from other Abdominal Conditions.—A large, thin-walled *ovarian or parovarian cyst*, if so large as to fill a great part of the abdomen, may cause great difficulties in diagnosis. In the case of an ovarian cyst the history may shew that the swelling definitely began in one situation, that it arose out of the pelvis and then spread upwards. The outline of the cyst may be felt, especially on deep inspiration. In a doubtful case a vaginal examination may reveal a cyst with pelvic attachments. The abdomen is prominent in an antero-posterior direction, while in simple ascites the bulging is also in a lateral direction.

The dulness is in or near the middle line of the abdomen and not in the flanks; but, as already pointed out, resonance in the loin may persist in ascites. The maximum abdominal girth is below the umbilicus, while in ascites it is at or above this level. In ascites the umbilicus is in its normal position, viz. one inch nearer to the pubes than to the ensiform cartilage, while with an ovarian cyst this relation may be greatly altered in the opposite direction. When an ovarian cyst is on either side of the middle line, it may displace the umbilicus, so that it is nearer one anterior

[1] Merklen et Gougelet. *Bull. Soc. méd. d. hôp. de Paris*, 1901, 3. s., xviii, 952.

superior spine than the other. This displacement may only be revealed by careful measurement, and not be manifest on mere inspection. In ovarian cysts the thrill may be absent, and when present is less marked than in ascites. There is little constitutional disturbance in ovarian cysts, the ill effects being almost entirely due to mechanical pressure. When an ovarian cyst is complicated by ascites, the diagnosis is extremely difficult. Rupture of the cyst with extravasation of its contents into the peritoneal cavity may occur spontaneously in thin-walled cystadenomas and parovarian cysts, or from trauma. If the fluid is non-irritating, it is absorbed, with the result that polyuria follows; but if irritating, peritonitis is set up.

Solid or Semi-solid Abdominal Tumours simulating Ascites.—Fatty, fibro-fatty, and myxo-lipomatous tumours, though comparatively rare, may, when they grow to a considerable size—and some of them have weighed as much as 40 pounds—very closely imitate ascites. In fact, many of the recorded examples have been tapped fruitlessly, and several of them more than once. Of the fatty tumours, of which Proust and Trèves [1] collected 89 examples, about one-third arise from the fat around the kidneys, the remainder take origin from the retroperitoneal and other tissues. The tumours, whether originally fatty or fibrous, are prone to become oedematous and undergo myxomatous degeneration and so readily fluctuate.

Diffuse colloid carcinoma or endothelioma of the peritoneum is very rare; it may give rise to great enlargement of the abdomen and to dulness on percussion, but fluctuation and thrill are not present unless there is concomitant ascites. In some cases there is no difficulty in feeling definite tumours, and then there is no resemblance to ascites. In Pye-Smith's [2] case of colloid carcinoma involving the peritoneum tapping was performed thirty-six times.

Encysted peritonitis and the localised tuberculous peritonitis in the lower and front portions of the abdomen [3] (Tait's "allantoic cysts") differ in the extent of the peritoneal cavity involved and in the fact that the dulness due to the effused fluid does not alter with changes in the position of the patient.

Hydatid Cysts.—Murchison described an enormous cyst starting from the liver and passing through the foramen of Winslow into the general peritoneal cavity, which it almost filled. In its fully developed or latest stage it resembled ascites, but the history shewed that the abdominal swelling was at first localised to the right side.

Various abdominal cysts, such as pancreatic, omental, chylous, urachal, mesenteric cysts, are seldom, if ever, so large as to resemble ascites. A large pyonephrosis or hydronephrosis is so unilateral that it should not be mistaken for ascites. In very exceptional instances a dilated stomach, a dilated gall-bladder, and a very large hepatic abscess (Powell,[4] Hatch [5]) have been diagnosed as ascites.

[1] Proust et Trèves. *Rev. de gyn. et de chir. abdom.*, 1908, xii, 93.
[2] Pye-Smith. *Trans. Path. Soc.*, 1893, xliv, 116.
[3] Doran, A. *Med.-Chir. Trans.*, Lond., 1898, lxxxi, 320.
[4] Powell. *Ind. Med. Gaz.*, 1898, xxxiii, 41.
[5] Hatch. *Ibid.*, 1898, xxxiii, 205.

From a Pregnant Uterus with Hydramnios.—The outline of the enlarged uterus may be made out by palpation through the abdominal walls. Other signs of pregnancy, such as mammary enlargement and engorgement, a soft and patulous os uteri, should be looked for.

Obesity.—When the abdominal walls are laden with fat, the detection of a small amount of ascitic fluid is difficult and often impossible. On the other hand, a feeling of semi-fluctuation may be obtained through the pendulous fatty walls and suggest ascites. To control this the hand of an assistant should be placed with the ulnar side downwards on the abdominal wall between the two hands of the observer. Inspection alone should assist in the diagnosis. When there is much fat in the abdominal parietes, the umbilicus is buried, whereas in ascites it tends to be everted.

Diagnosis of Ascites due to Cirrhosis from that due to other Causes.—Under the following heads attention will chiefly be paid to the main points that are in favour of the various conditions which may imitate cirrhosis by inducing ascites.

Acute peritonitis can hardly be confounded with the ascites due to cirrhosis, for the onset is sudden, the constitutional symptoms are prominent, and the abdominal distension is due to paralytic dilatation of the intestines with gas rather than to the quantity of fluid. It should be mentioned, however, that ascites may sometimes come on rapidly in cirrhosis, especially when complicated by portal thrombosis. Unlikely as it would appear, the sudden onset of ascites in a case of alcoholic cirrhosis with subacute gastritis has simulated intestinal obstruction.

The ascites due to the various forms of *chronic peritonitis* is extremely likely to be mistaken for that of cirrhosis. Chronic peritonitis and universal perihepatitis (*vide* p. 161) frequently cause ascites, usually in association either with adherent pericardium or with arteriosclerosis and granular kidney. In a doubtful case albuminuria is therefore against the existence of cirrhosis as the primary cause. In chronic peritonitis the ascites recurs again and again after tapping; cases are on record in which the abdomen has been tapped fifty or even a hundred times. This is the most reliable criterion in distinguishing chronic peritonitis from cirrhosis. Enlargement of the spleen, which is comparatively frequent in cirrhosis, is not a prominent feature in chronic peritonitis, unless there is some complication, such as lardaceous disease. Haematemesis hardly ever occurs in chronic peritonitis; hence the association of haematemesis and ascites points to cirrhosis. In cases in which haematemesis is associated with frequently recurring ascites chronic peritonitis is probably complicated by some other condition, such as gastric ulcer or cirrhosis.

Tuberculous peritonitis may supervene in the course of cirrhosis, and is then very likely to be regarded as simple ascites. In 584 cases of common cirrhosis peritoneal tuberculosis was present in 53, or 9 per cent (*vide* p. 223). The primary lesion here is cirrhosis, which disposes the

peritoneum to tuberculous infection. In these cases the liver is markedly cirrhosed, while the peritonitis is of more recent date. Although in tuberculous peritonitis a slight secondary hepatic fibrosis is sometimes seen, it is microscopic rather than macroscopic.

The mistake that has often occurred is to do laparotomy on a child with cirrhosis and ascites in the belief that it is tuberculous peritonitis. If such a thing occurs, it would be advisable to take the opportunity of uniting the liver and great omentum to the abdominal wall so as to lead to vascular adhesions (*vide* p. 260).

Tuberculous peritonitis in adults, except when secondary to cirrhosis, is most commonly seen in women, and often spreads from the uterine appendages. The following points are in favour of tuberculous peritonitis: evidence of tuberculosis elsewhere; abdominal pain and tenderness, especially in the lower part of the abdomen and about the right iliac fossa; pain on micturition; fever; enlarged glands in the abdomen or groin; a moderate degree of effusion; a hard cord due to the rolled-up omentum; induration, redness of the skin, and evidence of a small abscess around the umbilicus. When drawn off, the fluid is more turbid, of a higher specific gravity (1020 instead of 1010), and richer in albumin than in cirrhosis. A preponderance of lymphocytes points to tuberculosis; the presence of numerous lymphocytes and of some endothelial cells is in favour of the association of cirrhosis and tuberculous peritonitis. Ordinary examination for tubercle bacilli is often negative, but injection into guinea-pigs gives rise to tuberculosis. The method of inoscopy,[1] or bacteriological examination of the clot formed in the fluid, may give positive results when ordinary methods fail (*vide* p. 248).

In ascites due to multiple nodules of malignant disease in the peritoneum a primary source may be manifest in the stomach (symptoms of dyspepsia, pyloric obstruction, absence of HCl in vomit), in the rectum, and in women in the pelvic organs. The umbilicus may be hard and infiltrated with growth, and sometimes small subcutaneous tumours can be felt in the line of the falciform ligament or elsewhere in the abdomen. Small masses of fat, however, may very closely imitate these minute secondary growths. In malignant disease there is more emaciation and pigmentation of the face is more frequent than in cirrhosis. The spleen is not enlarged and there is no history of haematemesis. Sometimes the glands in the groin are enlarged, and occasionally multiple subcutaneous tumours are present.

In *malignant disease of the liver* the presence of deep jaundice together with ascites, the enlargement and irregularity of the liver, the progressive hepatic enlargement and more rapid emaciation, help to differentiate it from ascites due to cirrhosis. Other points in favour of malignant disease are evidence of growth elsewhere, induration of the umbilicus, and absence of splenic enlargement. In cases with ascites it is often impossible to distinguish between cirrhosis and malignant disease of the liver until the abdomen has been tapped. A large nodular liver points to new-growth.

[1] Jousset. *Arch. de méd. expér. et d'anat. path.*, 1903, xv, 289.

Syphilitic disease of the liver may cause ascites. The presence of syphilitic lesions elsewhere and a positive Wassermann reaction call for antisyphilitic treatment, which may clear up the diagnosis. When enlarged from gummatous or lardaceous change, or from both combined, the liver is firm and may be irregular, and may be mistaken for malignant disease.

Lardaceous disease of the liver does not often give rise to ascites in adults. The following case of lardaceous liver closely imitated cirrhosis:

A woman aged forty-seven under my care in St. George's Hospital, June-July 1900, had the facial aspect of cirrhosis; there were signs of chronic pulmonary tuberculosis at both apices, oedema of the feet which preceded by two weeks the onset of ascites, and albuminuria. There was a history of haematemesis which in the light of the necropsy was probably haemoptysis. The ascites required tapping twice; the liver and spleen could not be felt. The patient was thought to have cirrhosis. The patient died semi-comatose. The necropsy shewed lardaceous liver (53 ounces) and kidneys, due to chronic pulmonary tuberculosis, with three or four vomicae in both upper lobes. There were slight thickening of the capsule of the liver and opacity of the peritoneum, but not enough chronic peritonitis to account for the ascites. There was no cirrhosis of the liver.

The history of past suppuration or of syphilis, evidence pointing to lardaceous disease of the kidneys (albuminuria) or of the intestines (diarrhoea), are important points in making a diagnosis.

Thrombosis of the portal vein is rare, but when it does occur is probably associated most often with portal cirrhosis of the liver (*vide* p. 56). When the trunk of the portal vein is affected, ascites, if not already present, rapidly develops. The spleen enlarges from obstruction of the splenic vein, and haematemesis may occur. The severity of the symptoms and their onset in a person whose past history shews neither cause for nor evidence of cirrhosis would be in favour of primary thrombosis of the portal vein. But it will always be difficult to be sure that the case is not one of latent cirrhosis. The difficulty of a correct diagnosis in some cases of portal thrombosis supervening in the course of cirrhosis is illustrated in the following case:

A man aged fifty-six, in a state of great weakness and considerable emaciation, was admitted under me at St. George's Hospital complaining of "dropsy, stoppage of the bowels, and difficulty in passing water." He had noticed oedema of the feet five weeks before; this was followed by constipation and difficulty in passing water. He had been quite a moderate consumer of beer, and denied syphilis. He was found to have marked ascites; nothing else abnormal could be felt in the abdomen, and he was thought to be probably the subject of malignant abdominal disease. He died thirty-six hours after admission. At the necropsy there were chronic peritonitis, marked portal cirrhosis, and thrombosis of the portal vein; the liver weighed 4 pounds and the spleen 4 ounces.

Ascites from ovarian papilloma may recur very frequently, and thus differs from the ascites of uncomplicated cirrhosis. The diagnosis can

be clinched by vaginal or rectal examination and the detection of irregular masses of growth choking up the pelvis, or by the recognition of pieces of the characteristic villous growth in fluid withdrawn from the abdomen.

Pye-Smith [1] recorded a remarkable case of papillomatous tumours of both ovaries which gave rise to ascites in a woman aged thirty-five, lasting nine years and necessitating 299 tappings. At the necropsy there were numerous implantation growths over the parietal peritoneum.

Ascites due to backward pressure of tricuspid regurgitation, etc., should be recognised by examination of the heart and the recognition of mitral or obstructive lung disease—emphysema, chronic interstitial pneumonia, or pneumonokoniosis. In some cases of cirrhosis failure of the heart, such as may occur from alcoholism, may induce ascites, so that cirrhosis and ascites are associated, though not related as cause and effect. In such cases it is difficult to decide their relation until the alcoholic dilatation of the heart has been successfully treated.

In *renal disease* ascites is part of the general dropsy which typically affects the face. The character of the urine and the cardio-vascular changes proper to renal disease should prevent any mistake in diagnosis. As pointed out elsewhere (p. 224), renal disease may coincide with portal cirrhosis.

In *splenic anaemia* of adults ascites very occasionally appears before the terminal cirrhosis of the liver, which is known as Banti's disease, has developed, as shewn by post-mortem examination of cases of uncomplicated splenic anaemia. Inasmuch as periodic haematemesis also occurs in that disease, the resemblance to cirrhosis when ascites develops might be thought to be very close. Clinically the anaemia and splenic enlargement are so much greater in splenic anaemia that ordinary cirrhosis is only likely to be diagnosed by those who are not familiar with the fact that ascites and periodic attacks of haematemesis may occur in splenic anaemia.

The **prognosis** of ascites due to uncomplicated cirrhosis is very bad; as a rule, death follows within a short time of its onset—usually within three to four months, and sometimes much sooner.

A distinction has rightly been drawn, more especially by Hale White [2] and Campbell Thomson,[3] between ascites due to cirrhosis and ascites associated with cirrhosis, but due to some other cause, such as chronic peritonitis. In ascites associated with chronic peritonitis tapping may be required frequently, and occasionally recovery may occur; whereas in ascites due to cirrhosis tapping is seldom required more than two or three times, and is followed by death sooner than in the first category.

In 38 cases of uncomplicated cirrhosis the average number of days of survival after the appearance of ascites was 98·6; in 31 of these cases paracentesis was necessary, and the average duration of life after the first tapping was 46

[1] Pye-Smith. *Trans. Path. Soc.*, 1893, xliv, 111.
[2] Hale White. *Guy's Hosp. Rep.*, 1893, xlix, 1.
[3] Thomson, Campbell. *Med.-Chir. Trans.*, Lond., 1901, lxxxiv, 251.

days. Whereas in 13 cases of cirrhosis, complicated with chronic peritonitis, the average number of days for the same interval came to 360 and 288 (Ramsbottom [1]).

It is, however, possible that in some cases of cirrhosis with chronic peritonitis and ascites, the ascites causes the chronic peritonitis, and not vice versa. A persistent ascites might in virtue of contained toxins or bacteria set up some chronic peritonitis. If this is so, the prognosis of ascites in cirrhosis is not so gloomy as is usually supposed. Since oedema of the feet in the course of cirrhosis is a sign of general toxaemia, the prognosis in a case of cirrhosis with ascites and oedema of the feet is worse than in cirrhosis with ascites alone, inasmuch as the latter may be a case of cirrhosis associated with ascites due to some other factor, such as chronic peritonitis. The presence or absence of oedema of the feet may thus be useful in determining whether, in any case of ascites due to cirrhosis, the termination is likely to come rapidly, or whether several tappings may be required with a possible chance of recovery. In the section on the general prognosis in portal cirrhosis the prognosis of ascites is referred to again (p. 295).

The **treatment** of ascites may be divided into: (i) paracentesis and drainage of the ascites; (ii) operations for producing vascular adhesions around the liver; (iii) diuretics and purgatives. The first and last of these methods are merely directed to the removal of the ascitic fluid. The production of artificial vascular adhesions is intended to prevent the peritoneal exudation, and is therefore a more radical method.

(i) *Advisability of performing Paracentesis.*—Formerly paracentesis of the abdomen was postponed as long as possible, partly because infection of the peritoneum sometimes followed tapping, and partly because the patient often went downhill extremely rapidly after the withdrawal of the ascitic effusion. With antiseptic precautions the likelihood of peritonitis resulting is minimised, while the occurrence of death comparatively shortly after paracentesis must be considered to be due to the natural course of the disease, and not to the removal of ascites.

Other reasons given for only adopting paracentesis as a last resource were that (*a*) the removal of fluid entailed the loss of a considerable amount of albumin, an argument that might also be used against opening an abscess (Murchison), and (*b*) that the intra-abdominal pressure of ascites prevented further transudation of fluid (Frerichs). Opinion has changed, and at the present time tapping is performed as soon as it is required in order to prevent the bad effects of excessive ascites.[2] It is a much more effective method than purgation, or the attempt to drain off the fluid by the kidneys, and does not tend to weaken the patient's strength as violent purging does.

[1] Ramsbottom. *Med. Chronicle*, Manchester, 1906, xlv, 7.

[2] Austin Flint was the first vigorous advocate of tapping comparatively early in the course of the disease. Vide *Am. Journ. Med. Sc.*, 1863, xlv, 331; and *Brit. Med. Journ.*, 1883, ii, 565.

Bad Effects of Excessive Ascites.—The results of ascites have been already referred to; they are largely mechanical in the first instance and due to pressure on the abdominal and thoracic viscera; the functions of these organs are interfered with, and are therefore imperfectly performed. The renal veins are pressed upon and the urinary excretion impeded, much in the same way as in the backward pressure of heart disease.

Indications for Paracentesis.—When the patient complains of marked discomfort, the abdomen should be tapped; but apart from this there are other conditions, such as diminished amount of urine associated with oedema of the legs, signs of thoracic embarrassment, such as dulness at the bases of the lungs due to collapse, dyspnoea, rales at the bases of the lungs, and in rare instances haemoptysis from collapse of the lungs, which should make the practitioner tap the abdomen. In cases with considerable ascites in which haematemesis occurs, the abdomen should be tapped, as by this means venous engorgement may be diminished.

Method of performing Paracentesis.—The most satisfactory treatment is tapping the abdomen with a Southey's trocar and cannula, the fluid draining slowly away through a fine india-rubber tube into a bucket placed by or underneath the bed. Occasionally—I have seen three such cases—the abdominal wall is so enormously thick that a Southey's trocar fails to reach the peritoneal cavity, and a specially long trocar is required. In one such case in which I used the trocar of a Dieulafoy's aspirator the abdominal wall, as it became lax from the removal of the ascitic fluid, collapsed in thick folds on the trocar and bent it out of shape.

The skin should be carefully washed and an antiseptic dressing (1 in 40 carbolic) put over the area where the trocar is to be introduced, and the trocar and cannula should be boiled in a test-tube containing water and left to cool in a solution of carbolic 1 in 40. The trocar is usually inserted in the middle line between the symphysis pubis and the umbilicus, but sometimes, from the presence of omental or other adhesions, little or no fluid may be drawn off in this situation; in such instances it will be necessary to tap the abdomen in the linea semilunaris on one or other side. It has been suggested that the spot selected should be on a line joining the umbilicus and the anterior superior spine of the ilium on the left side, so as to avoid any danger of wounding the caecum or the liver (Plicque [1]). Puncture of the abdominal wall at the centre of this line has in at least two recorded cases caused fatal haemorrhage from a wound of the deep epigastric artery (Boidin,[2] Lian [3]). The middle line is therefore a safer site for the tapping. It is, of course, essential that the area selected should be dull, and it should be ascertained, if necessary by passing a catheter, that the dulness is not due to a distended bladder.

Under ordinary conditions and with reasonable care there should never be any danger of wounding the liver. I have, however, seen its effects at a necropsy, in which there was very considerable extravasation

[1] Plicque. *Presse méd.*, Paris, 1900, p. 28.
[2] Boidin. *Bull. Soc. Anat.*, Paris, 1903, lxxviii, 415.
[3] Lian. *Ibid.*, 1907, lxxxii, 665.

from puncture of a large branch of the portal vein. As a rule, little or no harm results.

Goodhart,[1] indeed, refers to the case of a woman who, when apparently in a very advanced stage of the disease, was tapped, but only blood came away, and it was thought that the trocar had passed into the liver. However, from that time the patient steadily improved. Possibly this fortunate result was due to the wound producing vascular adhesions around the liver.

In very rare cases excessive haemorrhage may result from the trocar wound of the abdominal wall; this is likely to occur in patients in a haemorrhagic state.

A man aged forty-nine years, on the verge of a third attack of delirium tremens, had a number of subcutaneous haemorrhages, and had recently had profuse epistaxis. His abdomen was tapped in the middle line between the umbilicus and the symphysis pubis for ascites. When the cannula was withdrawn there was a spurt of arterial blood which was found to come from a branch of the deep epigastric in the substance of the rectus muscle; the artery was ligatured in two places, but the man died three hours afterwards. At the necropsy there were two pints of dark blood mixed with ascitic fluid in the peritoneal cavity; the liver (76 oz.) was remarkably cirrhotic, the veins of Sappey were dilated, and the body intensely anaemic. The blood appeared to have come from a wound of the deep epigastric veins, and to have passed through the track of the trocar into the abdomen. [St. George's Hospital P.M. Book, 1906, No. 371.]

The patient lies on his back, and the cannula should be fixed by means of plaster. During the drainage the abdomen should be compressed by a many-tailed bandage, or by a binder, which must be tightened from time to time, so as to avoid tympanites.[2] When the cannula has ceased to run from the small amount of fluid left in the abdomen, and not from displacement or blocking of the tube, which can be ascertained by passing a probe down the cannula, it should be withdrawn and the small wound covered with a plug of absorbent cotton-wool saturated with collodion. The binder should be kept on for two or three days to prevent flatulent distension of the intestines. Continuous strapping of the abdomen has indeed been recommended as a means of preventing the re-accumulation of fluid. If any distension occur, a dose or two of the sulphates of magnesium and sodium, a dram and a half of each, should be given. If the abdomen is nearly emptied, the small trocar wound heals up, and no trouble from leakage results. When, however, from adhesions the fluid is not satisfactorily removed, leakage from the wound may give considerable inconvenience, although the cannula has ceased to run. After paracentesis, from the increased absorption of fluid from the bowel and from the flaccid condition of the abdominal muscles, there is occasionally troublesome constipation.

[1] Goodhart. *Guy's Hosp. Gaz.*, June 7, 1897.

[2] This practice appears to have been first employed by Dr. R. Mead [*Medical Works*, p. 518, 1762]; also see *The Gold-headed Cane*, p. 66, 1st ed., 1827.

Injection of adrenalin chloride into the peritoneal cavity after removal of the ascites has been followed by good results in cases thought to be cirrhosis; a dram of 1 in 1000 solution in ½ oz. of water may be used.

Use of a Large Trocar.—In former times a large trocar, like that employed for withdrawing the contents of an ovarian cyst, used to be plunged into the abdomen and the fluid rapidly drawn off. This is chiefly of historical interest; personally I have never seen it employed. The rapid withdrawal of fluid sometimes led to collapse, possibly from a large quantity of blood being drawn into the splanchnic veins.

Treatment by Continuous Drainage.—The wound has been kept open and the fluid allowed to run away continuously by Caillié, Elliot, Urso, Cheadle,[1] and others. But it has grave drawbacks.

Of Urso's 9 cases, 4 died directly; the best result seems to have been prolongation of life for nine months. Elliot's cases were both fatal. In some of Cheadle's cases in which the puncture remained open the results were satisfactory except for the manifest discomfort.

A modification of permanent drainage is described by Jaboulay[2] under the title "Cicatrice à filtration." In a man with ascites from cirrhosis the skin of the abdomen was incised transversely below the left costal arch, the muscles and peritoneum were divided lower down, and a piece of omentum was attached outside the peritoneal cavity, and the wound closed with hardly any escape of ascitic fluid. The skin healed over the artificially produced interstitial hernia of the great omentum, and the ascites diminished by escaping into the subcutaneous tissues of the abdominal wall. A week after the operation a small external fistula in the stitch wounds developed and the fluid gained an external exit. The man left the hospital in fair health. Narath in 1905 adopted a somewhat similar technique (*vide* p. 262). Paterson[3] drained the ascitic fluid into the subcutaneous tissues of the abdomen by means of a short glass tube with projecting flanges at each end. Permanent drainage into the tissues of the thigh through the femoral ring has also been employed (Wynter[4] and Handley). Routte's operation consists in making an anastomosis between the peritoneal cavity and the saphenous vein, and has been recommended in bad cases (Soyesima[5]). In 1911 Celso[6] collected 10 cases, only 2 of which were successful.

(ii) *The Surgical Treatment of Ascites by the Production of Vascular Peritoneal Adhesions.*—This method of treatment, as conceived by Drummond and Morison,[7] was based on the assumption that ascites was due to portal obstruction, and was an attempt to increase the collateral circulation between the portal vein and the general systemic veins. The operation was original in Morison's hands, but it had been previously planned by Talma and carried out by Van der Meulen in 1889, by Schelkley in 1891,

[1] Cheadle. *Brit. Med. Journ.*, 1900, i, 895.
[2] Jaboulay. *Lyon méd.*, 1900, xciv, 499.
[3] Paterson. *Lancet*, Lond., 1910, ii, 1273.
[4] Wynter. *Proc. Roy. Soc. Med.*, 1908, i (Clin. Sect.), 49.
[5] Soyesima. *Deutsche Ztschr. f. Chir.*, 1909, xcviii, 390.
[6] Celso. *Morgagni*, Milan, 1911, Riv., liii, 675.
[7] Drummond and Morison. *Brit. Med. Journ.*, 1896, ii, 728.

and by Lens in 1892. It is often called Talma's operation, or the Talma-Morison operation.

Technique of the Operation.—It is convenient to tap the abdomen before the operation so as to remove the ascites, though this is by no means essential. An incision parallel to the right costal margin is probably more convenient than one in the long axis of the body. The liver should be examined to confirm the diagnosis of cirrhosis, for the operation will do no good if the ascites is due to chronic peritonitis. The peritoneum over the liver and diaphragm is scraped so as to set up adhesive inflammation, and the surfaces are brought in contact by stitching the round ligament to the abdominal parietes or by passing stitches through the liver. The great omentum may be utilised to multiply the vascular adhesions by interpolating it between the diaphragm and the convexity of the liver. The numerous veins in the great omentum will assist in the development of a compensatory anastomosis. No bad effects, such as intestinal obstruction, result from limitation of the scope of the transverse colon's movement. In a case reported by Talma [1] the spleen remained of considerable size until at a second laparotomy the spleen was sutured to the abdominal parietes, after which it became smaller. It has therefore been thought that the peritoneum should be scraped widely so as to allow of the formation of vascular adhesions with the parietal peritoneum around the spleen and intestines (Ito and Omi [2]), as well as around the liver, but the production of widespread peritoneal adhesions is not advisable. The peritoneal cavity should be drained either by means of a glass tube inserted into the wound or by a separate suprapubic incision into the peritoneum so as to prevent the ascitic fluid separating the roughened peritoneal surfaces and interfering with the formation of vascular adhesions. The patient should also, as far as possible, be kept in a sitting posture, so as to prevent re-accumulation of fluid in the upper part of the abdomen.

It has been suggested by Murrell [3] that the development of a collateral circulation may be accelerated by rubbing the skin of the abdomen with ung. capsici or with cajeput oil. This would, of course, not be done until the operation wound had completely healed.

Epiplopexy is a slighter operation which requires less time and manipulation and is therefore applicable to advanced cases with little power of resistance. Its object is to increase the compensatory collateral circulation between the radicles of the portal veins and the systemic veins. The operation consists in suturing the great omentum to the anterior abdominal wall (Roberts [4]). In 1901 Schiassi [5] fixed the great omentum under the abdominal muscles and external to the parietal

[1] Talma. *Berlin. klin. Wochen.*, 1898, xxxv, 833.
[2] Ito und Omi. *Deutsche Ztschr. f. klin. Chir.*, 1902, lxii, 141.
[3] Murrell. *Lancet*, 1902, i, 1602.
[4] Roberts, J. B. *Phila. Med. Journ.*, 1901, vii, 163.
[5] Schiassi. *Semaine méd.*, Paris, 1901, xxi, 145.

peritoneum; and in 1905 Narath[1] introduced the omentum into a subcutaneous pocket in the abdominal wall. These operations can be performed without general anaesthesia.

Discussion of the Manner in which the Talma-Morison Operation improves the Condition of the Patients.—Does the improvement which sometimes results both in the general health and the disappearance of ascites depend solely on the increased collateral circulation and the resulting fall in the pressure in the portal vein? Against this interpretation it may be argued (*a*) that ascites does not occur when the blood-pressure in the portal vein is presumably highest—viz. early in the course of the disease when haematemesis is most often met with, and that experimental ligature of the portal vein does not necessarily produce ascites. Cirrhosis may exist for many years without ascites, which may appear quite suddenly; whereas if ascites were a purely mechanical effect of increased pressure in the portal vein, it should develop gradually and earlier in the course of the disease. It would therefore appear that the good effects of the collateral circulation are not solely due to relieving the pressure in the portal vein. (*b*) That ascites is a late manifestation and appears to be due to a toxaemic rather than a purely mechanical result of increased portal blood-pressure, and that it is caused by a poison in the blood exerting a lymphagogue action.. The toxaemic state depends on hepatic insufficiency—in other words, on the inability of the cirrhotic liver to destroy poisons that are continually passing to it from the alimentary canal; these poisons, therefore, reach the general circulation and lead to oedema of the feet, ascites, and to constitutional and nervous symptoms. If the collateral circulation between the peripheral parts of the portal vein and general systemic veins is markedly increased, less blood will go through the liver and the toxaemia will be increased. In fact, the collateral circulation between the portal and general venous system is carried to its logical conclusion in Eck's fistula. In this experiment the portal vein is interrupted in the portal fissure; its proximal end is closed, and its distal end is put into communication with the inferior vena cava. In other words, the portal circulation through the liver is short-circuited and all the blood from the intestinal area enters directly into the inferior vena cava. As shewn by the experiments of Hahn, Massen, Nencki, and Pawlow[2] on dogs, this procedure tends to induce a disposition to uraemia. Thus, feeding the dogs on meat caused severe nervous disturbance, depression, asthenia, clonic and tonic spasms, and coma, and sometimes death. One of Morison's[3] patients was alternately excited and depressed for three weeks after the operation; similar depression has been noted in other cases, and may be explained as being due to the passage of poisons, manufactured in the intestine, directly into the general circulation without the intervention of the liver. Eck's fistula has been carried out on a man by Vidal,[4] the patient surviving for four months.

[1] Narath. *Centralbl. f. Chir.*, 1905, xxxii, 433.
[2] Hahn, Massen, Nencki, und Pawlow. *Arch. f. exper. Path. u. Pharmak.*, 1893, xxxii, 161.
[3] Morison. *Lancet*, 1899, i, 1426. [4] Vidal. *Semaine méd.*, Paris, 1903, xxiii, 351.

Thus, since it appears that the increase in the collateral circulation between the portal vein and the general systemic system would tend to induce a general toxaemia, the improvement in general health that follows the operation must be due to some cause other than the formation of anastomotic channels between the portal vein and the general systemic veins.

Thomson [1] suggested that the operation may prevent ascites by the simple method of producing universal adhesions and obliterating the peritoneal cavity. That this is possible is shewn by the cases, such as Dickinson's [2] and Weber's,[3] in which ascites disappeared and cirrhosis with universal peritoneal adhesions was found at the necropsy.

In 1899 Mr. G. R. Turner and I [4] suggested two other ways in which the development of a collateral circulation in adhesions around the liver might be beneficial to the economy: (1) By somewhat diminishing the flow of blood through the liver it may enable that organ to deal more satisfactorily with the blood passing through it, and so reduce the toxaemia, which is probably the important factor in inducing ascites. (2) That the presence of vascular adhesions over the surface of the liver would relieve venous engorgement and so allow a freer supply of arterial blood to the liver. The nutrition of the liver cells would thus be improved and they would be under better conditions to undergo compensatory hyperplasia. The compensatory hypertrophy of the liver [5] will enable the organ to perform more efficiently its important antitoxic functions, and so lead to a latency of the symptoms.

Early Performance of Operation Desirable.—It is important that the operation should be done comparatively early and not postponed until the patient is too debilitated to withstand it, for patients with cirrhosis are, at the best of times, far from good subjects. Thus patients may die from peritonitis or from shock immediately after the laparotomy. Another reason for not delaying operative interference is the importance of intervening before the liver tissue is so degenerated that it is unable to undergo compensatory hyperplasia as the result of the improved blood-supply provided by the adhesions. In suitable cases for operation medical measures should only be persisted in while the diagnosis is open to doubt, and they should always be directed to counteract any possible syphilitic disease of the liver. When medical treatment and a course of iodide of potassium have not benefited a case of ascites which is thought to be due to either syphilis or cirrhosis, the question of operative interference should be considered.

[1] Thomson, H. Campbell. *Med.-Chir. Trans.*, Lond., 1901, lxxxiv, 265.
[2] Dickinson, W. H. Allbutt's *System of Medicine*, 1898, v 691.
[3] Weber, F. P. *St. Barth. Hosp. Rep.*, 1898, xxxiv, 321.
[4] Rolleston and Turner. *Lancet*, Lond., 1898, ii, 1660.
[5] It is interesting to note that in a case of hepatic cirrhosis, in which it was suggested that the symptoms were arrested as the result of universal peritoneal adhesions, the liver weighed 89 ounces and presented nodules on its surface which may be interpreted as due to compensatory hyperplasia. The patient died from poisoning by mussels. (F. P. Weber. *St. Barth. Hosp. Rep.*, Lond., 1898, xxxiv, 321.)

When cirrhosis can be diagnosed with fair certainty in the pre-ascitic stage, and when there are evidences of the disease, such as haematemesis and splenic enlargement, operative interference has a much better chance than in the late stages.

The *contra-indications* to the performance of the operation are: (i) An advanced stage of the disease, shewn by debility, wasting, and marked toxaemia. (ii) Considerable jaundice. (iii) Definite heart or renal disease.

Results of the Operation.—A large number of cases have been operated upon, and in some instances the operation has been done on cases in which ascites was due to some other cause.

Sinclair White [1] collected 227 cases of cirrhosis operated upon, and found that 37 per cent were cured and 13 per cent improved, whilst in 15 per cent the operation failed, and in 33 death followed. At the French Surgical Congress in 1904 very divergent views were expressed: on the one hand, Monprofit [2] estimated that complete recovery followed in 35 per cent of 224 cases operated upon; on the other hand, Willems [3] quoted statistics to the effect that only 10, or 4 per cent, of 250 cases operated upon were successful. In 288 instances in which the operation had been performed, about 70 per cent being cirrhosis, Bunge [4] estimated that cure occurred in 30 per cent, and improvement in a further 14 per cent.

On the whole, the results are somewhat disappointing, but this may in part be due to the fact that the operation is so often undertaken as a last resource, and late in the course of the disease, when the fatal termination is already near. The earlier the operation is undertaken, the better the chance of improvement or even arrest of the disease.

(iii) *Treatment by Diuretics.*—In moderate ascites diuretics may be tried; it is also advisable to give them directly after paracentesis has been performed. In considerable ascitic effusion, diuretics have little effect, possibly because the renal veins are pressed upon, and from the resulting venous engorgement the kidneys are placed at a disadvantage. For this reason they are often much more effective after paracentesis than before. Diuretics should never be employed to the exclusion of paracentesis. Many diuretics have been employed. A pill containing digitalis, squill, and mercury is one of the most popular diuretics in ascites. This pill is called Baillie's pill at St. George's, or Addison's pill at Guy's Hospital. Small doses of calomel may be given not only for their antiseptic action, but also to increase the output of urine, especially when combined with citrate of caffeine. Potassium salts, such as the acetate, citrate, and bitartrate, are recommended by some, but their diuretic effect is inferior to that of many other available drugs, and the depressing and toxic effect of potassium is a distinct drawback. It is better not to give spirituous solutions, such as spirit of juniper, spiritus aetheris nitrosi, as

[1] White, Sinclair. *Brit. Med. Journ.*, 1906, ii, 1287.
[2] Monprofit. *Rev. de chir.*, 1904, xxiv, 602.
[3] Willems. *Ibid.*, 606.
[4] Bunge. *Die Talma-Drummondsche Operation*, 1905.

it is possible they might, like alcoholic drinks, do further damage to the liver. Copaiba resin in 10 to 15 grain doses has been advocated as a valuable remedy in ascites. It should be given in keratin capsules, which resist the action of the gastric juice, so as to avoid irritation of the stomach. Apocynum is a powerful diuretic, as its name the "vegetable trocar" implies. It has the disadvantage of irritating the stomach; in order to prevent this, a small dose of cannabis indica should be combined with it. The tincture can be given in 15 to 30 minims three times daily, or the fluid extract (U.S.P.) in 10 minim doses may be employed instead. I have been disappointed with its effects in the ascites of cirrhosis. Asparagus has often been used as a diuretic. Hare [1] has seen improvement in ascites of cirrhosis after a dram of a liquid extract of asparagus given three times daily. Urea, on account of its diuretic action, has also been recommended. I have tried it without marked effect in several cases, and Goggi has seen bad results follow its administration. Diuretin has been tried, but is not of any particular use in the ascites of cirrhosis. Good results have been reported from nucleinic acid (Mezernitzky [2]). Liver substance or extract has been given by the mouth or by subcutaneous injection. Polyuria and diarrhoea result, and ascites may be much diminished. In 14 cases collected by Mouras [3] ascites disappeared in 7 (*vide* also p. 301).

Treatment by Purgatives.—The ancient treatment of attempting to remove ascites by free purgation has been abandoned, and vigorous drugs like elaterium and gamboge are no longer given. The excessive diarrhoea thus produced necessarily starves and weakens the patient, while it lessens the urinary excretion and so may tend to induce or increase retention of toxic substances in the blood and lead to toxaemia. Cheadle speaks of cases being "purged to death." Further, violent purgatives readily light up catarrh of the intestine, and so do harm. Repeated small doses of calomel may be given and exert a beneficial antiseptic action as well as clearing out the bowels. Saline purgatives such as sulphate of sodium or magnesium may be employed. Compound jalap powder in one-dram doses is an effectual purge. Turpeth, the Ipomoea turpethum of the Colonial and Indian Pharmacopoeias, is recommended in 20 grain doses (Murrell [4]).

Restriction of Fluid, etc.—Dickinson [5] records 6 cases of ascites due to cirrhosis treated by reducing the amount of liquid taken by the mouth down to one pint or less. In two cases the ascites disappeared. In one death occurred two years later from cerebral abscess, and the patient, a boy aged nine years, was found to have a hobnailed liver and universal peritoneal adhesions. The treatment was recommended not as a substitute for tapping, but as an adjuvant. The diminished fluid has distinct disadvantages, since it must tend to produce constipation, thereby

[1] Hare, H. A. *Therap. Gaz.*, 1899, xxiii, 589.
[2] Mezernitzky. *München. med. Wchnschr.*, 1910, lvii, 1032.
[3] Mouras. *Thèse de Paris*, 1901, No. 278.
[4] Murrell. *Lancet*, 1902, i, 1602.
[5] Dickinson. Allbutt's *System of Medicine*, 1898, v, 691.

increasing fermentation and autointoxication. Further, it must curtail the urinary excretion and so favour toxaemia.

It has been urged that the intake of chlorides should be restricted, as they are retained and tend to increase ascites,[1] but the results have not been very striking (Herringham and Hadfield[2]).

Haematemesis may be the earliest warning to the individual that he is the subject of any disease more serious than indigestion. A frequent sequence of events is that a man who for years has lived freely and has had attacks of gastritis and dyspepsia, due to alcoholic excess, has, while in his usual state of health or after a little uneasiness in the stomach or faintness, a copious haematemesis. Haematemesis may be preceded by abdominal discomfort, febrile disturbance, enlarged spleen, and evidence of gastritis. In such cases gastritis, due to toxic or infective agents, is probably the exciting cause of the haemorrhage. The haematemesis is sometimes repeated during the next few days, but usually there is a single large haematemesis. When haematemesis is often repeated the condition is either not cirrhosis, or, if there be hepatic cirrhosis, it is complicated by some factor, such as gastric ulcer, superficial gastric erosions, or ulcerated varicose oesophageal veins.

Incidence.—Haematemesis does not appear from statistics to be so frequent in the course of cirrhosis as is usually imagined. It is such a striking event that it is rather surprising to find that it occurs less often than jaundice and in about one-fourth of all patients dying with a cirrhotic liver.

In 243 cases, obtained by combining Yeld's[3] (85), Sears and Lord's[4] (78), and my own (80) cases, haematemesis occurred in 64, or 26·3 per cent.

It occurs rather more frequently in cases dying directly from the effects of cirrhosis.

In 80 cases of cirrhosis fatal from the effects of the disease, examined after death at St. George's Hospital, 26, or 32·5 per cent, had had haematemesis. In 4 of the 26 cases death was directly due to haematemesis. Men suffered more frequently than women; thus, of 51 men, 19, or 37 per cent, had haematemesis, whilst of the 29 women, only 7, or 24 per cent, had haematemesis.

Haematemesis is rare in children, possibly because alcoholism, which is certainly more frequent in adults, favours haemorrhage by reducing the coagulability of the blood.

Saunal[5] recorded fatal haemorrhage from an oesophageal varix in a girl aged twelve years with cirrhosis. In the Norfolk and Norwich Hospital Museum

[1] Olmer et Audebort. *Rev. de méd.*, Paris, 1904, xxiv, 199.
[2] Herringham and Hadfield. *St. Barth. Hosp. Rep.*, 1905, xli, 23.
[3] Yeld. *Ibid.*, 1898, xxxiv, 215.
[4] Sears and Lord. *Boston Med. and Surg. Journ.*, 1902, cxlvii, 285.
[5] Saunal. *Thèse de Paris*, 1892.

there is a specimen (No. 59) of dilated oesophageal veins from a girl aged eight years who died after a succession of haematemeses. The liver was hobnailed and weighed 36 ounces, the spleen weighed 18 ounces, the skin was slightly tinged, but there was no real jaundice.

After haematemesis the patient is left in a condition of secondary anaemia, the degree of which varies with the amount of blood lost. It is not easy to estimate the amount of blood lost, for though a considerable proportion of it may be vomited up, some always passes into the duodenum and gives rise to melaena, and may thus escape notice, and is necessarily difficult to estimate. After the haematemesis the patient sometimes feels relieved and loses any feeling of oppression and heaviness that he may have previously had in the abdomen. Enlargement of the spleen detected before haematemesis may diminish very greatly as the result of the loss of blood.

Although haematemesis is usually an early symptom, it may supervene late in the disease, and even prove fatal in a patient with ascites.[1]

A man aged fifty-four years was admitted into St. George's Hospital. He had jaundice, ascites, and albuminuria. Paracentesis to 10½ pints was performed, and after this the fluid did not collect again. He got weaker, and eventually died immediately after a large haematemesis. This was the only occasion on which he brought up blood. At the necropsy the liver was cirrhotic and weighed 6 pounds 10 ounces. The spleen, 10 ounces, the kidneys, 10 ounces each, appeared normal.

The blood is probably generally poured out slowly into the stomach, and thus has time to clot and to be acted upon by the gastric juice. It is for these reasons darker in colour than the blood in gastric ulcer, which is rapidly extravasated from the gastric arteries. The quantity of blood brought up is practically always considerable, for the vomiting is chiefly due to the mechanical distension of the stomach by the blood. When a small quantity is poured out the blood is not as a rule vomited, but passes into the bowel and gives rise to melaena. After a small haemorrhage the patient may vomit from some other cause, and bring up a little black or "coffee-ground" vomit, but this is somewhat exceptional. Very large amounts of blood may be vomited in the haematemesis due to cirrhosis. Thus Osler[2] refers to a case in which 10 pounds were lost in seven days. It is noteworthy that collapse is not so frequent or so marked as in the haematemesis of gastric ulcer, in which blood is rapidly poured out. When a varicose oesophageal vein is opened and very large quantities of blood are lost, sometimes at repeated intervals, death may follow, but this does not invalidate the general statement just made that in the ordinary haematemesis of cirrhosis alarming symptoms are rare.

After haematemesis the temperature is, as a rule, depressed from shock, but after a few days it becomes normal. It may then remain normal or become raised. Fever after haematemesis should suggest the

[1] H. Fagge. *Principles and Practice of Medicine*, ii, 134, 1st ed., 1886.
[2] Osler. *Practice of Medicine*, p. 558, 5th ed., 1905.

presence of some complication, such as tuberculosis, a pleural effusion, especially on the right side, endocarditis, or an infective process in the tonsils, teeth, or elsewhere. Fever may, however, depend on rapidly progressing changes in the liver, especially when the spleen remains enlarged or increases in size. Haematemesis and rapid hepatic changes may be due to an infection falling on a liver in which cirrhosis was quiescent. In such cases ascites may soon appear.

Possibly a slight and transient elevation of temperature after hæmatemesis may depend on constipation and the retention in the intestines of a considerable quantity of blood, and consequent microbic multiplication. Haematemesis may be such a severe shock to a patient who has been drinking steadily as to set up delirium tremens which may prove fatal.

Etiology of Haematemesis in Cirrhosis.—(1) *Gastritis.*—The haematemesis may follow a debauch and be due, in part at least, to an exacerbation of a chronic gastritis. In such a case the after-history may indicate whether acute gastritis alone or cirrhosis and gastritis together were responsible for the haemorrhage. Haematemesis apparently solely due to gastritis is by no means rare, but in any given case it must be borne in mind that haematemesis may after all have been disposed to by a cirrhotic liver, which subsequently became arrested and gave rise to no further symptoms.

Bad teeth and pyorrhoea alveolaris are not infrequently responsible for infective gastritis; and toxic gastritis may, of course, be set up by a drinking bout. In haematemesis from gastritis the blood is thought to be derived by oozing from the capillaries and small veins of the gastric mucous membrane. The haemorrhage is probably determined by minute areas of necrosis and ulceration in the course of a toxic or infective gastritis. When no source for haemorrhage can be found in the stomach or oesophagus it may depend on toxaemia, which shews itself elsewhere by haemorrhage from the gums, into the skin, etc.

It is unlikely that haematemesis is ever due solely to increase of venous blood-pressure in the walls of the stomach; some inflammatory or degenerate change in the gastric mucosa is a necessary factor. Often, of course, no determining cause is forthcoming; but sometimes fever, gastritis, and splenic enlargement may precede it; Gauthier[1] suggests that toxins unaltered by the liver damage the intestinal blood-vessels and so set up haemorrhage.

(2) *Minute Erosions.*—Haematemesis in cirrhosis may be due to superficial erosions of the gastric mucous membrane. These may be so small as to be easily overlooked, especially as the stomach is blood-stained and somewhat sodden. The stomach should be left for some hours in Müller's fluid, after which small erosions will become evident.

Deguy[2] reported fatal haematemesis in a case of latent cirrhosis with a minute superficial ulcer $\frac{8}{10}$ of a millimetre in size. Mathieu[3] recorded fatal

[1] *Journ. de méd.*, March 10, 1896.
[2] Deguy. *Bull. Soc. anat.*, Paris, 1898, lxxiii, 767.
[3] Mathieu. *Semaine méd.*, 1897, xvii, 170.

haematemesis in a woman aged thirty who was thought to be the subject of gastric ulcer; the necropsy shewed cirrhosis, oesophageal varices, and numerous haemorrhagic erosions on the lesser curvature and posterior wall of the stomach. Microscopically there was acute interstitial gastritis, which was the apparent cause of the ulceration. In a man with enormously tortuous veins near the cardia fatal haemorrhage occurred from a small erosion; gastro-enterostomy had been done for a supposed ulcer. The liver was cirrhotic. The patient was a total abstainer (Taylor [1]).

(3) *Gastric and Duodenal Ulcers.*—Gastric ulcer rarely occurs in patients with cirrhosis of the liver.

Among 56 cases of gastric ulcer examined after death at St. George's Hospital there were 2 with hepatic cirrhosis (T. C. English). According to the Fenwicks [2] cirrhosis of the liver is present in 9 per cent of cases of gastric ulcer.

Duodenal Ulcer.—In rare instances, of which I have seen one, copious haematemesis may occur in the course of cirrhosis from a duodenal ulcer. In 184 cases of duodenal ulcer collected by G. M. Cullen,[3] hepatic cirrhosis was present in 2·2 per cent.

(4) *Varicose oesophageal veins* are the most important cause of haematemesis in cirrhosis, being present in the great majority (80 per cent) of the fatal cases in which a thorough necropsy is made (Preble [4]). Exceptionally varicose oesophageal veins are found when the liver is healthy.

Graham and Weir Mitchell [5] recorded cases of fatal haematemesis from this cause in a boy aged seventeen years and in a child with healthy livers. In adults oesophageal varix may be due to chronic alcoholism without any cirrhosis of the liver (Letulle [6]). It has been thought that this phlebectasis is due to the caustic action of alcohol on the mucous membrane of the oesophagus (G. Muller [7]).

This compensatory collateral circulation serves a useful end in relieving portal engorgement, but, like other compensatory mechanisms, it may fail. Severe haemorrhage may be due to ulceration of the mucous membrane covering the varices, and may be precipitated by the passage of rough masses of food through the oesophagus. These oesophageal varices and severe haemorrhages are commoner in association with large than with small cirrhotic livers.

The blood may well up from the oesophagus when the patient is lying quiet in bed, and not be vomited up as it is in gastric ulcer. But in this event the blood does not enter the stomach and will be alkaline. As the varicose oesophageal veins are practically always near the cardiac

[1] Taylor. *Trans. Coll. Phys.*, Phila., 1906, xxviii, 17.
[2] Fenwick, S. and S. *Ulcer of the Stomach and Duodenum*, p. 76, 1900.
[3] Cullen. *Scot. Med. and Surg. Journ.*, 1897, i, 637.
[4] Preble. *Am. Journ. Med. Sc.*, 1900, cxix, 263.
[5] Graham and Weir Mitchell. *Trans. Assoc. Am. Phys.*, 1896, xi, 215.
[6] Letulle. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1890, 3. s., vii, 783.
[7] Muller. *Gaz. hebd. de méd.*, Paris, 1900, v, 470.

orifice, the blood usually runs into the stomach and is vomited as in ordinary haematemesis. An ulcerated varicose vein can be seen with the oesophagoscope (Abrand [1]). The loss of blood may be so profuse as to prove fatal.

It is highly probable that in many of the cases regarded as due to a general venous oozing, an ulcerated oesophageal varix was overlooked. The ulceration may be very small and may escape notice at the necropsy. Letulle says that the ulcer may only become apparent after the oesophagus has been left for twenty-four hours in Müller's fluid.

The first haemorrhage may be so profuse as to be immediately fatal. This was so in one-third of Preble's 60 fatal cases of gastro-intestinal haemorrhage in cirrhosis. In other cases repeated haemorrhages occur. In rare instances there are considerable intervals of good health between the attacks of haematemesis ; in Garland's [2] case haemorrhage took place at intervals for seven years. Repeated haemorrhages at brief intervals may kill the patient in a short time from the first symptom of illness (Marmasse [3]). In fatal gastro-intestinal haemorrhage from cirrhosis the primary disease is often latent. The latency of cirrhosis in cases with varicose oesophageal veins shews the value of this compensatory mechanism. In only 6 per cent of 35 cases of cirrhosis with varices were the clinical symptoms characteristic, viz. ascites, enlarged spleen, subcutaneous abdominal veins, etc. (Preble). The following case illustrates the latency of cirrhosis until fatal haematemesis from an ulcerated oesophageal varix occurs :

A man, aged thirty-three, was brought in dead into St. George's Hospital, having vomited up a large quantity of blood shortly before death. There were dilated varices at the lower end of the oesophagus, one of which was ulcerated. The veins at the cardiac end of the stomach were somewhat varicose and there was a very minute abrasion of the mucosa over one of them, but the vein, though exposed, was not perforated. The intestines contained blood. There was no ascites. The liver, $4\frac{1}{2}$ pounds, was finely cirrhotic with bright yellow nodules. Microscopically there was multilobular fibrosis with much fatty degeneration of the liver cells. The spleen, $9\frac{1}{2}$ oz., was shrunken as if it had been larger. The kidneys, $7\frac{1}{2}$ oz. and $8\frac{1}{2}$ oz., were hypertrophied but healthy. There was caseous tubercle at the apex of the right lung.

In the following instance death was due to haemorrhage from an ulcerated oesophageal vein in a patient under treatment for cirrhosis :

Charles W., fifty-one years, a farm labourer, was admitted under my care in St. George's Hospital on September 15, 1900, with slight ascites and oedema of the legs. He had been a moderate drinker, and had never had syphilis. In July 1900 he had haematemesis and melaena ; before this he had not suffered from dyspepsia or morning vomiting. He was a weather-beaten man with a large liver and slight ascites. The spleen was not palpable. There was oedema

[1] Abrand. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1909, 3. s., xxvi, 378.
[2] Garland. *Trans. Assoc. Am. Phys.*, 1896, xi, 206.
[3] Marmasse. *Bull. Soc. Anat.*, Paris, 1899, lxxiv, 75.

of the feet, but no neuritis. Pulse 96, low tension, artery tortuous and somewhat atheromatous. Urine 1008, no albumin. The oedema of the feet went down and the man's condition improved; he was indeed feeling particularly well, when on September 21 haematemesis occurred; he was given suprarenal extract by the mouth and morphine hypodermically; on the next day he again had haematemesis and became very blanched, so that concealed haemorrhage was suspected. He was transfused, but died the same day. At the necropsy there was a small ulcer in the oesophagus, elevated so as to look like a miniature volcano, situated about one inch from the cardiac orifice of the stomach. This opened into a vein; the other veins at the lower end of the oesophagus were not varicose. The stomach and the intestines were full of blood. The liver, 80 oz., was pale, finely granular, and intensely cirrhotic, with numerous haemorrhagic spots in it. The portal vein was normal. The kidneys were pale but free from arteriosclerotic change. Spleen large. The cavity of the peritoneum contained two pints of ascitic fluid. Testes normal.

(5) *Varicose Gastric Veins.*—Haemorrhage from varicose veins in the stomach is very rare in cirrhosis. Letulle[1] described two fatal cases in men aged twenty-three and thirty-nine respectively. Other cases have been recorded by Marchiafava, Hillier, Blake, Jackson, Revillout, Minot, Taylor.[2]

Haemorrhage from the Pharynx.—Bouchard[3] pointed out that small angiomas are frequently present at the back of the pharynx and that haemorrhage from them may give rise to haematemesis. The pharynx of cirrhotic patients with haematemesis should therefore be carefully examined, as the cause of the haemorrhage, if found, can be satisfactorily treated by local styptics.

It has thus been seen that haematemesis in cirrhosis may occur (i) when there is no morbid lesion visible to the naked eye except gastritis. (ii) From small superficial abrasions of the gastric mucous membrane. (iii) In very rare instances from gastric or duodenal ulcer. (iv) From rupture or ulceration of varicose veins at the lower end of the oesophagus; this is the most important cause. (v) From ulcerated varicose veins in the stomach. (vi) From the pharynx, the blood being swallowed and subsequently vomited.

Diagnosis of Haematemesis of Hepatic Cirrhosis from that due to other Causes.—Without mentioning all the possible causes of haematemesis it will be useful to refer to the causes which are most likely to be confused with hepatic cirrhosis.

(A) *Gastric ulcer* in men of mature years runs a very chronic course, gives rise to continued pain and dyspepsia, but very rarely goes on to perforation. In some cases that I have seen there was an absence of tenderness on palpation, although the ulcer, as verified at the necropsy, was large and adherent to adjacent parts. Haemorrhage from the

[1] Letulle. *Presse méd.*, Par., 1898, ii, 313.
[2] Taylor. *Trans. Coll. Phys.*, Phila., 1906, xxviii, 17.
[3] Bouchard. *Rev. de méd.*, Par., 1902, xxii, 837.

stomach in these cases may give rise to a suspicion of cirrhosis. When a patient with entirely latent cirrhosis dies from very copious haematemesis, it is impossible to diagnose the condition from gastric ulcer except on the greater probability of cirrhosis giving rise to haematemesis in a middle-aged man than gastric ulcer.

The occurrence of repeated haemorrhages and painful dyspepsia are against cirrhosis. Enlargement of the spleen militates against gastric ulcer. In young women gastric ulcer is far more frequent than cirrhosis. When cirrhosis occurs in them, there is usually considerable enlargement of the liver and spleen and evidence of alcoholic excess. Pressure over the gastric ulcer in young women causes sharp pain, compared by the patient to that of a knife, which is quite different from the diffuse tenderness elicited on deep pressure in gastritis accompanying cirrhosis. The blood in haematemesis due to cirrhosis is black from the prolonged stay in the stomach and is often clotted, forming masses that may stick in the patient's pharynx. In gastric ulcer the blood is poured out more rapidly from a leaking artery, and is therefore brighter, less acted upon by the gastric juice, and not necessarily coagulated.

(B) From *pore-like erosions of the gastric arteries.* Very free and repeated haemorrhages may take place from minute erosions. In these cases there is no deep tenderness and there is a comparative absence of antecedent gastric symptoms (Dieulafoy,[1] Steven[2]). The chief distinction from the haematemesis of cirrhosis seems to be the occurrence of repeated and copious haematemesis in a patient who has none of the signs, symptoms, or history of portal cirrhosis.

(C) In *gastric carcinoma* the vomited blood is black, resembles "coffee-grounds," and is usually small in quantity, so that melaena is not noticed. In carcinoma of the pylorus haematemesis is in rare instances profuse; in such cases the stomach will probably be dilated and a tumour may be palpable. As a rule, carcinoma of the stomach is accompanied by so much pain and the vomited blood is so small in amount that the condition is not likely to imitate cirrhosis. If tested, the vomit will probably be found not to contain hydrochloric acid. Another important point in the diagnosis of gastric carcinoma is the presence of a tumour near or at the umbilicus, in the line of the falciform ligament, or on the surface of the liver, or enlarged glands above the left clavicle.

(D) In *splenic anaemia* periodic haematemesis may occur for years; sometimes there is very fair health in between the attacks; in some instances recurrent haemorrhages have occurred over a period of ten years. The anaemia is more marked and the splenic enlargement more considerable than in cirrhosis. The diagnosis from cirrhosis, which depends largely on these points, is important inasmuch as splenectomy appears, from Osler's[3] and Harris and Herzog's[4] observations, to offer

[1] Dieulafoy. (Exulceratio simplex.) *Presse méd.*, Par., 1898, i, 29.
[2] Steven, J. L. (Pore-like Erosions of the Gastric Arteries.) *Glasgow Med. Journ.*, 1899, li, 5.
[3] Osler. *Trans. Assoc. Am. Phys.*, 1902, xvii, 429.
[4] Harris and Herzog. *Ann. Surg.*, 1901, xxxiv, 111.

the best chance of cure. These cases usually occur in men between twenty and forty years of age, and so might easily be regarded as due to latent cirrhosis. Closely allied to chronic splenic anaemia of adults is the condition described by Banti,[1] and often spoken of as *Banti's disease*, in which splenic anaemia is after some years complicated by secondary cirrhosis of the liver.

In leukaemia, haematemesis and melaena may occur and be associated with both splenic and hepatic enlargement; the diagnosis from cirrhosis depends on an examination of the blood.

Prognosis.—Haematemesis is rarely fatal in cirrhosis; in 80 cases in which cirrhosis was the direct cause of death, haematemesis was the sole cause in only 4, or 5 per cent.

Treatment of Haematemesis from Cirrhosis.—The patient should be kept perfectly quiet in bed, and for two or four days nothing whatever should be given by the mouth. Ice should certainly not be sucked, as an indefinite quantity of water is thus taken, which necessarily sets up peristaltic contractions of the stomach, and so may give rise to fresh haematemesis, while, further, the cold water must abstract a considerable amount of heat from the patient, who is often already somewhat collapsed. Thirst, which is often a cause of distress to the patients, is a natural result of the loss of blood and of the draining of the tissues to replace the fluid part of the blood. The mouth should be cleaned by pads of moistened cotton-wool, and enemas of warm water should be given every four hours to relieve thirst. If necessary, subcutaneous transfusion with saline solution may be employed. In order to ensure rest a hypodermic injection of morphine is useful; this calms the natural mental disturbance and anxiety of a person who has unexpectedly brought up blood.

The administration of digitalis or digitalin, ergot, lead, or other drugs which constrict the vessels and raise blood-pressure, is useless if not dangerous. Nitrite of amyl, which dilates the small blood-vessels and lowers blood-pressure, has more in its favour.[2] Calcium salts increase the coagulating power of the blood, and so may lead to thrombosis in the bleeding vessels. A dose of a dram of the chloride may be added to one of the enemas of water given to relieve thirst, and may be repeated if haematemesis recurs and the patient's life is threatened from anaemia and exhaustion. As recurrent haematemesis in cirrhosis is usually due to ulcerated varices at the lower end of the oesophagus, it is advisable to try to act locally on the bleeding area by the administration of Ruspini's styptic, which is largely composed of gallic acid; the styptic may be given in half to one dram doses in an ounce of water by the mouth. Two successive half-dram doses may be given.

The various preparations of suprarenal gland substance may also be given by the mouth in recurrent haematemesis so as to obtain the local vaso-constrictive effect on the bleeding vessels. It should not be given hypodermically or per rectum, for, as its general effect is to raise the

[1] Banti, G. *Semaine méd.*, Paris, 1894, xiv, 318.
[2] Compare Hare, F. *Lancet*, 1904, ii, 522.

arterial blood-pressure, it would, if absorbed into the general circulation, tend to increase haemorrhage from any leaking vessel. Another remedy which may be given by the mouth is turpentine in twenty minim doses in spirit of chloroform (℥x.) and water (℥j.) every four or six hours.

The local application of an ice-bag to the abdomen has been recommended, but it may increase collapse. If there is great collapse after haematemesis, transfusion of normal saline solution subcutaneously or into the veins should be performed.

The lower bowel should be cleared out by a soap-and-water or by a glycerin enema, or when there is no recurrence of haemorrhage and there is any abdominal distension or slight fever, a blue pill followed by a saline draught containing sulphate of magnesium should be given on the third day. During the first three days it is better to give nothing by the mouth, rectal injections of water (10 to 20 ounces) being given to relieve thirst every four or six hours as seems necessary. Nutrient enemas or suppositories may also be given every six hours, but in many instances this is not really necessary, and the patient is more comfortable without. In fact, the mental influence of nutrient enemas is often more valuable than their physical effect.

If there is nothing to suggest gastric ulcer, cautious feeding by the mouth may usually be begun after the third day, provided there has been no return of haematemesis. Peptonised milk or peptonised milk gruel should first be given and the diet gradually improved. After a week or ten days, according to his general condition, the patient should be allowed to get up.

A most essential point is the after-treatment, which consists in a light, simple diet, abstinence from alcoholic stimulants and from highly spiced articles of food. The importance of change of life and of total abstinence should be clearly explained to the patient.

When, as sometimes happens, haematemesis occurs in patients with ascites, removal of the fluid by paracentesis may be followed by a cessation of haematemesis. In such cases congestion may be aggravated by the intra-abdominal pressure of ascites. Fatal gastro-intestinal haemorrhage has, however, occurred after paracentesis (Estachy [1]).

Haemorrhage from the bowel is common in cirrhosis. It may be divided into (i) melaena as ordinarily understood, viz. blood so altered that it is dark in colour; (ii) haemorrhage from piles or from the mucous membrane of the rectum, the blood being more or less of its normal colour.

Melaena (ἡ μέλαινα νόσος, the black disease) commonly accompanies or follows haematemesis. The blood, which, by distending, mechanically irritates the stomach, is expelled in two directions—into the oesophagus and into the duodenum. In other words, while haematemesis is going on the patient vomits into the duodenum. The haemoglobin of some of the blood-corpuscles is acted upon by the gastric juice and reduced to acid

[1] Estachy. *Bull. et mém. Soc. méd. de Vaucluse*, Avignon, 1906, ii, 432.

haematin ; there is hardly sufficient time for this to take place in the mass of the blood that is driven into the duodenum, so that the blackness and tarry appearance of the motions are largely the result of the iron of the haemoglobin being acted upon by sulphuretted hydrogen in the intestines and converted into some compound containing sulphide of iron.

Melaena from gastric haemorrhage may occur without concomitant haematemesis. When the volume of blood poured out is small, so that the stomach is not over-distended, it will pass into the duodenum mixed with the contents of the stomach and appear in the motions. In such cases the occurrence of melaena may escape observation or only be noticed accidentally, and may then be regarded as due to a latent duodenal or intestinal ulcer. It may be difficult or impossible to diagnose the source with certainty in the absence of other signs of cirrhosis. In duodenal ulcer there should be deep tenderness in the situation of the duodenum and pain two or three hours after food. Duodenal ulcer may complicate cirrhosis and give rise to melaena without haematemesis. I have seen one case in a man aged forty years in which this coincidence was present. The duodenal ulcer, undiagnosed during life, gave rise to very acute pain in the right loin.

Melaena in cirrhosis may depend on haemorrhages of considerable size from the mucosa of the intestines. It is usually seen about the same time as haematemesis, viz. in the pre-ascitic stage, but it may accompany considerable ascitic effusion, or occur after ascites has come and gone, and be a terminal phenomenon. Traces of blood are common in the ascitic stage (Crosa [1]) ; this occult blood, which cannot be detected by the naked eye, can be demonstrated by the delicate benzidine test.

A man aged fifty-two was admitted under my care with excessive ascites, which came on three months before, and melaena ; his abdomen was tapped, but he rapidly sank and died within forty-eight hours of the paracentesis. At the necropsy there was cirrhosis, a complete absence of any dilatation of the oesophageal veins, a chronic gastric ulcer at the pylorus, and close to it a small ulcer of more recent date from which the blood filling the stomach and intestines appeared to have come. The portal vein was normal.

In the following cases extensive haemorrhage from the rectum immediately preceded death :

A woman of alcoholic habits, aged forty-nine, under my care in St. George's Hospital, was tapped for ascites twice within a fortnight after admission. After this she lived for seven and a half weeks in an extremely drowsy condition, but did not again become ascitic. The day before her death she passed 2 pints of blood from the bowel. There were no subcutaneous haemorrhages at any time. At the necropsy the mucous membrane of the lower 6 inches of the rectum was inflamed, and though no definite ulcer could be found, the rectum must have been the source of the haemorrhage ; for no blood or blood staining was found

[1] Crosa. *Gazz. d. osp.*, Milano, 1909, xxx 1225.

higher up in the bowel. The liver was cirrhotic. In a man aged forty-four years death was immediately preceded by melaena. He had twice been tapped for ascites due to cirrhosis; he had successively haematuria, epistaxis, and lastly melaena.

Slight melaena may occur from small multiple haemorrhages from the mucosa of the intestines due to hepatic insufficiency. These extravasations are analogous to the multiple haemorrhage occurring under similar conditions into the skin and other tissues.

Piles occasionally cause some bleeding. It is remarkable that piles are not more frequent in cirrhosis, as it would naturally have been expected that portal obstruction would almost constantly lead to varicose haemorrhoidal veins. Frerichs,[1] Sappey, Thierfelder, Nothnagel,[2] and others are all agreed on the comparative rarity of piles in cirrhosis. It has been thought that haemorrhage from piles in cirrhosis serves a useful purpose by relieving hepatic engorgement, and that their cure by operation may be followed by haematemesis or by advance in the downward course of the disease; in other words, that piles in cirrhosis is a condition that it is dangerous to cure.

Treatment.—For considerable melaena without haematemesis a turpentine enema may be given. The patient should be kept quiet, if necessary, by morphine. If bleeding occurs from piles, the local condition should be attended to.

Haemoptysis in the course of cirrhosis is somewhat infrequent. When it does occur, it is usually comparatively slight. It may be due to various causes:—

1. *False Haemoptysis.*—This may depend on epistaxis from the posterior nares, or on haemorrhage from the mucous membrane of the naso-pharynx. These haemorrhages are not uncommon in the late stages, and may be due to the general toxaemia. Bouchard[3] insisted on the frequency of angiomas in the pharynx, from which haemorrhage may occur independently of grave toxaemia.

2. *Haemorrhage from the larynx* may be due to concomitant tuberculous disease, or to venous oozing depending on hepatic insufficiency. Dreyfuss observed a bleeding tumour in the larynx of a patient with cirrhosis.

3. *Haemorrhage from the lungs* due to (*a*) pulmonary tuberculosis; (*b*) extreme congestion accompanying pulmonary collapse secondary to abdominal distension; (*c*) venous oozing depending on hepatic insufficiency.

Haemoptysis in patients with cirrhosis should arouse a strong suspicion of pulmonary tuberculosis. It is, however, not always justified. In an alcoholic woman under my care who said she had had slight haemoptysis for years, the lungs were free from tuberculosis at the necropsy.

[1] Frerichs. *Diseases of the Liver*, ii, 47. Transl. New Sydenham Soc., 1861.
[2] Nothnagel. *Diseases of the Intestines and Peritoneum*, English transl., p. 308, 1907.
[3] Bouchard. *Rev. de méd.*, Paris, 1902, xxii, 837.

Bibliography.—Dreyfuss. *München. med. Wchnschr.*, 1898, xlv, 1022.—Galliard. *Union méd.*, Nov. 1889.—Lubet Barbon. *Ann. de laryngol. et d'otol.*, 1897 (Larynx).—Dieulafoy. *Manuel de interne path.*, ii, 689 (Larynx).—Debove et Trémolières. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1909, xxvi, 731 (Larynx).

Epistaxis is by no means infrequent in cirrhosis. It may be part of the general tendency to haemorrhage depending on hepatic insufficiency, but it may supervene before there is any other evidence of this toxaemia or be the first sign of this complication. It occurs from one nostril—usually, as was pointed out long ago, from the right. It usually comes from a point near the anterior extremity of the septum which can be easily compressed (Bouchard [1]). The haemorrhage may be due to ulceration of an arterial angioma, and may if uncontrolled be so severe as to lead to syncope. Relapses are very prone to occur. In a patient of Dieulafoy's [2] repeated haemorrhages occurred from an ulcerated angioma in the nostrils. Epistaxis may alternate with haemorrhages from other sources.

A man aged forty-four, under my care, had first haematuria, then epistaxis, and just before death melaena. His liver was markedly cirrhotic; he had been tapped twice for ascites.

Haemorrhages from other Situations.—Haematuria may occur from hepatic insufficiency, but it is rare.

In a man aged fifty years, who was under my care in 1903, with cirrhosis, transient haematuria occurred at the same time as epistaxis and oozing from the gums.

The following case is of interest as an example of haematuria and other forms of haemorrhage:

Cirrhosis. Haematuria due to Nephritis. Epistaxis. Fatal Melaena.—A man aged forty-four, of alcoholic habits, was admitted to St. George's Hospital under my care on June 20, 1900, with swelling of the abdomen, flatulence, pain near the umbilicus, swelling of the legs, and loss of flesh and strength dating from an attack of pneumonia eighteen months previously. He had the signs of cirrhosis with a large liver, but had very distinct haematuria with casts and a sp. gr. of 1009. The question arose whether there was cirrhosis with intercurrent nephritis or primary malignant disease of the kidney with secondary growths in the liver. There were no haemorrhages elsewhere. The abdomen required tapping twice. With rest in bed the haematuria passed away, but the patient's general condition got worse. On July 9 there was only a trace of albumin, and on July 11 none at all. On July 11 and 12 he had epistaxis, and on the latter day rapidly became comatose; though he revived a little after transfusion, he died on July 14 with considerable melaena. At the necropsy the liver, 68 ounces, was cirrhotic and finely granular; the portal vein was free from any thrombosis. The kidneys weighed 7½ and 8 ounces each, and shewed parenchymatous nephritis. The mucous membrane of the small intestine was pigmented, the change being more marked near the stomach. The spleen weighed 10 ounces.

[1] Bouchard. *Rev. de méd.*, Paris, 1902, xxii, 837.
[2] Dieulafoy. *Manuel d'interne pathologie*, 1901, ii, 669.

Menorrhagia and Metrorrhagia.—In the early stages of cirrhosis metrorrhagia is often seen; very possibly this is partly connected with chronic alcoholism. In the later stages of cirrhosis there is usually amenorrhoea, though when hepatic insufficiency supervenes, haemorrhages may occur from the uterine mucous membrane.

The occasional formation of a **haematoma in the rectus abdominis muscle** has already been referred to as a possible evil effect of the collateral circulation in connexion with the veins in the falciform ligament (*vide* p. 214).

In a case recorded by Lefas [1] in which portal cirrhosis was complicated by jaundice and grave toxaemia (icterus gravis) the cause of the haematoma was thought to be fatty degeneration of the endothelium of the intramuscular capillaries.

General Haemorrhages.—In the late stages of cirrhosis when the liver has become incapable of stopping poisons absorbed from the alimentary canal, a condition of hepatic toxaemia results. The blood shews a low fibrinogen content (Whipple [2]), the blood-vessels are damaged, and haemorrhages may occur all over the body. The general haemorrhagic condition may in some instances be due to haemic infection. Thus, in a case of cirrhosis with haemorrhagic bullae, Monnier [3] cultivated *Bacillus coli* and streptococci. In such cases there is fever. Petechial haemorrhages into the skin are frequent, and haemorrhages are often seen from the mucous membrane of the mouth, blood oozing from the gums or from cracks on the dry dorsum of the tongue. The sordes thus produced give rise to an offensive odour of the breath.

In an exceptional case recorded by Webber [4] haemorrhage took place from the external ears, in addition to haemoptysis and bleeding from the gums. Leudet [5] also reports haemorrhage from the external ear in cirrhosis.

Thrombosis and haemorrhages are usually associated with opposite conditions of the blood as regards coagulation, the blood coagulating more rapidly in thrombosis and less rapidly than normal in haemorrhage. In the following case they were associated:

An alcoholic woman aged forty years was admitted under my care for severe haematemesis thought to be due to cirrhosis; in two days' time she developed typical delirium tremens, from which she recovered under the administration of hyoscine $\frac{1}{75}$ gr. sub cutem. After her recovery from delirium she had numerous haemorrhages all over the body; it was noticeable that there were several small thrombosed veins in the neighbourhood of some large cutaneous haemorrhages. There were thrombosed veins on the front of the abdomen, on the right mamma, and right arm. The veins of the legs were not affected.

[1] Lefas. *Bull. Soc. anat.*, Paris, 1902, lxxvii, 586.
[2] Whipple. *Arch. Int. Med.*, Chicago, 1912, ix, 390.
[3] Monnier. *Compt. rend. Soc. Biol.*, 1896, xlviii, 65.
[4] Webber. *Lancet*, 1894, i, 1000.
[5] Leudet. *Ann. mal. de l'oreille et du larynx*, Paris, 1890.

The *treatment* of haemorrhages is partly local and partly general; the local treatment consists in the application of remedies such as adrenalin to bleeding spots when they can be reached. The general treatment consists in giving lactate of calcium in half-dram doses three times a day for six doses, and in attempting to reduce the general toxaemia by diuretics such as citrate of caffeine, purgatives, and subcutaneous transfusion if necessary.

Nervous Symptoms.—Various nervous manifestations may occur in the course of cirrhosis; as a rule the more striking are noticed late in the disease and are associated with advanced toxaemia. The slighter nervous symptoms, such as headache, giddiness, muscular weakness and tremor, disturbance of mental power, disordered sensation, pruritus, may occur earlier in the course of cirrhosis. It may not be easy to determine satisfactorily in every case whether symptoms are solely due to the liver and its functional failure, to other factors, such as alcoholic excess or renal disease, or to hepatic inadequacy combined with one of these additional factors. Thus, delirium tremens is due to recent alcoholic excess, and other forms of delirium may be most satisfactorily explained as due to hepatic or renal inadequacy. As long as the kidneys excrete toxic bodies which the liver fails to stop, the patient may remain fairly free from nervous symptoms, but headache, mental torpor, and depression are readily produced by food which has no bad effects in a healthy person. Failure in the excretion of urine increases toxaemia and often precedes the onset of acute nervous phenomena.

Slight mental disturbance is common, but it is natural to ascribe loss of memory, failure of will-power and of intellectual ability, solely or in part to the effects of alcohol. As in other morbid conditions of the liver, mental depression and hypochondriasis are common. Muscular tremor is not infrequent, and is often largely alcoholic and due to sleeplessness or to nights disturbed by nightmares and bad dreams.

Pruritus.—Itching of the skin is generally associated with jaundice, but may occur in its absence; it is not a common symptom, and when it does occur is usually seen late in the course of the disease.

Hanot[1] speaks of a case in which it occurred, and was persistent, a year before symptoms of cirrhosis developed, without any jaundice.

The more severe nervous symptoms are coma, delirium, convulsions, and paralyses. It has been thought that a large cirrhotic liver is more prone to be associated with grave nervous symptoms, but there is probably not enough to justify this view.

Coma.—Cases of cirrhosis which run their full course usually die with coma, often when ascites has disappeared (post-ascitic stage) or is stationary and small in amount. Coma is due to grave toxaemia, which may be purely hepatic and depend on the destruction of the hepatic cells being so widespread that the liver fails to stop poisons manufactured in the alimentary canal, as a result of which the circulation becomes flooded

[1] Hanot. *Arch. gén. de méd.*, 1896, clxxvii, 67.

with them. If the kidneys are active, the poisons may be got rid of, but in many cases coma is precipitated by failure in the excretory activity of the kidneys. Though coma is more commonly a terminal phenomenon, it may be transitory and be removed by treatment. I have several times seen coma disappear after intravenous transfusion; the same result may follow bleeding. A patient in a drowsy, semi-comatose condition may wake up sufficiently to try to get out of bed and then relapse into coma. Before the onset of coma there may be extreme irritability and restlessness, due to toxaemia and resembling that seen in uraemia.

Delirium may be terminal and precede coma, or more rarely it may temporarily supervene in the course of the disease and disappear. In the case of transient delirium it must be borne in mind that delirium tremens is not uncommon in the course of cirrhosis. I have seen short bouts of fever associated with delirium lasting two days or so, recur in a patient with cirrhosis before ascites developed. The character of the delirium varies; usually it is low and wandering, but occasionally it is very violent. The character of the delirium may change, or quiet and noisy phases may alternate.

Delirium tremens may occur in various circumstances in the course of cirrhosis. It may come on in the usual way from continued drinking in a patient with latent cirrhosis, or even when the disease has advanced into the stage of ascites. It may follow haematemesis, and then be more of the nature of traumatic delirium[1] and comparable to the delirium which is precipitated, so to speak, by a fractured thigh or pneumonia in an alcoholic subject. In other cases in which haematemesis is not very profuse, a mild form of delirium tremens may develop and may possibly be due to the treatment—viz. deprivation of food by the mouth for a few days.

Convulsions are sometimes seen at the close of the disease. Delirium often passes into coma, and convulsions may be added shortly before death.

Paralysis.—In addition to paraplegia due to peripheral neuritis of alcoholic origin, other forms of paralysis occasionally complicate cirrhosis. Cerebral haemorrhage or thrombosis may supervene, but usually when the cirrhosis is latent. In very rare instances hemiplegia occurs without any gross change to account for it.

In an alcoholic woman aged fifty-three, under my care in St. George's Hospital, with cirrhosis, the onset of right hemiplegia and aphasia suggested cerebral haemorrhage. At the necropsy no naked-eye morbid change could be found in the brain. The liver was markedly cirrhotic (weight, 70 ounces). Lévi[2] records terminal coma and facial paralysis in a man aged seventy with an alcoholic history and cirrhosis, and without any cerebral change except oedema.

It is possible that cirrhosis might dispose to cerebral haemorrhage by producing a haemorrhagic tendency. I have seen a case of cirrhosis in a

[1] Compare West, S. *Clin. Journ.*, 1895–6, vii, 58.
[2] Lévi. *Arch. gén. de méd.*, Paris, 1896, clxxviii, 165.

girl aged nine years in whom there were multiple cerebral haemorrhages, fever, and probably a terminal infection. Haemorrhagic pachymeningitis may be associated with cirrhosis; Heitz,[1] who has collected 7 cases of these combined lesions, regards them as independent results of alcoholism. It has been thought that thrombosis in the cerebral vessels may be disposed to by hepatic cirrhosis.

In a girl aged twelve years hemiplegia was due to thrombosis of the cerebral veins. There was ascites due to hepatic cirrhosis, and it was thought by Fisher[2] that the thrombosis depended on absorption of organic bodies from the peritoneal cavity.

There is an interesting group of cases, in which cirrhosis is latent and the symptoms are entirely nervous. It is usually familial, but is not hereditary, and may be sporadic. Gowers[3] described it as "tetanoid chorea," S. A. K. Wilson[4] as "progressive lenticular degeneration." Wilson collected 11 cases, about equally divided between the two sexes and proving fatal in the second or third decade. A mixed cirrhosis of the liver and symmetrical degeneration in the lenticular nuclei are constantly found. Homén[5] thought that the disease depended on hereditary syphilis; but Wilson, who excludes syphilis and alcohol, invokes a toxin probably not microbic (for clinical features *vide* p. 335).

Duration.—Portal cirrhosis commonly lasts a considerable time; one two, or more years usually intervene between the appearance of symptoms due to the liver, if indeed their first appearance can be accurately determined, and the termination of the case. The progress of the lesion in the liver may become arrested, and from compensatory changes the disease may become latent. Sometimes, however, the disease runs a very rapid course; in such cases there are a certain amount of fever, abdominal pain on the right side, enlargement and tenderness of the liver, oedema of the legs, haemorrhages, and the early development of ascites. These cases are more often seen in comparatively young subjects, who have been drinking heavily, and may run their course in two to six months. This condition of acute cirrhosis is allied to subacute diffuse hepatitis (*vide* Symmers[6]). When cirrhosis runs a very rapid course, degenerative changes take place in the liver cells and the condition is much the same as icterus gravis, only less acute.

Termination and Method of Death.—As has been pointed out (p. 227), cirrhosis may be latent owing to compensation having been effected. The compensatory anastomosis of the oesophageal veins with the gastric veins may be a source of danger, and sometimes very profuse and even fatal haematemesis may result from ulceration or rupture of an

[1] Heitz. *Rev. de méd.*, Paris, 1904, xxiv, 580.
[2] Fisher, T. *Lancet*, 1901, ii, 845.
[3] Gowers. *Rev. Neurol. and Psychiat.*, Edin., 1906, iv, 249.
[4] Wilson, S. A. K. *Brain*, Lond., 1912, xxxiv, 295.
[5] Homén. *Neurol. Centralbl.*, 1890, lx, 514.
[6] Symmers, D. *Am. Journ. Med. Sc.*, Phila., 1908, cxxxv, 251.

oesophageal varix. In such cases cirrhosis may be quite unsuspected, although the fatal issue is a direct result of hepatic cirrhosis.

In only 6 per cent of 35 cases of haematemesis from oesophageal veins were the cases typical of cirrhosis from a clinical point of view (Preble [1]).

Haematemesis is rarely directly fatal. In 80 cases fatal from the direct effects of cirrhosis examined at St. George's Hospital, 4, or 5 per cent, only were due to haematemesis; but Preble has collected 60 cases of fatal gastro-intestinal haemorrhage in cirrhosis. Death may occur after a single large haemorrhage or after a series of repeated haemorrhages. In a third of the cases collected by Preble death followed a single haemorrhage.

Before the onset of ascites, death may be due to various complications (*vide* p. 283), which frequently throw any symptoms due to cirrhosis into the shade. Some of these complications are due to alcoholism; thus, there can be little doubt that alcoholism is in great measure responsible for the frequency of tuberculosis, peripheral neuritis, and cardiac failure. Generalised tuberculosis may carry off a patient with cirrhosis long before loss of flesh and impairment of general nutrition have appeared. I have several times seen generalised tuberculosis in fat patients with cirrhosis.

When chronic renal disease is associated with cirrhosis of the liver, the clinical aspect is mainly that of kidney disease, and death usually results from uraemia, which, it may be noted, is very much like the late toxaemic stage of cirrhosis.

Acute infections, such as erysipelas and pneumonia, when they occur in the subjects of cirrhosis, are extremely likely to prove fatal. It has been said that acute infections of this kind are more fatal in portal cirrhosis than in hypertrophic biliary cirrhosis, since the liver cells are in a better state of preservation in the latter disease. Occasionally acute infection may fall on the liver itself and set up acute degenerative changes in the liver cells, and so give rise to symptoms resembling those of acute yellow atrophy. But inasmuch as the liver is not healthy previous to the acute infection, as is the case in acute yellow atrophy, it is perhaps more convenient to speak of the condition as icterus gravis. An acute infection may attack the smaller bile-ducts without affecting the liver cells to such a degree as to produce acute yellow atrophy, though the clinical resemblance is considerable.

An alcoholic waiter, aged forty-seven, had had haematemesis seven weeks before death; ascites, jaundice, and oedema of the feet subsequently developed; he was admitted into St. George's Hospital and was tapped; he remained jaundiced, and for the last three weeks of his life was delirious. The liver, 60 oz., shewed multilobular and unilobular cirrhosis, with inflammation of the small bile-ducts, which contained inspissated masses of bile. The spleen weighed 10 oz. and was soft.

[1] Preble. *Am. Journ. Med. Sc.*, 1900, cxix, 263.

When ascites has developed, death usually follows before the patient requires tapping more than twice. Indeed, if paracentesis has to be repeated several times, the case is either complicated with some degree of chronic peritonitis or is not one of cirrhosis at all. After one or two tappings the fluid may not reaccumulate and the patient may linger on for a time in a drowsy and very feeble condition—a post-ascitic stage. Death is usually due to increasing weakness and coma. There is often low, muttering delirium; active delirium is rare, but I have known it to be maniacal. More often the patient becomes more and more insensible and passes into deep coma. Occasionally while in this toxaemic state death may be precipitated by profuse haemorrhages from the stomach or rectum. Death may be due to some complication; in rare instances acute peritonitis results from infection by the trocar, but it occurs independently of tapping, and is then due to infection from within, either by the blood-stream or in rare instances from some lesion, such as tuberculous ulceration of the intestines, which allows micro-organisms to pass into the peritoneal cavity. Acute infections, such as pneumonia and erysipelas, may also prove fatal in a patient with ascites due to cirrhosis.

From a degenerated and fatty condition of the heart muscle sudden death may occur; this is by no means common in my experience; in 53 fatal cases of cirrhosis Cheadle[1] found that death occurred suddenly in this way in 6. More often a patient dies slowly with a failing heart but in a general toxaemic condition.

COMPLICATIONS.—**Tuberculosis.**—The liability of patients suffering from cirrhosis to be affected with tuberculosis of the lungs and peritoneum has been already referred to (*vide* p. 222). In about 12 to 14 per cent of cases with cirrhosis death is directly due to pulmonary tuberculosis; in many of these cases the cirrhosis is latent and is only discovered after death. In other instances pulmonary tuberculosis may escape detection or give rise to very few signs. Tuberculous peritonitis may not be suspected, as the ascites is very naturally regarded as due to cirrhosis. In tuberculous peritonitis supervening in cirrhosis there may be fever and more abdominal pain than in ordinary ascites, the onset of ascites may be very rapid, and if tapping be performed, the fluid is found of a higher specific gravity (1020) than in ordinary cirrhosis (1010); cytological examination shews that the predominating cells are lymphocytes instead of endothelial cells as in uncomplicated cirrhosis. In the following cases ascites was due to tuberculous peritonitis supervening in the course of cirrhosis:

A fat woman, aged forty-nine, with a marked alcoholic aspect, was admitted under my care at St. George's Hospital on January 9, 1902, with ascites, oedema of the feet, paraesthesia in the legs, and bronchitis. The liver was enlarged, the breath very foul, and there was morning sickness. She was treated as a case of cirrhosis, and on January 17 the abdomen was tapped;

[1] Cheadle, W. B. *Some Cirrhoses of the Liver*, 1900, p. 51.

the fluid was turbid and of a specific gravity of 1020 ; owing to the thickness of the abdominal wall it was difficult to get a trocar sufficiently long to reach the peritoneal cavity, and only about a pint of fluid was withdrawn. Death occurred on January 19. At the necropsy the liver (68 oz.) was markedly cirrhotic and microscopically contained much fat ; the spleen weighed 12½ oz. Some chronic peritonitis and recent generalised tuberculous peritonitis, old tubercle at the apices and much bronchitis in the lower lobes of both lungs, were found.

A man, aged forty-seven, considered himself as well till September 7, 1908, when the abdomen suddenly became swollen. He was admitted into St. George's Hospital on September 14 with extensive ascites and was tapped the same day, 20 pints of fluid being removed. The predominating cells were lymphocytes ; there were a few endothelial cells and polymorphonuclear cells. He had a dry tongue, a persistently raised temperature between 100° and 102° F., and died after thirty hours of coma on September 30, twenty-three days after the onset. The necropsy shewed old cirrhosis, recent tuberculous peritonitis, and an old vomica at the apex of one lung.

Generalised Tuberculosis.—In cirrhosis the possibility of generalised tuberculosis should be thought of when there is continued fever and the patient rapidly goes downhill without any appreciable ascites. Generalised tuberculosis may prove fatal in fat patients.

Bronchitis.—Some degree of bronchitis is not uncommon and may be an accidental accompaniment. On the other hand, it may be directly related to the cirrhosis, and may be due to collapse of the bases of the lungs from upward displacement and impaired movement of the diaphragm due to ascites, flatulence, or an enlarged liver. It may be part of a general catarrh from alcoholic excess or be the result of backward pressure from a failing heart. Since what appears to be bronchitis may be really rapid pulmonary tuberculosis, it is advisable to test the sputum for tubercle bacilli in cases of bronchitis in cirrhosis. In the following case rapid tuberculosis gave rise to the signs of general bronchitis :

A fat alcoholic man, aged fifty, who had had delirium tremens, was under my care for a few days in St. George's Hospital in March 1900. He had oedema of the feet and a haemorrhagic eruption on the legs, a dilated heart, a large liver, and general bronchitis ; the sputum contained a little blood. The urine (1020) was free from albumin. He was thought to have cirrhosis of the liver and backward pressure from cardiac dilatation, with possibly a pulmonary apoplexy. After being in for three days, with delirium at night, he quite suddenly died. At the necropsy the liver (108 oz.) shewed multilobular cirrhosis with much fatty change ; the left lobe overlapped the spleen, which weighed 28 oz. The kidneys weighed 9 oz. each and were healthy. There was no ascites. There was a pint of clear fluid in each pleural cavity and very dense adhesions at both apices. There were small cavities at both apices and recent firm caseous masses in the lower lobes and miliary tubercles throughout both lungs. There was no pulmonary apoplexy. There was bronchitis and tuberculous ulceration of the larynx. The heart (17 oz.) shewed fatty infiltration and degeneration and was dilated, but was free from valvular disease. Examination of the lungs shewed tubercle bacilli.

Pleurisy with Effusion is not uncommon and is often a manifestation of concomitant pulmonary tuberculosis. It is more frequent on the right side, and this is very probably due, as suggested by Villani,[1] to a spread of inflammation or infection from the liver through the diaphragm. The pleurisy may be acute and accompanied by pain and fever, or of an indolent and chronic character. In the latter event the condition is much like a hydrothorax, but, as already mentioned, it is often tuberculous.

James[2] records a curious case of ascites and right pleural effusion, in which a communication was thought to exist between the right pleura and the peritoneal cavity, inasmuch as tapping the pleura emptied the abdomen, and, in fact, seemed to be more effectual than paracentesis abdominis.

The fluid may be serous, sero-fibrinous, or in rare cases haemorrhagic. Haemorrhagic pleurisy is usually due to tuberculosis (Barjon and Henry,[3] Jean[4]), though it is possible that in the late stages it may be due to hepatic insufficiency. It has been suggested that the haemorrhagic character of the pleural effusion is sometimes due to alcoholism (Fernet[5]). A pleural effusion, especially on the right side, is more likely to be haemorrhagic than a concomitant ascites. The following case illustrates the relationship of tuberculosis and a haemorrhagic pleural effusion:

A man, aged forty-nine, died in St. George's Hospital with cirrhosis of the liver and tuberculosis. At the necropsy there was a pleural effusion on both sides—serous on the right side, haemorrhagic on the left side; there were numerous tubercles in the lung on the side of the haemorrhagic effusion.

In the following case the haemorrhagic character of the pleural effusion probably depended on trauma:

A billiard marker, aged forty-three, was admitted under my care with fever, a large right-sided pleural effusion, enlargement of the liver, and ascites. The effusion was twice tapped, and clear fluid was drawn off on both occasions, which contained neither tubercle bacilli nor pneumococci. He passed into a toxaemic condition, and although transfused, died without any improvement. His abdomen never required tapping. The right pleura contained much dark blood-stained fluid; the lung was collapsed and covered with lymph, which was haemorrhagic in one place and suggested that the blood had come from a newly formed vessel; there was a little obsolete tubercle at the apex. There was serous ascites, no chronic peritonitis, a multilobular cirrhotic liver (65 oz.) with small bilirubin-calcium calculi in the gall-bladder. The round ligament contained a big vein the size of the little finger (*vide* Fig. 35).

Taylor[6] records a case of haemorrhagic pleural effusion which was independent of tuberculosis and probably due to an acute infection.

[1] Villani. *Rif. med.*, Napoli, 1895, ix, pt. i., 686.
[2] James. *Trans. Med.-Chir. Soc.*, Edin., 1898–99, xviii, 191.
[3] Barjon et Henry. *Lyon méd.*, 1898, lxxxviii, 258.
[4] Jean. *Thèse de Paris*, 1891.
[5] Fernet. *Bull. Soc. méd. des hôp. de Paris*, 1900, 3. s., xvii, 781.
[6] Taylor, F. *Guy's Hosp. Rep.*, 1896, lii, 45.

The presence of a right-sided pleural effusion in a doubtful case is in favour of cirrhosis as against simple thrombosis of the portal vein, since it does not occur in the latter condition unless complicated by cirrhosis. It should, however, be borne in mind that some degree of dulness on percussion, loss of vocal vibrations and of breath sounds at the right base, may be due to upward projection of a large cirrhotic liver, or to a small cirrhotic liver pushed up by ascites, and not to any pleural effusion. In the same way friction at the right base may be due to local peritonitis and not to pleurisy.

Peripheral Neuritis.—The minor degrees of peripheral neuritis are often thrown into the shade by ascites or other effects of cirrhosis on which attention is focussed, and so pass undetected. Cramps, muscular tenderness, and loss of the tendo Achillis and knee jerks may occur in cases of cirrhosis admitted for ascites or haematemesis, and are, generally speaking, to be referred to alcoholism. Peripheral neuritis in the early stages of cirrhosis is usually alcoholic and may be associated with psychical symptoms, thus constituting Korsakoff's syndrome or polyneuritic psychosis. Well-marked alcoholic neuritis is commoner in women and is often associated with pulmonary tuberculosis; in such cases the liver is nearly always fatty and rarely cirrhotic, and the clinical picture is, in the main, that of neuritis.

In 114 cases in which the liver was cirrhotic at the necropsy there were 3 (females) cases in which death was due to alcoholic neuritis (Rolleston and Fenton). In 82 cases of cirrhotic livers at Charing Cross Hospital, there were 4 (2 males, 2 females) in which death was due to alcoholic neuritis (Candler [1]).

The terminal stages of cirrhosis are marked by symptoms due to hepatic insufficiency, such as epistaxis and other haemorrhages, delirium, and coma. The toxic coefficient of the urine will, if the kidneys be healthy, become increased as a result of the liver failing in its antitoxic function, and a toxaemic neuritis may result. If alcohol has been taken recently, the neuritis must be considered to be due to this cause, but in the absence of this factor hepatic insufficiency with resulting toxaemia is a satisfactory explanation. Very little alcohol may cause neuritis in advanced cirrhosis.

In a case of Gouget's [2] neuritis came on two weeks before death in a woman previously alcoholic, who, however, had had no stimulant for the two months that she had been in hospital. The arms and legs were simultaneously affected, which is unusual in the alcoholic form. Hayem observed the same type of neuritis in a case of primary carcinoma of the liver.

Delirium tremens has been dealt with on p. 280.

The occurrence of **chronic peritonitis** in the bodies of patients dying

[1] Candler. *Arch. Neurol. Claybury*, 1907, iii, 441. The literature of polyneuritis in cirrhosis is given by Klippel and Lhermitte, *Semaine méd.*, Paris, 1908, xxviii, 13.

[2] Quoted in Lévi's *Paris Thèse*, 1896.

with cirrhosis of the liver is referred to elsewhere (p. 223). The presence of chronic peritonitis in cirrhosis accounts for ascites, which lasts much longer than in cases of uncomplicated cirrhosis. As a result of chronic peritonitis the omentum may become rolled up and form a firm mass running across the abdomen.

In a case, recorded by Benham,[1] of cirrhosis complicated by chronic peritonitis the omentum and mesentery were thickened and matted together, and formed a pulsating mass during life.

Renal Disease.—The occurrence of albuminuria (*vide* p. 233), and the morbid lesions of the kidney (*vide* p. 224) in cirrhosis have been dealt with elsewhere. A priori it would naturally be expected that death would occur earlier in cirrhosis complicated by renal disease than in ordinary cirrhosis, inasmuch as the toxaemia depending on hepatic inadequacy would not be obviated by the excretion of toxic bodies by the kidneys. This hypothesis, however, is not supported by statistics. Both in Yeld's[2] figures from St. Bartholomew's Hospital and in the cases at St. George's Hospital the average age of patients dying with the combined conditions was higher than in those patients who succumbed to uncomplicated cirrhosis of the liver. When the two diseases are met with in the same person, the clinical symptoms are rather renal than hepatic. This is in accord with the hypothesis that in the combined condition the toxaemia would be more marked.

Gout not unnaturally figures in the history of some patients who come under observation with the symptoms of cirrhosis. Frank gout, however, is very rare in patients with active cirrhosis. A large liver, which may in some instances be due to early or latent cirrhosis, is not infrequent in gouty subjects.

In 43 cases of cirrhosis tabulated by Yeld the joints were healthy in 34 and contained uratic deposit in 9, or 21 per cent. In 5 of the 9 cases the kidneys were granular.

Terminal Infections are far from rare in cases of cirrhosis. Probably the bactericidal power of the blood is diminished as it is in chronic heart and kidney disease. Suppurative or fibrinous peritonitis is not a very uncommon termination; Garnier and Pignot[3] collected six examples of terminal pneumococcic peritonitis; streptococcic peritonitis may also occur; both of these forms may be independent of paracentesis. As already pointed out, tuberculous peritonitis may supervene in the course of cirrhosis.

Acute infection of the liver itself, giving rise to degeneration of the liver cells and to icterus gravis (Pitt,[4] Weber[5]), are probably not

[1] Benham, F. L. *Trans. Clin. Soc.*, 1895, xxviii, 226.
[2] Yeld, R. A. *St. Barth. Hosp. Rep.*, 1898, xxxiv, 215.
[3] Garnier et Pignot. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1911, 3. s., xxxi, 469.
[4] Pitt, G. N. *Trans. Path. Soc.*, Lond., 1889, xl, 351.
[5] Weber, F. P. *Ibid.*, 1899, l, 136.

very infrequent. Erysipelas, pericarditis, pneumonia, infective endocarditis, are also occasionally met with.

In 65 fatal cases of infective endocarditis tabulated by Kelynack [1] cirrhosis was found in 4. In the museum of St. Bartholomew's Hospital there is a spleen (2295 h) containing a mass of laminated blood-clot the size of an orange from a man who had cirrhosis of the liver and streptococcic endocarditis of the aortic valves.

In a case of cirrhosis of the liver Councilman [2] found infection with streptococci giving rise to purulent infiltration of the retroperitoneal glands, thrombosis of iliac veins and inferior vena cava, with secondary embolic infarcts in the lungs.

Thrombosis.—Thrombosis is rare in cirrhosis. Portal thrombosis when it occurs is frequently associated with cirrhosis, but it only occurred in 10, or 3·3 per cent, of 334 cases of cirrhosis examined after death at St. Bartholomew's Hospital (Langdon Brown [3]). I have seen severe phlebitis of the leg in the late stages of cirrhosis. A case of multiple thrombosis and haemorrhages was referred to on p. 278.

DIAGNOSIS.—Dyspepsia, often associated with evidences of alcoholic excess, of considerable duration, haematemesis which cannot be explained satisfactorily on other grounds, and enlargement of the liver and spleen, are the broad lines on which the disease can be diagnosed in the pre-ascitic stage. The onset of ascites in a patient who has manifested the above symptoms and is, in addition, more or less cachectic leaves little room for doubt that a late stage of cirrhosis has been reached.

The **differential diagnosis** of cirrhosis from other conditions has already been partially dealt with under the heads of ascites (p. 251) and haematemesis (p. 271). The diseases which simulate cirrhosis, in so far as the production of ascites and of gastro-intestinal haemorrhage are concerned, such as chronic peritonitis, in which is included perihepatitis, and gastric ulcer, have thus been considered.

From Hypertrophic Biliary Cirrhosis with Chronic Jaundice.—Portal and hypertrophic biliary cirrhosis, though distinct, may in certain instances be combined, and cases shew a transition from one to the other. It may be pointed out that the same blending of distinct types is seen in the case of kidney disease. Chronic parenchymatous nephritis, which may be compared to hypertrophic biliary cirrhosis, and the granular (arterio-sclerotic) kidney, which may be likened to portal cirrhosis, may overlap, run into each other, or be combined.

The clinical and anatomical features of the diseases may both be found in the same person; thus, in hypertrophic biliary cirrhosis a secondary portal cirrhosis frequently develops before death, and the patient, who has for years presented the symptoms and signs of biliary cirrhosis, dies with ascites and perhaps gastro-intestinal haemorrhage.

[1] Kelynack. *Encyclopaedia Medica*, 1900, iv, 365.
[2] Councilman, W. T. *Trans. Assoc. Am. Phys.*, 1896, xi, 213.
[3] Brown, Langdon. *St. Barth. Hosp. Rep.*, 1901, xxxvii, 62.

Cases of portal cirrhosis with a large liver and rather persistent jaundice occasionally occur and very closely imitate hypertrophic biliary cirrhosis; the distinction between the two depends on the jaundice not being permanent, on the slighter degree of splenic enlargement, and on the occurrence of ascites or other characteristic evidences of portal cirrhosis. In cases of portal cirrhosis which run an acute course, or in which more acute inflammatory changes supervene on portal cirrhosis of some standing and affect the bile-ducts, the clinical and anatomical features may shew a combination of biliary and portal cirrhosis (compare p. 323).

From other Enlargements of the Liver.—A patient may come under observation, say for examination for life insurance or for digestive disturbance, and be found to have an enlarged liver without any other manifestation of cirrhosis. The question then arises whether there is latent cirrhosis or some other morbid change in the liver. If there is proof or history of alcoholic excess, the enlargement may be due to fatty change, to early or to latent cirrhosis, or to temporary engorgement. If the organ is smooth, free from tenderness and pain, and the spleen is not palpably enlarged, the probabilities are in favour of fatty enlargement. Tenderness is in favour of engorgement or of early cirrhosis; enlargement of the spleen points to cirrhosis or to malarial hepatitis.

Malarial Enlargement.—As a result of chronic and severe malaria very considerable enlargement of the liver with tenderness on palpation results. This is combined with splenic enlargement and usually with irregular fever. The patient is much run down in health and weight, and the condition presented is very like that of early but advancing cirrhosis. The history that the patient, often a young man and not specially alcoholic, has been the subject of continued malaria abroad is important. Examination of the blood is of course essential. These cases often improve very rapidly under treatment in England, and the enlargement of the liver is much diminished or disappears entirely.

Chronic Venous Engorgement.—The enlarged liver due to the backward pressure of obstructive heart or lung disease may imitate a cirrhotic liver; especially as there is not infrequently a transient systolic apical murmur in cirrhosis. In forming a diagnosis the history and appearance of the patient and the presence of other signs of cirrhosis or of heart disease are important. Thus alcoholism, haematemesis, and an enlarged spleen point to cirrhosis, while rheumatic fever in the past, haemoptysis, and beneficial results from digitalis or strophanthus, are in favour of chronic venous engorgement.

In *leukaemia* the liver is often much enlarged, and epistaxis and haematemesis may occur. In the myeloid form the spleen is greatly enlarged, while in the chronic lymphatic form the superficial lymphatic glands are enlarged. The diagnosis is easily made by examination of the blood.

Malignant Tumours.—In the late stages when the patient is cachectic and ascites and jaundice are both present, the resemblance to malignant disease may be very close. In a patient over sixty years of age these

signs are in favour of malignant disease. Enlarged glands above the clavicle are strongly in favour of carcinoma. A history of chronic alcoholism, long-continued dyspepsia, and splenic enlargement suggest cirrhosis. In many instances doubt must exist until the abdomen is tapped and the liver can be thoroughly palpated.[1] If it is small, it is probably cirrhotic; if large and smooth, it might be either cirrhosis or massive cancer growing inside the organ, but the former is much more probable, both because primary cancer is rarer and because it need not give rise to either ascites or jaundice. Enlargement of the liver with multiple umbilicated nodules points to malignant disease (*vide* also p. 520).

A *hydatid cyst* deeply embedded in the substance of the liver expands the affected lobe, makes it prominent, firm, and enlarged, usually in a downward direction. In cirrhosis the enlargement is more uniform, affecting both lobes, and the surface is slightly irregular. It must, however, be remembered that when a large hydatid destroys a considerable amount of liver substance, compensatory hyperplasia of the other lobe may occur, and that the resulting enlargement may appear uniform, as in cirrhosis. A large cirrhotic liver, unless displaced forward by a flatulent stomach, which is only a temporary condition, or by some other cause, is not nearly so prominent as in hydatid disease. In hydatid the general health is good, whereas in cirrhosis there is usually some impairment, or signs of chronic alcoholism.

Syphilis of the Liver.—A history of syphilitic infection, manifest lesions elsewhere, or a positive Wassermann reaction would point to this explanation of an enlarged liver. In syphilitic disease the liver is often irregularly enlarged, whereas the two lobes of the liver are generally uniformly affected in latent cirrhosis. Pain is more frequent in syphilitic disease, and albuminuria, if present, is of diagnostic value as pointing to the probable existence of lardaceous disease. Sometimes all external manifestations of syphilis are wanting and the only clinical evidence forthcoming is diminution of the enlarged liver under a tentative course of anti-syphilitic remedies, which should always be employed in a case of doubtful nature.

In *splenic anaemia*, in which recurrent haematemeses are frequent, the splenic enlargement and the anaemia are more marked than in cirrhosis, and there is usually a diminution in the number of white blood-corpuscles, or leucopenia. The diagnosis between splenic anaemia and portal cirrhosis may be rather difficult, since, on the one hand, splenic anaemia may terminate in cirrhosis of the liver (Banti's disease), and, on the other hand, both haematemesis and ascites may occur in cases of splenic anaemia in which fibrosis of the liver is absent, as shewn after death. Splenic anaemia with periodic haematemesis is chiefly distinguished from portal cirrhosis by the greater degree of anaemia and of splenic enlargement.

Kala Azar.—In countries where this disease is endemic, the diagnosis from cirrhosis must depend on the presence or absence of the Leishman-

[1] Compare Landrieux. *Journ. des praticiens*, 1899, p. 737.

Donovan body. In Egypt there is a form of cirrhosis which must be distinguished from kala azar (Cummins [1]).

Intrahepatic Suppuration.—In acute cirrhosis accompanied by fever and considerable enlargement of the liver the diagnosis from intrahepatic suppuration might present difficulties. Haematemesis and an alcoholic history point to cirrhosis, while a hectic temperature, localised hepatic tenderness, leucocytosis, and a history of residence abroad and dysentery, or of conditions, such as recent appendicitis, suppurating piles, or gall-stones, which might lead to pylephlebitis or to suppurative cholangitis, are in favour of intrahepatic suppuration.

Carrington [2] described the case of a woman who had an enlarged liver and a temperature oscillating between 98·4° and 104°; pylephlebitis was diagnosed, but after death the liver weighed 72 ounces and shewed rapidly progressing cirrhosis and a fatty condition of the liver cells.

Enteric Fever.—In acute cirrhosis with a raised temperature there may be considerable resemblance to enteric fever. In patients who have been drinking heavily and present an enlarged liver and spleen, fever, and diarrhoea, a rapid diagnosis from enteric fever is sometimes only possible by means of a blood-culture or the agglutination test (Widal's reaction). In children with fever, diarrhoea, and swollen abdomen the suspicion of a perforating typhoid ulcer has even arisen (*vide* p. 220).

Intestinal obstruction has been suspected in a patient with repeated vomiting from alcoholic gastritis and abdominal distension from ascites. Considerable tympanites may come on rapidly with the onset of ascites. Careful examination of the patient's history and general condition should, however, correct a first impression of this kind and lead to appropriate treatment for the pressing gastric symptoms. Intestinal obstruction might conceivably occur from strangulation by a band of peritoneal adhesions in connexion with perihepatitis; and, of course, intestinal obstruction may occur in a patient with cirrhosis.

In Lusseau's [3] case of cirrhosis the third part of the duodenum was compressed by a cicatricial band.

Prognosis depends in great measure on the reparative power of the body and on its ability to compensate for the lesions of cirrhosis. Some discussion on the compensatory mechanisms is therefore necessary in order to obtain a clear idea of the problems involved in the prognosis.

The organism attempts to compensate for the evil effects of cirrhosis in two ways: (i) By a further development of the normal anastomoses between the tributaries of the portal vein and the general systemic veins (*vide* p. 209). (ii) By hyperplasia of the liver cells.

(i) Dilatation of the communications between the tributaries of the

[1] Cummins. "Kala Azar in the Anglo-Egyptian Sudan," *Third Report of Wellcome Research Lab., Gordon Memorial College, Khartoum*, 1908, p. 100.
[2] Carrington. *Guy's Hosp. Rep.*, 1883–4, series iii, xxvii, 337.
[3] Lusseau. *Progrès méd.*, Paris, 1879, vii, 545.

portal vein and the general systemic veins compensates for the mechanical obstruction to the passage of portal blood through the cirrhotic liver. It thus relieves the engorgement of the portal area, and should thereby tend to obviate haematemesis, and probably to delay the onset of ascites and possibly to assist in its removal.

If the effects of hepatic cirrhosis were chiefly mechanical and due to venous engorgement of the portal area, the more extensively the portal vein was put into communication with the inferior vena cava, the better would be the result. But a most important element in the pathological results of cirrhosis is the destruction of the liver cells and the necessary loss of their various functions, especially their antitoxic action, or the power of stopping poisons absorbed from the alimentary canal and preventing their entry into the general circulation. If, therefore, this collateral circulation be carried to its logical extreme, namely, by making the portal vein open directly into the inferior vena cava, or Eck's fistula, so that the portal circulation is short-circuited and the liver is virtually put outside the circulation, the results, as obtained by Hahn, Massen, Nencki, and Pawlow[1] on dogs, are very striking. The symptoms were much like those of uraemia; the urine contained carbamic acid, which is normally changed by the liver into urea. Similar symptoms were produced by intravenous injection of carbamic acid, and hence it was regarded as the cause of the toxic manifestations.

It is therefore probable that the good effects of the collateral circulation in cirrhosis are not purely mechanical. Possibly diversion of some of the blood from the liver relieves congestion of that organ and so enables it to deal more satisfactorily with the remaining blood that still passes to it. It is also conceivable that the state of nutrition of the organ is improved by relieving the congestion of the portal vein, and that it is thus able not only to be more active functionally, but to undergo compensatory hyperplasia to greater effect. This subject was also dealt with in considering the way in which the Talma-Morison operation for the relief of ascites does good (*vide* p. 260).

(ii) The second anatomical change by which an attempt is made to compensate for the evil effects of cirrhosis is multiplication of the liver cells (*vide* p. 207). As a result of this hyperplasia the liver increases in size. This attempt at compensation in cirrhosis is very general, but its success is variable; in many instances it is in vain. Though for a time it staves off the evil day and the disease remains latent, there is always the danger that the cirrhotic process may spread to the hyperplastic areas and that they may become engulfed like the rest of the liver; further, the adenomatous nodules may outgrow their nutrition and become necrotic; or they may undergo fatty change from some general cause such as toxaemia, for example in the nodular cirrhosis sometimes seen in tuberculosis.

In some instances the compensation is sufficiently good to restore a

[1] Hahn, Massen, Nencki, und Pawlow. *Arch. f. exper. Path. u. Pharmak.*, 1893, xxxii, 161.

fair equilibrium, and the disease is latent so long that it may be thought to be cured. There is hardly a return to perfect health, for there is a want of reserve power, and the compensation, if strained, may give way. The importance of this compensatory hyperplasia is well expressed in Hanot's dictum that the diagnosis of hepatic cirrhosis is made from the state of the connective tissues, and that the prognosis depends on the condition of the cells of the liver.

Period of the Disease.—In ordinary cirrhosis the prognosis is, generally speaking, gloomy, but there are several special points which must be taken into consideration. Thus the prognosis is necessarily different at an early and at a late period of the disease. It is quite possible for the earliest symptom of importance—haematemesis—to be succeeded by many years of life, and even for the cirrhosis, which gave rise to it, to remain permanently latent. But, though the disease may become latent, and remain so for years, the condition is not one of real cure. The morbid change in the liver, though compensated for, is still there, and may be restarted, or the compensatory mechanisms may fail. Thus, fatal haemorrhage may occur from dilated and varicose oesophageal veins, or, as just mentioned, fibrosis and fatty change may invade the areas of hyperplastic liver cells. The prognosis in the late stages is very bad, and ascites due to cirrhosis uncomplicated by chronic peritonitis is usually followed by death within a short time. A drowsy, sleepy condition points to a general toxaemia, and though it may be temporarily removed by treatment, it is prone to recur and pass into coma, and is therefore an extremely grave sign.

The **effect of treatment** has an important bearing on the prognosis from the point of view of preventing any further aggravation of the disease. Complete abstinence from alcohol is most essential, and on the patient's power of obedience his future will to a great extent depend. Marked improvement from iodides makes the prognosis good because it tends to alter the diagnosis of portal cirrhosis into that of syphilitic disease of the liver.

General Nutrition.—A well-nourished patient has naturally a much better prospect than an emaciated subject. The appearance of the face, haggard and sunken about the eyes and temporal fossae in cases rapidly going downhill, is an instinctively recognised guide in forming a very grave prognosis, while the nutrition of the skin elsewhere, and of the muscular development generally, is of considerable value. The presence of stigmata on the face has been said to be of bad prognosis, but as an isolated manifestation this has seemed to me of little value; a dirty, earthy tint of the skin is more significant of a general nutritional change.

Age has some influence on the prognosis. Thus, Cheadle[1] found that the average age of 37 cases in which temporary or prolonged improvement occurred was thirty-nine years, or nearly ten years less than the average age of fatal cases of cirrhosis. It is possible that in these cases

[1] Cheadle. *Some Cirrhoses of the Liver*, p. 72, 1900.

the cirrhosis developed rapidly as the result of heavy drinking, and that the process was not so advanced as in older subjects, in whom the fibrosis is formed more slowly. A comparatively early age is more favourable, inasmuch as the general nutrition is probably fairly preserved, and reparative and compensatory processes can be carried out efficiently. On the other hand, the prognosis in children is bad.

Size of the Liver.—From what has been said about compensatory hyperplasia it would appear probable that enlargement of the liver improves the prognosis, since it is more likely to be associated with latency of the disease than a small one. But this is not a hard-and-fast rule, since enlargement may be temporary and due to alcoholic excess, to absorption of poisonous products from the alimentary canal, or to complications such as cardiac failure and backward venous pressure. Further, in the early stage when the cirrhotic process is actively advancing, the liver is considerably enlarged. But in the absence of constitutional symptoms, complications, or other signs that the cirrhosis is active and progressive, the outlook is better in a case with a large than with a small liver. This is borne out by the fact (*vide* p. 197) that the liver is larger in persons affected with cirrhosis but dying from accident or from independent diseases than in patients dying directly from the disease. Most of the cases of cirrhosis reported as recoveries have enlarged livers. According to Hanot and Gilbert [1] and Cheadle, two-thirds of the cases conform to this statement. Cheadle dealt with no less than 30 cases in which recovery, either temporary or prolonged, resulted after tapping.

Enlargement of the spleen is present in progressive cases, and is absent, as a rule, in latent cases in which compensation has taken place. Its size is, therefore, an indication of some value, and in cases thought to be latent, splenic enlargement should suggest the possibility of approaching haematemesis, ascites, or toxaemia. It should be regarded as a danger-signal and as an indication for purgation by which portal engorgement and intestinal fermentation can be diminished or obviated. If the spleen remain enlarged after haematemesis, the possibility of a recurrence or of the near advent of ascites should be borne in mind.

Haematemesis is usually an early symptom; often, indeed, the first indication to the patient that he has anything serious the matter. In such cases the immediate prognosis is usually good, for the patient recovers, and may by a careful life escape any further manifestations of cirrhosis for years, or possibly for ever. Haematemesis is rarely fatal, but when it is so, the fatal haematemesis is usually the first. Haematemesis frequently repeated at short intervals is probably due to an ulcerated oesophageal vein, and the prognosis is worse than in the ordinary single haematemesis. When haematemesis occurs in patients with ascites, the prognosis is even more gloomy than it was before, as its occurrence makes it probable that the ascites is due to cirrhosis of the liver and not to concomitant chronic peritonitis.

Multiple or general haemorrhages, from the gums, throat, nose, skin,

[1] Hanot et Gilbert. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1890, 3. s., vii, 492.

etc., make the prognosis very grave, as they point to an advanced toxaemia, which may be succeeded by coma.

With the onset of **ascites** the patient's days are, as a rule, numbered. According to Hale White,[1] indeed, cases of uncomplicated cirrhosis, *i.e.* without chronic peritonitis, never survive to be tapped more than once. Though this may not be strictly in accord with general impression, and though recovery after paracentesis has often occurred in cases in which the existence of cirrhosis has subsequently been established after death from other causes, the gravity of ascites due to cirrhosis can hardly be overestimated.

But the onset of ascites in a patient thought to have cirrhosis must not be regarded as necessarily the equivalent of a death warrant. Many recoveries after paracentesis for ascites thought to be due to cirrhosis have been recorded (Bristowe,[2] Millard,[3] and Cheadle[4]).

An instructive case is mentioned by Hawkins[5] of a man who had been a hard drinker and was under Murchison in St. Thomas's Hospital with ascites. After this he became a total abstainer and lived in fair health for twelve years. At his death from pericarditis and granular kidneys, the liver was found to weigh 59 ounces, its capsule was much thickened and adherent to the diaphragm, and on section it shewed multilobular cirrhosis. Ehret[6] reports the details of a man who thirty years before his death, which was due to carcinoma of the oesophagus at the age of seventy-two, had jaundice, ascites requiring several tappings, and pain over the liver and spleen ; he became temperate. The liver was small and cirrhotic, the spleen large and surrounded by firm adhesions.

When, as in Hawkins' case, death subsequently occurs from some other cause, and the diagnosis of cirrhosis is confirmed, we must conclude that the compensatory mechanism is sufficient to explain the cure. It must be remembered that ascites associated with cirrhosis may be due to some concomitant cause, such as chronic peritonitis or mitral disease. In such cases death is less likely to supervene rapidly than in cases in which there is no cause for ascites other than cirrhosis. In ascites due to chronic peritonitis repeated tappings may be required, and the outlook as regards prolongation of life is better than in ascites due solely to cirrhosis.

If in a case thought to be cirrhosis the ascitic effusion is loculated from the presence of adhesions, it is probable that for this reason the prognosis is better than in cases in which there are no grounds to suspect adhesions. But, on the other hand, it is difficult to be certain that cases of loculated or encysted ascites are not entirely due to chronic peritonitis, to the exclusion of cirrhosis.

Oedema of the legs is, apart from any local cause, of bad omen, for it either points to a general toxaemia, cardiac debility, or is associated

[1] Hale White. *Guy's Hosp. Rep.*, 1892, xlix, 1.
[2] Bristowe. *Trans. Med. Soc.*, 1892, xv, 271.
[3] Millard. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1892, 3. s., ix, 153.
[4] Cheadle. *Some Cirrhoses of the Liver*, p. 69, 1900.
[5] Hawkins, H. P. Allbutt's *System of Medicine*, 1897, iv, 180.
[6] Ehret. *München. med. Wchnschr.*, 1903, xxxix, 321.

with, and possibly due to, pressure of the ascitic exudation on the inferior vena cava. In these conditions the outlook is extremely bad.

Functional activity of the kidneys, or renal permeability, is an important factor in the prognosis, and the urine should always be measured and examined, so that any feature in its amount and in its solid contents may be at once detected and treated. So long as the kidneys remove the toxic bodies which the cirrhotic liver allows to pass into the general circulation, the patient is in a fairly satisfactory state; but failure in the urinary excretion brings on a condition of hepatic toxaemia which resembles uraemia. The presence of diacetic acid, as shewn by a port-wine colour on the addition of ferric chloride, in the urine makes the prognosis very grave, as acid intoxication is imminent and may lead to coma.

Fever is met with in cases which run a comparatively acute course, or in the presence of some complication such as tuberculosis, and is therefore of bad prognosis.

Complications, such as pulmonary tuberculosis and peripheral neuritis, make the prognosis graver. When a granular kidney is associated with cirrhosis, the age at death is higher than in cases fatal from uncomplicated cirrhosis, and clinically the renal symptoms are more prominent. It need hardly be added that any acute infection, such as peritonitis, pericarditis, erysipelas, or pneumonia, necessarily makes the outlook extremely bad.

The integrity of the hepatic cells is of great importance in recovery from erysipelas (Roger and Garnier [1]). In ordinary cirrhosis in which the cells are much affected erysipelas is usually fatal. Ten cases of ordinary cirrhosis attacked with erysipelas all terminated fatally (Bridiers de Villemor [2]), whereas in hypertrophic biliary cirrhosis, in which the liver cells may remain intact and actively functional, recovery may be hoped for.

TREATMENT will be considered under the following heads:—

1. To prevent any further advance in the morbid change in the liver. This includes abstinence from alcohol, careful dieting, and special attention to the alimentary canal so as to prevent or minimise autointoxication. In the early pre-ascitic stage of cirrhosis these measures may be spoken of as prophylactic.

2. The palliative or symptomatic treatment. The treatment of conditions such as haematemesis (p. 273) and ascites (p. 257) will be found under those headings.

3. To promote the compensatory mechanisms by means of which the disease becomes latent.

1. **To Prevent and Remove Factors which favour the Morbid Change in the Liver.**—Irritating or toxic substances, such as alcoholic drinks and spicy or stimulating food, must be avoided. Alcohol must be entirely prohibited, and care should be taken not to give the patient

[1] Roger et Garnier. *Rev. de méd.*, Paris, 1901, xxi, 97.
[2] Bridiers de Villemor. *Thèse de Paris*, 1893–94, No. 428.

alcohol in his medicines. Thus, tinctures, alcoholic extracts and spirituous solutions, such as spiritus chloroformi, should be avoided, and infusions or watery extracts substituted. If it is impossible to prevent the patient taking some stimulant—a relaxation of his strict duty to the patient—the medical attendant should see that it is taken after meals and largely diluted. On a patient's power of will to become a total abstainer his future will largely depend. It may be very difficult, from the nature of their occupation, for some persons, such as those engaged in the liquor traffic and commercial travellers, to become teetotallers. In such instances change of occupation or retirement from business is advisable.

Most writers agree that in the last stages of the disease alcohol is necessary; according to Cheadle,[1] indeed, total deprivation of alcohol hastens the final collapse. The administration of alcohol in the very last stage, when death seems imminent in a few days, is really only a kindly act and directed to inducing euthanasia. Any attempt at curative treatment is over, and the passing of the bar is thus made easier.

Diet is a most important part of the treatment. The object is to minimise autointoxication and to prevent further progress of the cirrhotic process. Milk is the ideal diet; as the fat in it is well emulsified absorption takes place, even under the difficulties presented by intestinal catarrh. The protein of milk is much less harmful than the proteins of meat, since the putrefactive products derived from it are minimised and the liver is less taxed in the production of urea. Milk has some diuretic action on the kidneys and leaves little residue, so that gastro-intestinal autointoxication is much reduced. A patient should be put on milk diet and kept on it till his condition has markedly improved. Difficulty will often arise in getting the patient to carry out the strict diet, from its monotony. Four pints of milk may be given during the twenty-four hours, or a larger quantity of skimmed milk. Milk may be diluted with mineral waters, such as soda, Apollinaris, Vichy, Vals. A little bicarbonate of sodium may be added with advantage and may do good by antagonising acidosis. Milk may be given as junket, in the form of milk jelly, or flavoured with a little tea, coffee, or cocoa, or as a soup with a vegetable flavouring. Milk should be given every two or two and a half hours during the waking hours. When digestion is defective, milk should be peptonised or given in the form of Benger's food. In some persons milk gives rise to nausea. Herter[2] finds that this can be obviated by substituting skimmed milk. The percentage of fat is thus reduced from 4 to 1 per cent. Kumiss, or fermented mare's milk, may also be given when ordinary milk disagrees, but should not be continued longer than necessary. It is very readily absorbed, and may be given in much larger quantities than ordinary milk. Whitla[3] recommends buttermilk, or the kumiss made in Ireland by mixing half a pint of water, half a pint of buttermilk, and four pints of fresh milk, and one ounce of loaf sugar, leaving in a warm

[1] Cheadle. *Brit. Med. Journ.*, 1900, ii, 693.
[2] Herter, C. A. *Lectures on Chemical Pathology*, p. 88, 1902.
[3] Whitla, W. *Dictionary of Treatment*, p. 502, 3rd ed., 1896.

place for thirty-six hours and occasionally shaking. A trustworthy form of soured milk may be tried.

It has been said that a restricted milk diet is well borne by French and Italian, but not by German, patients. A milk diet should be maintained until improvement occurs; eggs and some easily digested farinaceous and protein foods should be added to the diet, and if these are well borne, pounded fish should be given after an interval. Beef-tea, meat essences, strong soups, and butcher's meat are not advisable. As a change, fruit and vegetables may be occasionally allowed. Stimulating and spicy food, such as curries, pickles, anchovies, pickled fish, vinegar, ginger, should be avoided. Fatty food, inasmuch as by fermentation it may give rise to fatty acids, such as acetic, lactic, butyric, valerianic, should be avoided. Coffee and tea should be taken in small quantities freely diluted with milk.

Carbohydrate Food.—The glycogenic function of the liver is well preserved in spite of the marked histological changes in the organ, and theoretically sugar and starchy foods should be readily assimilated. In practice carbohydrate food should be given in very small quantities and only increased if it is well borne. From the frequency of gastro-intestinal catarrh, fermentation is very likely to take place in sugary food and to give rise to dyspepsia, flatulence, and the production of acids, which when absorbed may further degenerative and cirrhotic changes in the liver.

A grapé cure, as much as 5 lbs. of ripe grapes daily, has been employed with some success by Cavazzini,[1] who ascribes good results to the sugar and the ferments in the grape juice.

Drugs.—Iodide of potassium should always be tried in cases thought to be cirrhosis of the liver, on the chance that the condition is in reality syphilitic. Whether iodides do any good in ordinary cirrhosis is very problematical, and no reliance can be placed on this drug or on chloride of ammonium, though it is well to give them a trial. Cases of early cirrhosis often improve under chloride of ammonium, but the other hygienic measures adopted may in reality have been responsible for the good effects ascribed to that drug. Iodoform has been employed internally instead of iodides, but has no advantage over them and may disturb gastric digestion. It is probable that the potash and ammonia given in these drugs are of definite value in counteracting incipient acidosis due to the formation of organic acids of the fatty acid series which tend to diminish the alkalinity of the blood. Whenever the urine gives a port-wine colour with ferric chloride (the fallacy of the reaction with salicylates and other drugs being eliminated), due to the presence of diacetic acid, bicarbonate of sodium should be given in large doses so as to counteract this acidosis.

It is very important to prevent or remove gastro-intestinal catarrh,

[1] Cavazzini. *Riv. crit. di clin. med.*, 1907, viii, 17.

which by the production of toxic bodies aggravates the changes in the liver. This can be most satisfactorily obtained by keeping the bowels freely open by salines, such as sulphate of sodium and of magnesium, natural Carlsbad or other mild purgative waters, and by giving fractional doses ($\frac{1}{40}$ to $\frac{1}{20}$ grain) of calomel, which prevent fermentation without purging or interfering with digestion. Arsenic, salicylates, capsicum, and the tinctures and spirituous solutions of drugs should be avoided.

Spa Treatment.—In the very early stages of the disease considerable benefit may be obtained from a course at one of the numerous spas. The regulated life enjoined when taking the cure and the effects of mildly purgative water in reducing portal engorgement and diminishing intestinal catarrh and fermentation are factors for good in the spa treatment of early cirrhosis, but little real benefit is likely to result in the later stages of the disease, and the fatigue necessitated by the journey is likely to diminish the failing powers of the patient. The following spas may be mentioned:—Harrogate, Llandrindod Wells, Vichy, Vals, Ems, Neuenahr, Homburg, Wiesbaden, Baden-Baden, Kissingen, Carlsbad, Marienbad, Franzensbad, Tarasp.

Splenectomy.—In cirrhosis due to poisons manufactured in the spleen (*vide* p. 188) removal of the spleen is a logical, if heroic, form of treatment. Out of seven patients thus treated two died from the operation (Jullien[1]).

2. **Palliative and Symptomatic Treatment.** — *Dyspepsia.* — The treatment of dyspepsia must depend on its nature; if it is irritative and due to gastritis, bismuth, dilute hydrocyanic acid, bicarbonate of sodium, are indicated. When it is atonic and due to inactivity of the gastric mucous membrane, tonics, such as dilute nitrohydrochloric acid, quassia, liquor strychninae, should be taken after meals, and pepsin in various forms may be given with food. For the relief of flatulence intestinal antiseptics, such as guaiacol, creosote, thymol, salol, naphthalene tetrachloride, and salicylate of bismuth, are often recommended; but it is better to give minute doses ($\frac{1}{40}$ to $\frac{1}{20}$ grain) of calomel twice or three times a day or saline purges.

Vomiting from gastritis should be treated by starvation for a time and by drugs, such as bismuth, bicarbonate of sodium, dilute hydrocyanic acid, or a little morphine. When food is resumed, after a few hours' rest, peptonised milk in small quantities should be given cold. The application of an ice-bag over the stomach has been thought to act as a sedative.

In the earlier stages *constipation* should be prevented by plenty of water, abdominal massage, and gentle exercise. Mild purgatives and laxatives should be employed if necessary, but powerful drugs, such as elaterium, should be avoided, as they may set up enteritis and exhausting diarrhoea. Salines, such as Epsom or Carlsbad salts; a mixture of two drams each of sulphate of magnesium and of sulphate of sodium; tartrate of sodium, or waters, such as Hunyadi János, Friedrichshall, Püllna,

[1] Jullien. *Arch. prov. de chir.*, Paris, 1911, xx, 90.

Æsculap, Apenta, and Franz Josef, may be taken with advantage before breakfast. If these means are not sufficient, a blue pill may be taken overnight in addition, or recourse may be had to small doses ($\frac{1}{6}$–$\frac{1}{2}$ grain) of calomel, or to cascara, rhubarb, scammony, euonymin, podophyllin, iridin.

Early in the disease *diarrhoea* or looseness of the bowels may be due to chronic alcoholism; if this is troublesome, bismuth, aromatic chalk and opium mixture, dilute sulphuric acid, tannigen, or, if really necessary, the enema opii should be given. The diet should, however, be supervised in the first instance, and alcohol strictly tabooed. In the late stage, when toxaemia has developed, diarrhoea may set in and kill the patient. But when slight, it is not always advisable to check the diarrhoea, as it may serve a useful purpose, like diarrhoea in advanced renal disease, in diminishing toxaemia.

Pain over the liver or the minor discomfort of weight and fulness may be relieved by the application of leeches or dry cupping. When the liver is enlarged relief may be experienced from the application of a bandage to support the organ. Hepatic pain and discomfort may be connected with active congestion of the liver, and should be treated by saline purges and by a few 20-grain doses of chloride of ammonium.

The drowsy, semi-comatose condition, due to toxaemia from hepatic insufficiency, may be relieved or even removed by transfusion of saline solution into the muscles or into the veins, the former being the more suitable; the transfusion may be repeated after twenty-four hours. I have seen a patient so improved that he went out of the hospital well: six months later he died of lobar pneumonia; at the necropsy the liver weighed 88 ounces and was markedly cirrhotic. In another case life was prolonged for seven and a half weeks after ascites had disappeared. On the other hand, transfusion often fails or gives rise to transient improvement only. Copious enemas of water may be given, but are not very successful. When diacetic acid is present in the urine, bicarbonate of sodium (℥ij to the pint) should be added to the water used for transfusion, so as to counteract acid intoxication. Hot-air baths often make the skin act and sometimes relieve the drowsy, toxaemic condition. Perspiration may be much accelerated by giving a hypodermic injection of pilocarpine ($\frac{1}{8}$–$\frac{1}{6}$ grain) before the bath; its depressing effect may be prevented by combining it with liquor strychninae.

Portal engorgement manifested by hepatic enlargement and tenderness, ascites, dyspepsia, and delay in the absorption of food (*vide* opsiuria, p. 232), is treated by saline purges. The increased osmosis into the bowels diminishes the pressure in the portal vein. Sulphate of magnesium and sulphate of sodium combined may be given on an empty stomach, alone or after a dose of calomel. The good effects are shewn by a considerable diminution in the size of the liver.

Direct puncture of the liver has been occasionally, but usually unintentionally, performed. In a case, mentioned by Goodhart,[1] in which it was done accidentally in tapping, the woman, who was evidently dying,

[1] Goodhart. *Guy's Hosp. Gaz.*, May 28, 1898.

was greatly improved by the withdrawal of blood from the liver. It is, however, dangerous, and should not be countenanced. Abstraction of blood from the spleen by means of a trocar has also been described as giving satisfactory results,[1] but it is dangerous and cannot be recommended. Massage to the abdomen, and especially to the liver, has been advocated to diminish the portal congestion which precedes haematemesis (Lecerf[2]).

Administration of Liver Substance.—Attempts have been made to compensate for the disturbance of hepatic function in cirrhosis by giving liver substance by the mouth, or injecting an extract of liver (hepatin) under the skin.

Mouras[3] collected 14 cases of cirrhosis treated in this manner, and though none could be regarded as cured, the results were encouraging; in 7 ascites disappeared and in the others improvement followed. The amounts of urine and of urea were increased, and the quantity of urobilin in the urine was diminished. In 26 cases collected by Gyr[4] in 1908 cure was reported in 13, a more optimistic estimate. Three or more ounces of pulped liver may be given daily. The only bad effect appears to be diarrhoea.

3. **To Promote the Compensatory Mechanisms by means of which the Disease becomes Latent.**—Nature's compensatory efforts in cirrhosis are (*a*) increase in the collateral circulation between the branches of the portal vein and the general systemic veins (*vide* p. 209) and (*b*) hyperplasia of the liver cells. These compensatory mechanisms have already been discussed in the section on Prognosis, and the operation for promoting vascular adhesions around the liver was described in the section on the Treatment of Ascites (p. 260).

Hyperplasia of the Liver Cells.—There is no drug, as far as is known, that can safely be employed for this purpose, though one would naturally turn to arsenic as likely, from its power of stimulating growth elsewhere, to have this effect. But it might set up gastro-intestinal irritation and autointoxication; and, indeed, there is reason to believe, both from increased frequency of ascites during the epidemic of arsenical poisoning in the north of England in 1899–1900 and from experimental results, that arsenic may cause cirrhosis. In the present state of our knowledge the administration of arsenic in cirrhosis is contraindicated. As was pointed out elsewhere, it is theoretically possible that the surgical production of vascular adhesions around the liver may improve the circulatory conditions and favour hyperplasia of the hepatic cells. It is hardly necessary to add that the general health should be improved as far as possible, and that fresh air, sun, and careful feeding are important factors in the treatment.

[1] Remlinger. *Journ. des praticiens*, 1901, p. 659.
[2] Lecerf. *Thèse de Paris*, 1901.
[3] Mouras. *Thèse de Paris*, 1901.
[4] Gyr. *Rev. méd. de la Suisse Rom.*, Genève, 1908, xxviii, 413.

PIGMENTED CIRRHOSIS

In the description of the histological appearances of portal cirrhosis it was pointed out that pigmentation of the liver cells and of the fibrous tissue may occur under certain conditions, and that some slight pigmentation of the cells is not uncommon in ordinary examples of the disease. Pigmentation of a cirrhotic liver may, in exceptional instances, be due to foreign particles of carbon, stone, or metals reaching it by the blood-stream (*vide* Cirrhosis anthracotica). Some degree of pigmentation with haemosiderin, an iron-containing derivative of haemoglobin, may be seen in cirrhotic livers after local haemorrhages into the substance of the organ. In the foregoing instances the amount of pigmentation is comparatively small and of little importance. The more important forms of pigmented cirrhosis are (i) that occurring in haemochromatosis and bronzed diabetes, and (ii) malarial pigmentation of a cirrhotic liver.

Cirrhosis Anthracotica.—In this very rare condition cirrhosis of the liver is associated with the presence of small masses of carbon in the organ. It is analogous to anthracosis of the lungs (coal-miner's lung). Welch [1] described such a case, and Adami [2] speaks of a similar condition in relation to silicosis. The condition is probably not so rare as the paucity of recorded cases would suggest, as it may not be detected unless the liver is microscopically examined.

A chimney-sweep aged forty-seven was admitted to St. George's Hospital on June 4, 1892, with a transverse fracture of the left leg; a month later he had parotitis, and on September 8 he became jaundiced and ascitic; ten days later the abdomen was tapped, and on September 25 he died from asthenia. The trachea, lungs, and stomach were deeply pigmented. The liver (59 oz.) was cirrhotic, but not pigmented to the naked eye. Microscopically there was old multilobular cirrhosis with rather extensive pigmentation of the fibrous tissues. The pigment was black and amorphous, quite different from the yellow pigment

[1] Welch, W. H. *Johns Hopkins Hosp. Bull.*, 1891, ii, 32.
[2] Adami, J. G. *Sajous' Annual*, 1898, ii, 313, article "Cirrhosis."

of haemochromatosis, and was probably soot conveyed by the portal vein to the liver. It is quite possible that such pigmentation of sweeps' livers in some degree is not uncommon. Alburger [1] described a case in a woman and suggested that the carbonaceous pigmentation depended on disease of the bronchial glands whereby their normal filtering action is impaired.

PIGMENTARY CIRRHOSIS OF HAEMOCHROMATOSIS.—*Synonym*: Diabète Bronzé.—**History and Etiology.**—Bronzed diabetes, or diabète bronzé, was first noticed by Troisier [2] in 1871, and was referred to by Trousseau in his clinical lectures. Hanot and Chauffard [3] in 1882 described two cases of diabetes with enlarged and pigmented cirrhotic livers. In 1886 Hanot,[4] in collaboration with Schachmann, described a further case and defined the condition as a morbid entity under the name "diabète bronzé." They took the view that the diabetes was the primary lesion, and that as a result the hepatic cell became stimulated to an increased production of pigment. Letulle [5] believed that as a result of hyperglycaemia the pigment was formed from the haemoglobin by the cells of various organs, and that it was stored up in the liver cells, though not produced there. In France the association with diabetes has been mainly insisted on. In Germany more attention has been paid to general pathological pigmentation without glycosuria. In 1889 v. Recklinghausen [6] described the condition of haemochromatosis, which consists in infiltration of the organs with pigment.

Opie [7] suggested that a toxin both causes haemolysis and acts on the cells of the liver and other organs so that they transform the soluble blood pigment reaching them into insoluble haemosiderin. Repeated injections of toluylenediamine into dogs have produced some pigmentation of the liver and other organs with an iron-containing body (Auscher and Lapique,[8] Meunier,[9] Biondi [10]); but the results are not comparable to haemochromatosis. Adami [11] and M. Abbott [12] regard bacterial activity as the cause both of the haemolysis and of the degenerative changes in the cells of the pigmented viscera, and suggest that it is a chronic intestinal infection. Examination of the blood, however, does not shew evidence of anaemia, haemolysis, or of haemolysins (Elmer [13]); and the bone marrow does not shew hyperplasia. Sprunt [14] suggests that haemochromatosis is a metabolic disease causing pigmentary degeneration

[1] Alburger. *Proc. Path. Soc.*, Phila., 1905, p. 137.
[2] Troisier. *Bull. Soc. Anat.*, Paris, 1871, xlvi, 231.
[3] Hanot et Chauffard. *Rev. de méd.*, Paris, 1882, ii, 385.
[4] Hanot et Schachmann. *Arch. de physiol. norm. et path.*, Paris, 1886, 3. s., vii, 50.
[5] Letulle. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1897, 3. s., xiv, 205.
[6] Von Recklinghausen. *Tagebl. d. Versamml. deutsch. Naturf. u. Aerzte*, Heidelberg, 1889, S. 324.
[7] Opie. *Journ. exper. Med.*, 1899, iv, 279.
[8] Auscher et Lapique. *Compt. rend. Soc. Biol.*, Paris, 1895, xlvii, 402.
[9] Meunier. *Thèse de Paris*, 1898.
[10] Biondi. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1895, xviii, 176.
[11] Adami. *Journ. Am. Med. Assoc.*, 1899, xxxiii, 1506.
[12] Abbott, M. *Journ. Path. and Bacteriol.*, Edin. and Lond., 1901, vii, 55.
[13] Elmer. *Interstate Med. Journ.*, St. Louis, 1911, xviii, 912.
[14] Sprunt. *Arch. Int. Med.*, Chicago, 1911, viii, 75.

of the cells followed by a reactive fibrosis of the organs, and not the result of blood-destruction. In the light of chronic haemolytic jaundice, the absence of jaundice in haemochromatosis militates against the existence of haemolysis. Potter and Milne,[1] who collected 51 cases of bronzed diabetes, consider that hepatic cirrhosis is the primary change and that there is an exaggeration of the siderosis often present in that disease (*vide* p. 207). There is not any evidence that suprarenal insufficiency is responsible for haemochromatosis.

Pigmentation occurs in the cells of the liver, pancreas, and secreting glands, in the interstitial tissue of these organs, in the lymphatic glands, in the heart muscle, intestines, and least of all in the skin. There are two pigments. The cells and interstitial tissue of the liver, pancreas, secreting and lymphatic glands contain a ferruginous pigment, haemosiderin. Whereas in the muscular fibres of the intestines and heart, and sometimes in the liver (Potter and Milne), an iron-free pigment called haemofuscin is found. The iron-containing pigment is present in much larger amount than the iron-free pigment. The relation of these two pigments offers scope for discussion; the iron-free may be only a later stage of the iron-containing pigment (M. B. Schmidt[2]), or they may be independent. Goebel[3] found this iron-free pigment in the smooth muscular fibres of various organs in old persons, so it may be regarded as more or less physiological.

The pigmentation of the skin is due to an iron-free pigment, apparently the same as the normal (Opie). The muscular fibres of the heart contain both haemosiderin and haemofuscin. In the earlier stages of haemochromatosis the pigment accumulates in the cells of the organs, the liver being most affected. The general opinion as to the sequence of events is that as the cells become infiltrated with pigment, they progressively degenerate, undergo necrosis, and liberate the pigment, which passes into the interstitial fibrous tissue of the organ; and that interstitial fibrosis of the liver and pancreas develops in the wake of the pigmentary change. It has, however, been thought that the pigmentation is secondary to the hepatic cirrhosis (Potter and Milne). When the fibrosis of the pancreas reaches an extreme degree, with disappearance of the islands of Langerhans, diabetes results. Diabetes mellitus is therefore a late result of the haemochromatosis. The condition is not common; in 1897 Letulle collected 30 cases, in 1906 Futcher[4] 35 cases, and 1911 Sprunt 50 cases of bronzed diabetes and 13 without diabetes.

A man aged fifty-two died in a drowsy state after paracentesis for ascites in 1902 under my care in St. George's Hospital. The liver was cirrhotic and of a greenish-blue colour. Multilobular cirrhosis with very well-marked haemo-

[1] Potter and Milne. *Am. Journ. Med. Sc.*, Phila., 1912, cxliii, 46.
[2] Schmidt, M. B. *Virchows Arch.*, 1889, cxv, 397.
[3] Goebel. *Ibid.*, 1894, cxxxvi, 482.
[4] Futcher. *Am. Journ. Med. Sc.*, Phila., 1907, cxxxiii, 78.

chromatosis was then found. During life there had been no glycosuria, and the skin, though somewhat earthy in colour, was not noticeably pigmented. The pancreas was not kept for microscopic examination, as the body was decomposed and no suspicion of haemochromatosis arose until after microscopic examination of the liver. In 1907 I saw in consultation a man aged sixty-six with ascites, an alcoholic history, diabetes, and diacetic acid in the urine ; the skin was somewhat pigmented. The abdomen was tapped twice and he died comatose. At the necropsy there was old cirrhosis of the liver with marked haemochromatosis ; the pancreas was much pigmented, and the intestines were of a leaden colour. Loehlein [1] has collected 3 cases of primary carcinoma in livers with cirrhosis due to haemochromatosis. I have seen extensive haemochromatosis with cirrhosis in a liver shewing secondary endotheliomatous growths (Fig. 72). In the museum of St. Bartholomew's Hospital there is a piece of liver shewing a simple cyst, which has the characteristic brick-red colour of the liver in haemochromatosis.

Probably pigmentation of the liver often assumed to be due to past malaria is in reality caused by haemochromatosis.

Age.—Haemochromatosis occurs chiefly between forty and fifty years of age.

Sex.—In Futcher's 35 cases of bronzed diabetes there were 33 males and 2 females ; about the authenticity of the 2 female cases there is room for suspicion. Since then Roberts [2] described a case in a woman. In M. Abbott's case of haemochromatosis and cirrhosis in a woman diabetes had not appeared.

Morbid Anatomy.—The liver is nearly always enlarged, sometimes considerably ; the left lobe may be larger than the right. It has a striking deep-red or maroon colour, resembling that of brick dust or iron rust, and shews multilobular cirrhosis. As might naturally be expected, the pigmented liver is less permeable to Röntgen rays than a normal one (Jeanselme [3]). Microscopically there is a brownish-yellow pigment, which gives the reaction for iron with ferrocyanide of potassium and hydrochloric acid (Perl's test) in the liver cells, in the endothelial cells lining the vessels, in Kupffer's star-like cells, and in the fibrous tissue enclosing the lobules. The pigment collects first in the liver cells in the periphery of the lobules ; as it accumulates the cell nucleus shews signs of degeneration, and eventually the cells necrose and break up. The pigment is picked up by endothelial leucocytes which collect in the lymphatics and mechanically damage the connective tissues so that proliferation of the fibroblasts follows (Mallory [4]). The hepatic artery shews endarteritis obliterans. The muscular coat and adventitia of the arteries and veins contain haemofuscin.

The *spleen* is enlarged, firm, and pigmented. The *pancreas* is enlarged, pigmented, and shews chronic interstitial fibrosis. The *suprarenals* do not shew any constant change. The *intestines* are pigmented

[1] Loehlein. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1907, xlii, 539.
[2] Roberts, M. *Brit. Med. Journ.*, 1911, ii, 1248.
[3] Jeanselme. *Presse méd.*, Paris, 1897, p. 58.
[4] Mallory. *Johns Hopkins Hosp. Bull.*, Balt., 1911, xxii, 71.

from haemofuscin in the muscular fibres and haemosiderin in the epithelial cells of the glands.

The **symptoms** may be those of cirrhosis or of diabetes (diabète bronzé). The signs are generalised pigmentation with enlargement of the liver and spleen. The pigmentation of the skin is chiefly on the exposed parts of the body, and its occurrence may perhaps be determined by sunlight (Potter and Milne); it may be of a slaty colour and might suggest the rare condition of argyria, in which the skin becomes permanently dis-

FIG. 38.—Pigmentation of the liver cells and fibrous tissue in cirrhosis of haemochromatosis. Some of the pigmented cells shew degeneration, and in some instances the outlines of the cells around the collections of pigment have gone. (From case described by Dr. Maude Abbott, who kindly provided me with some of the liver.) × 220.

coloured as a result of the medicinal use of silver salts. Generalised pigmentation is present in most but not in all the cases; when it is absent the existence of pigmented cirrhosis is only discovered after death.

The liver is usually, but not always, bigger than in health. The enlargement of the liver and spleen is usually progressive and relatively equal (Osler [1]). In a certain number of cases haemorrhages occur, and in a few instances there have been recurrent attacks of purpura, especially on the legs (Anschutz [2]). Abbott's case died of haemorrhage from an ulcerated oesophageal varix. There may be ascites, which has been found to contain sugar (Margain [3]), and the subcutaneous abdominal

[1] Osler. *Am. Journ. Med. Sc.*, 1902, cxxiv, 766.
[2] Anschutz. *Deutsches Arch. f. klin. Med.*, Leipz., 1899, lxii, 411.
[3] Margain. *Rev. de méd.*, Paris, 1905, xxv, 214.

veins may be dilated. There may be dyspepsia and pain on the right side of the abdomen. Diabetes is a late phenomenon and does not always supervene ; when it does, it usually appears a year before death. It is severe in form, and is nearly always accompanied by acidosis. The onset may be somewhat abrupt, with weakness, diarrhoea, oedema of the legs, and may lead to death from coma or from destructive lung changes.

Diagnosis.—Signs of cirrhosis, glycosuria, and pigmentation of the skin justify a certain diagnosis. In cases of cirrhosis with cutaneous pigmentation, but with no glycosuria, the disease may be suspected, but unless the pigmentation is very considerable cannot be positively diagnosed, since a dirty earthy colour is not uncommon in ordinary cirrhosis, and past jaundice may discolour the skin. As bearing on the question of diagnosis it may be mentioned that diabetes occurs in 2 per cent of all cases of cirrhosis (Potter and Milne), that cirrhosis occurs in 5 per cent of all cases of diabetes (Simmonds [1]), and that Futcher noted bronzing twice in 256 cases of diabetes.

Differential Diagnosis.—From *Addison's* disease the enlargement of the liver and spleen and glycosuria should distinguish it. In some instances of *hypertrophic biliary cirrhosis* the colour of the skin may resemble that of haemochromatosis, but the existence of jaundice as shewn by the conjunctivae should prevent a mistake. In *chronic splenic anaemia* there is sometimes cutaneous pigmentation, possibly from the effects of arsenic given medicinally, and some resemblance to haemochromatosis without glycosuria might result. The spleen is greatly enlarged in splenic anaemia, and only moderately in haemochromatosis, while the course of the disease is usually prolonged in splenic anaemia.

In most exceptional cases alcaptonuria may be associated with remarkable pigmentation of the face, ears, and internally of the costal cartilages (*ochronosis*, Virchow). In these cases the reduction of copper by the urine might suggest bronzed diabetes ; further examination of the urine would, however, prove the absence of sugar.

Prognosis is bad. Life may be prolonged for years and death may occur from gastro-intestinal haemorrhage as in cirrhosis. When diabetes appears, the fatal termination is usually not delayed beyond a year.

Treatment.—If there is diabetes, the treatment should be directed to that condition by appropriate dieting, opium, and alkalis. Before the onset of glycosuria the treatment should be the same as that of early cirrhosis, viz. a bland diet and drugs directed to prevent intestinal fermentation and putrefaction.

Malarial Pigmentation of a Cirrhotic Liver. — In the past malaria was regarded as an established cause of hepatic cirrhosis, and several forms of malarial cirrhosis were described. Frerichs, Lancereaux, Phillips,[2] and Kelsch and Kiener [3] recognised malaria as a cause of hepatitis, and the two latter described in great detail the changes induced

[1] Simmonds. *Berlin. klin. Wchnschr.*, 1909, xli, 531.
[2] Phillips, L. P. *Records of the Egyptian Government School of Medicine*, 1904, ii, 47.
[3] Kelsch et Kiener. *Arch. de physiol. norm. et path.*, 1878, p. 571 ; 1879, p. 354.

in the liver by chronic malaria. In one form, called "hyperhémie phlegmasique," the liver is large, shews perihepatitis, cloudy swelling of the liver cells, and small-celled infiltration of the portal spaces. In another form, nodular parenchymatous hepatitis, the liver is large, soft, and contains small nodules composed of liver cells undergoing hyperplasia; cirrhosis may subsequently develop. Kelsch and Kiener believed that the fibrosis was due to metaplasia of the liver cells, but the view that connective tissue is formed from epithelial cells is entirely opposed to modern pathological teaching. The resulting cirrhosis is described as either unilobular or multilobular. Both the fibrous tissue and the liver cells are infiltrated with pigment.

As Barker[1] points out, the degenerative and necrotic changes in the liver cells produced by severe malarial infection are exactly the conditions favourable to the production of chronic fibrosis of the liver. Further, in malaria there may be considerable gastro-intestinal disturbance which might lead to cirrhosis of the liver, and it has also been thought that the production of poisons in the spleen might cause secondary cirrhosis (Chauffard,[2] *vide* p. 188). Barker suggested that the pigmentation of the liver cells, which is most marked in the peripheral parts of the lobules, may act as an irritant and set up fibrosis of the organ, in the same way that the inhalation of carbon particles induces pneumoconiosis. Osler,[3] on the other hand, says that during fifteen years' practice at the Johns Hopkins Hospital there was no case of advanced cirrhosis due to malaria. Welch is quoted by Barker as having seen only one case of malarial cirrhosis in New York, and that in an Algerian.

Without denying the possibility that the necrotic changes in the liver cells induced by malaria may be succeeded by cirrhosis, this sequence of events is evidently so rare that when cirrhosis occurs in a malarial subject the question must arise whether it is cirrhosis caused by malaria or merely cirrhosis in a malarial patient. Alcohol and intestinal toxaemia may be potent causes of hepatic cirrhosis in patients suffering from chronic malaria, or a patient with latent cirrhosis may contract malaria. In either of these events the liberated blood pigment may be deposited in the liver and produce a pigmented cirrhosis. Clinically there is nothing very special in cirrhosis in a malarial subject. The signs are those of ordinary portal cirrhosis terminating with ascites. From the influence of malaria the spleen is more markedly enlarged than in ordinary portal cirrhosis.

[1] Barker. *Johns Hopkins Hosp. Rep.*, 1895, v, 221.
[2] Chauffard. *Semaine méd.*, Paris, 1899, xix, 177.
[3] Osler, W. *Practice of Med.*, p. 557, 5th ed., 1905.

BILIARY CIRRHOSIS

Biliary cirrhosis will be considered under two distinct heads: (i) Hypertrophic biliary cirrhosis, and (ii) obstructive biliary cirrhosis.

Hypertrophic Biliary Cirrhosis

It is sometimes spoken of as "hypertrophic cirrhosis." This is likely to lead to confusion, as there are several other kinds of large cirrhotic livers; in common or portal cirrhosis the organ is often much enlarged, a fatty cirrhotic liver is of very considerable size, and the pigmented cirrhotic liver in haemochromatosis is also entitled to the adjective hypertrophic. The term "hypertrophic cirrhosis" should therefore be given up.

Definition.—The disease is characterised by chronic jaundice, periodic febrile attacks, absence of ascites, enlargement of the liver and spleen, and by its preference for young persons. There is no gross obstruction in the larger bile-ducts, and histologically the cirrhosis is more unilobular than in portal cirrhosis.

History.—Although the condition was recognised by Requin[1] in 1846, by Todd[2] eleven years later (1857), and by Hayem in 1874,[3] it attracted little attention until Hanot[4] (1875) sharply struck out the disease in his thesis on "Hypertrophic Cirrhosis with Chronic Jaundice."

Hanot's thesis was based on 15 cases, 4 of which he had observed during life; in 3 of the 4 a necropsy was obtained.

In 1893 Kiener[5] suggested that the disease should be called Hanot's disease. Since then somewhat different though allied forms of hypertrophic biliary cirrhosis have been described in France (*vide* p. 310), and discussion has arisen as to the channel by which the cause of the disease reaches the liver. For some years the opinion has been growing that the description given by Hanot was too crystallised, and that few cases conform to the rigid type he erected. It has also been suggested that the symptoms and signs do not correspond to any one anatomical change in the liver, but may be associated with various forms of cirrhosis. Oertel[6] denies that the morbid appearances are sufficiently characteristic to justify the recognition of a special form; Meyer[7] takes the same view, and some writers in this country consider that no real distinction

[1] Requin. *Pathologie méd.*, tome ii, p. 748.
[2] Todd. *Med. Times and Gaz.*, 1857, xv, 571.
[3] Hayem. *Arch. de physiol. norm. et path.*, Paris, 1874, 2. s., i, 126.
[4] Hanot. *Thèse de Paris*, 1875.
[5] Kiener. *Semaine méd.*, Paris, 1893, xiii, 345.
[6] Oertel. *Arch. Int. Med.*, Chicago, 1908, i, 394.
[7] Meyer. *München. med. Wchnschr.*, 1908, lv, 2276.

can be drawn between portal and hypertrophic biliary cirrhosis. Further, the clinical features of hypertrophic biliary cirrhosis occur in cases which on necropsy shew portal cirrhosis. This discrepancy between the clinical picture and the morbid changes is probably due to the fact that cirrhosis, wherever it begins, will after a time spread and lead to a mixed cirrhosis. Thus, there is a special tendency for changes presumably beginning in the small bile-ducts to become complicated in course of time by those of portal cirrhosis. After much consideration of the question I have come to the conclusion that there is an essential difference, both clinically and pathologically, between portal and hypertrophic biliary cirrhosis, and that Hanot and the French school are fully justified in their contention. No doubt transitional forms between the two types of cirrhosis occur, just as they do between the arteriosclerotic (granular) kidney and that of chronic parenchymatous nephritis (large white kidney); but it would be incorrect to assume that they are different manifestations of the same process. Although different types exist, it is advisable to give an inclusive description of the disease as a whole, and to draw attention to the varieties which may occur.

Different Forms of Hypertrophic Biliary Cirrhosis.—A number of cumbrous names have been coined to distinguish varieties of the disease. These varieties depend on differences in the degree of the splenic and hepatic enlargement, and on the relationship between the enlargement of the two organs, both in size and in the date of appearance. The following forms were described by Gilbert,[1] Chauffard,[2] and Lereboullet. *Ordinary form of hypertrophic biliary cirrhosis*, described by Hanot, in which the liver and spleen are both enlarged. *Splenomegalic form*, in which the splenic enlargement is the predominant feature. *Hypersplenomegalic form*, in which the spleen is actually larger than the liver. *Metasplenomegalic form*, in which splenic enlargement precedes any manifest change in the liver. *Hepatomegalic* or *microsplenomegalic form*, in which the enlargement of the liver is the prominent feature; the spleen may not be enlarged (asplenomegalic form). *Presplenomegalic form*, in which the enlargement of the liver precedes that of the spleen. *Atrophic biliary cirrhosis*, in which the liver is small. A special *juvenile type* with great splenic enlargement was described by Gilbert and Fournier.[3]

In the cases in which the spleen is considerably enlarged before the liver is noticed to be affected — metasplenomegalic hypertrophic biliary cirrhosis—Chauffard believes the hepatic cirrhosis to be due to poisons manufactured in the spleen, and that the disease is a different one from the ordinary type. There is a gradual transition from the less marked examples of metasplenomegalic biliary cirrhosis to Banti's disease or splenic anaemia with a terminal cirrhosis. Cases without jaundice, "Cirrhose biliaire anictérique," have also been described.

[1] Gilbert. *Semaine méd.*, Paris, 1900, xx, 154.
[2] Chauffard. *Ibid.*, 1900, xx, 176.
[3] Gilbert et Fournier. *Compt. rend. Soc. Biol.*, 1895, xlvii, 419.

Some Forms of Disease possibly allied to Hypertrophic Biliary Cirrhosis.—As in many other diseases, there are less characteristic cases ("fruste" or larval) which present some of the features of biliary cirrhosis, but are incomplete and wanting in others. Thus, as just mentioned, there may be transitional cases between splenic anaemia and hypertrophic biliary cirrhosis. Barlow and Shaw[1] published two cases of recurrent attacks of jaundice and abdominal crises with enlargement of the liver and spleen, in a mother and son, which seem to form a connecting link between hypertrophic biliary cirrhosis and chronic splenic anaemia. Chronic haemolytic jaundice (*vide* p. 537) also resembles biliary cirrhosis, especially the metasplenomegalic form in which the spleen is enlarged before the liver.

Incidence.—Genuine cases of hypertrophic biliary cirrhosis are distinctly rare; this contrasts with the frequency of portal cirrhosis. The rarity of the disease is perhaps not fully recognised since cases of ordinary cirrhosis with large livers but without persistent jaundice are not infrequently confused with it.

Etiology.—*Age.*—It is commonest between the ages of twenty and thirty and is rare after forty, thus again contrasting with common cirrhosis in which the average age is about forty-eight years. A considerable number of cases occur in young children (Gilbert and Fournier's juvenile form).

Sex.—In children the incidence of the disease falls fairly equally on the two sexes. In 22 cases collected by Morley Fletcher,[2] including Gilbert and Fournier's 7 cases, there were 13 male and 9 female children. In adult life males are more often attacked. In Schachmann's[3] 26 cases only 4 were females.

Heredity.—The disease may be found in more than one generation (Boix, Boinet), but probably this depends on the surroundings more than on direct heredity. The disease is sometimes familial or met with in several members of the same family when exposed to the same conditions.

Finlayson[4] described 3 cases in one family. Dreschfeld[5] recorded the disease in two brothers, and Osler[6] had a similar experience in America. Boix,[7] Boinet,[8] and Hasenclever[9] also published similar groups of cases. In Brahmin infants in India a form of cirrhosis described as biliary is very common, and is especially apt to attack members of the same family. But these cases are not the same as Hanot's disease, and may be kala azar. The condition is referred to elsewhere (p. 335).

[1] Barlow and Shaw. *Trans. Clin. Soc.*, Lond., 1902, xxxv, 155.
[2] Fletcher, H. Morley. *System of Medicine* (Allbutt and Rolleston), 1908, iv, part i, 185.
[3] Schachmann. *Thèse de Paris*, 1887.
[4] Finlayson. *Glasgow Hosp. Rep.*, 1899, ii, 39.
[5] Dreschfeld, J. *Med. Chron.*, 1896, N.S., v, 19.
[6] Osler. *Practice of Medicine*, p. 561, 6th ed., 1905.
[7] Boix. *Compt. rend. Soc. Biol.*, Paris, 1898, l, 297.
[8] Boinet. *Arch. gén. de méd.*, 1898, clxxxi, 358; and 1903, cxci, 362.
[9] Hasenclever. *Berlin. klin. Wchnschr.*, 1898, xlv, 997.

In other members of the same family who have no symptoms of disease the spleen may be enlarged (Boix, Boinet); this is analogous to the loss of knee-jerk in apparently healthy members of a family containing some children affected with hereditary ataxia.

In one family the father and two children had fully developed hypertrophic biliary cirrhosis, and three other children had big spleens (Boinet).

Lereboullet[1] described the "cholaemic family," the members of which are supposed to be specially susceptible to infection of the bile-ducts, much in the same way as other families are rheumatic or tuberculous. The subjects of this diathesis are probably more likely to have hypertrophic biliary cirrhosis than ordinary persons (*vide* p. 40).

Alcoholism.—Although the antecedents of patients with hypertrophic biliary cirrhosis sometimes include heavy drinking, there is no reason to regard alcoholism as related to the disease in the same way as it is to common cirrhosis. Alcoholic excess may dispose to infection by reducing the resisting power of the body as a whole and of the liver in particular. Of the two brothers recorded by Dreschfeld, one was a hard drinker while the other was temperate. Boix put forward the view that the infection is introduced into the body in water; and it has been thought that cold and damp houses favour the occurrence of the disease.

Malaria, etc.—In some instances malaria has preceded the onset of the disease, but in the majority of instances this can be ruled out of court. Géraudel[2] revived Lancereaux's view of 1871—that the signs and symptoms ascribed to the disease are malarial in origin.

There is no reason to believe that syphilis or tuberculosis plays any special part in the causation of the disease. In a few cases it has been noticed to develop after typhoid fever (Boinet, and Gilbert and Lereboullet[3]). Odon[4] collected 9 cases; as *B. typhosus* causes cholecystitis and cholangitis, it appears probable that it may produce analogous changes in the small intrahepatic ducts and that the infective process once started may become mixed and shew other microbes such as *B. coli*.

Pathogeny.—Hanot originally regarded the initial lesion as a catarrhal inflammation of the small bile-ducts. In favour of an infective origin for this cholangitis the following points may be urged: the frequency of fever; the considerable splenic enlargement, which indeed may precede or be more marked than that of the liver; and glandular enlargement, not only in the portal fissure, but occasionally in more distant parts of the body.

There are two views as to the path by which the infective or toxic agent reaches the liver: (*a*) A descending cholangitis, or an inflammation beginning in the small intrahepatic bile-ducts due to an irritant reaching

[1] Lereboullet. *Les Cirrhoses biliaires, Thèse de Paris*, No. 180, 1902.
[2] Géraudel. *Thèse de Paris*, 1902.
[3] Gilbert et Lereboullet. *Compt. rend. Soc. Biol.*, Paris, 1905, lviii, 706.
[4] Odon. *Thèse de Paris*, 1905–6, No. 77.

them by the blood-stream, as in experimental toluylenediamine poisoning. The changes in the liver and spleen would then be the local results of a general toxaemia or infection. In cases in which the spleen becomes manifestly enlarged before the liver (metasplenomegalic biliary cirrhosis), the liver is probably more resistant to infective or toxic influences than in the ordinary cases of biliary cirrhosis. (*b*) That hypertrophic biliary cirrhosis is due to a local infection of the bile-ducts from the duodenum—an ascending cholangitis—by bacilli of the colon group (Gilbert and Fournier,[1] Potain[2]). The enlargement of the spleen is regarded as secondary to the local infection of the liver and due to micro-organisms or their poisons absorbed from the infected bile-ducts. In some cases in which the gall-bladder has been drained, micro-organisms such as the *Bacillus coli* and *Diplococcus pneumoniae* have been found in the biliary tract; there may be some question whether all the 17 cases included in Greenough's[3] list of operations were genuine examples of hypertrophic biliary cirrhosis, but the marked success in 13 of the cases is in favour of an ascending infection (*vide* p. 326).

Against the view that it is an ascending infection might be urged the comparative infrequency of antecedent dyspepsia, the absence of duodenitis at necropsies, and that the spleen may be enlarged before the liver, and before there is any jaundice. Further, if the condition were due to an ascending infection from the duodenum, the pancreatic duct should also become infected, and as a result chronic interstitial pancreatitis with increase in the size of the head of the pancreas should occur.

Guillain[4] described such a condition, under the name of "Sclérose hépato-pancréatique hypertrophique avec hypersplénomégalie," in a temperate woman aged fifty-two years; there were hypertrophic biliary cirrhosis and enlargement of the pancreas to double its normal size. He regarded the condition as due to an ascending infection.

In biliary cirrhosis there is some chronic pancreatitis, but the pancreas is not enlarged (Lefas[5]).

Possibly some of the forms of hypertrophic biliary cirrhosis are like Guillain's type, due to an ascending infection, but the majority are, like scarlatinal nephritis, due to a haemic infection or intoxication of a chronic nature. This is conveyed by the hepatic artery; for the cirrhosis induced by poisons arriving by the portal vein is nearly always multilobular.

Bacteriology.—Although anticipated, no microbic cause has yet been satisfactorily established. The colon bacillus has been found in blood withdrawn by puncture from the liver during life and subsequently in the liver and spleen in the same case (Gilbert and Fournier). But

[1] Gilbert et Fournier. *Compt. rend. Soc. Biol.*, 1897, xlix, 692.
[2] Potain. *Semaine méd.*, 1896, xvi, 101.
[3] Greenough. *Am. Journ. Med. Sc.*, 1902, cxxiv, 979.
[4] Guillain. *Rev. de méd.*, 1900, xx, 701.
[5] Lefas. *Arch. gén. de méd.*, Paris, 1900, clxxxv, 539.

further evidence is necessary before the colon bacillus can be regarded as the specific cause. Hayem,[1] in his cases of chronic infective jaundice with splenic enlargement and exacerbations, which is perhaps allied to hypertrophic biliary cirrhosis, found the *Diplococcus pneumoniae* in blood aspirated from the spleen during life. A diplococcus was also described by Kirikoff.[2]

Morbid Anatomy.—The *liver* is uniformly enlarged; but one lobe, usually the left, may be more affected than the other. It usually weighs from 80 ounces upwards, even to eight pounds or more.

In very exceptional cases the liver is described as smaller than natural—"atrophic biliary cirrhosis." It does not seem clear that Weber's[3] case, in which the liver of a girl aged fourteen years was hobnailed and weighed $26\frac{1}{2}$ ounces, was not one of portal cirrhosis.

Perihepatitic adhesions uniting the liver to the diaphragm are not uncommon, but otherwise the surface is fairly smooth, and is at most finely granular. It does not present the gnarled and hobnailed appearance of common cirrhosis. In long-standing cases secondary portal (multilobular) cirrhosis supervenes and the surface may be irregular. It is of a dark-green colour and on section is firmer than natural and has an aspect like granite, due to the fine mesh of the fibrosis.

The portal vein, hepatic artery and veins are normal. The gall-bladder contains bile and is usually healthy, though its walls are sometimes thickened. The larger bile-ducts appear normal. As there is cholangitis it is remarkable that bilirubin-calcium calculi are not more often present in the ducts. Gall-stones have been found in some cases, but are a secondary formation; as they are not constant, they cannot be regarded as the cause of the cirrhosis.

Microscopic Appearances.—The liver shews fibrosis, which in the earlier stages is unilobular and tends to surround each lobule, much in the same way, though not so diagrammatically, as in a pig's liver. In the early stages the unilobular arrangement is well seen. But in long-standing cases the fibrosis is often irregular and there is usually multilobular cirrhosis. This confusing picture no doubt accounts for the difficulty experienced by many writers in accepting hypertrophic biliary cirrhosis as a distinct pathological type. I regard this multilobular cirrhosis as a secondary change, which may very plausibly, on Chauffard's hypothesis of splenogenous cirrhosis (*vide* p. 188), be referred to the action of poisons manufactured in the enlarged spleen and conveyed to the liver by the portal vein. In cases fatal from accident or from some intercurrent disease the unilobular cirrhosis, described by Hanot, may be seen unobscured by the secondary multilobular cirrhosis which supervenes in long-standing cases.

[1] Hayem. *Presse méd.*, Paris, 1898, i, 121.
[2] Kirikoff. *St. Petersb. med. Wchnschr.*, 1900, xvii, 353.
[3] Weber, F. P. *Trans. Path. Soc.*, Lond., 1896, xlvi, 71.

The connective tissue of the unilobular cirrhosis is delicate and fibrillar, somewhat like neuroglia, and has an open structure. In some parts it invades the lobules and becomes unicellular; Kaufmann[1] regards this as characteristic of Hanot's cirrhosis. As compared with the fibrosis of multilobular cirrhosis it is much less dense, but is more intimately related to the lobules and cells of the liver. The delicate connective tissue contains branching anastomosing elastic fibres, which invade the lobules and form a fine network between the cells. The elastic tissue is derived especially

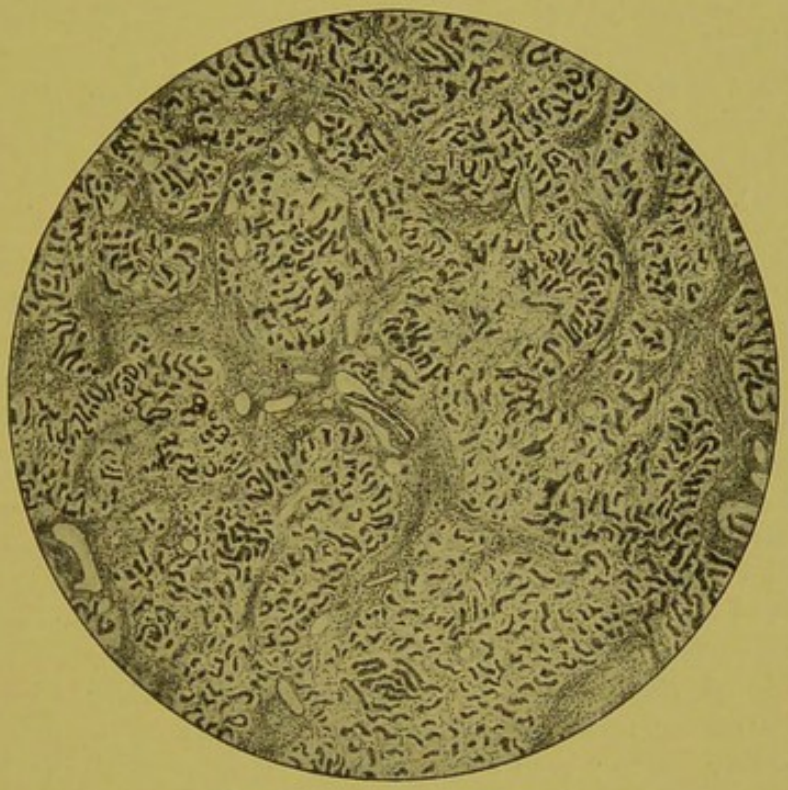


FIG. 39.—Unilobular cirrhosis with some invasion of the lobules by delicate connective tissue. The liver cells are shrunken from the effects of the hardening agent (absolute alcohol). × 25.

from the sheaths of the bile-ducts (Carnot and Amet[2]), and may also spread in from the capsule, where it is normally present. There is less newly formed elastic tissue in biliary cirrhosis than in portal cirrhosis (Flexner[3]). The small bile-ducts are surrounded by small round cells and fibrosis; some shew obliterative cholangitis, others are dilated (Lereboullet[4]). The bile capillaries often contain plugs of inspissated bile.

Pseudobile Canaliculi.—Around the margins of the lobules and in the fibrillar interlobular connective tissue there are columns of small,

[1] Kaufmann. *Lehrbuch d. spez. path. Anat.*, 1907.
[2] Carnot et Amet. *Arch. de méd. expér. et d'anat. path.*, Paris, 1906, xviii, 763.
[3] Flexner. *Univ. Med. Mag.*, Phila., 1900, xii, 614.
[4] Lereboullet. *Les Maladies du foie et leur traitement*, p. 325, 1910, Paris.

deeply staining cells. The cells, which surround a potential lumen, are either cubical or elongated so as to lie parallel to the long axis of the column. Occasionally the lumen is dilated, and, though ordinarily empty, may contain minute biliary calculi. The columns of cells twist and branch in the neighbourhood of the lobules. Though they are particularly well marked in hypertrophic biliary cirrhosis, and are only exceptionally absent in that disease, their presence is not pathognomonic of it, for they are met with in many morbid conditions of the liver, such as portal cirrhosis, abscess, acute yellow atrophy, gumma, and tuberculosis, which tend to destroy the liver cells or interfere with their functional activity. The histological appearances of the so-called new bile-ducts are the same in all these various conditions and differ from normal bile-ducts in that there is either a complete absence of a covering of elastic fibres or a very imperfect development of this tissue around them (Flexner). A great deal of discussion has taken place as to their nature and origin (*vide* p. 205).

Hanot and Gastou[1] regard these so-called new bile-ducts as the first results of irritation of the liver cells, and explain their frequency in hypertrophic biliary cirrhosis as a direct consequence of the exacerbations in the course of the disease.

Hanot insisted that the liver cells are for a long period extremely well preserved, and when the patient dies from some other cause, do not shew the fatty and degenerative changes seen in portal cirrhosis. In many cases acute degenerative or toxic changes occur shortly before death. The integrity of the liver cells has been disputed, and it has been asserted that this statement is based on examination of cells shewing attempts at regeneration (Kaufmann[2]).

Relation of Banti's Disease to Hypertrophic Biliary Cirrhosis. — In chronic splenic anaemia a terminal multilobular cirrhosis may supervene, probably as the result of poisons manufactured in the spleen; this is called Banti's disease. Hypertrophic biliary cirrhosis is essentially unilobular, but in the late stages a secondary multilobular cirrhosis, probably of splenic origin and like that of Banti's disease, may supervene.

The *spleen* is much larger than in portal cirrhosis; its weight commonly varies between 15 and 40 ounces, but may be considerably more. The organ may thus weigh twice to six times its normal weight, whereas the liver is seldom more than twice or three times its ordinary weight. The spleen is therefore relatively heavier than the liver. In some rare cases the spleen is absolutely bigger and heavier than the liver; this is more likely to be met with in children than in adults. To this condition Gilbert[3] applied the term hypersplenomegalic hypertrophic biliary cirrhosis.

[1] Hanot et Gastou. *Compt. rend. Soc. Biol.*, Paris, 1893, xlv, 741.
[2] Kaufmann. *Lehrbuch der spez. path. Anat.*, 1907.
Gilbert. *Semaine méd.*, Paris, 1900, xx, 124.

In F. Taylor's [1] case the spleen weighed 87½ ounces and the liver 40 ounces, and in a case recorded by Milian and Landrieux [2] the spleen weighed 94½ ounces and the liver 65½ ounces. In a very chronic case of hypertrophic biliary cirrhosis, in which jaundice, enlargement of the spleen down to the umbilicus, and clubbing of the fingers were noticed seven years before death, the liver weighed 65 ounces and the spleen 77 ounces (Roger Smith [3]).

There are frequently perisplenic adhesions from local peritonitis and thickening of the capsule with local exaggerations of this change or lamellar fibromas. In uncomplicated cases, *i.e.* when death is not due to acute infection, the spleen is firmer than natural.

Microscopically there is fibrosis, with distension of the sinuses with blood. The Malpighian bodies in an early stage are hyperaemic; later they may undergo fibrotic atrophy, a process which occurs in other chronic toxaemias, and has been obtained experimentally by Pilliet [4] as a result of poisoning by metatoluylenediamine, paraphenylene, and nitrate of sodium. There is also some endothelial hyperplasia in the pulp.

The *lymphatic glands* in the portal fissure are usually enlarged, but are so soft that they do not press on the bile-ducts. They are dark in colour and oedematous; and microscopically shew fibrosis and pigmentation. The pigment is probably derived from destruction of the red blood corpuscles (haemolysis), but differs from the pigmentation of general haemochromatosis in not involving the liver and spleen. The lymphatic glands around the pancreas may also be similarly affected, and glandular enlargement has been noted in the mesentery, groin, axilla, mediastinum, and neck (Popoff [5]).

The *alimentary canal* is usually free from signs of past inflammation. Hanot noted that the duodenum in the region of the biliary papilla was not affected by catarrh; Debove's experience, however, is rather in the opposite direction.

The *pancreas*, as a rule, is not increased in size or weight, but it is far from normal. It is indurated and may be united by adhesions to neighbouring organs. There is an intimate fibrosis of an embryonic type spreading from the ducts. In addition to this form of fibrosis there are some proliferation of the cells lining the ducts and fatty degeneration of the cells of the acini (Lefas [6]). In exceptional cases, as in Guillain's [7] hypertrophic cirrhosis of the liver and pancreas with extreme splenic enlargement, the pancreas may be enlarged.

The *kidneys*, except for bile-staining, are healthy and may shew hypertrophy (Milian [8]). All the organs are bile-stained.

Clinical Picture.—The *onset* may be gradual, and before jaundice

[1] Taylor, F. *Guy's Hosp. Rep.*, 1900, liv, 5.
[2] Milian et Landrieux. *Semaine méd.*, Paris, 1900, xx, 124.
[3] Smith, H. Roger. *Trans. Clin. Soc.*, Lond., 1898, xxxi, 264.
[4] Pilliet. *Compt. rend. Soc. Biol.*, Paris, 1894, xlvi, 331.
[5] Popoff. *Sovrem. klin.*, St. Petersburg, 1895.
[6] Lefas. *Arch. gén. de méd.*, Paris, 1900, clxxxv, 539.
[7] Guillain. *Rev. de méd.*, Paris, 1900, xx, 701.
[8] Milian. *Bull. Soc. Anat.*, Paris, 1901, lxxvi, 323.

sets in malaise, loss of strength, and, in some cases, dyspepsia, abdominal distension or pain, and pruritus may be noticed. Occasionally pain is first noticed in the left hypochondrium, and physicial examination shews that there is considerable enlargement of the spleen. Usually, however, the patient first seeks medical advice after the appearance of jaundice. The onset of jaundice may be almost imperceptible; in other cases it may be sudden and be accompanied by gastro-intestinal disturbance, thus resembling catarrhal jaundice, or be accompanied by abdominal pain and some fever, so as to imitate an attack of intermittent hepatic fever due to a calculus in the common bile-duct.

Gilbert[1] described three modes of onset: (i) The hepatic, with jaundice and pain over the liver; (ii) the gastro-intestinal, with loss of appetite, sickness, diarrhoea, and abdominal pain; and (iii) the splenic, with pain in the left hypochondrium and enlargement of the organ.

The *course* of the disease is characteristically slow. For a considerable time—often for years—the general health is fairly maintained in spite of persistent jaundice. At intervals crises or attacks of abdominal pain with fever and increase in the jaundice occur; these exacerbations, like those in pernicious anaemia and in Addison's disease, lower the general health and nutrition. The periodic exacerbations become more frequent and the disease makes steady though slow progress, wasting and loss of strength appear, and the general state becomes very unsatisfactory. Death may be due to intercurrent disease, to the gradual development of complete hepatic insufficiency and the resulting toxaemia, or during one of the exacerbations acute degenerative changes in the liver cells may lead to icterus gravis. In the last event jaundice deepens, delirium and nervous symptoms appear, and a "typhoid" or comatose condition ushers in death.

Symptoms.—The tongue is often furred, but may be clean for long periods. The appetite is sometimes poor, but is frequently normal and in some instances has been very excessive. There is not the marked distaste for fatty food met with in ordinary obstructive jaundice. Dyspepsia is much less frequent than in portal cirrhosis. Hayem stated that hyperacidity is constant, but Kirikoff's[2] results were entirely opposed to this. Nausea and vomiting are occasionally present. Haematemesis is rare; it may occur late in the disease as the result of secondary portal cirrhosis and even prove fatal. Milian[3] recorded fatal haematemesis from an oesophageal varix. Attacks of diarrhoea on slight provocation are not uncommon. The motions contain stercobilin, though from intercurrent catarrhal jaundice the stools may be temporarily pale. In 26 cases collected by Schachmann[4] the faeces were colourless in only two.

The abdomen is prominent and distended, especially in the upper

[1] Gilbert. *Semaine méd.*, Paris, 1900, xx, 186.
[2] Kirikoff. *St. Petersburg. med. Wchnschr.*, 1902, xxvii, 357.
[3] Milian. *Progrès méd.*, April 14, 1900.
[4] Schachmann. *Thèse de Paris*, 1889.

quadrants, partly from the large size of the liver and spleen, and partly from tympanites and weakness of the abdominal walls. Until late in the disease ascites is absent or very slight, and is then due to intercurrent attacks of perihepatitis and perisplenitis. Towards the termination of the disease ascites may be considerable from the development of secondary portal cirrhosis and toxaemia.

There is a sense of weight in the right hypochondrium, and periodic attacks of pain with tenderness over the liver and spleen, which may even suggest biliary colic, occur. There may be little or no enlargement of the subcutaneous veins around the umbilicus, but it cannot be said that this feature of portal cirrhosis is completely absent in hypertrophic biliary cirrhosis. It may develop as the result of superadded portal cirrhosis in the later stages of the disease.

Physical Signs.—The *liver* is much and uniformly enlarged, and, as a rule, smooth and firm to the touch, but occasionally somewhat irregular from perihepatitic adhesions. Its dulness often extends upwards to the fourth rib in the right nipple line, and downwards to the umbilicus or even lower, and as far as the crest of the ilium. The pressure of the enlarged organ pushes the costal arch out. On palpation there is slight general without any localised tenderness. The gall-bladder is not distended. The enlargement of the liver is, generally speaking, progressive; it may vary from time to time, and increase in size during the exacerbations. Late in the disease it sometimes diminishes in bulk from some degree of contraction of the fibrous tissue, probably of that constituting the multilobular cirrhosis.

The *spleen* is firm, smooth on the surface, but not so hard as in myeloid leukaemia. When attacks of inflammation of the capsule supervene, friction may be heard with the stethoscope, and in some instances a soft blowing murmur may be audible over the spleen. It is very considerably enlarged—much more so than in common cirrhosis. It is more marked in children, in accordance with the fact that its capsule is more distensible than in adults. The spleen may, indeed, be not only relatively but absolutely heavier than the liver. The splenic enlargement may precede any enlargement of the liver; Boix[1] and Popoff[2] insist that it always does. Lereboullet[3] describes the following forms of the disease, based on the relative size of the spleen and liver: (i) The ordinary or hepatic type, in which the liver and spleen are both considerably enlarged, Hanot's disease. (ii) Hypersplenomegalic biliary cirrhosis, in which the splenic enlargement is the predominant feature, the spleen being actually larger than the liver. (iii) Microsplenic biliary cirrhosis, in which the enlargement of the liver is the predominating feature. The spleen may not be enlarged. (iv) Atrophic biliary cirrhosis, in which the liver is small and the spleen large.

[1] Boix. *Compt. rend. Soc. Biol.*, 1898, I, 297.
[2] Popoff. *Leçons cliniques*, St. Petersburg, 1896. Quoted by Boix.
[3] Lereboullet. *Les Maladies du foie et leur traitement*, p. 315, 1910, Paris, Baillière et fils.

Chauffard [1] insists on the time relations between the hepatic and splenic enlargement and divides the cases into three groups: (i) The spleen and liver are simultaneously and equally affected. (ii) The spleen is affected first and in a greater degree—metasplenomegalic hypertrophic biliary cirrhosis; the cirrhosis he believes to be secondary to poisons manufactured in the spleen. (iii) The liver enlarges first and probably determines the splenic enlargement—presplenomegalic hypertrophic biliary cirrhosis.

Jaundice is slight at first and becomes more marked as the disease progresses; it is permanent, but varies in degree, being intensified during the exacerbations. After these crises it recedes a little, but, on the whole, slowly progresses. The jaundice may eventually become very dark or green. There may be considerable brown discoloration of the skin, resembling that of Addison's disease. This melanodermia may occur early, before the onset of jaundice (Roger Smith), but usually it is combined with the icteric staining of the skin. There may be troublesome itching, and from scratching the skin may become covered by an eczematous or lichenous eruption. Long-continued jaundice may lead to xanthoma. I have seen it in a case in which moderate jaundice had existed for nine months. It is said that in some cases of otherwise typical hypertrophic biliary cirrhosis jaundice is absent.

Haemorrhages.—In the later stages there may be cutaneous petechiae, epistaxis, bleeding from the gums and throat, and in exceptional instances haemoptysis, haematuria, and haematemesis.

Physical Development.—The patients are thin, badly nourished, and, when not adults, frequently small for their age. As in other conditions, such as cretinism, hereditary syphilis, and congenital morbus cordis, growth and bodily development may be greatly interfered with and the onset of puberty and in girls menstruation postponed. To this condition the term "infantilism" is applied. The skin is dry. Oedema of the feet may occur in the late stages.

Clubbing of the Fingers.—Some cases of long standing shew clubbing of the terminal phalanges of the fingers and toes. The terminal phalanx may be expanded and broadened so that the digit resembles a spoon or even a pendulum. The nails may be overcurved and longitudinally striated; in extreme instances the nails have been compared to a parrot's beak. This change is the same as that in congenital morbus cordis and chronic lung disease, and is sometimes spoken of as "Hippocratic fingers." It is relatively common in biliary cirrhosis; Gilbert and Lereboullet [2] were able to refer to 40 cases in 1901. It is met with more often in children, in whom it was first described by Gilbert and Fournier,[3] than in adults. Skiagraphy shews that there is no bony enlargement of the terminal phalanges (F. Taylor,[4] Boutron [5]). The

[1] Chauffard. *Semaine méd.*, 1900, xx, 176.
[2] Gilbert et Lereboullet. *Gaz. hebd. de méd.*, 1902, xlix, 1.
[3] Gilbert et Fournier. *Rev. mens. des mal. de l'enf.*, Paris, 1895, xiii, 309.
[4] Taylor, F. *Guy's Hosp. Rep.*, 1900, liv, 13.
[5] Boutron. *Thèse de Paris*, 1899, No. 513.

clubbing is due to thickening of the soft tissues, and on the analogy of its occurrence in bronchiectasis and empyema the change is probably due to the action of toxins. But it is not associated with intra-thoracic disease, and there is no reason to think that it is due to embarrassment of the right lung by the upward pressure of the enlarged liver. Neither is it confined to this form of hepatic disease, for it was well marked in a boy aged seventeen, with syphilitic stricture of the bile-ducts (*vide* Fig. 49), and in very rare instances it has occurred in portal cirrhosis (p. 229). In a few cases of hypertrophic biliary cirrhosis bulbous fingers have been associated with perforating ulcer of the foot and neuritis.

Reference for the subject of clubbed fingers in biliary cirrhosis may also be made to Roger Smith, *Trans. Clin. Soc.*, 1898, xxxi, 258; Parmentier et Castaigne, *Sem. méd.*, 1901, xxi, 94; Rhorassandri, *Thèse de Paris*, 1900, No. 160; Ebstein, E., *Deutsches Arch. f. klin. Med.*, Leipz., 1906, lxxxix, 67.

Arthritis, Hypertrophic Osteo-Arthropathy, etc.—Enlargement of the ends of the bones, synovitis, and pain in the joints, so-called biliary rheumatism, has been described (Gilbert and Fournier).

Wynn[1] collected 11 cases of biliary cirrhosis with hypertrophic osteo-arthropathy. The change has been referred to toxic absorption from the alimentary canal. But against this view it must be borne in mind that gastro-intestinal disturbance is much more constant in portal than in biliary cirrhosis, and that bulbous fingers are extremely rare and osteo-arthropathy almost unknown in portal cirrhosis (*vide* p. 230), which is a very common disease as compared with biliary cirrhosis.

In a man aged twenty-three years, who rapidly developed the clinical picture of hypertrophic biliary cirrhosis, the right shoulder, pelvis, and hip were depressed without any spinal curvature to account for it. The patient was unconscious of the condition and could by an effort temporarily correct it. Sicard and Remlinger[2] thought that the enlarged liver might possibly have some part in bringing about this curious attitude, though it had not been noticed in cases with much bigger livers.

Nervous System.—As a rule, there is nothing special to note with regard to the nervous system. As the result of jaundice there may be some mental depression and failure of memory, and occasionally emotional disturbance. Marked drowsiness is not very rare. In the terminal stages toxaemic symptoms, such as delirium, coma, and convulsions, appear. I have seen peripheral neuritis with numbness of the fingers, but this appears to be quite unusual.

The *heart* tends to dilate, and a systolic mitral murmur or haemic murmurs may be heard at some time during the course of the disease. The *pulse* is regular, of fair tension, and not slow.

Blood.—There is usually a secondary anaemia, the red corpuscles being reduced to between 4,500,000 and 2,200,000, and the colour-index is below 1.

[1] Wynn, W. H. *Birmingham Med. Rev.*, 1904, lv, 283.
[2] Sicard et Remlinger. *Rev. de méd.*, Paris, 1897, xvii, 693.

Emerson [1] met with high counts—7,800,000 and 8,500,000—in 2 out of 5 cases; in one the count was as low as 1,504,000. Hayem and Cabot [2] found that in exceptional instances the amount of haemoglobin may be relatively excessive. Thus in Hayem's case there were 1,884,000 red corpuscles with 50 per cent of haemoglobin; the diagnosis was confirmed by a necropsy.

There is no poikilocytosis (Milian [3]); the blood is less coagulable than in health. Hanot stated that leucocytosis was present, but it appears that leucocytosis is not constant, and may be absent. When present, it is not high, varying between 9,000 and 15,000, and is due to an increase in the polymorphonuclears (Milian).

Hanot and Meunier [4] found leucocytosis in 5 cases, Cabot in 4 out of 6 cases, and Da Costa [5] in 2 out of 6. It was absent in cases reported by Taylor, and Milian and Kirikoff [6] found that leucocytosis was only present when there were complications, and that a normal count or leucopenia was the rule. Bigart's [7] observation of increase in the number of mast cells appears to be unique and may have been due to some independent factor.

Respiratory System.—There may be shortness of breath, due to the upward displacement of the diaphragm, anaemia, and cardiac dilatation. Occasionally, as part of the general haemorrhagic tendency, haemoptysis may occur. Cough is sometimes persistent, and suggests tuberculosis, but tubercle bacilli are very rarely found in the sputum.

Urine.—The quantity passed varies considerably; usually it is increased, but during the exacerbations it may be diminished. Milian [8] lays stress on polyuria as a characteristic feature. It is high-coloured and rich in urinary pigments. Urobilin and indican are both occasionally present. Bile pigment is practically always present. Unlike the concentrated urine of portal cirrhosis, there is little tendency to deposit urates. There is usually no albuminuria; when present, it has been noticed to be intermittent. Casts, if carefully looked for, are nearly always found; their presence appears to depend on the jaundice. The amount of urea varies; it may be normal or at times be diminished. Glycosuria does not occur. As the liver cells preserve their nutrition for a considerable period, alimentary glycosuria, induced by giving three ounces of sugar on an empty stomach, cannot be produced in most cases.

The toxicity of the urine is said to be feeble, and this has been used as an argument against the view that hypertrophic biliary cirrhosis is primarily due to a general haemic infection. The freezing-point of the urine, or its cryoscopic value, has been found to be high (Ferrannini [9]).

[1] Emerson. *Clinical Diagnosis*, p. 587, 1906.
[2] Cabot. *Examination of the Blood*, p. 250.
[3] Milian. *Bull. Soc. Anat.*, Paris, 1903, 6. s., v, 13.
[4] Hanot et Meunier. *Compt. rend. Soc. Biol.*, Paris, 1895, xlvii, 49.
[5] Da Costa. *Clinical Hematology*, p. 352, 1892.
[6] Kirikoff, *Ztschr. f. klin. Med.*, 1898–99, xxxvi, 444; Kirikoff und Korobkoff, *Russ. Arch. f. Path., klin. Med., u. Bakt.*, St. Petersburg, 1902.
[7] Bigart. *Compt. rend. Soc. Biol.*, 1902, liv, 1529.
[8] Milian. *Bull. Soc. Anat.*, Paris, 1901, lxxiv, 323.
[9] Ferrannini. *Zentralbl. f. inn. Med.*, 1903, xxiv, 273.

Termination.—In uncomplicated cases the disease slowly progresses until a fatal toxaemic condition results from destruction of the liver cells. The "typhoid" state develops and the patient becomes more jaundiced, drowsy, and passes into coma. During this stage ascites may appear, or in rare instances death may be precipitated by fatal gastro-intestinal haemorrhage.

A married, childless woman, aged thirty-two, who had had one miscarriage, was admitted to St. George's Hospital with jaundice of four months' duration, a greatly enlarged and tender liver, enlarged spleen and no ascites, but a history of several attacks of haematemesis. The urine was bile-stained and contained a trace of albumin. There were no distended abdominal veins. There was a systolic murmur over the pulmonary artery. There was no definite history of alcoholism, but it was suspected. A few days after admission haematemesis recurred and was often repeated; the patient became delirious and finally comatose, and in spite of being bled from one arm to about a pint and transfused to two pints in the other arm, she died. At the autopsy there was no ascites. The liver, weight 7 pounds 9 ounces, was slightly irregular on the surface and on section shewed fine cirrhosis; it was deeply bile-stained. The bile-ducts were pervious and the gall-bladder contained dark bile but no calculi. Portal vein healthy. Microscopically, liver cells very fatty, no signs of acute atrophy, numerous so-called new bile-ducts. Cirrhosis, comparatively slight, was mainly unilobular.

Death may be due to some acute infection, such as pneumonia, erysipelas, or peritonitis. Erysipelas is very prone to attack patients with chronic jaundice, and, from their want of resistance, to prove fatal; but in hypertrophic biliary cirrhosis erysipelas, though a severe complication, is not necessarily fatal. If acute infection falls on the liver itself, the symptoms of icterus gravis result. Primary carcinoma in a liver shewing hypertrophic biliary cirrhosis has been recorded (Goldzieher and Bókay [1]).

Diagnosis.—Chronic jaundice without complete biliary obstruction, as shewn by the colour of the faeces, the occurrence of periodic exacerbations, and considerable enlargement of the liver and spleen, without any evidence of cholelithiasis, especially in a young person, are the essential points on which to base a diagnosis of hypertrophic biliary cirrhosis.

Differential Diagnosis.—In cases of *portal cirrhosis* with big livers and intercurrent jaundice the diagnosis depends on the jaundice being transitory and not permanent, on the comparatively slight splenic enlargement, and on the history and presence of signs of common cirrhosis. It cannot, however, be maintained that the two diseases (portal and biliary cirrhosis) are always distinct, either anatomically or clinically. Sometimes they are combined, and not infrequently the two diseases overlap in the same way as the parenchymatous and interstitial forms of nephritis.

The following case presented features of both diseases, but it might

[1] Goldzieher und Bókay. *Virchows Arch.*, 1911, cciii, 75.

also be interpreted as a case of portal cirrhosis with acute and recent inflammation of the intrahepatic bile-ducts:

A man aged forty-seven died in St. George's Hospital; he had had haematemesis and ascites which required tapping; for the last three weeks of his life he was delirious and jaundiced. His liver weighed 50 ounces and was typically hobnailed; microscopically it shewed multilobular and unilobular cirrhosis, a large number of pseudobile canaliculi, and microscopic calculi in the bile capillaries. The spleen weighed 18 ounces.

In *haemochromatosis* there is widespread pigmentation of the body with secondary cirrhosis of the liver and pancreas, the liver is enlarged and some of the symptoms resemble those of hypertrophic biliary cirrhosis. The skin, however, though pigmented, is seldom jaundiced, and in five-sixths of the cases there is glycosuria (bronzed diabetes).

In *obstructive jaundice* the liver may be enlarged and swollen from retained bile; but this condition differs from hypertrophic biliary cirrhosis in the acholic faeces, the absence of splenic enlargement, and in many cases an enlarged gall-bladder can be made out.

Chronic jaundice due to a calculus in the common duct may imitate hypertrophic biliary cirrhosis in the periodic attacks of intermittent hepatic fever, and in the fact that the stools are not necessarily devoid of bile. Calculi usually occur later in life than biliary cirrhosis, the periodic attacks of pain are more severe than in hypertrophic biliary cirrhosis, and the spleen is not enlarged.

In *alveolar hydatid* jaundice and splenomegaly may occur, but the condition is excessively rare (*vide* p. 425).

In *ordinary hydatid disease* the spleen is not enlarged, the periodic attacks of fever and pain are absent, and jaundice when present is either due to rupture of a cyst into the duct, in which case there is usually continued fever, or due to pressure on the larger ducts with complete exclusion of bile from the intestines.

In *prolonged catarrhal jaundice* the spleen is either not enlarged or very slightly, and bile is absent from the faeces.

In *chronic splenomegalic haemolytic jaundice* the liver is either not enlarged or only slightly and temporarily, the blood shews fragility of the red corpuscles, the urine is free from bile, and pruritus, xanthoma, and mal-development do not occur (*vide* p. 537).

In *Weil's disease* the clinical course is rapid and acute, whereas in hypertrophic biliary cirrhosis it is a matter of years, not of days.

Malaria can be eliminated by examination of the blood and by the failure of quinine to affect the disease.

Some rather exceptional cases of *syphilitic disease of the liver with chronic jaundice* and very considerable enlargement of the liver and spleen may imitate hypertrophic biliary cirrhosis. Syphilitic lesions elsewhere, a positive Wassermann reaction, albuminuria as pointing to lardaceous disease as the cause of splenic enlargement, irregularity of the surface of the liver from gummas, the presence of enlarged veins near the umbilicus,

and the beneficial effects of antisyphilitic treatment point to syphilis. In the case described on p. 380, the presence of gummas on the limbs pointed to syphilis, but in other respects the features resembled those of Gilbert and Fournier's splenomegalic type of hypertrophic biliary cirrhosis.

Tuberculosis implicating the Liver.—Géraudel[1] has collected a number of cases in which tuberculosis gave rise to hepatic and splenic enlargement and chronic jaundice.

Banti's Disease.—There is a gradual transition between (*a*) cases of so-called metasplenomegalic biliary cirrhosis, in which the splenic enlargement precedes any manifest change in the liver, and (*b*) cases of chronic splenic anaemia which eventually develop a terminal cirrhosis of the liver and jaundice—so-called Banti's disease. To distinguish between the two a reliable history is necessary. Chronic splenic anaemia presents anaemia of the chlorotic type, an absence of leucocytosis or even a diminished number of leucocytes (leucopenia), and recurrent gastro-intestinal haemorrhages before the development of jaundice; whereas in metasplenomegalic biliary cirrhosis there would be practically an absence of symptoms during the period in which splenomegaly is the only physical sign.

Duration.—Though the disease must be regarded as incurable, it is essentially chronic, and jaundice may exist for ten years or even longer; Goluboff[2] speaks of twelve years' duration. The average duration is about five years. In a few instances the disease runs an acute course, and then proves fatal within two years.

The **prognosis** is bad; the disease is incurable, but its progress is often extremely slow, and patients may retain fair strength for years. The patient's environment influences the outlook; careful treatment and supervision may be followed by improvement. An easy life in a healthy locality will prolong life, whereas overwork, exposure to cold and wet, and insanitary conditions will surely lead to deterioration.

The patient's general nutrition has, of course, an important bearing on the prognosis. Wasting and the recurrence of exacerbations and of haemorrhages at shorter intervals shew that the disease is advancing towards its termination. The incidence of complications, such as pneumonia, peritonitis, or erysipelas, makes the outlook very serious. Erysipelas may be recovered from if the urinary excretion is well maintained. Clubbing of the fingers is only met with in long-standing cases, and is an indication that the course of the disease has been slow.

The general lines of **treatment** are much the same as in portal cirrhosis. In certain points there are differences: thus, a more generous diet may be allowed than in portal cirrhosis, while itching of the skin due to jaundice is more, and ascites and haematemesis less, likely to require treatment than in ordinary cirrhosis. In the early stages an attempt

[1] Géraudel. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1909, xxvi. 24.
[2] Goluboff. *Ztschr. f. klin. Med.*, Berl., 1894, xxiv. 353.

may be made to put the patient in more healthy surroundings and to remove him from the conditions, among which the water-supply may play a part, that favoured the onset of the disease. Fresh air is important, but exposure to chills, and especially to cold and damp weather, should be avoided, and the patient should be warmly clad. A course at Homburg, Ems, Neuenahr, Kissingen, Vichy, Vals, Harrogate, may be tried. If the patient goes to Carlsbad, the course must be comparatively mild.

The *diet* should be simple and nourishing; irritating and unduly stimulating articles of food should be carefully excluded. Milk should be given freely, eggs, bread and butter, simple puddings, fish, and occasionally meat may all be taken. Alcohol should be avoided; or if taken at all, in small quantities and well diluted. Water should be drunk freely, but it will be advisable to have it boiled when the patient is still living in the house where the disease developed.

Intestinal fermentation and putrefaction should be prevented by careful dieting, correction of constipation, and by minute doses of calomel ($\frac{1}{40}$–$\frac{1}{20}$ of a grain) three times a day; rather larger doses ($\frac{1}{6}$–$\frac{1}{2}$ grain) may be employed in single doses to combine its antiseptic and purgative properties. Calomel is preferable to salol, β-naphthol, betol, and the synthetic intestinal antiseptics. Saline purgatives, such as sulphate of magnesium and sulphate of sodium in combination, are also useful in preventing intestinal fermentation, while mineral waters may be employed with the same object. The catarrhal condition of the small bile-ducts should be treated by drugs which, when excreted into the intrahepatic ducts, disinfect the ducts; for this purpose urotropin in combination with salicylate of sodium should be given.

Itching of the skin may be treated externally by warm baths or fomentations with carbolic acid lotion; internally lactate of calcium in 20-gr. doses or antipyrin, grs. v.–x., may be employed. Small hypodermic injections of pilocarpine have also been recommended (*vide* p. 567).

Surgical Treatment.—Terrier[1] and Delagénière[2] drained the gall-bladder in some cases with good results. Thus, in 13 cases tabulated by Maurice Guillot[3] 10 were cured; Greenough[4] adds 4 cases, making up a total of 17 cases, of which 13 were relieved. It is not certain that all the cases were of the same type; some of them may possibly have been examples of chronic infective cholecystitis and cholangitis and not of genuine biliary cirrhosis (*vide* Michaux[5]). The drainage of the gall-bladder was continued for periods varying from ten days to three months, and in some instances the bile, which was at first infected, became aseptic.

[1] Terrier. *Rev. de chir.*, Paris, 1892, xii, 553.
[2] Delagénière. *Arch. prov. de chir.*, Paris, 1897, vi, 310.
[3] Guillot, M. *Gaz. hebd. de méd.*, Paris, 1902, N.S., vii, 49.
[4] Greenough. *Am. Journ. Med. Sc.*, 1902, cxxiv, 979.
[5] Michaux. *Rev. de chir.*, Paris, 1901, xxiii, 126.

Obstructive Biliary Cirrhosis

By obstructive biliary cirrhosis is meant a fibrosis spreading from the bile-ducts around the lobules of the liver and due to obstruction of the large bile-ducts.

History.—The conception of cirrhosis due to biliary obstruction was first prominently brought forward by Charcot and Gombault[1] in 1876, though three years previously Wickham Legg[2] in England had described a clinical case with full pathological details. In 1882 Mangelsdorf[3] collected 184 cases, and in 1901 W. W. Ford[4] and in 1903 Weber[5] argued in favour of this sequence of pathological events.

Experimental Ligature of the Bile-ducts.—As bearing on the production of obstructive biliary cirrhosis, numerous experiments have been performed in which the bile-ducts have been ligatured and the liver subsequently examined for any fibrosis. The conclusions thus arrived at are by no means uniform.

Mayer[6] in 1872 ligatured the common bile-duct of cats and produced dilatation of the bile-ducts with intralobular and extralobular fibrosis. Charcot and Gombault's[7] (1876) results, like the earlier experiments of Wickham Legg[8] (1873), shewed that ligature of the duct led to dilatation of the intrahepatic ducts with fibrosis around the individual hepatic lobules (insular cirrhosis) and into their substance (intralobular cirrhosis). The lobules tended to undergo atrophy, while numerous newly formed bile-ducts in the perilobular tissue passed by a gradual transition into the liver cells at the margin of the lobule. Somewhat similar results were obtained by Chambard, and by Foa and Salvioli. Charcot and Gombault referred these changes to the irritating properties of the retained bile, and incidentally mentioned that the bile contained "vibrios." Maffucci[9] also induced cirrhosis by ligaturing the bile-duct.

As these results were obtained before the days of antiseptics, it has often been urged that the cirrhosis was due, not to mechanical pressure and irritation exerted by the retained bile, but to infection. Thus, Steinhaus[10] found that after ligature of the bile-ducts in guinea-pigs, who were killed at periods varying from six hours to ten days, no interstitial hepatitis was produced unless infection occurred. The interval of ten days is very short, but as most of the animals died within a fortnight after ligature of the common duct, this was unavoidable. In order to keep animals alive longer Josselin de Jong[11] ligatured individual branches of the hepatic duct instead of the common bile-duct and obtained much the same results as Steinhaus. Similar experiments in the

[1] Charcot et Gombault. *Arch. de physiol. norm. et path.*, 1876, 2. s., iii, 272.
[2] Legg, Wickham. *St. Barth. Hosp. Rep.*, 1873, ix, 161.
[3] Mangelsdorf. *Deutsch. Arch. f. klin. Med.*, 1882, xxxi, 522.
[4] Ford, W. W. *Am. Journ. Med. Sc.*, 1901, cxxi, 60.
[5] Weber, F. P. *Trans. Path. Soc.*, 1903, liv, 103.
[6] Mayer. *Med. Jahrb.*, Wien, 1872, ii, 133.
[7] Charcot et Gombault. *Arch. de physiol. norm. et path.*, Paris, 1876, 2. s., iii, 272.
[8] Legg, W. *St. Barth. Hosp. Rep.*, 1873, ix, 161.
[9] Maffucci. *Gior. internaz. delle sc. med.*, 1882, N.S., iv, 889.
[10] Steinhaus. *Arch. f. exper. Path. u. Pharm.*, 1891, xxviii, 432.
[11] Josselin de Jong. *Inaug. Diss.*, Leyden, 1894. Quoted by Harley and Barratt.

hands of Nasse,[1] and of Vaughan Harley and Barratt,[2] shewed that intralobular fibrosis resulted. The latter observers ligatured the left hepatic duct in cats and kept them alive for four to sixteen months, and in dogs without any jaundice resulting ; microscopic sections of the left and of the healthy right lobe could then be compared. The changes observed were not absolutely constant, but in many instances well-marked interlobular fibrosis, hyperplasia of the interlobular bile-ducts, and atrophy of the hepatic lobules, beginning at the periphery, were present in the area of the liver corresponding to the ligatured bile-duct. Ligature of the common duct in frogs, guinea-pigs, and rabbits under antiseptic precautions gave rise to some fibrosis (Lahousse,[3] Beloussow,[4] Gerhardt [5]).

There is thus considerable difference of opinion whether or not fibrosis is produced. In some cases in which the ligature is applied to the duct near the duodenum the part of the duct above the ligature may contain micro-organisms, so that although the ligature itself is aseptic, the conditions are complicated. Lamacq [6] points out that in dogs the liver may normally contain infective nodules. His results shew that when infection is avoided, ligature leads to necrosis of the liver cells in rabbits when the bile pressure is relatively high, but that in dogs necrosis is rare and when present not marked. No leucocytic infiltration or fibrosis occurred around the areas of necrosis and no proliferation of bile-ducts. The same results were obtained by Ribadeau-Dumas and Lecène [7] in guinea-pigs. By aseptic ligature of the common bile-duct M. Richardson [8] produced cirrhosis in rabbits, and Milne [9] in cats.

To sum up the effects of ligature of the bile-ducts : fibrosis may be absent, it may be present and be due to infection, or may, even where infection is absent, be found in varying degrees. This fibrosis following aseptic ligature may be explained in several ways : it may be regarded merely as a fibrous replacement, perhaps more apparent than real. In cases such as Nasse's and Harley's and Barratt's, in which one hepatic duct is ligatured and the fibrosis is limited to the corresponding part of the liver, this may be the explanation. Harley and Barratt, however, referred the fibrosis to the continued slight irritation of the bile. In other instances the cirrhosis may be due to toxic influences which are brought into existence by failure of the liver properly to perform its antitoxic function of stopping and destroying poisons brought to it by the blood, especially that of the portal vein ; in such an event the poisons would reach the liver a second time by the hepatic artery. Or, again, when the common bile-duct is tied the cirrhosis may be due to poisons absorbed from the alimentary canal, where, as the result of interference with the flow of bile, fermentation and putrefaction have

[1] Nasse. *Arch. f. klin. Chir.*, 1894, xlviii, 885.
[2] Harley and Barratt. *Journ. Path. and Bacteriol.*, 1901, vii, 203.
[3] Lahousse. *Arch. de biol.*, Paris, 1887, vii, 187.
[4] Beloussow. *Arch. f. exper. Path. u. Pharmak.*, 1881, xiv, 211.
[5] Gerhardt. *Ibid.*, 1892, xxx, 1.
[6] Lamacq. *Arch. de méd. expér. et d'anat. path.*, Paris, 1897, ix, 1135.
[7] Ribadeau-Dumas et Lecène. *Ibid.*, 1904, xvi, 191.
[8] Richardson, M. *Journ. Exper. Med.*, N.Y., 1911, xiv, 401.
[9] Milne. *Quart. Journ. Med.*, Oxford, 1911–12, v, 415.

been excessive. Lastly, the fibrosis may be entirely independent of ligature of the bile-ducts and due to extrinsic causes developing after the duct has been ligatured.

Incidence.—The statistics of Mangelsdorf[1] shewed that up to 1882 the published cases of cirrhosis which could be ascribed to biliary obstruction numbered 184; between 1882 and 1900 W. W. Ford[2] collected 21 more and added 3 fresh examples. From his 21 cases collected from literature 10 may be deducted, since 9 belong to the group of congenital obliteration of the ducts and one was an example of congenital cystic disease of the liver. Cases of cirrhosis due to biliary obstruction are therefore not often described. The general opinion is that mechanical biliary obstruction seldom or never causes genuine cirrhosis, and that although fibrosis may be detected on microscopic examination, it is not of any clinical or practical significance.

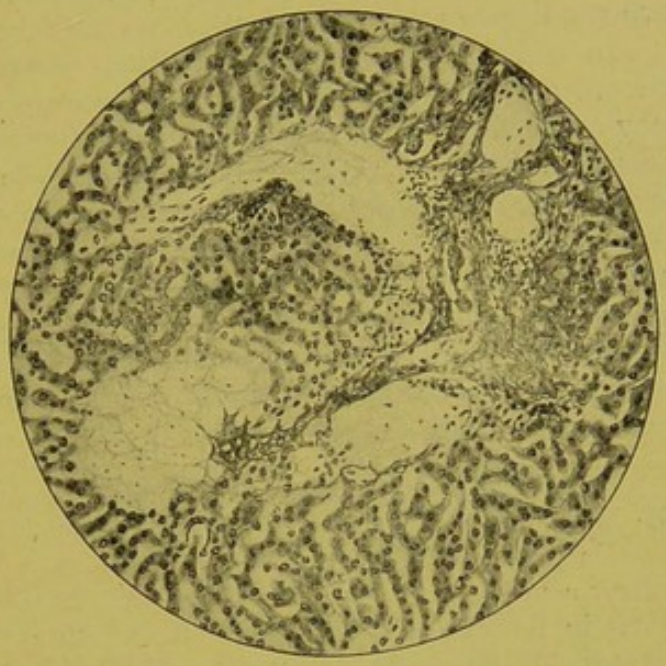


FIG. 40.—Focal necrosis due to biliary obstruction. From a guinea-pig whose bile-duct was compressed by a cyst. The pale areas shew complete necrosis of the liver cells; there is some small-celled infiltration around the portal space. The bile-ducts contained inspissated bile. (From a specimen kindly lent by Dr. J. H. Drysdale.)

The **effects of biliary obstruction on the human liver**, like those obtained by experimental work on animals, are not uniform, but there is very little evidence that biliary obstruction *per se* causes cirrhosis. When the common bile-duct is completely occluded from without, for example, by malignant disease of the head of the pancreas, there is dilatation of the ducts, but as a rule little or no fibrosis, while the liver cells are degenerated, atrophied, and occupied by bile pigment. The liver substance is atrophied and the organ is in a condition comparable to that of hydronephrosis. It is somewhat strange that manifest microbic infection does not occur more often, since the biliary stagnation must dispose to infection by micro-organisms reaching the liver by the blood-stream.

Malignant disease of the pancreas with complete biliary obstruction is not rare, but it is remarkable that it is hardly ever associated with cirrhosis of the liver. If biliary obstruction *per se* produced fibrosis of

[1] Mangelsdorf. *Deutsch. Arch. f. klin. Med.*, 1882, xxxi, 522.
[2] Ford, W. W. *Am. Journ. Med. Sc.*, 1901, cxxi, 60.

the liver, the association should be often seen. The cases are so few that it seems possible that when hepatic cirrhosis and malignant disease of the pancreas are found in the same person, the cirrhosis was the older lesion and was latent, and that the growth in the pancreas developed subsequently. Maffucci [1] and Legrand [2] have recorded cases in which these two conditions were associated.

In addition to the possibility that bacterial infection of the dilated bile-ducts, when obstructed by the pressure of a tumour from without, may occur from the blood-stream, it must be remembered that as complete obstruction entails absence of bile from the intestine, putrefactive and fermentative processes in the bowel become excessive and might lead to the production of poisons, which, when carried to the liver, would set up the ordinary portal or multilobular cirrhosis. This change would, indeed, in all probability be met with more often, were it not that the liver, being flooded with bile which has acquired toxic properties, as shewn by the focal necroses of the liver cells, is incapable of such reaction.

The cirrhosis of the liver found in association with congenital obliteration of the bile-ducts has been regarded by Thomson, Beneke, Ford, and Lavenson as secondary to the biliary obstruction and as a good example of obstructive biliary cirrhosis. It is, however, quite as reasonable to believe that the process starts in the smaller ducts, where it sets up pericholangitic fibrosis and then spreads to the larger ducts and gall-bladder, where it sets up obliterative cholangitis and cholecystitis (*vide* p. 651).

On the other hand, when a gall-stone is lodged in the common bile-duct, the results are not so constant; sometimes the changes are the same as in aseptic closure of the common duct, but other cases shew cholangitis and pericholangitis, which, if the process is chronic, result in fibrosis around the ducts. There seems to be very little doubt that the factor which determines fibrosis around the intrahepatic ducts in gall-stone obstruction is infection. As the result of prolonged biliary stasis, icteric necrosis of the liver cells occurs and fibrosis of a diffuse character may thus be favoured.

Mangelsdorf tabulated 54 cases of hepatic cirrhosis associated with gall-stones, in 16 of which calculi were found in the ducts. Parkes Weber [3] collected 12 cases of biliary cirrhosis from obstruction of the larger ducts by gall-stones.

Hypertrophic biliary cirrhosis has been associated with gall-stones,[4] but it is rare, as Naunyn [5] has never seen it; the gall-stones in such cases must be regarded as secondary to, and not the cause of, the biliary cirrhosis.

[1] Maffucci. Quoted by Ford, *Am. Journ. Med. Sc.*, 1901, cxxi, 60.
[2] Legraud. *Rev. de méd.*, Paris, 1889, ix, 165.
[3] Weber, F. P. *Trans. Path. Soc.*, Lond., 1903, liv, 105.
[4] Compare Sharkey. *St. Thomas's Hosp. Rep.*, 1888, xviii, 245.
[5] Naunyn. *Cholelithiasis*, p. 163, Transl. New Sydenham Soc., 1896.

Morbid Anatomy.—*The liver* in mechanical obstruction of the bile-ducts, though enlarged in the early stages, is small at the necropsy, unless occupied by secondary growths or by a hydatid cyst. Its surface is irregular, shews dilated and varicose bile-ducts filled with mucus, and is of a dark green colour. The dilatation of the ducts is not always uniform; it may indeed be localised, often near the margin of the left lobe.

In a case examined in St. George's Hospital there was an area, the size of the palm of one's hand and roughly divided into two by the falciform ligament, on the convexity of the liver, which was entirely composed of dilated bile-ducts.

Occasionally there are perihepatitic adhesions. On section of the organ the dilated ducts are prominent and give the liver a sponge-like or honeycombed appearance; it is usually somewhat flabby from atrophy of the secreting cells, and cuts very differently from an ordinary cirrhotic liver. The liver parenchyma around the dilated bile-ducts shews atrophy, condensation, and some pericholangitic fibrosis. When acute infection has been superadded, there may be suppuration in or around the bile-ducts, and minute abscesses. The naked-eye appearances are therefore very different from those of hypertrophic biliary cirrhosis.

Further, the histological changes are not the same as those of hypertrophic biliary cirrhosis. In calculous obstruction the ducts are dilated and tend to become progressively more so in proportion to the duration of the obstruction, whereas in hypertrophic cirrhosis this does not occur. In biliary obstruction the larger ducts are chiefly affected and may shew cholangitis and pericholangitis, whereas in hypertrophic biliary cirrhosis the smallest intrahepatic ducts are inflamed. Degeneration of the liver cells and focal necroses are prominent in mechanical obstruction of the larger ducts, whereas in hypertrophic biliary cirrhosis the liver cells maintain their nutrition for long periods.

The changes consist in dilatation of the bile capillaries around the intralobular veins, rupture of them, and escape of bile into the lymph spaces between the sinusoids and the liver cells (Mallory[1]). The liver cells shew degeneration and infiltration with bile pigment (Carnot and Harvier[2]). The columns of small cubical cells, known as "pseudobile canaliculi," are described in many cases, but are certainly not always present. When fibrosis occurs it spreads out from the larger bile-ducts and may give rise to multilobular cirrhosis or to a more diffuse form of cirrhosis which not only tends to surround the individual lobules, but invades their substances and passes between the hepatic cells. From his study of 184 cases of cirrhosis, thought to be due to biliary obstruction, Mangelsdorf concluded that no particular form of cirrhosis could be said to depend on biliary obstruction.

The spleen is sometimes small or of normal size, but in cases in which

[1] Mallory. *Johns Hopkins Hosp. Bull.*, Balt., 1911, xxii, 70.
[2] Carnot et Harvier. *Arch. de méd. expér. et d'anat. path.*, Paris, 1907, xix, 76.

considerable fibrosis of the liver coexists with obstruction of the larger ducts, as in Weber's cases, there may be enlargement, though not to the same degree as in hypertrophic biliary cirrhosis.

The pancreas in cases in which a calculus occupies the lower end of the bile-duct or the ampulla of Vater may, from obstruction combined with infection of its duct, shew dilatation of the duct and fibrosis with atrophy of the secreting tissue of the organ. This chronic interstitial pancreatitis is perilobular and somewhat coarse; only in very late stages does it become interacinous; as a rule diabetes mellitus is not produced.

Clinical Features.—When cirrhosis of the liver, whether pericholangitic or portal, occurs in a patient with biliary obstruction, it does not, as a rule, reveal itself by any special signs or symptoms, the features being those of biliary obstruction (*vide* p. 540). Complete aseptic obstruction of the common bile-duct leads to dilatation of the intrahepatic ducts and to focal necrosis of the liver cells. The functional activity of the liver is thus very gravely interfered with and, as a result of this hepatic inadequacy, cholaemia or biliary toxaemia results, a condition which is more rapidly fatal than cirrhosis. The symptoms are those of complete obstructive jaundice and cholaemia; the gall-bladder is usually dilated; this and the history should distinguish it from impacted gall-stone.

Cases of long-standing gall-stone obstruction of the common bile-duct associated with ordinary portal cirrhosis undoubtedly occur. As a rule, symptoms of portal cirrhosis are absent or cast into the shade by those of biliary obstruction. When the clinical features of ordinary portal cirrhosis follow obstruction, due to gall-stones or other causes, the cirrhosis is reasonably explained as the result of poisons manufactured in the intestines and carried to the liver by the portal vein.

Ford collected 10 cases in which ascites and other symptoms of portal cirrhosis were associated with obstruction of the common bile-duct. In 6 of these the obstruction was by gall-stones, and in 4 by tumours, glands, or a cicatrix pressing on the duct from without.

In instances in which a gall-stone passes into the common bile-duct without any history of colic diagnosis may be difficult. As time progresses, bile may escape by the side of the stone into the duodenum and the faeces are no longer pale; they then contain stercobilin, just as in hypertrophic biliary cirrhosis. In differentiating these two conditions, the size of the spleen is important; it is much enlarged in hypertrophic biliary cirrhosis, whereas in gall-stone obstruction splenomegaly, if present, is relatively insignificant. In hypertrophic biliary cirrhosis the liver is greatly increased in size; in biliary obstruction it may be swollen from retention of bile, but in the late stages it becomes smaller.

The **treatment** is that of obstructive jaundice by operative measures and by symptomatic remedies (*vide* p. 566). In the rare cases with ascites and symptoms pointing to ordinary cirrhosis the treatment should be on the lines of that disease.

HEPATIC CIRRHOSIS IN CHILDREN

CIRRHOSIS in children is probably not so rare as might be concluded from C. West's[1] experience of only 4 examples among 70,000 cases of children's diseases. In fact, at the Hospital for Sick Children, with which West was connected, there were in forty-five years 40 cases of cirrhosis among 5500 necropsies, or ·73 per cent (Forbes[2]). In 17,891 necropsies in children there were 33 cases of cirrhosis, or ·18 per cent (Jones[3]). In 1889 Hatfield[4] was able to refer to 156 examples, including Palmer Howard's[5] 63 cases, of cirrhosis in children. In 1906 Jones collected from the European and American literature of fifty years, 300 cases of various forms of cirrhosis. Musser's[6] 529 cases included Ghose's 400 cases of biliary cirrhosis in infants in India, a special and common disease in Calcutta, but on a somewhat different footing from the sporadic cases seen in temperate climates (*vide* p. 335). Children are affected by the forms of cirrhosis seen in adults, and in the main react in very much the same manner. The following summary will be confined to points deserving special attention.

The various forms of cirrhosis of the liver seen in children may attack more than one member of the family; this depends on hereditary factors, of which syphilis is pre-eminent, and on influences favouring cirrhosis, such as alcohol and improper food, which form part of the family environment.

The unicellular cirrhosis of hereditary syphilis and the lesions of delayed hereditary syphilis are dealt with elsewhere (p. 370); after recovery from unicellular cirrhosis the liver is probably left with its resistance so diminished that it may readily become affected by ordinary portal cirrhosis, the resulting change being neither due to syphilis nor curable by antisyphilitic treatment, but disposed to by the influence of former syphilis, and therefore parasyphilitic and comparable to tabes dorsalis and general paralysis of the insane. Some cases of portal cirrhosis in early life may thus be related to syphilis (cf. Payne[7]).

There are other forms of intra-uterine or *congenital cirrhosis.* It occurs in congenital obliteration of the bile-ducts, and in cases which clinically resemble that group, but anatomically do not present obliteration of the ducts. It is reasonable to believe that the change is due to poisons conveyed from the mother to the fetus (*vide* p. 651).

Vanverts and Ramond[8] record a case of congenital ascites and hepatic cirrhosis in which the fetus' abdomen had to be tapped before it could be

[1] West, C. *Lectures on Diseases of Infancy and Childhood*, p. 654, 1884.
[2] Forbes. *Trans. Path. Soc.*, Lond., 1906, lvii, 354.
[3] Jones. *Brit. Journ. Child. Dis.*, 1907, iv, 1.
[4] Hatfield. *Cyclopaedia of Children's Diseases*, 1889, iii, 488.
[5] Palmer Howard. *Am. Journ. Med. Sc.*, Phila., 1887, xciv, 350.
[6] Musser, J. H. *Supplement to Cyclopaedia of Children's Diseases*, p. 798, 1899.
[7] Payne. *Trans. Path. Soc.*, Lond., 1900, li, 366.
[8] Vanverts et Ramond. *Bull. Soc. Anat.*, Paris, 1896, lxxi, 153.

delivered. The liver was enlarged and cirrhotic. There was no evidence of syphilis, alcoholism, or tuberculosis in the parents.

Portal cirrhosis is rare; among 12,461 necropsies, during the forty years 1866–1905 at St. George's Hospital, there were only 8 cases under twenty-one years. In Woolley's[1] 90 collected cases under twenty-one years of age there were 48 males and 42 females, the average age was eleven years, and was practically the same in the two sexes; 70, or 77·8 per cent, occurred between the ages of six and fifteen years. As in adults, the liver may be larger than normal, or may be small and markedly hobnailed. In cases with pronounced nodular hyperplasia the liver may look as if occupied by multiple new-growth. In some cases the cirrhosis can be traced to precocious alcoholism, or to some specially irritating kind of food, such as fish soaked in vinegar. It is, therefore, not surprising that occasionally two or more children in the same family suffer from portal cirrhosis (*vide* p. 180). Jones has collected 74 cases of alcoholic cirrhosis in children. In many cases alcoholism can be excluded and some other cause must be sought for, such as gastro-enteritis or the specific fevers. Probably some of the cirrhotic livers of early life are, like granular kidneys in childhood, in reality parasyphilitic (*vide* p. 381). On the other hand, portal cirrhosis is not, like chronic interstitial nephritis and interstitial keratitis (Nettleship[2]), commoner in female than in male children.

Clinical Features.—Haematemesis seems less frequent than in adults, possibly because the spleen is more distensible and therefore accommodates relatively more portal blood than in the adult. Saunal,[3] however, recorded fatal haemorrhage from an oesophageal varix in a girl aged twelve years (*vide* p. 266). Haemorrhages elsewhere, from the nose and into the skin, and depending on severe toxaemia, are quite as frequent as in adults. Spider-like angiomas on the skin of the face are not so often seen in children as in adults. Enlargement of the liver and spleen is more prominent than in adults. This may in part depend on the liver being relatively larger in children and on greater power of repair and hyperplasia of the liver in early life. The spleen is more readily distended in early life. In children cases of mixed portal and biliary cirrhosis are not infrequent; this, again, bears on the more marked enlargement of the liver and spleen.

Fever is more frequent in children than in adults, and may be so marked as to suggest enteric fever or generalised tuberculosis.

In a case of Wickham Legg's[4] a boy aged twelve years was first thought to have enteric fever and later acute tuberculosis. Another case regarded as enteric fever occurred at St. George's Hospital (*vide* p. 220).

Ascites is common, and is very likely to be regarded as evidence of tuberculous peritonitis. In Woolley's 90 cases there was ascites in 59,

[1] Woolley. Unpublished Thesis for M.D. Cantab., 1906.
[2] Nettleship. *Roy. London Ophthalmic Hosp. Rep.*, 1904–6, xvi, 1.
[3] Saunal. *Thèse de Paris*, 1892.
[4] Legg, Wickham. *St. Barth. Hosp. Rep.*, 1877, xiii, 148.

in 12 tuberculous peritonitis was diagnosed. Pulmonary tuberculosis is a very rare complication, but infection of the peritoneum may occur. In some cases a terminal suppurative peritonitis is met with. A curious symptom sometimes observed is ravenous appetite. Marked jaundice is rare; diarrhoea is more often associated with cirrhosis in children than in adults. The prognosis is probably worse than in adults.

In an interesting group of cases described by Ormerod,[1] Homén,[2] Gowers, and S. A. K. Wilson,[3] the symptoms are nervous, and cirrhosis is entirely latent. Gowers[4] described them as "tetanoid chorea," Anton[5] as "dementia choreo-asthenica," and S. A. K. Wilson as "progressive lenticular degeneration." The disease is familial but not hereditary. The clinical features are bilateral tremor and spasticity, and in the late stages contractures. There is dysphagia and anarthria; but no real paralysis. There is symmetrical degeneration of the lenticular nucleus and multilobular and unilobular cirrhosis of the liver. Homén considered that the disease was the result of congenital syphilis. Wilson, who has collected 11 cases, excludes alcohol and congenital syphilis as causes, and believes that a toxin, probably not microbic and possibly a lipoid, exerts a selective action on the lenticular nuclei, comparable to the selective bile-staining of the lenticular nucleus in "Kernicterus" (*vide* p. 569).

Hypertrophic biliary cirrhosis is relatively a commoner form of cirrhosis in children than in adults; it presents some special features which Gilbert and Fournier[6] described as the juvenile type of the disease. Development is arrested and "infantilism" results. The cases may run an extremely protracted course, and the type of the disease may change, and eventually present the features of ordinary or portal cirrhosis (*vide* p. 314). For the account of the disease *vide* p. 309.

Cirrhosis in Young Children in India.—A peculiar form of cirrhosis among young native children in India, attacking chiefly Hindus, has been described by Gibbons,[7] Ghose,[8] and others.[9] It occurs especially in, but is not confined to, Calcutta. It is common—Ghose has seen as many as 400 cases—and extremely fatal, often killing off one child after another in the same family; about 95 per cent of those attacked die from the disease before the end of the second year of life. In 1891–93 it caused 1748, and in 1907, 636 (Pearse) deaths in Calcutta; only six of Ghose's 400 cases recovered. It is not due to syphilis, alcohol, or malaria. It has been thought to depend on irritating bodies in the food, especially as the

[1] Ormerod, J. A. *St. Barth. Hosp. Rep.*, 1890, xxvi, 57.
[2] Homén. *Neurol. Centralbl.*, 1890, ix, 514.
[3] Wilson, S. A. K. *Brain*, Lond., 1912, xxxiv, 295.
[4] Gowers. *Diseases of Nervous System*, 1886, ii, 656; *Rev. Neurol. and Psychiat.*, Edin., 1906, iv, 249.
[5] Anton. *München. med. Wchnschr.*, 1908, lv, 2369.
[6] Gilbert et Fournier. *Compt. rend. Soc. Biol.*, Paris, 1895, xlvii, 419.
[7] Gibbons, J. B. *Scientific Memoirs by Medical Officers of the Army of India*, 1891, part vi; and the *Ind. Lancet*, 1896, vii, 426.
[8] Ghose. *Lancet*, Lond., 1895, i, 321.
[9] Nil Ratan Sircar, *Ind. Lancet*, 1896, viii, 3; Mackenzie, *Lancet*, Lond., 1895, i; Pearse, *ibid.*, 1909, i, 265.

nursing mothers restrict themselves to a dry diet, and take a decoction of black pepper. It has been suggested that it may be due to kala azar (Castellani and Chalmers [1]). The change begins as a unicellular cirrhosis, and then becomes interlobular; the amount of fibrous tissue may be very large, there is great destruction of the liver cells, and extensive formation of new bile-ducts. Kundrat and Paltauf of Vienna, to whom Gibbons shewed his specimens, regarded the change as an undescribed form of biliary cirrhosis. The spleen is usually enlarged. The disease is not congenital, but generally begins about seven months of age with fever and enlargement of the liver and spleen. Constipation, nausea, and jaundice, which eventually becomes intense, occur, and a terminal ascites may develop.

In **rickets** the liver is enlarged, in addition to being somewhat displaced downwards by deformity of the chest. As the result of absorption of toxic products from the alimentary canal there is some fatty change in the liver cells and fibrous hyperplasia in the portal spaces.[2] Hogben [3] seems alone in describing the change as a biliary cirrhosis. The change seems to be temporary and does not appear to be the precursor or first stage of cirrhosis. The changes in the liver secondary to morbus cordis and spoken of as cardiac cirrhosis, pericarditic hepatic pseudo-cirrhosis, and cardio-tuberculous cirrhosis (*vide* p. 101) are chiefly met with in children.

TUBERCULOSIS OF THE LIVER AND BILE-DUCTS

Synopsis

Introduction.

Paths by which tubercle bacilli reach the liver.

By the umbilical vein (congenital tuberculosis); hepatic artery; portal vein; lymphatics; bile-duct.

Forms of hepatic tuberculosis.

(I) Miliary tuberculosis.

(II) Local tuberculosis.

- (*a*) Involving the bile-ducts.
- (*b*) Caseous tuberculous masses.
- (*c*) Tuberculous abscess.

Other changes in the liver associated with tuberculosis.

Focal necrosis. Fatty, lardaceous change.

Tuberculosis and cirrhosis.

Introduction.—Tuberculosis of the liver has little clinical importance, can seldom be diagnosed with certainty during life, and when found after death is usually part of generalised tuberculosis. Larger tuberculous

[1] Castellani and Chalmers. *Tropical Medicine*, 1910.

[2] *Vide* W. H. Dickinson. "Enlargement of the Viscera in Rickets," *Med.-Chir. Trans.*, Lond., 1869, lii, 359.

[3] Hogben. *Birmingham Med. Rev.*, 1888, xxiv, 65.

masses seldom give rise to clinical manifestations. In the exceptional instances in which a tuberculous mass or abscess has produced enlargement of the liver, some commoner result of tuberculosis, such as fatty or lardaceous change, would probably be diagnosed. The comparative infrequency of advanced tuberculous changes in the liver might suggest that, like the thyroid gland, the liver is inimical to the growth of the tubercle bacillus. This, however, is doubtful, for in lower animals, especially in birds, hepatic tuberculosis is common, and Sergent [1] shewed experimentally that the bile is not more antagonistic to the growth of tubercle bacilli than of other micro-organisms. It is probable that the reason why advanced tuberculous changes are rare in the liver is that the liver does not, like the mesenteric glands, lie in the direct line of the lymphatic vessels conveying lymph from the intestines. The lymphatic glands in the portal fissure receive the efferent lymphatic vessels conveying lymph away from the liver. In order that tuberculous infection should pass into the liver along the lymphatics of the portal fissure the bacilli would have to work their way against the flow of lymph. Possibly this does occur, but in most cases in which the intestines, the liver, and the lymphatic glands in the portal fissure are tuberculous, the tubercle bacilli have probably travelled from the intestine to the liver by the portal vein, set up tuberculous foci in the portal canals, and so infected the lymphatic glands in the portal fissure.

Marmorek,[2] however, finds from experiment that there is a certain amount of immunity to tuberculous infection on the part of the liver which cannot be satisfactorily explained on the anatomical grounds mentioned above. He believes that chemical factors inhibit the growth of tubercle bacilli in the liver.

Paths by which Tubercle Bacilli can reach the Liver.—Tubercle bacilli may reach the liver from various sources.

By the Umbilical Vein.—During fetal life, if there is tuberculous disease of the placenta, the bacilli reach the liver by the umbilical vein. This is very rare and is chiefly interesting from Baumgarten's view that tubercle bacilli are retained in the liver from early fetal life in the form of spores. Experimentally tuberculosis of the liver in the fetus has followed local tuberculous infection of the genital organs in guinea-pigs (D'Arrigo [3]). Cases of hepatic tuberculosis in children within the first fortnight of life have been described (Sabouraud,[4] Horl), and are undoubtedly due to infection during fetal life. Bar and Rénon [5] found tubercle bacilli in the blood of the umbilical vein of two fetuses of tuberculous mothers.

By the Hepatic Artery.—In generalised tuberculosis tubercle bacilli reach the liver by the hepatic artery. It is probable that tubercle bacilli often reach the liver when, although a number of bacilli have gained entrance to the general circulation, generalised tuberculosis does not result. Thus, in chronic

[1] Sergent. *Thèse de Paris*, 1895–6, No. 92; *Compt. rend. Soc. Biol.*, Paris, 1895, xlvii, 351.
[2] Marmorek. *Arch. gén. de méd.*, Paris, 1903, ii, 2945.
[3] D'Arrigo. *Centralbl. f. Bakt.*, 1900, xxviii, 683.
[4] Sabouraud. *Compt. rend. Soc. Biol.*, Paris, 1891, xliii, 674.
[5] Bar et Rénon. *Ibid.*, 1895, xlvii, 505.

pulmonary tuberculosis tubercles in the liver may be due to bacilli which have strayed into the blood-stream. The miliary tubercles are scattered through the liver both inside the lobules and in the portal spaces. It is possible that when a number of tubercles thus arise in the portal spaces they may increase in size and form a caseous mass which bursts into the bile-ducts and thus gives rise to the condition described as tuberculous cholangitis. Pilliet[1] suggested that tubercle bacilli might be excreted from the blood into the ducts and that tuberculous cholangitis then results. Microscopic examination, however, of such cases, viz. in which the ducts are involved (*vide* p. 341), shews that the tuberculous process always begins outside the ducts. It is only exceptionally that tuberculous cholangitis or abscess is due to bacilli reaching the liver by the arterial blood.

By the Portal Vein.—In tuberculous ulceration of the intestine tubercle bacilli readily pass by the portal vein to the liver, and there set up either miliary tubercles, or the larger and more chronic tuberculous changes in connexion with the bile-ducts. Tubercle bacilli can pass through the mucous membrane of the intestine without any gross lesion of the mucous membrane.

By the Lymphatics.—In tuberculous peritonitis bacilli may possibly pass through the lymphatic vessels of the capsule into the liver. It is also conceivable that tuberculosis of the glands in the portal fissure, secondary to intestinal disease, might extend to the inside of the liver against the current of lymph.

By the Common Bile-duct.—It has been suggested that tubercle bacilli from the duodenum pass up the bile-ducts, work their way through the mucous membrane of the ducts into the portal spaces, and there give rise to caseous tubercles. This view, which is improbable as tubercle bacilli are non-motile, has been disproved by Sergent's[2] injections of tubercle bacilli into the bile-ducts, which shewed that unless the walls of the ducts were previously damaged, as by ligature, they did not allow tubercle bacilli to pass through them. It is noticeable that the extra-hepatic ducts are not affected by tuberculosis except in the rarest instances, and that there is no condition of ascending or descending tuberculous cholangitis to correspond with tuberculous disease of the ureter.

To sum up: Tubercle bacilli reach the liver by the hepatic artery in generalised tuberculosis and in conditions which fall short of generalised tuberculosis. The portal vein also conveys tubercle bacilli to the liver, but there is no evidence that tubercle bacilli travel up the bile-duct and very little that hepatic tuberculosis is conveyed through the lymphatics.

Forms of Hepatic Tuberculosis

It might be thought more methodical to consider hepatic tuberculosis under two heads—(i) tuberculous disease of the liver substance proper and (ii) tuberculosis of the bile-ducts. But since, as will be shewn later, the ducts themselves are not affected primarily and only suffer as the result of extension from without, whether the starting-point is in the liver substance, the portal space, or in exceptional instances the lymphatic glands in the hilum, it is more practical to divide the subject of hepatic tuberculosis into—

[1] Pilliet. *Thèse de Paris*, 1891.
[2] Sergent, E. *Thèse de Paris*, 1895, No. 92.

(I) Miliary tuberculosis—(*a*) part of acute generalised tuberculosis; (*b*) due to infection from the intestine.

(II) Local tuberculosis—(*a*) involving the ducts; (*b*) not involving the ducts.

I. Miliary Tuberculosis

The presence of miliary tubercles in the liver is part of generalised tuberculosis, and though sometimes not seen on naked-eye examination, they will be found constantly in microscopic sections. Miliary tubercles are found in the liver in chronic pulmonary tuberculosis as a result of two processes: (*a*) tubercle bacilli reaching the liver by the hepatic artery, and (*b*) tubercle bacilli derived from secondary tuberculous ulcers in the intestine and passing to the liver by the portal vein.

Simmonds[1] found hepatic tubercles in 82 per cent of 476 cases of tuberculosis, 76 per cent in adults, 92 per cent in children. Zehden[2] found miliary tubercles in 50 per cent of all fatal cases of pulmonary tuberculosis, thus corresponding fairly with the frequency of tuberculous ulceration of the intestine in that disease. My own experience would put the occurrence of miliary hepatic tubercles in fatal cases of ordinary pulmonary tuberculosis lower than 50 per cent.

Miliary tubercles in the liver at birth have been referred to on p. 337.

Morbid Anatomy.—Miliary tubercles in the liver are small and isolated, grey, and when older yellow in colour, and are better seen on the surface of the capsule than on section of the organ. In some instances the liver may be crowded with minute miliary tubercles which can only be seen when microscopic sections are made; to the naked eye the liver may merely shew cloudy swelling. In the substance of the liver the tubercles are nearly always situated inside the lobules and thus form a contrast to the local and chronic form of tuberculosis of the liver occupying the portal spaces. Miliary tubercles are not very rare in cirrhotic livers. The liver is generally fatty and rather increased in weight; there may be considerable venous engorgement from terminal failure of the right side of the heart. Usually there is little or no tuberculous perihepatitis, but this may coexist with miliary tubercles in the substance of the liver in two conditions: (*a*) When there is chronic tuberculous peritonitis in which the capsule of the liver shares, or (*b*) in rare instances a subacute fibrinous peritonitis associated with acute miliary tuberculosis of the capsule of the liver. It is possible that the miliary tubercles in the hepatic substance may, if the generalisation is not very acute, have time to unite into small caseous areas which may soften down and form small tuberculous abscesses.

In a child aged three months who died in St. George's Hospital with advanced tuberculous bronchopneumonia, the liver contained a large number of

[1] Simmonds. *Centralbl. f. Path.*, 1898, ix, 865.
[2] Zehden. *Ibid.*, 1897, viii, 468.

miliary tubercles and two tuberculous cavities stained with bile, rather larger than a pea. The intestines were free from tuberculosis. Sergent described a unique case of confluent miliary tuberculosis of the liver.

Histology.—In their earliest stage tubercles consist of small round cells, like masses of lymphoid tissue, with a delicate reticulum. The cells are produced by proliferation of the connective-tissue cells; Metchnikoff regards the cells as phagocytes derived from vascular endothelium. After a time larger endothelioid cells are found in the miliary tubercle. When the tubercle grows larger, according to McWeeney,[1] 0·2 mm., giant cells appear. The giant cells are due to union of pre-existing cells, though it has been thought that continued growth and nuclear division without cellular division in endothelioid cells might account for them. The central part of the giant cells becomes homogeneous and caseous, while the nuclei form prominent objects around the periphery. It is often impossible to demonstrate bacilli in perfectly typical tubercles. The liver cells at the margin of the tubercles are compressed and may be fatty. In some cases the fatty change is widely diffused throughout the liver.

Signs and Symptoms.—There are *no clinical signs or symptoms* which can be relied upon to indicate the presence of miliary tubercles in the liver. Hilton Fagge[2] and Fränkel[3] have seen it associated with jaundice, and recently Warthin[4] states that some degree of jaundice is present in 80 per cent of the cases; this is quite contrary to general experience. A large number of tubercles on the surface of the liver may possibly give rise to a friction rub.

II. Local Tuberculosis

(*a*) Involving the bile-ducts. (*b*) Caseous tuberculous masses.
(*c*) Tuberculous abscess.

(*a*) Tuberculous Disease involving the Bile-ducts

Synonyms: Tuberculous Cavities in the Liver; Tuberculous Cholangitis or Pericholangitis.

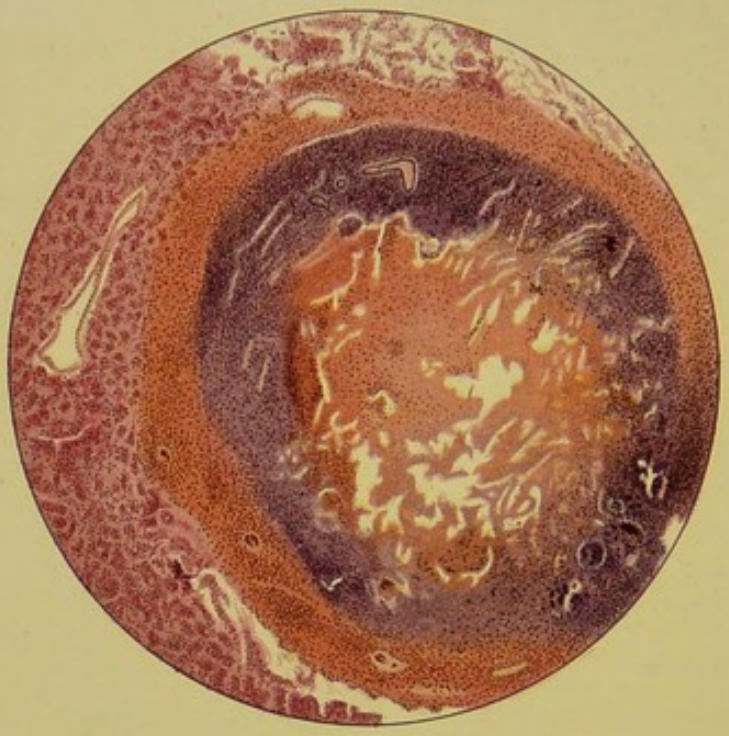
Incidence and Etiology.—Though this condition was described by Bristowe[5] in 1858, who found it in 12 out of 167 cases of tuberculous ulceration of the intestines, it has not attracted much general attention, probably because it has no clinical features. It is a commoner condition than the number of recorded cases would suggest. The tubercle bacilli reach the liver by the portal vein, being derived from the intestines, which in most instances shew tuberculous ulceration. They settle down

[1] McWeeney. *Brit. Med. Journ.*, 1900, i, 844.
[2] Hilton Fagge. *Textbook of Med.*, 1886, ii, 270.
[3] Fränkel, A. *Ztschr. f. klin. Med.*, 1882, v, 107.
[4] Warthin. *Internat. Clin.*, Phila., 1911, s. 21, i, 89.
[5] Bristowe, J. S. *Trans. Path. Soc.*, Lond., 1858, ix, 241.

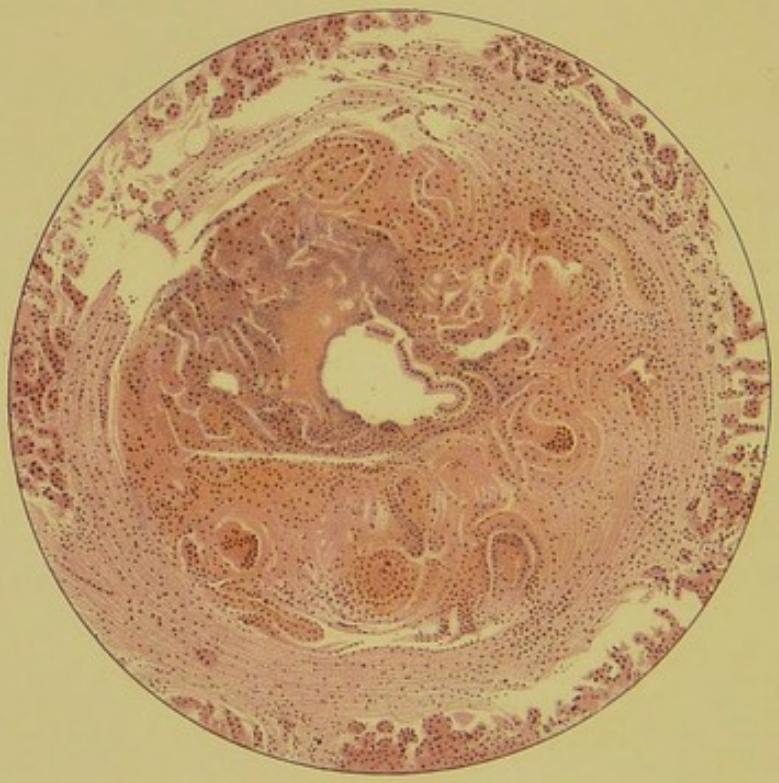
PLATE III.

Section of Liver Shewing Tuberculous Cavities in Portal Spaces, Communicating with the Bile-ducts, and Stained Green with Bile.

From a case recorded by Dr. Dudgeon. Painted by L. Jones, M.S.



1



2.

1. Advanced Stage of a Tuberculous Cavity in the Liver.

There is a dense fibrous capsule derived from the portal space which surrounds tuberculous granulation-tissue; more internally there is a mass of caseous debris.

2 Earlier stage, shewing tuberculous granulation-tissue occupying the portal space and opening into the bile-duct.

(These figures, from *Trans. Path. Soc.*, Lond. 1899, l, 160, were kindly lent by Dr. Morley Fletcher.)

in the portal spaces and produce miliary tubercles, and later masses of tuberculous granulation-tissue. The condition might well be spoken of as tuberculosis of the portal spaces.

Sergent[1] insists that the first step is tuberculous pylephlebitis and thrombosis of the intrahepatic branches of the portal vein, and that at a later stage tuberculous granulation-tissue develops in the portal spaces.

The tuberculous granulation-tissue caseates, softens down, and eventually breaks into the bile-ducts from without inwards. The discharge of the tuberculous foci into the ducts is analogous to rupture of a caseous focus in the lung into the bronchi. The ducts become infected and may be entirely destroyed locally. The communication between the cavities thus formed and the ducts is not always visible, but from the bile-stained condition of the "vomicae" there can be no doubt this has occurred. (Compare Wethered's case.[2])

As stress has been laid on the statement that the bile-ducts are invaded from without or are secondarily involved in tuberculous disease of the liver, it should be mentioned that Lancereaux[3] described a case of tuberculosis of the common bile-duct, gall-bladder, and cystic duct in a woman aged thirty-two years, which he regarded as directly due to infection from the duodenum.

Morbid Appearance.—The liver is usually somewhat larger than natural, and on section shews a number of white caseous areas or of bile-stained cavities with caseous walls. In the earlier stages, before the tubercles have opened into the ducts, the tuberculous material is firm and resembles, and is therefore sometimes regarded as, lymphadenoma; in the later (excavation) stage, when they have opened into a bile-duct, their walls have a greenish-yellow colour from bile-staining, and exceptionally a purple colour from haemorrhage. In their early stage the tubercles may be $\frac{1}{6}$ to $\frac{1}{4}$ inch in diameter; the cavities subsequently formed are larger and may measure an inch or even two inches across.

Structurally the masses are enclosed in a capsule representing the fibrous tissue of the portal space, and contain caseating granulation-tissue surrounding a cavity which can be seen opening into a bile-duct; the epithelium of the bile-duct may be well preserved except at the point of perforation from without. The tuberculous process is therefore primarily pericholangitic, not cholangitic. Further, the bile-duct is not affected throughout its course in the way that a tuberculous ureter is, but is locally infected at the spot where it is invaded from without. The larger extrahepatic ducts are very seldom involved; a softened tuberculous gland in the hilum of the liver may exceptionally open into the bile-duct.

Köster[4] has recorded a case which would bear this interpretation. A boy aged three years had jaundice, due to pressure of tuberculous portal glands, and

[1] Sergent. *Thèse de Paris*, 1895, No. 92.
[2] Wethered, F. J. *Trans. Path. Soc.*, Lond., 1889, xl, 139.
[3] Lancereaux. *Traité des maladies du foie et du pancréas*, 1899, p. 662.
[4] Köster. *Centralbl. f. inn. Med.*, 1896 xvii, 213.

tuberculous pneumonia. The liver contained tubercles, the ducts were dilated, and the lower end of the common bile-duct opened into a caseous cavity.

Macroscopic Diagnosis.—Tuberculous masses and cavities in the liver sometimes closely resemble other conditions. The deep bile-staining is extremely suggestive of tuberculous cavities in connexion with the bile-ducts, but before this staining has occurred the masses may resemble nodules of lymphadenoma, etc. The tuberculous masses are whiter and may break down, which lymphadenoma never does. In cirrhosis with multiple adenoma fatty change in the nodular areas of hyperplasia has often given rise to a mistaken diagnosis of tuberculous masses. In exceptional instances secondary carcinoma may closely imitate tuberculous masses and necessitate microscopic examination. The rare condition, chronic pericholangitis, of which Strangeways Pigg and I,[1] and Morley Fletcher,[2] have recorded examples, exactly imitates tuberculous cavities in the liver. Psorospermial disease of the bile-ducts in tame rabbits closely imitates tuberculous lesions, and though it is extremely rare in man, it is conceivable that some examples of this protozoan infection have been erroneously called tuberculous. Actinomycosis and the suppurating foci in pylephlebitis and cholangitis are hardly likely to be mistaken for tuberculous cavities, though abscesses at first regarded as tuberculous have been subsequently shewn to be actinomycotic.[3] Cysts lined with epithelium and containing clear fluid may occur in tuberculosis of the liver (Merle [4]), and may be due to obstruction of the ducts exerted by the tuberculous tissue.

Histologically the portal space is occupied by tuberculous granulation-tissue containing giant cells and undergoing caseation. This surrounds the bile-duct and opens into it. Eventually the bile-duct may be destroyed, and at this stage the portal space contains a central mass of caseous debris, stained with bile and surrounded by tuberculous granulation-tissue.

Clinical Features.—There are very seldom any definite symptoms pointing to the liver. It is indeed remarkable that jaundice is constantly absent, inasmuch as there is very definite obstruction in, at any rate some of, the bile-ducts.

It seems possible that the reason why jaundice is not met with is that the lymphatic vessels which should carry the bile from the obstructed ducts are themselves compressed and are unable to convey the bile into the general circulation. If this be the case, the liver substance should be bile-stained. Since this does not occur in cases of tuberculous cavities in the liver, this explanation cannot be urged.

It is true that occasionally attacks of abdominal pain have been reported in cases in which tuberculous cholangitis was found after death. These attacks of pain are not accompanied by jaundice or by bile in the urine and are not likely to suggest biliary colic. The abdominal pain is

[1] Rolleston and Strangeways Pigg. *Journ. Path. and Bacteriol.*, 1898, v, 221.
[2] Morley Fletcher. *Trans. Path. Soc.*, Lond., 1901, lii, 193.
[3] Harley, J., *Med.-Chir. Trans.*, 1886, lxix, 135; Shattock, S. G., *Trans. Path. Soc.*, Lond., 1885, xxxvi, 260.
[4] Merle. *Arch. de méd. expér. et d'anat. path.*, Paris, 1909, xxi, 353.

very probably due to tuberculous ulceration of the intestines or concomitant tuberculous peritonitis. Ascites may result from tuberculous peritonitis, or conceivably from compression of the portal vein by enlarged tuberculous glands. As a rule, the clinical aspect of the cases presenting this condition after death is that of pulmonary, abdominal, or generalised tuberculosis.

I examined after death a child aged nine months who had advanced tuberculous disease of the lungs, tuberculous ulcers in the intestine, caseous mesenteric glands, and tuberculous cavities in the liver. During life the signs were those of consolidation of the lungs ; there was no diarrhoea or jaundice. Winternitz [1] records a case of tuberculous cavities in the liver associated with tuberculous ulcers of the stomach. In Dudgeon's specimen of tuberculous cavities in the liver (*vide* Plate III) from a girl aged two years, there were tuberculous ulcers in the intestine, tuberculous peritonitis, and adenitis of the lymphatic glands in the portal fissure.

(*b*) Caseous Tuberculous Masses

Under this heading it will be convenient to consider comparatively large masses of caseous material which do not communicate with the bile-ducts. It is true that such masses might soften down and effect a fistulous communication with the bile-ducts, but it would then be impossible to be certain that the tuberculous process had not started near the bile-ducts. Although sometimes called "solitary tubercle," there may be a number of these caseous masses in the liver. This form of local tuberculosis, in which the portal spaces and bile-ducts are not specially involved, is rare, but is common in some animals.

Masses of hard caseous tubercle are very common in birds ; in fact, the liver is the chief, and in 20 per cent of the cases examined by W. Hutchinson [2] the only, organ affected in avian tuberculosis. In bovines large caseous masses are found in the liver ; they soften from suppuration and have a thick fibrous capsule.

Cases in man have been recorded by Craven Moore, Clement, Zehden, Simmonds (2), Fischer [3] (2), Thayer,[4] Felberbaum.[5] I have certainly seen two. F. Craven Moore's [6] case was extremely interesting in that there were 8 tuberculous masses in the liver of a man who died with carcinoma of the pylorus. It was thought that the tubercle bacilli were absorbed from the ulcerated surface in the stomach and that the absence of HCl in the gastric juice rendered this infection more feasible. Clement [7] described an almost exactly similar case. Inasmuch as tubercle bacilli were not found in Moore's or Clement's cases, the possibility arises that there may have been some other cause for the caseous masses, such as the pseudo-tuberculosis bacillus described by A. Pfeiffer and by

[1] Winternitz. *Johns Hopkins Hosp. Bull.*, 1908, xix, 223.
[2] Woods Hutchinson. *Studies in Human and Comparative Pathology*, p. 304.
[3] Fischer. *Arb. a. d. Geb. der path. Anat. und Bakteriol.*, Leipz., 1908, vi, 621.
[4] Thayer. *Bull. Johns Hopkins Hosp.*, Balt., 1911, xxii, 146.
[5] Felberbaum. *Med. Rec.*, N.Y., 1911, xxx, 1248.
[6] Craven Moore. *Med. Chronicle*, 1899, 3. s., ii, 5.
[7] Clement. *Virchows Arch.*, 1895, cxxxix, 35.

Klein. Klein[1] found a bacillus in Thames and Lea water which produced caseous masses in the liver, lung, and lymphatic glands.

The following are examples of multiple tuberculomas in the liver :

A boy aged eight years was admitted under my care in St. George's Hospital with pericarditis and advanced renal disease ; he recovered from the pericarditis, and multiple tuberculous lesions of the limbs, skull, and vertebrae gradually appeared. It was noticeable that as the tuberculous lesions advanced his renal symptoms receded. There was never any jaundice. He eventually died of exhaustion. The liver (20 oz.) was much enlarged as compared with his emaciated body. There was tuberculous perihepatitis with large white caseous masses, unstained with bile, in the liver. They were the size of filbert nuts and had been felt during life. No communication with the bile-ducts could be made out ; the mesenteric, tracheal, inguinal, and axillary glands were also tuberculous.

Milian and Hertz[2] recorded the case of a man aged fifty-eight with emaciation, an enlarged spleen, and fever unaffected by quinine. The clinical aspect suggested malaria or tuberculosis, but no signs were found in the lungs. The liver contained miliary tubercles and others as big as a horse-chestnut ; the spleen was also affected ; but there were no tubercles in the alimentary canal or lungs. In a somewhat similar case—a woman aged sixty-six years—described by Tolot,[3] there were no intestinal or pulmonary lesions.

Around the white caseous masses there is a thin fibrous capsule, and outside this the liver substance is compressed and the cells elongated and flattened. The caseous masses may be fairly easily enucleated. They closely resemble gummas, and must be distinguished from the appearance presented in nodular hyperplasia when fatty degeneration has occurred in the hyperplastic liver cells. In a few instances encysted caseous masses have also been found in the spleen (Milian and Hertz ; Tolot).

The **clinical aspect**, as has been shewn by the foregoing cases, is not characteristic. The liver may not be made out to be enlarged. Exceptionally a tuberculous mass may be sufficiently large to be felt through the abdominal walls during life. In Bunzl's[4] case there was so much pain that operation was necessary.

Thus, in a case related by T. L. Anderson[5] a mass the size of a tangerine orange in the left lobe of the liver was distinctly felt during life. The patient, a man aged forty-one, had extensive intestinal tuberculosis.

In a few cases the spleen is palpably enlarged. Jaundice is most exceptional ; it occurred in Thayer's case, which was thought to be one of malignant disease ; a diagnosis can hardly be made. As a rule, the patients suffer from increasing weakness, loss of appetite, and general debility.

[1] Klein, E. E. *Lancet*, 1899, ii, 1297.
[2] Milian et Hertz. *Bull. Soc. Anat.*, Paris, 1900, lxxv, 153.
[3] Tolot. *Lyon méd.*, 1902, xcix, 323.
[4] Bunzl. *München. med. Wchnschr.*, 1908, lv, 451.
[5] Anderson, T. L. *Australas. Med. Gaz.*, 1899, xviii, 93.

Excision of a tuberculous mass has been carried out with success (Rome,[1] Bunzl, Ransohoff[2]).

(c) Tuberculous Abscess

The caseous masses may become secondarily infected with pyogenetic micro-organisms, soften down, and form abscesses; this occurred in H. Mackenzie's[3] case, in which the cavities were purple and contained blood but not bile. In rare instances tuberculous abscesses may reach a considerable size, and cause local perihepatitis or even perforate into the peritoneal cavity. A tuberculous abscess of the liver may be either entirely inside the liver, or when near the surface of the organ may set up a localised perihepatic or a subphrenic abscess. A single tuberculous abscess of the liver is very rare. Some of the cases that have not been examined microscopically may have been softened gummas or actinomycotic abscesses (*vide* p. 386). A tuberculous abscess closely simulating actinomycosis is in the Pathological Museum of the University of Birmingham.

Mayo Robson[4] operated upon a tuberculous hepatic abscess which was evidently single, as the patient was in good health more than two years afterwards.

There may be other evidences of tuberculosis in the body, such as advanced pulmonary disease, or, on the other hand, the liver may be exclusively or almost exclusively affected. Tuberculous abscesses are usually small and multiple and belong to the group of local tuberculosis involving the bile-ducts.

Effects on the Liver of Tuberculosis elsewhere in the Body

Tuberculosis elsewhere in the body may lead to other changes in the liver besides the secondary development of tubercles.

1. Focal necrosis and coagulation-necrosis due to the virulent action of bacilli on the liver cells; this has been studied experimentally by Pilliet and is the same as that described by Hanot in other infective disorders.

2. Fatty change. The fatty liver met with in pulmonary tuberculosis is well known. It is discussed on page 427.

3. Lardaceous change is not uncommon in advanced cases with long-continued suppuration. This change is due not to the tuberculous toxin, but in all probability to toxins derived from secondary infection of tuberculous abscesses or vomicae with pyogenetic cocci.

Tuberculosis and Cirrhosis

As has been already pointed out, portal cirrhosis is frequently complicated by tuberculosis. It has, however, been thought that tuberculosis

[1] Rome. *Ann. Surg.*, 1904, xxxix, 98.
[2] Ransohoff. *Med. News*, N.Y., 1904, lxxxiv, 727.
[3] Mackenzie, H. W. G. *Trans. Path. Soc.*, 1890, xli, 156.
[4] Mayo Robson. *Trans. Clin. Soc.*, Lond., 1895, xxviii, 83.

may cause hepatic cirrhosis; in dealing with this question it will be clearer to consider it under two heads:

(A) Cirrhosis of the liver associated with tuberculosis of the liver.

(B) Cirrhosis of the liver associated with tuberculosis elsewhere, but not in the liver.

(A) *Cirrhosis associated with Tuberculosis of the Liver.*—In a patient with latent cirrhosis generalised tuberculosis may arise, and miliary tubercles develop in the liver in common with the other viscera. Tubercle bacilli may also be carried to a cirrhotic liver from the intestines. In children with nutmeg livers from backward pressure in heart disease, infection of the portal spaces with tuberculosis may supervene. The fibrosis is not great and the condition is essentially a complication of chronic venous engorgement of the liver; it is referred to under the name of "cardio-tuberculous cirrhosis" (p. 101). A large fatty cirrhotic liver containing miliary tubercles is sometimes seen. The two processes of hepatic cirrhosis and tuberculosis are probably independent of each other, but are both disposed to by alcoholism. Hanot and Gilbert[1] described a large fatty liver with small-celled infiltration and fibrous hyperplasia of the portal spaces and miliary tubercles as a morbid entity, due to tuberculosis, under the names "hypertrophic fatty tuberculous hepatitis" or "hypertrophic fatty cirrhosis." Clinically there is enlargement of the liver, slight jaundice, and a little ascites, the disease running a rapid course in about six weeks. They further described two less acute forms of tuberculous cirrhosis: (*a*) Without any enlargement of the liver, and (*b*) with more fibrosis than in the previous form, but with similar fatty change and tuberculous infiltration. The two latter forms only differ in the fact that one shews marked nodules, like those seen in cirrhosis with adenoma. There is no doubt that these forms occur, but I believe that, generally speaking, the cirrhotic changes are not due to the tuberculosis. Around tuberculous masses in the liver there is local fibrosis which sometimes spreads diffusely into the surrounding liver tissue.

On the other hand, it is quite reasonable to believe that tubercle bacilli might, under certain conditions, such as high resistance of the liver or a low degree of microbic virulence, cause fibrosis in the liver just as in the lungs. This does not very often happen in man, since if the resistance of the liver is good or the vitality of the bacilli feeble, the latter would probably be destroyed outright. Still there are experimental grounds for believing that tubercle bacilli may under some conditions have a sclerogenic effect on the liver. Hanot and Gilbert[2] found that in guinea-pigs the bacilli of avian tuberculosis produced a markedly cirrhotic liver with deep scars, whereas tubercle bacilli from man induced fatty change and coagulation-necrosis (Pilliet[3]). Stoerk[4] also produced a progressive fibrosis of the liver in guinea-pigs by the use of tubercle bacilli; at first there was definite tuberculosis of the liver, but as time went on the fibrosis advanced and the tuberculosis receded. Gougerot[5] obtained much the same results. A small deeply scarred liver with lobulation and cicatrices like those of acquired syphilis was found by Hanot to be associated with scattered

[1] Hanot et Gilbert. *Arch. gén. de méd.*, Paris, 1889, clxiv, 513.
[2] *Idem. Compt. rend. Soc. Biol.*, Paris, 1892, xliv, 72.
[3] Pilliet. *Thèse de Paris*, 1891.
[4] Stoerk. *Wien. klin. Wchnschr.*, 1907, xx, 847.
[5] Gougerot. *Rev. de méd.*, Paris, 1909, xxix, 81.

miliary tubercles in the substance of the organ. It resembles, in fact, the lesion produced in guinea-pigs by avian tubercle bacilli.

The following case, recorded by Collet and Gallavardin,[1] may perhaps be regarded as an example of cirrhosis due to tuberculosis. In a woman aged sixty in whom the spleen (4½ pounds) shewed massive tuberculosis the liver was greatly enlarged and contained small caseous tubercles in connexion with the portal spaces and a diffuse and rather delicate fibrosis. The hepatic changes were regarded as secondary to those of the spleen, and might be considered as an example of cirrhosis of splenic origin (*vide* p. 188). Isaac[2] described haematogenous tuberculosis of the liver, lasting 3½ years, and inducing cirrhosis.

(B) *Cirrhosis associated with Tuberculosis elsewhere, but not in the Liver.*—The association of hepatic cirrhosis and tuberculosis elsewhere in the body is common; in most cases in which the tuberculous process is active it has developed subsequently to the cirrhosis of the liver. In other instances there may be obsolete and latent tuberculosis of old date and independent cirrhosis of the liver, which are only discovered at the necropsy. In a certain number of cases old tuberculous lesions in the lungs are lighted up and make rapid progress in the course of alcoholic cirrhosis.

Nodular cirrhosis is sometimes found in fatal cases of pulmonary tuberculosis. Toxins generated in the lungs may lead to extensive fatty change in the proliferated liver cells forming the adenomatous projections on the cirrhotic liver. The appearance thus produced may imitate very closely that of multiple nodules of growth. It is conceivable that tuberculous lesions in other parts of the body may, by the production of chemical poisons, induce cirrhosis of the liver without any tuberculosis of that organ. Thus, in pulmonary tuberculosis, in which streptococcic infection of cavities is very common, toxins may be absorbed from the suppurating surfaces and carried to the liver by the general circulation. In most cases of such absorption from the lungs fatty degeneration of the liver, or even acute necrotic changes with toxaemic jaundice (Weber[3]), without any fibrosis, result; but in very chronic cases it is conceivable that cirrhosis might be brought about. Again, expectoration when swallowed may not only be the source of toxic bodies, which may subsequently be carried to the liver by the portal vein, but may set up gastro-enteritis and follicular, not necessarily tuberculous, ulceration of the intestines, and thus give rise to dyspeptic cirrhosis of the liver. Mouisset and Bonnamour,[4] however, believe that cirrhosis in tuberculous patients is nearly always due to concomitant alcoholism. Lavenson and Karsner[5] in 50 cases of tuberculosis of various parts of the body found some periportal fibrosis in 48, or 92 per cent, a higher percentage than in a number of control non-tuberculous patients; in 9 cases, or 18 per cent, the fibrosis was marked.

Hanot[6] described lobulation of the liver in 7 cases of chronic tuberculosis and believed that fibrosis was due to the tuberculous toxin. I have notes of one such liver in a man with chronic phthisis in whom there was no history of syphilis and no gummas in the body; there was, however, a scar on the penis,

[1] Collet et Gallavardin. *Arch. de méd. expér. et d'anat. path.*, Paris, 1901, xiii, 191.
[2] Isaac. *Frankfurter Ztschr. f. Path.*, Wiesbaden, 1908, ii, 125.
[3] Weber, F. P. *St. Barth. Hosp. Rep.*, 1908, xliv, 55.
[4] Mouisset et Bonnamour. *Rev. de méd.*, Paris, 1904, xxiv, 337.
[5] Lavenson and Karsner. *Univ. Penna. Med. Bull.*, Phila., 1909, xxii, 167.
[6] Hanot. *Gaz. des hôp. de Paris*, 1893, lxvi, 902.

and there can be little doubt that it was in reality syphilis. Possibly some of Hanot's cases may have been examples of delayed hereditary syphilitic disease of the liver with secondary tuberculosis. At any rate, such a condition in tuberculosis pure and simple must be very rare.

In conclusion, although from a pathological point of view tuberculosis, both in the liver and when confined to some other part of the body, may in certain circumstances set up some fibrosis in the liver, there is no reason to think that genuine cirrhosis of clinical importance is primarily produced in this way. Tuberculosis, whether in the liver or elsewhere, may produce degenerative changes in the liver cells, and when there is pre-existing cirrhosis, considerable damage may be done in this way.

SYPHILIS OF THE LIVER

History.—That syphilis affects the liver is a very ancient idea; according to Frerichs,[1] as old as the history of syphilis itself. But the earlier views naturally differed from those of the present day. Fallopius[2] in the sixteenth century considered that the liver was primarily affected in syphilis and so corrupted the humours of the body that ulcers occurred on the genitals. Subsequently Morgagni opposed the view that the liver was affected in syphilis. Later van Swieten, Portal, and Ricord described syphilitic lesions of the liver, but very little attention was directed to the visceral lesions of syphilis until Dittrich[3] in 1849, and S. Wilks[4] in this country, described gummas in the internal organs. The distinction between gummas and nodules of malignant growth dates from this time; previously gummas were regarded as cancerous nodules or even as evidence of healing of malignant growths.

Syphilitic disease of the liver will be considered under the two main heads of (i) the acquired and (ii) the congenital or hereditary forms.

Hepatic Lesions in Acquired Syphilis

The hepatic changes due to acquired syphilis will be considered under the heads of (i) the secondary and (ii) the tertiary manifestations, while brief reference will be made to the possibility that remote—parasyphilitic—changes in the liver may be due to syphilitic infection.

The Secondary Manifestations of Syphilis in the Liver.—Diffuse intercellular cirrhosis similar to that of congenital syphilis occurs in the acquired form. But opportunities for examining the liver in the secondary stage of acquired syphilis are rare.

[1] Frerichs. *Diseases of the Liver* (Transl. New Sydenham Soc.), 1861, ii, 150.
[2] Fallopius. *Tract. de Morbo Gallico*, Padua, 1584.
[3] Dittrich. *Vrtljschr. f. d. prakt. Heilk.*, Prag, 1849, 1; 1850, 33.
[4] Wilks, S. *Trans. Path. Soc.*, Lond., 1857, viii, 240.

Hermann Weber[1] many years ago described a case of acquired syphilis in a man aged twenty, in whose liver the lesions appear to have been intercellular. I have examined a few cases in which the liver of syphilitic subjects has shewn diffuse unicellular cirrhosis without any gumma.

Since then few cases are examined during the secondary stage, and since it is a lesion from which recovery is quite possible, it is not unlikely a priori that the condition occurs temporarily and usually passes away. In support of this it may be pointed out that in the rare cases of acute yellow atrophy supervening after syphilis the microscopical appearances are at least compatible with the view that there has been unicellular cirrhosis and that excessive necrosis of the hepatic cells has supervened.

In a man aged forty-seven, who died of cerebral haemorrhage and had gummatous testes, the liver shewed very diffuse intercellular fibrosis which varied in different areas, but was compatible with the views that there had been partial acute atrophy with recovery, or that it was intercellular cirrhosis. Dr. Parkes Weber,[2] who kindly shewed the slides to me, pointed out that the situation of the fibrosis, viz. around the capillaries of the hepatic artery, resembled that of lardaceous change and suggested that the poison was carried by the hepatic artery.

In the secondary stage of acquired syphilis the liver may be affected so as to give rise to jaundice, either innocent or malignant; unicellular cirrhosis may occur, and in exceptional cases gummatous lesions are present (*vide* p. 360).

Jaundice in the Secondary Stage of Syphilis.—Jaundice may occur early in the secondary stage and at the same time as the cutaneous roseola. Paracelsus (1510) and Sanchez in the eighteenth century are credited[3] with having noticed the association between early syphilis and jaundice, but our knowledge really dates from Gubler's[4] memoir containing 5 cases in 1853. It is, however, uncommon, and more so in Germany than in France; in 15,799 cases of syphilis Werner[5] met with jaundice in 57, or only 0·37 per cent; and Goldstein[6] in 20 out of 7462 cases of syphilis, or 0·26 per cent. In 1868 Lancereaux[7] collected 21 cases, and in 1900 Lasch[8] referred to 49 cases, almost all from French literature. These figures suggest that jaundice during the roseolous stage is far rarer than it is in reality.

There are numerous views to explain the occurrence of jaundice in the early stages of syphilis. Inasmuch as it often coincides with the exanthem, it was first thought that it is due to a somewhat similar

[1] Weber, H. *Trans. Path. Soc.*, 1871, xvii, 152.
[2] Weber, F. P. *Brit. Med. Journ.*, 1899, i, 728.
[3] *Idem. Proc. Roy. Soc. Med.*, 1909, ii (Path. Sect.), 116.
[4] Gubler. *Mém. Soc. Biol.*, 1853, v, 235.
[5] Werner, S. *München. med. Wchnschr.*, 1897, xliv, 736.
[6] Goldstein. *Wien. med. Wchnschr.*, 1904, liv, 1861.
[7] Lancereaux. *Syphilis*, 1868, i, 182; transl., New Sydenham Soc.
[8] Lasch, O. *Berlin. klin. Wchnschr.*, 1894, xxxi, 904; *Selected Essays*, New Sydenham Soc. Library, 1900, p. 145.

condition in the mucous membrane of the bile-duct (Gubler); or, in other words, a specific cholangitis. A condyloma of the bile-duct has also been suggested. According to another view, pressure is exerted on the ducts by syphilitic enlargement of the lymphatic glands in the portal fissure; in favour of this it may be mentioned that out of Werner's 57 clinical cases of syphilitic jaundice there was marked enlargement of the superficial lymphatic glands in 41.

In Talamon's[1] case of acute yellow atrophy in a girl aged seventeen with a secondary cutaneous eruption and other signs of syphilis the glands in the portal fissure were enlarged but did not compress the common bile-duct.

It has been thought to be haemolytic in origin, and due either to increased fragility of the reds or to a haemolysin in the blood (Gaucher and Gougerot[2]). It is probably not simple catarrhal jaundice occurring in a person who has recently contracted syphilis, since the successful treatment is that of syphilis and not of catarrhal jaundice. But it might be due to changes in the small intrahepatic bile-ducts caused by general syphilitic hepatitis. When this intercellular infiltration is excessive, it may run on into acute yellow atrophy; about 50 cases of this severe sequel have been recorded, only 10 being in males (Fischer[3]; *vide* also p. 577). There is no proof that the jaundice is due to the administration of mercury, for in only 4 of 49 cases of benign jaundice occurring in the early stage of syphilis, collected by Lasch, had mercury been given before the icterus appeared.

Sex.—In Lasch's 49 cases 25 were men and 24 women, but as more cases of syphilis are seen in men, syphilitic jaundice is proportionately more frequent in women.

Its onset is usually sudden without any apparent cause and is not accompanied by any special disturbance, such as is seen in cholelithiasis or catarrhal jaundice. It comes on simultaneously with the cutaneous roseola and may coincide with a particularly copious eruption. It may appear as soon as five weeks after infection, or later up to the sixth month.

Clinical Features.—The jaundice is well marked, and unless treated with mercury, tends to become chronic; thus it may last three months if treated with the ordinary remedies for catarrhal jaundice. The aspect of the patient with a jaundiced syphilitic eruption is very characteristic and somewhat repulsive. There is an absence of gastro-intestinal symptoms and of itching; the appetite is well preserved, though distaste for fatty food may be experienced. The liver is usually slightly enlarged and the spleen may be palpable. In two exceptional cases there was transient ascites (Quincke,[4] Gembarski[5]). Bile is absent from the urine or only temporarily present.

[1] Talamon. *Méd. mod.*, Paris, 1897, viii, 97.
[2] Gaucher et Gougerot. *Ann. des mal. vén.*, Paris, 1911, vi, 326.
[3] Fischer. *Berlin. klin. Wchnschr.*, 1908, xlv, 905.
[4] Quincke. *Die Krankheiten der Leber*, Wien, 1899.
[5] Gembarski. *Rev. de méd.*, Paris, 1910, xxx, 689.

Diagnosis.—The important point is to recognise that in a patient with recent syphilis jaundice may be a specific manifestation and not an independent attack of catarrhal jaundice. From the presence of the roseola and enlarged glands the recognition of syphilis is easy.

The *prognosis* is good, as a rule, but in some rare cases the jaundice passes into acute yellow atrophy. There are probably intermediate grades between the benign jaundice and the acute yellow atrophy occurring in the early stage of syphilis.

The *treatment* is that of secondary syphilis; it is noteworthy that the ordinary treatment of catarrhal jaundice is without any good result. If the mercurial treatment is prematurely discontinued, jaundice may recur.

The Tertiary Lesions of Syphilis in the Liver.—The specific tertiary lesions in the liver are polymorphic and include gumma, gummatous infiltration, cicatrices, and a combination of gummas and cicatrices (sclero-gummatous form). Lardaceous disease, which may be considered as a parasyphilitic lesion, is often combined with gummas and with cicatrices.

The manifestations of tertiary syphilis in the liver may be divided into (*a*) those that are progressive and (*b*) those that are merely the relics of past syphilitic activity. In other words (*a*) the late secondary and tertiary lesions seen in the gummas and gummatous infiltration of the organ and (*b*) the cicatrices, calcified remains, and deformities left behind by the first-named lesions are both included under the tertiary manifestations. Lardaceous disease, which is a sequel of syphilis, is dealt with elsewhere (*vide* p. 433).

Gumma.—The word gumma was employed in its present sense by Fallopius in 1584. But it was not generally used until comparatively recent times. In 1852 Budd[1] described gummas under the name of "encysted knotty tumours of the liver," and separated them from cancerous growths, with which they had been generally confounded, but did not recognise their syphilitic origin or speak of them as gummas.

Method of Formation of a Gumma.—The early stage of the future gumma is a mass of syphilitic granulation-tissue of a pink colour, sharply localised, and contrasting with the healthy liver substance. At this stage it is better to speak of it as a syphiloma, since the word gumma describes a caseous mass surrounded by a fibrous capsule. After a time necrosis occurs in the centre of the syphiloma; this is partly due to syphilitic endarteritis in the neighbourhood whereby the blood-supply is cut off, so that the process has been compared to infarction (Beriel and Laurent[2]), and probably in part to an increase in amount or concentration of the syphilitic poison. At this stage there is a yellowish-white centre surrounded by pink granulation-tissue. Later there is a caseous mass surrounded by a fibrous capsule, a condition resembling a caseous

[1] Budd. *Diseases of the Liver*, 1852 ed. ii, 407.
[2] Beriel et Laurent. *Lyon méd.*, 1910, cxiv, 1291.

tubercle of some duration. By the union of several gummas a large gummatous area may result.

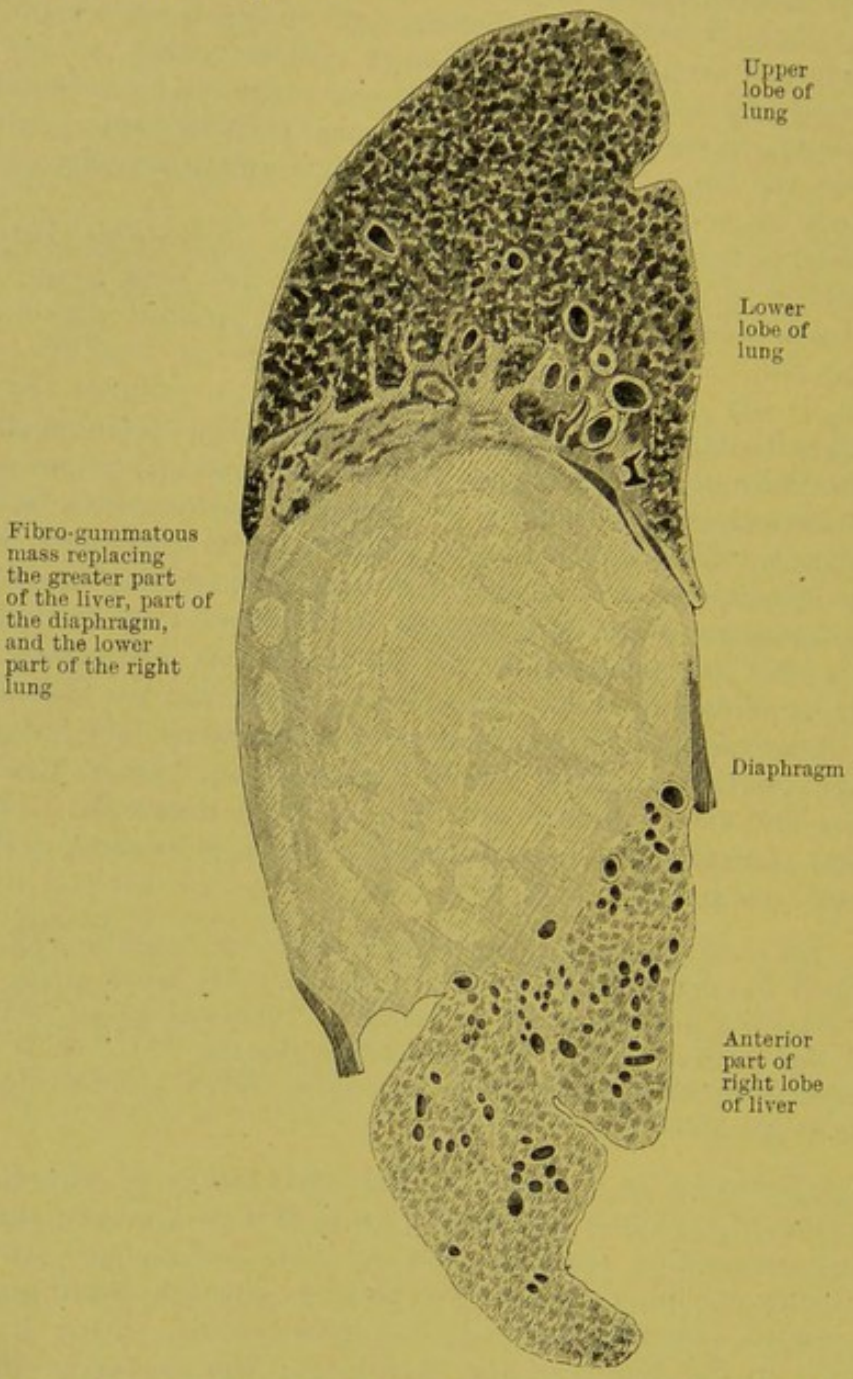


FIG. 41.—A large gumma of the liver extending through the diaphragm into the lower lobe of the right lung. From a specimen (Series ix, 183 g) in St. George's Hospital Museum.[1]

Structure, etc.—A well-marked gumma consists of a firm, yellowish-white mass, not unlike the section of a potato, surrounded by a fibrous capsule which spreads out for a short distance into the surrounding liver tissue. In rare instances the caseous part of a gumma is yellow from

[1] I am indebted to Professor S. Delépine for this block, which appeared in the *Transactions of the Pathological Society of London*, 1891, xlii, 151.

bile-staining (Marie[1]). There are thus three zones in a gumma: (1) The central area of necrosed or necrosing granulation-tissue; (2) the surrounding fibrous capsule; (3) the invasion of the surrounding parts of the liver by interstitial fibrosis.

Old gummas consist of the central caseous portion and the well-formed fibrous capsule without any advancing margin. In recent gummas in which the capsule is indefinite there is, on the other hand, well-marked infiltration of the liver tissue.

The amount of fibrous tissue enclosing a gumma varies; in large and advancing gummas it may be slight and indistinct, in old gummas it is firm and dense. As it contracts it presses on the caseous centre, and at the same time, if near the capsule of the liver, produces thickening, puckering, and cicatrices on the surface of the organ. Perihepatitis and thickening of the capsule are thus produced; in rare instances, of which an example is given on page 165, there may be chronic universal perihepatitis. Adhesions frequently form between the liver and adjacent organs, the diaphragm, and the anterior abdominal wall; in rare instances gummas may behave like malignant tumours and invade the anterior abdominal wall, the diaphragm, or adjacent organs.

In a specimen (series ix, 183 g) in St. George's Hospital Museum an immense gumma of the right lobe of the liver passed through the diaphragm and extensively infiltrated the lower lobe of the right lung (Delépine and Sisley[2]; *vide* also Fig. 41). In a case reported by Bruhl and Lyon Caen[3] a softened gumma put a bile-duct and bronchus into communication and so gave rise to a broncho-biliary fistula. In a case of late hereditary syphilis with the usual tertiary changes, recorded by Post,[4] gummatous inflammation extended into the anterior abdominal wall and produced a definite tumour.

Gummas are usually in the substance of the liver; occasionally, however, they project from the surface of the organ. To the naked eye gummas may sometimes closely resemble primary massive carcinoma or multiple carcinomatous growths in the liver.

Gouget[5] described a case in which columnar-celled carcinomatous growths were at first thought to be gummas; I have seen similar appearances on several occasions. As a rare coincidence secondary growths may occur in a liver containing gummas. Microscopical examination is necessary before deciding that both gummas and secondary new-growths are present. In 1891 I examined such a case; a man had primary carcinoma of the colon with small secondary growths in a scarred and gummatous liver. The left testis also contained gummas.

[1] Marie, R. *Bull. Soc. Anat.*, Paris, 1901, lxxvi, 628.
[2] Delépine and Sisley. *Trans. Path. Soc.*, 1891, xlii, 141.
[3] Bruhl et Lyon Caen. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1909, xxviii, 295.
[4] Post. *Boston City Hosp. Rep.*, 1898, p. 233.
[5] Gouget. *Bull. Soc. Anat.*, Paris, 1898, lxxiii, 605.

The *microscopic appearances* of a gumma differ according to its age. In the stage when caseation has begun, the central necrotic part, which to the naked eye appears white, is fibrillar or granular, shews a few nuclei but is otherwise structureless, and does not stain properly ; around it there is a mass of cells due to proliferating fibroblasts, and containing lymphocytes, plasma cells, and occasionally eosinophil and giant cells. These giant cells, which are rare in gummas, are formed from the endothelium of the small blood-vessels and possibly lymphatic vessels. The giant cells in gummas are not so large as in tuberculosis. Necrosis and caseation may be seen to be extending into this surrounding granulation-tissue in young gummas, while in older ones organisation is going on and

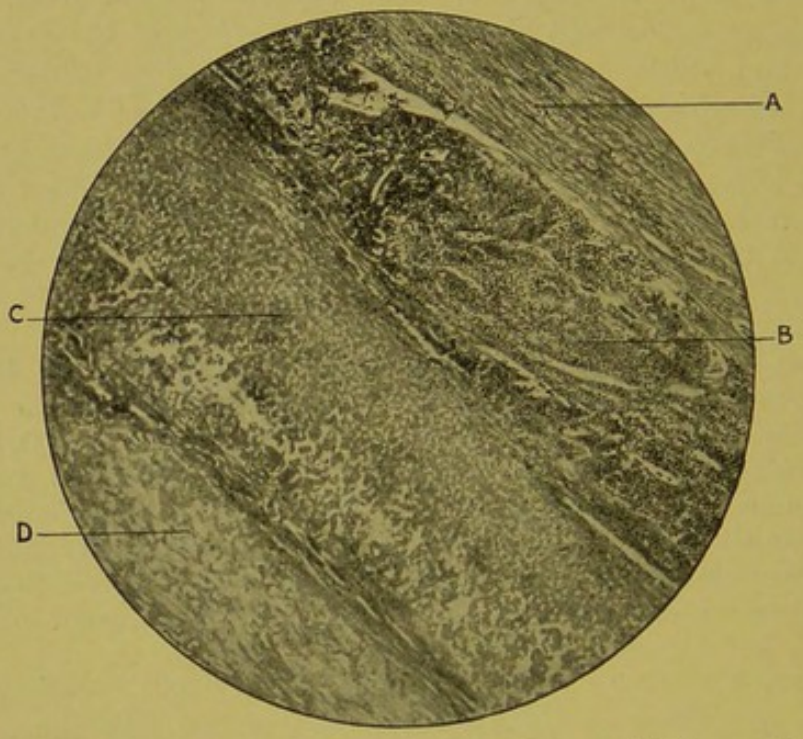


FIG. 42.—Recent gumma of liver. × 30. A, Fibrous capsule ; B, syphilitic granulation-tissue ; C, caseating granulation-tissue ; D, caseous centre.

a capsule of connective tissue is formed around the caseous mass. The fibrous capsule contains elastic fibres and globules of fat.

The granulation tissue spreads into the surrounding liver tissue for a short distance, so that there is intercellular cirrhosis in the immediate neighbourhood of the gumma. Later groups of liver cells become surrounded by bands of young connective tissue, and in recent cases the solid columns of small cubical cells (pseudobile canaliculi) which stain deeply are prominent objects at the margin of a gumma. The liver cells near the margin of a gumma are flattened from pressure and may be spindle-shaped. The *Treponema pallidum* may be found at the margin of the necrotic areas.

The small arteries at the margin of a gumma shew well-marked endarteritis obliterans. There is sometimes lardaceous change immedi-

ately around the gumma. In old gummas which are no longer advancing, the fibrous capsule is dense and well formed, there is no small-celled infiltration around the gumma, and no giant cells. The caseous material and the proliferating zone around it contain a good deal of fat and thus differ from tuberculous caseation, in which fatty change is slight, the degenerative change being of a hyaline nature (Gaylord and Aschoff [1]). Bile-stained cavities are very rare; they may be due to escape of bile into a softened gumma, or may be the outcome of a gummatous pericholangitis (Brault and Legry [2]).

Retrogressive Changes in Gummas.—The caseous material may diminish

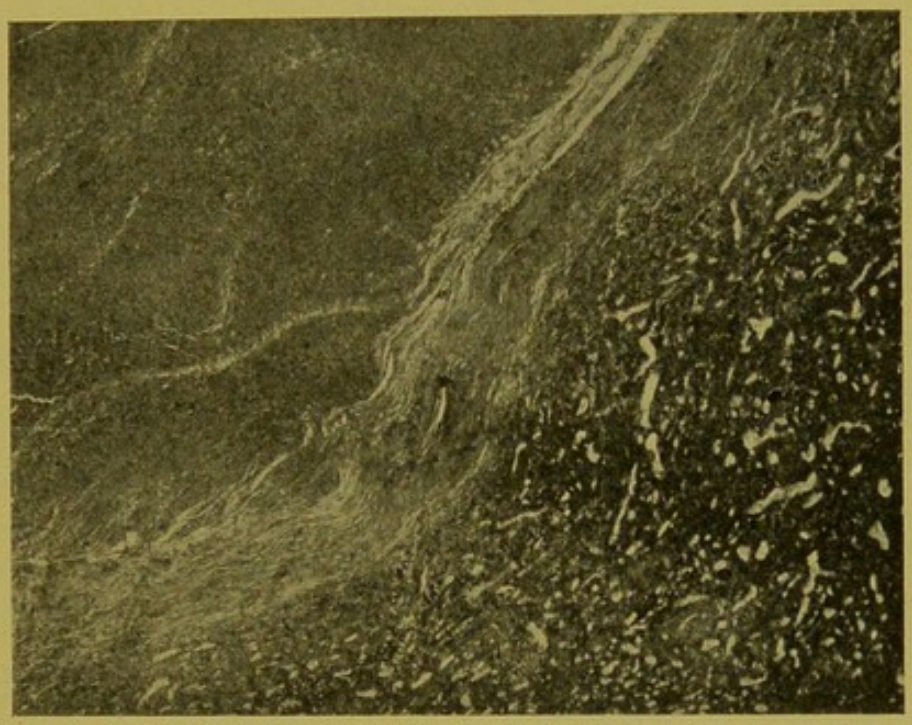


FIG. 43.—Old gumma of liver. The lighter part is the caseous material; it is surrounded by a dense fibrous capsule which extends into the surrounding liver substance. (Photomicrograph by Dr. S. G. Penny.)

in amount from the circumferential pressure exerted upon it by the contraction of its fibrous capsule; at the same time it becomes drier from absorption of fluid. Calcareous change is not very rare, but it is usually only in small particles which do not offer any real resistance to the knife. In these cases the presence of calcareous matter is best seen in microscopic sections. In other instances calcification is best seen in the capsule of the gumma (*vide* Cambridge Museum, Nos. 504, 505). In exceptional cases calcification is very prominent.

Dr. Fooks kindly sent me the liver of a woman aged fifty-nine who died in the Brentford Union Asylum, Isleworth, in April 1898. It weighed 31½ ounces and was two-thirds the natural size. The surface was scarred and puckered all

[1] Gaylord and Aschoff. *Pathological Histology*, p. 95, 1902, Lond.
[2] Brault et Legry in *Manuel d'histologie pathologique*, Paris, 1912, iv, part ii, 899.

over, especially on the right side. These cicatrices were all calcified; a section of the organ exposed several calcareous masses the size of a walnut. The youngest case in which I have seen calcified gummas was in a girl aged nineteen years, who died from the effects of lardaceous disease in St. George's Hospital in 1905. The liver, 44 oz., contained two calcified gummas. A cicatrix was found on the genitals and there were no signs of congenital syphilis.

Targett[1] described diffuse calcification of the liver which probably supervened on gummatous change (*vide* Fig. 44). Calcification of the liver may in very rare instances occur independently of syphilis (*vide* p. 440) and is met with in animals.

Occasionally gummas soften down; this may very probably be the result of treatment with iodides, and be a stage in the process of absorption. It may also be due to infection, and when it occurs in a large gumma the condition is practically a chronic abscess.

Fig. 44.—Diffuse calcification of liver probably subsequent to gummatous infiltration. St. George's Hospital Museum, Series ix, 172 B. (Drawn by Dr. E. A. Wilson.)

Moxon[2] described a large gumma, which softened down and communicated with a bile-duct.

Unless the gumma is very large, it is slowly absorbed. This is carried on by autolysis and phagocytosis, and depends on the neighbouring blood-vessels and lymphatics being permeable and not obstructed by syphilitic changes. The more the gumma contracts, the more it resembles the scars and cicatrices which are in many cases the only remains of obsolete gummas. This probably accounts for the rarity of gummas in old persons. The scars may, however, result from the organisation of inflammatory products without any central caseation having taken place.

Number and Situation.—Gummas may be circumscribed and multiple, or there may be diffuse gummatous infiltration of a large part of one or even of both lobes. The right lobe is much more often affected and the anterior surface far more frequently than the under aspect. They are much more often multiple; in 100 cases of hepatic gummas collected by Tresawna[3] only 11 were single. The liver of a soldier aged thirty-two, who had contracted syphilis ten years previously, weighed 67 oz. and contained small caseous gummas, estimated at 268 in number [St. George's Hospital Post-mortem Book, 1905, No. 334]. It is said that the neighbour-

[1] Targett. *Trans. Path. Soc.*, Lond., 1889, xl, 123.
[2] Moxon. *Ibid.*, 1872, xxiii, 153.
[3] Tresawna, W. S. Unpublished Thesis for M.B. degree, Cambridge, 1907.

hood of the falciform ligament is a favourite situation for gummas, but I have not noticed any special localisation of gummas except the anterior surface. They may occur in any part and may, when near the portal fissure, press on the main trunks or branches of the bile-ducts or portal vein. In W. G. MacCallum's[1] case a gumma in the liver pressed on the inferior vena cava and gave rise to thrombosis.

Syphilitic Cicatrices.—Deep furrows on the surface of the liver, due to cicatricial contraction, are the result of organisation of syphilitic granulation-tissue. Cicatrices may be formed directly from syphilomas or be the last stage of a gumma which has undergone absorption. The

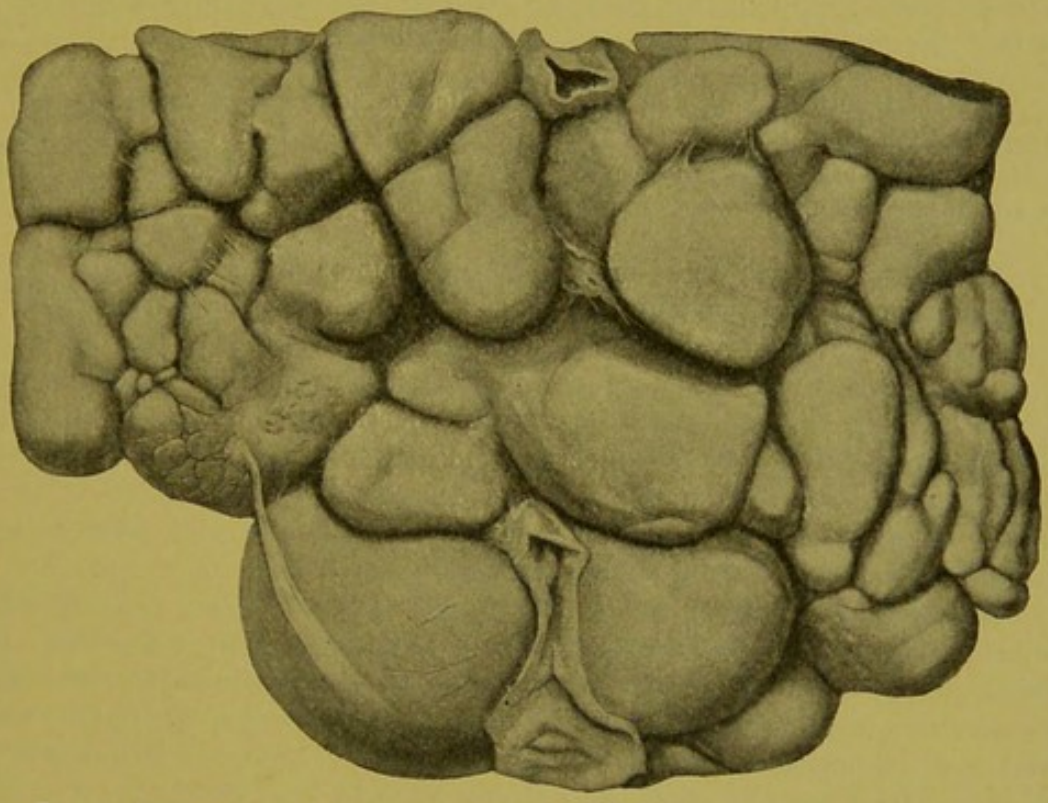


Fig. 45.—Liver with syphilitic cicatrices. St. George's Hospital Museum, Series ix, 174 e.

cicatrices may be linear or may be star-like. The linear cicatrices may divide a lobe into a number of lobules; the star-like cicatrices are depressed with well-formed fibrous tissue radiating into the capsule on all sides of it. The liver may be so widely fissured and lobulated by cicatrices that it has a slight resemblance to the coarse hobnailed liver of portal cirrhosis, but the irregularity of this diffuse syphilitic fibrosis, or "syphilitic cirrhosis," as it is often called, distinguishes it from genuine portal cirrhosis. Like gummas, these scars are said to be frequent in the neighbourhood of the falciform ligament. When they occur near the portal fissure, they may involve the portal vein, giving rise to ascites, or the bile-ducts, thus producing jaundice; or if they occur near the

[1] MacCallum. *Johns Hopkins Hosp. Bull.*, Balt., 1903, xiv, 88.

coronary ligament, they may lead to narrowing or obliteration of the hepatic veins (*vide* p. 50).

Bosanquet[1] records obliteration of the inferior vena cava by syphilitic cicatrices spreading from a gummatous liver.

The scars may contain a central caseous mass, shewing that they are receding gummas; sometimes calcification has commenced in the caseous material. The older the scar, the denser it is, and the more depressed the surface of the liver over it.

Gummas and Cicatrices combined (Sclero-Gummatous Form).—The contraction of syphilitic cicatrices and gummas may lead to great deformity, so that the organ is nodular and irregularly lobulated.

In a girl aged twenty-five years who died under my care in St. George's Hospital with syphilitic stenosis of both bronchi[2] the liver (52 oz.) was occupied by multiple caseous gummas and was so extensively scarred that as many as 16 lobes could be counted on its anterior surface.

The shape of the liver may be altered out of all recognition. The relative size of the two chief lobes of the liver may be greatly altered; thus, the left lobe may be almost entirely destroyed by fibrous contraction, or enlarged from gummatous infiltration or from hyperplasia of the liver substance to compensate for extreme destruction of the right lobe. Schorr[3] and Milne[4] have collected some cases of compensatory hypertrophy of one lobe when the other is destroyed by gummatous or cicatricial change. As a rule, the syphilitic lesions and enlargement are much more marked in the right than in the left lobe.

Association of Gumma and Lardaceous Change in the Liver.—As already pointed out, local lardaceous change may be found around a gumma. In other instances gummas may be found in a universally lardaceous liver. In 86 cases of gummas collected by J. L. Allen the liver was lardaceous in 12, or 14 per cent. In Flexner's[5] 88 cases the liver was lardaceous in 7 or 8. In these 174 cases the percentage is 11·2.

Incidence of Gummas in Universally Cirrhotic Livers.—It might naturally be supposed, since alcoholic excess and exposure to syphilitic infection are frequently associated, that gummas would be common in universally cirrhotic livers. This, however, is not the case, and it is remarkable how seldom gummas and ordinary portal cirrhosis coexist in the same liver.

Among 174 cases of hepatic gumma, obtained by combining J. L. Allen and Flexner's cases, there were 13, or 7·5 per cent, with genuine cirrhosis. Dr. Trevor has shewn me a universally cirrhotic liver containing several large gummas and adenomas.

[1] Bosanquet, W. C. *Edin. Med. Journ.*, 1902, N.S., xii. 250.
[2] Rolleston and Ogle. *Trans. Clin. Soc.*, 1899, xxxii, 158.
[3] Schorr. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1907, xlii, 179.
[4] Milne. *Journ. Path. and Bacteriol.*, Cambridge, 1909, xiii, 129.
[5] Flexner. *New York Med. Journ.*, 1902, lxxv. 101.

Incidence of Tertiary Hepatic Lesions.—Though well recognised and exhaustively described, the tertiary hepatic manifestations are by no means very common. It is true that cicatrices of old gummas are usually entirely latent, so that they are less frequently detected clinically than in the post-mortem room. Cicatrices are apparently more often seen than gummas, though in many instances gummas and cicatrices are present in the same liver. But even in the post-mortem room they are rare.

In an examination of the post-mortem records of St. George's Hospital, dealing with a period of fifty years (from 1857 to 1906), J. L. Allen and W. S. Tresawna found 44 cases only of undoubted hepatic gummas ; during this same period there were 13,960 necropsies ; there were, in addition, 34 other cases in which cicatrices alone were present. Among 9500 necropsies at Guy's Hospital in the twenty years 1885–1904 there were 23 cases with gummas, and 72 with cicatrices (Hale White [1]). Among 11,300 necropsies performed at the Middlesex Hospital between 1854 and 1900 gummas were noted in the liver in 40 cases.[2] In a period of thirty-five years during which there were 5088 necropsies at the Philadelphia Hospital, Flexner [3] found gummas in 23 cases, cicatrices in 38, and in all 88 cases of hepatic syphilis, half this number being cases of diffuse syphilitic fibrosis. Thus, out of a total of 39,848 necropsies gummas occurred in 130 cases only, or 0·33 per cent. But when syphilitic lesions are found in the body after death the liver is affected in more than half the cases ; in 87 such cases examined at Manchester the liver shewed syphilitic changes in 51, or 58·6 per cent (Brockbank [4]).

There is indeed a great contrast between the frequency of hepatic lesions in congenital and in acquired syphilis.

Predisposing Causes.—It has been thought that previous disease of the liver, or conditions such as alcoholism, malaria, or jaundice, would, by diminishing the resistance of the liver, render it more likely to be affected. Trauma, such as blows or previous injury to the liver, may very probably, as elsewhere in the body, determine the occurrence of gummas in the organ. It is interesting to note that gummas have been found in the pendulous portion of the right lobe seen in the tight-laced or corset livers of women. But hepatic gumma is more often seen in men than in women.

In 141 cases of gumma of the liver collected from various sources by W. S. Tresawna 100 were males and 41 females ; he could not find any evidence that tight lacing disposed the liver to gummatous change.

It is difficult to prove the influence of injury in determining the incidence of gumma in the liver, but the greater frequency of hepatic gumma in the male sex, nearly 3 to 1, and on the anterior surface of the liver, certainly favours this hypothesis.

[1] Hale White. *Common Affections of the Liver*, p. 192, 1908.
[2] *Arch. Middlesex Hosp.*, 1905, v, 136.
[3] Flexner. *New York Med. Journ.*, 1902, lxxv, 101.
[4] Brockbank. *Med. Chronicle*, Manchester, 1909, l, 319.

In a case recorded by Pitt[1] the irritation of an old hydatid cyst in the liver seemed to have determined an extensive syphilitic formation around it.

Age Incidence.—The great majority of hepatic gummas are found between the ages of twenty-five and fifty years. In 78 cases of hepatic gumma collected by J. L. Allen, 69, or 88·5 per cent, occurred within this limit. The average age of these 78 cases was thirty-nine years, and was almost the same in the two sexes. The cases were arranged as follows :—

Age.	Number of Cases.	Age.	Number of Cases.
15–20	1	46–50	11
21–25	2	51–55	3
26–30	15	61–65	1
31–35	10	66–70	1
36–40	21	71–75	1
41–45	12		

Gummatous disease in the liver has been observed at the advanced age of eighty-nine (Wagner[2]).

Interval between Infection and the Appearance of Gummas.—Usually several years, from ten to twenty, elapse between the primary chancre and evidence of gummas in the liver ; but exceptionally gummas have been found within a year of infection.

Key[3] found a gumma the size of a walnut in the liver of a woman aged twenty-six who died of generalised tuberculosis six months after infection ; and Fleischhauer,[4] a gumma in the liver of a man who died seven months after infection. These cases are analogous to the rare instances of hepatic gummas in fetuses and stillborn children (*vide* p. 370).

Clinical Manifestations.—Clinically the occurrence of manifestations due to hepatic lesions, apart from lardaceous disease, is comparatively rare in tertiary syphilis.

Mauriac,[5] combining the statistics of Fournier, Ehlers, and Hjalmann, found that in 7497 cases of tertiary syphilis symptoms pointing to the liver occurred in only 41.

It is remarkable how rare syphilitic lesions in the liver are in cases of locomotor ataxia, and it has been suggested that there is some kind of antagonism between hepatic syphilis and parasyphilitic lesions of the nervous system. Gummas and especially cicatrices are not uncommonly latent, and are only found after death as a surprise.

The factors which determine symptoms are : (1) the size and extent and (2) the position of syphilitic lesions in the liver. (1) If a gumma is

[1] Pitt. *Trans. Path. Soc.*, Lond., 1886, xxxvii, 276.
[2] Wagner. *Arch. f. Heilk.*, 1864, v, 126.
[3] Key. *Schmidts Jahrb.*, 1874, clxi.
[4] Fleischhauer. *XII. Congr. f. inn. Med.*, Wiesbaden, 1893.
[5] Mauriac. *Gaz. hebd. de méd.*, Paris, 1888, 2. s., xxv, 564.

large, it will give rise to the signs of a tumour, and by irritating the capsule of the liver to perihepatitis and pain; the morbid metabolism inside it may lead to the production and absorption of poisons which cause constitutional symptoms, such as anaemia, asthenia, and fever. (2) A cicatrix or small gumma on the convexity of the liver may not cause any symptoms, but if situated in the portal fissure, jaundice and ascites may follow. There is a great difference between the relative importance of the symptoms produced by a caseous gumma and by an old cicatrix; for symptoms due to the pressure of a gumma may be relieved or disappear under treatment, whereas it is highly improbable that an old cicatrix will be influenced.

As just pointed out, there is usually a considerable interval (ten to twenty years) between the primary infection and the onset of symptoms; it may be postponed for thirty or forty years, so that it has been said that no one can be regarded as cured of syphilis until he has been examined after death. Some cases shew signs of hepatic involvement within three years of infection, and exceptionally hepatic symptoms develop with great rapidity. In the early stages of the disease, before very definite localising symptoms and signs appear, there is very commonly weakness, general loss of health, failure of appetite, and gastro-intestinal disturbance. According to Marcuse,[1] two-thirds of the cases shew gastro-intestinal symptoms in the early stages. As gummas nearly always reach the surface of the liver, local perihepatitis is common, which, according to its intensity, accounts for discomfort, pain, and tenderness in the right hypochondrium; the pain may radiate to the right shoulder, and is sometimes accompanied by local tenderness. Pain is one of the most frequent symptoms in tertiary syphilis of the liver.

The clinical manifestations of tertiary syphilitic disease of the liver are protean, and for convenience may be grouped under the following headings:—(I) With symptoms suggesting portal cirrhosis, or simple chronic peritonitis and perihepatitis. (II) Presenting widespread lardaceous disease. (III) Suggesting tumour of the liver, such as malignant growth, hydatid, or enlarged gall-bladder. (IV) Imitating suppuration in the liver. (V) Resembling cholelithiasis. (VI) Simulating chronic splenic anaemia. (VII) With clinical features resembling hypertrophic biliary cirrhosis.

I. **Cases imitating Cirrhosis.**—These cases are frequent and important, as they probably account for some of the reputed cures of ordinary cirrhosis. There is ascites which is serous, but in rare instances has been noticed to be chyliform (Veil, Galvagni,[2] Poljakoff[3]) or even haemorrhagic. Other signs of portal obstruction, such as haematemesis, dilated veins in the abdominal walls, and dyspepsia, are much less frequent than in cirrhosis. Among 42 cases of hepatic syphilis in which full clinical

[1] Marcuse. *Wien. med. Wchnschr.*, 1900, l, 2219.
[2] Veil, Galvagni. Quoted by Boix. *Arch. gén. de méd.*, Paris, 1903, cxci, 1302.
[3] Poljakoff. *Berlin. klin. Wchnschr.*, 1900, xxxvii, 9.

notes were available 2 only had had haematemesis (Tresawna). In a case reported by Ebstein [1] a necrotic gumma appeared to have given rise to extensive haemorrhage into the biliary system and melaena. There may be enlargement of the spleen. Jaundice is very infrequent. Ascites may be produced in several ways: (i) by the pressure of cicatrices or gummas on the intrahepatic branches of the portal vein, or in some instances on the trunk of the vein in the portal fissure of the liver; there was hepatic syphilis in 7 out of 68 cases of portal thrombosis collected by Lissauer; [2] (ii) by constriction of the hepatic veins; (iii) by perihepatitis over gummas; this is usually local, but may be more widespread and give rise to some chronic peritonitis.

Under iodide of potassium the gumma undergoes absorption, and the symptoms will pass off unless there is enough cicatricial tissue left to exert permanent pressure on the portal vein or its branches. In a number of cases the absorption of the gumma leads to relief; these cases are responsible for some of the reputed cures of portal cirrhosis, for iodides are commonly given in that disease. In other instances in which there is no means of knowing that there is a firm cicatrix, and not a gumma, embarrassing the portal circulation, antisyphilitic treatment fails, and the case more closely resembles common cirrhosis.

The Differential Diagnosis of Syphilitic Disease of the Liver from Ordinary Cirrhosis.—The history and other signs of syphilis, including a positive Wassermann reaction, should always suggest a syphilitic disease of the liver and lead to adequate antisyphilitic treatment. In syphilis the liver may be irregularly enlarged, especially the right lobe, while in cirrhosis enlargement is more uniform. Definite enlargement of the spleen in the absence of lardaceous disease, which itself points to syphilis and should then be accompanied by albuminuria, is rather in favour of cirrhosis. An alcoholic history and dyspepsia of long standing are also in favour of cirrhosis. Ascites which frequently recurs after paracentesis is probably not due to cirrhosis, but to chronic peritonitis and perihepatitis or to syphilitic disease of the liver. When ascites is due to cirrhosis, the patient is usually thin or emaciated, whereas in syphilitic disease of the liver nutrition may be fairly well preserved.

Cases resembling Simple Chronic Peritonitis and Perihepatitis.—Cases of syphilitic disease of the liver in which ascites recurs will closely resemble simple chronic peritonitis, of which chronic universal perihepatitis is only a part. Chronic and recurrent ascites only occurs in a certain proportion of the cases of hepatic syphilis, while it is constant in simple chronic peritonitis. There must, therefore, be undoubted evidence of syphilis, such as a positive Wassermann reaction, or enlargement and irregularity of the liver, which point to gummatous disease, before the diagnosis of syphilitic disease is made in preference to chronic peritonitis. A thorough course of iodides should, however, always be tried. But failure of this treatment does not absolutely put syphilitic disease out of court. Uni-

[1] Ebstein. *Deutsches Arch. f. klin. Med.*, Leipz., 1908, cxii, 236.
[2] Lissauer. *Virchows Arch.*, 1908, cxcii, 276.

versal chronic perihepatitis may in some rare instances be associated with and possibly due to syphilis (*vide* p. 165). Cheadle[1] considered syphilis the most important cause of perihepatitis. My own experience is that gummas commonly cause local perihepatitis, but that syphilitic infection is quite an exceptional cause of universal perihepatitis. In 22 cases collected by Hale White[2] syphilis was the apparent cause in 3.

II. **Cases with the Features of Lardaceous Disease.**—When a gummatous liver is associated with lardaceous disease, the renal affection gives rise to albuminuria and dropsy, and the aspect of the case may be that of renal disease. In these circumstances the presence of a gumma in the liver may naturally be unsuspected. Albuminuria in syphilis is not, however, undeniable proof of lardaceous disease, since it may be due to a syphilitic nephritis. In some cases in which the liver and spleen are both very considerably enlarged, the clinical aspect has been described as that of Hanot's hypertrophic biliary cirrhosis but without jaundice (Boix[3]). The following is a well-marked case of syphilitic gummas of the liver combined with lardaceous disease:

A man aged forty-two years was under my care in St. George's Hospital, with ascites, albuminuria, and casts; there was no trace of jaundice and his facial aspect was that of cirrhosis. There was no cardiac disease or hypertrophy; the blood-pressure was low. It was thought possible that he had lardaceous disease of the kidneys and syphilitic disease of the liver, but the diagnosis was open to doubt, as there was no history or signs of lues veneris. The spleen could not be felt. The liver was somewhat enlarged. He was put on iodide of potassium, but without any improvement, and his abdomen was tapped; a week later he vomited, complained of abdominal pain, and as there was considerable ascites, he was again tapped; the fluid withdrawn was turbid and contained numerous pus corpuscles; the patient rapidly died. At the necropsy there was recent peritonitis. The liver, 8 lb. 10 oz., was somewhat scarred, and shewed a gumma, the size of a cocoanut, in the posterior part of the right lobe, which compressed the right branch of the portal vein and had running through its centre a large bile-duct. There were other small gummas in the liver, which was lardaceous. The spleen (20 oz.) shewed diffuse waxy change. The left kidney was atrophied; the right (15 oz.) was lardaceous.

III. **Gummas, etc., imitating Hepatic Tumours.**—The irregularities produced by gummas on the anterior surface of the liver may be readily felt through the abdominal wall. The elevations of the liver substance due to the contraction of cicatrices are also easily palpable. A large gumma or gummatous infiltration of a lobe or part of a lobe may suggest primary massive carcinoma. If a Wassermann reaction is positive, iodides and mercury should be given in full doses. Jaundice and ascites, especially together, are more likely to be met with in malignant disease; other points in favour of growth are rapid increase in the size of the liver, marked constitutional symptoms, and signs of a growth elsewhere. In a

[1] Cheadle. *Some Cirrhoses of the Liver*, pp. 41, 43, 1900.
[2] Hale White. Allbutt's *System of Medicine*, 1897, iv, 121.
[3] Boix. *Arch. gén. de méd.*, Paris, 1903, cxcii, 1302.

syphilitic subject an enlarged and irregular liver may be due either to gummatous disease or to new growth, for syphilis in no way protects against malignant disease. The vigorous administration of iodides and mercury should decide the question, diminution in size of the liver settling the diagnosis in favour of gumma.

An eminent member of the medical profession who had been unfortunately inoculated with syphilis died with hepatic cancer, which he had naturally at first hoped and believed to be gummatous disease.

Enlargement of the spleen, from lardaceous or gummatous change, is more likely to accompany syphilis than malignant disease of the liver. When gummas are associated with lardaceous change in the same liver the enlargement may be extreme, and the resemblance to carcinoma very close. The irregularities produced by cicatrices in a lardaceous liver also imitate malignant disease. In such cases albuminuria points to lardaceous disease, and is therefore in favour of syphilis. Moreover, albuminuria is rare in malignant disease of the liver.

A man aged forty-one who had had a sore on the penis followed by a bubo, but no other history or signs of syphilis or suppuration, was admitted to St. George's Hospital with ascites and albuminuria. After tapping, nodules were felt on an enlarged liver and the tentative diagnosis of cirrhosis was given up in favour of malignant disease. At the necropsy the irregularities felt as nodules were due to peritoneal adhesions over the convexity of the liver; the liver weighed 9 lbs., was fatty and lardaceous, but presented no fibrosis, gumma, or growth. The spleen (13 oz.), kidneys, suprarenals, and intestines were lardaceous. One testis shewed fibroid change.

Difficulty sometimes arises in deciding between gummatous infiltration of a lobe of the liver and a *hydatid cyst* embedded in the liver. The general health in hydatid is unaffected, unless suppuration has occurred, and the liver is smooth, whereas in syphilis, a positive Wassermann reaction, other signs of the disease, and irregularity of the liver should be present. In any doubtful case iodides should be given at once. Gummatous and cicatricial deformity of the right lobe may suggest malignant disease of the gall-bladder. A gumma projecting from the liver close to the gall-bladder may also suggest a primary carcinoma of the latter viscus. A gumma in the left lobe of the liver may imitate carcinoma of the stomach. Gummas, when adherent to the stomach, may cause much dyspepsia (Curtis [1]).

IV. **Cases with Fever, resembling Hepatic Suppuration.**—Occasionally irregular fever occurs in gummatous disease of the liver,[2] and may perhaps be due to secondary infection of a gumma. The fever may suggest hepatic suppuration, pylephlebitis, malaria (Cabot [3]), latent tuber-

[1] Curtis. *Clin. Journ.*, Lond., 1911, xxxviii, 43.

[2] Bristowe, *Trans. Clin. Soc.*, Lond., 1886, xix, 249; Gerhardt, *Berl. klin. Wchnschr.*, 1900, xxxvii, 1046; Klemperer, *Ztschr. f. klin. Med.*, 1904, lv, 177; Weber, F. P., *Lancet*, Lond., 1907, i, 728 (Bibliography); Breccia, *Riv. crit. di clin. med.*, Firenze, 1907, viii, 665, 692; Edwards, *Amer. Journ. Med. Sc.*, Phila., 1910, cxl, 527; Riley, *Trans. Chicago Path. Soc.*, 1911, viii, 91 (References).

[3] Cabot. *Journ. Am. Med. Assoc.*, Chicago, 1910, lv, 1343.

culosis, lymphadenoma, or enteric fever. It is, as a rule, removed by antisyphilitic treatment. When secondarily infected, a gumma may soften and imitate an abscess.[1] The association of a fluctuating swelling in the region of the liver and a raised temperature would render the resemblance to an ordinary hepatic abscess so close that unless the patient was known to have had syphilis there would be no reason to delay surgical treatment. A softened gumma may present anteriorly or may perforate through the ribs and project posteriorly or laterally.

The abdomen of a woman, aged twenty-six years, who had a history of syphilis, was opened and a small gumma excised from the anterior margin of the liver. A hard mass was felt in the right lobe posteriorly and was thought to be a gumma. She was put on iodide of potassium and the right base was aspirated several times, but without success. At the necropsy there was an empyema on the right side and a suppurating gumma, apparently communicating with the empyema, in the posterior part of the right lobe of the liver (Newbolt[2]).

Tropical hepatitis around a previously quiescent gumma may imitate an abscess, and the true state of affairs be only revealed when caseous material instead of pus is removed at operation.

V. **Cases resembling Gall-stones.** — Jaundice is not common in tertiary syphilis of the liver, but occasionally the pressure of a gumma or the traction exerted by syphilitic cicatrices in the portal fissure may cause obstructive jaundice. In rare cases this obstructive jaundice is accompanied by attacks of pain resembling biliary colic, but not due to gall-stones. In any case of probable cholelithiasis with well-marked signs of tertiary syphilis iodides should be given before proceeding to operation. The following case recorded by Billings[3] bears on this point:

A single man, aged thirty-seven, who had contracted syphilis a year and a half previously, had constant pain in the region of the gall-bladder with attacks of colic followed by jaundice and accompanied by intermittent fever. A tumour was felt in the region of the gall-bladder; Finger operated for cholecystitis and calculi in the gall-bladder and cystic duct, and found multiple gummas; the largest gumma was at the edge of the liver, close to the gall-bladder. The main ducts, however, did not appear to have been pressed upon, so the obstruction must have been in their branches. Similar cases have been described by Riedel,[4] Parker,[5] Lilienthal,[6] Munro,[7] and Schrager.[8]

VI. **Cases resembling Chronic Splenic Anaemia.**—In some cases

[1] Barry, C., *Ind. Med. Gaz.*, 1904, xxxix, 298; Thompson, *Lancet*, Lond., 1910, ii, 1415.
[2] Newbolt. *Med., Surg., and Path. Rep. Roy. Southern Hosp.*, Liverpool, 1901, pp. 143, 248.
[3] Billings. *Phila. Med. Journ.*, 1900, vi, 671.
[4] Riedel. *Mitth. a. d. Grenzgeb. d. Med. u. Chir.*, Jena, 1904, xiv, 1.
[5] Parker, R. *Lancet*, 1899, i, 301.
[6] Lilienthal. *Ann. Surg.*, 1902, xxxvi, 132.
[7] Munro. *New York State Journ. of Med.*, 1908, viii, 183.
[8] Schrager. *Journ. Amer. Med. Assoc.*, Chicago, 1912, lviii, 681.

of syphilitic disease of the liver the spleen is greatly enlarged from lardaceous disease, or in rare instances from gummatous change, while the liver is little, if at all, enlarged. In such cases there may be a considerable resemblance to chronic splenic anaemia which is characterised by anaemia of the chlorotic type, leucopenia or a diminution in the number of leucocytes, and great splenic enlargement. In a case of Coupland's[1] the spleen was removed for supposed splenic anaemia with great apparent benefit; subsequently, when the woman died from haematemesis and ascites, the liver was found to be syphilitic. Osler[2] also refers to examples of syphilis imitating chronic splenic anaemia in adults.

VII. **Cases resembling Hypertrophic Biliary Cirrhosis.**—In rare instances syphilis may lead to an enlarged liver with chronic jaundice and splenic enlargement (Hanot[3]). There may be signs of syphilis elsewhere in the body, the progress of the case is more rapid than in hypertrophic biliary cirrhosis, and the splenic enlargement is not so marked.

A good example of syphilitic disease imitating hypertrophic biliary cirrhosis is given on p. 380. Ferrannini described the case of a woman aged forty-eight years, with jaundice, clay-coloured stools, a large spleen and liver which resembled hypertrophic biliary cirrhosis. At the necropsy the enlargement of the liver and spleen was found to be due to syphilis and the jaundice to a retention cyst in the head of the pancreas compressing the common bile-duct.

Diagnosis.—A history of syphilitic infection, the evidence of syphilitic lesions in some accessible part of the body, such as the skin, tongue, throat, testes, or bones, or a positive result with the Wassermann serum reaction, in an obscure case of hepatic enlargement or tumour, should always be regarded as an indication for antisyphilitic treatment. A patient may deny infection or may be entirely ignorant that he has contracted the disease.

In the following case the patient complained of hepatic pain, had an enlarged liver without jaundice or ascites, and denied syphilitic infection. A labourer aged fifty was under my care in St. George's Hospital in October 1900. For a month he had constant pain in the right hypochondrium, worse at night when lying on the right side and on respiration. Married, no children, but his wife has had four miscarriages. The liver extends below the costal arch in the nipple line and is tender. Spleen not enlarged. Testes not enlarged. There is a rupial scar near the umbilicus. The tongue is greatly deformed and cannot be put out; it is scarred, shews superficial glossitis, and is lobulated, but not ulcerated. The tongue had been sore for six months; this was ascribed by the patient to heavy smoking. On full doses of iodide and mercury the hepatic pain and the condition of the tongue rapidly improved.

[1] Coupland, S. *Brit. Med. Journ.*, 1896, i, 1445.
[2] Osler, W. *Amer. Journ. Med. Sc.*, 1902, cxxiv, 765.
[3] Hanot. *Presse méd.*, 1896, p. 505.

Hepatic syphilis is probably very commonly overlooked, the disease being regarded as cirrhosis or early new-growth. It is therefore important to bear in mind the possibility of syphilis in all obscure enlargements of the liver and to have the Wassermann test done. Moreover, in doubtful cases invaluable assistance to diagnosis is obtained by watching the effects of a thorough course of mercurials and iodides, or salvarsan. In the early stages of malignant disease it may be quite impossible to come to a correct decision until these have been tried. The differential diagnosis of syphilitic disease of the liver from cirrhosis, chronic peritonitis, malignant disease, etc., has already been referred to under the description of the clinical aspects of syphilitic disease of the liver.

Prognosis.—When properly treated the prognosis is much better than in most of the conditions which resemble it, such as carcinoma, cirrhosis, chronic peritonitis, and perihepatitis. Gummas undergo absorption and the bad effects due to their mechanical effects will disappear. On the other hand, firm cicatrices will, as has already been pointed out, not be affected, and the results of antisyphilitic treatment are therefore disappointing, and, in addition, misleading if absence of a good result be regarded as necessarily eliminating syphilis. The prognosis of syphilitic enlargement, which is often gummatous, is therefore rather better than that of ascites or jaundice thought to depend on syphilitic disease of the liver, since the latter may be due to cicatrices.

Treatment.—Mercurial inunction and iodide of potassium internally should be employed. The three iodides, of potassium, sodium, and ammonium, may be given in combination, or iodide of potassium may be given with spiritus ammoniae aromaticus so as to avoid the depressing effects of potassium. In any event ammonia in some form should be given, as it is said to double the effect of the iodides. The usual course is to begin with fifteen grains of the combined iodides three times daily, which is increased until thirty grains are being taken three times a day. If mercurial inunction be not employed at the same time, liquor hydrargyri perchloridi should be added to each dose of the medicine. The medicine should be taken shortly before meals. If taken after meals, dyspepsia may occur, possibly because some free iodine is liberated by the action of the hydrochloric acid of the gastric juice on the iodides.

The use of iodide of potassium in tertiary syphilis appears to have been first discovered in 1831 by R. Williams, of St. Thomas's Hospital (Sir J. Paget [1]) ; though Wallace, of Dublin, who employed it in 1832 and published his results in the *Lancet* in 1836, is generally credited as the first to use this drug.[2]

[1] Sir James Paget. *Address to the Abernethian Society of St. Bartholomew's Hospital*, 1885, p. 19 ; privately printed. Quoted by Howard Marsh in obituary notice of Sir J. Paget, *St. Barth. Hosp. Rep.*, 1900, xxxvi, 6.

[2] See Lancereaux. *Syphilis*, 1869, ii, 300. New Sydenham Society.

The good effects of iodides and mercury may not appear for a considerable time. It is essential, therefore, that several weeks' thorough treatment should be insisted upon before it can be concluded that the condition is not syphilitic.

An interesting speculation is opened up by a consideration of the marvellous way in which iodides produce absorption of gummatous material. This action can hardly be considered specific in the strict sense of the term, inasmuch as a similarly marked effect follows its adequate administration in actinomycosis. Possibly iodides prevent further disease of the vessels in the neighbourhood, and this may enable the natural process of absorption to go on unchecked by endarteritis of the neighbouring vessels, while it prevents further syphilitic manifestations. Stockman [1] believes that iodides act by increasing the thyroid secretion, which has a powerful absorptive action. If this be the case, thyroid extract should be given in gummas. Flexner [2] attributes the absorption of gummas to autolysis or the action of intracellular ferments, and supposes that this ferment action is accelerated by iodides.

Intravenous injections of salvarsan ("606") may be given with due precautions. If the patient is anaemic, iron should be given, iodide of iron being a convenient form. When gummas develop with great rapidity and soon after infection, subcutaneous, or better intramuscular, injection of various mercurial salts may be employed.

Pain due to perihepatitis may be relieved by hot fomentations, by poultices, or by the application of a few leeches over the painful area. The general health should be maintained by a generous diet and by fresh air, preferably that of the sea. Alcohol should be avoided unless there are special reasons for its use. In severe cases with cachexia the medicinal treatment may with advantage be carried out at spas of high elevation, such as Barèges, Cauterets, Bagnères-de-Luchon, or Wildbad-Gastein. Aix-la-Chapelle and Wiesbaden are well adapted for the treatment of visceral syphilis.

Surgical Treatment.—Removal of a gumma may be possible when the anterior margin of the liver is affected, and when the lesion is single and localised, but it is only likely to be performed when an exploratory operation has been undertaken for purposes of diagnosis and when a tumour of uncertain nature is found and can be fairly easily removed. In exceptional instances when a breaking-down gumma is ulcerating through the abdominal wall, scraping out the gummatous sloughs, as in a case described by W. G. Spencer,[3] is advisable, inasmuch as toxic absorption is thus prevented.

In a case in which an exploratory operation revealed a very large gumma 4 or 5 inches across, R. Parker [4] removed some, but not all, of the caseous contents; antisyphilitic remedies were given and the man recovered. In a

[1] Stockman. *Glasgow Hosp. Rep.*, 1899, ii, 69.
[2] Flexner. *Am. Journ. Med. Sc.*, 1903, cxxvi, 214.
[3] Spencer, W. G. *Brit. Med. Journ.*, 1898, ii, 1686; and *Trans. Clin. Soc.*, 1899, xxxii, 46.
[4] Rushton Parker. *Lancet*, Lond., 1899, i, 301.

remarkable case recorded by Curtis[1] a gumma of the liver firmly adherent to the stomach was removed; the patient left off taking iodides, and three years later a gumma of the liver adherent to the caecum was removed.

Removal of a localised gumma or of a gummatous constriction lobe in cases in which laparotomy has been undertaken to clear up the diagnosis, or under the impression that some other condition was present, is admissible, inasmuch as it may accelerate the cure by antisyphilitic treatment. But very thorough antisyphilitic treatment should be carried out before an operation is undertaken for removal of a gumma.

In 1907 Cumston[2] collected 32 cases in which resection of the liver had been performed for gumma. In most cases operation was undertaken under the idea that the hepatic condition was other than a gumma. Steiner[3] collected 13 cases in which laparotomy was planned on what turned out to be errors of diagnosis.

Parasyphilitic Affections.—By parasyphilitic or metasyphilitic lesions are meant changes which are not pathognomonic of syphilis, but which develop when the soil has been prepared by syphilis; such are tabes dorsalis and general paralysis of the insane. The question of parasyphilitic multilobular cirrhosis occurring in the subjects of congenital syphilis is discussed on p. 381. Pathologists have rightly insisted on the difference between ordinary portal cirrhosis and the specific forms of hepatic fibrosis—namely, unicellular cirrhosis in hereditary syphilis and multiple scarring by cicatrices. This may explain why so little attention has been paid to multilobular cirrhosis as a parasyphilitic sequel. That it not uncommonly happens that a person who has had syphilis becomes the subject of ordinary multilobular cirrhosis is quite natural, since syphilis does not protect in any way against the effects of alcoholism, and, moreover, Bacchus and Venus are frequently worshipped by the same devotees. It is reasonable to believe that parasyphilitic multilobular cirrhosis may occur in adults, but there are considerable difficulties in recognising it or in establishing its existence. Fabris[4] has recorded a case.

Lardaceous Disease.—With the advance of surgery prolonged suppuration has become so infrequent that syphilis is responsible for a much larger proportion of cases of lardaceous disease than formerly. Lardaceous liver is considered on page 433; it need only be stated here that lardaceous change may accompany gummatous and other syphilitic lesions in the liver and that in some instances the lardaceous change is found only around gummas.

[1] Curtis. *Clin. Journ.*, Lond., 1911, xxxviii, 44.
[2] Cumston, C. G. *International Clinics*, 1907, 17. s., ii, 124.
[3] Steiner. *Thèse de Paris*, 1902, No. 380.
[4] Fabris. *Arch. per le sc. med.*, Torino, 1908, xxxii, 471.

Congenital Syphilis of the Liver

The hepatic lesions due to congenital or hereditary syphilis may conveniently be considered as: (1) Those found in infants at the same time that other manifestations of congenital syphilis are common. (2) Those of delayed or late congenital syphilis. (3) Multilobular cirrhosis in children with a history or signs of former hereditary syphilis; this constitutes parasyphilitic cirrhosis. The first of these categories is far the most important and is what is ordinarily understood by the liver of congenital syphilis.

History.—Gubler[1] first gave a full account of the lesions of the liver in hereditary or congenital syphilis in 1852. Bamburger, Virchow, and Parrot further described the condition, and in Great Britain Sir S. Wilks recorded a case in 1866. The reader will find references to the history of hereditary hepatic syphilis in Lancereaux's[2] work. More recently the tertiary effects of congenital syphilis on the liver have been specially described in cases of syphilis hereditaria tardiva.

The Ordinary Hepatic Manifestation of Congenital Syphilis

Incidence.—The liver is affected in a very high proportion of the infants dying with congenital syphilis.

In infants with congenital syphilis the liver has been found to be affected in from 39 per cent (Hofmeister[3]) to 65 per cent (Feige[4]).

This contrasts with acquired syphilis, in which the liver very frequently escapes. It is generally considered that antenatal syphilis may be either (i) hereditary, and due to the spermatozoon being the carrier of the syphilitic parasite to the ovum, while the mother escapes though rendered immune to further infection; or (ii) congenital, and due to the syphilitic parasite passing from the mother through the placenta into the umbilical vein of the fetus. The frequency of hepatic lesions in antenatal syphilis is an argument in favour of the view that the infection is maternal, and passes through the placenta into the umbilical vein, damaging the liver, which is the first organ of the fetus with which it comes in contact; a further argument in favour of this view is that the liver generally contains a larger number of *Treponema pallidum* than the other organs of the infant (McIntosh[5]); if the ovum were primarily infected by a syphilised spermatozoon it is improbable that the embryo would survive; and further, if it did, the *Treponema pallidum* would reach the liver by the hepatic artery, and the liver, being thus exposed to the same risk of

[1] Gubler. *Mém. Soc. de Biol.*, Paris, 1852, iv, 25.
[2] Lancereaux. *Syphilis*, 1869, ii, 132, 151. Transl. New Sydenham Soc.
[3] Hofmeister. *Dissertation*, Kiel, 1886. Quoted by Quincke in Nothnagel's *Encyclopaedia of Practical Medicine*, English translation, p. 745.
[4] Feige. *Dissertation*, Kiel, 1896. *Ibid.*
[5] McIntosh. *Journ. Path. and Bacteriol.*, Cambridge, 1909, xiii, 245.

infection as in postnatal syphilis, should be affected in much the same proportion as in the acquired disease. In postnatal syphilis when the disease is conveyed by a wet-nurse, by inoculation, or other means, the lesions are the same as in the acquired disease.

Morbid Anatomy.—*Liver.*—There is very considerable variation in the changes found in the livers of infants dying with congenital syphilis; but the two main points in regard to the morbid anatomy are, (i) that the change tends to be diffuse, and (ii) that it is a secondary syphilitic manifestation. Congenital hepatic syphilis thus differs markedly from the circumscribed lesions of the liver characteristic of the tertiary stage of the acquired disease. The appearance of the liver is by no means constant; sometimes there is little or no manifest change to the naked eye, and microscopic examination alone may make it certain that there is syphilitic infection. The liver is enlarged, usually retains its shape, and weighs more than natural, being one-twelfth or one-sixteenth instead of one-twenty-fifth of the body-weight at birth. The surface may shew adhesions, due to intrauterine perihepatitis and peritonitis, but except for these adhesions the liver is smooth, and is firmer and more resistant than normal. The healthy colour is altered; occasionally, in the early stages of the disease, it is congested, but usually its tint is lighter than in health; it may be violet, greyish-yellow, and approaching the colour of flint (*foie silex* of Gubler) or yellow. On section it is firmer than natural and resistant, but not to the same extent as in cirrhosis or in congenital obliteration of the bile-ducts. The organ tends to be uniformly affected, but often some parts are more affected than others, so that a mottled appearance is presented. The alteration in colour is the same as described above, but the mottling may be more marked; areas presenting the yellow change may alternate with parts preserving the more or less healthy red colour, and the appearance may suggest primary sarcoma. In other instances the glistening, semi-translucent aspect suggests lardaceous change.

On carefully examining the cut surface small grey spots like grains of semolina are generally visible; they are small granulomas or syphilomas and composed of small round cells; in some instances the central portions of these granulomas shew caseation and may then be spoken of as miliary gummas. The left lobe is said to be more often affected with these syphilomas. To the naked eye these look like small miliary tubercles, and microscopically they so far resemble them in being localised collections of small round cells. Tuberculosis may indeed be associated with intercellular cirrhosis, and the distinction between these small syphilomas and miliary tubercles depends on the presence of the corresponding parasite. In rare instances caseous gummas have been found in infants and even in stillborn children and premature fetuses.

Canton[1] figured multiple hepatic gummas in a child of seven weeks, and T. Barlow[2] described "receding gummata" in a child twelve weeks old.

[1] Canton E. *Trans. Path. Soc.*, 1861-2, xiii, 113. [2] Barlow, T. *Ibid.*, 1877, xxvii, 202.

Bittner [1] recorded gummas in the liver of a stillborn child and in a six months fetus. Other cases are given by Lancereaux [2] and by Hutinel and Hudelo.[3]

The *microscopic appearances* vary greatly according to the duration and virulence of the infection. In the earliest stage there is capillary congestion with perivascular small-celled infiltration, which subsequently becomes diffuse. These newly formed cells are the outcome of proliferation of (*a*) the pre-existing connective-tissue cells of the organ ; (*b*) of the endothelium of the capillaries and lymphatics inside the hepatic lobules, whilst Kupffer's star-like cells, which are intimately connected with the en-

Fig. 46.—Microscopic appearances in intercellular cirrhosis. There is delicate connective tissue between the small groups of liver cells.

dothelial lining of these vessels, share in this process. This diffuse infiltration closely resembles an infiltrating sarcoma, and naturally, since proliferation of the connective tissues during fetal life or soon after birth leads to a formation which is structurally much the same as that of a sarcoma. It is extremely probable that some cases described as diffuse sarcoma in early life were in reality examples of the hepatic lesion of hereditary syphilis. By appropriate staining methods numbers of *Treponema pallidum* (*Spirochaeta pallida*) can be seen (*vide* Fig. 46) in the connective tissue between the liver cells and the sinusoids. Erythroblastic foci are present (Erdmann).

At a rather later stage the fibroblasts separate the individual liver

[1] Bittner. *Prag. med. Wchnschr.*, 1877, xviii, 581.
[2] Lancereaux. *A Treatise on Syphilis*, ii, 152. Transl. New. Syd. Soc., 1869.
[3] Hutinel et Hudelo. *Arch. de méd. expér. et d'anat. path.*, Paris, 1890, x, 509.

cells from each other. There is thus a pericellular, unicellular, or intercellular cirrhosis. This appearance is occasionally seen in the secondary stage of syphilis, and locally in some cases of ordinary portal cirrhosis. Sometimes the microscopic appearances of intercellular cirrhosis at this stage are like those of an infiltrating carcinoma.

As time goes on the organisation of young connective tissue may advance and lead to well-formed fibrous tissue. The chronic nature of the inflammation, if allowed to run its course, is often well shewn by the presence of both well-formed fibrous tissue and recent inflammatory or granulation tissue in the same specimen. The fibrous tissue of Glisson's

FIG. 47.—Section of liver in congenital syphilis shewing *Treponema pallidum* (E. O. Jordan).

capsule in the portal canals is also increased in amount. In places there may be collections of small round cells—syphilomas—or, as they are often called, miliary gummas, though the word "gumma" should be reserved for the further stage of necrosis and caseation. These small syphilomas may be found in association with early intercellular infiltration, or later, when there is well-formed fibrous tissue.

The hepatic lesions which can be regarded as a remote result of congenital syphilis will be referred to again under the heading of "Delayed Congenital Syphilis," but here it may be pointed out that although ordinary cirrhosis may very probably supervene in a liver recovering from intercellular cirrhosis, it does not appear reasonable to imagine that intercellular cirrhosis can be directly transformed into multilobular or unilobular cirrhosis. Extensive fibrosis of the liver producing a tumour-like mass is sometimes seen as the result of congenital syphilis. Some

cases of the kind have been described as fibroma of the liver. Marchand [1] has insisted on the syphilitic nature of these cases.

As an example of very extensive fibrosis Morley Fletcher's [2] case of a child aged eight weeks may be referred to. The mother had had seven other healthy children and one stillborn infant, but no other evidence of syphilis was forthcoming. The liver was much enlarged and easily felt. There was no jaundice or ascites. The liver (28 oz.) microscopically shewed great fibrosis, the fibrous tissue being well formed ; in addition, there were areas with much small-celled infiltration. The hepatic cells were greatly atrophied, compressed, and in many places formed columns resembling pseudobile canaliculi (*vide* Fig. 48) ; there was a considerable amount of extravasation of red corpuscles. The spleen was not enlarged. The right suprarenal was enlarged to the size of its corresponding kidney and there were fibrosis and extravasation into the medulla. In this case, as in those recorded by Marchand, some doubt as to the existence of syphilis might arise.

The liver cells are atrophied, compressed, and may shew granular and degenerative changes. Fatty change is not frequent, and when present is usually quite sporadic and localised. As the result of necrosis they may disappear from considerable areas, their place being taken by organising granulation-tissue. The liver cells may be so compressed that they closely resemble newly formed bile-ducts. In rare instances the liver cells shew great enlargement and contain many nuclei (Binder,[3] Oppenheimer,[4] Ménétrier and Rubens-Duval [5]). The giant or plasmodial liver cells have been thought by Binder to be due to fusion of hepatic cells, and by the other observers mentioned as the result of nuclear division without cell-division, the process being due to the action of the syphilitic toxin.

The hepatic artery is normal and is free from endarteritis, a change which would naturally be expected if the syphilitic virus reached the liver from the general circulation. In exceptional instances, however, endarteritis and periarteritis and phlebitis are present (Oberndorfer [6]). There is an increase in the amount of fibrous tissue and in exceptional instances marked inflammatory changes around the bile-ducts and portal vein in the portal spaces. Endophlebitis of the branches of the hepatic veins sometimes occurs, and if allowed to progress, may eventually lead to stenosis of the orifice of these veins (*vide* p. 50).

The variations met with in the liver in congenital syphilis depend on the severity of the infection and its duration. The following conditions may be recognised :

I. The commonest change is a diffuse embryonic infiltration which develops into young connective-tissue cells separating the individual liver cells ; this is intercellular, unicellular, or pericellular cirrhosis.

[1] Marchand. *Centralbl. f. allg. Path.*, 1896, vii, 273.
[2] Morley Fletcher, H. *Trans. Path. Soc.*, Lond., 1899, l, 138.
[3] Binder. *Virchows Arch.*, 1904, clxxvii, 44.
[4] Oppenheimer. *Ibid.*, 1905, clxxxii, 237.
[5] Ménétrier et Rubens-Duval. *Arch. de méd. expér. et d'anat. path.*, Paris, 1907, xix,
[6] Oberndorfer. *Centralbl. f. allg. Path. u. path. Anat.*, 1900, v, 145.

II. The previous condition may be combined with small collections of round cells or miliary gummas.

III. Further organisation of the intercellular infiltration leads to widespread or local areas of fibrosis.

IV. Occasionally well-formed caseous gummas like those seen in adults are present.

V. A combination of gummas with fibrosis (gummatous hepatitis) not affecting the whole organ, but forming circumscribed areas which may imitate a tumour.

The diffuse intercellular cirrhosis is, like the lesions of secondary

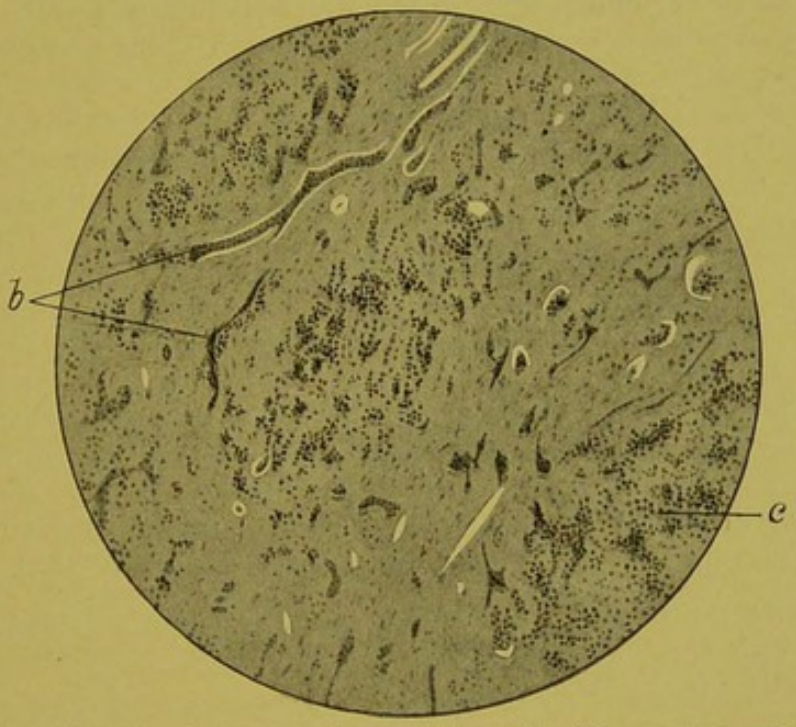


FIG. 48.—Microscopic section from a case of congenital syphilis. Shews extensive fibrosis, areas of small-celled infiltration (*c*), compressed liver cells, and columns of cells resembling small bile-ducts (*b*). (Drawing kindly lent by Dr. H. Morley Fletcher.)

syphilis elsewhere, essentially curable if treated with mercury. It may, however, pass into the tertiary lesions, and gummas, cicatrices, and lardaceous change may develop (*vide* p. 378).

The *spleen* is generally enlarged; according to Marfan the spleen of stillborn syphilitic infants weighs four times the normal. From fibrosis it becomes firmer than natural. Lardaceous disease may be seen in older children. Gummas are extremely rare; Still [1] could only find two cases in infants. There may be adhesions between the capsule and adjacent parts. Microscopically there is fibrosis.

The *kidneys* may also present interstitial fibrosis. This is of interest in connexion with Payne's [2] view that granular kidneys in young children depend on hereditary syphilis. There may be diffuse small-celled infiltration

[1] Still. *Trans. Path. Soc.*, Lond., 1897, xlviii, 205.
[2] Payne, J. F. *Ibid.*, 1900, li, 364.

in the pancreas and testes, and changes in the lungs are comparatively frequent. The suprarenals are enlarged, and may shew small-celled infiltration, haemorrhage, or fatty change.

Clinical Features.—When the infection is advanced, the child may be stillborn or die a few days after birth. In many cases the child is healthy when born and subsequently develops evidences of congenital syphilis. For some unknown reason girls are more prone to congenital syphilis than boys. As a general rule, signs pointing definitely to the liver, such as jaundice and ascites, are absent, and it is only on examination that the liver and spleen are found to be enlarged. The clinical features may be summarised thus: the well-known manifestations of hereditary syphilis are present, and, in addition, there is enlargement of the spleen and liver.

The enlarged liver may reach down to the iliac crest; Carpenter[1] found the liver enlarged in 47 per cent of the cases of inherited syphilis under six months of age; and in 148 cases it was palpably so in 48 (Hochsinger[2]). It must be borne in mind that in young children the liver normally projects further down than in adults; this is not merely due to the relatively larger size of the organ in children, but also to the more horizontal position of the ribs, which leaves the organ less covered. Hence slight apparent enlargement is not of importance in the absence of other evidence. The degree of hepatic enlargement corresponds with that of the other manifestations of the disease, and may therefore be taken as an index of the severity of the infection. The liver is firm, tender, and somewhat resistant. In very rare cases there is a localised tumour formation which is readily felt during life (*vide* p. 373).

In a child three months old, icterus, ascites, and cerebral symptoms were associated with a gummatous projection from the under surface of the right lobe of the liver (Cohn[3]).

The spleen is commonly enlarged in hereditary syphilis. This was pointed out by Gee[4] in 1867, who found clinical evidence of splenic enlargement in one-fourth of his cases.

More recently the incidence of splenic enlargement in congenital syphilis has been estimated at 45 per cent by Still,[5] 50 per cent by Marfan,[6] and at 63 by Coutts.[7]

Jaundice occasionally occurs, and is probably not so extremely rare as is often stated. It may be due to various factors. It may possibly depend on pressure of enlarged glands in the portal fissure on the ducts, or on pressure exerted by masses of syphilitic granulation-tissue, but is more probably due to inflammatory changes in the small bile-ducts which

[1] Carpenter. *Syphilis in Children*, p. 53, 1901.
[2] Hochsinger. *Wien. med. Wchnschr.*, 1896, xlvi, 345.
[3] Cohn, M. *Virchows Arch.*, 1896, cxlvi, 468.
[4] Gee, S. *Brit. Med. Journ.*, 1867, i, 435.
[5] Still. *Practitioner*, 1904, lxxiii, 101.
[6] Marfan. *Rev. mens. des maladies de l'enfance*, 1903, xxi, 211.
[7] Coutts. *Brit. Med. Journ.*, 1896, i, 1026.

form part of the diffuse unicellular hepatitis. In the latter case it is much the same as the jaundice occasionally seen in the secondary stage of acquired syphilis. I have seen death from haematemesis in jaundice due to congenital syphilis. Secondary infection may cause jaundice in congenital syphilis; it may be due to *B. coli* or *B. proteus* (Milon,[1] Bar and Rénon [2]). The micro-organisms may enter through the umbilical vein and find a suitable nidus in the liver, the resistance of which has been reduced by the syphilitic lesion. The development of jaundice is thus comparable to icterus gravis supervening in ordinary cirrhosis. The aspect of the case may then be one of multiple haemorrhages and resemble the acute umbilical infections in the newly born. Perry and Shaw [3] refer to a case of this kind in an infant two weeks old.

When jaundice is met with in congenital syphilis, it is usually present at birth, but it may not come on until some weeks later. In rare cases the jaundice may pass away and return again.

Still [4] refers to a boy who was jaundiced for the first six weeks of life; he then recovered and appeared perfectly healthy until the age of two years and three months, when he again became attacked by jaundice, which, after lasting some weeks, proved fatal. Microscopically the liver shewed intercellular cirrhosis.

Ascites is very rare; it may be due to concomitant peritonitis and perihepatitis, which are not very rare in severe cases, or possibly to the pressure of enlarged glands in the portal fissure. In intrauterine life hepatic syphilis may so interfere with the circulation through the umbilical vein as to produce hydramnios, and a number of premature deaths are thus accounted for. But in infants which survive there is not sufficient phlebitis of the portal vein to produce ascites. The abdomen is somewhat distended, partly from enlargement of the liver and spleen, and partly from tympanites. Prominence of the subcutaneous abdominal veins is sometimes noticeable. The usual symptoms and signs of congenital syphilis, such as debility, wasting, the cutaneous, mucous, and bony lesions, anaemia, and in some cases multiple haemorrhages, vomiting, and diarrhoea, are present.

Diagnosis.—This is usually very much easier than in acquired syphilis of the liver in adults, inasmuch as there are usually well-marked signs of syphilis elsewhere in the infant. In the absence of these signs other causes for enlargement of the liver and spleen, such as rickets, tuberculosis, gastro-intestinal infection, must be considered and as far as possible eliminated. Caseous tubercle in the liver in young infants has imitated syphilitic disease almost exactly (Hochsinger [5]). In cases in which there is jaundice from birth without any manifest signs of syphilis, simple jaundice and congenital obliteration of the ducts must be

[1] Milon. *Thèse de Paris*, 1897, No. 434.
[2] Bar et Rénon. *Compt. rend. Soc. Biol.*, Paris, 1895, xlvii, 379.
[3] Perry and Shaw. *Guy's Hosp. Rep.*, 1893, l, 226.
[4] Still. *Clin. Journ.*, 1901, xvii, 322.
[5] Hochsinger. *Wien. med. Bl.*, 1894, xvii 255.

borne in mind. A positive Wassermann reaction practically clinches the diagnosis.

Prognosis.—The prognosis depends on the general state of nutrition and on efficient and prompt antisyphilitic treatment. If the liver and spleen are greatly enlarged, the prognosis is grave. Visceral enlargement may be regarded as an index of the severity of the infection. Haemorrhages are of bad omen, and cases with jaundice usually do badly.

Treatment.—The treatment is that of congenital syphilis; mercury may be given by inunction or by the mouth. Hydrargyrum cum cretâ may be given in the form of a powder: to a child under two months ½ grain twice a day; after that age the dose is increased to one grain. Liquor hydrargyri perchloridi may be given instead or the French preparation of Liqueur de Van Swieten in doses of 10 minims daily for a child of one month old, increasing the doses by 5 or 10 minims every month or so. A more satisfactory method, both because it acts more rapidly and is less likely to lead to salivation, is mercurial inunction. Mercurial ointment is rubbed on with flannel, into the axillae, over the liver, and over the spleen, a fresh situation being selected daily. To begin with, about 15 grains of the ointment should be used every day. The mercurial treatment should be carried out daily for three months, and then relaxed gradually; in the fourth month the treatment being intermitted for a week at a time, and in the fifth month for two weeks. In the second year of treatment mercurial inunction should be performed during one month out of three, and small doses of iodide of potassium given. In the third year the dose of the iodide may be increased, and in the fourth year the mercurial treatment may be dropped, while the iodide is continued. In this way the appearance of tertiary manifestations should be prevented. In order to prevent both abortion and syphilitic infection of the fetus a pregnant woman known to be the subject of syphilis should go through a course of antisyphilitic treatment.

Salvarsan has been injected into syphilitic infants; but in sucklings it is safer to inject the mother first, as some therapeutic substance is evidently contained in the milk; if no improvement occurs or if it is slight, the infant can then be injected with less risk (McIntosh and Fildes[1]).

The Hepatic Manifestation of Delayed Congenital Syphilis

Synonym: Late Hereditary Syphilis.

Description.—The changes in the liver are the same as in the tertiary stage of the acquired disease, but they occur in the subjects of undoubted hereditary syphilis.

History.—Probably the first case was recorded in 1863 by S. Wilks,[2] in a girl aged twelve years whose mother had had secondary syphilis.

[1] McIntosh and Fildes. *Syphilis from the Modern Standpoint*, 1911, p. 189, Lond.
[2] Wilks, S. *Guy's Hosp. Rep.*, 1863, ix, 24.

The child's liver was much deformed and contained gummas and numerous cicatrices.

H. Morris'[1] case was one of the earlier examples of tardive hereditary syphilis. The patient was a girl aged twenty years with a family history of syphilis and a personal history of interstitial keratitis. The liver was noticed to be enlarged at eighteen, and ascites appeared in the course of the next year. At the necropsy the liver, which weighed 39 ounces, was fissured, puckered, lardaceous, and contained gummas; the kidneys and spleen were also lardaceous.

Incidence.—A considerable number of cases, probably about 70, have been recorded. In 1886 Fournier[2] collected 25, and in 1890 Hudelo[3] referred to 49 cases. The liver is affected in about a third of the cases; out of 132 cases of delayed inherited syphilis the bones were affected in 39 per cent, the liver coming next in 34 per cent (Forbes[4]).

The hepatic lesions are tertiary in character and are the same as those seen in the acquired disease. In order to be sure that the case is one of delayed congenital syphilis there must be some other evidence of the congenital affection, such as interstitial keratitis, otherwise the disease might have been acquired in early life; for example, from a wet-nurse.

Morbid Anatomy.—The liver is nearly always enlarged and is changed in much the same way as in the tertiary stage of the acquired disease. It may be very greatly deformed and cut up into numerous lobes; it is highly probable that some of the recorded anatomical abnormalities of multiple lobulation (as many as 16 lobes have been described) can be thus explained. The lesions are gummas, cicatrices, fibrosis, intercellular cirrhosis, and lardaceous change in varying degrees and combinations. It is well to remember that, as in early congenital syphilis, the naked-eye appearance of the liver may suggest malignant disease; this was the first naked-eye diagnosis in a boy aged fifteen years with delayed hereditary hepatic syphilis described by H. W. G. Mackenzie.[5] In order to exclude caseous tubercles, Devic and Froment[6] consider a microscopic examination necessary; of 53 recorded cases of late hereditary syphilis these authors consider 25 probable and only 6 certain examples. Perihepatitis is common and may be the means by which gummatous inflammation spreads to the abdominal wall. The other organs may shew syphilitic lesions and advanced lardaceous disease.

Clinical Features.—The subjects of delayed hereditary syphilis of the liver usually display copious signs of syphilitic infection in the bones, sense organs, or in the existence of widespread lardaceous disease. They

[1] Morris, H. *Trans. Path. Soc.*, Lond., 1879, xxi, 214.
[2] Fournier. *La Syphilis héréditaire tardive*, 1886.
[3] Hudelo. *Thèse de Paris*, 1890. Quoted by Chauffard, *Traité de Médecine* (Bouchard, Brissaud), v, 265.
[4] Forbes. *St. Barth. Hosp. Rep.*, 1902, xxxviii, 37.
[5] Mackenzie, H. W. G. *Trans. Path. Soc.*, Lond., 1892, xliii, 84.
[6] Devic et Froment. *Ann. de dermat. et de syph.*, Paris, 1906, 4. s., vii, 97.

are ill developed, look much less than their years, and are examples of what has been called infantilism. The usual age is between ten and twenty years. The liver is nearly always enlarged and may even appear as a tumour.

In Post's [1] case, a boy aged twenty-two years, the subject of late hereditary syphilis, there were gummas in various bones, in the pancreas, and in the liver. A gumma in the liver had become adherent to and invaded the abdominal wall, giving rise during life to a very definite tumour. Besides gummas the liver shewed very diffuse fibrosis. The patient died from an acute streptococcic infection. Bristowe's [2] patient, a boy aged fifteen years, had a tumour of uncertain nature connected with the liver which yielded nothing on aspiration. The temperature was hectic. On antisyphilitic treatment the signs and symptoms all disappeared.

FIG. 49.—Clubbing of the fingers in a case of late hereditary syphilis. (Photographed by DR. H. G. Drake Brockman.)

The spleen is enlarged either from lardaceous change or independently, as in the following case,[3] which imitated hypertrophic biliary cirrhosis.

A boy aged seventeen years had chronic jaundice of some years' duration, subcutaneous gummas, periostitis, enlarged spleen and liver, and clubbed fingers. He was the subject of congenital syphilis. Death was due to erysipelas complicated by pericarditis and peritonitis. The liver weighed 5 pounds, the right lobe was much scarred by gummas and was small, a fibrous mass compressed the common hepatic duct just at its commencement and obstructed the entrance of the two hepatic ducts into it. The spleen weighed 45 ounces. None of the organs were lardaceous.

There may be oedema of the feet, evidence of lardaceous disease of the kidneys, and eventually uraemia. Jaundice is rare, but ascites is very common. Jaundice and ascites may be due to pressure exerted by gummas or cicatrices in the portal fissure, while ascites may be part

[1] Post. *Boston City Hosp. Rep.*, 1898, 233.
[2] Bristowe. *Brit. Med. Journ.*, 1886, i, 878.
[3] Lazarus-Barlow, W. S. *Trans. Path. Soc.*, 1899, l, 158.

of the general dropsy of lardaceous kidney disease. There may be fever as in the acquired form (*vide* p. 364). In some instances there is widespread arteriosclerosis, with so much endarteritis obliterans that the pulses in the limbs may be absent. Death may be due to secondary infections, such as erysipelas, or be due to uraemia, cardiac failure, or asthenia.

In a well marked case of delayed hereditary syphilis, with hepatic gummas and lardaceous disease, in a girl aged twenty years in St. George's Hospital death was due to terminal peritonitis.

Diagnosis rests on the evidence of congenital syphilis, namely, interstitial keratitis, Hutchinson's teeth, deafness, and infantilism, together with hepatic enlargement. If evidences of syphilis common to the congenital and the acquired forms, such as gummas and lardaceous disease, are present and none of the stigmata of the congenital form are obvious, the infection may have been acquired in early life. But from the point of view of treatment an accurate distinction between them is unnecessary. The following case illustrates the difficulties which may arise in classification :

There was late hereditary syphilis, but the hepatic lesions were of the secondary and not of the tertiary stage. Clinically the hepatic enlargement must have appeared to have been undoubtedly of a tertiary nature. In a case of the congenital syphilitic disease with Parrot's pseudo-paralysis, deafness, and other stigmata in a girl aged twenty-one years, recorded by Touche,[1] the liver, which weighed 104 ounces, only shewed intercellular cirrhosis, although gummas and tertiary lesions were present in the bones.

When, as is often the case, the most prominent features are those of enlarged liver, ascites, and lardaceous disease, the diagnosis turns on evidence of past syphilis ; failing this and any other cause for lardaceous disease, such as prolonged suppuration, late hereditary syphilis should be thought of.

The *differential diagnosis* must be made from hydatid cyst and possibly from sarcoma, or, if there be fever, from abscess ; from cirrhosis and tuberculous peritonitis, when ascites is the predominating feature ; and from chronic nephritis, when dropsy and albuminuria are due to lardaceous disease.

Prognosis.—The prognosis is not so favourable as in acquired tertiary syphilis of the liver ; the effects of the poison are more widespread, and the frequency with which extensive lardaceous disease is present makes the outlook very grave.

The **treatment** is that of acquired syphilis in its tertiary stage (*vide* p. 367).

Parasyphilitic Multilobular Cirrhosis

Multilobular cirrhosis in young subjects with congenital syphilis is of considerable interest. The diffuse intercellular cirrhosis of infants

[1] Touche. *Bull. Soc. Anat.*, Paris, 1900, lxxv, 852.

suffering from congenital syphilis is, like the lesions of the secondary stage of the acquired disease, a curable condition. Microscopic examination of the livers of children formerly affected with hereditary syphilis may not shew any disease. On the other hand, every now and again the liver of a child with stigmata of congenital syphilis shews ordinary cirrhosis. The arrangement of the two lesions is so dissimilar that intercellular cirrhosis cannot be thought to be transformed into multilobular cirrhosis; it would rather lead to diffuse fibrosis or gummatous change. It seems probable that the intercellular cirrhosis undergoes absorption, but that some vulnerability or diminished resistance of the liver is left behind. If causes that tend to produce ordinary cirrhosis then arise, this change will be readily produced. In other words, the multilobular cirrhosis is a parasyphilitic lesion, and is comparable to general paralysis of the insane, in that, though not syphilitic, it is favoured by syphilisation of the soil (cf. Payne [1]).

Sometimes multilobular cirrhosis due to its ordinary causes may supervene in a liver in which intercellular cirrhosis still exists. This would account for some cases of very extensive fibrosis, chiefly of the multilobular type, but in which there are in addition areas of fibrosis suggesting that intercellular cirrhosis has gone on to organisation. Occasionally in multilobular cirrhosis in the subjects of congenital syphilis there is early lardaceous change in the organ.

The *clinical features* are much the same as those of portal cirrhosis in children. Parkes Weber [2] describes syphilitic splenomegaly with recurring attacks of jaundice and portal cirrhosis. What proportion of the cases of advanced portal cirrhosis of the liver in children have a syphilitic substratum it is difficult to determine; but the reported cases shew that direct evidence of syphilis is often absent. The following case illustrates the marked cirrhosis that may develop in the wake of congenital syphilis and the importance of a microscopic examination in distinguishing this condition from late hereditary syphilis:

A boy aged thirteen years, who had never taken alcohol, was the third child of his mother, who had four miscarriages after his birth. In May 1898 the abdomen enlarged, he became languid, and in August he became short of breath, and haematemesis and melaena occurred. On admission to St. George's Hospital the liver was much enlarged, reaching three finger-breadths below the costal arch, and dilated veins were present on the abdominal wall. He was twice tapped for ascites; death occurred three weeks after the last tapping. There was no oedema of the feet or albuminuria. At the necropsy the liver (42 oz.) was enlarged, granular on the surface, and on section shewed white areas suggesting gummatous infiltration. These were especially well marked around the hepatic veins, and by narrowing them had induced thrombosis. Microscopically, however, these areas did not shew any caseation, but a high degree of multilobular and intercellular fibrosis. There was no lardaceous change. The spleen (16 oz.) was enlarged, and contained a large

[1] Payne. *Trans. Path. Soc.*, Lond., 1900, li, 366.
[2] Weber, F. P. *Brit. Journ. Child. Dis.*, Lond., 1911, viii, 97.

fibrous area. The oesophageal veins were dilated. The testes and kidneys were healthy. The liver is in St. George's Hospital Museum, Series ix, 174[1], and was described by Dr. Lazarus-Barlow.[1]

Diagnosis.—It may be difficult to differentiate between these cases of cirrhosis in individuals with other manifest signs of congenital syphilis, on the one hand, and cases of late hereditary syphilis with hepatic lesions and ascites, on the other hand. In the latter there may be excessive lardaceous disease, as shewn by albuminuria. Iodide of potassium and mercury should be tried; improvement will point to hepatic gummas due to late hereditary syphilis, and the treatment must then be pushed.

The **prognosis** of these cases is very bad.

The **treatment** is that of ordinary cirrhosis, viz. milk diet, no alcohol or irritating food. Constipation should be prevented by seeing that plenty of water is taken, and if necessary by calomel and saline purges. Flatulence and excessive intestinal fermentation and putrefaction should be prevented by relieving constipation or by minute doses of calomel ($\frac{1}{20}$ to $\frac{1}{40}$ grain) or of perchloride of mercury. Mercury and the iodides of potassium, sodium, and ammonium should be given to prevent if possible any further progress in the disease. But as the lesion is parasyphilitic rather than syphilitic, iodides cannot be expected to remove the fibrosis. Weber advises caution in antisyphilitic treatment and recommends iodide of iron. In other respects the treatment is on the same lines as in portal cirrhosis.

ACTINOMYCOSIS

Incidence.—Actinomycosis (*ἀκτίς*, a ray, *μύκης*, a fungus) is rather rare in Great Britain and America; less so in Germany, Austria, Russia, and Norway. In France its reputed rarity appears to be due to the disease having escaped recognition; Duvau[2] has collected 146 cases observed in that country. Acland[3] collected 109 cases recorded in Great Britain. In 1902 Erving[4] collected 100 cases in America. In 1094 cases of human actinomycosis collected by Ruhrah,[5] 604, or 56 per cent, were in the head and neck, 223, or 20 per cent, in the digestive tract, 164, or 15 per cent, in the respiratory tract, 26, or 2 per cent, in the skin; and 63, or 6 per cent, were doubtful.

Etiology.—Actinomycosis is about three times commoner in men than in women.

[1] Lazarus-Barlow, W.S. *Trans. Path. Soc.*, 1899, l, 146.
[2] Duvau. *Thèse de Lyon*, 1902, No. 92.
[3] Acland. *System of Medicine* (Allbutt and Rolleston), 1907, ii, part i, 332.
[4] Erving, W. *Johns Hopkins Hosp. Bull.*, 1902, xiii, 261.
[5] Ruhrah. *Ann. Surg.*, 1899, xxx, 417.

On the basis of 405 cases Leith[1] estimated that 73 per cent were males and 27 per cent females.

It is most frequent between the ages of twenty-five and forty-five years.

It is generally stated that the infection is conveyed into the body by grain and other vegetable material. Homer Wright[2] considers this erroneous, and believes that the specific micro-organism—*Actinomyces bovis*—is a normal inhabitant of the alimentary canal.

Actinomycosis of the liver is rare. In 1903 Auvray[3] was only able to collect 31 published cases, but in Acland's 109 cases, collected from Great Britain only, the liver was invaded in 32.

Method of Origin.—Actinomycosis of the liver must be either metastatic, the infection being conveyed by the blood-stream from a mucous or cutaneous surface, or due to the direct spread of the disease from a focus in the neighbourhood. In the majority of instances the primary focus is in the alimentary canal, from which infection may spread either by the blood-stream or by continuity. In the latter event there may be a mass of inflammatory tissue extending between the affected part of the bowel, usually near the caecum, and the liver. In rare instances there is a direct spread of the actinomycotic growth from the skin of the abdominal wall or from the base of the right lung into the liver. In exceptional instances the infection has entered through the female genital tract. (Grainger Stewart and Muir,[4] and a case in St. George's Hospital, *vide* p. 386.) The primary focus, usually in the intestine, may heal so that it is very difficult or impossible to determine its situation. Such cases, of which Aribaud collected seven, have been called primary actinomycosis of the liver.

In 30 cases of hepatic actinomycosis collected by Aribaud[5] the growth was derived from the intestinal tract in 20. In 12 of these it spread by metastases and in the remaining 8 by direct extension.

Actinomycosis in the head and neck very seldom leads to infection of the liver.

Moodie[6] recorded a case in which a small circumscribed primary actinomycotic tumour of the upper jaw gave rise to a large actinomycoma of the liver.

Actinomyces or the ray fungus belongs to the streptothrix group and presents pleomorphous characters. It may appear as filaments, as cocci, or clubs. The clubs are often absent in human actinomycosis. For a description of the parasite the reader should refer to bacteriological text-

[1] Leith. *Edin. Hosp. Rep.*, 1894, ii, 121.
[2] Wright, J. H. *System of Medicine* (Osler and M'Crae), 1907, i, 327.
[3] Auvray. *Rev. de chir.*, Paris, 1903, xxiii, 1.
[4] Grainger Stewart and Muir. *Edin. Hosp. Rep.*, 1893, i, 96.
[5] Aribaud. *Thèse de Lyon*, 1897.
[6] Moodie, E. L. *Journ. Path. and Bacteriol.*, 1902, viii, 239.

books. Cases of infection with branched filamentous organisms somewhat resembling, but not, *Actinomycosis bovis*, and sometimes described as pseudo-actinomycosis, are now called nocardiosis (Wright).

Morbid Anatomy.—The liver is enlarged and shews adhesions on the surface. The morbid condition varies very considerably. The actinomycotic abscess has a characteristic honeycombed aspect and has been compared to a sponge soaked in pus. The alveolar appearance is due to the coalescence of a number of small abscesses. The suppurative process spreads by continuity, and is accordingly more or less localised; but sometimes small abscesses are seen away from the main collection, or there may be multiple abscesses, like those seen in pyaemia.[1] The individual abscesses vary in size from a pin's head to that of a walnut.

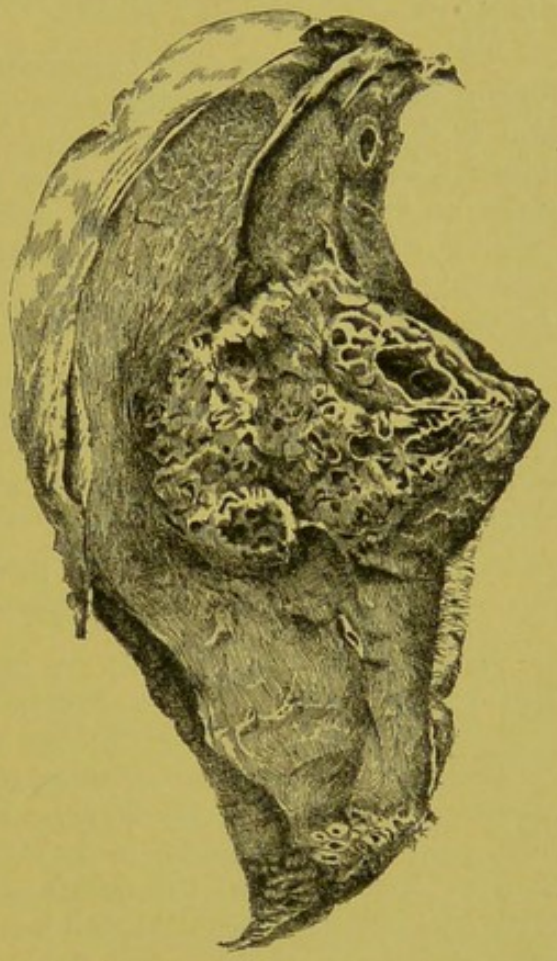


Fig. 50.—Actinomycosis of the liver, from a specimen (Series ix 182a) in St. George's Hospital Museum. (Drawn by Dr. E. A. Wilson.)

Inflammation of the capsule of the liver and adhesions to adjacent organs are very common. When situated anteriorly, the actinomycotic lesion readily extends, after adhesions have been formed, to the abdominal wall and may lead to an abscess. This may be the first evidence of disease, so that caution is necessary in assuming that the hepatic lesion is secondary to an abscess of the abdominal wall. Rupture of an actinomycotic abscess near the surface of the liver into the general cavity of the peritoneum causes acute peritonitis, as in Grainger Stewart and Muir's case. But from the frequency with which perihepatic adhesions are found it is more usual to get localised collections of pus near the liver, such as a subphrenic abscess. An actinomycotic abscess may even perforate into the stomach.

In Duckworth and Marsh's[2] case an actinomycotic abscess in the left lobe of the liver eroded the stomach wall from without inwards; there was also a

[1] Stewart, H. M. *Guy's Hosp. Rep.*, 1897, liv, 303.

[2] Duckworth and Marsh. *Brit. Med. Journ.*, 1900, ii, 1189; *Trans. Clin. Soc.*, 1901, xxxiv, 1.

subphrenic abscess of the same nature. In a man under my care an actinomycoma of the right lobe discharged into the stomach.

The abscess or abscesses in the liver may extend through the diaphragm into the lung or pleural cavity. Cases of hepatic actinomycosis may thus first present themselves as chronic empyemas of obscure origin. An actinomycotic tumour in the posterior part of the right lobe may spread into the right suprarenal, and even reach the right kidney.

The pus contains the characteristic granules composed of the ray fungus, and often pyogenetic cocci. It has been thought that suppuration is due to secondary infection, but there may be no evidence of mixed infection. Around the areas of suppuration there is fibrosis with pigmentation. Microscopically there are intercellular fibrosis and atrophy of the liver cells. The remainder of the liver may be fatty or lardaceous. In rare cases actinomycosis may be pyaemic and spread by the blood-vessels.

In Kanthack's[1] case it was not clear whether the abscess originated in the right lobe of the liver or at the base of the right lung; from this it had spread by continuity into the right suprarenal, and had given rise to pyaemic abscesses over the body. In Boari's[2] case there were secondary pyaemic abscesses due to pyogenetic cocci and not containing actinomyces.

Actinomycotic lesions in the liver have sometimes been regarded as tuberculous or ordinary hepatic abscesses.[3]

A plate published in 1838 of "an organic disease of the liver of an obscure kind as yet undescribed," and shewing "breaking down of a peculiar tubercular matter," is clearly actinomycosis.[4]

Clinical Picture.—Before there are any symptoms or signs indicating disease of the liver there may be evidence of abdominal disturbance, such as pain, constipation, or localised swelling imitating appendicitis. Stewart laid stress on the occurrence of two stages in the disease—an early period just referred to, and a later one when the liver is definitely affected. Between these two stages there may be an interval of fair health. The first symptoms of hepatic actinomycosis may be those of an empyema, subphrenic abscess, of an abscess in the abdominal wall, or, when the portion of the liver near the kidney is involved, of a perinephritic abscess. The liver may be enlarged, and with fever and pain over the liver the resemblance to an ordinary hepatic abscess may be very close.

A girl, aged twenty-one, was admitted into St. George's Hospital in October 1904 with a history of three acute attacks of abdominal pain in the past twelve

[1] Kanthack. *Trans. Path. Soc.*, Lond., 1894, xlv, 233.

[2] Boari. *Atti Accad. d. sc. med. e nat. in Ferrara*, 1895–6, lxx, 247.

[3] *Vide* Harley, *Med.-Chir. Trans.*, 1886, lxix, 135; Shattock, *Trans. Path. Soc.*, Lond., 1885, xxxvi, 260.

[4] Anatomical Drawings from Collection in the Army Medical Museum at Chatham. 3rd Fascic., 1838. Printed by Taylor, London.

months. The abdomen was opened and the appendix found to be normal, and a bilateral pyosalpinx removed but not examined. In January 1905 she was operated upon for a right subphrenic abscess, but she became very anaemic, and continued to have a hectic temperature until June 16, when she died with thrombosis of the right femoral vein and gangrene of the foot. At the necropsy there were subphrenic and hepatic abscesses shewing actinomyces, and the pyosalpinges which had been kept were then examined and found to be actinomycotic; the disease was therefore probably primary in the genital tract.[1]

Jaundice is extremely rare. Ascites has been noted late in the disease (Eve [2]), but is usually absent. Anaemia is an important feature of the disease. There is leucocytosis. Latimer and Welch [3] described a case of actinomycosis of the liver combined with myeloid leukaemia.

The **prognosis** of actinomycosis of the liver is very bad. Duvau [4] collected 40 cases of hepatic actinomycosis, all of which proved fatal. Presumably the prognosis should be less gloomy if the disease could be recognised in an early stage and treated vigorously with iodide of potassium, and secondary infection with pyogenetic micro-organisms prevented. For when the latter event has occurred the prognosis is bad. Though much commoner in animals, actinomycosis is rather more virulent in man.

The **diagnosis** depends on finding the fungus in the pus either from the liver or from a discharging abscess elsewhere. Before this has been done the condition is hardly likely to be thought of, and recorded cases shew that the disease has been regarded as empyema, pulmonary tuberculosis, sarcoma of the kidney (Leith), perinephritic abscess, hepatic abscess, suppurative cholangitis due to gall-stones, suppurating hydatid, or gumma of the liver. It has been observed that the subjects of actinomycosis react to Koch's tuberculin (Kahler, Arloing); this might lead to an erroneous diagnosis of massive tuberculosis of the liver.

Treatment.—The effect of iodide of potassium on actinomycosis is extremely marked and does fully as much good as it does in tertiary syphilis. It should be given in large doses, as much as two drams, or even more daily. In addition, 15 to 30 minims of a 1 per cent aqueous solution of iodide of potassium may be injected into the affected part, at first at intervals of three or four days, but later more frequently (Sawyer [5]). The effects of iodides internally combined with *x*-rays have been very encouraging.

When an actinomycotic abscess has been opened, the necrotic tissue may be scraped away with advantage, while of course iodides should be given freely. Iodoform may be employed locally, and carbolic acid or other disinfectants should be applied in order to minimise the risks of

[1] *Vide* Symes-Thompson. *Brit. Med. Journ.*, 1907, i, 984.
[2] Eve. *Trans. Path. Soc.*, Lond., 1889, xl, 405.
[3] Latimer and Welch. *Trans. Assoc. Am. Phys.*, 1896, xi, 328.
[4] Duvau. *Thèse de Lyon*, 1902.
[5] Sawyer. *Journ. Am. Med. Assoc.*, 1901, xxxvi, 1314.

infection. In a few cases tuberculin has seemed to have a good effect; Ziegler found the injection of a protein body obtained from cultures of *Staphylococcus pyogenes aureus* of use, and a cure has followed the use of an autogenous vaccine (Wynn,[1] Harbitz and Grøndahl[2]). Arsenic has also been recommended (Braun).

LYMPHADENOMA

Synonyms: Hodgkin's Disease, Lymphomatosis granulomatosa.

In generalised lymphadenoma the liver may contain nodules of white growth. As a rule the growths are small, discrete, and do not lead to any enlargement of the organ during life, but there may be a large diffuse mass.

Congenital lymphadenoma has been described (Bouvain and Ducloux,[3] Brault[4]), but the cases may have been pseudoleukaemia or lymphocytoma rather than lymphadenoma in the strict sense in which it is used in this article.

Morbid Anatomy.—The appearances of lymphadenomatous nodules in the liver may imitate caseous tuberculous masses and secondary new-growth. They are firm, white, and do not soften or become bile-stained; in these particulars they differ from what is often seen in advanced caseous tubercles. Tuberculosis may be combined with lymphadenoma in the liver (Andrewes[5]), as is well shewn in a specimen (No. 2223[c]) in St. Bartholomew's Hospital Museum. Lardaceous change may be found in a liver affected with lymphadenoma, and from the absence of any other factor, such as suppuration or syphilis, it would appear that lymphadenoma, or its underlying cause, may induce the lardaceous change.

Microscopical Appearances.—The growth starts in the portal spaces and extends outwards, passing between and eventually into the neighbouring lobules. The margin of the invaded lobules has an appearance like that of intercellular cirrhosis. Gradually the growth infiltrates the lobules, and the liver cells atrophy. The columns of deeply staining cubical cells, the so-called new bile-ducts, shew up prominently in the growth and at its advancing margin. In an early stage the growth is composed of small cells like lymphocytes, and the nodule closely resembles that of the earliest (miliary) collections of lympho-

[1] Wynn. *Brit. Med. Journ.*, 1908, i, 554.
[2] Harbitz and Grøndahl. *Am. Journ. Med. Sc.*, Phila., 1911, cxlii, 386.
[3] Bouvain et Ducloux. *Presse méd.*, Paris, 1901.
[4] Brault. *Manuel d'histologie pathol.*, Paris, 1912, iv, part i, 1014.
[5] Andrewes, F. W. *Trans. Path. Soc.*, Lond., 1902, liii, 313.

cytic leukaemia. Retiform tissue with cells like large lymphocytes and

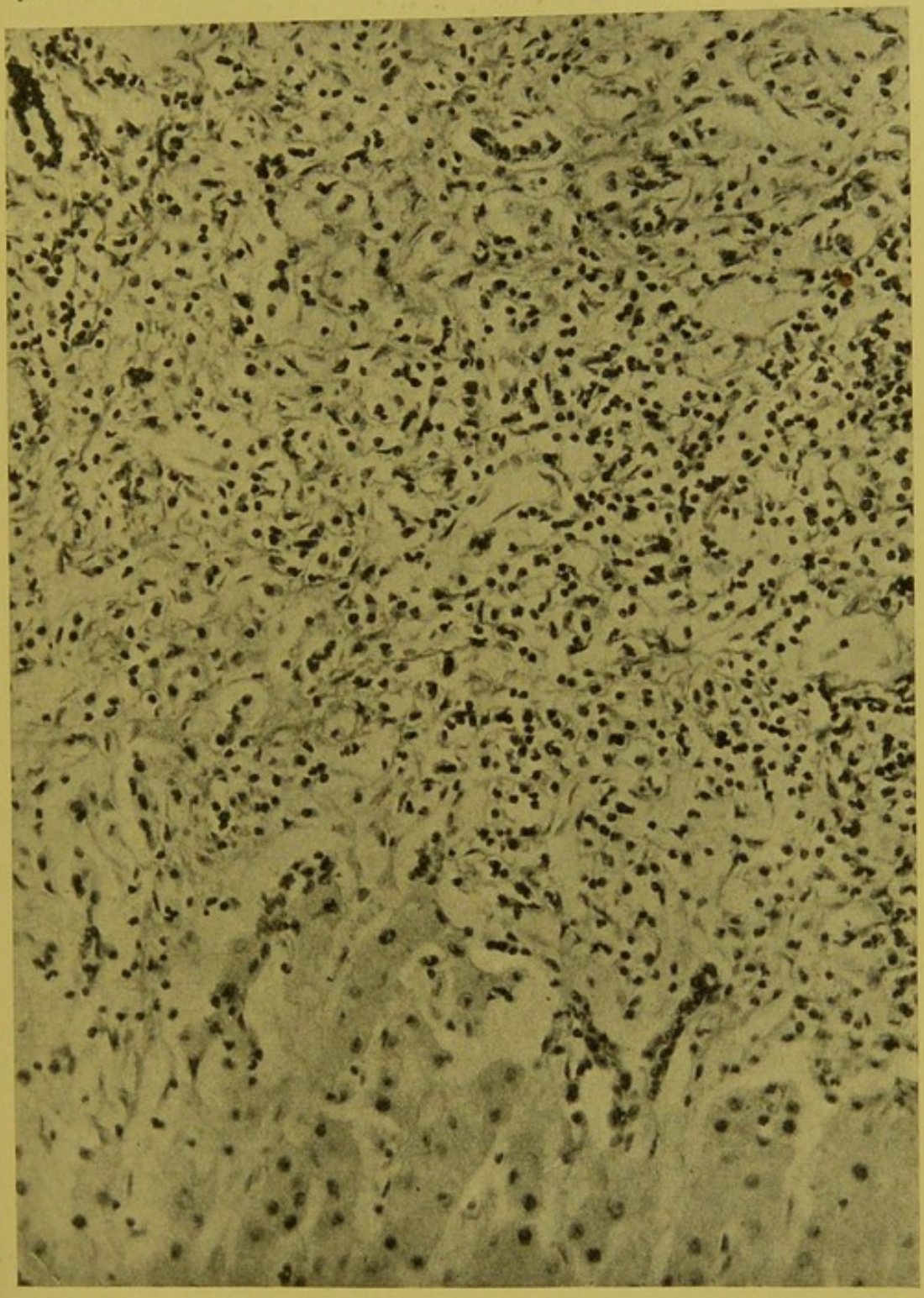


FIG. 51.—Margin of lymphadenomatous nodule. The endothelial and connective-tissue cells forming the growth are well seen. There is a reticulum between the cells. In one part the formation of deeply staining pseudobile canaliculi from the liver cells can be seen. High power. (Dr. H. Spitta.)

multinuclear (lymphadenoma) cells then appear ; and in very chronic cases

which are rare there is mainly fibrous tissue (M. Clarke[1]). Lymphadenoma may so infiltrate the liver that it has been thought that transformation into a mixed-celled sarcoma occurs (Yamasaki,[2] Karsner[3]). Compensatory hyperplasia of the liver cells may occur around the lymphadenomatous foci (Milne[4]). For a full description of the histology of lymphadenoma the reader should consult Andrewes', Reed's,[5] and Longcope's[6] papers.

Clinical Picture.—Lymphadenoma usually gives rise to slight enlargement only of the liver. When the liver is affected there is not uncommonly relapsing pyrexia of various types. Exceptionally the organ is very considerably enlarged, and if the superficial lymphatic glands are but little affected, the clinical aspect of the case, especially when there is a swinging temperature, may suggest pylephlebitis or hepatic abscess, as in two cases under my observation. Lymphadenomatous enlargement with fever may imitate hepatic syphilis with fever (*vide* p. 364), a Wassermann would exclude syphilis. Lymphadenoma of the liver and fever in a boy with inherited syphilis have given rise to great difficulty in diagnosis from syphilitic disease of the liver with syphilitic fever. Suchard and Teissier[7] met with a case imitating carcinoma of the liver; I have seen a patient on whom an exploratory operation for malignant disease has been performed.

Ascites may be present, but may be due to lymphadenoma of the intra-abdominal lymphatic glands and lymphatic obstruction; in such cases the effusion may be milky and resemble chyle. Ascites may be associated with compression of the portal vein by enlarged lymphatic glands, as in a case reported by Purser.[8] Jaundice does not often occur, but enlarged glands in the portal fissure may press on the bile-duct and produce biliary obstruction. I have seen periodic jaundice coincide with fever and enlargement of superficial lymphadenomatous glands.[9] Lymphadenomatous enlargement of the liver and spleen with jaundice must be distinguished from biliary cirrhosis by the rapid course and high temperature.

The **treatment** is the same as in lymphadenoma, but the **prognosis** is very bad when the liver is involved.

[1] Clarke, M. *Journ. Path. and Bacteriol.*, 1908, xii. 95.
[2] Yamasaki. *Ztschr. f. Heilk.*, 1904, xxv, 269.
[3] Karsner. *Arch. Int. Med.*, Chicago, 1910, vi, 175.
[4] Milne. *Journ. Path. and Bacteriol.*, Cambridge, 1909, xiii, 132.
[5] Reed. *Johns Hopkins Hosp. Rep.*, 1902, x, 133.
[6] Longcope. *Bull. Ayer Clin. Lab.*, 1903, i, 4.
[7] Suchard et Teissier. *Bull. Soc. Anat.*, Paris, 1897, lxxii, 940.
[8] Purser. *Lancet*, 1908, i, 1554.
[9] Rolleston. *Proc. Roy. Soc. Med.*, 1909, ii (Clin. Sect.), 155.

HYDATID CYSTS

HYDATIDS (ὑδατίς) are the cystic, larval, or bladder stage of a tapeworm which in its adult stage is found in the intestine of the dog, and also occurs in the wolf, the fox, and the jackal.

Life-History.—This tapeworm—the *Taenia echinococcus*—is small, measuring about 4 millimetres, or $\frac{1}{6}$ inch, in length, and composed of not more than four segments, the head and three proglottides, the last or terminal one being larger than the others put together, and containing fully developed sexual organs and, when fecundated, ova to the number of 500. The first segment, or head, has a prominent rostellum surrounded by two rows of hooklets, there being about 20 hooklets in each series. There are also four suckers. When the terminal proglottis breaks off from the tapeworm and is carried along with the faeces, the contained ova are liberated.

The ova after their exit from the bowel of the host are scattered about, and may find their way into the alimentary canal of man, when eaten on lettuce, water-cress, or other vegetables, or drunk with water. When the ova get into the stomach, their chitinous envelopes are dissolved, and an oval-shaped embryo, with six spines arising from one of its poles, is set free. The spines are directed backwards and thus allow the embryo to bore its way into the coats of the bowel, but prevent it from returning along the passage it has made. The embryos get into the portal vein and are conveyed to the liver. That they pass by the portal vein is largely assumed because the liver is *par excellence* their destination. If they simply bored their way straight through opposing structures, it would be natural to find them equally distributed throughout the surrounding organs. Possibly, moreover, conditions for their further development are more favourable in the liver than elsewhere, just as in the case of the free embryos of trichinella the muscles are the place of selection.

It has been thought that injury will favour the evolution of an embryo into a hydatid cyst by reducing the resistance of the liver. When the embryo reaches the liver and comes to rest, it proceeds to become transformed into the bladder or hydatid. The embryo loses its hooklets and enlarges so as eventually to form a small cyst; the outer surface becomes laminated and is called the ectocyst, while more internally the granular endocyst is evolved, and the contents undergo liquefaction. When reproductive changes leading to the production of daughter cysts commence, the first change is the formation of brood-capsules in the endocyst. These are small buds, lined internally by material resembling the ectocyst, and externally by the endocyst, so that it appears like an invagination of the cyst. The cavity of the brood-capsule contains fluid. From the outer surface of the brood-capsule the scolices develop; they are the early stage of the head of the future tapeworm and are provided with hooklets. The scolices arising from the outer surface of the brood-capsule eventually become invaginated into its interior. They readily become detached from the wall of the brood-capsule, and as a result of rupture of the brood-capsules become free in the cavity of the cyst. A scolex is about 0·3 mm. long and consists of two segments; the segment originally attached to the wall of the brood-capsule often contains crystals of carbonate of lime, while the

free segment has a crown of hooklets and four suckers. The hooklets measure 0·04 mm. Should the scolex reach the intestine of a dog it develops into an adult tapeworm by lengthening and transverse segmentation of its posterior end.

Daughter cysts are produced either inside the original cyst, endogenous formation, which is the usual way, or more rarely by external budding off, exogenous formation. The two processes may both occur in the same cyst. The daughter cysts are derived either from the scolices or brood-capsules, which become vesicular, or from invagination of the parenchymatous endocyst. The daughter cysts may become detached from the endocyst and become free in the cavity of the parent cyst, and may contain granddaughter cysts.

Exogenous formation of daughter cysts is rare in man, though common in sheep. Cysts are formed in the deeper layers of the ectocyst, become filled with fluid, and work their way outwards; they finally project from the surface of the mother cyst and become surrounded by an adventitious fibrous capsule. The mother cyst thus becomes knobby from the projection of daughter cysts, some of which may become disconnected from it. It is possible, however, that the so-called exogenous appearance is really only due to the cyst growing irregularly and sending out processes in the lines of least resistance. Pseudopodium-like processes of a single cyst might thus travel along the portal spaces in the liver, there being a continuous cavity throughout. Later the communication between the cyst and its process might become constricted, and in this way the appearance of a secondary cyst attached to the main cyst, but with an independent cavity, might be produced.

It was once thought that the extremely rare disease, alveolar hydatid, was a form of the exogenous proliferation of the hydatid cyst. In connexion with the exogenous mode of growth it may be pointed out that the presence of two or more hydatid cysts in the same liver is probably due to two distinct embryos having reached the liver and not to exogenous formation of one from the other.

Sterile Hydatid Cysts.—When no multiplication or reproductive changes take place in the cyst, it is spoken of as being sterile or as an acephalocyst, though the latter term is not often used now. The fluid does not contain any daughter cysts or scolices, and the nature of the cyst, whether hydatid or not, must be determined by microscopic examination of its wall. Failure in reproduction probably depends on imperfect nutrition. Pedunculated hydatid cysts which hang down from the under surface of the liver are more likely to be sterile than those embedded in the substance of the liver.

Warty ingrowths from the cyst wall are sometimes observed; they are probably abortive daughter cysts.

In the museum of Surgeons' Hall, Edinburgh, there is a part of the wall of a hydatid cyst shewing this papillomatous appearance. The cyst was a large one and contained many hundreds of small cysts (No. 1885).

On the other hand, it is possible that in some of the cases the warty growths were due to commencing degenerative changes and that the process is due to involution and not to imperfect evolution.

Structure of Hydatid Cysts.—The wall of the true parasitic cyst consists of the outer cuticle, or ectocyst, and an inner lining, or endo-

cyst. The cysts have an opalescent whitish-blue colour, and unless considerably thickened, tear easily. The ectocyst is elastic and tends to curl up when it is incised. Structurally it has a characteristic laminated appearance. There are wavy bands of homogeneous, hyaline material which, like the wall of the original ovum, is chitinous.

The endocyst forms the parenchymatous or granular internal lining of the ectocyst; from it the brood capsules are developed. It may contain crystals of carbonate of calcium like those seen in the mature cestoda and in the scolices. According to Loeper[1] the presence of glycogen shews that the cyst is living. The fluid in a living hydatid cyst is clear, of a low specific gravity, 1002 to 1015, contains no albumin, but a considerable quantity of chloride of sodium; for other details see page 405. When the cyst becomes inflamed or dies, the fluid becomes albuminous and may be turbid.

Outside the parasitic cyst, as a result of compression and irritation of the tissues of the liver, a fibrous capsule is produced which extends for a short distance into the surrounding liver substance. A hydatid cyst projecting from the surface of the liver may have a thick fibrous covering with the consistence of cartilage, which resembles a corneal fibroma of the spleen and may be calcified. The remains of the hydatid cyst may escape notice, and the true nature of these thick-walled cysts be overlooked. When embedded in the substance of the liver the fibrous capsule contains pseudobile canaliculi and mononuclear and eosinophil cells (Loeper, Bodin and Fiessinger[2]). This local eosinophilia is not constant, and corresponds in this respect more or less with the presence or absence of haemic eosinophilia (Dévé[3]). In addition, there may be giant cells whose function is to attempt absorption of the cyst; they do not contain tubercle bacilli, and differ from the giant cells of tuberculous granulation-tissue in that their nuclei are in the centre and not at the periphery. In rare instances the mother cyst may disappear; Stirling[4] reports a case with more than 28,000 daughter cysts in which barely a shred of the mother cyst could be detected.

Two cysts arising in close contact to each other may be enclosed in the same pseudocyst or capsule derived from the tissues of the liver by pressure irritation. Occasionally a hydatid cyst is divided into two parts by a constriction, and thus resembles an hour-glass or a shirt stud. This may depend either on two cysts, originally separate, opening into each other, or, as pointed out in speaking of exogenous formation of daughter cysts, on irregular growth due to differences in the resistance offered by the surrounding tissues.

Situation of Hydatid Cysts in the Liver.—The cysts may be deeply embedded in the liver, and are naturally, from the greater size of the right lobe, commoner there than in the left lobe. Cysts in the upper and

[1] Loeper. *Clinique médicale de l'Hôtel-Dieu*, 1906, v, 264.
[2] Bodin et Fiessinger. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1908, xxv, 182.
[3] Dévé. *Compt. rend. Soc. Biol.*, Paris, 1905, lvii, 49.
[4] Stirling. *System of Medicine* (Allbutt and Rolleston), 1907, ii, part ii, 1004.

back part of the right lobe push the diaphragm up. Not uncommonly a hydatid cyst hangs down from the liver like a dilated gall-bladder.

Number.—There may be one cyst only, but it is not by any means rare to find two or three. As many as forty small cysts have been found in the liver (Dolbeau [1]).

Size.—A single hydatid cyst may reach a very large size indeed. The largest hydatid cyst of the liver on record appears to be one containing 36 pints; it occupied three-quarters of the abdomen and was successfully operated upon by H. B. Robinson;[2] four years previously it had been tapped and 40 litres (70 pints) removed with only very temporary relief.

Spontaneous Death.—Inasmuch as hydatids are most commonly present in the liver, being found there in 57 per cent of all the cases of the disease, it is natural that hydatid cysts which have become latent, and undergone involution changes ending in spontaneous cure, are commoner in the liver than elsewhere.

It has also been thought that they are more often found in the liver because their natural evacuation is less easy than in the case of the lung or kidney, from which they may be coughed up or passed into the ureter. But there is not much difference between the lumen of the common bile-duct and of the ureter, except that the larger end of the ureter, the pelvis of the kidney, is directed towards the hydatid in the kidney, whereas the intrahepatic bile-ducts are small. This explanation of the frequency of hepatic hydatids is not worth much, for natural evacuation is rare in any organ and much less common in the lung and kidney than in the liver.

Causes of Spontaneous Death.—Possibly the cause may sometimes be inherent in the individual parasite, which, being of poor vitality, runs its allotted course and dies before reaching the ordinary size. For death with spontaneous cure is most often seen in small cysts which have not given rise to symptoms during life. This, however, is not a universal rule, and a large hydatid, if not operated on, may gradually undergo involution changes and shrivel up.

A patient had been seen when eleven years old by Sir Astley Cooper, and his liver was then said to be four times its natural size and was thought to contain fluid; no operation was done. The tumour gradually got smaller and forty-five years later, when Murchison [3] saw the patient, there was a mass as hard as bone in connexion with the right lobe of the liver.

The usual term of life of a hydatid cyst is not known, but it has been thought to be as long as twenty years. Of the causes acting from without and impeding the growth or possibly poisoning the parasite outright, the most commonly recognised is the entrance of bile into the cyst. The constant pressure exerted by the contents of the tense cyst leads to atrophy of the tissues intervening between the cavity of the cyst and an adjacent bile-duct and allows of the entry of bile into the cyst, and sometimes of a discharge of the contents of the cyst into the bile-duct (*vide*

[1] Dolbeau. *Bull. Soc. Anat.*, Paris, 1857, xxxii, 116.
[2] Robinson, H. B. *Trans. Clin. Soc.*, Lond., 1897, xxx, 16.
[3] Murchison. *Lectures on Diseases of the Liver*, p. 130, 1877.

p. 418.) As evidence of the entrance of bile into the cyst the occurrence of crystals of bilirubin and biliverdin may be forthcoming.

On the other hand, dead cysts may not contain any trace of bile, and spontaneous cure of hydatid cysts may occur in other organs, where, of course, bile can play no part. Further, the parasiticidal action of bile appears to be slight, as Dévé[1] finds that scolices continue to grow in a mixture of equal quantities of bile and hydatid fluid. Secondary hydatid cysts can develop in the peritoneum when there is a bile-stained peritoneal effusion from rupture of a hydatid cyst, already communicating with a bile-duct, into the peritoneal cavity. It therefore seems probable that bile has little to do with spontaneous death of hydatid cysts in the liver. In some instances the entrance of bile is subsequent to the death of the parasite.

Chemical alterations in the lymph bathing the outside of the cyst have also been suggested, and it has been thought that poisonous products absorbed from the bowel, such as alcohol, might play such a part; but the resistance of hydatid cysts to any form of drug renders this doubtful. The entrance of fluids, such as blood, into the cavity of the cyst may so disturb the equilibrium necessary for the continued life of the parasite as to lead to its death. Of the occurrence of past haemorrhage into a hydatid cyst there is no very satisfactory evidence, as the crystals of haematoidin and bilirubin are identical. It appears probable that in cases in which "haematoidin" is described in cysts the crystals are really bilirubin.[2] Absorption of the contained hydatid fluid has been thought to be the cause of spontaneous death of the parasite; this view is supported by cure after simple tapping of a cyst, but, on the other hand, there is no proof that under ordinary conditions absorption of the fluid can occur from a living cyst.

The rapid proliferation of the daughter cysts so that they increase out of all proportion to the surrounding fluid and produce heightened pressure, and so exert an inhibitory influence on the life of the parasite, has been put forward as a cause of spontaneous death.[3] That this is not a universal cause is shewn by the fact that dead cysts may contain few or even no daughter cysts. Changes in connexion with the fibrous capsule of the cyst, such as cicatricial contraction and calcification, have also been thought to interfere with the nutrition of the parasite, but it is difficult to prove the relation between the two processes.

Changes following Death of a Hydatid Cyst.—The fluid of a living hydatid cyst under ordinary conditions is practically free from albumin; after death, however, it becomes albuminous. From the albuminous fluid removed from a hydatid cyst which had previously been killed by electrolysis Boinet[4] obtained crystals of a toxic body analogous to mytilotoxin, probably the result of cleavage of the albumin. The albuminous fluid in

[1] Dévé. *Compt. rend. Soc. Biol.*, Paris, 1903, lv, 75.
[2] *Vide* Dickinson, W. L. *Trans. Path. Soc.*, Lond., 1894, xlv, 259.
[3] Murchison. *On Diseases of the Liver*, p. 62, 1885.
[4] Boinet. *Rev. de méd.*, Paris, 1898, xviii, 845.

the cyst becomes turbid and cloudy from the precipitation; later, absorption occurs and the contents become less fluid and more gelatinous and the parent cyst shrinks, while fatty metamorphosis of the albumin gives the contents a buttery, caseous, or putty-like character; various stages, from a glairy or colloid state to complete solidity, may be met with as time goes on. The contents are frequently yellow in colour. These changes in the mother cyst are subsequently repeated in the daughter cysts. The putty or gelatiniform material may contain crystals of cholesterin, stearin, bile pigment, tyrosine, Charcot's crystals;[1] and calcification may extend from the outer adventitious capsule into the contents of the cyst.

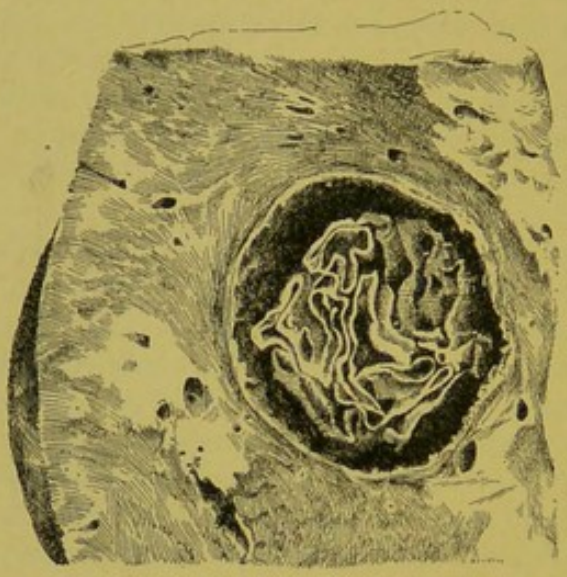


FIG. 52.—An obsolete hydatid cyst in the liver. From a specimen (Series ix. No. 179e) in the Museum of St. George's Hospital. (Drawn by Dr. E. A. Wilson.)

Contraction and shrinking of the outer fibrous capsule lead to a folding of the cyst wall compared to the appearance of a corpus luteum. The outer capsule may become extremely hard from infiltration with carbonate and phosphate of lime. Good specimens of the calcified shells, so to speak, of hydatid cysts are to be found in most museums; there is one (No. 2234) in St. Bartholomew's Hospital Museum of multiple calcified cysts. Usually the process of spontaneous cure is unaccompanied by any inconvenience or clinical signs.

In a case recorded by Mitchell Bruce and Sheild[2] the contents of a very large cyst became gelatiniform. The tumour was so large, and was, contrary to what would naturally be expected, increasing in size, that laparotomy was performed. The diagnosis of a solid hydatid cyst had previously been made by aspiration of colloid matter containing hooklets.

In rare cases a spontaneously cured hydatid suppurates and, if in communication with the bile-ducts, may cause suppurative cholangitis.

Condition of the Remainder of the Liver.—The pressure exerted by a large cyst causes atrophy of the liver in its immediate neighbourhood, and in this way a whole lobe may become excavated and destroyed. In extreme instances the organ may become so deformed that its anatomical features are quite obliterated. Compensatory hypertrophy of other parts of the liver readily occurs, and the resulting hypertrophy is often considerably in excess of the normal amount of liver substance. The left

[1] Carwardine. *Trans. Path. Soc.*, 1898, xlix, 132.
[2] Mitchell Bruce and Sheild. *Med.-Chir. Trans.*, Lond., 1892, lxxv, 175.

lobe has been found to weigh as much as a normal liver (Zadoc-Kahn [1]). The compensatory hyperplasia occurs with greater ease in hydatid disease of the liver than in cirrhosis, malignant disease, or abscess. This is probably because there is no depressing factor, such as toxins, to reduce the vitality of the liver cells. The compensatory hypertrophy is better developed at some distance from the cysts, and since cysts are usually in the right lobe, the left is frequently greatly hypertrophied, though the quadrate and Spigelian lobes share in the compensatory process. This compensation accounts for the absence of constitutional symptoms in the disease. On the other hand it is possible that the hyperplasia of the liver cells may be so excessive as to give rise to primary carcinoma, as in Loehlein's case. With very rapidly growing hydatid cysts there may not be time for compensatory hypertrophy to occur, and the amount of liver substance may for a time be greatly diminished. Hydatid cysts have been found to be associated with universal cirrhosis of the liver (Cayley, Weir, S. Savage [2]), and with malignant disease.[3] In Necker's [4] case there were two hydatid cysts, cirrhosis, secondary spindle-celled sarcoma, and a primary carcinoma derived from the bile-ducts. In a man aged forty-nine who died in St. George's Hospital from pyloric carcinoma with extensive secondary infection of the liver, which weighed 10 pounds, there was a dried-up hydatid cyst in the right lobe close to the gall-bladder. In a case recorded in St. Thomas's Hospital Reports primary carcinoma of the liver was associated with several calcified hydatid cysts.[5] In Loehlein's case of a very large hydatid of the liver there was hyperplasia of the liver cells and a primary carcinoma derived from the liver cells. Loehlein [6] quotes 4 other cases by Bamberg, Dibbelt, Necker, and Fränkel.

In a case recorded by Pitt [7] the irritation set up by a cyst in the left lobe of the liver of a man aged thirty-nine years, who had contracted syphilis thirteen years before death, seemed to have caused a remarkable syphilitic growth enclosing the cyst.

Relative Frequency of Hepatic to Hydatid Cysts Elsewhere.—The liver is more often the site of hydatid cysts than the whole of the remainder of the body. The percentage incidence of hydatids in the liver is variously estimated at 74 per cent (Lyon [8]) to 44 per cent (Davaine [9]).

[1] Zadoc-Kahn. *Arch. gén. de méd.*, Paris, 1897, clxxix, 171.

[2] Cayley, W., *Trans. Path. Soc.*, Lond., 1874, xxv, 129; Savage, S., *Brit. Med. Journ.*, 1899, i, 1030; Weir, *Med. Rec.*, N.Y., 1899, lv, 149; Stevens, *Brit. Med. Journ.*, 1901, i, 1139.

[3] Habran, *Bull. Soc. Anat.*, Paris, 1868, p. 437; Florand, *ibid.*, 1886, 4. s., xi, 677; Longuet, *Gaz. hebd. de méd.*, Paris, 1874, xxi, 774; Russell, J. W., *Brit. Med. Journ.*, 1907, i, 311; Cranwell, *Bull. et mém. Soc. de chir. de Paris*, 1909, xxxv, 3.

[4] Necker. *Ztschr. f. Heilk.*, Wien u. Leipzig, 1905, xxvi (Abt. path. Anat.), 351.

[5] *St. Thomas's Hosp. Rep.*, 1891, xxix, 141.

[6] Loehlein. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1907, xlii, 531.

[7] Pitt, G. N. *Trans. Path. Soc.*, Lond., 1886, xxxvii, 276.

[8] Lyon. *Am. Journ. Med. Sc.*, 1902, cxxiii, 124.

[9] Davaine. *Traité des Entozoaires*, Paris, 1878.

In 1897 cases of hydatid disease Davies Thomas[1] found the liver affected in 1084, or 57 per cent, the lungs being next with 220, or 11·6 per cent. Finsen estimated the incidence of hydatids in the liver at 69 per cent, Peiper[2] at 66·4 per cent, Neisser[3] at 50 per cent, and Cobbold, on the basis of his own and Davaine's cases, at 46 per cent.

The frequency with which the liver is infected is due to its filtering the blood from the intestines and thus arresting the embryos which have got into the portal vein. If the embryo is not stopped by the liver, it passes to the capillaries of the lung and may come to rest there.

Etiology.—*Geographical Distribution.*—In England hydatid disease is said to be commoner in London than in most country districts, but in the Fen districts around Cambridge it is comparatively common.

Murchison in 2100 necropsies at the Middlesex Hospital recorded 13 bodies with hydatids, or 1 in 161 ; in 7 of these, or 1 in 300, they were the cause of death. From an examination of the statistics of in-patients at St. Bartholomew's Hospital, London, for thirty years, W. S. Church[4] found that one case of hydatid disease was admitted in 1100. The disease appears to be getting rarer in London.

In Scotland hydatids are very rare, but in Shetland they are comparatively common (H. Stiles[5]). In Russia they are not infrequent. In Switzerland and South Germany, where the alveolar form occurs, the cystic form is not common. In Iceland they are extremely common ; estimates vary from one-sixth to one fifty-eighth of the entire population, one-thirtieth being the mean and more probable figure. The great frequency of hydatid disease depends on the enormous number of dogs which are very frequently infected with taeniae. It is said to be common in Turkey. Hydatid cysts are rare in South Africa, but are becoming more frequent in Algiers, and are not uncommon in Egypt. In Australia they are very frequent, being commonest in South Australia. In 1000 necropsies mentioned by Stirling and Verco hydatids were found in 49, or 5 per cent. In Victoria one case of hydatid occurs in every 175 admitted to hospital, in New South Wales 1 in 380. The proportion in New Zealand and Tasmania is also very high (Church). Stirling and Verco[6] lay stress on the presence of large numbers of sheep as an important factor in the incidence of hydatid disease. In North Queensland it is almost unknown.

In North America hydatid disease is rare, and when it is met with is in the bodies of foreigners.

Up to July 1891, Osler[7] could only find evidence of 85 cases ; since the migration of Icelanders into Winnipeg the disease has become more frequent in

[1] Thomas, Davies. *Hydatid Disease*, Adelaide, 1894.
[2] Peiper. *Thierische Parasiten*, 1904, S. 158.
[3] Neisser. *Echinococcenkrankheiten*, Berlin, 1877.
[4] Church, W. S. *Clin. Journ.*, Lond., 1900, xv, 337.
[5] Stiles, H. *Scot. Med. and Surg. Journ.*, 1903, xii, 131.
[6] Stirling and Verco. *System of Medicine* (Allbutt and Rolleston), 1907, ii, part ii, 997.
[7] Osler, W. *Practice of Medicine*, ed. ii.

that locality. Ten years later Lyon[1] collected notes of 241 cases of hydatid disease occurring in the United States and Canada up to July 1, 1901. Most of the patients were either Icelanders or Germans.

In the Argentine Republic hydatid disease has been becoming increasingly common; in the years 1890–1907 there was 3195 cases treated in the hospitals of Buenos Aires (Cranwell[2]). This depends on the large number of sheep and dogs there. Hydatid disease is very rare in India, and doubt has been expressed as to its origin there at all; it may be found in persons dying in India who have acquired the disease elsewhere. W. J. Buchanan[3] records an undoubted case of hydatid cyst of the liver in a native of India who had never been out of the country; a very large abdominal hydatid cyst, possibly hepatic in origin, was recorded by Sorabji[4] in a native Indian woman. It is very rare in China.

There is nothing to suggest that the natives of Iceland or Australia, where the disease is most prevalent, are in the slightest degree immune from hydatid disease. In 1897 Verco and Stirling[5] stated that except for accident and tuberculosis, hydatid disease was responsible for all deaths of the aborigines in the Adelaide Hospital.

Method of Infection.—The ova derived from the dried and scattered faeces of dogs may settle on vegetables or contaminate drinking-water. Lettuce and especially water-cress may, if not carefully washed, serve as vehicles for the transmission of the disease. Persons in contact with dogs and other animals, the subjects of *Taenia echinococcus*, are in danger of becoming the hosts of the bladder stage of the tapeworm. There is some risk in the possession of pet dogs, as infection may be conveyed by a dog licking the hands and face of its master. Dévé[6] collected a number of instances of two cases of hydatid disease occurring in the same family.

It has been suggested that when portions of hydatid cysts embedded in the livers of sheep or oxen are eaten, the scolices may develop in the alimentary canal of man and give rise to auto-infection. This hypothesis requires for its confirmation the recognition of scolices in the human alimentary canal, and has not yet been justified. Offal from slaughter-houses, however, containing hydatid cysts is a most important factor in the causation of the tapeworm in dogs, and so indirectly of the cysts in man.

Sex.—The incidence of hydatid disease in the two sexes depends on their relative exposure to infection, which is generally more marked for men. In Australia, where the water-supply in the bush is the great source of infection, the ratio is 100 men to 77 women. In America Lyon found the incidence 60 per cent in men and 40 per cent in women.

[1] Lyon. *Am. Journ. Med. Sc.*, 1902, cxxiii, 124.
[2] Cranwell. *Bull. et mém. Soc. chir. de Paris*, 1909, xxxv, 3.
[3] Buchanan. *Lancet*, 1900, ii, 19.
[4] Sorabji. *Lancet*, Lond., 1908, i, 97.
[5] Verco and Stirling. Allbutt's *System*, 1897, ii, 1114.
[6] Dévé. *Arch. gén. de méd.*, Paris, 1907, cxcviii, 673.

In France Davaine[1] found the incidence equal in the two sexes. In Berlin women were more often affected than men in the ratio of 65 to 35 (Neisser[2]), and in Iceland women are twice as often affected (71 per cent) as men (29 per cent) (Finsen[3]).

Age.—The disease becomes more frequent up to about fifty years of age and then declines, the majority of cases occurring between twenty and forty. It is rare under fifteen. In children it is said to be less rare in girls than in boys, and to attract attention chiefly about eight years of age.

Pontou[4] collected 22 cases in children in 1867, and a large number have since been recorded. In Australia during seven years Downs[5] operated upon 25 cases. Cases of two cysts in the liver of a boy aged six years (H. B. Robinson[6]) and a boy aged seven years (Cheney[7]) have been recorded. Of 948 cases in the Argentine 135 occurred in the first and 200 in the second decade of life (Vegas and Cranwell).

Clinical Picture.—**Symptoms.**—A hydatid cyst of the liver may remain entirely latent, so that its presence, even when involution or spontaneous cure have not supervened, may be only revealed at the necropsy, or be suspected for the first time when the abdomen is examined, in the course of life insurance routine or in a pregnant or recently delivered woman. Even when the cyst is large, there may be nothing to attract the patient's attention, except perhaps the increasing size of the abdomen, or a feeling of weight or of dragging in the hepatic region. When the capsule of the liver is inflamed, tenderness and pain on respiration are present, but acute perihepatitis is infrequent in the absence of suppuration. Pain in the right hypochondrium shooting to the right shoulder may be due to adhesions caused by the toxic action of hydatid fluid (Quénu[8]). Maclaurin[9] found that pain occurred in 62 out of 102 cases. Pain is quite rare in children. The contrast between the marked physical signs and the freedom from symptoms and from constitutional disturbance has already been referred to. Pressure symptoms are, as a rule, absent; this probably depends on the slow growth of the cyst. Pressure on the stomach and intestines may, however, give rise to dyspepsia, vomiting, and constipation. Obstruction is a most exceptional result of hydatid cysts, but Reichold[10] recorded the case of a woman in whom intussusception had been diagnosed. Upward pressure on the diaphragm may greatly encroach on the pleural cavity and produce considerable dyspnoea. This will be more marked when the abdomen is

[1] Davaine. *Traité de Entozoaires*, Paris, 1877.
[2] Neisser. *Die Echinococcenkrankheiten*, 1877.
[3] Finsen. Quoted by Lyon.
[4] Pontou. *Thèse de Paris*, 1867. Quoted in *Traité des maladies de l'enfance*, iii, 195.
[5] Downs. *Austral. Med. Journ.*, 1911, xvi, 127.
[6] Robinson, H. B. *Lancet*, Lond., 1899, i, 767.
[7] Cheney. *Arch. Pediat.*, 1897, xiv, 851.
[8] Quénu. *Rev. de chir.*, Paris, 1910, xlii, 945.
[9] Maclaurin. *Austral. Med. Gaz.*, 1909, xxviii, 295.
[10] Reichold. *München. med. Wchnschr.*, 1897, xliv, 441

distended from some other cause, such as pregnancy. The irritation of a large hydatid cyst may set up slight pleurisy and give rise to pain and cough. As in some other hepatic conditions, the pain may be referred to the right shoulder. Epistaxis, haematemesis, melaena, and metrorrhagia have been recorded, but are extremely rare.

In a case recorded by Hillier[1] haemorrhage took place into a hydatid cyst and ran along the hepatic duct, which opened into the cyst, to the duodenum. The patient died from haematemesis and melaena. At the necropsy the cyst contained 37 ounces of blood-clot.

The **physical signs** of hydatid cysts are more prominent than the symptoms. In many instances the upper segment of the abdomen on the right side and in the epigastrium is prominent and firm, and there is bulging of the costal arch on the right side. In great abdominal distension lineae albicantes may be present. Dilated subcutaneous veins are very exceptional, but a prominent "caput Medusae" has been noted when the inferior vena cava is compressed by a large cyst.

The liver is enlarged, its form and outline varying, of course, with the position of the cyst or cysts. A cyst near the convexity of the liver displaces the diaphragm upwards. A cyst in the right lobe may compress the lower lobe of the right lung and imitate a pleural effusion. In rare instances a cyst in the left lobe has simulated a pericardial effusion.

When the cyst is deeply embedded in the substance of the right lobe, the liver is expanded and pushed forwards as if occupied by a solid growth. When the cyst projects from the under surface of the right lobe, the liver is pushed forward, and when it protrudes beyond the lower border it may imitate an enlarged and distended gall-bladder, a tumour of kidney, uterus, or ovary, or a pancreatic cyst. A pendulous hydatid cyst may, like a distended gall-bladder, be accompanied by a linguiform lobe of the liver. A cyst growing from the anterior surface bulges the hypochondrium out, or when in the left lobe, the epigastrium forwards, in a remarkable manner. In such cases the enlargement of the liver is not uniform, as in cirrhosis, but is localised and may be manifestly due to a tumour, in size varying from that of an orange upwards. The hepatic enlargement does not depend entirely on the position of the cyst, though of course it is chiefly due to its presence. When the right lobe is occupied by a large hydatid cyst, marked compensatory hypertrophy of the left lobe may render it easily palpable. Chauffard recorded such a case in which the left lobe weighed almost as much as a normal liver.[2]

Usually the tumour is tense and elastic; it may, especially when thick-walled and covered by liver tissue, give the impression of a solid tumour; as already mentioned, the contents may in exceptional cases undergo gelatinous change, although the cyst is increasing in size. Occasionally, on the other hand, it may fluctuate so as to imitate an abscess. On percussion the cyst is almost always dull; the entrance of air from

[1] Hillier. *Trans. Path. Soc.*, Lond., 1856, vii, 22.
[2] Chauffard. *Semaine méd.*, Paris, 1896, xvi, 265.

rupture into a hollow viscus, bronchi, or intestine being so rare as to make it probable that when the cyst appears to be resonant it is really covered by stomach or intestine. Gas has, however, been found in suppurating hydatid cysts without there being any communication with the intestinal tract, and can be explained as the result of infection with the *Bacillus aerogenes capsulatus* or other, usually anaerobic, organisms.

Dévé [1] collected 48 cases of gaseous hydatid cysts of the liver; 24 of these were closed suppurating cysts, 11 had ruptured into the bronchi, 7 into the alimentary canal, and 6 had been operated upon.

The "hydatid thrill," discovered by Blatin in 1801, is an inconstant sign and, even when present, is not pathognomonic. It is brought out by percussing the middle finger of the left hand when placed over the cyst; a peculiar vibration is then communicated to the finger percussed. This thrill was thought by Briançon [2] to be due to the impact of contained daughter cysts, but it can be obtained in sterile hydatid cysts, in tense cysts of other kinds, such as hydronephrosis, and sometimes in encysted ascites, or, according to Chauffard,[3] in general ascites under certain conditions, such as an elastic state of the abdominal walls in young persons. The "hydatid thrill" is not very often obtained, but the conditions required for its production are more often realised in hydatid than in other cysts; so that its presence, though not absolute evidence, strongly suggests a hydatid cyst. Lancereaux [4] obtained it twice in a personal experience of 60 cases; many observers have never met with it. A thrill is said to be relatively less rare in early life than in adult patients (Broca [5]). It has been thought that the occurrence of suppuration, by altering the conditions inside a hydatid cyst, will remove the thrill (Milian [6]). After tapping a cyst a thrill sometimes becomes evident, though previously absent.

When two or more hydatid cysts are either in or in connexion with the liver, the signs may be very confusing, and from the irregularity of the surface suggest malignant disease, cirrhosis with great enlargement, displacement of the liver, or affections of other organs.

In a case of multiple hydatids in the liver encroaching above on the pleural cavity, the downward projection of two large cysts from the right lobe of the liver left a notch between them which during life was taken for the notch between the two lobes of the liver, the organ being thought to be displaced downwards by a pleural effusion. Two hydatid cysts in a boy aged seven projecting from the anterior surface of the right lobe gave rise to a sulcus which when felt through the abdominal walls imitated the colon passing over a tumour of the right kidney (Cheney [7]).

[1] Dévé. *Rev. de chir.*, Paris, 1907, xxxv, 529.
[2] Briançon. *Thèse de Paris*, 1828.
[3] Chauffard. *Traité de Médecine* (Bouchard et Brissaud), 1902, v, 303.
[4] Lancereaux. *Traité des maladies du foie et du pancréas*, p. 738, 1899.
[5] Broca. *Semaine méd.*, 1901, xxi, 89.
[6] Milian. *Bull. Soc. Anat.*, Paris, 1900, lxxv, 911.
[7] Cheney. *Arch. Pediat.*, 1897, xiv, 851.

Pressure on the bile-duct producing jaundice, on the portal vein inducing ascites or haemorrhoids, or on the inferior vena cava causing oedema of the legs, is very rare. The position of the cyst has an important bearing on the production of these pressure symptoms; thus, a cyst in the portal fissure or in the Spigelian lobe will readily give rise to these results (Tuffier[1]). Pressure symptoms are relatively less infrequent in children than in adults. In 502 collected cases of hydatid cyst there were 44, or 8·7 per cent with jaundice (Quénu[2]). Jaundice is almost constant when a hydatid ruptures into and discharges daughter cysts into the ducts, but is rare apart from this.

Stirling[3] describes a large cyst with calcareous walls springing from the under surface of the left lobe, which pressed on the common bile-duct and thus produced jaundice. A man with jaundice of eleven months' duration and well-marked xanthoma multiplex had three hydatid cysts in the liver; one of these projected into the portal fissure and completely obliterated the common hepatic duct (W. Legg[4]). It has been thought that osmosis of hydatid fluid into the tissues around the cyst may cause cholangitis and jaundice (Quénu).

A large cyst may in rare cases compress the inferior vena cava and produce oedema of the lower limbs and the trunk, and a plexus of dilated veins over the abdomen (Pheasants[5]), but complete obliteration of the inferior vena cava without oedema of the feet has been recorded (Dévé[6]). A pendulous cyst is rather more likely to press on the inferior vena cava or right iliac veins than a cyst embedded in the liver. Ascites is practically always due to some complication; thus it occurs when there is leakage of the cyst after aspiration or spontaneous rupture. When suppuration has supervened in the cyst, ascites may be due to concomitant local peritonitis. Large cysts naturally displace neighbouring viscera, the amount of displacement depending on the size and situation of the cyst. The diaphragm is frequently pushed up on the right side, and when a large cyst occupies both lobes of the liver the two sides of the thorax may be greatly encroached upon. In such cases or when the cyst is in the left lobe the heart may be greatly displaced upwards. In Knaggs'[7] case the cardiac dulness was in the first and second intercostal spaces. A large cyst may displace the stomach, the right kidney, and the other abdominal viscera. Occasionally urticaria is the first indication of a hydatid cyst, and may be seen in a case without any proof that the cyst has ruptured or leaked. In McMurray's[8] case pruritus and a papular rash existed for two years and disappeared the day after an unruptured hydatid cyst was removed. Of 132 cases a rash occurred in 10 per cent,

[1] Tuffier. *Semaine méd.*, Paris, 1906, xxv, 121.
[2] Quénu. *Rev. de chir.*, Paris, 1910, xli, 241.
[3] Stirling. *Intercol. Med. Journ. Australasia*, 1899, iv, 96.
[4] Legg, W. *Trans. Path. Soc.*, Lond., 1874, xxv, 155.
[5] Pheasants. *Bull. Johns Hopkins Hosp.*, Balt., 1909, xx, 292.
[6] Dévé. *Bull. Soc. Anat.*, Paris, 1903, 6. s., v, 197.
[7] Knaggs. *Trans. Clin. Soc.*, Lond., 1890, xxiii, 173.
[8] McMurray. *Austral. Med. Gaz.*, 1896, xv, 185.

usually after operation (MacLaurin [1]). It has been thought that urticaria is relatively less rare in children than in adults affected with hydatid disease.

As a rule, there is no change in the blood, but some cases shew eosinophilia. In some cases eosinophilia has been slight in degree and it is most exceptional to get such a high count as in Palazzo's [2] case (68·3 per cent) and in Augier's [3] and in Seligmann and Dudgeon's [4] cases, in which the percentage was 57. The occurrence of eosinophilia has no relation to a hydatid rash. After the cyst is opened the eosinophilia falls. In 10 cases examined by Ramsay [5] there was eosinophilia in two only, 28·2 and 6·2 per cent respectively. In 2 of the 10 cases the cysts were suppurating, and, as might be expected from Opie's observations, there was no eosinophilia. Eosinophilia has a definite relation to the presence of animal parasites in the body, and has been thought to play a part in protecting against toxins manufactured by the parasites (Gulland [6]). If this is so, it should occur only when absorption of the contents of a hydatid cyst is going on, and this has been supported by the observation that it is almost always present when the cyst has ruptured into the peritoneum (Barling and Welsh [7]). Eosinophilia is by no means constant, and though its presence is in favour of the view that a doubtful tumour is a hydatid, its absence does not exclude this diagnosis. The blood-serum of patients with hydatid disease contains a specific precipitin (Fleig and Lisbonne [8]), which is thrown down if the blood-serum is mixed with a suitable hydatid fluid. Welsh and Chapman [9] found this test to be positive in 9 cases of hydatid disease. A negative result is inconclusive, but a positive reaction is absolute proof of a hydatid (Welsh, Chapman, and Storey [10]). The reaction of fixation of the complement can also be employed (Laubry and Parvu [11]).

The urine is normal unless there is some complication. A suppurating hydatid may by absorption lead to albuminuria or conceivably to albumosuria. The pressure of a large hydatid on the right renal vein may cause temporary albuminuria.

In Praetorius' [12] case albuminuria disappeared after incision and drainage of a hydatid cyst of the liver.

In very rare cases pressure on the inferior vena cava or on the renal veins has been thought to explain great diminution in the excretion of urine (Davis [13]).

[1] MacLaurin. *Austral. Med. Gaz.*, 1909, xxviii, 295.
[2] Palazzo. *Giorn. internaz. d. sc. med.*, Napoli, 1909, xxxi, 19.
[3] Augier. *Journ. des sc. méd. de Lille*, 1908.
[4] Seligmann and Dudgeon. *Lancet*, Lond., 1902, i, 1764.
[5] Ramsay. *Intercol. med. Journ.*, 1906, xi, 380.
[6] Gulland. *Brit. Med. Journ.*, 1902, i, 831.
[7] Barling and Welsh. *Lancet*, Lond., 1910, ii, 1001.
[8] Fleig et Lisbonne. *Compt. rend. Soc. Biol.*, Paris, 1907, lxii, 1198.
[9] Welsh and Chapman. *Lancet*, Lond., 1908, i, 1338.
[10] Welsh, Chapman, and Storey. *Ibid.*, 1909, i, 1103.
[11] Laubry et Parvu. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1908, 3. s., xxvi, 391.
[12] Praetorius. *Berlin. klin. Wchnschr.*, 1898, xxxv, 312.
[13] Davis. *Lancet*, Lond., 1900, ii, 1014.

As an interesting coincidence Girard's[1] case of clubbed fingers associated with hydatid of the liver without any pulmonary changes may be mentioned.

To sum up: the physical signs of a hydatid cyst in the liver are out of proportion to the symptoms; there may be great enlargement with an absence of constitutional disturbance. The most marked clinical manifestations are produced when the cyst ruptures into adjacent organs or cavities, or suppurates—complications which will be described later.

DIAGNOSIS.—The diagnostic features are the presence of a cystic tumour in the liver which is considerably enlarged, and a marked absence of constitutional disturbance. The diagnosis cannot be made with absolute certainty unless fragments of the cyst or hooklets have been obtained by paracentesis or as the result of rupture of the cyst into the alimentary tract or in other positions. In the absence of this criterion the diagnosis is largely one of exclusion, and will be considered under the differential diagnosis.

Diagnosis of a Hydatid Cyst by Examination of Fluid drawn off by an Exploratory Puncture.—An exploratory puncture with a fine syringe should not be undertaken, inasmuch as very severe symptoms and even death may follow the escape of a small quantity of fluid into the peritoneal cavity. The characteristics of hydatid fluid from a living cyst are as follows: It is colourless, slightly opalescent, and neutral in reaction, with a specific gravity of 1002 to 1015, with about 1 per cent of solids. It contains mucin, but no albumin, small quantities of sugar, inosite, succinic acid, succinate of calcium, and sometimes traces of cholesterin, leucine, and tyrosine. About half the total solid matter is chloride of sodium. According to Loeper[2] the fluid from a living cyst contains glycogen which rapidly changes into dextrose. Scolices and hooklets are not free in the living cysts and only become detached by paracentesis or when the parasite dies. The detection of hooklets is much facilitated by centrifuging the fluid; the scolices can be seen as small white dots by the naked eye. When the parasite dies, the fluid becomes albuminous and turbid, and a toxic body, comparable to mytilotoxin, may appear. When suppuration supervenes, the percentage of albumin of course increases. In the absence of hooklets, scolices, and membrane, it may be difficult to distinguish the hydatid fluid from that of some hydronephroses and from cerebrospinal fluid. The laminated membrane of the ectocyst may be discharged from a suppurating hydatid and a microscopic section presents a characteristic and beautiful appearance.

Differential Diagnosis.—A large number of conditions, such as tumours and cysts in or close to the liver, may imitate a hydatid cyst of the liver. A hydatid cyst may (I) project from the anterior surface of the liver, (II) be deeply seated in the substance of the organ, (III) project upwards towards the thorax, or (IV) downwards into the

[1] Girard. *Semaine méd.*, Paris, 1903, xxiii, 32.
[2] Loeper. *Clinique de l'Hôtel-Dieu de Paris*, 1906, v, 264.

abdomen. The conditions which may be confused with these four groups will now be considered seriatim.

(I) **When the cyst projects from the anterior surface** of the liver diagnosis is comparatively easy. There are, however, a number of conditions which may possibly be confused with it. *Simple cysts* of the liver, though rarely of such dimensions as to resemble a hydatid, cannot be accurately diagnosed until their contents or their walls are examined. In cystic disease of the liver the concomitant enlargement of the kidneys should suggest the true nature of the hepatic disease. In *malignant disease* there is usually cachexia, whereas in hydatid the general health is good. In addition, multiple malignant growths often are umbilicated, and there is generally pain, neither of which is present in uncomplicated hydatid disease. The distinction, however, may sometimes be very difficult.

Thus, Sargnon[1] describes a case in which hydatid was diagnosed and laparotomy performed; the liver, when exposed, presented the appearance of multiple growth, and the abdomen was accordingly closed; subsequently at the autopsy the growths were found to be multiple hydatid cysts.

Cholecystitis.—As a rule, inflammation of and about the gall-bladder does not suggest a hydatid cyst of the liver. It is only in the presence of a great deal of inflammatory adhesions around the gall-bladder and of the tongue-shaped elongation of the right lobe that difficulty is likely to arise. Pain is prominent in most cases of chronic cholecystitis, and rare in hydatid disease.

In a woman, aged fifty years, who was under my care the liver was much enlarged and extremely hard, but her general condition was so good that malignant disease seemed unlikely. She had been tapped without any result by a general practitioner. Laparotomy was performed, and a greatly thickened gall-bladder containing a large number of calculi found. The calculi were removed and the patient recovered. Microscopic examination of part of the wall of the gall-bladder removed at the operation only shewed chronic inflammation.

From Conditions in the Anterior Abdominal Wall.—Suppuration in the sheath of the rectus and in the anterior abdominal wall is more superficial than a hydatid, does not move with respiration in the same way, and may make the skin red and oedematous. Suppuration in the rectus is not common, and when it does occur, is usually below the umbilicus. A hydatid in the anterior abdominal wall is small and can be made out to be distinct from the liver and not to move with it. Phantom tumours and localised spasm of the right rectus abdominis muscle disappear gradually under an anaesthetic and are resonant on percussion. Localised paralysis of the rectus over the liver has been described by Potain[2] as resulting from rheumatism of the vertebral joints, in hysterical

[1] Sargnon. *Lyon méd.*, 1898, lxxxvii, 254.
[2] Potain. *Semaine méd.*, Paris, 1896, xvi, 209.

subjects, and in cardiac dilatation from local inflammation of the peritoneal covering of the liver; the bulging and local distension which result imitating a hydatid cyst of the liver.

(II) **When the cyst is deeply embedded in the substance of the liver,** especially in the posterior part of the right lobe, and expands and pushes the liver forwards, the diagnosis is more difficult. *Massive carcinoma* in the substance of the liver is accompanied by severe constitutional disturbance and cachexia, and runs a rapid course (*vide* p. 472). A *large cirrhotic liver*, when pushed forwards by flatulent distension of the stomach, may imitate enlargement due to a hydatid. In cirrhosis the enlargement is more uniform, affecting both lobes, and the surface is not perfectly smooth; other signs of cirrhosis may be present and the general health is not so good as in hydatid disease. *Gummatous enlargement* is usually painful, and would be accompanied by a positive Wassermann reaction. If any doubt exists, a course of iodide of potassium and mercury should be tried.

The *enlargement* due to lardaceous disease, leukaemia, and cardiac affections should be readily distinguished by signs of the primary diseases and examination of the urine, blood, and heart. Enlargement of the spleen would militate against ordinary, but not against multilocular, hydatid of the liver, and would be greatly in favour of lardaceous disease and leukaemia. The various forms of *suppuration in the liver*, such as a large tropical abscess, suppurative pylephlebitis, and cholangitis, are practically always accompanied by fever, often by rigors, and the constitutional disturbance is very considerable. The history of residence abroad, dysentery, appendicitis, or cholelithiasis would favour suppuration. But fever and constitutional symptoms are the points of most importance. Suppuration in a hydatid cyst of the liver is the same as a hepatic abscess, and it can only be diagnosed by a history of a cyst having existed in the liver for a considerable time. In *subphrenic abscess* the fever and constitutional disturbance, the history of acute onset, of symptoms pointing to gastric ulcer, and in some cases the presence of air (subphrenic pyopneumothorax), are sufficient to distinguish it from an ordinary hydatid cyst. A suppurating hydatid may by leakage set up a subphrenic abscess.

Aneurysm of the hepatic artery is very rare, and is nearly always accompanied by pain and jaundice, and the symptoms are only likely to resemble rupture of a hydatid cyst into one of the bile-ducts.

(III) **Hydatid Cyst Projecting Upwards into the Thorax.**—When a hydatid cyst projects from the convexity of the right lobe, or in rare instances from the upper surface of the left lobe, it may be difficult to distinguish it from a pleural effusion, since it may displace the diaphragm upwards, lead to extensive collapse of the lung and to dulness over the greater part of the right side of the chest, without producing any downward displacement of the liver. In such cases the diagnosis may only be arrived at when the contents of the cyst are seen; for example, when rupture into the lung leads to expectoration of pieces of hydatid mem-

brane or when hooklets are found in fluid drawn off by an aspirator. Skiagraphy, by shewing the upward displacement of the diaphragm on the right side and its relation to the shadow cast by the heart, is more likely to assist in arriving at a correct diagnosis than any other means short of exploration at our disposal. When a hydatid cyst gives rise to the signs of a small pleural effusion and to considerable enlargement of the liver, the diagnosis is easier; but in a case with these signs the hepatic enlargement might be due to some other cause, such as cirrhosis, and the dulness in the chest to a small effusion. The dulness due to a pleural effusion differs somewhat from that of a hydatid cyst in the liver, which displaces the diaphragm upwards. If the line of dulness is highest in the axilla and falls somewhat both towards the spine and sternum, a pleural effusion is more probable; dulness at the base behind with a rounded summit is in favour of a cyst in the liver (Fowler and Godlee [1]).

The diagnosis between a hydatid cyst in the upper and back part of the right lobe of the liver and one in the substance of the right lung, especially when near the base, is very difficult, as the clinical signs and symptoms are very much the same. There is said to be more cough in cases of pulmonary hydatid, and there may be a band of resonance below the dulness corresponding to the cyst, owing to the presence of some resonant lung below the hydatid. Haemoptysis may be an early symptom in hydatid of the lung, while it is not likely to occur with a hydatid of the liver except from extreme congestion of collapsed lung; [2] it is rare then, and would only occur late in the disease, when the diaphragm is displaced upwards to a marked degree, viz. to the level of the second rib or even of the clavicle. From constant pressure exerted by the cyst the diaphragm may atrophy so as to allow the hydatid to project into the pleural cavity or to communicate with the lung without any suppurative or ulcerative process.

What has been said about hydatids in the lung and the diagnosis from hydatid of the upper surface of the liver applies in the case of *hydatid of the pleural cavity*. As in the case of the lung, the question is more likely to arise on the right side. In Luff's [3] case, however, a hydatid in the left pleura, containing six pints of fluid, gave rise to signs of hydatid of the liver with probable extension into the left pleura. It is impossible to distinguish betwixt a hydatid between the liver and diaphragm and a cyst projecting from the convexity of the liver. In both cases the liver is depressed and the pleural cavity encroached upon. A cyst between the layers of the suspensory ligament of the liver may have started in the superficial part of the liver and grown up out of it.

(IV) **When the cyst projects downwards into the abdomen** it is usually more readily recognised, but confusion may easily arise between it and other conditions, such as a dilated gall-bladder, renal tumour or

[1] Fowler and Godlee. *The Diseases of the Lungs*, p. 478, 1898.
[2] Galliard. *Arch. gén. de méd.*, Paris, 1890, clxv, 409.
[3] Luff, A. P. *Lancet*, Lond., 1896, i, 1134.

displacement, and various other abdominal tumours. There is also the greater likelihood that cysts in this position may press upon the neighbouring viscera and thus complicate the diagnosis. A dilated gall-bladder may closely resemble a hydatid cyst hanging down from the under surface of the liver; usually, however, it is not so prominent, and there may have been attacks of biliary colic or of icterus in the past; though both these symptoms may follow rupture of a cyst into the bile-ducts. A dilated gall-bladder is pear-shaped and much more movable than a hydatid cyst. During a laparotomy a pendulous hydatid cyst arising near the gall-bladder may be mistaken for that viscus even by an experienced observer (*vide* p. 628). A hydatid cyst with local peritonitis may imitate calculous pericholecystitis (Longe [1]).

Hydronephrosis of the right kidney when it passes forwards towards the abdominal wall may closely resemble a hydatid; for the colon need not necessarily lie in front of a large renal tumour. A hydronephrosis will project much more into the loin, the urine may be of a low specific gravity, and the occurrence of inflammation in the kidney or the transition of a hydronephrosis into a pyonephrosis would be shewn by pyuria. A copious discharge of urine associated with disappearance of the tumour is characteristic of an intermitting hydronephrosis. A soft *renal or suprarenal* growth on the right side may imitate a hydatid cyst projecting from the right lobe of the liver.

A man aged twenty-five had a fluctuating tumour below the liver, which was at first thought to be hydatid, but puncture only brought blood away. After death I found a large cystic endothelioma arising from the right suprarenal and invading the right lobe of the liver.

Renal and suprarenal growths probably move less on respiration than those connected with the liver, and tend to bulge into the loin; a bimanual examination should therefore always be made. A floating kidney might cause difficulty in diagnosis; Potain described a form of nephroptosis, "anteversion of the kidney," which is especially likely to resemble a hydatid of the liver unless a bimanual examination is insisted on.

Pancreatic and Peripancreatic Cysts.—Cysts in connexion with the pancreas or a collection of fluid in the lesser sac of the peritoneum (peripancreatic cyst) are usually more prominent towards the left, and are only likely to be confused with hydatid cysts attached to the left lobe of the liver. Pancreatic and other abdominal cysts and tumours should be separated from the liver by a zone of resonance, whereas a hydatid cyst should be continuous with it. Again, a pancreatic cyst is more deeply placed and should lie behind the stomach, while a hydatid cyst would be in front. In case of doubt the stomach should be inflated with air. In the following case a suppurating hydatid attached to the back of the left lobe of the liver imitated a pancreatic cyst:

[1] Longe. *Rev. de méd.*, Paris, 1910, xxx, 757.

A woman aged forty-nine, the mother of ten children, was admitted under my care at St. George's Hospital on November 30, 1901. Four months previously she suddenly had an attack of very severe pain accompanied by rigors and followed by jaundice. The attacks were repeated at intervals of about two weeks. The tumour was noticed after the first attack, and was thought to have varied in size from time to time. She was a fat woman with a large, tense tumour between the umbilicus and the ensiform cartilage; close to the latter it was dull on percussion, but elsewhere it was resonant; it could not be separated from the left lobe of the liver and did not bulge into the loin. This was important, since when asked a leading question the patient said it varied from time to time according to the amount of water, sometimes excessive, that she passed. There was no jaundice or bile in the urine. The diagnosis lay between a peripancreatic cyst, a hydronephrosis, and a hydatid cyst dependent from the left lobe of the liver. It was thought to be a peripancreatic effusion into the lesser sac of the peritoneum following pancreatitis, which possibly occurred as the result of the passage of gall-stones four months before. Accordingly on December 9 Mr. Sheild made an incision over the left linea semilunaris and came down on coils of intestines somewhat matted together; on separating them stinking pus with numerous daughter cysts welled up from a cyst attached to the left lobe of the liver. This cavity was drained. For a time the patient did well, but the discharge was very copious and she became very weak, eventually dying on December 21. At the necropsy there was a large subphrenic abscess between the diaphragm and the right lobe of the liver. In the left lobe of the liver there was a suppurating hydatid cyst which passed backwards and was adherent to the pancreas which appeared healthy. The liver was fatty, swollen, and weighed 7 pounds. The cystic and the common bile-ducts were much dilated, but there were no gall-stones in the gall-bladder. The spleen, 4 ounces, was healthy.

A large hydatid cyst should hardly be mistaken for *ascites* unless the cyst is so large that it almost fills the abdomen, and even then the dulness will not reach to the flanks. Chemical examination of fluid drawn off by a trocar will settle the question. *A large ovarian cyst* may resemble a pendulous hydatid cyst, especially one that has contracted adhesions to the lower part of the abdomen. The history of the tumour as indicating the situation where it was first noticed, whether near the liver or the pelvis, the connexion of the tumour with the liver or with the uterus, and vaginal examination may assist in making a diagnosis. An ovarian cyst under ordinary conditions will not move on respiration.

Duration and Prognosis.—It is difficult to estimate how long a hydatid cyst may remain alive and capable of active growth, but it may be twenty years.

A man aged thirty-five died in St. George's Hospital with a hydatid, the size of an adult's head, full of daughter cysts, in the right lobe; close to it there was a small, dried-up cyst. Nineteen years before he had been tapped, and presumably the small cyst had been then evacuated. Probably the two cysts were of the same age; but even if the larger cyst was due to infection at the time of tapping the other, it must have existed for nineteen years.

The prognosis of a large hydatid cyst largely depends on whether it is operated upon or not. If not operated upon, it may die, shrivel up, and give rise to no further trouble, but a cyst which has remained quiescent or latent may suppurate without any manifest cause. Suppuration is a dangerous complication, and its possible incidence in the remote future must be faced in deciding not to call in surgical interference.

The size, rate of growth, and the possibility of rupture or suppuration supervening require consideration. If the cyst is sufficiently large to be diagnosed and is rapidly increasing in size, the danger of rupture is sufficient to make operation desirable. When a cyst gets smaller under observation, it may be undergoing spontaneous cure, and may be left alone without any immediate prospect of danger, but it is safer to remove it, for if suppuration supervenes, the conditions are then less favourable for successful operation. The situation of the cyst influences the prognosis: if it is deeply situated and in the upper and posterior part of the right lobe, it is both more likely to encroach on the thorax and more difficult to operate upon. Another important point which often cannot be determined is whether there is one cyst or whether they are multiple.

If a cyst is not growing rapidly, and is therefore not interfered with, there is the possible danger of traumatic rupture of the cyst, or of rupture into some viscus to which it has become adherent. Rupture always affects the prognosis and gives rise to anxiety, though the gravity of the prognosis varies according to the situation of the rupture. Thus, rupture into the pericardium is nearly always rapidly fatal. Dévé[1] has shewn that death is not inevitable when a cyst ruptures into the inferior vena cava, if the cysts discharged are few and small. Rupture into the peritoneum or even into the pleura may prove fatal very rapidly, and if the patient does survive, there is danger of peritonitis or of empyema. The effects of escape of hydatid fluid into the peritoneal cavity are considered on p. 413. Traumatic rupture of a living cyst may cause comparatively little disturbance, but rupture of a dead cyst, the contents of which have become toxic or infected, is most dangerous. Rupture into parts of the peritoneum cut off by adhesions is, of course, much less grave, but it may then be difficult to be sure that this has occurred. Gradual leakage into the general peritoneal cavity is not necessarily followed by severe symptoms. Rupture into the bile-ducts is very prone to cause suppurative cholangitis, and is therefore a grave complication. Ruptures into the lungs, alimentary tract, and externally are less serious. Cyr[2] estimated the mortality at 90 per cent when rupture occurred into the peritoneum, 80 per cent into the pleura, 70 per cent into the bile-ducts, 57 per cent into the bronchi, 40 per cent into the stomach, 15 per cent into the intestines, and 3 per cent on to the surface of the body. Suppuration also makes the outlook very gloomy. Some observers, especially in France, have noticed that pul-

[1] Dévé. *Bull. Soc. Anat.*, Paris, 1903, 6. s., v, 185.

[2] Cyr. Quoted by Hoppe-Seyler, Nothnagel's *Practical Encyclopedia*, "Diseases of the Liver," p. 802. English translation, 1903.

monary tuberculosis not uncommonly follows a hydatid cyst (Routier[1]); but it is possible that the hydatid disease is really due to infection conveyed in the dietetic treatment of tuberculosis.

If the cyst is operated upon, the prognosis depends on the operation adopted, on complications arising from the operation, while there is, further, the possibility of there being other cysts which, though latent at the time of the operation and not then attracting attention, may subsequently give rise to trouble.

TREATMENT.—The treatment of hydatid cysts is essentially surgical, and consists in the evacuation or removal of the cyst. No drugs given by the mouth have any effect on the parasite. A number of different methods have been employed.

I. Simple **puncture with a trocar** and removal of some or all of the fluid contents of the cyst. This method, which is the oldest, has been much employed, and has naturally met with approval, as it is simple and easy to perform. After the withdrawal of the fluid the parasite, under favourable conditions, dies and the cyst shrivels up. Though in many cases cure results from simple tapping, there is an element of risk, since severe symptoms and even death have followed this simple operation. Dieulafoy[2] considers that the bad effects of simple tapping are due to the cyst having been only partially evacuated, and that as a result some of the residual fluid has escaped into the peritoneal cavity; he, therefore, insists on complete evacuation of the cysts, and directs that an aspirator should be used. The safe course, however, is to have the cyst fully exposed by a surgeon and then treated as the details of the case, thus plainly seen, shew to be the proper course. Simple puncture may also be followed by suppuration.

II. A modification, or rather an addition to the simple procedure of tapping, consists in the injection of antiseptic fluids into the interior of the cyst. In this method a little of the fluid is removed by means of a small puncture, and a small quantity of some fluid is then introduced with the object of killing the parasite. This method, advocated by Baccelli, was successfully practised by Bókay,[3] who injected a solution of perchloride of mercury 1 in 1000. Other fluids, such as ox-bile, so as to imitate one supposed cause of spontaneous cure, iodine solution, carbolic acid, alcohol, formaline, have been used with the same object. These methods are dangerous and are only mentioned to be avoided. Suppuration, and even fatal mercurial poisoning, have been recorded.

III. **Acu-puncture.**—The insertion into the cyst of long needles which are withdrawn after about a quarter of an hour. This probably acts by allowing the cyst to leak into the peritoneum. It is a dangerous practice.

IV. **Electrolysis.**—Hilton Fagge and Durham[4] employed this method

[1] Routier. *Bull. et mém. Soc. chir. de Paris*, 1909, xxxv, 3.
[2] Dieulafoy. *Bull. Acad. de méd.*, Par., 1899, 3. s., xli, 530.
[3] Bókay. *Arch. f. Kinderh.*, 1897, xxiii, 310.
[4] *Med.-Chir. Trans.*, Lond., 1871, liv, 1.

with success in 7 or 8 cases. It consisted in introducing two needles into the cyst and then passing a constant current through the cyst, the needles being attached to the negative pole, while the positive pole of the battery was connected with a sponge placed on the skin of the abdomen over the cyst. Electrolysis acts in the same way as simple acu-puncture, and not, as was at first imagined, by decomposition of the fluid in the cyst.

Accidents and Bad Effects following Simple Tapping.—When a hydatid cyst is tapped and the fluid is partially drawn off, some of the residual fluid not uncommonly escapes into the peritoneal cavity, and its presence may be shewn by some shifting dulness and fluctuation in the flanks and lower part of the abdomen. There are usually no bad symptoms, but intense itching followed by urticaria lasting a few hours to two days may result; sometimes peritonismus, or signs of false peritonitis, follows tapping, and in rare cases death preceded by convulsions and collapse has occurred. The fluid in a living hydatid cyst does not contain albumin or hooklets, does not produce toxic effects when injected into animals, and is usually without any bad effects on man (Kirmisson, Kornach, Martini, Maury, Boinet and Chazoulière).

Chauffard,[1] however, met with a most exceptional case in a man aged thirty-five years; a hydatid cyst was punctured and 10 c.c. of clear fluid drawn off; epileptic convulsions set in and death followed within twenty-five minutes from the time of puncture of the cyst. The cyst contained clear fluid which was without any poisonous action on animals.

When the hydatid cyst dies and undergoes aseptic necrosis without the introduction of micro-organisms, the characters of the fluid, both physical and physiological, change. The fluid becomes turbid, yellow, syrupy, contains hooklets, albumin, and a toxic body which is analogous to mytilotoxin found in the livers of poisonous mussels, and gives rise to the urticaria and other symptoms sometimes manifested after the escape of hydatid fluid into the tissues. This poison has been found by Boinet and Chazoulière[2] to crystallise in long, silky needles. Physiologically when injected into animals it induces convulsions, loss of motor and sensory power, followed by slowing of the heart, rapid respirations, dilated pupils, fall of blood-pressure, prostration and collapse, and in larger doses death. Viron[3] found a toxin in hydatid fluid from sheep which produced acute inflammation of the tissues.

In a man aged twenty-three years with jaundice, dangerous collapse followed exploratory paracentesis of a hydatid cyst, and subsequently profuse urticaria appeared on the abdomen, legs, and extensor surfaces of the arms, and lasted for some hours (L. Humphry[4]). Two weeks later $\frac{1}{50}$ grain of atropine was injected to prevent recurrence of these severe symptoms and paracentesis was

[1] Chauffard. *Semaine méd.*, Paris, 1896, xvi, 265.
[2] Boinet et Chazoulière. *Rev. de méd.*, Paris, 1898, xviii, 845.
[3] Viron. *Arch. de méd. expér. et d'anat. path.*, Paris, 1892, iv, 136.
[4] Humphry. *Lancet*, 1887, i, 120.

successfully performed. Injection of the fluid into guinea-pigs and a dog caused marked toxic symptoms. Bryant[1] recorded sudden death five minutes after paracentesis of hydatid of the liver; the trocar passed through the portal vein, and it is possible that the hydatid fluid entered directly into the circulation.

The bad effects of hydatid fluid are probably due to anaphylaxis or hypersensitiveness, and are comparable to those produced by the injection of a foreign protein or serum. The symptoms may be grouped under three headings: (*a*) Cutaneous—pruritus and urticaria; (*b*) Cerebrospinal—epileptiform convulsions; and (*c*) collapse and cardiac failure.

As mentioned above, a hydatid rash has in very rare instances been seen without rupture or leakage of the cyst[2]; usually it is due to one or other of these events. It has been produced by contact with the fluid, as in the case referred to by Achard of two individuals who suffered from urticaria after making a necropsy on a case of hydatid cyst. Fatal toxic symptoms supervened five days after abdominal operation and drainage of a hydatid cyst in a case recorded by Fuster and Godlewski. A trocar has also been known to wound a large branch of the portal or hepatic vein and induce fatal haemorrhage. Puncture may be followed by suppuration in the cyst, and thus not only is time lost, but a dangerous complication results.

Surgical Treatment.—As already pointed out, the more satisfactory method of dealing with hydatid cysts of the liver is by surgical means, the abdomen being opened and the cyst exposed. For the various methods of dealing with the cyst the reader should refer to a surgical textbook. In a few instances the whole of the cyst, including the external adventitious capsule, has been removed. Generally the incision of the cyst and the removal of the parasite and daughter cysts are performed. There are dangers connected with the operation, of course, such as haemorrhage from veins in the capsule of the cyst, and extensive and prolonged leakage of bile due to free communications between the cyst and the larger bile-ducts. The loss of bile from a cyst, if continued, may lead to emaciation if it is so extensive that all or nearly all the bile escapes from the body by this channel. This result need not occur if a fair proportion of the bile enters the duodenum. As a possible danger due to the operation, long-continued suppuration leading to lardaceous disease may be mentioned, but is much less likely to occur now than in former times.

Prophylaxis.—Raw vegetables should be carefully washed, so as to prevent the possibility of ova being conveyed by them. As the ova are almost entirely derived from the faeces of dogs, care must be taken by those who keep dogs in the house. In places where hydatid disease is frequent, drinking-water, one of the chief means by which the disease is spread, should be filtered or boiled, and fruit and vegetables should not be eaten unless boiled or washed with filtered or boiled water.

[1] Bryant, T. *Trans. Clin. Soc.*, 1876, xi, 230.
[2] McMurray. *Australian Med. Gaz.*, 1896, xv, 185.

Legislation should make it obligatory on the officials of slaughter-houses to burn the offal of sheep and oxen infected with hydatid cysts, and to prevent dogs getting access to this source of infection. Strict measures of this kind should be employed to stamp out the disease and prevent it obtaining a foothold in countries like America, where as yet it is not widespread. Another beneficial measure would be the destruction of stray and homeless dogs.

Complications.—The chief complications are rupture and suppuration of the cyst.

Rupture may occur into the peritoneum, into adjacent hollow viscera, or after perforation of the diaphragm, into the pleura, lung, or pericardium. In order to open into the serous cavities on the other side of the diaphragm the cyst must first become adherent to the under surface of the diaphragm and then penetrate the muscular and serous coats, just as a cyst has to work its way through the coats of the stomach or intestine to rupture into these organs. The process of perforation depends on atrophy, from constant pressure, of the tissues of the diaphragm or intestine, which have become adherent to the cyst by local adhesive peritonitis. Suppuration renders perforation and rupture much easier, and in rare instances a suppurating cyst may perforate the abdominal wall.

Rupture into the peritoneal cavity may be divided into two categories: (*a*) Into the general peritoneal cavity; the cyst may rupture freely or merely leak. (*b*) Rupture into a localised part of the abdominal cavity which has been cut off by previous local peritonitis. A localised or subphrenic abscess may thus result.

Rupture of a hydatid cyst into the peritoneal cavity apart from trauma or suppuration is rare, and, as already pointed out, is more readily produced in a suppurating cyst. A hydatid cyst which is not suppurating may rupture as the result of direct or indirect violence, or even spontaneously without any manifest cause. It has been known to occur in pregnancy and may possibly be precipitated by increased intra-abdominal pressure. Usually, however, there is a history of a blow on the abdomen immediately preceding the onset of pain and collapse.

The escape of hydatid fluid into the general cavity of the peritoneum may be rapidly followed by either (i) very severe symptoms of collapse succeeded by fatal syncope or by peritonitis, or (ii) comparatively trivial symptoms. The factor which determines whether severe or comparatively trivial symptoms follow the escape of hydatid fluid into the peritoneal cavity is probably the character of the contents of the cyst. If the parasite is dead, the fluid becomes toxic, whereas the fluid from a living cyst is harmless. Rupture of a suppurating cyst, or of one in connexion with an infected bile-duct, into the peritoneal cavity naturally sets up acute peritonitis. The sudden acute symptoms might, in the event of the presence of a hydatid cyst in the abdomen being unknown, be mistaken for irritant poisoning or perforation of an abdominal viscus. In the absence of an urticarial rash the real nature of the condition

would probably only appear when the abdomen was opened. The following case illustrates the occurrence of death from peritonitis and the danger that attaches to postponing operative interference:

A woman aged thirty-four had a swelling in the upper part of the abdomen for thirteen years; it began in the epigastrium and gradually enlarged. She was admitted into St. George's Hospital on October 19, 1893, and a large hydatid was diagnosed. Operation was advised, but she was alarmed and left the hospital, only to return five days later in collapse with urticaria; the tumour could no longer be felt. Mr. Turner performed laparotomy and found a ruptured hydatid cyst which occupied the whole of the left lobe of the liver. The patient died next day. There was general peritonitis. No other hydatid cysts were found in the viscera.

The leakage of a cyst into the peritoneal cavity may give rise to collapse and symptoms suggesting intestinal obstruction (peritonismus). The rupture is accompanied by sudden pain, but if the contents are not toxic or infective, recovery may follow with or without the significant, but comparatively trivial, incident of an urticarial eruption (*vide* p. 403). Eosinophilia appears to be almost constant (Barling and Welsh [1]). Rupture of a large cyst may cause considerable ascites which lasts for some time and reaccumulates after tapping. Debove and Soupault [2] described such a case in which tuberculous peritonitis was diagnosed. The rupture may be complicated by the escape of bile into the abdominal cavity (choleperitoneum). The communication of the cyst with the bile-duct may take place before or after the rupture of the cyst into the peritoneum; Dévé [3] believes that the latter is most often the case and compares it to the escape of bile into a cyst after tapping. The effusion of bile does not necessarily set up peritonitis. When the bile is sterile and there is no peritonitis, the abdomen gradually swells, and after days or weeks requires tapping; the effusion has a great tendency to recur. It is curious that there is no jaundice, for the peritoneum has great powers of absorption and the quantity of bile in these cases is often considerable.

Two remote effects of rupture of a hydatid cyst into the peritoneum are: (I) infection of the peritoneum with daughter cysts; and (II) echinococcic pseudo-tuberculosis of the peritoneum.

Secondary infection of the peritoneum with numerous daughter cysts may eventually cause considerable trouble. Doubt has been thrown on the secondary infection of the peritoneum with daughter cysts from rupture of a hydatid cyst of the liver, and it has been suggested that what appear to be secondary implantations are really independent cysts,[4] but this is not in accordance with the clinical facts that some years after rupture of a hydatid cyst in the liver other cysts may be found scattered over the peritoneum. The favourite situations for these secondary cysts

[1] Barling and Welsh. *Lancet*, Lond., 1910, ii, 1001.
[2] Debove et Soupault. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1892, 3. s., ix, 855.
[3] Dévé. *Rev. de chir.*, Paris, 1902, xxvi, 67.
[4] Potherat. *Bull. et mém. Soc. de chir. de Paris*, 1900, xxvi, 54.

are the great omentum and the pelvis. It probably takes about two years for the cysts to develop sufficiently to give rise to signs or symptoms. It is somewhat remarkable that secondary infection of the peritoneum with daughter cysts may occur in cases in which the original cyst has been in communication with a bile-duct and the daughter cysts exposed to the action of the bile.

Dévé[1] has seen secondary cysts develop in the peritoneum in cases with a bile-stained peritoneal effusion due to rupture of a hydatid cyst, already in communication with a bile-duct, into the peritoneal cavity. He found that scolices still continued to grow in a mixture of equal parts of hydatid fluid and bile.

Pseudo-tuberculosis of the peritoneum[2] after rupture or leakage of a hydatid cyst is a rarely recognised though interesting condition. It consists in small granulomas covered over by the endothelium of the peritoneum and containing pieces of hydatid membrane or hooklets. Histologically there are giant, endothelioid, and small round cells. The process may be regarded as an attempt to absorb the bits of membrane and the hooklets.

Rupture into the pleura of course usually occurs on the right side. The effusion into the pleura may be clear or may become purulent; in the latter event the pleural cavity may be much like a large suppurating hydatid cyst with numerous daughter cysts floating on it. Such an empyema may burst into the lung, and I have known suffocation result. If, as fortunately usually happens, the patient survives, a pyopneumothorax or a broncho-biliary fistula may result. Rupture of a hydatid cyst into the pleura may lead to an extravasation of bile into the pleural cavity; Dévé[3] quotes two such cases recorded by Cruveilhier and Douart.

Rupture into the Lung.—If the lower part of the pleural cavity is obliterated by adhesions and the cyst perforates the diaphragm, rupture into the lung may follow and set up a pneumonic or even a gangrenous condition in the neighbourhood. The hydatid fluid may pass into the lung and give rise to serious dyspnoea, and hydatid membranes, which may be bile-stained, may be coughed up. Impaction of the membranes or daughter cysts in the bronchi or trachea may give rise to suffocative dyspnoea. When a hydatid cyst freely communicates with a bronchus, bile may pass into the lung and a broncho-biliary fistula may result. Out of 35 cases of broncho-biliary fistula collected by Graham,[4] 11 were due to hydatid cysts of the liver. These fistulous communications between the lung and hydatid cysts are more likely to occur when the hydatid projects from the convexity of the liver. Dévé[5] has collected 11 cases in which the cyst became gaseous after rupture.

[1] Dévé. *Compt. rend. Soc. Biol.*, Paris, 1903, lv, 75.

[2] *Vide* Dévé. *Rev. de chir.*, 1902, xxvi, 79; *Arch. de méd. expér. et d'anat. path.*, Paris, 1907, xix, 347.

[3] Dévé. *Rev. de chir.*, Paris, 1902, xxvi, 67.

[4] Graham, J. E. *Trans. Assoc. Am. Phys.*, 1897, xii, 247.

[5] Dévé. *Rev. de chir.*, Paris, 1907, xxxv, 549.

Jones[1] recorded rupture of a suppurating hydatid of the liver into a bronchus in a girl aged eight years. The chest wall was incised and the cyst eventually extracted from the lung; recovery followed.

Rupture into the pericardium is very rare, and is fatal either directly from shock or later from pericarditis.

Rupture into the Bile-ducts.—The frequency with which this occurs is difficult to estimate, for it often gives rise to no clinical manifestations, or may be mistaken for biliary colic due to gall-stones. When the communication between the cyst and the bile-duct is small, the fluid in the cyst may run quietly away and the cyst may shrivel up; on the other hand, the cyst may be infected from the bile-duct and suppurate. The characteristic cases are those in which the communication between the cyst and the duct is sufficiently large to allow daughter cysts to escape into the duct and pass along its lumen. This gives rise to biliary obstruction, jaundice, colic, and may easily be regarded as due to gall-stones. In some cases there is fever from infective or suppurative cholangitis. Fragments of cysts or hooklets have, in rare cases, been found in the vomit, but are more often detected in the stools. The cysts may remain in the ducts and cause considerable biliary obstruction and dilatation of the ducts. Possibly the hydatid fluid may, in the first instance, irritate the mucous membrane, in virtue of toxic bodies formed in the dead cysts, and set up a descending cholangitis. But in most cases cholangitis is due to infection, very possibly ascending from the duodenum, which is favoured by the presence of the grape-skin-like membranes in the larger bile-ducts. Cholangitis may spread into the evacuated cyst and cause suppuration. The suppurating cyst or ducts may perforate or leak into the peritoneal cavity and give rise to acute peritonitis or a localised subphrenic abscess. The hydatid membranes may remain impacted in the common bile-duct or even in the hepatic duct of one lobe of the liver.

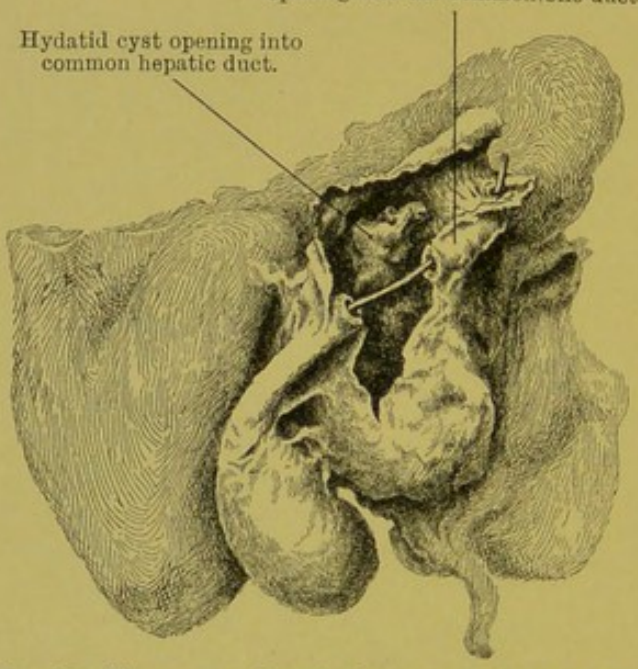


FIG. 53.—The common hepatic duct greatly dilated from the presence of part of a hydatid cyst which has ruptured into it. The cystic duct has been cut across so as not to obscure the view. From a specimen (Series ix, 196A) in St. George's Hospital Museum. (Drawn by Dr. E. A. Wilson.)

[1] Jones. *Lancet*, Lond., 1899, ii, 1435.

In a case under my care it seemed probable that they had for a considerable time remained in the left hepatic duct and shortly before death moved into the common duct, for the ducts in the left lobe which contained a small cyst were all dilated and suppurating, while those in the right lobe were normal.

When in the common bile-duct the membranes may project into the duodenum through the biliary papilla and pass into the intestine or they may remain in the duct. The cyst may, after rupturing into the bile-duct, perforate the diaphragm and so give rise to a broncho-biliary fistula.

Sudden death from rupture of a hydatid cyst into the left hepatic duct occurred in a man aged forty-four, and was explained by Gouraud and Rathery[1] as due to absorption of the hydatid fluid by the intestines. This exceptional result is comparable with sudden death from rupture of a hydatid cyst into the peritoneal cavity (*vide* p. 415).

The symptoms of colic followed by jaundice so strongly suggest gall-stones that the true state of affairs is not likely to be suspected unless the existence of a hydatid cyst has previously been recognised, and unfortunately hydatid cysts in the portal fissure or Spigelian lobe, positions which favour rupture into the ducts, are specially difficult to diagnose. The condition cannot be diagnosed unless pieces of bile-stained hydatid membrane are found in the faeces or in the vomit. Calculi may coexist with hydatid cysts in the bile-ducts and be secondary to cholangitis set up by the rupture of the cyst into the duct (Terrier,[2] Hinder[3]). The bile-staining of hydatid membranes is in favour of their having passed down the ducts, but is not absolutely pathognomonic, for a cyst already in connexion with a bile-duct might discharge into the stomach or bowel. When suppurative cholangitis has supervened, the underlying cause may be thought to be cholelithiasis, or the fever, rigors, and jaundice might be referred to pylephlebitis; but pain and jaundice are less frequent in suppurative pylephlebitis than after rupture of a hydatid into the bile-ducts.

As the diagnosis is difficult and is usually made on the post-mortem table, the number of reliable published cases of passage of hydatid cysts by the bile-ducts in which recovery has occurred is comparatively small. I have notes of nine cases in which complete recovery followed. Cyr estimated the mortality at 70 per cent. It is probable that as more cases of jaundice due to obstruction of the larger ducts are now operated upon, more examples of the collapsed cysts obstructing the bile-ducts will be forthcoming.

Stirling[4] published a case which recovered after cholecystotomy and the subsequent discharge of hydatid membrane from the wound. The first symptom

[1] Gouraud et Rathery. *Bull. Soc. Anat.*, Paris, 1900, 6. s., ii, 307.
[2] Terrier. *Bull. et mém. Soc. de chir. de Paris*, 1906, xxxii, 848.
[3] Hinder. *Trans. viii. Australasian Congress*, 1909, i, 317.
[4] Stirling. *Intercolonial Med. Journ. Australasia*, 1899, iv, 98.

—pain like biliary colic—came on suddenly nine days before the operation, and was followed by jaundice and rigors. In a woman aged forty, operated upon by F. T. Stewart,[1] the hepatic and common bile-ducts contained hydatid cysts, while the gall-bladder contained both gall-stones and free hydatid cysts. It is probable that the previous passage of gall-stones through the cystic duct had dilated the duct and thus enabled the cysts to pass out of the common hepatic duct through the cystic duct into the gall-bladder. Under ordinary conditions hydatid membranes would never be able to work their way up a normal cystic duct.

Persistent discharge of bile from the wound after operation on a hydatid cyst may be due to impaction of a daughter cyst in the common bile-duct.

Rupture into the stomach is rare, and is more likely to occur when the cyst is in the left lobe of the liver. Of 11 cases referred to by Davaine, 6 were fatal. When rupture has taken place, the cyst may become tympanitic from the entry of air, and pieces of hydatid membrane, which may be bile-stained, may be recognised in the vomit or in the faeces.

Rupture into the intestines is also rare. The prognosis seems to be better than when rupture occurs into other hollow viscera, for of 15 of Davaine's[2] cases only one died. Rupture into the duodenum is very rare, and an exact diagnosis during life is hardly possible.

In a case reported by Hale White[3] a hydatid in the left lobe was opened during life, the patient eventually died, and a second, suppurating, hydatid cyst was found in the right lobe. The cyst in the left lobe communicated by a rather long passage with the duodenum. In a man aged twenty-six years who died jaundiced and emaciated there were two cysts, one containing bile which was opened during life. After death a large hydatid cyst, which had opened into the duodenum, was found in the right lobe.[4]

When rupture into the colon occurs, the prognosis would seem to be very good, since in 21 cases collected by Letanneur[5] no deaths took place. On the other hand, the diagnosis of these cases, unless confirmed by necropsy, is open to doubt; some of them may be cases of rupture into the bile-ducts.

Rupture into the inferior vena cava or the hepatic veins is very rare. Of 11 cases collected by Dévé[6] the cyst opened in 7 into the inferior vena cava, and in 4 into the hepatic veins. In 8 of these cases death occurred very rapidly; this may be due to impaction of cysts in the right side of the heart or to pulmonary embolism; but in some cases there is no evidence of embolism and death may have been due to toxic bodies in the hydatid fluid. Rupture into these veins need not necessarily give

[1] Stewart. *Phila. Med. Journ.*, 1899, iv, 433.
[2] Davaine. *Traité des Entozoaires*, Paris, 1877.
[3] Hale White. *Trans. Path. Soc.*, 1885, xxxvi, 252.
[4] *St. Barth. Hosp. Rep.*, 1899, xxxv, Registrar's Report, p. 214.
[5] Letanneur. Quoted by Potain, *Journ. de méd. et chir.*, Sept. 10, 1900.
[6] Dévé. *Bull. Soc. Anat.*, Paris, 1903, 6. s., v, 185.

rise to sudden death if the daughter cysts discharged into the blood-stream are few and quite small.

There is a specimen (No. 1371) in the Museum of the London Hospital of rupture of a hydatid cyst in the right lobe of the liver into the inferior vena cava.

In very rare cases (Seidel, Vegas and Cranwell[1]) fatal pulmonary embolism has been due to thrombosis of the inferior vena cava, set up by compression of the vein by a cyst. In most exceptional instances a hydatid cyst has ruptured into the pelvis of the kidney, the gall-bladder, or the portal vein. Rupture through the abdominal wall is practically unknown, as a cyst would now be treated surgically long before it had penetrated the abdominal wall. It is the most favourable place for spontaneous rupture; of 21 cases collected by Murchison, 13 recovered.

Suppuration in a hydatid is a serious complication, as it converts the case into one of hepatic abscess. The symptoms are much the same in both cases, but in hydatid there is a marked tendency to perforate or rupture into adjacent organs or cavities; but since adhesions are less frequent around ordinary hydatid cysts, a suppurating one is not so likely to point through the skin as an ordinary hepatic abscess.

Mechanism of Suppuration in a Hydatid Cyst.—Suppuration may be set up in several ways: It may be due to direct infection from without after paracentesis or incision. It may be due to rupture of the cyst into the ducts, or may follow injury to the liver. In the latter instance the resistance of the tissues around the cyst is so reduced that any micro-organisms in the neighbourhood are able to multiply and set up inflammation. Suppuration may be due to infection of the liver itself or of the bile-ducts.

In a woman successfully operated upon in St. George's Hospital by Mr. L. Jones for gall-stones in the gall-bladder and common duct, there supervened, after an interval of six weeks' normal temperature, suppuration in a small hydatid cyst previously latent.

Petit[2] has described the spread of infection from the pleura, but in most cases of associated empyema and suppurating hydatid cysts the pleura is secondarily involved. Suppuration may occur as the result of haemic infections; for example, in enteric fever, infective endocarditis, and the puerperal state. When there are several cysts in the liver, suppuration may be confined to one or may extend to the others.[3] A suppurating mother-cyst may contain daughter cysts which are not purulent. Suppuration has occurred in a cyst which appeared to have undergone spontaneous cure.

The results of bacteriological examination of suppurating hydatid cysts are somewhat divergent. In some instances no micro-organisms have been found, and it has been suggested that suppuration is due to

[1] Quoted by Dévé. *Bull. Soc. Anat.*, Paris, 1903, 6. s., v, 196.
[2] Petit. *Rev. mens. de méd. et de chir.*, 1877, i, 678.
[3] For illustrative case *vide* Sinclair White, *Brit. Med. Journ.*, 1897, ii, 398.

chemical poisons (Chauffard and Widal[1]); and, as already mentioned, Viron[2] found a toxin in the hydatid fluid from a sheep which set up acute inflammation. But it is more probable that the organisms have died out. In some cases, streptococci, *Staphylococcus pyogenes aureus* and *citreus*, pneumococcus, and *Bacillus coli* have been isolated in pure or mixed cultures. The extremely fetid character of the pus may depend on the presence of anaerobic micro-organisms.

In a fetid but not gaseous suppurating hydatid cyst in a boy aged eleven years Hallé and Bacaloglu[3] found, in addition to *B. coli* and streptococci, two strictly anaerobic microbes—*Staphylococcus parvulus* and *Bacillus fragilis*.

Haemorrhage into a suppurating hydatid cyst is not uncommon, and as a result the contents have a dark purplish-red colour not unlike that in tropical abscess. Production of gas in a suppurating hydatid cyst is very rare; this may be due to the *Bacillus aerogenes capsulatus* or to other anaerobic organisms; Garnier[4] described *Bacillus moniliformis* in a gaseous suppurating hydatid. The physical signs are an amphoric note on percussion and a bell note over the cyst. Suppurating gaseous hydatid cysts (pyopneumohydatid) have been recorded by Habershon,[5] Lippmann,[6] Gilbert and Weil,[7] Griffon.[8] In 1907 Dévé[9] collected 24 examples of gaseous suppurating hydatid cysts in the liver, which had no communication with the lungs, intestines, or exterior.

A suppurating hydatid cyst by leaking may give rise to a subphrenic abscess, or exceptionally to a subphrenic pyopneumothorax.

Tuffier and Barbarin[10] described the case of a woman who was operated upon for a gaseous subphrenic abscess on the right side, which displaced the liver backwards. After death it was found that this depended on a suppurating hydatid cyst which had also set up general peritonitis.

For the general clinical features of suppurating hydatid cysts the reader should refer to the description of hepatic abscess.

ALVEOLAR HYDATID

Synonym: Multilocular Hydatid.

History.—Cases of this rare disease were formerly regarded as examples of colloid carcinoma of the liver, until Virchow, in 1856, demonstrated their parasitic nature.

[1] Chauffard et Widal. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1891, 3. s., viii, 168.
[2] Viron. *Arch. de méd. expér. et d'anat. path.*, Paris, 1892, iv, 136.
[3] Hallé et Bacaloglu. *Ibid.*, 1900, xii, 689.
[4] Garnier. *Ibid.*, 1907, xix, 785.
[5] Habershon, S. H. *Practitioner*, 1902, lxviii, 178.
[6] Lippmann. *Compt. rend. Soc. Biol.*, Paris, 1902, liv, 218.
[7] Gilbert et Weil. *Ibid.*, 1898, l, 657.
[8] Griffon. *Clinique médicale de l'Hôtel-Dieu*, Paris, 1906, v, 67.
[9] Dévé. *Rev. de chir.*, Paris, 1907, xxxv, 529.
[10] Tuffier et Barbarin. *Bull. Soc. Anat.*, Paris, 1898, lxxiv, 689.

Incidence.—The disease is very rare, though possibly it is occasionally overlooked or regarded as malignant disease or multiple hydatids of the ordinary kind. In 1901 Melnikow-Raswedenkow [1] collected 235 cases. It is met with in the south of Germany, Bavaria and Würtemberg, Hanover, Switzerland, Austria, and, according to Posselt,[2] in the Tyrol. Dieulafoy [3] was only able to refer to two cases of alveolar hydatid disease in France—one of the liver (Bruyant [4]), the other of the lung and pleura (Rénon [5]). It was formerly regarded as rare in Russia, but in 1901 70 cases were collected by Melnikow-Raswedenkow, who considers that it is more often met with there than elsewhere. It is generally stated that no case has been recognised in England. There are specimens of this disease in the Army Medical Museum at Netley (Nos. 1230, 1239).

Hilton Fagge [6] examined a specimen of colloid cancer in the museum of Guy's Hospital which Frerichs had suggested might be alveolar hydatid, but found nothing to support this view.

In America 6 cases have been reported, chiefly in Germans (Osler [7]). Its geographical distribution differs from that of the common echinococcus, and it is noteworthy that no case has been found in Australia or Iceland, where the ordinary hydatid is specially common. It has been described in cows, sheep, and pigs; it has been thought that the infection is thus conveyed to man (Posselt).

Nature.—A good deal of discussion has taken place as to the nature of alveolar hydatid disease, *i.e.* whether it is merely an exogenous form of the ordinary echinococcus (Virchow) or an entirely distinct parasite. Klemm [8] found the ordinary *Taenia echinococcus* in the intestine of a dog fed on the alveolar hydatid, but it is possible that the taenia was present in the dog previously; for Mangold,[9] and subsequently Müller,[10] by giving the scolices to animals, obtained a taenia different from that of the ordinary echinococcus. The geographical distribution of the two forms does not correspond, as it should do, on the supposition that alveolar hydatid is merely the result of exogenous multiplication of the ordinary echinococcus. Melnikow-Raswedenkow, from exhaustive researches, concludes that the alveolar hydatid is quite distinct from the ordinary echinococcus cyst. According to his views, it should be regarded as belonging to the class of the infective granulomas, and be comparable to tuberculosis, actinomycosis, and syphilis, since it manufactures a special toxin which causes inflammation followed by coagulation-necrosis.

The embryo reaches the liver by the portal vein, becomes embedded

[1] Melnikow-Raswedenkow. *Studien über den Echinococcus alveolaris*, 1901.
[2] Posselt. *Deutsches Arch. f. klin. Med.*, 1899, lxiii, 457.
[3] Dieulafoy. *Manuel de pathologie interne*, tome ii, p. 773.
[4] Bruyant. *Bull. hist. et scientif. de l'Auvergne*, 1899.
[5] Rénon. *Compt. rend. Soc. Biol.*, 1900, lii, 167.
[6] *A Textbook of Medicine*, by Fagge and Pye-Smith, 1902, ii, 459.
[7] Osler. *Practice of Medicine*, p. 37, ed. vi, 1905.
[8] Klemm. *Inaug. Dissert.*, München, 1883.
[9] Mangold. *Berlin. klin. Wchnschr.*, 1892, xxix, 50.
[10] Müller. *München. med. Wchnschr.*, 1893, xl, 225.

in one of the portal spaces, and develops into a chitinous multilocular mass which corresponds to a proglottis of a taenia and not to a hydatid cyst. The parasite becomes encysted and produces ova which are spherical or oval, and measure from 170 to 1000 μ in diameter; an embryo encysted in the liver may produce 15 to 16 ova. In the production of ova when in the human body this cestode resembles the trematode worms, such as the liver fluke (*Fasciola hepatica*). The embryos, being endowed with amoeboid movement, invade the tissues, set up inflammatory and degenerative changes, and may be destroyed by phagocytosis. When the embryos get into the hepatic veins, they may set up metastases in the lungs, brain, etc.

As already pointed out, alveolar hydatid leads to an exogenous formation of cysts, and thus contrasts with the endogenous production of daughter cysts inside the parent cyst which characterises the ordinary echinococcus in man.

Morbid Anatomy.—The liver is enlarged, but may not be otherwise abnormal externally; it may be nodular from the projection of the parasite, and from perihepatitis be adherent to the diaphragm or to surrounding parts. According to Posselt's statistics, the right lobe is affected alone in 65 per cent of the cases, and the left lobe exclusively in 10 per cent. The posterior part of the right lobe is the seat of election. The tumour is surrounded by a fibrous capsule containing an alveolar arrangement of irregular cavities, some of which are occupied by the gelatinous hydatid cysts, others by caseous, purulent, or bile-stained debris. The appearance is much like that of colloid carcinoma. The contents of degenerated cysts may eventually resemble mortar from admixture with lime salts. The liver is hard from fibrosis, which may involve more distant parts of the organ, and may grate under the knife from calcareous infiltration. Occasionally large cystic spaces may form. The unaffected part of the liver undergoes compensatory hypertrophy. The bile-ducts are often compressed, and inflammation may spread to the vessels in the portal spaces and set up endophlebitis, lymphangitis, and obstruction and obliteration. The naked-eye appearances may suggest colloid carcinoma, or, from the sponge-like structure, actinomycosis.[1] Secondary alveolar hydatids may occur in the lymphatic glands, lungs, peritoneum, kidneys, brain. By direct extension the right adrenal may be infected.

Histology.—The parasite shews a structureless wavy membrane, which is covered both internally and externally by an embryonic parenchymatous layer giving rise to scolices. The alveolar hydatid thus differs fundamentally from the ordinary hydatid which has an internal parenchymatous layer (or endocyst) only (Melnikow-Raswedenkow). The outer parenchymatous produces scolices, living amoeboid embryos, and toxins, and thus sets up extensive inflammation in the surrounding tissues and metastases. The scolices are developed in the outer parenchymatous layer, and are therefore exposed to the action of phagocytes, and as a result are difficult to find. The tumour is alveolar, the fibrous tissue being derived from the

[1] Compare Wynne. *St. Barth. Hosp. Rep.*, 1889, xxv, 159.

liver; the spaces contain colloid material—the chitinous vesicles of the parasite—which, as the result of coagulation-necrosis and caseation, forms a mass like a gumma. By softening a cavity may result, and in the debris calcareous granules, cholesterin, and haematoidin crystals may be seen. The periphery of the tumour shews active proliferation of the connective-tissue cells with the production of fibroblasts, giant cells, and endarteritis obliterans. The liver cells may be fatty.

Clinical Features.—The disease is usually seen in persons between twenty-five and fifty years of age, and occurs more often in men than in women, according to Vierordt, in the proportion of 3 (males) to 2 (females). The onset is very gradual, and usually the first symptoms are referred to the region of the liver, and consist of pain, weight, and discomfort. On examination the liver is enlarged and feels hard and resistant and its edge firm; the surface may be smooth, or nodular when the parasite invades the capsule. In the latter event it will be tender, and pain may be due to perihepatitis. In rare cases fluctuation and softening appear in the hepatic tumour. Dévé refers to 2 cases in which there was a gaseous abscess.[1]

The spleen is said to be enlarged in 90 per cent of the cases (Posselt). Jaundice occurs in four-fifths of the cases. It may be the first thing noticed and tends to become deep. As a result cholaemia with multiple haemorrhages may develop. In rare instances the jaundice intermits and varies from time to time. As jaundice may depend on obstruction inside the liver, bile may still pass into the duodenum. Ascites is much less frequent than jaundice; it may be due to pressure on the portal vein, or to chronic or tuberculous peritonitis (Teutschlaender[2]). Oedema of the legs may occur in the late stages of the disease, and in rare instances depends on pressure on the inferior vena cava. The urine may be of low specific gravity and so copious as to imitate diabetes insipidus. Eosinophilia is inconstant. Some cases shew irregular fever and excessive perspiration; in this connexion it should be remembered that tuberculosis is said to supervene in 3 per cent of the cases (Posselt). Emaciation is a late event, and thus contrasts with the course of events in malignant disease of the liver. Digestive disturbances are not uncommon, such as dyspepsia, nausea, vomiting, diarrhoea, or constipation. In some instances there is thirst or a voracious appetite, and in these cases the bodily weight may increase.

Course and Duration.—The disease is very chronic, and may last for ten or more years. Death may be due to increasing weakness or to cholaemia.

Diagnosis is extremely difficult, and the disease will probably be regarded as malignant until the liver is carefully examined. This mistake has been made even when the liver has been exposed by laparotomy. The slow course of the disease may arouse a suspicion as to its real nature. Removal of a fragment of the growth at a laparotomy and microscopic examination have established the diagnosis, but mere puncture

[1] Dévé. *Rev. de chir.*, Paris, 1907, xxxv, 556.
[2] Teutschlaender. *Corr.-Bl. f. schweiz. Ärzte*, 1907, xxxvii, 406.

is of no value. It may also be mistaken for hypertrophic biliary cirrhosis or cysts of the pancreas. If the liver is enlarged and no localised tumour is palpable, the presence of jaundice and splenic enlargement may suggest biliary cirrhosis. But the jaundice is much deeper than in biliary cirrhosis, and the enlargement of the spleen comes on later in the course of the disease.

Prognosis.—The difficulty of diagnosis accounts for the fact that most cases are recognised after death, and that, as far as our knowledge goes, the prognosis is bad. But it is to be hoped that comparatively early operation and excision of the growth will give good results.

Treatment consists in excision of the affected part of the liver, and should be undertaken as early as possible. Bruns[1] successfully treated a case by excision of the parasite. Merely tapping has not been found to be successful. Injection of formalin into the tumour has given encouraging results.

FATTY LIVER

UNDER the heading of "fatty liver" it will be convenient to consider together the changes formerly described separately as fatty infiltration and fatty degeneration. It will be well, however, to state briefly what is meant by the two terms. Fatty infiltration or accumulation is an exaggeration of the physiological storage of fat in the hepatic cells; it is normally present in young children, in pregnant and nursing women, sometimes in healthy adults who have died suddenly from accidents, and constantly in obesity. Fatty degeneration, originally regarded as the pathological production of fat at the expense of the protoplasm of the liver cells, may be described as the appearance of fat in injured cells, the fat being an index rather than the direct result of the cell degeneration (Christian[2]). For a full consideration of the subject of fat metabolism the reader should consult Adami's *Principles of Pathology*, 1911, i, 905. The histological differences between the two conditions are described on page 430, but in practice they are frequently combined. It is better, therefore, to speak of pathological fatty change in the liver.

Etiology.—Pathological fatty change in the liver is met with in a number of conditions which have in common the presence of toxins in the blood. Thus, a fatty state of the liver cells is the most constant change found in the bodies of alcoholic persons, and experiment shews that this must be regarded as due to the effect of alcohol as a protoplasmic poison. Numerous other poisons lead to the same change, *e.g.* phosphorus, arsenic, antimony, copper, chloroform, iodoform, sulphuric, oxalic, carbolic, tartaric, and other acids, sulphonal.[3]

[1] Bruns. *Beitr. z. klin. Chir.*, 1896, xvii, 201.

[2] Christian, H. A. *Johns Hopkins Hosp. Bull.*, 1905, xvi, 6.

[3] Taylor and Sailer, *Contributions from the William Pepper Laboratory*, Philadelphia, 1900, p. 120; and Garrod, *Lancet*, 1900, ii, 1323.

Rosenfeld [1] has proved experimentally that the fatty change produced in the liver by phosphorus and phloridzin is not due to the local formation of fat from the protoplasm of the hepatic cells but to the transport of fat from other parts of the body ; for if the animal is previously starved no accumulation of fat occurs in the liver.

A certain amount of fatty change is induced by numerous bacterial toxins, and may occur in typhoid fever, pneumonia, puerperal fever, cholera, diphtheria, small-pox,[2] scarlet fever, erysipelas, and streptococcic infections.[3] Fatty change in the liver is very frequent in pulmonary tuberculosis. Louis found it in 40 out of 120 fatal cases. It is thought to be more frequent in female than in male patients (Budd [4]). It is very striking to find extensive fatty change in the liver of an emaciated patient with little or no subcutaneous fat. Frerichs [5] regarded the fatty condition of the liver as due to the absorption of fat from the subcutaneous and other parts of the body and sometimes to imperfect secretion of bile. This explanation will not stand against the facts that in cases of emaciation and jaundice, as, for example, carcinoma of the head of the pancreas compressing the bile-duct, there is often no fatty change in the liver. The administration of fatty food and cod-liver oil can hardly account for the change, inasmuch as cod-liver oil was not used in Louis' time (Wilson Fox [6]). Insufficient oxidation depending on the condition of the blood cannot be an exclusive or essential cause, since fatty change in the liver is much less marked in emphysema, chronic bronchitis, and congenital morbus cordis than in pulmonary tuberculosis. The fatty liver in tuberculosis is at the present time referred to retrogressive or degenerative changes set up by poisons reaching the liver. Whether this is due to the tuberculous toxin alone seems doubtful.

Péron [7] found that intravenous injections of cultures of virulent tubercle bacilli lead to extensive fatty degeneration of the liver, an effect which was prevented if the cultures had previously been raised to 100° C. for five minutes ; but Carrière [8] as a result of injection of tuberculin produced cloudy swelling, vacuolation, and necrosis of the liver cells, but never any fatty or lardaceous change. The latter experiments suggest that the fatty degeneration is due to the effects of toxins other than those of the tubercle bacillus, such as might result from secondary streptococcic infections.

Fatty change in the liver cells is met with in intestinal diseases, such as dysentery and diarrhoea, and would therefore appear to be due to the action of poisons absorbed from the alimentary canal.

[1] Rosenfeld. *Ztschr. f. klin. Med.*, 1895, xxviii, 256.
[2] Arnaud. *Marseille méd.*, 1899, p. 39.
[3] Roger et Garnier. *Rev. de méd.*, 1901, xxi, 97.
[4] Budd, G. *Diseases of the Liver*, p. 304, ed. iii, 1857.
[5] Frerichs. *Diseases of the Liver*, vol. i, pp. 285, 301. Transl. New Sydenham Soc., 1860.
[6] Wilson Fox. *Treatise on Diseases of the Lungs and Pleurae*, p. 620, 1891.
[7] Péron. *Compt. rend. Soc. Biol.*, 1898, 10. s., v, 446.
[8] Carrière. *Arch. de méd. expér. et d'anat. path.*, Paris, 1897, ix, 65.

Thus, in 32 cases of gastro-enteritis in children Thiemich[1] found fatty change in 23 ; Freeborn[2] noted a similar condition in 50 per cent of cases of diarrhoea in children under three years of age. Freeman[3] found that out of 496 children dying of various diseases the liver was fatty to the naked eye in 202, or 41 per cent, and that this change was common in acute infectious diseases and in disease of the alimentary tract, but rare in other chronic wasting disorders. Menetrier[4] described fatty liver due to a grave infection of appendicular origin.

Fatty change is also met with in grave anaemia, and is probably due to the poisons giving rise to the anaemia. It is also well marked in cases fatal from the status epilepticus (Mott[5]), in diabetic coma, in fatal cases of acid intoxication after anaesthesia in children,[6] and in cyclical vomiting,[7] all of which are toxic conditions.

Fatty change in the liver is frequent in the bodies of pregnant women, and is very probably due to the diseases or morbid conditions responsible for death. As pointed out in other parts of this work, fatty change is frequently associated with other lesions of the liver, such as cirrhosis, lardaceous disease, and chronic venous engorgement. It is then due to some poison, to impaired nutrition, or to both factors. In some instances acute fatty transformation of the liver cells occurs and proves fatal with much the same clinical manifestations as acute yellow atrophy. In some cases there is no clear evidence as to the nature of the toxic or infective cause. It has been noted after operations, and has been thought to be due to chloroform, iodoform, carbolic acid, or to a combined action of toxins due to disease and of chloroform (*vide* also p. 579).

Stiles and M'Donald[8] argue that the fatty change in the liver is entirely due to the action of chloroform on a previously healthy liver. Wells[9] suggests that chloroform kills the cells but leaves their intra-cellular enzymes intact, so that self-digestion or autolysis occurs ; he further suggests that the oxidising enzymes are acted upon while the lipase is free to form fat.

Morbid Anatomy.—When the liver cells rapidly undergo fatty change the organ is much enlarged, for example, in phosphorus poisoning, and in extreme cases a weight of even 10 pounds has been reached.

In 1890 a woman aged sixty-seven, who for years had been a heavy drinker and lately had consumed a bottle of whisky a day, was admitted into St. George's Hospital deeply jaundiced, unconscious, and with scarcely audible

[1] Thiemich. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1896, xx, 179.
[2] Freeborn. *Acad. Med. New York*, Jan. 1897.
[3] Freeman. *Arch. Pediat.*, 1900, xvii, 81.
[4] Menetrier. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1903, 3. s., xx, 1115.
[5] Mott. *Arch. Neurol. Claybury*, 1899, i, 491.
[6] Compare cases and remarks by L. G. Guthrie, *Lancet*, 1894, i, 193, 257 ; and 1903, ii, 10 ; *Clin. Journ.*, 1907, xxx, 129 ; Brackett, Stone, and Low, *Boston Med. and Surg. Journ.*, 1904, cli, 2 ; Bevan and Favill, *Journ. Amer. Med. Assoc.*, 1905, xlv, 754.
[7] Langmead. *Practitioner*, 1912, lxxxix, 29.
[8] Stiles and M'Donald. *Rep. Soc. Study Dis. Child.*, Lond., 1904, iv, 208.
[9] Wells. *Journ. Am. Med. Assoc.*, 1906, xlvi, 341.

heart sounds ; the urine did not contain leucine or tyrosine. At the necropsy which I performed, the liver weighed $10\frac{3}{4}$ pounds and floated in water ; microscopically, besides very extensive fatty change, there was some apparent increase in the amount of the fibrous tissue. The heart, 16 ounces, shewed fatty degeneration. The process was probably acute, though less so than in acute yellow atrophy. Such cases might perhaps be called acute yellow hypertrophy.

The enlargement affects all parts equally and the normal shape of the liver is retained, the edges becoming rounded and thicker. When the fatty change comes on slowly, enlargement is much less marked and some fatty livers are of a normal size or occasionally small. A fatty liver is usually uniformly smooth on the surface, and as seen after death, anaemic. The consistency varies, being sometimes firm, and this without any fibrosis ; sometimes soft and friable.

In a boy aged three years who died as the result of poisoning from the absorption of iodoform from a wound the liver weighed 30 ounces and was remarkably firm, keeping its shape and impressions like His' model. Microscopically there was marked fatty change but no fibrosis or lardaceous disease. During life high temperature, delirium, and wasting were present.

These differences in the consistency of a fatty liver may depend on conditions preceding death, such as infective agencies leading to acute changes, or may be the result of post-mortem decomposition. On section the lobules are often very distinctly mapped out so that the surface has a granular appearance exactly like that of unilobular cirrhosis. It is often impossible to be certain as to the existence of cirrhosis or not until microscopic sections have been made. In other cases in which the fatty change affects the cells of the lobules universally the cut section is uniform and has no resemblance to cirrhosis. The specific gravity of the liver is diminished and the organ may float in water. When cut into, the surface of the section may be soft and yielding, or in some instances firm. The dry blade of a knife is rendered greasy by the exuding oil when the organ is soft. If put into a flame, the fat melts, may burn in a spluttering manner, and if allowed to drop on paper, leaves an oily stain. The fat may amount to 25 to 30 per cent of the weight of the liver. There may be local haemorrhages and focal bile-staining due to extravasation, depending on degeneration and rupture of these vessels. Local areas of fatty change are not uncommon in the liver in infective cases ; they are due to the local action of the toxins produced on the spot by micro-organisms in the vessels of the liver.

Histologically the liver cells contain globules of fat of varying sizes which are refractive and stain black with osmic acid, red with Sudan III and Scharlach R, and various colours with basic aniline dyes by Lorrain Smith's[1] method. The fat is found most often in the central zone, least often in the median zone of the lobule (M'Crae and Klotz[2]).

A distinction has been drawn between fatty degeneration and fatty

[1] Lorrain Smith. *Brit. Med. Journ.*, 1906, ii, 149.
[2] M'Crae and Klotz. *Journ. Exper. Med.*, N.Y., 1910, xii, 746.

infiltration of the liver cells. Thus, in fatty infiltration the cells chiefly at the periphery of the hepatic lobules are occupied by globules of fat of considerable size, whereas in fatty degeneration the fat occurs in small granules which, according to M'Crae and Klotz, do not run together to form globules. These granules are most frequent in the central zone. In fatty infiltration the protoplasm of the liver cells is mechanically displaced to the side of the cell by the deposited fat. In fatty degeneration the cells are degenerated, their cytoplasm granular, and the nucleus shews chromatolysis, but is in its ordinary position. After removal of the fat in cases of infiltration the cells return to their normal state, whereas in degeneration they break up. Well-marked examples of the two processes are quite distinct, but they are frequently combined and it is often impossible to draw a rigid line between them.

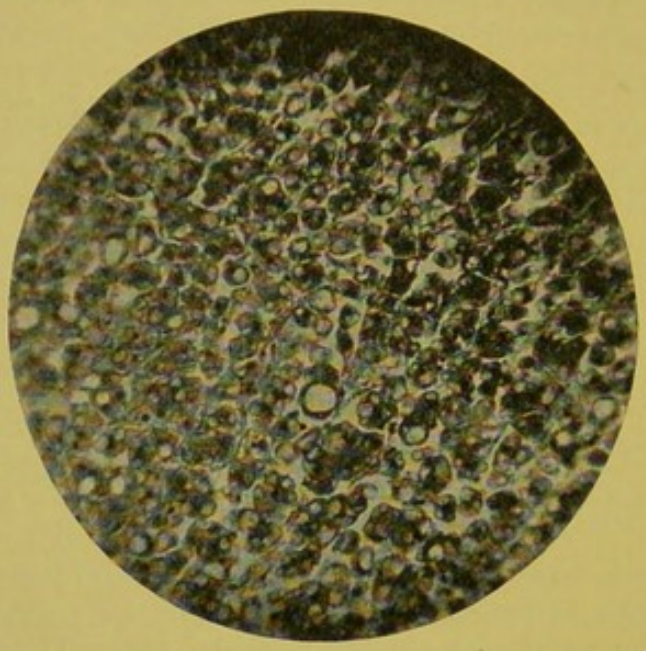


FIG. 54.—Extensive fatty change in the liver cells, the result of acute toxic changes. (Photomicrograph by Dr. S. G. Penny.)

A review of the pathology of fatty degeneration and infiltration shews that there is no proof that fat arises directly from degeneration of the protein molecule of the liver cell. The factors which lead to so-called "fatty degeneration" lower the vitality of the cells and thus favour deposit of fat (lipins), which, owing to injury, the cell cannot utilise. Instead of "fatty degeneration" the term "degenerative fatty infiltration" should be employed (Herxheimer and Walker Hall [1]).

The fibrous tissue of the portal spaces shews up so as to suggest some old fibrosis, and frequently there is some small-celled infiltration in and around the portal spaces; this is due to wasting and atrophy of the essential liver parenchyma, and may be called a "replacement fibrosis." Though in miniature much the same as hepatic cirrhosis, it is unimportant, and should be regarded as dependent on the fatty change and should not be spoken of as fatty cirrhosis, but as fatty liver. In this way any confusion between this condition and genuine cirrhosis with superadded fatty change is avoided.

Clinical Picture.—*Signs.*—In cases of general obesity the liver may be made out by percussion to be enlarged, but it may be difficult to feel the

[1] Herxheimer and Walker Hall. *Med. Chronicle*, Manchester, 1904, xl, 227.

edge distinctly, both because the abdominal walls are overloaded with fat and because during life the enlarged fatty liver is often soft. Fatty liver is indeed very often latent and unsuspected. The skin may be greasy, the arterial pressure is usually low, and the heart sounds distant or feeble. Fat women often have remarkably small chests, and in the dead-house the contrast between the enormous fatty covering and the size of the thoracic cavity is most striking.

In cases in which a fatty liver is associated with definite disease, such as pulmonary tuberculosis, the liver is enlarged and smooth, but is less firm than in lardaceous disease or cirrhosis, and therefore not so easily

FIG. 55.—Microscopical appearances of extensive fatty change in the liver cells. Some groups of cells are free from change, while in others hardly any protoplasm is left. There is an apparent increase of the interlobular fibrous tissue, suggesting slight multilobular cirrhosis. ×72.

felt. The spleen is not enlarged. The stools are light. Jaundice does not occur in uncomplicated cases; and there is no portal obstruction, so that there is no ascites or enlargement of the subcutaneous abdominal veins. Piles have been said to occur, but this is probably a coincidence. Addison[1] laid stress on the condition of the skin accompanying fatty liver—bloodless, looking like fine polished ivory, almost semi-transparent, and exquisitely smooth, like satin. This change was earliest seen and best marked on the backs of the hands. Addison also referred to recurring attacks of oedema in cases of fatty liver, especially in alcoholic patients. Possibly the oedema was due to peripheral neuritis or cardiac dilatation. It has been suggested that an enlarged fatty liver may inter-

[1] Addison, T. *Guy's Hosp. Rep.*, 1836, i, 476.

fere with the action of the diaphragm, and so cause massive collapse of the lower lobe of the right lung (Goodall and Kingsbury [1]).

The ammonia in the urine may be increased at the expense of the urea. This should be regarded not as evidence of failure in the urea-forming power of the liver cells, but as evidence that the morbid process underlying the fatty change, for example, phosphorus poisoning, leads to the formation of organic acids which fix the ammonia and prevent its conversion into urea.

Lépine and Eymonnet [2] described excess of glycero-phosphoric acid in the urine; this is derived from lecithin, which they found to be present in excess in fatty livers. Haematoporphyrinuria is often seen,[3] and may be due to failure of the fatty liver to arrest the urobilin which reaches it from the alimentary canal.

The **symptoms** are those of the condition or disease responsible for the secondary change in the liver. No doubt the various functions of the liver are not so well performed as in health, but there is no constant or pre-eminent failure of function. When the degeneration is very acute and extensive, the symptoms approach those of acute atrophy, although actually the liver is much larger than normal. But the condition then ceases to be one of ordinary fatty liver.

The diarrhoea formerly thought to depend on fatty liver is probably the cause rather than the effect. There is no pain associated with fatty liver.

As a result of severe trauma fat from the liver might pass into the hepatic veins and give rise to fat embolism of the lungs (Engel [4]).

In delayed chloroform poisoning the cases fall into two groups: (*a*) with fatty change in the periphery of the lobules, mainly in children, presenting the signs of acid intoxication, and hardly ever jaundice; (*b*) mainly in young adults with jaundice and the symptoms and gross morbid appearances of acute yellow atrophy (chloroform necrosis of the liver; H. G. Wells [5]).

Diagnosis.—Painless enlargement of the liver, with a smooth, comparatively soft surface, in an individual in whom one of the known causes of a fatty liver, such as alcoholism or pulmonary tuberculosis, is active, should suggest its presence. It must be diagnosed by exclusion of the following conditions:

(1) Leukaemic infiltration of the liver leads to a firmer condition and can be at once recognised by examination of the blood.

(2) Lardaceous disease. The liver is much firmer than in fatty liver, and there may be signs of lardaceous disease of the kidneys (albuminuria), splenic enlargement, or diarrhoea.

(3) Cirrhosis, especially an enlarged cirrhotic liver with latency of the

[1] Goodall and Kingsbury. *Brit. Med. Journ.*, 1911, ii, 815.
[2] Lépine et Eymonnet. *Lyon méd.*, 1882, xli, 15.
[3] Garrod. *Lancet*, 1900, ii, 1323.
[4] Engel, H. *München. med. Wchnschr.*, 1901, xlviii, 1046.
[5] Wells, H. G. *Arch. Int. Med.*, Chicago, 1908, i, 594.

symptoms. In the absence of symptoms the diagnosis is very difficult, and turns chiefly on the surface of the liver; if it is smooth, fatty change is probable; if irregular, cirrhosis is indicated. In numerous instances fatty change is associated with cirrhosis.

(4) A displaced liver if movable is at once recognised, but if displaced by some undetected cause, such as a pleural effusion or pneumothorax, it might be regarded as a large fatty liver.

(5) Enlargement due to a deep-seated hydatid cyst or abscess. Here the liver is much more prominent and more easily felt and mapped out, while there may be signs of pressure, pain, or fever.

Prognosis.—Patients with fatty livers, being often chronic alcoholics, are bad subjects for operation and bear severe illness—such as pneumonia, and erysipelas, and accidents—very badly. Symonds,[1] Verneuil,[2] and L. Guthrie[3] insisted on the danger of operations on these patients; and Guthrie, who has pointed out that chloroform narcosis is specially dangerous in patients with fatty livers, has recorded a series of cases in children in which symptoms suggesting acid intoxication followed operations, and in which a fatty liver was found after death. Gilbert and Lereboullet[4] have drawn attention to the frequency with which pneumonia proves fatal in cases in which the liver is fatty, and insist that death results in such cases, not from hepatic disease, but because of it. Apart from the dangers attending operations and acute illness the prognosis of fatty liver is that of the accompanying disease or condition.

The **treatment** of fatty liver is that of the primary cause, such as obesity or pulmonary tuberculosis. In cases in which symptoms of acid intoxication come on after chloroform or ether narcosis, large doses of bicarbonate of sodium should be given by the mouth, rectum, or intramuscular transfusion; glucose 6 per cent solution may also be given by the mouth or rectum (Beddard[5]).

LARDACEOUS DISEASE

Synonym: Amyloid, Waxy, Chondroid (Wells) Disease of the Liver.

Hope figures an undoubted case of lardaceous disease in his work on "Morbid Anatomy" (1834) as "hypertrophy of the red substance of the liver." In 1857 Budd[6] described it as "scrofulous disease of the liver."

Incidence and Etiology.—The liver is not so often affected as the

[1] Symonds. *Med. Times and Gaz.*, 1860, ii, 351.
[2] Verneuil. *Gaz. méd. de Paris*, 1892, 8. s., i, 447.
[3] Guthrie, L. *Lancet*, 1903, i, 10; 1905, ii, 583. *Clin. Journ.*, 1907, xxx, 129.
[4] Gilbert et Lereboullet. *Bull. et mém. Soc. méd. des hôp.*, 1902, 3. s., xix, 577.
[5] Beddard. *Lancet*, Lond., 1908, i, 782.
[6] Budd, G. *Diseases of the Liver*, p. 312, ed. iii, 1857.

spleen and kidneys. In the combined statistics of Birch-Hirschfeld, Loomis, Dickinson, Goodhart, and Turner, there are 795 cases of lardaceous disease, in which the spleen was affected in 585, the kidney in 539, and the liver in 387.

The causes of lardaceous change in the liver are those of lardaceous disease generally, namely, prolonged suppuration and syphilis without necessarily any associated suppuration; and grave cachectic conditions due to chronic and severe toxaemias occasionally appear to be responsible for it. Tuberculosis *per se* does not give rise to the lardaceous change, but when a tuberculous lesion becomes secondarily infected lardaceous disease may develop. This is seen in chronic pulmonary tuberculosis, hip-joint disease, or caries of the spine with psoas abscess.

Incidence in chronic pulmonary tuberculosis: in 326 cases tabulated by West[1] lardaceous disease was met with in 20, or 6·2 per cent; in Wilson Fox's series of 91 cases the percentage was as high as 15.

The lardaceous change is usually produced slowly after months of suppuration, but it has been found in the liver one month after the onset of osteomyelitis (Soyka). This acute lardaceous change has also been produced in animals (Krawkow,[2] A. B. Green[3]).

Prolonged suppuration is now so comparatively infrequent that lardaceous disease is less common, and relatively more often due to syphilis than formerly. As a result of congenital syphilis, lardaceous change is seen as a late result, but it hardly ever occurs in association with the intercellular cirrhosis. In delayed hereditary syphilis it may be combined with gummas or with parasyphilitic multilobular cirrhosis (*vide* p. 379). The lardaceous change may be local in the liver around a gumma, an abscess, or a suppurating hydatid. This points to the conclusion that the change is due to a toxin derived from the abscess or gumma. Lardaceous disease is occasionally seen in other infective conditions, such as chronic malaria. Brault and Legry[4] suggest that grave intestinal lesions, such as tuberculous ulceration, are specially prone to produce lardaceous change in the liver.

Lardaceous change may be associated with lymphadenoma in the liver without any other cause,[5] and I have seen it in chronic lymphatic leukaemia. Early lardaceous change has been described in four cases of fatal rheumatic fever (Beattie[6]).

Pathogeny.—The lardaceous substance is a glycoprotein containing chondroitin-sulphuric acid, and is apparently due to the action of a poison or poisons on protoplasm. Krawkow[7] considered that infection was absolutely necessary,

[1] West. *Diseases of the Respiratory Organs*, 1902, ii, 426.
[2] Krawkow. *Arch. de méd. expér. et d'anat. path.*, Paris, 1896, viii, 106.
[3] Green. *Journ. Path. and Bact.*, Edin. and Lond., 1901, vii, 184.
[4] Brault et Legry, in *Manuel d'histologie pathologique*, Paris, 1912, iv, 829.
[5] Buchanan, *Glasgow Med. Journ.*, 1889, ii, 117; Fagge and Pye-Smith's *Textbook of Medicine*, ii, 647, ed. iv.
[6] Beattie. *Brit. Med. Journ.*, 1906, ii, 1444.
[7] Krawkow. *Centralbl. f. allg. Path. u. path. Anat.*, 1897, xl, 195.

and that the lardaceous change did not follow aseptic suppuration such as that set up by turpentine. He regarded the change as due to the absorption of microbic poisons, and, like Czerny, looked upon lardaceous disease as an infiltration rather than a local degeneration.

Morbid Anatomy.—The liver is enlarged and may weigh more than twice its normal amount; it has been known to weigh 14 pounds (Wilks[1]). The surface is smooth, usually anaemic, and may shew a few stellate veins. The enlargement is uniform, and the shape of the organ is so well preserved that the impressions of adjacent viscera recall His' anatomical model. The margins of the liver are firm and rounded. It is extremely firm and can be cut into thinner slices than a healthy organ. It has a rubbery feel, but is not so resistant to the knife as a cirrhotic liver. Its specific gravity is increased, and has been found to be 1080 (Wilks) instead of the normal 1055. The liver is anaemic, but its colour varies with the degree of anaemia; it may resemble the fat of bacon or, when less anaemic, smoked salmon. The lobular arrangement is accentuated. The connective tissues of the walls of the gall-bladder and ducts are said to shew the change in a high proportion of the cases of widespread lardaceous disease, 11 out of 12 cases (Zabezynska[2]). The glands in the portal fissure may be considerably enlarged, but do not press on the bile-ducts or portal vein. As in other organs, the lardaceous change, when slight, may not be manifest to the naked eye, and microscopic examination or staining with iodine may be necessary.

Iodine Stain.—The existence of lardaceous disease of the liver should be tested for in the post-mortem room by the iodine reaction. A solution of iodine in water, containing a little iodide of potassium to dissolve it, the dilute liquor iodi of the Pharmacopoeia U.S.A., or Lugol's solution (iodine 1 part, iodide of potassium 2 parts, water 200 parts), should be used. The tincture of iodine should not be employed, since the spirit it contains partially coagulates albumin, and thus obscures the reaction. The cut section should first be washed to remove any blood, and since alkali interferes with the reaction, should be treated with dilute acetic acid. The solution of iodine should then be poured upon it, or, better, a thin slice of the liver should be placed in a beaker of the watery solution of iodine. The selective action of iodine is then well shewn; the healthy parts are coloured yellow, while the lardaceous parts become of a dark mahogany. The intermediate zone of the lobules stands up as a brown ring on a yellow ground. The colour changes on the addition of H_2SO_4, but does not actually turn blue, as was originally described, but becomes a dark violet or allied tint.

Microscopic Examination.—The chief brunt of the disease falls on the capillaries in the intermediate zone of the lobules, which appear swollen, homogeneous, and tortuous. They compress and to a great extent conceal the hepatic cells, while the narrowing of the lumen of the capillaries impedes the flow of blood through them, and as a result the liver cells

[1] Wilks, S. *Lectures on Pathological Anatomy*, p. 455, 3rd ed., 1889.
[2] Zabezynska. *Rev. méd. de la Suisse Rom.*, 1911, xxxi, 815.

atrophy and degenerate. On section the swollen homogeneous curves of the capillaries imitate the appearance that would be presented by swollen hepatic cells, but the latter can be made out in appropriately stained specimens between the enlarged capillaries, and never become lardaceous. The lardaceous change in the capillaries eventually spreads throughout the lobule, and may then invade the intralobular vein. The fibrous tissue of the portal space remains healthy, and cirrhosis does not occur as the result of the cellular changes.

Although the capillaries are the part of the hepatic vascular system chiefly attacked by the lardaceous change, examination of livers in which the change is commencing may shew that the first part to be affected is the middle coat of the small arteries, as is seen around a gumma, the muscular coat being irregularly attacked; eventually, if the change is excessive, it may attack the walls of the portal and hepatic veins. The lardaceous material lies between the muscular fibres of the media and not in them; it spreads inwards to the intima, but does not involve the endothelium, which may shew fatty change.

Microscopic sections may be examined fresh, with iodine solution, or preferably with methyl-aniline violet.

Staining Reactions.—With methyl-aniline violet in watery solution the lardaceous capillaries are stained red, while the healthy tissues are coloured violet; this stain is better shewn if the sections are washed in water acidulated with acetic or hydrochloric acid. It is a much more delicate stain than the iodine one, and it seems probable that it reacts to an earlier stage of lardaceous change than iodine. When the lardaceous change is very far advanced, the methyl-aniline violet reaction may fail, while the iodine reaction continues to be marked. Other substances, such as colloid or hyaline, occasionally stain like lardaceous tissue. Krawkow considers that the reaction is more easily obtained in fresh sections, and that slight degrees of it may not be shewn if the tissues are previously hardened. Gentian violet may also be employed; it has the same selective staining effect.

Clinical Picture.—*Symptoms.*—Lardaceous disease of the liver is usually subordinate either to the primary condition to which it is due or to the general manifestations of widespread lardaceous disease, for it is rare for the liver to be the only organ affected. There are no symptoms pathognomonic of lardaceous disease affecting the liver to the exclusion of the other viscera. Jaundice does not occur unless there is some other factor, such as a gumma. Ascites if present is in all probability due to concomitant cirrhosis, gumma, chronic peritonitis, or renal disease.

A boy under my care with a lardaceous liver due to psoas abscess had oedema of the legs, great development of the caval veins over the abdomen, and ascites. There was obliteration of the inferior vena cava. The ascites was due to extension of inflammation from the spine to the peritoneum and mesentery which was thickened. Tirard[1] recorded a somewhat similar case.

[1] Tirard, N. *Medical Treatment*, Lond., 1900, p. 338.

Ascites does, however, occasionally occur in uncomplicated instances of lardaceous liver. It may be part of general oedema, or terminal and due to extreme cachexia. Bolton [1] records 3 cases of extreme ascites in children, and points out that it is commoner in children than in adults. It is remarkable that although the liver is almost universally lardaceous, there is little clinical evidence of functional inadequacy. It has, it is true, been thought that the bile is diminished in amount, and that the faeces become pale. The liver is free from pain or tenderness unless there is some complication, such as abscess, perihepatitis, growth, or gumma.

Signs.—The only real evidence of lardaceous disease of the liver is its enlargement, which is uniform, smooth, and painless. It is only when combined with gumma, cirrhosis, perihepatitis, or in the rare event of a secondary growth in a previously lardaceous liver that the surface becomes rough and nodular. The left lobe of the liver may be so prominent as to suggest primary malignant disease (Musser [2]), or an enlarged spleen (Affleck [3]). Clubbing of the fingers with osteo-arthropathy has been observed in lardaceous disease of the liver secondary to spinal caries (Symes-Thompson [4]).

Diagnosis.—Under this heading the other forms of painless enlargement of the liver must be mentioned. In every case it is important to determine if the causes for lardaceous disease are or have been present, and if there are any signs of renal or intestinal disease of the same nature.

In the absence of anaemia and some degree of wasting the probabilities are against hepatic enlargement being lardaceous. In leukaemia the liver is enlarged, but a blood examination will settle any doubt. When lymphadenoma attacks the liver, there will almost certainly be enlarged glands elsewhere and fever. Simple fatty liver is less readily felt and, as a rule, is associated with obesity. In pulmonary tuberculosis an enlarged liver may be due to fatty change or to lardaceous disease, and to settle the question the other signs of lardaceous disease must be looked for; if all of them, such as albuminuria, dropsy, diarrhoea, enlarged spleen, are absent, it may be assumed that the liver is fatty.

A hydatid cyst deep in the substance of the organ may so displace the liver forwards as to imitate the physical signs of a lardaceous liver, but the other symptoms and causes of lardaceous disease are wanting, and the patient's general health is usually so good as to put lardaceous disease out of court. A large cirrhotic liver may, from its size and firmness, imitate a lardaceous liver. In both diseases the spleen may be enlarged, and when ascites occurs in lardaceous disease the condition may easily be regarded as cirrhosis. Evidence of past suppuration, albuminuria, and of past syphilis, are in favour of lardaceous disease; a history of alcoholism and haematemesis point to cirrhosis. The following

[1] Bolton. *Clin. Journ.*, Lond., 1907, xxxi, 117.
[2] Musser, J. H. *Proc. Path. Soc.*, Phila., 1898–9, n. s., ii, 202.
[3] Affleck, J. O. *Trans. Edin. Med.-Chir. Soc.*, 1898, xvii, 61.
[4] Symes-Thompson. *Med.-Chir. Trans.*, Lond., 1904, lxxxvii, 130.

case illustrates the difficulties which may arise in correctly diagnosing between these two conditions:—

A woman aged forty-seven was under my care in St. George's Hospital in June-July 1900 with ascites, oedema of the legs, albuminuria, and signs of pulmonary tuberculosis at both apices. There was a history of haematemesis, and the facial aspect was that of cirrhosis. She was tapped twice, and then passed into a drowsy condition from which she rallied temporarily after transfusion. At the autopsy there was lardaceous disease of the liver (53 ounces) and kidneys due to chronic pulmonary tuberculosis. Microscopically there was no fibrosis of the liver. There was slight thickening of the capsule of the liver and opacity of the peritoneum. It is possible that the lardaceous condition of the liver, together with the slight peritoneal change, was responsible for the ascites. It is probable that what was described as haematemesis was in reality haemoptysis.

Prognosis.—When the liver is enlarged so that it is readily felt, and there is reason, from the history, to believe that it is due to lardaceous disease, the prognosis is bad, since the disease is likely to attack the kidneys and the intestines. The affection of the liver itself does not make so much difference, but it is evidence that the disease is present and may affect more important organs.

Under appropriate treatment a lardaceous liver may diminish in size. Duckworth [1] recorded a case in which it diminished by half before death occurred, and previously Graves [2] described great improvement in cases which were probably of the same nature. Experimentally Lubarsch [3] has shewn that lardaceous disease may pass away; he excised a piece of a lardaceous spleen from an animal some weeks before death, and after death no evidence of lardaceous change was present.

Treatment.—The first step is to remove the cause if it is still present. Suppuration should if possible be submitted to surgical treatment so as to bring it to a rapid and satisfactory termination. When syphilis is the cause, iodide of potassium should be given, while good results have also been obtained from iodide of iron. If there be concomitant renal disease, the effect of iodide must be carefully watched, as an iodide eruption is then more readily produced. I have seen such an eruption closely resemble a uraemic rash. The general health requires careful attention; and sea air, good food and hygienic surroundings, bitter tonics, iron, and acids do good. Alkalis have been recommended, chiefly on theoretical grounds, but do not succeed better than, if so well as, acids. Budd and Warburton Begbie recommended chloride of ammonium, but its utility is very doubtful. Constipation may require attention, but mild laxatives should be given, otherwise severe diarrhoea may be set up. Diarrhoea may be very troublesome, and by exhausting the patient lead to a fatal issue; it may alternate with constipation, and should be treated by

[1] Duckworth. *St. Barth. Hosp. Rep.*, 1874, x, 57.
[2] Graves. *Clinical Medicine*, i. 518, New Sydenham Soc., 1884.
[3] Lubarsch. *Virchows Arch.*, 1897, cl, 471.

astringents, and if necessary with opium. General dropsy requires cardiac tonics, iron, and diuretics; the skin should be made to act freely by diaphoretics and hot baths, or the amount of fluid should be restricted.

PIGMENTATION

THE subject of pigmentation in association with cirrhosis is described under the head of Pigmented Cirrhosis (p. 302). It is merely necessary here to mention the various conditions in which the liver cells contain pigment. The pigments may be divided into: (I) Intrinsic, or those produced in the body and derived from the blood or bile; and (II) extraneous pigments introduced into the body; these are of comparatively little importance.

I. **Intrinsic pigments** are those derived from the blood, namely, haemosiderin, which contains iron, haematoidin, an iron-free body, and the bile pigment.

Haemosiderin.—The cells of the liver may contain haemosiderin—an iron-containing pigment derived from the destruction of red blood-corpuscles and the haemoglobin thus liberated—in a number of conditions. In a systematic examination of the liver in 300 cases, Castaigne [1] found that in 31, or more than 10 per cent, the liver cells contained haemosiderin. In portal cirrhosis haemosiderin is not uncommon in the liver cells (Abbott,[2] Kretz). The reaction (Perl's test) for haemosiderin consists in placing microscopic sections in a 2 per cent solution of ferrocyanide of potassium for three minutes, transferring to a 1 per cent solution of hydrochloric acid for two to five minutes, and washing in distilled water; the pigment granules take a bluish-green colour, which is well seen in the cells in the periphery of the lobule in pernicious anaemia. It also occurs in leukaemia, in some cases of enteric fever, and chronic intestinal disorders. Contact with iron lifters must be avoided in performing this test. Adami [3] considers that haemosiderin is deposited around the diplococcic form of the colon bacillus, described by him, in the liver cells. Bacterial haemolysis has been thought to account for haemosiderosis of the liver cells in ordinary cirrhosis (*vide* p. 207) and in haemochromatosis (*vide* p. 303). In haemochromatosis the liver cells also contain haemofuscin. Haemosiderosis of the liver is also seen after haemorrhage into the peritoneal cavity, in fatal purpura, and has been produced by experimental haemolysis; for example, by toluylenediamine (Meunier [4]). In some cases of new growth in the liver the hepatic cells in the neighbourhood of the growth shew haemosiderin. I have also seen it in lymphadenoma. In malaria the liver cells may contain

[1] Castaigne. Quoted by Chauffard, *Traité de Médecine* (Bouchard-Brissaud), v. 240, ed. ii, 1902.

[2] Abbott, M. *Journ. Path. and Bacteriol.*, Edin. and Lond., 1901, vii, 55.

[3] Adami. *Journ. Amer. Med. Assoc.*, 1899, xxxiii, 1506.

[4] Meunier. *Thèse de Paris*, 1897–8, No. 171.

haemosiderin, and it has also been described in association with suppuration. According to Biondi,[1] Kupffer's star-shaped cells take up haemosiderin.

Haematoidin.—This iron-free pigment is seen in and between the liver cells around the intralobular vein in chronic venous engorgement of the liver (*vide* p. 90.) It may also occur in the neighbourhood of haemorrhages, angiomas, scars of old abscesses, gummas, etc.

In the various forms of biliary obstruction the liver cells are degenerated and occupied by granules of *bile pigment.*

II. **Extrinsic Pigmentation.**—*In Anthracosis, Silicosis, etc.*—In rather rare instances particles of carbon or of other foreign substances have been found in otherwise normal livers; the liver of cirrhosis (*vide* p. 302) may shew impregnation with particles of carbon — cirrhosis anthracotica (Welch[2]); [Lancereaux[3] described this condition in copper-workers]; of stone (Adami[4]), and of silver after its medicinal use for epilepsy (Frommann[5]). Reference has been made elsewhere (p. 302) to a case of cirrhosis in a sweep with pigmentation, probably due to soot, of the fibrous tissue. These conditions are interesting curiosities, but have no clinical significance.

CALCIFICATION

This condition, which is a pathological curiosity, occurs in two forms—primary and secondary.

Primary calcification is very rare; it may occur in the liver cells, in the connective tissue, or in the walls of the vessels. In three cases this calcification was associated with chronic nephritis.

In a boy aged sixteen years who died with scarlatinal dropsy, Bristowe[6] found infiltration of the liver cells with an earthy salt which dissolved in acetic acid. In a boy aged seventeen years who died from chronic pulmonary tuberculosis and parenchymatous nephritis, Mihel[7] found that the liver, which grated under the knife and had the aspect of chronic venous engorgement, shewed calcareous infiltration of the liver cells around the intralobular veins. The infiltration appeared to be due to calcium phosphate. In a girl aged fourteen years who died with advanced interstitial nephritis the liver was found by Brill and Libman[8] to shew calcification with calcium phosphate around the branches of the hepatic artery, which was affected with endarteritis obliterans. The liver shewed chronic perihepatitis and chronic venous engorgement.

Babes[9] refers to a case, fatal from tuberculous disease of the hip, in

[1] Biondi. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1895, xviii, 174.
[2] Welch. *Johns Hopkins Hosp. Bull.*, 1891, iii, 32.
[3] Lancereaux. *Traité des maladies du foie et du pancréas*, p. 380, 1899.
[4] Adami. *Sajous' Annual*, 1898, ii, 313.
[5] Frommann. *Virchows Arch.*, 1859, xvii, 135.
[6] Bristowe, J. S. *Trans. Path. Soc.*, 1857, viii, 233.
[7] Mihel. Quoted *Phila. Med. Journ.*, 1901, vii, 199.
[8] Brill and Libman. *Journ. Exper. Med.*, N.Y., 1899, iv, 541.
[9] Babes. *Virchows Arch.*, 1886, cv, 511.

which the liver shewed areas of calcification, regarded as due to the deposit of salts absorbed from the affected bones. Sprunt [1] described calcification of the elastic tissue in the liver and spleen in a case of infective biliary cirrhosis due to a stone in the common duct. In a case of widespread calcification of the arteries and endarteritis associated with hydronephrosis in a child aged six months the hepatic artery was similarly affected, but the liver was microscopically healthy (Hale White and Bryant [2]). Though calcification of arteries in the liver is extremely uncommon in man, it is said not to be rare in horses.

In secondary calcification a deposit of calcareous salts occurs in inflammatory products of considerable age, such as gummas, the scars of cured abscesses, the walls of hydatid cysts, and in the walls of the gall-bladder as the result of past or chronic inflammation. A remarkable example of diffuse calcareous infiltration of the liver recorded by Targett [3] was probably secondary to syphilitic inflammation (*vide* Fig. 44).

Carrel [4] recorded a psorospermial tumour of the liver which underwent calcification. The tumour was removed in a laparotomy undertaken with the view that it was a calcified gall-bladder. Chemically the salts chiefly present were carbonate and phosphate of calcium.

Sometimes hard, coral-like masses, of about the size of a marble, are found embedded in the liver. They are probably the dried-up remains of biliary cysts or, in other words, intrahepatic calculi. Small bile cysts without any general biliary obstruction are occasionally seen; as time goes on their contents become more viscid and eventually solid. Small calcified masses with a fibrous capsule which represent the larvae of *Linguatula rhinaria* are not very rare in the liver (Kaufmann [5]).

LEUKAEMIC INFILTRATION

Synonym: Leucocythaemic Infiltration.

THE liver may be greatly enlarged in leukaemia, especially in the lymphocytic form; not uncommonly it weighs 5 or 6 pounds instead of $2\frac{1}{2}$, and may weigh much more; a weight of 13 pounds has been noted.

Murchison [6] described a case which, from the illustration given of the blood, was evidently myeloid leukaemia, with a liver that was smaller than natural, weighing 35 ounces. In the two following cases of myeloid leukaemia examined after death at St. George's Hospital the liver was much enlarged. The liver of

[1] Sprunt. *Journ. Exper. Med.*, N.Y., 1911, xiv, 59.
[2] Hale White and Bryant. *Guy's Hosp. Rep.*, 1901, lv, 17.
[3] Targett. *Trans. Path. Soc.*, Lond., 1889, xl, 123.
[4] Carrel. *Lyon méd.*, 1900, xciii, 89.
[5] Kaufmann. *Lehrbuch der spez. Path.*, 1907, S, 594.
[6] Murchison. *Diseases of the Liver*, p. 308, ed. ii, 1877.

a man aged twenty-six weighed 7½ pounds, and the spleen 6 pounds; scattered through both these organs were white spots resembling miliary tubercles, but due to dense infiltration with leucocytes. The liver of a woman aged twenty-seven weighed 10 pounds and the spleen 76 ounces. Together these two viscera occupied almost the whole of the front of the abdomen, a few coils of intestine only appearing above the pubes. There was no ascites. The enlargement of the liver was, contrary to what is usually seen, almost entirely of the right lobe and not of both lobes.

Morbid Anatomy.—The surface of the liver is pale and smooth. On section it is pale and may shew accumulations of leucocytes either in the larger portal spaces or in the substance of the liver. In rare instances there are pinkish white masses around the portal spaces; less rarely there are white spots exactly like miliary tubercles in the liver substance. Microscopically these are areas of dense leucocytic infiltration and not tuberculous granulation tissue. In the condition described as chloroma, which forms a connecting link between leukaemia and tumours, the portal canals have been found to be marked out as green tracks.

In a case of acute myeloid leukaemia there were tumour-like masses due to blood in the liver and spleen (Miller[1]).

Microscopically, the appearances are not always exactly alike. There may be a general and diffuse crowding of the capillaries with leucocytes with some increase at the periphery of the lobules; or there may be intense leucocytic infiltration around the portal spaces at the periphery of the lobules, with comparatively little blocking of the intralobular capillaries. When there is marked infiltration at the margin of the lobules the lobulation is clearly seen with the naked eye, and the microscopic appearances at first sight suggest interlobular inflammation, *e.g.* suppurative pylephlebitis. The leucocytes are chiefly large or small mononuclears; in myeloid leukaemia myelocytes are seen in the capillaries. The liver cells, especially in the centres of the lobules, may stain imperfectly, from degeneration depending on impaired nutrition, and may be fatty or atrophied. At the periphery of the lobule the hepatic cells are sometimes pigmented with haemosiderin and resemble the appearances in pernicious anaemia. On chemical analysis the amount of iron has been found to be increased. Milne[2] has observed extensive hyperplasia of the liver cells in lymphocytic leukaemia. Cirrhosis does not develop as the result of leukaemic infiltration, but Mosse[3] reported a case of lymphocytic leukaemia cured by *x*-rays, in which fatal cirrhosis followed and was thought to be due to damage done to the liver cells as a result of destruction of large numbers of leucocytes.

Clinical Features.—There is really nothing which can be specially correlated with leukaemic infiltration of the liver in a case of leukaemia

[1] Miller. *Journ. Path. and Bacteriol.*, Cambridge, 1912, xvi, 143.
[2] Milne. *Ibid.*, 1909, xiii, 131.
[3] Mosse. *Berlin. klin. Wchnschr.*, 1908, xlvi, 1219.

except the painless enlargement of the liver. Jaundice does not occur; in the latter stages of leukaemia ascites is not uncommon; it has been suggested that this may be due to pressure of leucocytic infiltration on the intrahepatic branches of the portal vein, or to pressure of enlarged glands in the portal fissure on the portal vein. But it seems more probable that it is due to some concomitant chronic peritonitis and to the cardiac debility and altered blood-state. It is conceivable that ascites might be in some degree determined by thrombosis in the terminal branches of the portal vein in the liver. The urine in a case of leukaemic

FIG. 56.—Liver in leukaemic infiltration. There is dense leucocytic massing around a vein and an excessive number of white blood-corpuscles in the capillaries. The liver cells stain badly. (Photomicrograph by Dr. S. G. Penny.)

infiltration of the liver was found to contain haematoporphyrin by Garrod,[1] who was inclined to regard this pigment as specially related to the hepatic change. The urine shews excess of uric acid.

The **diagnosis** of leukaemic infiltration of the liver depends on an examination of the blood. This should be done in a doubtful case of hepatic and splenic enlargement in order to prevent the disease being regarded as lardaceous or syphilitic and treated with iodide of potassium. In very acute leukaemia the liver may be tender as well as enlarged, and the fever and the severe constitutional condition may, if no glands are palpably enlarged, closely imitate hepatic abscess (Emerson[2]).

The **prognosis** and **treatment** are, of course, those of leukaemia.

[1] Garrod, A. E. *Lancet*, 1900, ii, 1323.
[2] Emerson. *Johns Hopkins Hosp. Bull.*, 1907, xviii, 80.

CYSTS

THE various forms of cysts which occur in the liver may be conveniently classified as follows:—

1. *Parasitic Cysts.*—Echinococcic or hydatid cysts (*vide* p. 391.)

2. *Cysts manifestly due to Biliary Obstruction.*—There may be widespread dilatation of the bile-ducts in the liver in long-standing biliary obstruction. The ducts stand out under the capsule and contain mucous fluid. This change is entirely secondary to the cause of the obstructive jaundice, such as carcinoma of the head of the pancreas, and will not be further discussed here. The effects of biliary obstruction may be more localised and give rise to definite cysts, which in exceptional instances may be of very considerable size; in North's[1] case a cyst containing five pints of coffee-coloured fluid was associated with a calculus impacted in the common bile-duct.

In a man aged thirty-nine who died in St. George's Hospital with jaundice supervening in the course of pancreatic diabetes complicated with rapid pulmonary tuberculosis, there were remarkably large intrahepatic calculi composed of bilirubin.[2] There were biliary cysts on the surface of the liver, with inflamed walls and fibrosis spreading outwards into the surrounding liver substance (*vide* Fig. 105). Merle[3] described cystic dilatation in a liver extensively tuberculous, presumably due to obstruction of the ducts.

3. A few words may be said about *cysts occurring in cirrhosis* of the liver. They are very rare and may arise in two distinct ways: (*a*) By biliary retention, and then resemble those just described; (*b*) by the softening down of the adenomatous masses seen in nodular cirrhosis. (*a*) These cysts are small, sometimes microscopic, and are only of pathological interest. The following is an example of macroscopic cysts:—

A woman aged forty-four years died with ascites and cirrhosis in St. George's Hospital. The liver, 41 ounces, was finely granular and shewed microscopically multilobular cirrhosis, passing in parts into unilobular cirrhosis. On the convexity of the right lobe near the falciform ligament there was a cyst the size of a hazel-nut with clear contents, and near it a dried-up cyst with thick walls and almost calcareous contents. The liver (Fig. 6) also shewed the effects of tight lacing.

Microscopic cysts or dilatations of the small bile-ducts are occasionally seen.

In making microscopic sections of a hobnailed liver weighing 41 ounces, I found dilatation of the bile-ducts in the portal spaces. This case shewed perihepatitis, chronic peritonitis, and small calculi in the gall-bladder, but there was no history or evidence of past biliary obstruction. (*See also* Fig. 34.)

[1] North. *Med. Rec.*, N.Y., 1882, xxii, 344.
[2] Rolleston. *Trans. Path. Soc.*, Lond., 1898, xlix, 133.
[3] Merle. *Arch. de méd. expér. et d'anat. path.*, Paris, 1909, xxi, 353.

(*b*) The adenomatous formations seen in nodular cirrhosis may soften down and form false cysts resembling those seen in degenerating new-growths; cysts due to degenerative changes in carcinoma and sarcoma of the liver are described on page 491.

4. *Simple Cysts.*—They are usually single or present in very small numbers; when there are a large number, the condition becomes that of cystic disease (*vide* p. 447). As a rule, the cysts are small and of no clinical importance. Larger simple cysts are sometimes met with. Probably some of those recorded are sterile hydatid cysts; microscopic examination of the cyst wall should decide the point. Cysts sufficiently large to contain many pints have been described.

In Bayer's[1] and Winckler's[2] cases there were 13½ pints, in Aldous',[3] 12 pints, and in North's, 5 pints of fluid.

Mode of Formation.—Simple cysts are usually regarded as due to retention from local obstruction of the bile-ducts. Bland-Sutton[4] suggests that the pressure exerted by the corset may lead to obstruction and dilatation of a bile-duct. Although in a fully developed stage they do not contain bile, they may do so in an early stage.

Thus, in a woman aged thirty-five years who died in St. George's Hospital in 1892, with peripheral neuritis and pulmonary tuberculosis, there was a small cyst containing bile in the left lobe of the liver.

The bile disappears from the cyst probably in the same way that it does in general biliary obstruction of long standing, and becomes replaced by clear albuminous fluid. It has been thought that a bile-containing cyst may be due to rupture of an intrahepatic bile-duct (Doran[5]). Other methods of origin have been suggested for simple cysts of the liver, such as dilatation of the glands of the larger bile-ducts or dilatation of aberrant bile-ducts (Moschcowitz, *vide* p. 454); the last view would explain the cysts as due to a congenital malformation. Again, some of the small single cysts with blood-stained contents may, as in the spleen, be the result of degenerative changes in angiomas. A large single cyst may be due to cystic change in an adenoma of the bile-duct, the papillomatous growth softening down in the same way as an adenoma of the thyroid.

Shattuck[6] reports such a cyst containing a gallon of clear fluid (*vide* p. 458).

Morbid Anatomy.—The cysts are commoner on the surface of the liver than in its substance, but they are seldom pedunculated; Doran refers to three large pedunculated cysts. A cyst, the size of a child's head, in the round ligament of the liver, described by Henderson,[7] was

[1] Bayer, K. *Prag. med. Wchnschr.*, 1892, xvii, 637.
[2] Winckler. Quoted by Doran.
[3] Aldous. *Brit. Med. Journ.*, 1911, ii, 688.
[4] Bland-Sutton, J. *Ibid.*, 1905, ii, 1167.
[5] Doran, A. *Med.-Chir. Trans.*, 1904, lxxxvii, 1.
[6] Shattuck. *Boston Med. and Surg. Journ.*, 1900, cxlii, 427.
[7] Henderson. *Ann. Surg.*, Lond., 1909, l, 550.

probably of a different nature from cysts in the liver. They are usually surrounded by a firm fibrous capsule which often contains numerous blood-vessels, and in cases of old standing may shew calcareous infiltration. The walls of recent cysts are thin. The inner surface is smooth, but is often ridged, possibly from the remains of partitions between originally separate cysts, and may resemble the inside of the auricles of the heart. It has an opaque white colour, except in very thin-walled cysts.

A typical specimen occurred in the liver of a man aged sixty-three who died of a thoracic aneurysm ; on the surface of the convexity of the liver, near the falciform ligament, there was a cyst the size of a hazel-nut, with traces of partitions but not completely multilocular. In a man aged seventy-eight years, who had granular kidneys with a few minute cysts, the liver, which otherwise appeared natural, contained four cysts ; three of them were on the surface of the liver, the other was deeply embedded in the substance of the right lobe ; it was the largest, and measured $\frac{3}{4}$ of an inch across. The contained fluid was straw-coloured and the walls were smooth.

The larger simple cysts must be distinguished from hydatid cysts by examination for hooklets and for laminated membrane, and during an operation the relations of the cyst must be noted in order to differentiate it from idiopathic dilatation of the extra-hepatic bile-ducts. The contents of these cysts vary considerably. They are usually clear and colourless, but may be bile- or blood-stained, green, reddish, or brown. From degenerative changes in the lining epithelium the contents may become syrupy, as in some renal cysts, and so dry up and form solid white encapsulated masses of small size. The fluid is albuminous and may contain blood or epithelial cells, haematoidin, bile pigment, cholesterin, tyrosine.[1] In Doran's case the cyst contained $2\frac{1}{2}$ pints of bile. It is probable that as the result of injury extravasation of blood or of bile may take place into a cyst with clear serous contents.

Microscopic Appearances.—The capsule is composed of laminated fibrous tissue which may contain bile-ducts, sometimes dilated, and occasionally blood pigment. The fibrous tissue invades the liver tissue for a very short distance, and is lined internally by a layer of epithelial cells which may be columnar, cubical, or polyhedral in the small cysts. In exceptional instances, of which Zahn[2] has collected 14 examples, the epithelium may be ciliated. In the larger cysts the cells are absent or much flattened.

Clinical Features.—Simple serous cysts are rarely large enough to give rise to signs or symptoms. When they do, the signs are usually like those of hydatid cysts, or occasionally of an ovarian cyst, and the treatment is the same. Rupture into the peritoneal cavity may occur, and when large, induce shock and collapse. In rare instances severe haemorrhage may occur into a large cyst and even prove fatal.

[1] Campbell M'Donnell. *Lancet*, 1900, i, 453.
[2] Zahn. *Virchows Arch.*, 1896, cxliii, 175.

Kilvington[1] mentions a case which died with symptoms like those of rupture of a large internal aneurysm, from haemorrhage into a large simple cyst of the liver.

Doran's[2] patient was markedly jaundiced.

Usually simple serous cysts are found accidentally at the autopsy, and more often in middle-aged persons. Durante[3] has met with one in an infant in whom there was no evidence of general cystic disease of the liver. Sharp[4] recorded a cyst containing three quarts of fluid in a boy aged seven years. Large cysts are more often seen in females than in males; in 10 cases 8 were females and 2 males.

Diagnosis.—When of such a size as to be palpable, they can only be distinguished from hydatid cysts by examination of the fluid (*vide* p. 405).

The *treatment* is excision of as much of the cyst wall as is possible; this can be carried out most successfully when the cyst is pedunculated. When embedded in the liver the cyst should be dealt with on the same lines as hydatid cysts.

Cyst of the Round Ligament.—A cyst the size of a child's head was removed from a man aged forty-one by Henderson.[5]

CYSTIC DISEASE

THE liver may be occupied by numerous cysts of varying sizes, and thus presents a contrast to the single or isolated cysts already referred to. This condition is spoken of as cystic disease of the liver.

Incidence.—From their age-incidence the cases may be divided into two categories—those seen in adult life and those found in the newly born—though it is probable that those seen in adult life are also congenital, but, being less marked, have survived.

Comparatively few cases have been reported in *newly born infants*; but the disease is doubtless often overlooked, as it may not be manifest until the liver is examined microscopically. I have seen two cases, in both of which the naked-eye appearances were rather those of fibrosis than of cystic disease. As some cases of cystic livers in infants have been associated with deformities, such as polydactylism, it is probable that if the livers of monsters and stillborn children were systematically examined microscopically, congenital cystic disease of the liver would be found to be less rare.

[1] Kilvington. *Intercolon. Med. Journ. Australasia*, 1902, vii, 557.
[2] Doran, A. *Med.-Chir. Trans.*, 1904, lxxxvii, 1.
[3] Durante. *Bull. Soc. Anat.*, Paris, 1902, lxxvii, 953.
[4] Sharp. *South African Med. Rec.*, 1906, iv, 39.
[5] Henderson. *Ann. Surg.*, 1909, l, 550.

Cases have been reported by Kanthack and myself,[1] Still (2),[2] Bar and Rénon,[3] Couvelaire,[4] Couvelaire and Porak,[5] Carré,[6] Brindeau and Macé,[7] Kilvington,[8] Bunting (2),[9] Sikes,[10] Meader.[11] In all these cases the kidneys were also markedly cystic. Borst[12] recorded a case in a child seven months old, Dudgeon[13] a case which was probably of this nature in a child of nine months in which the kidneys were normal; W. Müller[14] a case in a female child two years of age whose abdomen began to swell at ten months, and Batty Shaw[15] a case in a child aged three and a half years. These cases support the view that the less marked congenital cases may persist into adult life.

Possibly the case of a full-term child the subject of many abnormalities, including cystic kidneys, obliteration of the bile-duct, and communicating cysts, one in each lobe of the liver, belongs to this group; no microscopic examination, however, was made (Witzel[16]). Gueniot's[17] case may also belong to this category. A full-term fetus had 6 fingers and 6 toes, anencephaly, absence of external genitals, kidneys three times the normal size, and a cyst in each lobe of the liver; the cyst in the left lobe contained 40 grams and that in the right lobe 80 grams of clear fluid. This was the eighth child of a woman who married her nephew; none of the children, some of whom shewed abnormalities, survived.

Association with Cystic Disease of the Kidneys.—Real cystic disease of the liver is nearly always accompanied by a similar, and almost always more advanced, change in the kidneys. This association was first noted by Bristowe.[18] A few accidental cysts may occur in the liver without any similar change in the kidney, but this hardly constitutes cystic disease. In 85 cases the liver alone was affected in 10 (Moschcowitz[19]). Cystic kidneys not uncommonly occur without cystic disease of the liver.

In 63 cases of cystic kidneys collected by Lejars[20] 46, or 73 per cent, were free from cystic change in the liver. In 90 cases of congenital cystic disease of the kidneys Luzzatto[21] found 5 only in which the liver was similarly affected.

---

[1] Kanthack and Rolleston. *Virchows Arch.*, 1892, cxxx, 488.
[2] Still. *Trans. Path. Soc.*, 1898, xlix, 155.
[3] Bar et Rénon. *Compt. rend. Soc. Biol.*, 1894, xlvi, 835.
[4] Couvelaire. *Ann. de gyn. et d'obstét.*, 1899, lii, 453.
[5] Couvelaire et Porak. *Compt. rend. Soc. d'obstét. et de gyn. et de pédiat.*, Paris, 1901, p. 26.
[6] Carré. *Thèse de Paris*, 1901, No. 232.
[7] Brindeau et Macé. *Gaz. hebd. de méd.*, Paris, 1899, xliv.
[8] Kilvington. *Intercolon. Med. Journ. Australasia*, 1902, vii, 557.
[9] Bunting. *Journ. Exper. Med.*, N.Y., 1906, viii, 271.
[10] Sikes. *Brit. Journ. Child. Dis.*, 1906, iii, 304.
[11] Meader. *Johns Hopkins Hosp. Bull.*, 1907, xviii, 354.
[12] Borst. *Festschrift der phys.-med. Gesells.*, Würzburg, 1899.
[13] Dudgeon, L. *Trans. Path. Soc.*, 1903, liv, 296.
[14] Müller, W. *Virchows Arch.*, 1901, clxiv, 270.
[15] Shaw, H. B. *Lancet*, 1903, i, 1447.
[16] Witzel. *Centralbl. f. Gynäk.*, 1880, 561.
[17] Gueniot. *Bull. Acad. de Méd.*, Paris, 1891, xxv, 169.
[18] Bristowe, J. S. *Trans. Path. Soc.*, 1856, vii, 229.
[19] Moschcowitz. *Am. Journ. Med. Sc.*, Phila., 1906, cxxxi, 674.
[20] Lejars. *Thèse de Paris*, 1888.
[21] Luzzatto. Quoted by Boinet et Raybaud, *Rev. de méd.*, Paris, 1903, xxiii, 8.

Still[1] collected 35 cases of combined cystic change in the liver and kidneys, 3 being infants.

Concomitant cysts in other organs, such as the pancreas (Bunting (2), M'Crae[2]) and spleen (Blackburn, Peacock and Scott[3]) have been described in a few cases. I have seen the association of ovarian cysts and hydrosalpinges with cystic disease of the kidneys and liver, and of cystic disease of the liver and kidneys in a woman with acromegaly whose pituitary was represented by a large cyst.

Age.—Multilocular cystic disease is usually observed comparatively late in life, apart from the rare cases seen in infants. In 26 cases collected by Still, 17 were over fifty, and 4 over seventy, years of age; the youngest adult case was thirty-nine.

Sex.—Females are more often affected than males—according to Still, in the proportion of 3 to 1, 21 of his 28 cases being females.

Inheritance.—As in cystic kidneys, the disease may be hereditary and occur in several members of the same generation (Rolleston and Kanthack, Kilvington, Bunting).

Morbid Anatomy.—In congenital cystic disease in *infants* the liver is in a majority of the recorded cases little if at all enlarged, and may not present any naked-eye evidence of cystic change, or only a few minute cysts on the surface. In Porak and Couvelaire's case the liver was so large that it impeded delivery and had to be tapped before the fetus, which was greatly deformed, could be extracted. On section the portal spaces are prominent from fibrosis; a few cystic dilatations may appear, but most of them are microscopic. The naked-eye appearances are usually more suggestive of fibrosis than of cystic change. The larger bile-ducts and the gall-bladder are healthy. The contents of the cysts are clear and do not contain bile (*vide* p. 450).

In *adult* cases of cystic disease the liver may be very greatly enlarged, though this is not constant.

MacDonald[4] records a cystic liver weighing 14 pounds. A cystic liver in the Royal College of Surgeons Museum weighed 13 pounds 7 ounces, and in Roberts'[5] case the liver weighed 11½ pounds.

A cystic liver from an adult woman may shew the deformity of tight lacing (*vide* St. Bartholomew's Hosp. Museum, No. 2204 D).

The degree of cystic transformation is nearly always much less in the liver than it is in the kidneys. The kidneys are usually megalocystic, while the cystic liver is smaller in proportion. The cysts are, however, bigger than those seen in babies, probably from the union of several cysts originally separate. Their size varies very considerably; there may be many small ones, with one or more larger ones. When

[1] Still, G. F. *Trans. Path. Soc.*, 1898, xlix, 155.
[2] M'Crae, J. *System of Medicine* (Osler and M'Crae), 1909, vi, 36.
[3] Peacock and Scott. *Trans. Roy. Acad. Med. Ireland*, Dublin, 1909, xxvii, 317.
[4] MacDonald. *New York State Journ. Med.*, 1908, viii, 185
[5] Roberts. *Ann. Surg.*, 1894, xix, 251.

the liver is considerably enlarged there may be several as big as a walnut. In exceptional instances a very large cyst may be formed. In Cleaver's[1] case there were many small cysts and a single large one measuring 7½ inches in circumference.

The cysts appear on the surface of the organ and may thus give rise to considerable deformity. They are surrounded by a capsule of well-formed fibrous tissue. On section the liver is more or less honeycombed by independent cavities. The cysts usually contain clear albuminous fluid, which is sometimes brown, probably from haemorrhage, and may become colloid and inspissated like the contents of some cysts in megalocystic kidneys. They contain proteins, urea, chlorides, and sometimes blood and epithelial cells, cholesterin, oxalate of calcium, leucine, and creatinine,[2] but not bile. There is a considerable increase in the amount of fibrous tissue in the liver. The large bile-ducts and the gall-bladder are free from any special change. The association of tuberculosis of the liver with cystic disease has been described (Merle[3])

Fig. 57.—Section of cystic disease of the liver in an adult. (Photographed by Dr. H. Morley Fletcher.)

Microscopical Appearances. — In the cystic livers of *newly born infants* there are a number of tubules in the portal spaces which are lined with subcolumnar epithelium and are somewhat dilated. They closely resemble dilated bile-ducts, but are far more prominent and appear to be more numerous than the normal bile-ducts. In sections they may completely encircle the interlobular vein. From the portal space these dilated tubes can be traced into the interlobular tissue, and are accompanied by fairly well-formed fibrous tissue. These epithelial extensions between the lobules are at first somewhat dilated, but as they pass further away from the portal space they tend to become solid cylinders, and when cut obliquely, may appear to have more than one layer of lining cells. There are never any masses of bile in these tubes or cysts.

The fibrosis thus tends to be unilobular, with exaggerations around the larger portal canals ; there is no intercellular cirrhosis and no evidence of

[1] Cleaver. *Phila. Med. Journ.*, 1901, viii, 1139.
[2] Forbes, J. G. *St. Barth. Hosp. Rep.*, 1897, xxxiii, 207.
[3] Merle, P. *Arch. de méd. expér. et d'anat. path.*, Paris, 1909, xxi, 353.

congenital syphilis. In places blood is extravasated into the substance of the hepatic lobules. The liver cells are usually well preserved; exceptionally they shew vacuolation which is not due to fat, but may be explained as sections of dilated biliary capillaries which, having invaginated or indented the liver cells, give the impression of being inside the cells.

In the *adult form* the cysts are much larger, arise in the portal spaces, and are surrounded by well-formed fibrous tissue, while there may be numerous blood-vessels in the immediate neighbourhood. There is considerable fibrosis of the liver; Blackburn[1] described fibrous nodules due to the conversion of cysts into connective tissue. In the smaller cysts the epithelium is columnar, in the medium-sized cysts it becomes cubical or polyhedral, and in the larger ones it is degenerated, absent, or represented by a few flattened cells. In exceptional cases ciliated epithelium has been described in the cysts.[2] The bile-ducts in the liver are often dilated in parts, but this is not constant. The hepatic cells are, generally speaking, healthy, but have been found to shew the vacuolated appearance described in congenital cases.

FIG. 58.—Photomicrograph of congenital cystic disease of the liver. Shews portal space with increased quantity of well-formed fibrous tissue and with dilated tubes lined by columnar epithelium, which has separated from the walls in the process of hardening. The hepatic cells shew vacuolation. (By Dr. Harold Spitta.)

Pye-Smith[3] regarded this change as due to intracellular cyst formation and to be a degenerative process beginning long after adult life.

A point of interest is the connexion between congenital cystic disease and the similar anatomical condition more often met with in adults. They are so similar that it appears reasonable to regard the adult cases as congenital in origin, and to explain the survival by supposing that the change in the liver and kidneys is less extensive than in the rare cases fatal in infancy. Still regards cystic disease of the liver as a malforma-

[1] Blackburn, C. R. *Trans. Path. Soc.*, Lond., 1904, lv, 203.

[2] Lejars, *Thèse de Paris*, 1888, p. 34; Hanot et Gilbert, *Maladies du foie*, p. 295, 1888.

[3] Pye-Smith. *Trans. Path. Soc.*, 1881, xxxii, 112.

tion which is not progressive, and on this hypothesis it is obvious that, if the subject can survive the early effects, life may be prolonged for years.

The **pathogeny** of cystic disease of the liver has given rise to much discussion. It is so generally combined with a similar change in the kidneys that it is highly probable that the causal factor is the same in both. The following hypotheses bear on the causation of cystic disease of the liver.

Inflammatory Hypothesis.—The oldest view was that there was primary inflammation of the fibrous tissue surrounding the bile-ducts, which thus led to dilatation of the bile-ducts (Mihalkowicz,[1] Juhel-Renoy, Babinsky, Blackburn). The process might be described as one of pericholangitic inflammation leading to a biliary cirrhosis of the liver with dilatation of the bile-ducts. It might perhaps be possible to explain the process as a fairly acute cholangitic and pericholangitic inflammation during fetal life, which so weakens the walls of the small ducts that they then dilate and never recover their proper size, while the inflammatory products organise into firm fibrous tissue. Further, the inflammation might be followed by epithelial proliferation and the formation of new bile-ducts.

This explanation of the change in the liver is surrounded with difficulties. If it be regarded as biliary cirrhosis with subsequent dilatation, a form of "epithelial cirrhosis" analogous to cystic disease of the breast, the objection at once arises that in biliary and indeed in the other forms of cirrhosis dilatation of the ducts is extremely rare. A further objection is the absence of jaundice in cystic disease of the liver both in infants and in adults, whereas in congenital obliteration of the bile-ducts in which there is an intrauterine inflammation of the intrahepatic bile-ducts, practically identical with that postulated by this hypothesis, there is persistent jaundice. The absence of jaundice is rather surprising, whatever view is held as to the origin of the cysts, for if they are not obstructed ducts themselves but independent formations, the real ducts should be pressed upon. This, however, can hardly occur, for there is no bile-staining of the liver or accumulations of inspissated bile in microscopic sections of the liver. It is noteworthy that in the rare condition of chronic pericholangitis (*vide* p. 682), in which the bile-ducts must be compressed, there is no trace of jaundice either locally in the liver or elsewhere; it is possible that in both instances this anomaly depends on the lymphatics being obstructed so that bile cannot be absorbed.

Beale[2] injected the larger bile-ducts in Bristowe's case with Prussian blue and found that no injection passed into the cysts; from this he concluded that the formation of cysts did not depend upon closure of a part of the tube and the subsequent accumulation of secretion beyond this point. It is difficult to follow this argument, for if the cysts were due to retention, the injection would not be able to pass the obstruction and flow into the cysts. That injection does

[1] Mihalkowicz. *Thèse de Paris*, 1876.
[2] Beale, L. *Trans. Path. Soc.*, 1856, vii. 234.

not pass into the cysts does not, however, prove that the cysts are unconnected with the bile-ducts, for Barratt,[1] in experiments on normal livers, found that when the common bile-duct was injected, under pressures of from 45 to 300 mm. of mercury (the normal pressure under which bile is secreted being 10 to 20 mm. of mercury), with gelatin, none of the injection passed into the bile canaliculi.

Degenerative Hypothesis.—Pye-Smith,[2] described vacuolation of the liver cells, which by fusion with those formed by other cells led to the formation of cysts. This appearance may be seen in congenital cystic disease of the liver. The vacuoles are probably sections of dilated bile capillaries invaginating the liver cells. Pilliet[3] regards cystic disease as a result of atrophy of the liver, the liver cells becoming changed into newly formed bile-ducts and vasa aberrantia, which dilate into multiple cysts.

Hypothesis that the Cysts are a Tumour.—Rindfleisch[4] believed the cystic change to be a cystic sarcoma starting from the bile-ducts. A number of authors have regarded the changes in the ducts as of an adenomatous nature (Siegmund,[5] Nauwerk and Hufschmidt,[6] Workman,[7] v. Kahlden[8]). Malassez[9] and Claude[10] considered that the disease was cystic fibro-adenoma homologous with an ovarian cystadenoma. Claude regarded the cysts as dilated new bile-ducts and believed that the process had a special relation to arteriosclerosis. Sabourin[11] describes cystic disease of the liver as a cavernous biliary angioma, and regards it as due to irritation which leads to development of new bile-ducts from various sources, such as pre-existing bile canaliculi, possibly from their mucous glands or from vasa aberrantia. The ducts thus formed unite, anastomose, dilate, and lead to the formation of larger ones by the destruction and absorption of the intervening septa.

Developmental Hypothesis.—Still put forward an explanation on the same lines as Shattock's[12] view of the nature of cystic kidneys. According to the latter view, the mesonephros persists and its dilated tubules form the cysts, while the metanephros or real kidney is blended with and compressed by the fetal persistence. In the case of the liver, Still[13] supposes that some of the columns of hypoblastic cells forming part of the duodenal diverticulum develop irregularly and form the cystic tubes, while the bile-ducts proper develop in the ordinary way and can be seen in the portal spaces. The excess of fibrous tissue he regards as a

[1] Barratt, W. *Journ. Path. and Bact.*, 1898, v, 345.
[2] Pye-Smith. *Trans. Path. Soc.*, Lond., 1881, xxxii, 112.
[3] Pilliet. *Tribune méd.*, 1893.
[4] Rindfleisch. *Lehrb. d. path. Gewebeleh.*, S. 403.
[5] Siegmund. *Virchows Arch.*, 1889, cxv, 155 (1 plate).
[6] Nauwerk und Hufschmidt. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1893, xii, 1.
[7] Workman. *Glasgow Hosp. Rep.*, 1900, ii, 363.
[8] v. Kahlden. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1893, xiii, 291.
[9] Malassez. *Progrès méd.*, April 5, 1876.
[10] Claude. *Bull. Soc. Anat.*, Paris, 1896, lxxi, 117.
[11] Sabourin. *Arch. de physiol. norm. et path.*, Par., 1882, 2. s., x, 63, 213.
[12] Shattock, S. G. *Trans. Path. Soc.*, Lond., 1886, xxxvii, 287.
[13] Still. *Ibid.*, 1898, xlix, 155.

persistence of fetal mesoblastic stroma and not inflammatory. In other words, the change is a malformation, and is therefore not necessarily progressive. Hence if death does not occur in early life, the cystic change may be found as a persistent condition in the adult cases. The close association with cystic kidneys, also, according to Shattock's view, a malformation, is thus rendered intelligible. It is also significant that other malformations may coexist. Thus, in one case the remarkable association of polydactylism, occipital meningocele, and webbed toes was found; in another a misplaced kidney; in another an undescended testis;[1] and in several others polydactylism. These external malformations are not met with in adult cases, and are not constant in the cases fatal at birth. It may reasonably be supposed that the cases in which the developmental defects are comparatively slightly marked persist to adult life. Moschcowitz[2] described aberrant bile-ducts in the fibrous tissue of the portal spaces of cystic livers, which were not present in normal livers though they were in livers from cases with cystic kidneys. This observation might be considered to support Still's hypothesis. But my impression is that what Moschcowitz calls aberrant bile-ducts are the microscopic cysts of a cystic liver.

Some doubt has been expressed whether the change is more allied to a new growth or to a malformation, and possibly it may be regarded as having an intermediate position between these two processes. Most writers accept Still's explanation, but personally I am not convinced that this view is more tenable than that cystic disease of the liver is due to some special form of fetal cholangitis and pericholangitis.

Clinical Picture.—Cystic disease of the liver may be suspected in a patient with greatly enlarged and probably cystic kidneys who has vague uraemic symptoms and considerable enlargement of the liver. In rare instances the cysts in the liver may be so large as to imitate hydatid or ovarian cysts. In Schroeder's case the abdomen was so widely occupied by the cystic liver that double multilocular ovarian cysts were diagnosed. A single large cyst may imitate a dilated gall-bladder (Cleaver). In practically all cases symptoms pointing to the liver are absent, and death, if not due to some intercurrent affection, is from uraemia or cerebral haemorrhage.

In a woman, aged thirty-nine, who died under my care from rupture of a small aneurysm on the right vertebral artery, there were cystic kidneys, cysts in the liver, ovarian cysts, hydrosalpinges.

In Budd's[3] and Blackburn's[4] cases there was jaundice due to gall-stones. As far as I know, the adult cases do not shew malformations of the limbs.

The cystic kidneys may be felt in life and sometimes have been regarded as hydronephroses, or even as pyonephroses.

[1] Cases quoted by Still. *Trans. Path. Soc.*, Lond., 1898, xlix, 164.
[2] Moschcowitz. *Am. Journ. Med. Sc.*, Phila., 1906, cxxxi, 674.
[3] Budd. Quoted by Blackburn, *loc. cit.* p. 250.
[4] Blackburn. *Trans. Path. Soc.*, Lond., 1904, lv, 203.

A woman aged thirty-five was admitted into St. George's Hospital with pain of one week's duration on the left side of the abdomen, where a soft, obscurely fluctuating tumour could be felt in the region of the kidney. There was pus in the urine, but no fever or leucocytosis. There had been dragging pain in the back from time to time, and increased frequency of micturition, especially at night, for nine years. An exploratory operation shewed that both kidneys contained numerous cysts of considerable size, and that the liver also contained many cysts. A small piece of the liver containing some small cysts was removed. Microscopically I found that the cyst walls were composed of well-formed fibrous tissue and that in the immediate neighbourhood there was fibrosis around the portal spaces. No epithelial or other lining could be found in the cysts.

In the congenital case described by Kanthack and myself the infant, aged one month, was universally oedematous, had a large quantity of albumin in the urine, and was extremely drowsy, as if uraemic; and 3 previous children had died in a similar way soon after birth.

The **treatment**, if the condition be suspected, is that of chronic renal disease, the object being to prevent uraemia. Opening the cysts in the course of laparotomy has been done, but is useless, and should be avoided if the condition is recognised.

ADENOMA

THE subject of adenoma may be considered under the two heads of (I) single adenoma, (II) the so-called multiple adenomas which are nearly always associated with portal cirrhosis of the liver.

SINGLE ADENOMA.—An innocent encapsulated growth of epithelial cells may occur in the liver, but is decidedly rare; pathologically it is of great interest, but clinically it seldom attracts attention.

These adenomas may be divided according to their structure into: (I) those composed of liver cells; (II) those derived from the bile-ducts; (III) those due to the inclusion of adrenal "rests."

I. **Solitary Adenomas Derived from the Liver Cells.**—An adenoma composed of liver cells, apart from the multiple growths of this kind seen in association with cirrhosis, is rare. Such growths may be spoken of as "acinous adenomas" in contradistinction to those derived from the bile-ducts, or as "solitary adenomas" in order to distinguish them from multiple adenomas. They occur equally in the two sexes, and at any age, from six months to sixty-nine years (Barbacci [1]).

An adenoma, measuring 8 inches in diameter, in the left lobe of the liver gave rise to a tumour palpable during life in a patient in St. Thomas's Hospital.[2] A large adenoma, $6\frac{3}{4}$ inches in diameter, in a lardaceous liver

[1] Barbacci. *Clin. mod.*, Milano, 1900, vi, 297.
[2] *St. Thomas's Hosp. Rep.*, 1904, xxxiii, 83.

shewed the lardaceous change (Shattock [1]). Muir [2] described an adenoma measuring 4 × 3 × 3 inches in a girl aged nine years; it was composed of liver cells irregularly arranged; there were no bile-ducts; and Milne [3] an adenoma 3 inches in diameter in a child of six months. Mahomed [4] described a localised collection of cells surrounded by a fibrous capsule embedded in the liver which was "nutmeg"; the tumour did not share in this general change. I have seen a similar specimen. There is a specimen (2223*b*) of a single necrotic adenoma in St. Bartholomew's Hospital Museum. Specimens have also been described by Engelhardt [5] and others.

Possibly these tumours may be due to a piece of liver substance which was separated during fetal life from the main liver, becoming subsequently embedded in the organ. Small projections of liver substance, miniature lobes, are occasionally seen on the under surface of the liver; if these become implanted in the substance of the liver, the appearance of an encapsulated adenoma, composed of liver cells, would be produced.

Cristiani [6] refers to the existence of multiple nodules of hepatic tissue embedded under Glisson's capsule, which have been explained as congenital and due to the inclusion of tiny lobes. Pepere [7] supports the congenital origin of solitary adenoma and describes a case in which there were, in addition to one in the liver, innumerable minute encapsulated masses of liver tissue scattered over the peritoneum and omentum.

A simple adenoma is nearly always solitary; it is very rare that several are seen in the same liver. Multiple adenomas are nearly always accompanied by multilobular cirrhosis, and may be regarded as secondary to that condition and in the light of compensatory hyperplasias of the liver cells. A few examples of multiple adenoma without pre-existing cirrhosis are referred to on page 459.

In exceptional cases a solitary adenoma is found in a cirrhotic liver. Among twenty cases of solitary adenoma collected by Caminiti,[8] four were associated with cirrhosis (Jona,[9] Delaunay,[10] and two of his own). Possibly in some cases the association is a mere coincidence. Delaunay's case of a columnar-celled growth being probably of this nature. But in most cases it is probable that a "solitary adenoma" in a cirrhotic liver is only the initial stage of the multiple adenoma in cirrhosis. I have seen two cases bearing this interpretation.

[1] Shattock. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Path. Sect.), 153.
[2] Muir, R. *Journ. Path. and Bacteriol.*, Cambridge, 1908, xii, 303.
[3] Milne. *Ibid.*, 1909, xiii, 348.
[4] Mahomed. *Trans. Path. Soc.*, 1877, xxviii, 144.
[5] Engelhardt. *Deutsch. Arch. f. klin. Med.*, 1898, lx, 607.
[6] Cristiani. *Journ. d'anat. et physiol.*, 1891, xxvii, 271.
[7] Pepere. *Arch. per le sc. med.*, 1902, xxvi, 117.
[8] Caminiti. *Arch. f. klin. Chir.*, 1903, lxix, 630.
[9] Jona. *Gazz. d. osp.*, 1901, xxii, 88.
[10] Delaunay. *Bull. Soc. Anat.*, Paris, 1876, li, 241.

Morbid Anatomy.—The tumour, often the size of a walnut, projects from the surface of the liver usually from the right lobe. It is a yellowish or greenish white on section, and of the same consistence as normal liver, but usually does not share in any change, such as chronic venous engorgement, affecting the liver as a whole. It may shew much necrosis (Fig. 59). In the liver of a man with advanced pulmonary tuberculosis a single adenoma so closely resembled a tuberculoma that a microscopical examination was necessary to decide its nature. The presence or absence of a capsule depends on the rate of growth of the adenoma.

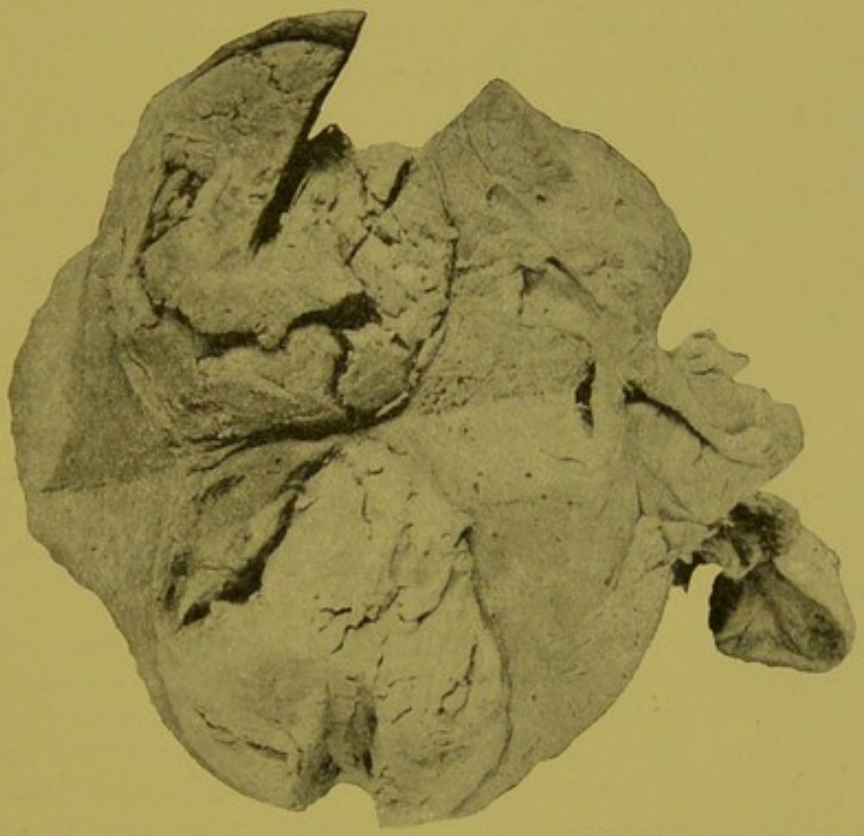


Fig. 59.—Large single adenoma of liver. (From a photograph kindly lent by Dr. I. Strauss.)

Microscopically the tumour is composed of liver cells which may, probably when the tumour is of some standing, be so modified as to form tubules lined by cubical epithelium; the structure approaches that of carcinoma with cirrhosis. Plugs of coagulated material containing bile-pigment may be present. The cubical character of the cells distinguishes this form of adenoma from the adenomas derived from the bile-ducts. In most cases the solitary adenoma derived from the liver cells is composed of cells of various sizes, but generally resembling liver cells. There is no definite arrangement, but there are capillaries and some strands of fibrous tissue running through the tumour.

II. Adenomas Derived from the Bile-ducts.—A papilloma springing from the inside of the extrahepatic bile-ducts would come under this heading, but is dealt with elsewhere (*vide* p. 687). Reference will be

made here to tumours arising from the intrahepatic bile-ducts, indenting and displacing, but not invading, the surrounding liver substance; they may be described as tubular adenomas lined by columnar cells. Cagnetto [1] described an adenoma with ciliated epithelium. It is possible that similar adenomas may be derived from the mucous glands in the walls of the larger bile-ducts. They may be single or multiple.

A *single adenoma* derived from the bile-ducts may become cystic; Leppmann [2] collected nine cases of this kind; such an adenoma may imitate malignant disease or hydatid cyst of the liver, a floating kidney, or an ovarian cyst (Kauffmann [3]). The nature of such tumors can only be determined by laparotomy. Cases of this kind have been recorded by Keen, Shattuck, Schmidt, Walker Hall and Brazil.[4]

Keen [5] removed a cystic adenoma, thought to be derived from the bile-ducts, from a woman aged thirty-one in 1891, who was alive in 1899. Clinically it simulated a floating kidney. Shattuck's [6] case is well worth quoting: A woman aged sixty-three presented a tumour reaching from the right costal arch to the iliac crest. It was smooth, not tender, and presented a fluctuating area in the centre. At the laparotomy a cyst containing a gallon of clear fluid was found and drained. After some time bile came away from the sinus. A second operation was followed by death from cardiac failure. At the necropsy the cyst arose from the liver near the falciform ligament and displaced the liver downwards. Microscopically the cyst wall contained numerous ducts and minute cysts, and it was regarded as a cystadenoma and not as a simple retention cyst.

It is quite possible that a large adenoma of the bile-ducts is sometimes regarded as primary carcinoma of the liver.

Peugniez [7] operated upon a woman aged fifty-nine for a tumour diagnosed as a gall-bladder; an encapsuled tumour the size of the fist was removed and the patient recovered. The tumour was regarded as a primary massive carcinoma of the liver, but the description and figures given are quite compatible with the view that it was a large adenoma of the bile-ducts, as in Keen's case.

Multiple adenomas derived from mucous membrane of the bile-ducts have been recorded (v. Hippel [8]). They may undergo cystic change, as in a remarkable case of Siegmund's [9] in a woman aged sixty-five. As has been pointed out (*vide* p. 453), multiple cystic disease of the liver was regarded by Malassez, Claude, and others as a fibro-adenoma of the bile-ducts.

III. Adenomas Due to Included Accessory Adrenals.—Schmorl,[10]

[1] Cagnetto. *Arch. per le sc. med.*, Torino, 1910, xxxiv, 495.
[2] Leppmann. *Deutsche Ztschr. f. Chir.*, 1900, liv, 446.
[3] Kauffmann. *Zentralbl. f. Gynäk.*, 1907, xxxi, 913.
[4] Walker Hall and Brazil. *Med. Chron.*, Manchester, 1903–4, xxxix, 243.
[5] Keen, W. W. *Ann. Surg.*, 1899, xxx, 267.
[6] Shattuck. *Boston Med. and Surg. Journ.*, 1900, cxlii, 427.
[7] Peugniez. *Bull. Soc. Anat.*, Paris, 1902, lxxvii, 456.
[8] v. Hippel. *Virchows Arch.*, 1891, cxxiii, 473.
[9] Siegmund. *Ibid.*, 1889, cxv, 155.
[10] Schmorl. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1891, ix, 523.

Oberndorfer,[1] Beer,[2] and Pepere[3] shewed that accessory adrenals are sometimes embedded in the liver. Schmorl found them in 4 out of 510 bodies, and Beer 6 times in 150. Encapsuled tumours of the liver derived from included suprarenal "rests" have been described by Schmorl and de Vecchi,[4] and it is probable that the development of simple adenomas in accessory suprarenals implanted in the liver is not very rare. Clinical symptoms are exceptional; Flemming[5] described a case in which an adenoma compressed the common bile-duct. Primary malignant tumours of the liver may arise in an accessory suprarenal (*vide* p. 481).

Multiple Adenomas of the Liver

Synonyms: Nodular Hyperplasia; Nodular Hepatitis; Hepatoma.

Multiple adenomas of the liver due to multiplication or hyperplasia of the liver cells are usually associated with cirrhosis of the liver, probably because cirrhosis is the commonest disease which destroys the liver cells and renders a compensatory hyperplasia necessary. Nodular hyperplasia may be met with in the absence of cirrhosis, as in some cases of malarial infection, in subacute atrophy, and in chronic venous engorgement of the liver.

A man aged thirty-seven died in St. George's Hospital in 1903 with advanced pulmonary tuberculosis and tuberculous peritonitis. The liver was at first thought to be stuffed with caseous tubercles. Microscopically these white areas were multiple adenomas; the liver shewed no cirrhosis.

As the result of injection of blastomycetes, Wlaeff[6] produced adenomatous tumours in the livers of guinea-pigs. J. Bartel[7] drew a distinction between multiple adenomas which are surrounded by a fibrous capsule, and nodular hyperplasia without any capsule.

Relationship of Multiple Adenomas and Cirrhosis.—Kelsch and Kiener,[8] and more recently Dieulafoy[9] and Engelhardt,[10] believe that the cirrhosis and the adenomas are due to the same poison and are the concomitant results of proliferation of the framework and of the cells of the liver respectively. In the Fuegians as the result of eating mussels, which at certain periods of the year contain a chemical poison, the liver is enlarged from hyperplasia of the cells and subsequently becomes cirrhotic (Segers[11]).

[1] Oberndorfer. *Centralbl. f. allg. Path. u. path. Anat.*, 1900, xi, 145.
[2] Beer. *Ztschr. f. Heilk.*, 1904, xxv, 381.
[3] Pepere. *Monitore zoolog. ital.*, 1903, xiv, 267.
[4] de Vecchi. *Virchows Arch.*, 1904, clxxvii, 133.
[5] Flemming. *Brit. Med. Journ.*, 1911, ii, 1475.
[6] Wlaeff. *Journ. de méd.*, Paris, 1901, p. 27.
[7] Bartel. *Wien. klin. Wchnschr.*, 1904, xvii, 613.
[8] Kelsch et Kiener. *Arch. de physiol.*, Paris, 1876, iii, 622.
[9] Dieulafoy. *Manuel de path. intern.*, 1901, ii, 734.
[10] Engelhardt. *Deutsches Arch. f. klin. Med.*, 1898, lx, 607.
[11] Segers. *Semaine méd.*, 1891, xi, 448.

Cornil and Ranvier,[1] Orth,[2] and Schmieden[3] regarded the adenomas as secondary to the cirrhosis. Brissaud[4] described multiple adenomas as a half-way house between cirrhosis and primary carcinoma, and the term "hepatoma" was suggested by Sabourin[5] to describe the transitional stage between adenoma and carcinoma. Lancereaux[6] and Marckwald[7] took the extreme view that cirrhosis was due to irritation set up by the presence of the adenomas.

There is some confusion in literature between cirrhosis with multiple adenomas and primary carcinoma with cirrhosis. It appears that Sabourin, who uses the former term, is sometimes describing cases which Hanot and Gilbert would call primary carcinoma with cirrhosis. The innocent condition of multiple adenoma in cirrhosis may eventually pass into primary carcinoma. When this occurs, there will be evidence of infiltration of the walls of the portal or hepatic veins, or of secondary growths in the lungs or elsewhere. Muir,[8] however, believes that no hard and fast line can be drawn between multiple adenomas in cirrhosis and primary carcinoma with cirrhosis, and that the first is potentially malignant from the outset.

Nature of Multiple Adenomas.—These multiple adenomas are usually associated with cirrhosis. Some reservation is necessary, since nodular hyperplasia or multiple adenomatous formations are found in other conditions (*vide* p. 459). The multiple adenomas ordinarily met with are exaggerations of the hobnails seen in portal cirrhosis, and represent a further stage of nodular hyperplasia. Multiplication of the more healthy liver cells occurs in common or portal cirrhosis and contributes to the size of the hobnails and to the increased weight of the liver in latent cirrhosis. It is when these hobnails undergo fatty degeneration and necrosis, and appear white on section, that they are particularly liable to attract attention, for when this change has occurred they do not, unless bile-stained, suggest cirrhosis, but resemble multiple new-growths or even caseous tubercles. Fatty change and necrosis of the hyperplastic nodules are particularly likely to occur when portal thrombosis complicates cirrhosis; hence the frequency with which portal thrombosis is recorded as associated with multiple adenoma, cancer with cirrhosis, etc. Thus in 15 cases of so-called adenoma of the liver analysed by Dr. Ll. Powell,[9] no less than 9 had thrombosis of the portal vein.

Those who regard the condition as one of primary carcinoma of the liver adduce the presence of hepatic cells in the portal vein and throm-

[1] Cornil et Ranvier. *Manuel d'histologie pathologique*, 1884, ii, 438.
[2] Orth. *Lehrbuch der path. Anat.*, 1887, quoted by Muir.
[3] Schmieden. *Virchows Arch.*, 1900, clix, 290.
[4] Brissaud. *Arch. gén. de méd.*, Paris, 1885, ii.
[5] Sabourin. *Thèse de Paris*, 1881; *Rev. de méd.*, Paris, 1884, iv, 321.
[6] Lancereaux. *Gaz. méd. de Par.*, 1868, 3. s., xxiii, 646.
[7] Marckwald. *Virchows Arch.*, 1896, cxliv, 29.
[8] Muir, R. *Journ. Path. and Bacteriol.*, Cambridge, 1908, xii, 287.
[9] Powell. Unpublished Thesis for M.B. Cantab., 1895.

bosis as further proof of its malignant character. But the presence of some hepatic cells in the portal vein does not absolutely prove that the growth is malignant, for the hobnails, being poorly nourished and having by rapid proliferation outgrown their blood-supply, soften down and may discharge into the portal or hepatic veins, and so induce thrombosis. Microscopic examination of the thrombus shews blood-clot with debris and large fatty liver cells.

Delépine[1] drew attention to this discharge of softened adenomas into the portal and hepatic veins, and F. C. Turner[2] described liver cells and fragments of liver tissue in the portal veins of cirrhotic livers and suggested that it was due to damage of the vessel walls by the infective process present in both his cases.

The proliferation of the liver cells is a compensatory process and occurs without the production of any transitional cells. When this process of regeneration is in progress, pseudobile canaliculi are usually prominent objects microscopically, and they have in the past been thought to be part of the compensatory process; but the general consensus of pathological opinion is adverse to this view.

Compensatory hyperplasia of the liver cells occurs in the most diverse conditions, which all have in common, interference with the functional activity or destruction of the liver cells. The effects of removal of portions of the liver in animals have been investigated by Tizzoni, Ponfick,[3] v. Meister,[4] Floeck,[5] Zadoc-Kahn,[6] and others; and Milne[7] has given a full account of the histology of regeneration of the liver in man. Proliferation begins and is most active, probably because nutrition is best there, in the liver cells at the periphery of the lobules.

When multiple adenomas in cirrhosis are seen at the necropsy of fatal cases of cirrhosis, the compensatory mechanism has in most cases broken down, and this is sometimes explained by thrombosis of the portal vein. The compensation may also be nullified by degenerative processes, fatty change, or softening in the hyperplastic hobnails, or by fibrosis spreading into them. No doubt the large size of livers in latent cirrhosis is partly due to this compensatory hyperplasia of the liver cells (see p. 196). Nodular cirrhosis is not very infrequent in cases fatal from pulmonary tuberculosis, and may be looked upon as a compensated cirrhosis. In such cases, if fatty degeneration attacks the hobnails, an appearance suggesting caseation results; it is quite possible that a naked-eye examination of the liver might result in a diagnosis of extensive tubercle or new growth of the organ.

[1] Delépine, S. *Trans. Path. Soc.*, Lond., 1890, xli, 362.
[2] Turner, F. C. *Ibid.*, 1884, xxxv, 22; and 1886, xxxvii, 262.
[3] Ponfick. *Virchows Arch.*, 1899, cxix, 193.
[4] v. Meister. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1893, xv, 1.
[5] Floeck. *Deutsches Arch. f. klin. Med.*, Leipz., 1895, lv, 397.
[6] Zadoc-Kahn. *Arch. gén. de méd.*, Paris, 1897, clxxix, 165.
[7] Milne. *Journ. Path. and Bacteriol.*, Cambridge, 1909, xiii, 127.

Morbid Anatomy.—The appearance of the liver is very striking and suggests multiple secondary new growths (*vide* Plate 5), gummas, or even caseous tubercle. The surface shews numerous projecting nodules, which, however, are not umbilicated. They are white on section, usually dry and friable, but may, especially when associated with portal thrombosis, be softened. The surrounding liver substance may be deeply congested, so that the contrast between the hobnails and the rest of the liver still further suggests secondary malignant disease. Adenomas in children with cirrhosis may be extremely prominent, and to the naked eye very closely resemble malignant disease; probably this active proliferation is part of a child's inherent power of repair and growth. The liver is usually enlarged, and sometimes to a very great extent. It is only rarely that it is actually smaller than natural. The conditions of hobnailed liver, nodular cirrhosis, and cirrhosis with multiple adenomas run into each other, and what one observer might speak of as extreme cirrhosis might by another be called cirrhosis with adenoma. The portal vein is frequently thrombosed, and microscopic examination of the clot may shew a few liver cells due to the discharge of one of the softened hobnails into the vein. Sometimes similar thrombosis is seen in the hepatic veins. The lymphatic glands in the portal fissure are not enlarged.

Microscopically the liver shews marked cirrhosis; the masses which to the naked eye suggest new-growth are altered liver cells surrounded by a fibrous capsule; the interstitial tissue contains pseudobile canaliculi and sometimes extravasated blood. In a hyperplastic nodule examined at an early stage the liver cells are larger than natural, in a good state of nutrition, with homogeneous protoplasm, and are undergoing proliferation, usually by direct nuclear division, but indirect nuclear division also occurs. This stage may be spoken of as nodular cirrhosis. In an early stage the naked-eye appearances are more striking than the microscopic. The first impression on looking at a microscopic section of nodular cirrhosis is often one of disappointment at finding little more than the changes of cirrhosis. The process of hyperplasia goes on in the periphery of the lobules. The liver cells around the "regeneration nodule" are often flattened from pressure and may become spindle-shaped. The normal arrangement of the hepatic lobule is lost, and tortuous columns of cells are seen which often tend to form irregular circles around the intralobular vein. The cells vary in size, some are smaller than normal, others are larger, and multinuclear cells are sometimes seen. Haemorrhage may occur into the adenomas or around them, and fatty change may appear in the cells forming the adenomas, especially when the portal vein is thrombosed. Fibrosis may extend into the substance of the adenomas.

Secondary Changes in Multiple Adenomas.—The fatty metamorphosis of the cells already mentioned may lead to softening down of the adenomas and the formation of the cystic spaces. The adenomas may discharge into the branches of the portal or hepatic veins and set up

PLATE V.

1

2

1. Surface of Liver with Nodular Cirrhosis.
The hobnails look like masses of secondary new-growth.

2. Section of Liver with Nodular Cirrhosis.
Shewing engorgement of fibrous tissue and white colour, due to fatty degeneration of the liver cells in the hobnails. Drawn by Dr. E. A. Wilson.

thrombosis. From vigorous proliferation of the cells in the adenoma the process may become carcinomatous (*vide* p. 474).

Clinical Aspect.—Since multiple adenoma is usually a result of cirrhosis, its age and sex incidence, its signs and symptoms, treatment, etc., are much the same as in that disease. It is found in a high proportion of cases of cirrhosis with thrombosis of the portal vein, and is therefore very frequently associated with ascites and haematemesis. An attempt has sometimes been made to establish a difference between the clinical features of ordinary cirrhosis and multiple adenomas, and the tendency has been rather to lay stress on the presence of hepatic pain and to present a picture approaching that of malignant disease of the liver. But no reliance can be placed on any such clinical differences. Hyperplastic tumours in subacute atrophy of the liver may reach a very large size; Barbacci [1] describes one as large as a fetal head; and Milne [2] mentions two cases in which operation for an abdominal tumor had been performed.

ANGIOMA AND CAVERNOMA

Synonym: Naevus.

An angioma or haemangioma is a true tumour with a new formation of arterioles; a cavernoma is a telangiectasis or dilatation of existing vessels; both occur in the liver (Adami [3]). The liver is more often the seat of these formations than any viscus in the body, but they are not very common in the liver; Lancereaux [4] saw 25 cases, and Adami 20 in 1400 necropsies. They are more frequent in the livers of cats. Hanot and Gilbert [5] say they are commoner in men, Thoma [6] that they are more frequent in women. They may be congenital and have been seen in fetuses, though this is exceptional. Veeder and Austin [7] collected 12 cases of solitary angiomas in infants, multiple angiomas are rarer. Usually they are found in old persons, and are then more probably acquired and may be due to a combination of local congestion of the hepatic vessels and atrophy of the liver cells. They are generally quite small. Large tumours are very occasionally seen.

In Fillipini's [8] case there was a tumour as large as an adult's head in the left lobe of the liver in a woman aged twenty-two. In Mantle's case [9] the

[1] Barbacci. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1901, xxx, 45.
[2] Milne. *Arch. Int. Med.*, Chicago, 1911, viii, 639.
[3] Adami. *Principles of Pathology*, 1911, ii, 488.
[4] Lancereaux. *Traité des maladies du foie et du pancréas*, 1899, p. 528.
[5] Hanot et Gilbert. *Études sur les maladies du foie*, p. 315, 1888.
[6] Thoma. *Pathology*, English Transl. by Bruce, i, 553, 1896.
[7] Veeder and Austin. *Am. Journ. Med. Sc.*, Phila., 1912, cxliii, 102.
[8] Fillipini. *Policlin.*, 1901; *Vide* Epitome, *Brit. Med. Journ.*, 1901, ii, No. 94.
[9] Mantle. *Brit. Med. Journ.*, 1903, i, 365.

tumour which had been growing for two years, in a man aged thirty-three years, was thought to contain 8 pints of blood.

They may be multiple, but more often are single. As many as 42 (Veeder and Austin) have been seen in the same liver. Of Schmieden's[1] 32 cases, 18 were single, 14 multiple. Angiomas may be found at the same time in other abdominal viscera and elsewhere.

In Payne's[2] case there were exceptionally large cavernous angiomas in the liver, which weighed 6 pounds, and angiomas in both ovaries and both adrenals; in Petroff's[3] case there were angiomas in the liver and in both adrenals. In Devic and Tolot's[4] case there were 30 angiomas in the liver, and others in the spleen, fat around the left kidney, mediastinum, left breast, skin of the back, and an angiosarcoma of the brain.

Morbid Anatomy.—They are usually immediately under the capsule, and often near the edge of the liver, on the convexity or in the neighbourhood of the falciform ligament. After death they become partially empty and are therefore slightly depressed below the level of the surrounding liver substance. In exceptional cases they are pedunculated. Lancereaux figures a pedunculated angioma attached to a liver which also contained other angiomas; and Journiac[5] also described this condition. They are round or wedge-shaped, with the base directed outwards and the apex inwards. On section they have a honeycombed appearance when the blood has been removed, like that of erectile tissue of the corpus cavernosum penis or of the placenta. They are dark red in colour; occasionally the surrounding liver substance is darkened by infiltration with blood pigment. They are sometimes encapsuled or encysted, and in connexion with this it is interesting to note that Berard[6] suggested that they were encysted splenic "rests." In large cavernous tumours there is usually a fibrous capsule; in smaller specimens there is often none, and the cavernous tissue is in immediate contact with the liver cells. The encapsulation is probably a secondary process, as in other innocent tumours. The capsule may shew calcification. The large angioma removed by Cripps[7] was so extensively calcified that until the microscopical examination it was thought to be an ossifying sarcoma. There is considerable difference of opinion as to the connexions of these tumours with the vessels in the liver; they have been said to be connected with the veins only, or to be in free communication with the hepatic artery and with the portal and hepatic veins (Virchow). Probably the blood supply varies in the different forms of angioma.

[1] Schmieden. *Virchows Arch.*, 1900, clxi, 373.
[2] Payne, J. F. *Trans. Path. Soc.*, 1869, xx, 203.
[3] Petroff. *Bolnich. Gaz. Botkina*, St. Petersb., 1899, No. 30; abstract in *Rev. de méd.*, Paris, 1901, xxi, 920.
[4] Devic et Tolot. *Rev. de méd.*, Paris, 1906, xxvi, 254.
[5] Journiac. *Arch. de physiol. norm. et path.*, Paris, 1878, 2. s., vi, 37.
[6] Berard. *Bull. Soc. Anat.*, Paris, 1828, p. 9.
[7] Cripps, W. Harrison. *Brit. Med. Journ.*, 1903, ii, 18.

There does not seem to be any tendency to malignant (endotheliomatous) change in them.

Besides the pigmented or "melanotic" and the encysted angiomas, another form is described—the fibrous angioma—in which the trabeculae increase markedly in thickness and thus lead to obliteration of the cavities or to its cure.

Histology.—The cavernoma, or ordinary hepatic blood-containing formation, shews a communicating meshwork of spaces containing red blood-corpuscles. The walls of the spaces are composed of fibrous tissue with some young connective-tissue cells and elastic fibres. Smooth

FIG. 60.—Drawing of cavernoma of the liver, shewing spaces containing coagulated blood with fibrous alveolar walls. It is encapsuled. × 21.

muscle fibres are described in some specimens. The spaces are lined by flattened endothelial cells covering the fibrous trabeculae. The structure is therefore that of cavernous tissue. The tumour may be separated from the liver cells by fibrous tissue which serial sections prove to be continuous with Glisson's capsule. In many specimens there is no limiting capsule and the blood-spaces are in direct contact with the liver cells. Bile-ducts and liver cells may thus appear to be embedded in the tumour. Pigment granules may be found in the fibrous trabeculae as well as in the surrounding liver cells; Hanot and Gilbert[1] give an illustration of this under the title of "melanotic angioma."

The haemangioma or true tumour may be entirely composed of newly formed arterioles.

[1] Hanot et Gilbert. *Études sur les maladies du foie*, p. 341, 1888.

Secondary Changes.—The blood may clot in the cavernous spaces and the endothelium may then creep over the remains of the clotted blood. When the blood-supply is interrupted by thrombosis, the cavernous tissue may become modified so as to contain serous fluid and imitate a lymph-angioma. In other cases the fibrous framework of the tumour may proliferate and compress and eventually obliterate the blood-spaces; in other instances hyaline degeneration may occur in the fibrous stroma.

Pathogeny.—As already mentioned, two forms occur in the liver: (i) The cavernoma, which is the commonest, due to dilatation of existing blood channels. This is due to congestion of the liver and atrophy of the hepatic cells. These telangiectases are usually acquired, and are seen in the atrophied livers of old persons; but some are congenital. (ii) Angioma or haemangioma, a real tumour or blastoma, due to the new formation of arterioles. They shew proliferation and power of independent growth.

Clinical Aspect.—In the majority of cases no symptoms can be ascribed to the presence of angiomas in the liver. It has been suggested that murmurs or venous hums heard over the hepatic region are sometimes produced in this way. In exceptional examples they have reached a considerable size (Steffen,[1] Chervensky,[2] Mantle, Cripps,[3] McWeeney).

In Petroff's[4] case of a woman aged thirty-eight years with symptoms of Addison's disease, jaundice was found to be due to the pressure exerted by a large angioma of the liver on the bile-ducts. There were cavernous angiomas in both suprarenals. In Tédenat's[5] case a fibrous angioma compressed the right hepatic and the cystic ducts and gave rise to jaundice, colic, and distension of the gall-bladder.

In some cases the condition has been diagnosed as hydatid or merely as a doubtful tumour of the liver.

I am indebted to Dr. Seymour Taylor for the notes of a man with a tumour in connexion with the liver which closely imitated a hydatid cyst; it was operated upon, and when exposed, still resembled a cyst; on puncture it bled profusely at every point. The patient left the hospital well.

In Sheppard's[6] case there was marked ascites, probably due to the angioma. Intraperitoneal haemorrhage from rupture of a large hepatic cavernoma has been reported (Roggenbau[7]). McWeeney's[8] case was fatal from haematemesis, for which no cause could be found.

The **prognosis** is fairly good in the cases which are operated upon, which are the only ones which can be diagnosed with certainty during life.

Treatment.—As it is only exceptionally that hepatic angiomas give

[1] Steffen. *Jahrb. f. Kinderh.*, 1882, n.f., xix, 348.
[2] Chervensky. *Arch. de physiol.*, 1885, ii, 553.
[3] Cripps, W. Harrison. *Brit. Med. Journ.*, 1903, ii, 18.
[4] Petroff. *Bolnichn. Gaz. Botkina*, 1899, No. 30; Abstract in *Rev. de méd.*, Par., 1901, xxi, 920.
[5] Tédenat. *Arch. gén. de méd.*, Paris, 1904, i, 579.
[6] Sheppard. *Bristol Med.-Chir. Journ.*, 1907, xxv, 46.
[7] Roggenbau. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1910, xlix, 313.
[8] McWeeney. *Journ. Path. and Bacteriol.*, Cambridge, 1912, xvi, 401.

rise to any signs or symptoms, the question of treatment rarely arises. As the presence of a large angioma would imitate a tumour of the liver, the only method of treatment is surgical, but there is considerable danger of profuse haemorrhage. If the tumour was thought to be an angioma, electrolysis might be tried. Keen,[1] in a list of 75 cases in which resection of the liver has been done for neoplasms, refers to 4 cases of angioma thus treated. In 1904 Tédenat quoted 6 cases in which excision had been carried out.

OTHER INNOCENT TUMOURS

Lymphangioma.—Maresch [2] described a pedunculated lymphangioma, diagnosed as an ovarian cyst, which was removed from the right lobe of the liver of a girl aged five years. It is conceivable that a tumour of this kind might result from degenerative changes in an angioma of the liver.

Myxoma.—A very large growth in the liver of a patient who had previously had a tumour removed from the breast by Nunn,[3] was described by the Morbid Growths Committee of the Pathological Society as a myxoma. Though probably a myxo-sarcoma, this specimen has often been referred to as a myxoma of the liver. A few other cases of myxoma have been described, but it seems probable that they are allied to sarcomatous rather than to innocent tumours. Cornil and Cazalis [4] described a primary myxoma in the liver of a child of nine months.

Fibroma of the liver has been described in a few cases, but caution must be exercised in accepting their existence. In infants this condition may be a manifestation of congenital syphilis and belongs to the group of cases described by Marchand.[5] Luschka's [6] case of fibroma in a child one month old was probably of this nature. It is possible that other cases would be more correctly described as fibro-sarcomas. It is conceivable that an angioma might undergo fibrotic atrophy and eventually form a small fibrous tumour. Small fibromas, like those seen in the medulla of the kidney, occur in the liver and enclose bile-ducts; Genewein [7] considers that they are not tumours in the ordinary sense of the term but fetal malformations, and speaks of them as hamartoma fibrocanaliculare.

Lancereaux [8] described a fibroma infiltrated with calcareous salts, in a woman aged twenty-eight years. On the under surface of the right lobe of the liver of a woman aged fifty-six Chiari [9] found a fibroma the size of an egg.

[1] Keen. *Ann. Surg.*, 1899, xxx, 276.
[2] Maresch, R. *Ztschr. f. Heilk.*, 1903, xxiv, 39.
[3] Nunn, T. W. *Trans. Path. Soc.*, Lond., 1873, xxiv, 120.
[4] Cornil et Cazalis. *Compt. rend. Soc. Biol.*, Paris, 1874, 5. s., iv, 22.
[5] Marchand. *Centralbl. f. allg. Path.*, 1896, vii, 273.
[6] Luschka. *Virchows Arch.*, 1858, xv, 168.
[7] Genewein. *Ztschr. f. Heilk.*, Wien u. Leipz., 1905, xxvi (*Abt. path. Anat.*), 430.
[8] Lancereaux. *Atlas d'anat. path.*, 1871.
[9] Chiari. *Wien. med. Wchnschr.*, 1877, xxvii, 365.

Four calcified fibromas, varying in size from a nut to a grain of wheat, were found in the liver of a tuberculous woman (Pisenti [1]). In a case of multiple neurofibromas the sympathetic nerves in the liver were beset with fibromas from the size of a bean to that of a millet seed (Ziegler [2]).

Lipoma.—Genuine fatty tumours do not occur in the liver. But what might be spoken of as a lipoma may be found indented on the surface, but outside the capsule, of the liver: these small tumours are in reality appendices epiploicae which have become detached from the colon and have come to rest between the diaphragm and the convexity of the liver.[3] I have seen several examples of this condition. An encapsulated mass of fat of about the size of a nut is found in a depression on the convexity of the liver, which it tightly fits. The capsule of the liver passes between the fatty body and the liver substance and there is no vascular connexion between the fatty tumour and the liver.

Localised areas of extreme fatty change in the liver cells are sometimes met with; they probably depend on vascular obstruction and microbic activity, and are not likely to be mistaken for real fatty tumours. Turnbull and Worthington [4] describe areas of atypical liver tissue, probably congenital anomalies, under the capsule, which are prone to fatty change. The fat which accompanies the obliterated umbilical vein in the falciform ligament sometimes increases in size so as to resemble a small fatty tumour. I have seen this in a woman who died after herniotomy.

Embryomas and teratomas are extremely rare in the liver.

Hanot and Gilbert [5] refer to a cyst in the liver containing hair, cartilage, and fatty material. In a baby aged six weeks Misick [6] found a lobular tumour the size of a man's fist in the right lobe of the liver; it contained bone, cartilage, and cysts derived from the hypoblast, but no epiblastic elements, so it should be described as a teratoma rather than a dermoid cyst. During life it was thought to be a tumour of the right kidney. Pye-Smith [7] described a teratoma adherent to, but not arising from, the liver in an infant one year old. During life the tumour had been tapped several times and the disease was regarded as cystic disease of the liver. It was an included fetus. Somewhat similar cases have been described by Philipp [8] and v. Hippel.[9]

The secondary implantation on the surface of the liver of fragments of a ruptured ovarian embryoma, which is not a malignant metastasis, has been described.[10]

[1] Pisenti. Quoted by Pepere, *I Tumori maligni primarii del fegato*, p. 25, 1902.
[2] Ziegler. *Special Pathological Anatomy*, translated by Macalister, part ii, p. 342, 1884.
[3] Rolleston. *Trans. Path. Soc.*, Lond., 1891, xlii, 160.
[4] Turnbull and Worthington. *Arch. Path. Inst. London Hosp.*, 1908, ii, 52.
[5] Hanot et Gilbert. *Études sur les maladies du foie*, p. 295, 1888.
[6] Misick. *Journ. Path. and Bacteriol.*, 1898, v, 128.
[7] Pye-Smith. *Trans. Path. Soc.*, 1886, xxxvii, 499.
[8] Philipp. *Jahrb. f. Kinderheilk.*, 1908, lxviii, 353.
[9] v. Hippel. *Virchows Arch.*, 1910, cci, 326.
[10] Hulke, *Trans. Path. Soc.*, 1873, xxiv, 157; Latham, *ibid.*, 1899, l, 232.

MALIGNANT TUMOURS

THIS subject will be considered in the following order: First the incidence and a detailed account of the morbid anatomy of primary malignant disease; then the incidence and a detailed description of the morbid anatomy of secondary malignant disease; thirdly, the general clinical picture; and, then, the points of distinction between the clinical manifestations of primary and secondary malignant disease of the liver.

PRIMARY MALIGNANT TUMOURS

Incidence.—Primary malignant tumours of the liver are rare. Every case requires critical post-mortem investigation to make sure that it is not secondary to some obscure growth elsewhere, and that the tumour did not, in reality, start in the gall-bladder or larger bile-ducts.

In 18,500 necropsies at Guy's Hospital, Hale White [1] found 24 cases of primary carcinoma of the liver, or 0·13 per cent. Eggel [2] estimates that primary carcinoma occurs once in 2000 necropsies, or 0·05 per cent.

The numerical ratio between primary and secondary carcinoma of the liver has been placed between 1:20 and 1:40 (*vide* p. 487).

Primary sarcoma, in which endothelioma is included, of the liver is rarer even than carcinoma.

Leith [3] collected 25 cases in 1897. In 1901 Vecchi and Guerrini [4] critically examined 45 published cases of primary sarcoma of the liver, but only accepted 21 cases as undoubted examples of this rare condition. I have notes of 64 cases of reputed primary sarcoma, of which 32 occurred in patients over ten years of age and 32 under that age. These cases do not include those described as primary melanotic sarcoma (*vide* p. 485) or any which were probably examples of hepatitis due to congenital syphilis.

Sex.—Primary malignant disease of the liver seems to be more frequent in men than in women, and contrasts with primary carcinoma of the gall-bladder, which, like gall-stones, is infinitely commoner in women—gall-stones and carcinoma of the gall-bladder being both about four times more frequent in women than in men.

In 74 cases of primary malignant disease in adults (42 carcinoma, 32 sarcoma) which I have collected, 42 were males and 32 females. The male sex was more often affected by carcinoma; of the 42 cases, 29 being males and 13 females. In Eggel's collection of 163 cases of primary carcinoma 63 per cent were males. Among my 32 cases of primary sarcoma 19 were females and 13 males.

---

[1] Hale White. *System of Medicine* (Allbutt and Rolleston), 1908, iv, part i, 215.
[2] Eggel. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1901, xxx, 506.
[3] Leith. *Lancet*, 1897, i, 170.
[4] Vecchi and Guerrini. *Med. News*, N.Y. 1901, lxxix, 816.

Age.—Primary carcinoma of the liver occurs in or after middle life and is rare before forty years of age.

In 42 cases of primary carcinoma (males 29, females 13) the average age was 47·2 years, being 42·1 among the females and 49·3 among the males. In Eggel's 163 cases the average age of the males was 53·11 years, and of the females 52·23.

The earlier observers described cases of cancer or "scirrhus" in very young children, but most of them were probably sarcomatous or due to congenital syphilis.

Prescott[1] recorded a congenital carcinoma of the left lobe of the liver in an infant of five months, and Miller and Cleland[2] cases of primary carcinoma in male infants aged nine and seven months; but it is probable that these cases were endotheliomas.

In older children portal cirrhosis with multiple adenoma very closely resembles carcinoma. H. Fussell and Kelly's[3] case of primary carcinoma in a girl aged sixteen years was regarded by Welch and Dock in this light.

Dr. Still has given me sections of a child's liver which looked exactly like malignant disease to the naked eye, but microscopically shewed cirrhosis with compensatory hyperplasia of the liver cells. Out of 29 reported cases of primary carcinoma of the liver in children, Philipp[4] accepts as genuine 12, namely, those of Koltmann, Wulff, Pye-Smith, Birch-Hirschfeld, Engelhardt, Acland and Dudgeon, Schlesinger, Grawitz, Burt, Mattirolo, Plant, Lubarsch. Since then cases have been reported by Weaver,[5] Karsner (2),[6] and Mair. This making 16 in all. Primary carcinoma in a woman of twenty-two was recorded by Gilbert and Claude.[7]

Primary sarcoma may occur at almost any age. The oldest case to which I have a reference was seventy-three years, while congenital cases have been recorded. Primary sarcoma of the liver may, like sarcoma of the kidney, be divided into two categories: (*a*) those which occur in adult life and (*b*) those met with very early in life.

The average age of 32 cases occurring in patients over fifteen years of age was 47·53 years (males, 51·6 years; females, 44·7 years), or exactly the same as the average age for primary carcinoma of the liver. In addition to these 32 cases I have tabulated 32 cases of primary sarcoma of the liver under ten years of age.

In 1883 Picot[8] collected 424 cases of malignant disease occurring under seventeen years of age; there were 13 of primary malignant disease of the

[1] Prescott. *Boston City Hosp. Rep.*, 1895, 6. s., 245.
[2] Miller and Cleland. *Arch. Path. Inst. London Hosp.*, 1906, i, 5.
[3] Howard Fussell and Kelly. *Univ. Med. Mag.*, Phila., 1895, vii, 838.
[4] Philipp. *Ztschr. f. Krebsforschung*, Berl., 1907, v, 326.
[5] Weaver. *Guy's Hosp. Rep.*, 1909, lxiii, 225.
[6] Karsner. *Arch. Int. Med.*, Chicago, 1911, viii, 238.
[7] Gilbert et Claude. *Arch. gén. de méd.*, 1895, clxxv, 513.
[8] Picot. *Rev. méd. de la Suisse Rom.*, 1883, iii, 660.

liver. R. Williams [1] referred to 29 cases of primary malignant disease of the liver under the age of fifteen years, the majority of which were probably sarcomatous. Noeggerrath [2] described a case of primary malignant disease of the liver in a baby which interfered with delivery; a congenital case was also observed by Jacobi.[3]

In connexion with sarcoma occurring in early life a caution must be thrown out as to the error of regarding as sarcoma the lesions of congenital syphilis. Cases of intercellular cirrhosis in infants have been described as primary sarcoma and lymphosarcoma. A diffuse intercellular cirrhosis in fetal life is, like sarcoma, an embryonic connective-tissue growth, so that the two processes have much in common. Severe visceral syphilis in early life may give rise to haemorrhagic enlargement of the suprarenals. Such a case might be regarded as sarcoma of the liver with secondary growths. The presence or absence of the *Treponema pallidum* will decide the question. Secondary growths in the adrenals may occur in primary sarcoma of the liver (Guy's Museum, No. 1571). There appears to be a group of cases, with growths in both the liver and adrenals, in which it is difficult to determine the site of the primary tumour. Pepper [4] collected 6 cases of congenital sarcoma of the liver and adrenals.

Etiology.—This is not the place to discuss the large and unsettled problem as to the true cause of malignant disease or to consider the "parasitic" or "habit of growth" hypotheses on the question. There is, however, one form of primary carcinoma in the liver, namely, that which develops in a previously cirrhotic liver, which favours the view that carcinoma is due to the acquired habit of proliferation of the liver cells, which, starting as a compensatory hyperplasia and thus giving rise to multiple adenoma in cirrhosis, eventually becomes so excessive as to constitute carcinoma.

In a few cases a definite history of a blow on the abdomen preceding the onset of malignant disease is forthcoming and may possibly have played some part in starting cellular proliferation.

Morbid Anatomy.—*Situation of the Growth in Primary Malignant Disease of the Liver.*—Primary malignant disease of the liver usually arises in the right lobe, but occasionally is limited to the left lobe.

As a curiosity, reference may be made to malignant disease arising in a tongue-like lobe. In a case of calculous cholecystitis and pericholecystitis the pendulous lobe in connexion with the gall-bladder was found to be the site of primary carcinoma; at first sight it was thought to have started in the gall-bladder, but Roux [5] satisfied himself that this was not the case.

On the other hand, the growth may infiltrate both lobes, so that it

[1] Williams, R. *Lancet*, 1897, i, 1328.
[2] Noeggerrath. *Deutsche Klinik*, 1854, vi, 496.
[3] Jacobi. *Therapeutics of Infancy and Childhood*, p. 371, 3 ed., 1903.
[4] Pepper. *Am. Journ. Med. Sc.*, 1901, cxxi, 287.
[5] Roux. *Rev. méd. de la Suisse Rom.*, 1897, xvii, 114.

is impossible to decide where it started, or there may be multiple primary growths in both lobes.

The morbid anatomy will be considered under the two heads of Primary Carcinoma and Primary Sarcoma.

Forms of Primary Carcinoma.—It will be most convenient to consider seriatim the morbid anatomy of the various forms of carcinoma which may arise primarily in the liver.

I. **Primary Massive Carcinoma (Synonym : "Cancer en Amande")** (Hanot and Gilbert).—There is a large white or yellowish tumour which expands the liver like a shell around it. The surface of the liver is usually smooth ; but in some cases the growth may project or there may be irregularities from secondary growths ; in the latter event there may be adhesions between the liver and adjacent structures, such as the diaphragm and stomach. The growth is more or less localised, and forms a mass as big as a cocoanut or the fetal head. There may be secondary growths in the liver. It usually starts in the right lobe, but in rare instances in the left lobe. According to Eggel, this form constitutes 23 per cent of the cases of primary carcinoma.

Fig. 61.—Photomicrograph of section of diffuse carcinoma of the liver. Shews a large quantity of hyaline fibrous tissue and groups of epithelial cells. (By S. P. Mummery, Esq.)

Structurally it is usually a polyhedral- or spheroidal-celled carcinoma of rapid growth, springing from the liver cells, or possibly from the cubical epithelium of the smaller bile-ducts. It has been suggested that embryonic relics derived from the duodenal diverticulum may be the starting-point of the growth. Exceptionally the growth is a columnar-celled carcinoma and has then arisen in connexion with the larger intra-hepatic bile-ducts.

Hanot and Gilbert[1] figure a giant-celled form of carcinoma in which the

[1] Hanot et Gilbert. *Études sur les maladies du foie*, p. 30, 1888, Paris.

largest cells measured as much as 100 μ. Sokoloff[1] and Cagnetto[2] described cases with ciliated epithelium. C. Powell White[3] described a primary carcinoma of the liver which softened down into a large cyst containing straw-coloured fluid ; some of the cells measured 30 to 40 μ in diameter. A primary carcinoma of the liver resembling a chorion-epithelioma has been described (Cruickshank and Teacher[4]).

The fibrous stroma may shew hyaline change, but does not contain elastic fibrils (Wrench).[5]

II. **Primary Infiltrating or Diffuse Carcinoma.**—In this form the growth is diffuse, and extends more widely than in the previous category. The tumour may be comparatively slow growing and so hard as to simulate cirrhosis. The whole of one lobe may become transformed into a hard yellow growth ; in such cases the liver may not be larger than natural.

Hilton Fagge[6] described such a case in which the liver weighed 36½ ounces and another weighing 62 ounces, but in his third case it weighed 186 ounces, and in Lee Dickinson's[7] case, 102 ounces.

It may, however, be rapidly growing and soft, and extend throughout the whole of the liver, uniformly enlarging it.

The liver of a man aged sixty-four had a uniform hobnail appearance and on section was universally altered. It weighed 151 ounces and microscopically shewed a rapidly growing spheroidal-celled carcinoma.[8]

Structurally, the infiltrating form of carcinoma of the liver is nearly always spheroidal-celled, though a few cases shew a transition from a columnar-celled to a spheroidal-celled type. In the hard forms the epithelial cells may be scanty and embedded in wide tracts of fibrous tissue, which may shew advanced hyaline change. This is the rarest form of primary carcinoma of the liver. Eggel estimated that it occurred in 12 per cent of the cases.

III. **Nodular or Multiple Primary Carcinoma.** — The appearance of the organ is like that seen when it is occupied by secondary growths, the difference being that there is no primary growth.

It is quite possible that in some instances multiple adenomas with cirrhosis have been regarded as this form of multiple primary carcinoma, since the naked-eye resemblance is very close. In other cases it is possible that one of the multiple nodules was primary and that the others are secondary, but have grown more rapidly and so come to rival it in size. It is conceivable that these multiple primary carcinomas may in some

[1] Sokoloff. *Virchows Arch.*, 1900, clxii, 1.
[2] Cagnetto. *Arch. per le sc. med.*, Torino, 1910, xxxiv, 495.
[3] White, C. P. *Brit. Med. Journ.*, 1899, ii, 1347.
[4] Cruickshank and Teacher. *Journ. Path. and Bacteriol.*, Cambridge, 1910, xiv, 282.
[5] Wrench. *Arch. Middlesex Hosp.*, 1905, v, 80.
[6] Hilton Fagge. *Trans. Path. Soc.*, Lond., 1877, xxviii, 137.
[7] Dickinson, L. *Ibid.*, 1894, xlv, 87.
[8] Rolleston. *Ibid.*, 1894, xlv, 92.

instances be due to proliferating cells derived from a focus in the mucous membrane of the alimentary canal, which, though irritated, does not shew any carcinomatous growth. As an example of "secondary growths without any primary focus" attention may be called to the fact that squamous-celled carcinoma may arise in the inguinal glands of sweeps whose scrota, though covered with warts from the irritation of soot, do not shew any definite carcinomatous growth (Butlin [1]).

This is the most frequent form of primary carcinoma of the liver. In Eggel's [2] collection of 163 cases it occurred in 104, or 64 per cent. In 41 cases from the Middlesex Hospital, however, it occurred in 15 or 36·5 per cent (Colwell [3]). The multiple tumours grow rapidly, are prone to degenerate, to undergo necrosis, and to become infiltrated with extravasated blood. Histologically, the growth is usually a spheroidal- or polyhedral-celled carcinoma. The cells are often of considerable size, and there is little interstitial connective tissue. The cells are probably derived from proliferation of the hepatic cells. In a few cases the growths are columnar-celled and are in all probability derived from the larger intrahepatic bile-ducts or possibly from mucous glands in their walls. In a case of multiple primary carcinoma shewing a transition from columnar- to spheroidal-celled growth, the origin was clearly from the bile-ducts (*vide* Fig. 62).

IV. **Primary Carcinoma Developing in a Cirrhotic Liver** (*Synonyms*: Primary Carcinoma with Cirrhosis; Malignant Adenoma; Cirrhosis Maligna; Cirrhosis Carcinomatosa).—This condition was described by Sabourin [4] under the title of Cirrhosis with Multiple Adenoma, and as Hepatoma by Rénon, Géraudel, and Monier-Vinard [5] who insist that it is not a carcinoma. "Hepatoma," also employed by Sabourin (p. 460), is a confusing title; Yamagiwa [6] uses it for primary carcinoma of the liver. Hanot and Gilbert,[7] who called it Carcinoma with Cirrhosis, state that a third of the cases of primary carcinoma of the liver are of this special variety. It occurred in 10 of the 41 Middlesex Hospital cases. It is probable that more than one condition has been described under this name. Some of the cases are probably that form of cirrhosis in which the hobnails are extremely well marked, and in which the hepatic cells in them have undergone a compensatory hyperplasia, or cirrhosis with multiple adenomas, and it is noticeable that in this class secondary growths are rare. This condition of nodular cirrhosis has a great naked-eye resemblance to multiple new-growths. The hobnails may undergo fatty degeneration, and may discharge their contents into the intrahepatic branches of the portal, or sometimes the

[1] Butlin, H. T. *Brit. Med. Journ.*, 1892, i, 1341.
[2] Eggel. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1901, xxx, 506.
[3] Colwell. *Arch. Middlesex Hosp.*, Lond., 1905, v, 125.
[4] Sabourin. *Thèse de Paris*, 1881; *Rev. de méd.*, Paris, 1884, iv, 321.
[5] Rénon, Géraudel, et Monier-Vinard. *Arch. de méd. expér. et d'anat. path.*, Paris, 1910, xxii, 311.
[6] Yamagiwa. *Virchows Arch.*, 1911, ccvi, 437.
[7] Hanot et Gilbert. *Études sur les maladies du foie*, p. 63, 1888.

hepatic, veins, and give rise to thrombosis; the presence of liver cells in the portal vein has been regarded by some as evidence that the change is carcinomatous, but without sufficient reason. In other cases of cirrhosis it seems probable that thrombosis of the portal vein is the

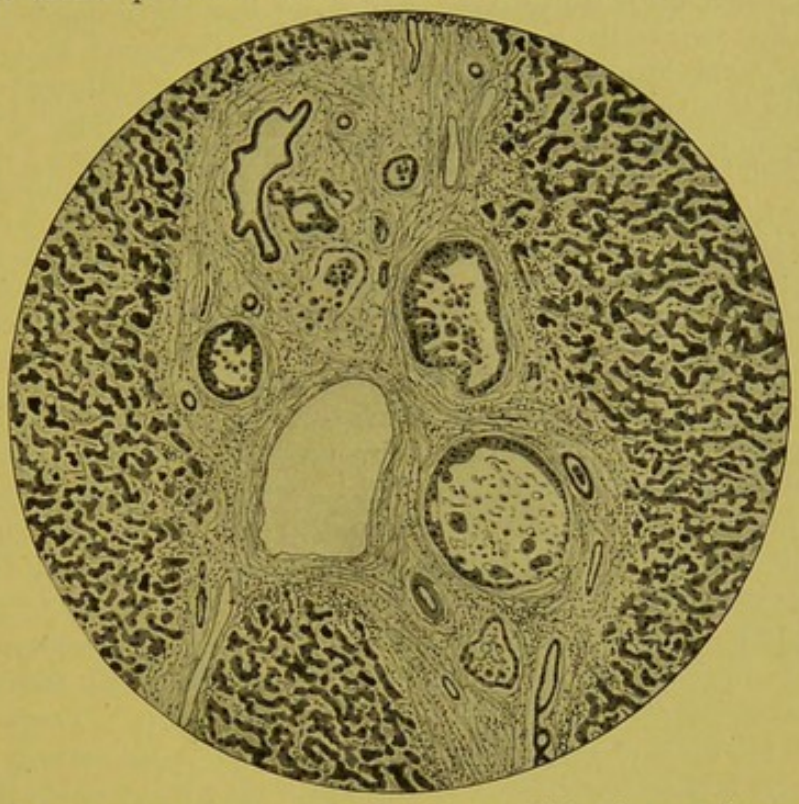


FIG. 62.—Pre-cancerous proliferation of the bile-ducts in multiple primary carcinoma. From a section kindly given me by Dr. L. S. Milne.

primary factor, and that this leads to necrosis and softening of the cirrhotic hobnails, which thus closely resemble masses of secondary new-growth.

Cirrhosis with compensatory hyperplasia of the liver cells forms a connecting link between cirrhosis, on the one hand, and carcinoma, on the other. Where the line separating the proliferation of the hepatic cells from carcinoma is transgressed, it may be difficult to determine, but that carcinoma may thus result is certain.

The relation of the carcinomatous growth to the fibrosis in carcinoma with cirrhosis has been regarded in the following lights :—

(*a*) That the cirrhosis and the carcinoma both develop at the same time and are due to irritation applied respectively to the interstitial connective tissue and to the cells of the liver (Hanot and Gilbert).

(*b*) That the carcinoma is the primary change, and that the cirrhosis is secondary to the irritation set up by the growth and is related to it in the same way that the interstitial tissue of a hard spheroidal-celled carcinoma is to the epithelial cells (Lancereaux [1]). Eggel, who does not recognise carcinoma with cirrhosis as a special form, found cirrhosis in about half his 163 cases of primary

[1] Lancereaux. *Gaz. méd. de Paris*, 1868, 3. s., xxiii, 646.

carcinoma. Against this view it may be urged that secondary growths are common in the liver with little or at the most only local fibrosis around them, whereas in primary carcinoma with cirrhosis the whole liver, and not merely the parts affected by the growth, is fibrotic.

(*c*) That cirrhosis is the primary change and that the compensatory hyperplasia of the liver cells becomes so excessive and atypical as to pass into carcinoma. The history and morbid anatomy of the cases are quite compatible with this view; the duration of the cases is much longer than in other forms of primary malignant disease of the organ; the symptoms are those of cirrhosis, and after death the cirrhosis is seen to be old and universal, while the carcinoma has the appearances of rapid growth. This view, which I have long held, is definitely stated by Turnbull and Worthington [1] who describe as successive stages, in the transition from regeneration to carcinoma in cirrhosis of the liver, (*a*) the regeneration nodule, (*b*) adenoma, (*c*) the carcinoma nodule.

Since it appears that cirrhosis is the primary change, and that carcinoma supervenes secondarily in much the same manner that carcinoma of the mamma follows chronic mastitis, it would, except for the objection to coining fresh names, be better not to speak of Primary Carcinoma with Cirrhosis, but to alter the title to Primary Carcinoma supervening in a cirrhotic liver, or on the analogy of Paget's disease of the nipple (dermatitis maligna), Cirrhosis Maligna, or on the analogy of carcinoma supervening on a gastric ulcer, to call it Cirrhosis Carcinomatosa.[2]

Morbid Anatomy.—The liver is usually little, if at all, enlarged; but in some instances it weighs twice its normal amount. There are commonly adhesions due to past perihepatitis. It is universally cirrhotic and presents multiple tumours, one of which may be so much larger that it would appear to be the primary; but Muir [3] definitely states that there are multiple independent foci of growth. The nodules of growth are not umbilicated; this is because they contain but little stroma, and hence cicatricial contraction, which is at any rate an important factor in umbilication, does not occur. In an early stage the nodules are firm and white; later they degenerate, undergo necrosis, soften down, and may be yellow or green in colour. They usually project on the surface of the liver, but they may be deeply embedded in its substance. The right lobe is far the most often affected. The growth does not tend to spread by the lymphatics to the glands in the portal fissure; but is specially prone to grow into the portal and hepatic veins and thus spreads through the liver and induces secondary growths. From the portal vein the growth may extend along pervious and dilated veins in the falciform ligament. The portal obstruction induces ascites, which is a constant feature of the disease. Extension into the hepatic veins is not uncommon. In Fabyan's [4] case the inferior vena cava was obstructed. Pennato [5] described three varieties of primary carcinoma with cirrhosis.

[1] Turnbull and Worthington. *Arch. Path. Inst. London Hosp.*, 1908, ii, 44.
[2] Rolleston. *Trans. Path. Soc.*, Lond., 1901, lii, 203.
[3] Muir, R. *Journ. Path. and Bacteriol.*, Cambridge, 1908, xii, 299.
[4] Fabyan. *Johns Hopkins Hosp. Bull.*, Balt., 1907, xviii, 351.
[5] Pennato. *Riforma med.*, 1897, xiii, 350.

The spleen is enlarged in about half the cases.

Secondary growths are said by Hanot and Gilbert to be as frequent as in other forms of primary carcinoma of the liver. After the liver, they are most frequently seen in the lungs or on the pleura, doubtless because the growth often extends into the hepatic veins. Secondary growths may also occur on the peritoneum.

When primary carcinoma supervenes in a cirrhotic liver, the minute structure is nearly always that described by Hanot and Gilbert[1] as *Epithéliome trabéculaire*. In some instances other histological forms have been met with (cylindrical-celled, Loehlein[2]), but there is evidently an intimate relation between trabecular carcinoma and cirrhosis, since its histological characters are hardly ever found in other forms of primary carcinoma of the liver.

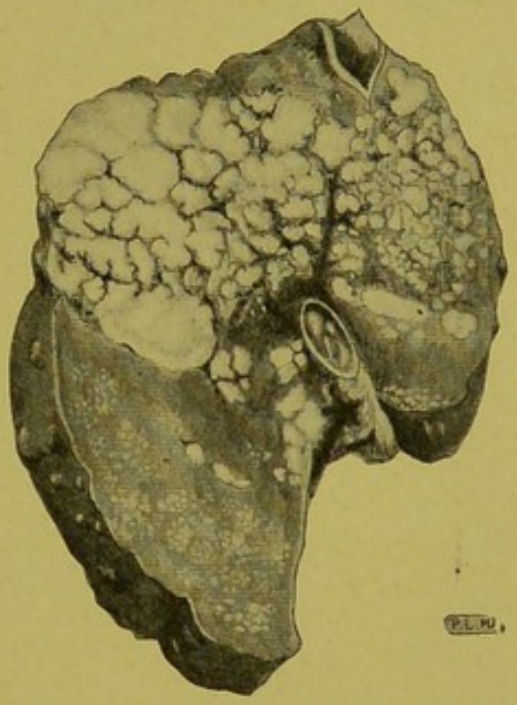


FIG. 63.—Section of the liver in carcinoma with cirrhosis. The growth invades the right lobe and the portal vein. (Drawn by P. L. Mummery, F.R.C.S.)

Tolot[3] has recorded a case of primary trabecular carcinoma without any cirrhosis in a man aged forty-seven years who had chronic pulmonary tuberculosis of seventeen years' duration and tuberculous ostitis of the vertebrae. The hepatic condition was latent.

There are tubular columns of polyhedral or subcolumnar cells arranged in a single layer around a lumen which is usually obliterated, but may contain inspissated bile. The nuclei of the cells are situated externally, at the periphery of the tubular column. These columns branch, twist, and are separated from each other by capillaries which may contain blood. Except for the capillary walls and occasionally well-formed venules, there is no intertubular stroma. The cells shew mitotic figures, stain well, like the pseudobiliary canaliculi, and are smaller than liver cells, being intermediate in size between them and the cells of the pseudobile canaliculi. Occasionally multinuclear cells are present. Both the growths in the liver (*vide* Fig. 66) and the secondary growths in the lung have been known to shew bile-stained contents (Cloin,[4] Ribbert,[5] Weber[6]). Muir,[7] however, is unable to confirm the

[1] Hanot et Gilbert. *Études sur les maladies du foie*, p. 41, 1888.
[2] Loehlein. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1907, xlii, 531.
[3] Tolot. *Rev. de méd.*, Paris, 1904, xxiv, 948.
[4] Cloin. *Prag. med. Wchnschr.*, 1901, xxvi, 261.
[5] Ribbert. *Deutsche med. Wchnschr.*, 1909, xxxv, 1607.
[6] Weber. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Path. Sect.), 147.
[7] Muir, R. *Journ. Path. and Bacteriol.*, Cambridge, 1908, xii, 299.

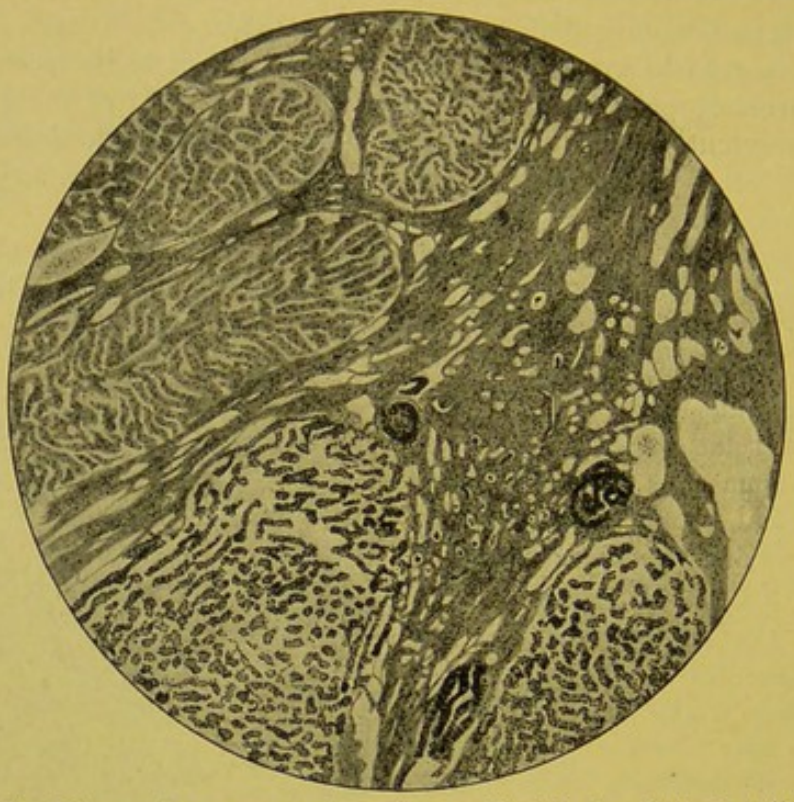


FIG. 64.—Microscopic appearances in carcinoma with cirrhosis. Cirrhosis to the left, carcinoma to the right. Under a very low power.[1]

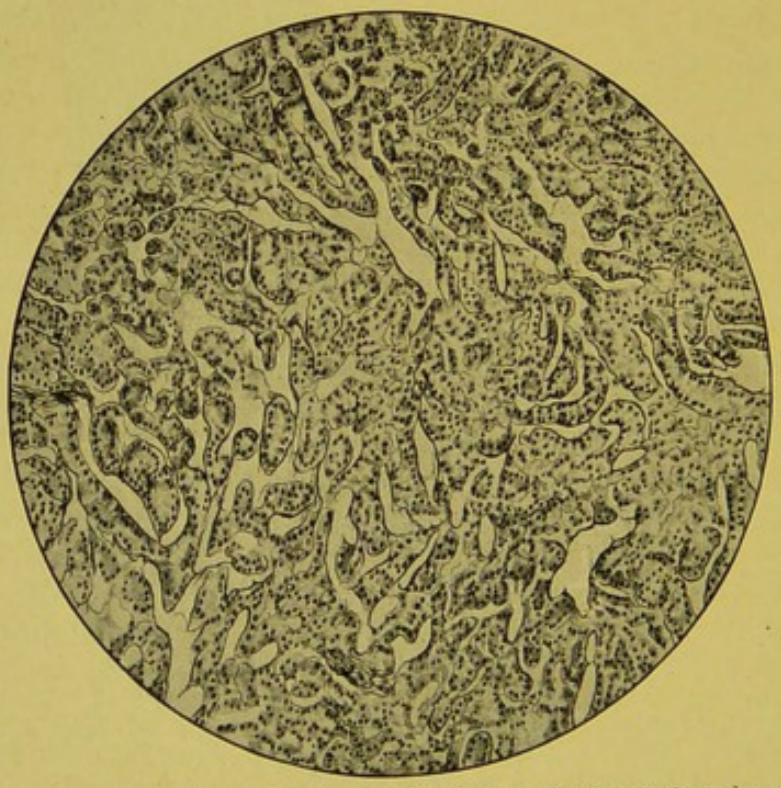


FIG. 65.—Microscopic structure of the growth under a higher power shews branching columns of subcolumnar cells separated by capillaries.

[1] For this block I am indebted to the Council of the Pathological Society of London. *Vide* Transactions, 1901, lii, 203.

production of bile in the secondary growths. There is a wide-meshed stroma containing abundant elastic fibrils which belong to the fibrosis of the pre-existing cirrhosis (M'Connell [1]). It thus differs from the stroma of other forms of primary carcinoma of the liver, which does not shew any new formation of elastic tissue (Wrench [2]).

Fig. 66. — Photomicrograph of carcinoma with cirrhosis. Shewing tubular columns of cells enclosing masses of inspissated bile. In the capillaries separating the columns of cells a few leucocytes are seen. (Dr. H. Spitta.) ×220.

This form of carcinoma is generally considered to be derived from the liver cells (Hanot and Gilbert,[3] Muir). Schmieden[4] traced the starting point of the multiple adenomas in a cirrhotic liver. In the first edition I stated my belief, which has not received any support from other writers, that the trabecular carcinoma might be a further development of the pseudobile canaliculi (*vide* p. 205). The development of carcinoma might be considered as an outcome of the habit of proliferation which began as a compensatory process.

When the growth is compressed or under pressure, the capillary walls may collapse and the structure of the growth is obscured. Degeneration of the cells may occur; the growth may become infiltrated with blood or invaded by fibrosis. Loehlein [5] collected 3 cases of primary carcinoma arising in the cirrhosis due to haemochromatosis; and Kusama [6] has recorded primary carcinoma in a liver shewing cirrhosis due to schistomiasis.

The *clinical aspects* of carcinoma with cirrhosis are practically the same as those of portal cirrhosis. It is only when the liver is large that nodules can be felt; as a rule, the liver is small. Ascites is constant;

[1] M'Connell. *Journ. Med. Research*, Boston, 1907, xvi, 13.
[2] Wrench. *Arch. Middlesex Hosp.*, 1905, v, 80.
[3] Hanot et Gilbert. *Études sur les maladies du foie*, p. 41, 1888.
[4] Schmieden. *Virchows Arch.*, 1900, clix, 290.
[5] Loehlein. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1907, xlii, 531.
[6] Kusama, quoted by Yamagiwa. *Virchows Arch.*, 1911, ccvi, 437.

in two cases (Travis,[1] Peabody [2]) it was markedly haemorrhagic. Jaundice and pain in the hepatic region are said to be more prominent than in simple cirrhosis. Carcinoma with cirrhosis occurs, as would naturally be expected from the greater incidence of cirrhosis in men, very much more frequently in the male than in the female sex. In 49 recorded cases of which I have notes 46 were in men.

V. **Primary Melanotic Carcinoma.**—Three cases have been recorded as primary melanotic carcinoma of the liver. The subject is one of great pathological interest and has given rise to a good deal of discussion. In two of the cases an eye had been removed, in one for glaucoma, in the other for a melanotic sarcoma.

Hale White's [3] case of primary melanotic carcinoma of the liver was in a man aged sixty-six whose eye, removed for glaucoma one year before, did not shew any sign of malignant disease. Fisher and Box's [4] case of multiple melanotic carcinoma of the liver (which weighed 12 pounds 6 ounces), bones, lungs, and heart in a man who had had an eye removed for melanotic sarcoma fourteen years before is open to obvious criticism. Goldzieher and Bókay [5] in 1911 described a case. Probably many would regard the growths as endotheliomatous rather than carcinomatous.

The Origin of Primary Carcinoma.—Primary carcinoma may arise from proliferation of the liver cells, of the cubical epithelium of the small bile-ducts, or of the columnar epithelium of the intrahepatic bile-ducts. There is much difference of opinion as to the relative frequency with which primary carcinoma of the liver arises from the liver cells and from bile-duct epithelium. Eggel from a review of 163 cases concluded that the proportion was 68 per cent from the liver cells, and 32 per cent from bile-duct epithelium. Pepere [6] considered the liver-cell origin 7 times commoner. Fischer [7] believed that all carcinomas arise from the bile-ducts, even those growths with cells resembling the liver cells. Spheroidal-celled carcinoma may be derived from the liver cells or from the small bile-ducts ; the larger-celled growths are probably derived from the liver cells. The trabecular form of carcinoma, seen in carcinoma with cirrhosis, is generally considered to be derived from the liver cells. Columnar-celled growths are derived from the larger intrahepatic bile-ducts or possibly from mucous glands in their walls.

In addition to the normal tissues of the liver it is, in accordance with Cohnheim's theory, conceivable that carcinoma might arise in pieces of other abdominal organs which have become included in the liver as the result of some irregularity in development. It has been suggested that embryonic relics of the duodenal diverticulum might persist and be the

[1] Travis, C. H. *Johns Hopkins Hosp. Bull.*, Balt., 1902, xii, 289.
[2] Peabody, G. L. *Trans. Assoc. Am. Phys.*, 1904, xix, 308.
[3] Hale White. *Trans. Path. Soc.*, Lond., 1886, xxxvii, 272.
[4] Fisher and Box. *Brit. Med. Journ.*, 1900, i, 639.
[5] Goldzieher und Bókay. *Virchows Arch.*, 1911, cciii, 109.
[6] Pepere. *I Tumori maligni primarii del fegato*, p. 171, 1902.
[7] Fischer. *Virchows Arch.*, 1903, clxxiv, 544.

starting-point of a carcinoma, or that a small piece of pancreas (Pepere [1]) might be included in the liver. Primary malignant tumours of the liver, homologous to malignant tumours in the kidney derived from adrenal "rests," have been described (Pepere,[2] Phillips and Spilsbury,[3] Powell White and Mair,[4] Hirschler [5]). But, just as the adrenal nature of the renal hypernephromas has been disputed, doubt has been thrown on the adrenal origin of these primary malignant tumours of the liver. Glynn [6] suggests that they are really derived from the liver cells.

A primary tumour of the liver with the structure of chorion-epithelioma has been reported (Marz [7]). Brault [8] calls these tumours angioplastic sarcoma.

Degenerative Changes in the Tumour.—The epithelial cells often shew fatty change, and necrotic changes are not uncommon; but, probably owing to rapid growth, colloid degeneration is not met with. From extensive necrosis the growth occasionally becomes cystic and some haemorrhage may take place. The fibrous tissue may undergo widespread hyaline change.

The Incidence of Secondary Growths in Primary Carcinoma of the Liver.—Secondary growths are common in the liver, and are found in other situations in more than half the cases. In Eggel's [9] collection metastasis occurred outside the liver in 66 per cent. Secondary growths are most frequent in the immediate neighbourhood; thus, infection may spread by the lymphatics to the glands in the hilum, which are often enlarged and may press on the portal vein and bile-ducts. Lymphatic glands elsewhere, in the upper part of the abdomen and in the thorax, may be infected. Metastasis also occurs by the blood-stream; the growth may extend directly into the portal and hepatic veins, and thus give rise—(i) to fresh growths in the substance of the liver, and (ii) by embolic masses of growth which pass *via* the hepatic veins to secondary nodules in the lungs.

In 21 cases of primary carcinoma of the liver Lancereaux [10] found growths four times in the gall-bladder, and twice each in the peritoneum, lungs, and spleen.

In a case of massive carcinoma of the liver there were innumerable secondary growths in the brain and nowhere else (Giachetti; [11] *vide* also p. 483). A secondary growth has been known to cause fracture of the femur (Goldzieher and Bókay [12]).

[1] Pepere. *Arch. per le sc. med.*, 1902, xxvi, 148.
[2] *Idem. Arch. de méd. expér. et d'anat. path.*, Paris, 1902, xiv, 763.
[3] Phillips and Spilsbury. *Brit. Med. Journ.*, 1905, i, 1274; and *Trans. Clin. Soc.*, Lond., 1905, xxxviii, 179.
[4] White (Powell) and Mair. *Journ. Path. and Bacteriol.*, Cambridge, 1907, xii, 107.
[5] Hirschler. *Frankfurt. Ztschr. f. Path.*, 1912, ix, 343.
[6] Glynn. *Quart. Journ. Med.*, Oxford, 1911–12, v, 157.
[7] Marz. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1904, xxxvi, 585.
[8] Brault. *Manuel d'histologie patholog.*, 1912, iv, part ii, 1008.
[9] Eggel. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1901, xxx, 506.
[10] Lancereaux. *Traité des maladies du foie et du pancréas*, p. 472, 1899.
[11] Giachetti. *Riv. di pat. nerv. e mentale*, Florence, 1907, xii, 149.
[12] Goldzieher und Bókay. *Virchows Arch.*, 1911, cciii, 75.

Extension of the primary hepatic growth into the portal or hepatic veins is much commoner in the special form of carcinoma with cirrhosis than in the other varieties of primary carcinoma. The growth in the vein may lead to very considerable dilatation of its walls, so that it is difficult to make out the exact limits of the vein in the substance of the liver.

Gilbert and Claude[1] recorded a case of extension of a massive carcinoma of the right lobe of the liver into the common bile-duct, which set up obstinate jaundice.

Incidence of Gall-stones in Primary Carcinoma of the Liver.—Although gall-stones occur in a high percentage—80–90 per cent—of cases of primary carcinoma of the gall-bladder, there is no special relation between cholelithiasis and primary carcinoma of the liver, gall-stones being merely a coincidence in malignant disease of the liver. Confusion has existed in the past, and primary carcinoma of the gall-bladder has sometimes been described as primary carcinoma of the liver, so any statistics, in which there is a high percentage of gall-stones in primary carcinoma, must be carefully criticised from this point of view.

In 41 cases of primary carcinoma of the liver examined at the Middlesex Hospital there was no case of cholelithiasis.[2] In 20 cases regarded as primary carcinoma of the liver, at St. George's Hospital, about two-thirds of which I saw or examined myself, 5, or 25 per cent, contained calculi in the gall-bladder.

Forms of Primary Sarcoma.—**I. Primary Massive Sarcoma.**—There is a large tumour, usually in the right lobe, which is analogous to the massive form of primary carcinoma (p. 472). There may be secondary tumours in other parts of the liver, but from their relative size there is no doubt as to the primary growth. In some instances the growth may project from the under surface of the liver so as to become pedunculated. A large proportion of the published cases of primary sarcoma appears to belong to this group. In 45 cases tabulated by Pepere,[3] 22 were in this category.

The cells may be small round, spindle, or of various shapes and sizes, mixed or irregular; sometimes, especially when growth is rapid, multinuclear giant-cells are present. Haemorrhage frequently takes place into the growth and gives rise to a mottled or red appearance. The growths are often spongy on section. Large sarcomatous tumours may be very haemorrhagic and break down into cystic cavities and even imitate abscesses.

A case recorded by Bramwell and Leith[4] simulated an abscess; aspiration was performed three times, with removal of 123 ounces of anchovy-coloured fluid.

In a woman aged sixty-four, in St. George's Hospital, there was a large cystic tumour continuous with the right lobe of the liver and reaching down to the

[1] Gilbert et Claude. *Arch. gén. de méd.*, Paris, 1895, clxxv, 513.
[2] Colwell. *Arch. Middlesex Hosp.*, 1905, v, 126.
[3] Pepere. *I Tumori maligni primarii del fegato*, p. 118, 1902, Napoli.
[4] Bramwell and Leith. *Lancet*, 1897, i, 170.

iliac crest. It was explored by Mr. Turner, and a large quantity of blood-stained fluid and a little growth removed; it was thought possible that it was a pancreatic cyst, but the fluid contained nothing but altered blood and had none of the characters of the fluid in a pancreatic cyst. Microscopically the growth was a mixed-celled sarcoma. At the necropsy there was an enormous cystic tumour, still containing brown, blood-stained fluid, projecting from the portal fissure and carrying the cystic and common bile-ducts and portal vein in front of it. There was, however, no jaundice or ascites. There were secondary growths in the retroperitoneal glands and in the lungs.

A woman aged fifty-nine years came under the care of Dr. Ogle in St. George's Hospital with paralysis of the left arm and leg of gradual onset, slight jaundice, ascites, a large liver and a tumour in the left hypochondrium, and oedema of the legs. Paracentesis to 20 pints was performed, and the patient

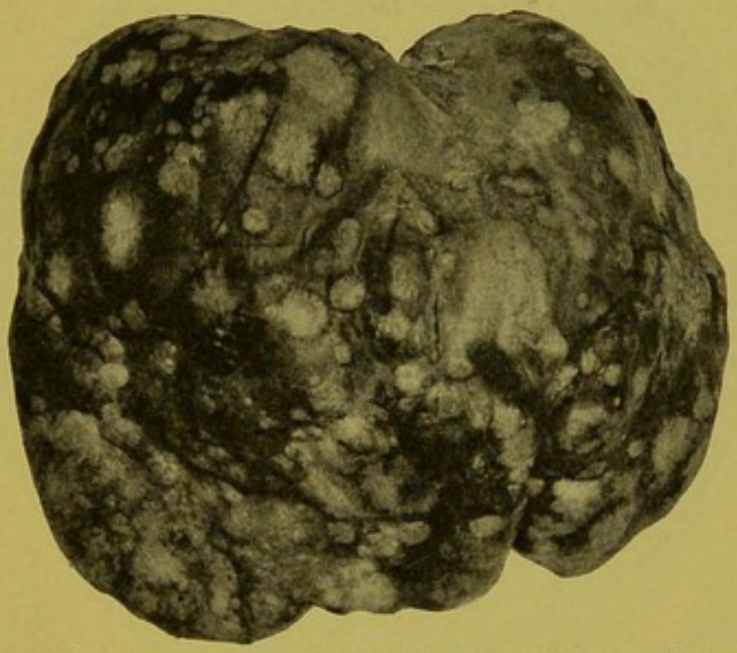


FIG. 67.—Multiple primary sarcoma of the liver shewing umbilication. (Photographed by Dr. W. R. Harris.)

gradually got weaker and died. The liver weighed 6 pounds 10 ounces; the left lobe was completely replaced by a whitish yellow growth which in parts was of cartilaginous firmness, there were discrete secondary growths in the right lobe and massive enlargement of the portal glands. There was a secondary growth the size of a walnut in the Rolandic area of the right cerebral hemisphere. Microscopically the growth in the liver was an angiosarcoma with areas of necrosis and of extensive fibrosis.

II. **Nodular, or Multiple, Primary Sarcoma.**—There are a number of discrete nodules scattered in the substance of the liver which are so much of the same size that no individual nodule can be regarded as primary and antecedent to the others. This is one of the two most frequent anatomical forms of primary sarcoma. It was present in 18 out of 45 cases of primary sarcoma tabulated by Pepere. Where the nodules are small and very numerous, they tend to become confluent and to produce

either a massive growth, like the form just described, or a more diffuse infiltration, in which the cut surface has an appearance not unlike granite.

Structurally, the cells of the growth may be of very various types—spindle, round, irregular, or giant cells.

The liver of a man, aged forty-seven, who died under the care of Dr. C. Ogle in St. George's Hospital, weighed 16¼ pounds and was full of white secondary growths which were umbilicated (Fig. 67). The only other growth was in the portal lymphatic glands. It was a small spindle-celled sarcoma. There is a good example of a multiple primary spindle-celled sarcoma of the

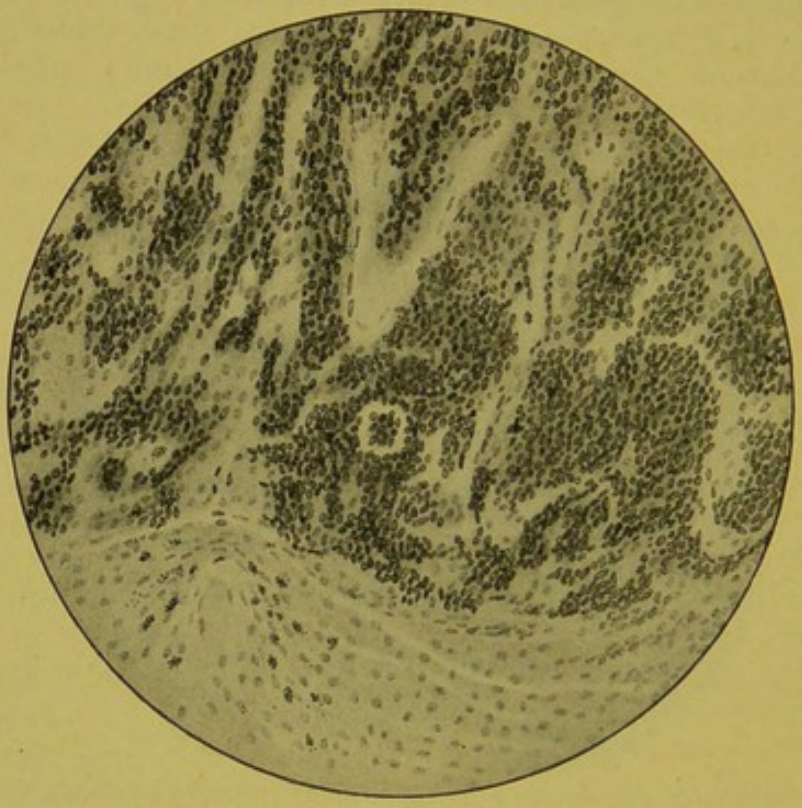


Fig. 68.—Drawing of a small spindle-celled sarcoma. The liver tissue is very lightly stained.

liver in the museum of the Royal Free Hospital. The late Miss Mabel Webb, M.B., curator of the Museum, kindly gave me a slide from this case which is reproduced above (Fig. 68).

III. **Diffuse or Infiltrating Primary Sarcoma.**—Sarcoma may uniformly infiltrate both lobes of the liver. This form is not infrequently seen in very early life, and must be carefully distinguished from the changes due to congenital syphilis. Some of the hard infiltrating growths, formerly spoken of as "scirrhus" of the liver, belong to this category, since they shew a structure like that of an endothelioma. There are large endothelial cells and much hyaline fibrous tissue.

IV. **Primary sarcoma arising in a cirrhotic liver** is very rare; in 1910 Dr. Trevor and I[1] collected 7 cases, all in males. Ascites occurred

[1] Rolleston and Trevor. *Journ. Path. and Bacteriol.*, Cambridge, 1911, xv, 247.

in 5 and was blood-stained in 3. In most of the cases the sarcoma appeared to start in the walls of the small blood-vessels; this militates against the natural assumption that the proliferation of the fibrous tissue in cirrhosis becomes so riotous as to pass into sarcoma. In Dominici and Merle's[1] case both sarcoma and carcinoma arose in a cirrhotic liver. These 7 cases were about equally divided into round- and spindle-celled growths, and in 5 some multinucleated giant-cells were described.

V. **Primary Melanotic Sarcoma of the Liver.**—I have references to 9 published cases,[2] but it is doubtful whether they are genuine and not secondary to a small growth in the uveal tract or in a cutaneous mole

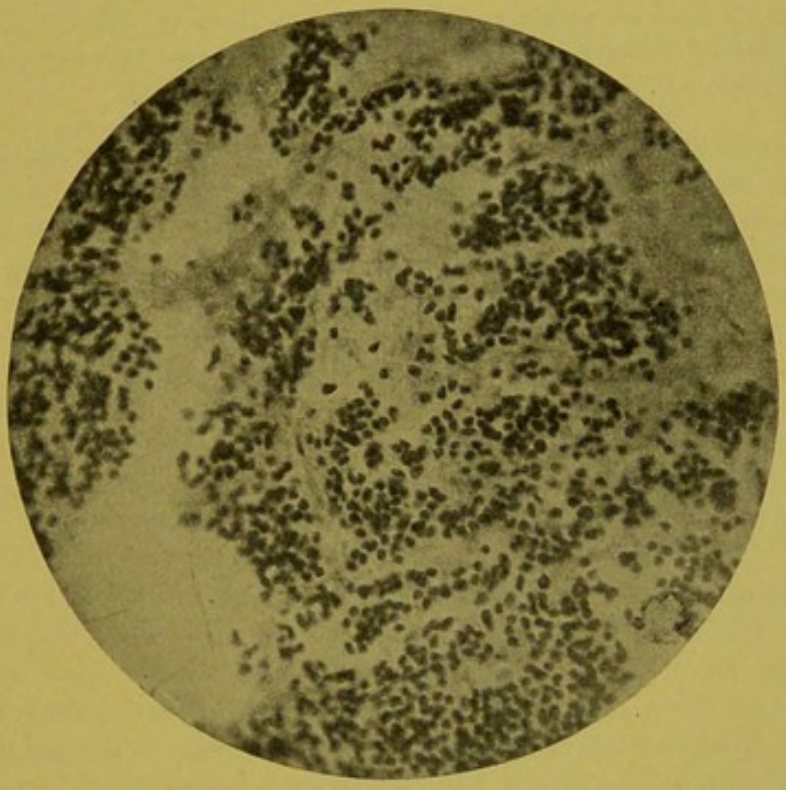


FIG. 69.—The edge of a small round-celled sarcoma infiltrating the liver diffusely in an infant. The growth was primary in the liver. (Photomicrograph by Dr. S. G. Penny.) × 200.

which has been overlooked. As shewn by Dr. Pitt's case (*vide* p. 501), a very minute growth in the uveal tract, which escapes ophthalmoscopic examination and gives rise to no symptoms during life, may produce great enlargement of the liver. Thus no case can be accepted unless it is clear that the eyes were specially examined after death, and this does not appear to have been done. In the recorded cases the most that is stated about the eyes is that there were no symptoms during life.

[1] Dominici et Merle. *Arch. de méd. expér. et d'anat. path.*, Paris, 1909, xxi, 136.

[2] Frerichs, *Diseases of the Liver*, ii, 326, Transl. New Sydenham Soc.; Block, O. C., *Arch. d. Heilk.*, 1875, xvi, 412; Legg, W., *St. Barth. Hosp. Rep.*, 1877, xiii, 160; Delépine, S., *Trans. Path. Soc.*, 1891, xlii, 161; Penrose, F. G., *ibid.*, 1891, xlii, 172, *Middlesex Hosp. Rep.*, 1891, p. 278; Holsti, *Brit. Med. Journ.*, 1895, i, epitome No. 395; Belin, *France méd.*, Paris, 1887; Sweet, *Brit. Med. Journ.*, 1909, ii, 1344.

Origin of Primary Sarcoma.—Sarcoma may arise from the general connective tissue of the liver in the portal spaces, from the perivascular connective tissue, and from the endothelium of the blood-vessels and lymphatics. The growths arising from the tissues of the vessels, angiosarcoma, may be further divided into—(i) those arising from the lining endothelium of the blood or lymphatic vessels, the endotheliomas, and (ii) those arising from the perivascular sheaths formed of endothelium covering the vessels externally, the peritheliomas. Probably a large proportion of the primary growths usually classed as sarcoma of the liver belong to the angiosarcomas.

Among 45 cases of primary sarcoma of the liver tabulated by Pepere,[1] 22 were regarded as derived from the vessels, and of these, 11 were endotheliomas and 8 peritheliomas.

Microscopically there is a general tendency for sarcoma in the liver to assume an alveolar arrangement and so to imitate carcinoma; it is, indeed, not unlikely that some cases of large or medium-sized round-celled sarcoma of the liver have been described as carcinoma, as there is often considerable difficulty in determining the nature of the growth in such cases. One reason why a sarcoma is often alveolar is that the growth is an endothelioma, derived from the endothelium lining the small blood-vessels or lymphatics.

The forms of sarcoma met with are very various; small round-celled, large round-celled, spindle-celled, irregular-celled sarcoma with giant-cells; lymphosarcoma, angiosarcoma, including under this head the endotheliomas, and melanotic sarcoma all occur.

Condition of the Remainder of the Liver in Primary Malignant Disease.—There may, of course, be secondary growths in parts of the liver remote from the main tumour. In some cases compensatory hyperplasia of the liver cells may form nodules which are with difficulty distinguished from secondary growths. The liver cells in the neighbourhood of the growth may contain haemosiderin. Local venous engorgement from pressure on the trunks of the intrahepatic veins, or local bile-staining from compression of the bile-ducts, may also be met with. The occurrence of cirrhosis has already been dealt with. As a curiosity, the association of primary malignant disease of the liver[2] with hydatid cysts in the organ may be mentioned (*vide* p. 397).

Growths in the liver may be invaded by micro-organisms; this may occur during life and give rise to suppuration. It is not uncommon for micro-organisms to gain access to the growth at or after death; they are then of no importance. Hebb[3] found long bacilli in a case of primary carcinoma, and Delépine[4] staphylococci in a melanotic sarcoma of the liver.

[1] Pepere. *I Tumori maligni primarii del fegato*, 1902, p. 118.

[2] *St. Thomas's Hosp. Rep.*, 1900, xxix, 141; Loehlein, *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1907, xlii, 531.

[3] Hebb, R. G. *Westminster Hosp. Rep.*, 1888, iii, 180.

[4] Delépine, S. *Trans. Path. Soc.*, 1890, xlii, 161.

Secondary Malignant Tumours of the Liver

Incidence.—*Numerical Ratio between the Incidence of Secondary and Primary Malignant Tumours of the Liver.*—Secondary malignant growths in the liver are very common, while primary growths of the liver are rare. The ratio between primary and secondary malignant disease of the liver is often stated to be about 1 to 20. Even this is rather overstating the frequency of primary malignant disease of the liver. Possibly cases of malignant disease of the gall-bladder or larger bile-ducts have been regarded as primary in the liver by some observers and so have tended to vitiate statistics.

Hale White[1] puts the proportion of undoubted primary to secondary carcinoma as 1 to 21. He found that primary malignant disease was the cause of death in 0·1 per cent, and that secondary growths were present in 3·47 per cent of patients examined after death at Guy's Hospital. Hansemann,[2] in twenty years—1870–1889—found that 258 necropsies shewing malignant disease in the liver had been performed in the Pathological Institute at Berlin; of these, either 6 or 4 were primary in the liver; this shews a ratio of primary to secondary growths of nearly 1 to 40.

Incidence of Secondary Carcinoma and Sarcoma in the Liver.—Secondary carcinoma is far more often met with than secondary sarcoma.

In 100 cases of secondary malignant disease of the liver abstracted from the post-mortem records of St. George's Hospital, 77 were carcinoma and 23 sarcoma. The cases of sarcoma include endothelioma, such as the malignant tumours of the suprarenal, of which there were 5. There were 3 cases of melanotic sarcoma. In Hale White's figures the percentage was 91·4 carcinomatous, and 8·6 sarcomatous, secondary growths. In his 361 cases of secondary growths in the liver at least 330 were carcinomatous.

The smaller incidence of secondary sarcoma in the liver is readily explained not only by the greater frequency of carcinoma, but also by the infrequency of primary sarcoma in the alimentary canal, or, in other words, within the territory of the portal vein. Sarcoma, like pyaemia, travels by the veins to and through the lungs, which filter out the micro-organisms or infecting cells and thus at their own expense protect the rest of the body.

Sex.—Secondary malignant disease of the liver is rather more frequent in women than in men.

During the years 1901–1909 there were, according to the Registrar-General's returns for England and Wales, 21,488 female and 14,139 male deaths from malignant disease of the liver; though these figures include malignant disease of the gall-bladder, which is much commoner in women, it is probable that they represent very fairly the sex-incidence of secondary malignant disease. Hale White estimated the ratio as 4 to 3.

[1] Hale White. *System of Medicine* (Allbutt and Rolleston), 1908, iv, part i, 204.
[2] Hansemann. *Berlin. klin. Wchnschr.*, 1890, xxvii, 353.

The greater frequency of secondary malignant disease of the liver in women depends not only on the greater incidence of malignant disease in that sex, but also on the special predominance of malignant disease of the mamma and female genital organs. Secondary growths in the liver often follow cancer of the mamma and genital organs, but rarely occur in malignant disease of lip, mouth, and tongue, which are much commoner in the male than in the female sex.

The incidence of cancer generally, and especially of the alimentary canal, is absolutely and steadily increasing (Payne [1]). According to the Registrar-General's statistics, although at the present time women suffer more severely from malignant disease than men in the aggregate, the incidence of malignant disease has increased more rapidly among men than in the other sex. It is, therefore, highly probable that secondary malignant disease of the liver is becoming more frequent in males than formerly.

In 100 cases of secondary malignant disease of the liver examined at St. George's Hospital and taken in continuity from the post-mortem records, 1892–1902, I was surprised to find that the number of males (66) was nearly double that (34) of the females. In 144 cases at Guy's Hospital 77 were in men and 67 in women (Weaver [2]).

Age.—Secondary malignant disease of the liver occurs most frequently after forty years of age.

The average age of 100 cases of secondary malignant disease of the liver examined at St. George's Hospital was 49·8 years. The average ages of the 66 males was 51·3 years, and of the 34 females, 47 years.

The average age is, as might be expected, higher in the cases of secondary carcinoma than in those of secondary sarcoma.

Among 100 cases of secondary malignant disease of the liver the average age of 77 cases of carcinoma was 51·9 years (50 male cases, average age, 53·1 years ; 27 female cases, average age, 48·5) ; while the average age of 23 cases of secondary sarcoma was 43 years (16 males, 43·8 years ; 7 females, 41·1).

Probably the earliest recorded case of secondary carcinoma of the liver is Zuppinger's [3] in a girl aged twelve years. The primary growth was a columnar-celled carcinoma of the sigmoid flexure. Ruczynski [4] reported a similar case in a boy aged thirteen years, the primary growth being in the splenic flexure.

Morbid Anatomy.—The liver is sometimes of the normal size, with a few secondary growths scattered over its surface. Often, however, the secondary growths in the liver increase very rapidly, and if the primary growth in the alimentary canal is comparatively stationary, the liver may reach a very large size ; in such cases it often weighs 16 pounds. The

[1] Payne, J. F. *Lancet*, 1899, ii, 765.
[2] Weaver. *Guy's Hosp. Rep.*, 1909, lxiii, 225.
[3] Zuppinger. *Wien. klin. Wchnschr.*, 1900, xiii, 389.
[4] Ruczynski. *Prag. med. Wchnschr.*, 1904, xxix, 531.

vascularity of the liver, the presence of glycogen, and the high temperature provide conditions specially favourable to rapid tumour growth. In cases, such as carcinoma of the breast or melanotic sarcoma of the uveal tract, in which the primary growth may have been removed after infection of the liver has actually taken place, the liver may subsequently become greatly enlarged. The largest livers known occur in secondary malignant disease. Osler[1] mentions a liver weighing 30½ pounds, and Christian[2] one of 33⅓ pounds. Richard Powell[3] refers to a liver weighing nearly 40 pounds but does not state the cause of enlargement.

Secondary invasion of the liver is hardly ever limited to a single nodule of growth. The liver may contain multiple and discrete growths, or may be diffusely infiltrated for a greater or less extent, as is sometimes well seen in carcinoma of the breast and in melanotic sarcoma. When widely infiltrated, the liver is enlarged, but preserves its general shape and anatomical outlines very fairly.

"Farre's tubercles" was formerly a well-known synonym for secondary growths in the liver. This writer described "Tubera circumscripta" and "Tubera diffusa," corresponding to the two forms mentioned above.[4]

In some instances nodules originally separate may unite into a large irregular mass. The growths are scattered throughout the liver, but are especially frequent near the surface of the organ, and are rarely seen on section when entirely absent from the surface. They grow rapidly and receive their blood-supply from the hepatic artery, which is sometimes considerably enlarged.

In this connexion it is interesting to refer to a plate of Bright's[5] shewing a large artery supplying a mass of secondary new-growth.

Whether carcinomatous or sarcomatous, the naked-eye appearances of the nodules have much in common. The peritoneum is often thickened and opaque over the nodules. They are usually white in colour, and are not infrequently bile-stained and may be speckled with blood or extremely haemorrhagic. In secondary melanotic sarcoma there may be isolated pigmented nodules, areas of diffuse melanotic infiltration, or both combined. In some cases the secondary melanotic growths are almost or quite devoid of pigment, at any rate to the naked eye. Sarcomatous growths are more likely to be haemorrhagic and to soften into pseudo-cysts; as a rule, they are not depressed in the centre or umbilicated, a change often seen in secondary carcinomatous growths on the surface of the liver. The statement that secondary sarcomatous nodules are never umbilicated, and may thus be distinguished from secondary carcinomatous growths in the liver, is too dogmatic and must admit of some exceptions.

[1] Osler. *Principles and Practice of Medicine*, p. 568, ed. vi, 1905.
[2] Christian, H. A. *Am. Med.*, Phila., 1903, v, 131.
[3] Powell, R. *Observations on Bile and its Diseases, and on the Economy of the Liver*, p. 17, 1800.
[4] Farre, J. R. *Morbid Anatomy of the Liver*, 1815, London.
[5] Bright. *Guy's Hosp. Rep.*, 1836, i, 638.

In St. Bartholomew's Hospital Museum there is the liver of a boy, aged ten years, enormously enlarged and studded with umbilicated nodules secondary to sarcoma of the kidney (No. 2215 c).

The dead-white colour of some secondary carcinomatous nodules, especially columnar-celled growths, may give rise to an appearance very like a gumma, so that considerable difficulty may arise in distinguishing between the two conditions, especially when only a limited examination can be made, as at exploratory laparotomies.

I have several times examined fragments removed during life which have turned out to be columnar-celled growths secondary to a latent carcinoma in the stomach or colon, and which it was naturally hoped might be gummatous. Gouget[1] described a columnar-celled carcinoma of the liver which was at first regarded as a gumma (*vide* p. 353).

The consistency of the growths varies considerably. Diffuse areas of infiltration may be hard, but as a general rule the larger the size of a secondary growth, the softer it is, since degeneration and necrotic changes are more prone to supervene than in smaller nodules. Small discrete nodules cut with the same kind of resistance as a cream cheese.

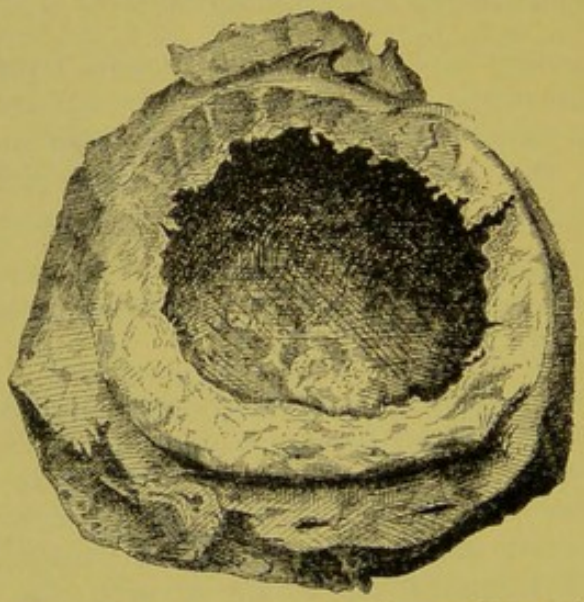


Fig. 70.—Cyst due to softening of a secondary carcinomatous growth in the liver, from a specimen in St. George's Hospital Museum. (Series ix, 184 L.) (Drawn by L. Jones, M.S.)

Degenerative Changes.—The central parts of the larger nodules readily undergo fatty degeneration and necrosis, and may have a caseous or softened appearance. The necrosed tissue readily undergoes autolysis or self-digestion by intracellular enzymes (proteases) of the dead cells. A rapidly growing mass of carcinoma may present the honeycombed and softened appearance of actinomycosis. Extreme softening may in some instances be due to suppuration from infection. The necrosed portions may be yellow or green from bile-staining, or may become infiltrated with blood. This haemorrhagic condition is more often seen in sarcoma, but it may also occur in secondary carcinomatous growths. Sometimes the haemorrhage into the degenerated growth is so profuse as to lead to serious syncope, but when this occurs, the growth has usually ruptured and allowed blood to pass into the peritoneal cavity. In other instances

[1] Gouget. *Bull. Soc. Anat.*, Paris, 1890, lxxv, 605.

a sanguineous ascitic effusion is due to comparatively insignificant leakage from a small nodule.

Colloid degeneration in a secondary growth in the liver is rare.

There is a mass of colloid carcinoma, the size of a man's fist, in St. Bartholomew's Hospital Museum, secondary to a growth in the rectum (No. 2216 H).

According to Schueppel,[1] diffuse colloid cancer of the peritoneum may spread by the lymphatics of the capsule of the liver and pass into its substance like strings. Eventually a whole lobe of the liver may become transformed into a colloid mass.

Myxomatous and hyaline degeneration may attack the fibrous tissue of a slow-growing secondary nodule of carcinoma, or occur in secondary endotheliomatous nodules even though growing rapidly.

Formation of Pseudo-cysts.—Degeneration and softening of secondary malignant growths may lead to the formation of cystic cavities. This may occur in any form of carcinoma, even in the squamous-celled variety, and in sarcoma. It is, however, rather rare.

In a case of carcinoma of the stomach recorded by Hawthorne[2] there were numerous cysts in the right lobe of the liver, due to softened new-growth; the largest had a diameter of $4\frac{1}{2}$ inches. Aspiration during life resulted in the withdrawal of 58 ounces of blood-stained fluid. The case imitated an abscess. In a case of carcinoma of the pylorus recorded by Nicaise[3] the liver (75 ounces) contained numerous secondary growths, and had a tongue-shaped lobe with a haemorrhagic cyst due to destruction of the growth. In a case of carcinoma of the cardiac end of the stomach in a woman in St. George's Hospital in 1909, secondary growths in the liver contained clear alkaline fluid. In a case of carcinoma of the liver, probably secondary to the pancreas, in a man aged fifty-one, there were numerous cystic spaces with caseous contents. Microscopically the growth was a carcinoma, shewing a transition from a columnar to a spheroidal type, with considerable fibrosis and extensive necrotic and cystic changes. The liver is in the Museum of the Royal Free Hospital. Voelcker[4] described secondary squamous-celled carcinomatous nodules with cystic change, a smooth thin layer of new growth alone being left as the wall of the cyst. In a similar case the cyst wall could easily be peeled out of the liver; it closely resembled a hydatid cyst and contained clear yellow fluid (Thomson[5]). There is a somewhat similar specimen with cysts the size of a tangerine orange in St. Bartholomew's Hospital Museum secondary to a growth in the oesophagus. In a case described by Sharkey[6] the liver was studded with cysts lined by squamous epithelium.

In St. Bartholomew's Hospital Museum there is a specimen (2215 E) of secondary sarcomatous growths which have broken down so extensively that the appearance is not unlike that of cystic disease of the liver in the adult; the primary growth was in the skin of the back. I have seen the same thing in a

[1] Schueppel. v. Ziemssen's *Cyclopaedia of Practical Medicine*, ix, 338. English transl., 1880.

[2] Hawthorne, C. O. *Clin. Journ.*, Lond., 1896, viii, 361.

[3] Nicaise, V. *Bull. Soc. Anat.*, Paris, 1900, 6. s., ii, 146.

[4] Voelcker, A. F. *Trans. Path. Soc.*, Lond., 1896, xlvii, 43.

[5] Thomson, H. C. *Practitioner*, 1899, lxii, 411.

[6] Sharkey, S. J. *Trans. Path. Soc.*, Lond., 1884, xxxv, 374.

secondary endothelioma of the liver which weighed 18 pounds, the primary growth being in the left kidney (*vide* p. 523). Von Horsch [1] describes extensive cystic changes in hepatic metastases secondary to sarcoma of the stomach.

Umbilication.—Not uncommonly secondary growths on the surface of the liver shew a central depression or umbilication. It occurs in comparatively slow-growing carcinomatous nodules and is very rare in secondary sarcoma (*vide* p. 489). According to Géraudel [2] it does not occur in secondary nodules due to lymphatic invasion from the surface of the liver.

This umbilication is due to the cells in the central part of the nodule undergoing degeneration and becoming compressed by the surrounding fibrous tissue, which, from the greater age of the growth in the centre, is better developed than in the more recent peripheral parts of the nodule. Another factor is the more exuberant cellular proliferation at the edge of the nodule, which leads to a heaping-up of growth. The depression of the oldest part of an oyster's shell, viz. that near the hinge, illustrates the production of umbilication (Wilks [3]). Umbilication is often absent in rapidly growing nodules of small size.

Effects of Secondary Growths.—Secondary growths on the surface of the liver frequently set up perihepatitis and so give rise to pain. It is very rare for a secondary growth on the surface of the liver to grow directly into the abdominal wall; this is probably prevented by the respiratory movements. It does, however, sometimes occur, and the diaphragm or anterior abdominal wall may be so firmly united by the growth to the liver that after death they can be separated only by the knife. A growth on the anterior surface of the liver may infect the opposed surface of the parietal peritoneum without any adhesions between the two, the growth being implanted by contact.

Growths in the liver frequently press on the branches of the portal vein and may thus help to cause ascites; pressure on the hepatic veins is often seen, and gives rise to local chronic venous engorgement. In a certain number of instances the secondary growths project into the veins and set up thrombosis; detachment of small pieces of growth projecting into the lumen of the hepatic veins leads to metastatic growths in the lungs. Occasionally a secondary growth may form a polypoid mass in the hepatic or portal veins.

Pressure on the intrahepatic bile-ducts is common and results in local bile-staining of the liver tissue. In rare instances malignant disease in the liver, after eating its way into the larger bile-ducts, may grow along the lumen of the duct without infiltrating the wall of the tube (Fauvel, Durand-Fardel,[4] Gilbert and Claude [5]). This process is like the downward projection of a renal growth into the ureter.

[1] v. Horsch. *Deutsche Ztschr. f. Chir.*, Leipz., 1907, xc, 98.
[2] Géraudel. *Arch. de méd. expér. et d'anat. path.*, Paris, 1910, xxii, 363.
[3] Wilks. *Pathological Anatomy*, p. 474, 1889.
[4] Fauvel, Durand-Fardel. Quoted by Devic et Gallavardin, *Rev. de méd.*, Paris, 1901, xxi, 570.
[5] Gilbert et Claude. *Arch. gén. de méd.*, Paris, 1895, clxxv, 513.

Histology.—Structurally the secondary nodules resemble the primary growth. When secondary to carcinoma of the stomach, the hepatic growths may be either columnar-celled or spheroidal-celled; when the colon is affected, the hepatic growths are columnar-celled; in both these instances, however, the secondary tumours may differ somewhat from the primary, the cells shewing a transition from the columnar to the spheroidal type. When secondary to carcinoma of the breast, the growth is spheroidal-celled; and when a primary growth in the lower part of the oesophagus infects the liver, the structure of the secondary nodules is that of a squamous-celled carcinoma. But here again from more rapid growth the cells may be spheroidal rather than squamous.

FIG. 71.—A secondary perithelioma of the liver. The primary growth was in the kidney (*vide* case on p. 526). (Photomicrograph by Dr. H. Spitta.)

Secondary sarcoma is very often alveolar in its arrangement; this depends on the growth starting from emboli inside the small vessels of the liver.

In some cases of secondary carcinoma the cells of the liver, which are atrophied and compressed by the invading cells, are considerably pigmented. This may be due to retained bile-pigment. In cases in which the liver is independently pigmented, as in malaria or in haemochromatosis, a secondary growth in the liver is not pigmented.

A man aged forty-six died under my care with a primary endothelioma in the spine. The liver was of a deep brick-red colour and had a number of minute white nodules in it, which are shewn in Fig. 67 to be quite free from pigment.

In some instances of secondary carcinoma there is proliferation of the liver cells in parts remote from the growth, which may be regarded as an attempt to replace the destroyed liver substance—a compensatory hyperplasia.

In a case of secondary sarcoma Cornil [1] observed proliferation of the hepatic cells and the formation of pseudobile canaliculi at a short distance from the growth (compare p. 496).

Brault [2] noticed that in some instances in which the cells of the secondary growths contain glycogen the hepatic cells contain none.

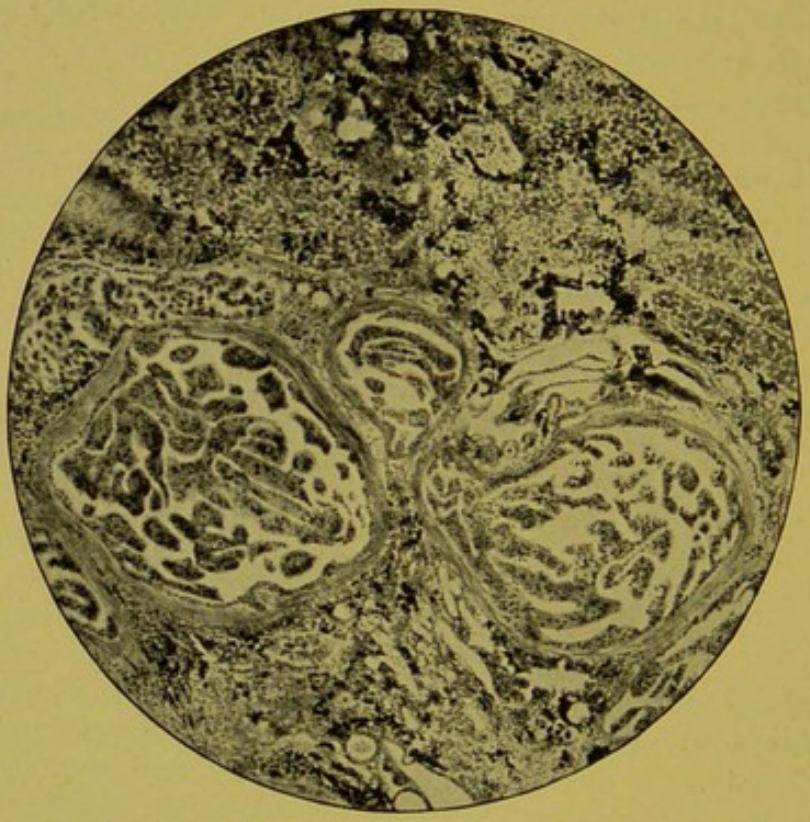


FIG. 72.—Liver with secondary endotheliomatous growths. The liver is pigmented from haemochromatosis; the small nodules of growth, entirely free from pigment, are mainly surrounded by remains of the fibrous tissue of the portal spaces. The primary growth was in the spine. ×28.

A certain amount of local fibrosis is common around carcinomatous nodules in the liver; this may be regarded as an attempt on the part of the organ to limit the extension of the growth. When this change is more general and there is obstinate jaundice, the fibrosis has been thought to be due to biliary obstruction set up by the tumour.[3]

Condition of the Remainder of the Liver.—From pressure on the bile-ducts the whole or parts of the liver may be bile-stained. The occurrence of local areas of chronic venous engorgement from pressure

[1] Cornil. *Bull. Soc. Anat.*, Paris, 1902, lxxvii, 195.
[2] Brault. *Arch. de méd. expér. et d'anat. path.*, Paris, 1902, xiv, 467.
[3] Gilbert et Claude. *Arch. gén. de méd.*, Paris, 1895, clxxv, 513.

on branches of the hepatic veins has just been referred to. In some instances the engorgement is so extreme that extravasation occurs in the immediate neighbourhood of nodules of growth and produces an appearance of a haemorrhagic infarct. Infarctions, both haemorrhagic and anaemic, have been met with in the liver, as a result of venous obstruction due to pressure, exerted by nodules of growth, on the portal or hepatic veins (*vide* p. 104).

Secondary malignant growths are very rare in cirrhotic livers; they occur, of course, in the special form of primary carcinoma with cirrhosis.

In 608 cases of secondary malignant disease of the liver the organ was cirrhotic in two (Colwell [1]). Hale White [2] mentions a case of a man with sarcoma of many bones with a growth in a cirrhotic liver. Poulain [3] met with a secondary nodule in a cirrhotic liver; the primary growth was a columnar-celled carcinoma of the stomach. Achard and Laubry [4] described secondary growths in a large cirrhotic liver, the primary growth being in the colon.

It is not very common to find cirrhosis of the liver in patients with intra-abdominal malignant disease; this is, of course, the main reason for the rarity of secondary growths in cirrhotic livers. It is conceivable that portal obstruction interferes with the passage of emboli of infecting cells from the colon and stomach, and that the cirrhotic liver is not a good soil for their development.

When, as not uncommonly happens, secondary growths occur in tight-laced livers, the constriction lobe attached to the right lobe may be quite free from growth, suggesting that its somewhat isolated position has prevented the advent of emboli of infecting cells by the blood-stream. On the other hand, secondary growths may be almost confined to the constriction lobe, as if its diminished resistance was specially favourable to the development of any embolic masses of new growth which gain access to it. Examples of these two different events are given in the section on the tight-laced liver (p. 9).

As a coincidence there may be secondary growths in a liver containing hydatids. I have met with one such case (*vide* p. 397), and Dr. R. N. Salaman has shewn me two specimens in which secondary nodules of carcinoma were in contact with old hydatid cysts. References to other recorded cases are given on p. 397. Secondary growths may arise in a syphilitic liver, and even in one containing gummas, but it is a rare coincidence.

A man aged forty who died with carcinoma of the colon had gummas in one testis and much scarring of the liver, which contained numerous gummas and nodules of new growth. The man was in St. George's Hospital in 1891. I did the necropsy and microscopically determined that there were both gummas and new growth in the liver.

[1] Colwell. *Arch. Middlesex Hosp.*, 1905, v, 135.
[2] Hale White. Allbutt's *System of Medicine*, 1897, iv, 208.
[3] Poulain. *Bull. Soc. Anat.*, Paris, 1899, 6. s., i, 1089.
[4] Achard et Laubry. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1902, 3. s., xix, 335.

Tuberculosis and secondary growths may exist in the same liver. There is no antagonism between the two processes, as was formerly thought.

Dalton [1] recorded a case of secondary columnar-celled carcinoma in the liver with miliary tubercles in the immediate neighbourhood. The primary growth was in the sigmoid flexure.

In very rare instances ordinary secondary growths, due to an extra-hepatic neoplasm, are associated with a primary carcinoma of the intra-hepatic bile-ducts.

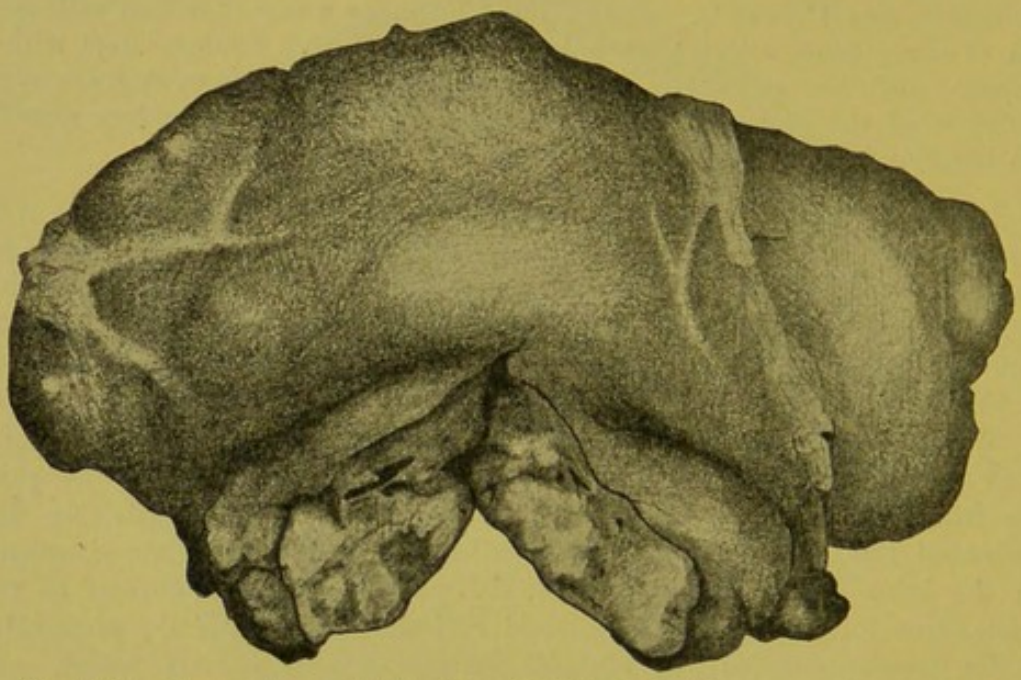


FIG. 73.—A liver shewing the constriction lobe divided and its halves separated so as to display large secondary carcinomatous growths in its substance. There were in addition two small white nodules only in the right lobe of the liver. The primary growth was carcinoma of the breast. (Drawn by L. Jones, M.S.)

In Necker's [2] case a cirrhotic liver contained two hydatid cysts, secondary spindle-celled sarcoma, and a primary carcinoma derived from the bile-ducts. In a secondary melanotic sarcoma of the liver primary carcinomatous nodules, derived from the bile-ducts and ascribed to the irritation of the secondary melanotic growths, have been described (Taylor and Teacher [3]).

The existence of two different kinds of secondary growths in the same liver must be excessively rare.

Simon [4] records the case of a woman who died, two years after removal of her right eye, with widespread melanotic sarcoma. The liver was greatly enlarged

[1] Dalton. *Trans. Path. Soc.*, Lond., 1885, xxxvi, 235.
[2] Necker. *Ztschr. f. Heilk.*, Wien u. Leipz., 1905, xxvi (*Abt. path. Anat.*), 351.
[3] Taylor and Teacher. *Journ. Path. and Bacteriol.*, Cambridge, 1908, xii, 441 ; 1910 xiv, 205.
[4] Simon. *Bull. Soc. Anat.*, Paris, 1900, xxiv, 213.

with melanotic sarcoma and contained a white nodule which microscopically had the structure of columnar-celled carcinoma. Unfortunately the stomach and intestines were not examined at the necropsy, so the site of the primary growth was not discovered.

Methods of Metastasis.—The dissemination of secondary growths is mainly due to embolism of the intrahepatic blood-vessels. In most cases, since the primary growth is within the territory drained by the portal vein, the emboli of carcinomatous cells travel up that vessel. When the primary growth is in the eye and in other distant parts of the

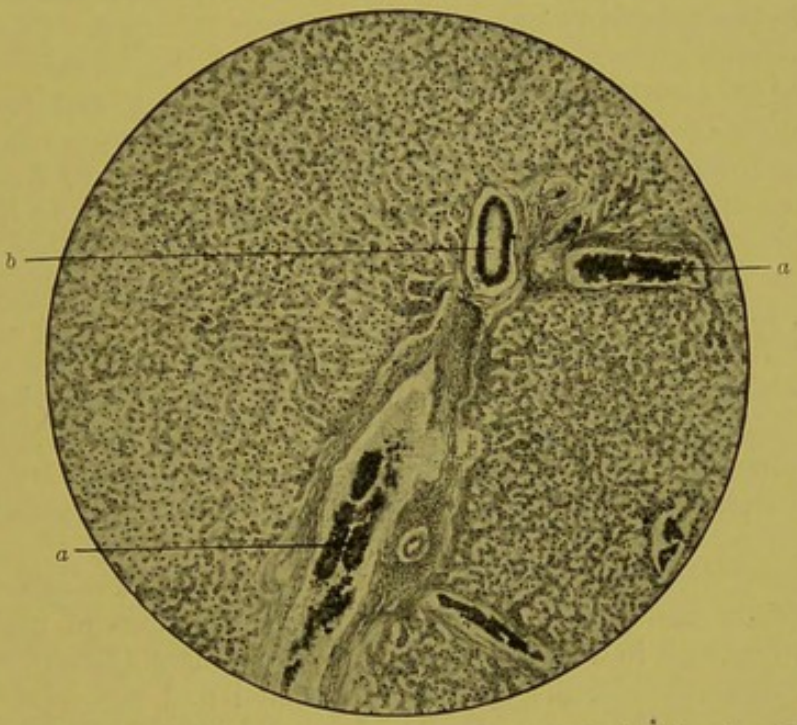


FIG. 74.—Minute emboli in the intrahepatic branches of the portal vein (*a*). A small bile-duct is represented at *b*. From a case of secondary carcinoma of the liver. The primary growth was in the stomach. × 50.

body, the emboli are distributed by the hepatic artery. It appears from Handley's[1] investigations that mammary carcinoma spreads by the lymphatics to the liver ("epigastric invasion"), and that the usual statement that it is embolic is erroneous. Primary carcinoma of the mamma may extend by the lymphatics to the linea alba and round ligament into the liver. With the exception of primary carcinoma of the mamma and probably of the oesophagus the dissemination of secondary growths in the liver, unlike the spread of carcinoma elsewhere, is not by way of the lymphatic vessels.

This depends on two factors: (i) That the liver does not receive the lymphatics of the other abdominal viscera, but sends its own out at the portal fissure; hence carcinoma would have to spread in against the direction of the flow of lymph. This does occur, but it is quite excep-

[1] Handley. *Lancet*, Lond., 1905, i, 1047.

tional. In carcinoma of the stomach growth can sometimes be seen tracking into the portal fissure. Colloid cancer of the peritoneum may pass into the subserous lymphatics of the capsule and invade the liver. (ii) That the primary carcinomatous growths in the alimentary canal frequently invade the radicles of the portal vein. When this has occurred, emboli readily pass up to the liver, inasmuch as there are no valves in the portal vein.

Secondary Growths due to Retrograde Embolism.—In rare instances a carcinomatous or sarcomatous embolus, when in the right auricle or inferior vena cava close to the diaphragm, is driven, by some expiratory effort, into the hepatic veins against the stream of blood. Thus Welch[1] refers to Heller's cases of malignant disease of the caecum in which a loose plug of growth was found in one hepatic vein, and to Bonome's case of cancer of the thyroid gland with metastatic growths in the liver developing from plugs in the hepatic veins. My friend Professor Adami has told me of a primary growth of an accessory adrenal which extended into the inferior vena cava and right auricle, where it ended in a ball-like termination and gave rise to secondary growths, evidently by retrograde embolism, in the liver.

Direct Invasion of the Liver by a Growth.—It is not very uncommon for a growth starting in the gall-bladder to infiltrate the liver by direct continuity, and in some instances the appearances have led to an erroneous diagnosis of primary malignant disease of the liver. Primary carcinoma of the extrahepatic bile-ducts may extend up into the liver.

Malignant disease of the stomach, especially at the cardiac end, may spread directly into the liver. In Fenwick's[2] 131 cases of gastric carcinoma this occurred in 13·7 per cent. In such cases the growth in the liver may undergo necrosis or become infected and give rise to a gangrenous abscess cavity and to fever. In rare instances carcinoma of the lower end of the oesophagus may extend directly into the liver. I have seen direct invasion of the liver occur in cases of primary endothelioma of the right suprarenal.

Situation of the Primary Growth in Secondary Malignant Disease of the Liver.—The most frequent sites of the primary carcinomatous growths are in the alimentary canal, viz. stomach, colon, oesophagus, pancreas, from which small emboli of infecting cells pass along the portal vein and form carcinomatous emboli in the capillaries of the liver; thus, secondary growths start and are for a time inside the hepatic capillaries, whereas primary carcinoma is outside the vessels, or extravascular.

In 100 consecutive cases of secondary malignant disease of liver abstracted from the post-mortem books of St. George's Hospital from 1892–1902 the following were the situations of the primary growths:

[1] Welch. Allbutt's *System of Medicine*, 1899, vi, 232.
[2] Fenwick. *Cancer and other Tumours of the Stomach*, p. 55, 1902.

Carcinoma.	
Stomach	24
Colon	12
Oesophagus	10
Pancreas	8
Gall-bladder	5
Uterus	4
Mamma	3
Kidneys	3
Bile-ducts	3
Biliary papilla	1
Vermiform appendix	1
Bladder	1
Ovary	1
Generalised	1
	77

Sarcoma.	
Suprarenals	5
Mediastinum	4
Melanotic	3
Generalised	3
Bone	2
Lung	2
Stomach	1
Liver	1
Thyroid	1
Uterus	1
	23

The *stomach* is the most frequent site of the primary growth in secondary malignant disease of the liver, about 25 per cent of the cases of secondary malignant disease of the liver are secondary to malignant disease of the stomach.

In malignant disease of the stomach there are secondary growths in the liver in about 35 per cent of the cases (Fenwick [1]). Welch gives 30 per cent, Perry and Shaw [2] 40 per cent, and Lebert 40·9 per cent. In 228 cases of primary carcinoma of the stomach examined after death at St. George's Hospital there were secondary growths in the liver in 71, or 31 per cent (Packe [3]); Colwell [4] found 86 metastases in 227 cases, or 37 per cent. In 47 fatal cases of gastric carcinoma tabulated by Osler and McCrae [5] the liver was affected in 23. According to Fenwick, the right lobe is involved in carcinoma of the pylorus and middle of the stomach and the left lobe when the cardiac end is the site of carcinoma.

Carcinoma of the colon is probably, after malignant disease of the stomach, the most frequent cause of secondary growths in the liver.

In 100 cases of secondary malignant disease of the liver the colon or rectum was the site of the primary growth in 12. In 100 fatal cases of primary carcinoma of the colon examined after death I found secondary growths in the liver in 34. But in many of these the secondary nodules were quite small and could not have given rise to any clinical manifestations. Of these 100 cases, 52 were males (19 secondary growths) and 48 females (15 secondary growths).

It is remarkable that secondary growths in the liver are more frequent and often more extensive when the primary growth in the colon is small than when it is large.

In a case mentioned by Weber [6] the liver weighed 27½ lbs., whilst the primary growth in the rectum was the size of a large cherry.

[1] Fenwick. *Cancer and other Tumours of the Stomach*, p. 182, 1902.
[2] Perry and Shaw. *Guy's Hosp. Rep.*, 1904, lviii, 155.
[3] Packe. *Med. Chronicle*, Manchester, 1907, xlvi, 213.
[4] Colwell. *Arch. Middlesex Hosp.*, 1896, vii, 157.
[5] Osler and McCrae. *Cancer of the Stomach*, p. 141, 1900.
[6] Weber, F. P. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Path. Sect.), 150.

A patient may be quite unconscious of a growth in the rectum when the liver is greatly enlarged. Hence the rectum should always be examined in suspected malignant disease of the liver when the site of the primary growth is not clear.

Metastatic growths in the liver are found in about half the cases of *primary carcinoma of the gall-bladder.*

In Musser's [1] 100 cases the liver contained secondary nodules in 52 and was directly invaded by the growth in 2 more.

Secondary growths are frequently found in the liver in fatal cases of *carcinoma of the breast.* Thus in 423 necropsies of mammary carcinoma tabulated by Gross [2] the liver was affected in 206, or 48·6 per cent; in 460 cases of carcinoma of the mamma examined after death at the Middlesex Hospital there were metastases in the liver in 215, or 46·7 per cent (Colwell [3]); in 735 cases investigated by S. Paget [4] the liver was involved in 241, or 34 per cent. This lower estimate is much the same as Beadles' [5] observation that in 100 cases of malignant disease of various parts of the body secondary growths in the liver were found in 36. In 422 cases of mammary carcinoma, tabulated by Handley,[6] the liver was affected in 90, or 21·3 per cent.

Carcinoma of the oesophagus is more likely to lead to metastases in the liver when the lower third of the gullet is the site of the growth.

In 85 cases of oesophageal carcinoma examined after death at St. George's Hospital there were secondary nodules in the liver in 17 instances; and in 28 out of 91 at the Middlesex Hospital; or a percentage of 25 in the 176 cases. In rare instances the oesophageal growth is so small as to be entirely latent while the liver is greatly enlarged.

Carcinoma of the uterus rarely gives rise to secondary growths in the liver; among 818 cases at the Middlesex Hospital there were 97 with hepatic metastases, or 12 per cent.

Secondary Sarcoma.—As already pointed out, secondary sarcoma is much less frequent in the liver than secondary carcinoma (*vide* p. 487). Hale White found 8·6 per cent of the cases of secondary malignant growths in the liver to be sarcoma. My figures, which give a much higher percentage of secondary sarcoma, viz. 23, include cases of endothelioma, for example, malignant growths primary in the suprarenals.

Melanotic Sarcoma.—The occurrence of secondary melanotic growths in the liver is well known, and is so striking that once seen—and all museums contain specimens—it is never forgotten. Since this is a matter

[1] Musser. *Boston Med. and Surg. Journ.*, 1889, cxxi.
[2] Gross. *Am. Journ. Med. Sc.*, Phila., 1888, xc, 235.
[3] Colwell. *Arch. Middlesex Hosp.*, 1905, v, 123.
[4] Paget, S. *Lancet*, Lond., 1889, i, 571.
[5] Beadles, C. F. *Trans. Path. Soc.*, Lond., 1896, xlvii, 77.
[6] Handley. *Lancet*, Lond., 1905, i, 1048.

of common knowledge, it might be thought that it is common in ordinary hospital work. This, however, is not the case.

In twelve years—1890–1901—3806 necropsies were performed at St. George's Hospital, and in 3 cases there were secondary melanotic growths in the liver, or in 0·08 per cent.

The primary sites of malignant melanomas are chiefly those where the pigment melanin is present, namely, in the uveal tract and in the skin, especially in pigmented moles. It may be mentioned that melanotic cutaneous growths, though from custom usually spoken of as sarcomas, are now generally regarded as pigmented endotheliomas. In rare instances a primary melanoma has been seen in the rectum or at the margin of the anus, but secondary growths in the liver are very rare in these cases.

De Buck and Vanderlinden [1] described a case with secondary growths in the liver. In neither Heaton's [2] case nor in one examined by myself were there hepatic metastases.

Recurrence in the liver usually occurs within three years of the appearance of the primary growth, and the prognosis is very bad. Occasionally long periods of immunity are met with. In one of the first published cases of secondary melanotic sarcoma there was an interval of eight or nine years between the removal of the eye and the occurrence of symptoms indicating hepatic growth.[3]

In Lilley's [4] case ten years elapsed between excision of an eye for melanotic sarcoma and death with growths in the liver. Lawbaugh [5] recorded a case in which seventeen years elapsed between enucleation of the eye for a melanotic sarcoma and death from the same growth in the liver. The most extraordinary case is one in which there were thirty-two years between the removal of the eye for melanotic sarcoma and death from the same disease in the liver. Wilder,[6] who mentions this case, saw the liver in Kundrat's laboratory at Vienna.

Very occasionally the liver may be widely infiltrated with secondary melanotic sarcoma, while the primary growth is very small and may escape notice.

The London Hospital Museum [7] contains a liver infiltrated with melanotic sarcoma and weighing 16 pounds; the primary growth in the eye was only discovered at the necropsy. Dr. Newton Pitt kindly shewed me a similar case. A man aged twenty-nine had cutaneous tumours, one of which was excised and found to be an alveolar melanotic sarcoma, and enlargement of the liver. Ophthalmoscopic examination of the eyes was negative. There was no melanin

[1] De Buck et Vanderlinden. *Belgique méd.*, Nov. 9, 1899.
[2] Heaton. *Trans. Path. Soc.*, Lond., 1894, xlv, 85.
[3] Murchison. *Ibid.*, 1873, xxiv, 123.
[4] Lilley. *Lancet*, Lond., 1911, ii, 363.
[5] Lawbaugh. *Journ. Amer. Med. Assoc.*, 1900, xxxv, 1363.
[6] Wilder. *Ibid.*
[7] Vide *London Hosp. Gaz.*, 1900, vii, *Clin. Supplement*, p. 1.

in the urine. At the necropsy there was widespread generalisation of the growth ; the liver weighed 16 pounds. There was a small growth in the outer edge of the uveal tract in the right eye.

Lawford's and Collins' statistics as to the results of melanotic sarcoma of the uveal tract shew that in 26 cases known to have died there was evidence that the liver was affected in 16.

In age-incidence malignant melanotic growths resemble carcinoma and rarely occur in early life.

In 103 cases of sarcoma of the uveal tract, all of which, except one, about which no note was made, being more or less melanotic, collected by Lawford and Collins,[1] the average age was 48·4 years, the extremes being 15 years and 84 years. In 35 cases of secondary melanotic growths in the liver which I collected, the average age was 48·7 years, or 46·7 years for the males and 53·3 for the females, the extremes being 27 years and 75 years.

Of Lawford's and Collins' 103 cases, 59 were males and 44 were females ; in my 35 collected cases in which the sex was stated, 25 were males and 10 were females ; this shews a greater preponderance of males than in the series of primary growths of the uveal tract. The right eye was affected 41 times and the left 60 times in Lawford's and Collins' cases, while in my cases of hepatic growths the right eye was rather more frequently the primary seat of growth, but the numbers are small.

Metastatic melanotic tumours of the liver are more often secondary to a primary growth in the uveal tract than in the skin. Thus, in 37 cases of melanotic sarcoma in the liver the primary growth was 24 times in the eye and 13 times in the skin. The growths in the liver following cutaneous melanosis are not so big or so striking as those secondary to melanotic sarcoma of the uveal tract. Primary cutaneous melanoma may, indeed, cause widespread metastases, the liver being one of the few organs not affected. In a case [2] in which the growth began in a left toe there were numerous growths in the skin elsewhere, the lungs, kidneys, and brain, but the liver and spleen were quite free. In most of my collected cases in which the liver contained growths secondary to cutaneous melanosis, the organ was little above the ordinary size, though in 2 cases it weighed over 7 pounds ; on the other hand, some of the largest livers recorded have been secondary to melanotic sarcoma originating in the eye. Thus, Litten [3] reported a liver weighing 27 pounds, Sayre [4] one of 23 pounds, and Hamburger [5] one of 22 pounds. I have examined 2 cases in which the weight was within a few ounces of 16 pounds. The average weight of the liver in 22 cases of melanotic growth secondary to a growth in the uveal tract was 13 pounds 3 ounces. This difference in the

[1] Lawford and Collins. *Roy. London Ophth. Hosp. Rep.*, 1893, xiii, 104, 395.
[2] Lévi. *Bull. Soc. Anat.*, Paris, 1899, lxxiv, 709.
[3] Litten. *Deutsche med. Wchnschr.*, 1889, xv, 41.
[4] Sayre. *Trans. New York Path. Soc.*, 1879, iii, 42.
[5] Hamburger. *Johns Hopkins Hosp. Bull.*, 1898, ix, 50.

liability to metastasis in the liver exhibited by melanotic sarcoma starting in the skin and in the eye is shewn in the two following cases:

Primary Growth in the Skin of the Big Toe; Widespread Metastasis.—A man aged sixty-four years had had his foot removed for a melanotic sarcoma starting in the big toe after an injury. The growth recurred in the stump, and at the necropsy, which I performed, there were metastases in the lungs, brain, left kidney, pancreas, abdominal glands, and liver. The liver contained numerous isolated growths, but weighed only 52 ounces. The growth was a spindle-celled sarcoma.

Primary Growth in the Eye, Excision, Recurrence in the Liver.—A man aged fifty-nine years was admitted under my care with the history that his right eye had been removed two years previously for a melanotic sarcoma. The liver was enormously enlarged and knobby, but there was no ascites. He had melanuria. The legs were oedematous. At the necropsy there were a few small secondary growths on the diaphragm, in the mucous membrane of the intestine, and in one adrenal. The liver was enormously enlarged, weighing 15 pounds 12 ounces, and was extensively occupied by growths of a spindle-celled melanotic sarcoma.[1]

The liver is a favourite site for secondary infiltration in melanotic sarcoma of the uveal tract. In a few cases it coexists with an intra-ocular growth, but it usually occurs within three years after removal of the eye and generally without there being any local recurrence in the optic nerve or orbit. It would thus appear that the infective cells of the growth must remain latent in the liver for some time. The liver may be the only organ in the body affected, or almost every viscus and tissue may shew metastases. It is remarkable that the cells of melanotic sarcoma being, as they usually are, larger than the cells of the other sarcomas which are stopped by the lungs, manage to pass through the pulmonary capillaries and to infect the liver. The liver evidently offers the most favourable situation for the growth of melanotic sarcoma.

The growths in the liver almost always progress very rapidly, but in Litten's[2] case there was evidence of a tumour in the liver for the exceptionally long period of four years.

The liver may be either nodular, from the presence of discrete growths, or diffusely infiltrated, so that the organ, though enlarged, is not altered in shape. When thus infiltrated, the liver substance presents a variegated appearance like that of granite, exceptionally it is so extensively infiltrated that it looks as if it had been soaked in tar. Not uncommonly the liver shews nodules in some parts and diffuse infiltration in others. As a rare event a pedunculated growth may be found attached to the liver. Sometimes parts of the growths are free from pigment and pale; in other cases the pigment is sparse and the tumours, to the naked eye, appear of a mottled grey or greenish colour. Perihepatitis is not common.

Histologically, secondary melanotic growths in the liver may be

[1] Rolleston. *Lancet*, Lond., 1899, i, 1273.
[2] Litten. *Deutsche med. Wchnschr.*, 1889, xv, 41.

sarcomatous or endotheliomatous; when sarcomatous, they may be spindle-celled, oval or oat-shaped, or round-celled. The cells start as emboli inside the hepatic capillaries, and hence the growth frequently has a more or less alveolar appearance.

Malignant Disease Primary in the Suprarenals.—In 26 cases of primary malignant disease (carcinoma, endothelioma, or sarcoma) of the adrenals collected by Marks and myself[1] the liver was the organ most frequently affected by secondary growths, namely, in 14, and was, in addition, invaded by direct continuity in 3. In 46 cases of sarcoma of the suprarenals collected by Pepper[2] there were metastases in the liver in 14. A suprarenal growth may extend into the inferior vena cava and give rise to retrograde embolism in the hepatic veins and so to secondary growths, as in Adami's case (p. 498).

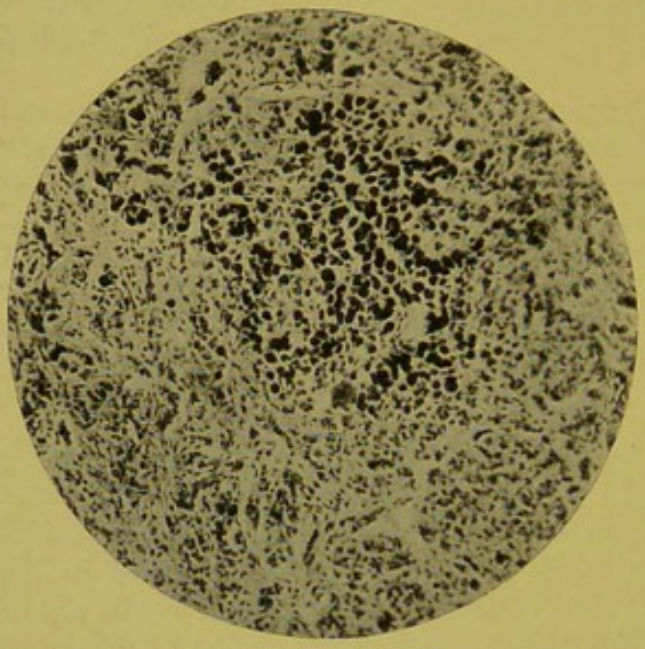


Fig. 75.—Secondary infiltration of the liver with a melanotic sarcoma. The cells are chiefly round-cells, and vary considerably in the amount of melanin they contain. The arrangement is more or less alveolar. The primary growth was in the uveal tract. (Photomicrograph by Dr. S. G. Penny.)

In generalised sarcoma the liver often contains discrete nodules of growth. The portal spaces may be infiltrated with green growth in chloroma, which has been regarded in the past as a round-celled sarcoma, but is a form of acute lymphocytic leukaemia. Trevithick[3] has reported a case of this kind.

An exceptional origin for secondary growths in the liver is so interesting that a brief reference may be made to it. Embryomas and teratomas in the abdominal cavity may become malignant and infect the liver.

Out of 10 cases of malignant teratoma collected by Montgomery,[4] 4 led to secondary growths in the liver. A non-malignant implantation-growth on the surface of the liver has followed rupture of an ovarian embryoma (Hulke,[5] Latham[6]). Abdominal dermoids (embryomas) are practically teratomas, as they are not composed of skin alone, but of tissues derived from all three layers of the embryo, and are really, as Wilms[7] shewed, complex tumours.

[1] Rolleston and Marks. *Am. Journ. Med. Sc.*, Phila., 1898, cxvi, 390.
[2] Pepper. *Ibid.*, 1901, cxxi, 287.
[3] Trevithick. *Lancet*, Lond., 1903, ii, 158.
[4] Montgomery. *Journ. Exper. Med.*, N.Y., 1898, iii, 259.
[5] Hulke. *Trans. Path. Soc.*, Lond., 1873, xxiv, 157.
[6] Latham, A. *Ibid.*, 1899, l, 232.
[7] Wilms. *Deutsche Arch. f. klin. Med.*, Leipz., 1895, lv, 289.

Clinical Features of Malignant Tumours of the Liver

It will be most convenient to describe the signs and symptoms of primary and secondary malignant tumours of the liver together, since the two conditions are so frequently indistinguishable, and to note the points of difference between them in a special section (*vide* p. 526). The latency of malignant tumours of the liver is dealt with on p. 519.

Physical Signs.—The facial aspect of a patient with advanced malignant disease of the liver is that of a grave and wasting illness. The eyes are usually sunken, and the skin dirty, sallow, or shewing varying degrees of jaundice. But in the earlier stages, even when nodular enlargement of the liver can be felt, there may be little to note in the patient's aspect except some anaemia, and it cannot be maintained that the facial aspect is characteristic at this early stage. Steady loss of flesh and weight are very common in malignant disease of the liver. The subcutaneous fat is absorbed, and as a result the cheeks and temples fall in and give the patient a hollow and haggard appearance. Absorption of fat helps to render the skin inelastic. During the emaciation an associated fatty tumour has greatly diminished in size (Bell [1]).

The patients may actually gain in weight as the liver increases in size.

A boy, aged fifteen years, with primary carcinoma of the liver, gained 19¾ pounds before his death; this was due to the enormous liver, which weighed nearly 16 pounds, or two-fifteenths of the total body weight, and also to ascites (Acland and Dudgeon [2]). A man who died in St. George's Hospital, under the care of Dr. C. Ogle, from multiple primary sarcoma of the liver, gained 7 pounds in the last three weeks of life. At the necropsy the liver weighed 16¼ pounds, and there was about one pint of ascitic fluid (*vide* Fig. 67).

The gain in weight of the individual as a whole, if not due to ascites and oedema, depends on the increase in the tumour growth more than counterbalancing the loss due to general emaciation. The same phenomenon is sometimes seen in rapidly growing renal sarcomas in infants. Some increase in weight and improvement in general nutrition may follow careful feeding, especially in the early stages of malignant disease of the liver.

Progressive emaciation is more marked in secondary malignant disease of the liver, for here there is in addition the effect of the primary growth, often in the stomach or colon, which has already, and perhaps for some considerable time, interfered with digestion and assimilation of food. In such cases nutrition may be so impaired that bed-sores develop; their occurrence is probably favoured by the fact that the patient generally lies in one position—on the back.

[1] Bell. *Brit. Med. Journ.*, 1902, i, 1588.
[2] Acland and Dudgeon. *Lancet*, Lond., 1902, ii, 1310.

Exceptionally, however, death may occur from secondary malignant disease of the liver when the patient is well nourished or even fat.

A man aged sixty-three years, a patient in St. George's Hospital, had enlargement of the liver and ascites. He had never had haematemesis and was not jaundiced. He was thought to have cirrhosis. At the necropsy, the abdominal walls, mesentery, etc., contained much fat. There was a primary carcinoma of the hepatic flexure, and the liver (10½ lbs.) was full of secondary growths.

In primary malignant disease the progress of the disease is so rapid, death often following even within three months of the first symptoms, that there may not be time for emaciation and there may be plenty of subcutaneous fat.

In a very rapid case which I examined after death some years ago the man —who was sent into the hospital for intestinal obstruction—was very fat. An enormously fat woman aged forty, weighing over 20 stone, died with multiple growths in the liver, which weighed 10 pounds 11 ounces. Except for a few minute nodules in the spleen, no other growth could be found elsewhere in the body. It was apparently a case of multiple primary carcinoma of the liver. Microscopically the growth was a rapidly growing carcinoma composed of cells shewing transitional forms from columnar to spheroidal type.

Cachexia is important in differentiating malignant from other enlargements of the liver, such as deeply seated hydatid cysts, hypertrophic biliary cirrhosis, and from some cases of nutmeg liver. The *progressive* character of the cachexia is of especial importance. The causation of cachexia is probably to be found in an auto-intoxication emanating from the rapidly proliferating epithelial growths. As is well known, the cells of many normal glands, such as the pancreas, thyroid, suprarenal, provide an internal secretion which passes directly into the lymphatics or veins, and helps to keep up the condition of equilibrium we know as health. When epithelial cells run riot and form atypical growths, or what might be called abnormal glands, it is not unreasonable to believe that they may produce a morbid internal secretion which, when absorbed, poisons the body generally, and gives rise to the cachexia of malignant disease. In support of this view it is noticeable that innocent tumours composed of normal tissues do not, however large they may be, give rise to cachexia, unless they mechanically interfere with absorption and nutrition. There are other ways in which poisonous substances can be supplied by malignant growths. As the result of necrosis and autolysis of growths, toxic bodies are probably produced which, when absorbed, will tend to produce toxaemia and cachexia.

Fever.—There has been a general impression that malignant disease of the liver is not accompanied by fever or only by transient elevations of temperature due to independent causes. This, however, is very far from being a rigid rule; Eggel[1] estimated that fever was present in 14 per cent of 147 collected cases of primary carcinoma of the liver, and

[1] Eggel. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1901, xxx, 506.

Russell[1] found some degree of pyrexia in nearly two-thirds of a small collection of various forms of malignant disease of the liver. Thus, fever may occur in malignant disease of the liver, whether primary or secondary, and its presence does not necessarily exclude new growth in favour of some form of hepatic suppuration. Fever in malignant disease of the liver may be divided into two categories: (i) Uncomplicated cases. The raised temperature may be due to the rapid growth and multiplication of cells inside the liver; cases occur in which no other cause is forthcoming; this may be seen in primary malignant disease of the liver. It is particularly likely to occur in rapidly growing sarcoma in young persons. The temperature, which rarely rises above 102° F., may continue for weeks. The liver forms a very suitable soil for rapid tumour growth and hence fever is more frequent in malignant disease of the liver than of other organs. As pointed out by Butlin and Colby,[2] fever is not very uncommon in cases of sarcoma of the femur and tibia. (ii) Complicated cases. Fever may be due to the absorption of poisons or micro-organisms from the ulcerated surface of the primary growth in the stomach, colon, or elsewhere. Again, the necrotic growths may become infected with micro-organisms either from the alimentary canal or from the blood-stream, and thus fever and rigors may result. Suppuration is occasionally associated with secondary growths in the liver. In some instances a primary growth in the stomach may directly nvade the liver and carry infection into that organ (*vide* p. 121).

A woman aged fifty-four had a primary spheroidal-celled carcinoma of the cardiac end of the stomach, which perforated directly into the under surface of the liver and produced a large abscess in close contact with numerous secondary nodules in the liver. The hepatic abscess leaked into the peritoneal cavity and set up fatal peritonitis.

Suppurative cholangitis may supervene in the course of malignant disease of the liver when the ducts are dilated from obstruction; this is more likely to occur in secondary malignant disease of the liver, since obstruction to the ducts is comparatively infrequent in primary growths of the liver substance.

Osler[3] refers to a case of cancer of the liver in which intermittent fever and rigors were so marked that the question of abscess was raised. After death, in addition to secondary growths, there were several abscesses caused by the growths compressing the bile-ducts.

A good example was seen in a woman aged forty-four who had jaundice due to growths in the portal fissure, secondary to carcinoma of the splenic flexure of the colon, compressing the hepatic ducts. The intrahepatic bile-ducts shewed suppuration. There was high fever in this case, which was under the care of my colleague, Sir Isambard Owen.

[1] Russell, J. W. *Brit. Med. Journ.*, 1907, i, 312.
[2] Butlin and Colby. *St. Barth. Hosp. Rep.*, 1895, xxxi, 31.
[3] Osler. *Johns Hopkins Hosp. Rep.*, Balt., 1891, ii, 1.

Primary carcinoma of the second part of the duodenum involving the biliary papilla (perivaterian duodenal carcinoma) is especially prone to set up suppurative cholangitis; usually it kills the patient in this way before there has been time for secondary growths to occur in the liver, but secondary growths may be found in association with suppurative cholangitis.

A man aged fifty-two was under the care of my colleague, Sir Isambard Owen, with jaundice, rigors, and a lump in the prostate. The necropsy revealed a primary columnar-celled carcinoma of the biliary papilla, secondary growths in the liver, suppurative cholangitis, empyema of the gall-bladder, and pyaemic abscesses in the prostate and kidneys.

Malignant dsiease and cirrhosis of the liver may both be accompanied

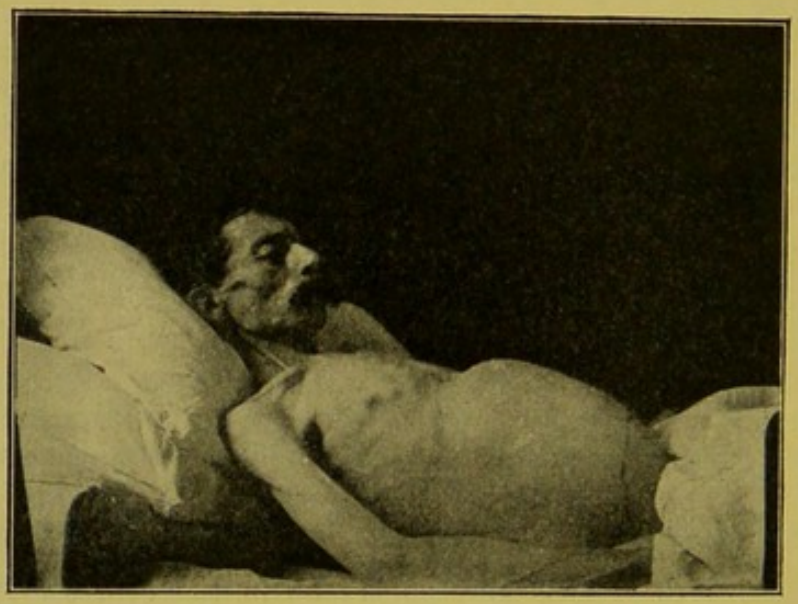


FIG. 76.—Primary multiple sarcoma of liver (*vide* fig. 67 on p. 483). The lower margin of the liver is marked on the skin. Cachexia is pronounced. The subcutaneous veins are enlarged. (Photograph by Dr. F. Golla.)

by fever. Cases of malignant disease of the liver with fever may simulate pylephlebitis, hepatic abscess, or even enteric fever (Guthrie [1]).

The *abdomen* may be greatly distended by the enlarged liver, the outline of which may even be visible, the skin is often tense, and enlarged veins, usually from obstruction of the inferior vena cava, may be visible.

The *liver* is enlarged; the enlargement is progressive, and may be so extreme that the organ eventually occupies most of the abdomen; it moves with respiration, and after death may not come down so low as in life, being drawn up by the last expiration. When the surface of the organ is irregular, the growth is in the great majority of cases secondary; the nodules may be felt to be umbilicated or depressed in the centre, and

[1] Guthrie. *Clin. Journ.*, Lond., 1908, xxxiii, 144.

thus can be distinguished from the hobnails of a cirrhotic liver, from which the progressive character of the enlargement further separates it. Sometimes, however, the depressions between hobnails on a cirrhotic liver convey the impression of umbilication, and umbilication cannot always be felt over secondary hepatic growths. In cirrhosis the enlargement is more uniform than in malignant disease which chiefly affects the right lobe.

In primary malignant disease of the liver there is usually a uniform, firm, and hard tumour in the position of the right lobe of the liver, and occasionally there are, in addition, nodules of secondary growth elsewhere on the surface of the liver. This condition cannot be distinguished from secondary malignant disease in which the primary growth is latent. Occasionally the growth is so soft that it fluctuates and imitates an abscess (*vide* p. 522). In rare cases it may pulsate, either because the growth is a haemorrhagic sarcoma or from transmitted pulsation.

Sir Lauder Brunton[1] met with a case of malignant disease of the left lobe of the liver with pulsation and a bruit over the tumour which imitated an abdominal aneurysm.

A mass of new growth may be found at the umbilicus in association with secondary malignant disease of the liver. Small outlying secondary growths may also form in the falciform ligament of the liver, and be felt during life near the linea alba; their presence greatly assists in forming a diagnosis of malignant disease. They may, however, be closely simulated by small islands of fat left intact when emaciation is rapid.

In a case of secondary malignant disease of the liver in which small masses were felt during life in the line of the falciform ligament I could not find after death the growths which I thought I had felt during life, and which had assisted in the diagnosis.

Nodules of new growth on the surface of the liver may be closely simulated by perihepatitic adhesions or by irregularities due to gummas and syphilitic cicatrices.

A *venous hum* or murmur is occasionally heard over the liver. It may be due to an excessively vascular or haemorrhagic growth, to pressure, exerted by nodules of growth or enlarged glands, on the portal vein, or possibly to constriction of the inferior vena cava where it is in contact with the liver. *Friction* from perihepatitis, set up by growths in the capsule, may be detected in some instances and is usually accompanied by pain and tenderness on pressure. It is commoner in secondary than in primary growths of the liver, not only because secondary growths are met with in such an overwhelming proportion, but because they are more likely to invade the capsule than primary growths.

Haemorrhages into the skin, mucous membranes, and other parts of the body may occur in association with jaundice and cholaemia. They may

[1] Lauder Brunton. *Trans. Med. Soc. Lond.*, 1896, xix, 117.

also be met with when there is little or no jaundice, though the liver is extensively infiltrated by growth, and when rapidly destructive changes in the liver cells are in progress, which interfere with the formation of fibrinogen. Exceptionally a haemorrhagic tendency is manifest in an early stage of malignant disease of the liver and then passes away. As the result of failure in the antitoxic function of the liver cells, poisons absorbed from the intestinal tract pass into the general circulation and give rise to cholaemia. The presence of bile in the circulation is quite subordinate in importance to these toxic substances.

Jaundice and *ascites* are not essential, but rather accidental, symptoms. They may be due to a growth pressing on the portal vein and bile-duct, or on their main branches; a secondary growth in the glands in the portal fissure may thus give rise to both. One or both of them may appear at almost any period of the disease. They are not evidences of the extent or severity of the disease, but only of its situation. They both occur in about 50 per cent of the cases.

Jaundice, if marked, is a severe complication, and by giving rise to cholaemia may accelerate the necessarily fatal issue. In 41 cases of primary malignant disease of the liver jaundice was present to some degree in 23, or 56 per cent (Colwell [1]); Eggel [2] found it in 61 per cent. Jaundice when present is usually comparatively slight and not of the marked character and prolonged duration sometimes seen in secondary malignant disease of the organ. Jaundice may depend on associated catarrh of the bile-ducts, and may then be relieved by treatment (Mayo Robson [3]), but during life it is generally explained by mechanical pressure. The onset of jaundice in malignant disease may be sudden and accompanied by sickness and vomiting, so as to simulate catarrhal jaundice very closely, but instead of disappearing, it persists and becomes deeper (*vide* p. 665).

In secondary malignant disease of the liver jaundice is rather more likely to supervene and to occur early when the primary growth is near the bile-ducts, for example, at the pylorus or in the gall-bladder. Primary growths in these positions are prone to spread directly to the portal fissure and to produce obstructive jaundice, whereas multiple embolic growths scattered over the periphery of the liver have much less tendency to induce biliary obstruction.

A man aged thirty-four years became jaundiced a few weeks before his death from primary spheroidal-celled carcinoma near the pylorus. The lesser omentum was $\frac{3}{4}$ inch thick from infiltration with growth which surrounded and compressed the common bile-duct. Microscopically the bile-duct was invaded by growth, the infiltration extending up to the neck of the gall-bladder and into the portal fissure. The gall-bladder and intrahepatic bile-ducts were distended, but the extrahepatic ducts were all compressed. The liver weighed

[1] Colwell. *Arch. Middlesex Hosp.*, 1905, v, 128.
[2] Eggel. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1901, xxx, 506.
[3] Mayo Robson. *Brit. Med. Journ.*, 1897, i, 641.

66 ounces and had a green, nutmeggy appearance; there were small masses of growth in the intrahepatic branches of the portal vein. This patient was in St. George's Hospital.

Obstruction to one of the intrahepatic bile-ducts may give rise to jaundice; in such a case the other bile-ducts convey bile into the intestine and the faeces are not clay-coloured. At the necropsy of such cases pressure on the gall-bladder will cause bile to flow into the duodenum.

A man aged fifty-five years, a barman, was admitted to St. George's Hospital with a large liver and distinctly palpable glands above the right clavicle. The liver was manifestly knobby, but no umbilication could be made out. The urine contained much urobilin; the faeces contained bile, and jaundice of no great intensity finally developed. Except for some difficulty in swallowing, there was nothing to suggest the site of the primary growth. At the necropsy the liver (14 lbs.) contained numerous secondary growths, some of which were umbilicated. Pressure on the gall-bladder brought bile out of the duodenal papilla. There were numerous growths in the liver near the portal fissure, which compressed some of the bile-ducts. No calculi; no cirrhosis of the liver, which was somewhat nutmeggy. The spleen shewed venous engorgement. There was a primary spheroidal-celled carcinoma in the middle third of the oesophagus, and a secondary growth, probably due to implantation but resembling to the naked eye another primary neoplasm, at the cardiac end of the oesophagus. There were a few ounces only of ascitic fluid.

On the other hand, experimental ligature of the left hepatic duct in cats performed by V. Harley and Barratt[1] did not cause jaundice. Possibly this was due to some collateral biliary anastomoses between the right and left lobes of the liver.

An interesting, but extremely rare, cause for jaundice is extension of malignant disease along the lumen of the bile-ducts in an analogous manner to the prolongation of a renal growth down the ureter. This has been known to occur in both primary and secondary malignant disease of the liver.

Gilbert and Claude[2] recorded primary carcinoma of the liver in a girl aged twenty-two, in whom attacks of biliary colic and obstinate jaundice were due to a process of the growth extending in a polypoid form into and blocking up the common bile-duct.

When jaundice is absent, the skin is usually anaemic, sallow, and sometimes dirty-looking; slight pigmentation, as in other forms of abdominal disease, is sometimes seen.

Legg[3] figures marked pigmentation suggesting argyria in a man with melanotic growths in a liver weighing 5700 grams (200 oz.) who also had melanuria. Williamson[4] lays stress on small black patches in the skin as diagnostic of internal melanotic growth.

[1] Harley and Barratt. *Brit. Med. Journ.*, 1898, ii, 1743.
[2] Gilbert et Claude. *Arch. gén. de méd.*, Paris, 1895, clxxv, 513.
[3] Legg. *Trans. Path. Soc.*, Lond., 1884, xxxv, 367.
[4] Williamson, R. T. *Lancet*, Lond., 1900, ii, 1874.

Ascites.—When the liver is extensively infiltrated with new growth its capillaries become obstructed over a correspondingly wide area, either by pressure from without, as in primary carcinoma, or from the presence of growth inside their lumen, as in secondary growth, and especially in one form of primary angiosarcoma (endothelioma), and in secondary melanotic sarcoma (Hektoen and Herrick [1]). In Eggel's 163 collected cases of primary carcinoma ascites occurred in 58·5 per cent. The obstructed portal circulation thus resembles that in portal cirrhosis, and an attempt at compensation by dilatation of the veins at the lower end of the oesophagus may result.

In a case under my care of secondary melanotic sarcoma of the liver which weighed 16 pounds, there were markedly varicose veins at the lower end of the oesophagus. Frerichs [2] records a similar case.

Portal thrombosis due to an extension of the growth from the intra-hepatic branches into the trunk of the portal vein may also account for ascites, but it is usually due to concomitant malignant disease of the peritoneum or to local inflammation of the capsule of the liver set up by an underlying growth. My own impression is that ascites is more frequent in secondary than in primary malignant disease of the liver. Eggel, however, estimates that ascites occurs in 58 per cent of the primary cases.

The ascitic fluid is usually serous and clear, like that in cirrhosis or in simple chronic peritonitis, but is bile-stained when there is jaundice. The effusion may be blood-stained from extravasation of blood into the growths, especially when they are necrotic and have ruptured into the general peritoneal cavity. In some cases, especially in sarcoma, the loss of blood, due to extravasation into the growths, may be so excessive as to give rise to faintness and collapse, while at the same time there is marked increase in the size of the hepatic tumour, which may even fluctuate and imitate very closely hepatic abscess (Byrom Bramwell,[3] Hawthorne [4]).

It has been stated that ascites is rare or even that it does not occur in melanotic sarcoma of the liver, but this is not borne out by the cases I have collected, for it was stated to be present in 10 of the 37 cases of secondary melanotic disease of the liver; and in at least four of the reputed primary melanotic growths of the liver there was ascites. Occasionally the ascitic fluid is of a dark colour, from the presence of melanin; more often it resembles ordinary ascitic fluid.

In a woman aged thirty-three who died with melanotic sarcoma of the liver there were 100 ounces of dark fluid in the peritoneal cavity and a pint of brown

[1] Hektoen and Herrick. *Am. Journ. Med. Sc.*, Phila., 1898, cxvi, 255.
[2] Frerichs. *Diseases of the Liver*, ii, 239, New Sydenham Soc., 1861.
[3] Bramwell, B. *Lancet*, Lond., 1897, i, 170.
[4] Hawthorne, C. O. *Clin. Journ.*, Lond., 1896, viii, 361

fluid in each pleura (*Middlesex Hosp. Rep.*, 1890–91, p. 278). Wickham Legg[1] and Senator[2] also recorded cases of brown ascitic fluid.

In melanotic sarcoma of the liver the ascitic fluid may be clear and yet contain cells with pigment granules inside them (Hektoen and Herrick). In a case under my care the ascitic fluid, though of the ordinary straw colour, contained melanogen, as shewn by the appearance of a dark ring on adding a watery solution of ferric chloride. On the other hand, Dr. Garrod tells me that in two similar cases with melanuria the ascitic fluid did not give the reaction.

In rare instances the ascitic effusion may be chylous as a result of transudation of chyle or even rupture of a lymphatic trunk, due to the pressure and obstruction exerted by a secondary growth in the course of the chyliferous trunks. A chyliform or fatty ascitic effusion, not due to the escape of chyle, but the result of fatty degeneration and disintegration of cells suspended in the peritoneal effusion, is not so rare. The fluid resembles chylous ascites to the naked eye, but differs from it microscopically in the size of the fat-globules, which are large and not in the fine emulsion characteristic of true chylous ascites. The oil-globules may be formed either in the cells of the growths and discharged into the peritoneal cavity, or in leucocytes. Corselli and Frisco[3] suggest that in malignant disease of the peritoneum, toxic bodies are formed which induce degenerative changes in the cells suspended in the ascitic fluid and so lead to fatty ascites.

In a case in St. George's Hospital a fatty milky effusion drawn off during life was found at the necropsy to be associated with numerous secondary growths in the liver, which weighed 15 pounds; there was also a large growth invading the receptaculum chyli, but no rupture of lymphatic vessels was forthcoming. The primary growth was in the gall-bladder.

In other cases there is milky ascites in which the opalescence is not due to fat but to the presence of a protein derivative or lecithin.

In a case of secondary carcinoma in a cirrhotic liver recorded by Achard and Laubry[4] the amount of fat—0·6 per cent—was too slight to account for the milkiness of the ascites.

The leucocytes in the ascitic fluid may be so numerous as to suggest a purulent ascitic effusion although there is no peritonitis (Gentès[5]). As the result of perforation of a viscus or infection, however brought about, an ascitic effusion in hepatic carcimona may be genuinely purulent.

The *blood* shews diminution of the red cells, with a more marked diminution in the amount of haemoglobin—a secondary anaemia. Leuco-

[1] Legg. *Trans. Path. Soc.*, Lond., 1878, xxix, 225.
[2] Senator. *Charité-Ann.*, Berlin, 1890, xv, 261.
[3] Corselli e Frisco. *Riforma med.*, Roma, 1896, iv, 630.
[4] Achard et Laubry. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1902, 3. s., xix, 335.
[5] Gentès. *Journ. de méd. de Bordeaux*, 1899, xxix.

cytosis may be present, but is not constant, and may be intermittent. It is usually moderate, but it may reach 36,000.

In 53 cases examined by Cabot [1] leucocytosis was present in 29. According to Da Costa [2] leucocytosis is more marked in hepatic carcinoma than in carcinoma of other organs.

The *urine* is usually diminished in amount, and occasionally shortly before death there may practically be suppression. It is high coloured, as a rule, and often lithatic, and may have a rather high specific gravity. When there is jaundice, bile-pigment is usually found in the urine, but when the jaundice is very slight, the urine may be acholic. When jaundice is marked, casts are found on centrifugalising the urine. Urobilin is present, sometimes in excess, unless the entrance of bile into the duodenum is entirely prevented. Indican is sometimes present.

Albuminuria is rare, and its presence in a doubtful case is in favour of some other condition, such as lardaceous disease, renal tumour, cystic disease, or hydronephrosis. It may, however, be induced by pressure on the inferior vena cava either by the liver or by enlarged glands. When the liver is so extensively infiltrated with growth that it is unable to stop poisons absorbed from the alimentary canal, the action of these poisons on the kidneys may result in albuminuria. In biliary obstruction with absence of bile from the intestines excessive fermentation may give rise to auto-intoxication and so to albuminuria. Teissier [3] described this "hepatogenous albuminuria." As already pointed out, albuminuria is rare in malignant disease of the liver, while these disposing conditions—hepatic insufficiency and jaundice—are fairly common; it would, therefore, appear that some other factor is necessary to produce albuminuria; the requisite factor is probably some primary feebleness or want of tone in the kidneys. Transient haematuria, on one or more occasions, may be the only indication that the primary growth is in the kidney. Hydronephrosis may in rare instances be due to the pressure of the greatly enlarged liver on the right kidney (Litten [4]). When the liver is extensively infiltrated with growth, the amount of urea may be diminished, and leucine and tyrosine have been found in the urine, probably from cell-destruction.[5]

Sugar is not found in the urine in uncomplicated cases of malignant disease of the liver. In this connexion it is interesting to note that Warthin [6] and Ohlmacher [7] found hypertrophy of the islands of Langerhans which they regarded as a compensatory mechanism for the

[1] Cabot. *Clinical Examination of the Blood*, p. 440, 1904.
[2] Da Costa. *Clinical Hematology*, p. 388, 1902.
[3] Teissier. *Semaine méd.*, Paris, 1899, xix, 282.
[4] Litten. Quoted in *Semaine méd.*, 1892, xii, 80.
[5] Compare Ulrich. *Nord. med. Ark.*, 1896, No. 11.
[6] Warthin. *Phila. Med. Journ.*, 1900, vi, 124.
[7] Ohlmacher, J. C. *Amer. Journ. Med. Sc.*, Phila., 1904, cxxviii, 287.

impaired hepatic function in their cases of extensive growths in the liver.

Creatine, which is not present in normal urine, has been found in large amounts in the urine of patients with malignant disease of the liver (Mellanby [1]).

In melanotic sarcoma the pigment melanin may appear in the urine (melanuria). The urine, when passed, is generally of the ordinary colour and gradually darkens on standing and exposure to the air. This darkening may be brought about rapidly by the addition of an oxidising agent, such as bichromate of potassium or nitric acid. A delicate test for melanin in the urine is the addition of a solution of ferric chloride, which even in dilute solutions produces a black colour. In very rare instances the urine is said to be black or dark brown when passed from the bladder. When the urine darkens after being passed the pigment is in the form of a colourless chromogen—melanogen—which by oxidation yields melanin. The melanin from the growth passes into the circulation, and may either be excreted as such, blackening the urine, or it may be changed by the tissues into melanogen and not produce any very manifest alteration in freshly passed urine. Melanuria may thus escape notice unless the urine is kept for a time or acted upon by oxidising agents. Nepveu and Chausel described pigment-granules in the blood and in the urine of patients with melanotic sarcoma.

In a man, aged fifty-nine years, under my care in St. George's Hospital, there were extensive melanotic sarcomatous growths in the liver, which weighed 16 pounds. The primary growth was a melanotic sarcoma of the eye removed twenty months before at Moorfields; the urine was clear when first passed, but darkened on standing and on the addition of nitric acid or ferric chloride.

Melanuria seldom occurs in the absence of secondary growths in the liver. The reasons for this probably are: (i) That there must be a considerable area of growth to provide a sufficiency of the pigment, and (ii) that the liver is more or less involved in most cases of generalised melanosis.

In one of the earliest cases described in this country as melanuria there was no hepatic growth (Hilton Fagge [2]). Melanuria was present in a case in which a large mass of melanotic growth occupied the left side of the chest, the liver being normal (Langdon Brown [3]).

The occurrence of melanuria does not depend on the presence of secondary growths in the kidneys and urinary tract, or on the kidneys being healthy, for it has been observed when the kidneys shewed the changes of arteriosclerosis. In some cases melanuria has been said to be intermittent.

The presence of melanin or of melanogen in the urine may be of great

[1] Mellanby. *Journ. Physiol.*, Cambridge, 1907, xxxvi; *Proc. Physiol. Soc.*, p. xxiii.
[2] Hilton Fagge. *Trans. Path. Soc.*, Lond., 1877, xxviii, 172.
[3] Brown, L. *Clin. Journ.*, Lond., 1909–10, xxxv, 191.

use in arriving at an accurate diagnosis in a case of enlarged liver. Thus in cases in which the primary growth in the eye remains latent, melanuria would shew that the enlargement was due to a melanotic growth. It has been stated that melanin occurs occasionally in the urine in cases in which no melanotic growth is present, but this is a mistake and is due to large quantities of indican in the urine (Garrod [1]). Urines which contain an excess of indican give with HNO_3 a reaction like that for melanin, but there is no colour reaction with ferric chloride, and in this way the two can be distinguished. The spontaneous darkening of the urine must be distinguished from that of alcaptonuria by the tests already given. In addition, alcaptonuric urine reduces Fehling's solution, but does not contain sugar, as shewn by the phenyl-hydrazine test. The toxicity of the urine has been stated to be increased (Charrin [2]).

Oedema of the feet is comparatively frequent in the later stages of the disease. It may be due to several causes, such as cardiac debility, or to toxaemia resulting from hepatic insufficiency; in the latter case the oedema is analogous to that in cirrhosis. Oedema, not only of the legs, but of the genitals, scrotum, and lower part of the trunk, may be mechanical and due to direct pressure exerted by growth, either in the liver or in the adjacent lymphatic glands, on the inferior vena cava and other venous channels, or to thrombosis of the inferior vena cava (*vide* case on p. 523), the iliac, femoral, or saphenous veins. Pheasants [3] collected 3 cases in which malignant disease of the liver extended into the inferior vena cava. It may also be due to the pressure of ascites on the inferior vena cava.

Thoracic Signs.—The large liver may encroach on the thorax and thus lead to collapse and hypostatic engorgement of the bases of the lungs, with signs of bronchitis. Concomitant ascites will tend to displace the thoracic viscera and to compress the lungs and produce pulmonary embarrassment; this may be temporarily relieved by tapping the abdomen. When the growth involves the capsule of the liver or the diaphragm, symptoms of pleurisy may result. Infection of the pleura may give rise to an effusion, usually blood-stained, and in very rare instances purulent. There may be reflex cough. Enlarged glands, infiltrated with growth, may be palpable above the clavicles, especially on the left side, the infection being conveyed by the thoracic or by the right lymphatic duct (compare Stevens [4]).

Symptoms.—Great weakness is not infrequent. It may be the result of such extensive destruction of the liver substance that the organ fails to stop poisons which in the ordinary course of events are absorbed from the alimentary canal and then destroyed or rendered innocuous. This hepatic inadequacy leads to general toxaemia and so to great feebleness. Hepatic inadequacy would also interfere with the absorption and proper

[1] Garrod. *St. Barth. Hosp. Rep.*, 1902, xxxviii, 25.
[2] Charrin. *Semaine méd.*, Paris, 1892, xii, 80.
[3] Pheasants. *Bull. Johns Hopkins Hosp.*, Balt., 1909, xx, 292.
[4] Stevens. *Brit. Med. Journ.*, 1907, i, 306.

assimilation of food. In many instances a primary growth in the alimentary canal impairs nutrition and so accounts for asthenia.

Gastric disturbance is common, there being loss of appetite, or even a marked distaste for food, especially for meat. In very rare instances there is great exaggeration of appetite, while in some cases the appetite remains unaffected or is sustained by a sort of auto-suggestion to counteract the wasting (Hanot[1]). Nausea is often present, and there may be vomiting. Spasmodic dysphagia, reflex in origin, has been reported. Chronic gastritis may for a time be the chief or only manifestation. The bowels are usually confined, and in the late stages it may be difficult to get them to act without disturbing the patient too much. Diarrhoea may be due to a primary growth in the colon. In the late stages obstinate hiccup may supervene; and thrush may invade the mouth and render swallowing difficult. I have seen the whole oral cavity lined by bile-stained thrush resembling wash-leather.

Hepatic pain may be caused by tension and stretching of the capsule, due to the presence of rapidly increasing tumours in the liver; but pain is mainly caused by perihepatitis set up by growths involving the capsule of the liver; in some instances sudden acute pain due to perihepatitis may be the first symptom. When the growth is deep-seated in the substance, as in some examples of primary carcinoma, pain may be slight or even absent throughout. Pain may be almost constant in the right hypochondrium, but is often especially felt in the back, in the shoulder, or in the loins, and may run down the right arm. It is more marked on exertion, and is worse at night. Pain is not present in all cases; but it has some bearing on the diagnosis, since there is comparatively little pain in cirrhosis, while in malignant disease of the liver pain may be persistent. Secondary growths in the diaphragm or an extension of the growth from the liver into the diaphragm may set up pleurisy and so cause a good deal of pain. Attacks of pain resembling those of biliary colic, but not due to gall-stones, are occasionally met with when the common duct is pressed upon from without.

V. Schultz[2] described attacks of false gall-stone colic in a man, aged forty-seven, due to secondary growths in the portal fissure which compressed the duct and set up jaundice. The primary growth was in the rectum.

Pruritus, or itching of the skin may be very troublesome, and a patient who is semicomatose may be continually scratching himself. It is usually associated with jaundice and occurs comparatively late in the course of the disease. Bouchard[3] speaks of it as sometimes present early in the disease, before sufficient data for the diagnosis are forthcoming.

It is very seldom that *peripheral neuritis* can be referred solely to failure of the detoxicating function of the liver. Most cases of

[1] Hanot. *Mercredi méd.*, Paris, 1893, iv, 417.
[2] Schultz. *Berlin. klin. Wchnschr.*, 1894, xxxi, 132.
[3] Bouchard. Congress at Rome, 1894.

peripheral neuritis complicating malignant disease of the liver are due to alcoholism.

Hayem [1] observed the acute onset of neuritis in both arms and legs in a case of primary carcinoma of the liver, which may have been due either to hepatic insufficiency or possibly to toxins derived from the growth.

In primary malignant disease the liver may be so extensively infiltrated with the growth that hepatic insufficiency is established. This accounts for the occurrence of haemorrhages, somnolence, and delirium in the last stages, and may render the diagnosis from cirrhosis difficult.

Charrin [2] described a case in which mental delusions occurred in an early stage of carcinoma of the liver and were thought to be due to toxaemia, as the toxicity of the urine was increased.

Duration.—Primary malignant disease of the liver runs a rapid course, and sometimes justifies the descriptive title "acute cancer." [3] From an analysis of his cases Hale White [4] concluded that the disease probably never lasts more than four months. In exceptional cases symptoms do not exist for as many weeks. The disease may remain latent; and in two instances there has been a history, possibly untrustworthy, of illness for a week only before death (Karsner [5]).

In secondary malignant disease of the liver the duration of life varies. Much depends on the nature and situation of the primary tumour, which may kill the patient before the growths in the liver have become manifest. On the other hand, if the primary growth has been removed or remains entirely latent, life may be prolonged for a year or even longer, after signs of a tumour in the liver have appeared. Usually, however, death occurs within six months of the first sign of hepatic enlargement.

Christian [6] reported a case of carcinoma of the liver secondary to an almost latent columnar-celled growth in the rectum, in which the liver was enlarged below the umbilicus thirty-five months before death. Taylor [7] mentions a case of three years' duration.

Sometimes the liver may be considerably enlarged and nodular, and the patient remains for weeks in much the same condition and then suddenly goes rapidly downhill. In other instances the liver steadily enlarges, and the patient's condition deteriorates. It has been stated that secondary growths in the liver grow with greater virulence during hot weather (Fenwick [8]).

[1] Quoted in Lévi's *Thèse de Paris*, 1896.
[2] Charrin. *Semaine méd.*, Paris, 1892, xii, 310.
[3] Rioufol. *Thèse de Lyon*, 1899 (Acute Cancer of Liver).
[4] Hale White. *Guy's Hosp. Rep.*, 1890, xlvii, 59.
[5] Karsner. *Arch. Int. Med.*, Chicago, 1911, viii, 238.
[6] Christian, H. A. *Am. Med.*, Phila., 1903, v, 131.
[7] Taylor, F. *Clin. Journ.*, Lond., 1912, xl, 17.
[8] Fenwick. *Cancer and Other Tumours of the Stomach*, p. 183, 1902.

Termination.—Death usually occurs from increasing asthenia and in coma, the patient often being unconscious for one or more days before the end comes. Sudden death has been known to occur while the patient is still well nourished.

Lambert[1] reported a case with fatal intraperitoneal haemorrhage from a secondary nodule of carcinoma in the liver; the immediate cause was thought to be straining in sea-sickness. A girl aged sixteen years was admitted into St. George's Hospital in 1911 with acute abdominal symptoms which came on after sitting up. Laparotomy revealed a large quantity of blood in the peritoneal cavity. At the necropsy the liver, which was full of peritheliomatous nodules and weighed 6 pounds, shewed a rent 4 inches long antero-posteriorly.

DIAGNOSIS.—The diagnostic signs of malignant disease in the liver are rapid and progressive enlargement, with evidence of definite tumour formation in the organ, pain, loss of weight and of constitutional strength, and, when the disease is not primary in the liver, evidence of malignant disease elsewhere. As pointed out already, the primary growth is latent in about half the cases of secondary malignant disease of the liver.

As a rule, malignant tumours of the liver, whether primary or secondary, give rise to some hepatic enlargement and pain, so that disease of the liver is at least suspected. When the growths are small and the liver is not enlarged, there may be no clinical evidence that the liver is affected; in such cases the patient dies from the effects of the primary growth.

In primary malignant disease of the liver the growth rarely remains entirely latent. It may, however, happen that the observer's attention is exclusively directed to secondary results or concomitant affections.

Sokoloff[2] described the case of a man aged seventy who had ascites and dropsy and was regarded as having arteriosclerosis. After death a primary columnar-celled carcinoma of the liver was found. Gouget[3] narrated a very similar case in a man aged fifty-three years, thought to have arteriosclerosis and bronchitis. At the necropsy the liver was of normal size and contained numerous growths of columnar-celled carcinoma; there were no growths in the body. H. G. Wells[4] reported a case of primary carcinoma with cirrhosis which was latent, the patient dying from uraemia. Hale White[5] recorded the case of a woman aged thirty-nine, thought to be suffering from the vomiting of pregnancy, who died after premature labour had been induced. Primary malignant disease of the liver, which weighed 126 ounces, was found. A man, aged sixty, after pain in the epigastrium, gradually passed into a condition suggesting general paralysis of the insane; at the necropsy there was a primary massive carcinoma of the liver and innumerable secondary growths in the brain and cerebellum (Giachetti[6]).

[1] Lambert. *Brit. Med. Journ.*, 1908, i, 81.
[2] Sokoloff. *Virchows Arch.*, 1900, clxii, 1.
[3] Gouget. *Bull. Soc. Anat.*, Paris, 1898, lxxii, 605.
[4] Wells, H. G. *Am. Journ. Med. Sc.*, Phila., 1903, cxxvi, 403.
[5] Hale White. *Trans. Path. Soc.*, Lond., 1885, xxxvi, 251.
[6] Giachetti. *Riv. di patol. nerv.*, Firenze, 1907, xii, 149.

Differential Diagnosis.—The diagnosis of malignant disease in the liver substance, whether primary or secondary, from other conditions will first be considered, and then the distinction between primary and secondary malignant disease will be dealt with.

Portal Cirrhosis.—When a patient comes under observation with the abdomen full of ascitic fluid it is often difficult to decide whether there is cirrhosis in a late stage or malignant disease of the liver. The diagnosis must then remain in doubt until the fluid is withdrawn; when this has been done, the liver can be carefully examined. A small or moderately enlarged liver, when associated with enlargement of the spleen, points to cirrhosis; a large and nodular liver, especially when combined with umbilication of the surface, indicates malignant disease. Emaciation and pain are more prominent in malignant disease, but wasting may be very considerable in cirrhosis. A large cirrhotic liver, when associated with some jaundice and ascites, closely imitates carcinoma, but the enlargement is more uniform and affects both lobes, the spleen is often enlarged, and cachexia is less rapid. The association of ascites and well-marked jaundice, however, should suggest malignant disease. Progressive increase in size is in favour of growth, more especially if it affect one lobe only. In the following case primary carcinoma imitated cirrhosis:

A cook aged forty-three years was admitted into St. George's Hospital with vomiting in the morning, loss of appetite, and emaciation. She had had piles for fifteen years. Alcohol had been taken in moderation. She was thin, had an enlarged, roughened liver, and some ascites which rapidly increased and required tapping. She became jaundiced and passed into a "typhoid" condition. At the necropsy, except for a few minute nodules in the lungs, there was no new growth in any part of the body, except in the liver, which weighed 106 ounces; there was no tumour in the gall-bladder or ducts; the right lobe contained extensive areas of whitish-yellow growth of firm consistency, and also small umbilicated nodules; the left lobe was a thin cake of about the size of a child's hand, and was nearly separated from the rest of the liver, and moved as if on a hinge; it also contained much growth. The liver was not cirrhotic. There was chronic gastritis.

In primary carcinoma supervening on cirrhosis, a diagnosis from cirrhosis is usually impossible, unless the liver is large and nodules of growth can be felt. Pain over the liver is often more prominent in these cases than in cirrhosis, and jaundice, though not always present, may be considerable.

From the large liver of *hypertrophic biliary cirrhosis* primary malignant disease differs in its more rapid growth, in the absence of splenic enlargement, and in the character of the jaundice. In malignant disease it is, generally speaking, either absent or, if present, obstructive, so that no bile passes into the blood. In biliary cirrhosis jaundice is constant, but not complete, and the faeces are not colourless. Hypertrophic biliary cirrhosis is met with much earlier in life than malignant disease.

Syphilis of the Liver.—Gummatous enlargement, especially when the

patient is cachectic, may suggest malignant disease. When the liver is hard and enlarged and the patient's general condition is good, gumma should be thought of and vigorous antisyphilitic treatment should be employed. In all cases of doubt iodides in large doses and mercury should be given. If, after a full course, the enlargement is still progressive, the case is almost certainly malignant. A history of syphilis and a positive Wassermann reaction are, of course, important, but the most decisive point is the effect of antisyphilitic treatment adequately carried out.

A large, firm, *lardaceous liver* in a cachectic patient might be mistaken for primary massive carcinoma of the liver at first sight, but the evidence of lardaceous disease elsewhere, as shewn by albuminuria and diarrhoea, the absence of pain and of rapid and progressive enlargement of the liver, together with a history of past suppuration or of syphilis, should lead to a correct diagnosis. A lardaceous liver with gummatous change or cicatrices may be so large and nodular that secondary malignant disease is closely imitated. The history and evidence of syphilis are important, but the effect of treatment is the only means of definitely deciding the point; if the liver progressively enlarges under full doses of iodide of potassium, malignant disease is almost certainly present. Other evidences of lardaceous disease, such as albuminuria, should also be looked for. Albuminuria is decidedly rare in malignant disease.

A *hydatid cyst* may suggest malignant disease of the liver, especially a primary massive carcinoma, in a comparatively early stage before constitutional symptoms have arisen; and multiple hydatid cysts may simulate the nodules of secondary malignant disease.

In hydatid the enlargement is slow and constitutional symptoms are absent. In malignant disease the tumour usually grows rapidly, other nodules may be felt, and cachexia is likely to supervene. Malignant disease occurs later in life than hydatid cyst of the liver; caution is, therefore, necessary before diagnosing hydatid in elderly persons. When the liver contains several hydatid cysts, some difficulty in arriving at a correct diagnosis must be expected.

In a case diagnosed as hydatid of the liver and operated upon, the appearances so closely resembled multiple malignant growths that the operation was abandoned; at the necropsy they were found to be multiple hydatids (Sargnon [1]). The coincidence of carcinoma and hydatid cysts in the same liver is referred to on p. 397.

Alveolar or multilocular hydatid has often been mistaken for malignant disease, both clinically and even when found after death. It has not been recognised in Great Britain. In most cases the spleen is enlarged, and its course is much slower than in malignant disease.

Cystic disease of the liver may cause very great enlargement. Considerable cystic change in the kidneys is nearly always present and the kidneys may be palpable. The condition is very chronic, and the symptoms are renal rather than hepatic.

[1] Sargnon. *Lyon méd.*, 1898, lxxxvii, 254.

Hepatitis due to chronic malarial infection occasionally gives rise to difficulty in diagnosis at first. But the history, examination of the blood, and the effect of quinine should clear up any doubt.

Influenzal hepatitis is not common, but it may closely imitate the early stages of malignant disease of the liver. The enlarged liver is accompanied by some fever, and a cautious opinion must be expressed until the course of events has been watched.

Intrahepatic Suppuration.—In rare instances the soft character of a rapidly growing tumour, or the formation of false cysts from necrosis or haemorrhage, may give rise to fluctuation, while fever, which is not very uncommon in malignant disease of the liver, may increase the resemblance to some form of intrahepatic suppuration, such as abscess and pylephlebitis; this is especially so in primary sarcoma of rapid growth in children or young adults. An exploratory laparotomy may be the only means of distinguishing between growth and suppuration. Suppuration may indeed be superimposed on malignant disease.

A man aged forty-one years began to suffer from sick headaches three months before his death; a month later he had flatulence and epigastric pain. When admitted into St. George's Hospital the patient, who was well nourished and free from jaundice, presented great enlargement of the liver, which projected markedly in the epigastrium. After admission the temperature became raised, and, an abscess being suspected, the liver was aspirated, but nothing but blood was withdrawn. As the temperature continued to rise, laparotomy was performed, and numerous growths on the surface of the liver were found. A small piece was removed, and found to be a spheroidal-celled carcinoma. The patient died a week later. At the necropsy the liver weighed 11 pounds 7 ounces; the left lobe was almost uniformly infiltrated by new growth, and the right lobe contained a number of discrete tumours. The only other growth was one in the middle of the body of the pancreas. Howard Marsh [1] reported the case of a soldier aged forty-three, who had been in India, and had an enlarged liver extending two inches below the ribs and forming a prominent swelling in the epigastrium, with exactly the appearance of an abscess pointing; it was soft, fluctuating, and the skin over it was dusky-red. Aspiration only brought away a little blood, and at the necropsy cancer of the liver was found. In Bramwell and Leith's [2] case an abscess was diagnosed and 53 ounces of chocolate-coloured fluid were removed by aspiration. There was a primary, irregular-celled sarcoma of the liver, which weighed 9 pounds. Hawthorne [3] published a somewhat similar case.

In the following case there was some resemblance to pylephlebitis:

A man aged twenty was admitted under my care at St. George's Hospital with anaemia, fever, and a large and tender liver. His history pointed to an attack of appendicitis five weeks before, followed by two rigors and by vomiting. It was thought that he had either a large appendicular abscess tracking up to the liver by the side of the colon, or pylephlebitis. At the operation there was

[1] Marsh, H. *St. Barth. Hosp. Rep.*, 1887, xxiii, 148.
[2] Bramwell and Leith. *Lancet*, Lond., 1897, i, 170.
[3] Hawthorne, C. O. *Clin. Journ.*, Lond., 1896, viii, 361.

no abscess, but the liver was large and bled readily when punctured ; on the convexity of the liver there was a raised area, thought to be either an early stage of an abscess or new growth. It was punctured, but nothing came out. The age of the patient militated against new growth. The patient survived for five weeks ; during the greater part of this period the temperature was intermittent, going up to 101° at night and becoming normal in the morning ; during the last week of life the temperature was almost normal. Oedema of the legs and back developed some weeks before death. At the necropsy the liver was occupied by numerous white growths shewing cystic degeneration, and weighed 18 pounds. The primary growth was in the left kidney. There was thrombosis of the inferior vena cava close to its bifurcation, thus accounting for the oedema. The portal vein was normal. Microscopically the growth was an endothelioma.

A large cystic sarcoma of the liver, such as that described on page 522 may very closely imitate an abscess or a sanguineous peritoneal cyst.

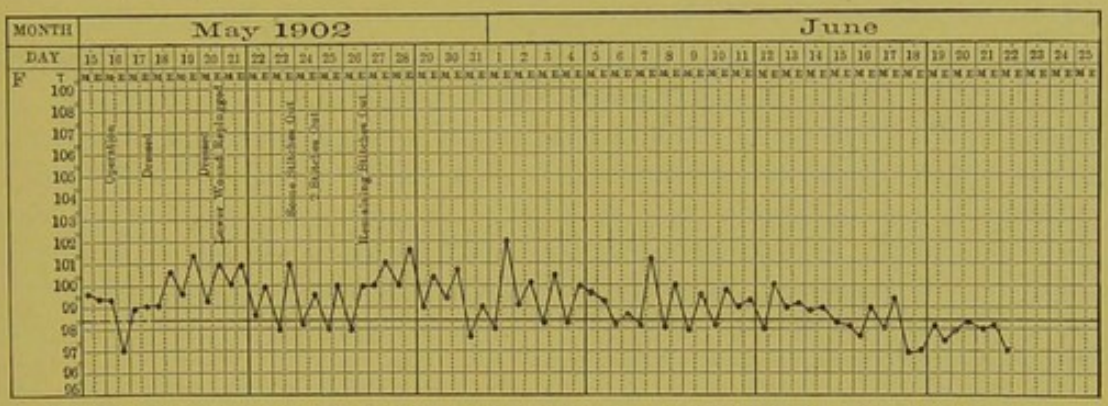


FIG. 77.—Temperature chart of a man, aged twenty years, with secondary endothelioma of liver imitating pylephlebitis. Primary growth in the left kidney.

If opened, the fluid from a cystic sarcoma will probably contain growth when examined microscopically, but even then it may be impossible to say whether the growth arose in the liver or invaded it, as a suprarenal or other retroperitoneal tumour might do. The diagnosis during life in these cases is extremely difficult. Conversely, slow abscess formation in the liver may be regarded as malignant disease and not operated upon for this reason.

Chronic Venous Engorgement.—The enlarged and tender liver of chronic venous engorgement, especially in the late stage of mitral disease, has, in rare instances, been regarded as malignant. This mistake is not likely to occur often, as the general aspect of the two diseases is so different. Difficulty is more likely to arise in cases of marked dilatation of the left ventricle without any mitral murmur. The presence of obstructive cardiac or pulmonary disease, and the effect of treatment by digitalis, strophanthus, purgatives, etc., in diminishing the size of the liver are points in the diagnosis on which further insistence is unnecessary.

A woman, aged forty, but looking fifteen years older, was under my care in St. George's Hospital with great pain and respiratory distress. Her appearance

suggested morbus cordis or a large pleural effusion, but the heart appeared healthy and there was only a little dulness at the right base. There was much resistance in the epigastrium and great pain on pressure, and as she had frequent retching, it was thought she might have malignant disease of the stomach and liver. Her condition prevented a thorough examination, and she was kept under the influence of morphine, but the pain seemed very severe. Three days before death she became jaundiced. At the necropsy there was no growth of any kind. The liver was enlarged and shewed some, but not advanced, chronic venous engorgement. The heart, 15 ounces, shewed extensive fibroid disease. The orifices of the coronary arteries were extremely small, and the ascending part of the aorta shewed gelatinous thickening, suggesting syphilitic or acute aortitis. There were a pulmonary apoplexy in the right lung and a pleural effusion. It is probable that the pain was cardiac and of the nature of angina.

In a girl, aged three and a half years, under my care a large firm liver was thought to be sarcomatous. The heart appeared normal and after death did not shew any disease. The liver shewed advanced chronic venous engorgement, the causation of which was obscure.[1]

Gall-stone in the Common Bile-duct; Intermittent Hepatic Fever.—Impaction of a gall-stone in the common bile-duct may occur without previous attacks of biliary colic. When this occurs in a person past middle life, it may be regarded as malignant disease of the liver, especially the form arising in the bile-ducts (*vide* p. 689). As time goes on, however, the jaundice tends to diminish, whereas in malignant disease it becomes deeper. In impacted gall-stone the liver, if enlarged at first, does not progressively increase in size, but rather diminishes, and there is an absence of irregularities on its surface.

A man aged sixty-seven became jaundiced at the beginning of 1890 after having felt weak for ten days; there had been no pain or colic. About May 17 he consulted the late Sir Andrew Clark, who, according to the patient, diagnosed cancer of the liver and gave him a month to live. When admitted to St. George's Hospital he was thin, jaundiced, and weak. The hepatic dulness began at the fifth rib in the right nipple line, and extended below the right costal margin, where there was a round, dull swelling extending downwards to within one inch of the umbilicus. No pain or tenderness existed. With rest in bed the jaundice cleared away and the tumour in the right hypochondrium receded, until, at the beginning of August, the skin was almost natural in colour. He then had spells of diarrhoea, which, however, were easily controlled by treatment. In September and October he had rigors on two occasions and fever at intervals, and he was losing flesh and strength from attacks of diarrhoea. On November 17 a severe bout of diarrhoea began; on the 19th he had a rigor, and on the following morning he died rather suddenly. At the necropsy I found a large calculus in the common bile-duct, close to the duodenum; it was loose and allowed bile to flow past it into the duodenum, as was proved by pressure on the gall-bladder. There was cholangitis, the liver shewed secondary pericholangitic fibrosis, and there were numerous adhesions around the gall-bladder and liver. There was no malignant disease in the body.

[1] Rolleston. *Trans. Med. Soc. Lond.*, 1909, xxxii, 19; and *Clin. Journ.*, Lond., 1908, xxxiii, 138.

A displaced or a wandering liver rarely imitates malignant disease. In Crawfurd's[1] case of anteverted wandering liver malignant disease was diagnosed during life. The association of jaundice and ascites with hepatoptosis is most unusual, but it may occur from kinking of the portal vein and bile-duct. The freely movable state of the liver should direct attention to the real condition. The severe constitutional symptoms in malignant disease and their absence in wandering and displaced livers should help to prevent any confusion.

A large *renal tumour* on the right side may appear to be in direct continuity with the liver. In some cases of extensive *cystic disease* of the kidneys the tumour may imitate a distended gall-bladder, or possibly, if tense cysts project from the surface of the kidney, secondary growths in the liver. A bimanual examination will shew that the renal tumour definitely bulges into the loin. The presence of bowel in front of the renal tumour is important; this may be made more manifest by filling the colon with air after removing its solid contents by means of an enema.

Tumours of the right suprarenal, by growing forwards, may closely resemble hepatic growths. In some cases the liver may be invaded by continuity, and secondary growths often occur in the liver.

In a large cystic sarcoma of the right suprarenal, which I examined post-mortem in 1891, the diagnosis was first hydatid of the liver, and subsequently malignant disease; there were secondary growths in the liver, as well as direct invasion of that organ.

Inflammatory thickening around the gall-bladder may be palpable as a hard mass, and thus may give rise to physical signs resembling carcinoma. The history of gall-stones and the fact that the patient's general state is not so grave as in carcinoma are important points to bear in mind.

Occasionally *faecal accumulation* in the transverse colon may imitate malignant disease; here the tumours may vary in position from time to time, can be indented by pressure, are capable of removal by purgatives or abdominal massage, and, when a careful examination is made, if need be under an anaesthetic, other masses can be made out in the course of the colon.

Improbable as it may appear, difficulty has arisen in distinguishing between *pregnancy* and secondary malignant disease of the liver.

In the following case[2] both conditions existed at the same time and the abdominal enlargement was naturally thought to be explained by pregnancy. A married woman aged thirty-nine years, who had had several children, was thought to be pregnant. She died, and a six-months fetus was found in the uterus. The liver weighed 17½ pounds and contained numerous secondary growths; the primary growth appears to have been in the colon. A case was reported by

[1] Crawfurd, R. P. *Lancet*, Lond., 1897, ii, 1182.
[2] Robinson. *Trans. Path. Soc.*, Lond., 1850, ii, 167.

Hale White[1] in which a woman was thought to be suffering from the vomiting of pregnancy until a primary carcinoma of the liver was found at the necropsy.

Diagnosis between Primary and Secondary Malignant Disease of the Liver.—In secondary malignant disease of the liver the primary growth may remain entirely latent during life. In such cases there are often no means of arriving at a correct diagnosis of secondary, rather than primary, malignant disease of the liver. These cases, which are clinically described as "malignant disease of the liver," tend, when included in statistics, to make primary malignant disease appear less rare than it really is. In about half the cases of secondary carcinoma of the liver the primary site cannot be determined during life. The primary growth may remain latent when it is in the stomach, pancreas, oesophagus, kidney, and, in exceptional instances, when in the colon.

A wasted old man aged sixty-two years was admitted under my care in St. George's Hospital on June 22, 1899, complaining of pain over the liver, inability to lie on his left side, shortness of breath, difficulty in digestion, and constipation. Six weeks previously his legs began to swell; this was followed by swelling of the abdomen. He had ascites which required tapping. The liver was much enlarged and extended nearly down to the umbilicus; nodules which seemed to be umbilicated were readily felt. On the skin over the free edge of the liver there was a meshwork of dilated vessels. There was dulness in both flanks. The urine was free from albumin; two days before his death, when his conjunctivae became jaundiced, bile-pigment appeared in the urine. He got steadily weaker, had little or no pain, completely lost his appetite, and died after being in a drowsy condition for forty-eight hours on July 6. At the necropsy the liver weighed 9 pounds 14½ ounces, and was packed with nodules of soft white growth which were not umbilicated. The right kidney weighed 8 pounds 5½ ounces, and was transformed into a large haemorrhagic growth which had broken down into pseudo-cysts. Some of the cysts contained cholesterin crystals. Microscopically the tumour was a perithelioma (*vide* Fig. 71). Kelynack[2] described a somewhat similar case in a woman, but the left kidney was affected and there was haematuria, so that the primary growth did not remain latent. The liver contained numerous cystic tumours and weighed 111 ounces. I have seen two other cases in which the primary growth in the kidney remained quite latent; this is very likely to happen when the right kidney is affected and is under cover of the enlarged liver, but it may occur when the growth in the left kidney is small.

From extreme sensibility and a mistaken sense of delicacy a woman may conceal a carcinoma of the breast and only complain of symptoms pointing to malignant disease of the liver.

Such a case is recorded by Pearson and Howes[3] in which an ulcerating carcinoma of the mamma was only discovered after death in a woman aged sixty who during life had been under treatment for a tumour in the liver with pain and ascites.

[1] Hale White. *Trans. Path. Soc.*, Lond., 1885, xxxvi, 251.
[2] Kelynack. *Journ. Path. and Bacteriol.*, 1897, iv, 236.
[3] Pearson and Howes. *Trans. Path. Soc.*, Lond., 1875, xxvi, 185.

Carcinoma of the stomach may remain quite latent when there are extensive secondary growths in the liver. According to Fenwick,[1] the changes in the liver are most marked when the tumour in the stomach is comparatively insignificant. Inasmuch as a pyloric growth is likely to lead to obstruction and symptoms, the latent growths are more often in the body or cardiac end of the stomach.

Secondary growths in the liver are not uncommon in carcinoma of the lower half of the oesophagus, but dysphagia is nearly always present.

In a man aged fifty-five years who died in St. George's Hospital with carcinoma of the oesophagus and numerous secondary growths in the liver, which weighed 14 pounds, there was nothing more definite than a distaste for solid food (*vide* p. 511).

The presence of an enlarged gland (Virchow's gland) above the clavicle should suggest the possibility of oesophageal carcinoma, but it may, of course, occur in other cases of generalised new growth. Enormous enlargement of the liver may be due to melanotic sarcoma secondary to a primary tumour in the uveal tract; in such cases the seat of the primary growth may easily be overlooked if the patient wears a glass eye and does not mention that his eye has been removed.

Multiplicity of nodules on the surface of an enlarged liver is much in favour of secondary growth, but unless there is definite evidence of primary neoplasm in the body, or of one having been removed, the diagnosis of secondary growths, though most probable, cannot be made with absolute certainty, since primary malignant disease may occur in a multiple nodular form. Deep jaundice and the association of ascites with jaundice are in favour of secondary malignant disease, whereas very rapid enlargement of the liver without emaciation is more frequent in primary malignant disease. It is true that the liver may increase in size very rapidly in secondary malignant disease, but since the primary growth is usually in the alimentary canal, there is generally considerable emaciation on this account before the liver is much or at all affected. When the primary growth is in the kidneys or in the uveal tract, emaciation is not so marked. In the enlargement of the liver due to melanotic sarcoma a clue to the nature of the disease, even in the absence of any history of an intra-ocular growth, may be obtained by the detection of melanin in the urine. To summarise the differential diagnosis of primary and secondary malignant disease of the liver:

Primary.	*Secondary.*
No sign or symptom of growth elsewhere in the body.	Some evidence of growth elsewhere.
A single tumour.	Multiple tumours.
Very rapid growth.	Less rapid growth.
Jaundice rare and slight.	Jaundice common.
Ascites not so frequent.	Ascites common.
Emaciation not so marked.	Emaciation marked.
Course rapid.	Course not so acute.

[1] Fenwick. *Cancer and Other Tumours of the Stomach*, p. 182, 1902.

Pepere[1] attempted to draw a clinical distinction between primary carcinoma and primary sarcoma of the liver on the grounds that primary sarcoma runs a more rapid course and is less frequently accompanied by jaundice or ascites than primary carcinoma. Bertelli[2] supports this distinction.

Prognosis.—When the diagnosis of malignant disease of the liver can be made at the bedside, the prognosis is always hopeless. It is true that when laparotomy reveals the presence of early primary malignant disease of the liver, malignant disease limited to a constriction lobe, or malignant disease of the gall-bladder invading the liver, there is a chance that removal will not be followed by recurrence. But even in these cases, which can hardly be diagnosed with any certainty before the abdomen is opened, the disease usually returns and kills the patients. Operation for removal of malignant growths from the liver, whether from its substance or when starting in the gall-bladder, is the only means at our disposal at present of mitigating the otherwise absolutely fatal prognosis. The prognosis is better when a growth originating in the gall-bladder is removed than in resection of the liver for a primary neoplasm. Death is more rapid in primary malignant disease than in the more familiar secondary growths in the liver.

How long life may be prolonged with secondary growths in the liver is uncertain (*vide* p. 518). In most cases death follows within six months of definite evidence of hepatic enlargement. The size of the liver and the constitutional condition are valuable guides as to the time left to the patient. The onset of oedema of the legs usually means that the end is near. It must be remembered that in some instances the liver may have been previously enlarged from some independent cause; a floating lobe or tight-laced liver might thus give rise to a fallacy.

In a case of secondary melanotic sarcoma of the liver recorded by Litten there was evidence of hepatic enlargement for four years before death, a period quite incompatible with the view that a secondary growth was present all the time.

On the analogy of the spontaneous disappearance of solid and inoperable growths in the abdomen having the appearance of malignancy—a remarkable event to which Greig Smith[3] drew attention—it is conceivable that malignant disease of the liver might occasionally disappear. In exceptional cases hepatic enlargement due to carcinoma has been noticed to pass away spontaneously (A. P. Gould,[4] Hodenpyl[5]).

Campbell quotes a case[6] in which influenza, supervening in the course of malignant disease of the liver, was followed by rapid diminution in the size of

[1] Pepere. *Arch. de méd. expér. et d'anat. path.*, Paris, 1902, xiv, 805.
[2] Bertelli. *Policlin.*, Roma, 1908, xxiv, 957.
[3] Greig Smith. *Med.-Chir. Trans.*, Lond., 1894, lxxvii, 139.
[4] Gould, A. P. *Clin. Journ.*, Lond., 1902, xx, 96.
[5] Hodenpyl. *Med. Rec.*, N.Y., 1910, lxxviii, 359.
[6] Campbell, H. *Brit. Med. Journ.*, 1898, i, 1126.

the liver. The patient indeed seemed to get well, but in one-and-a-half years' time the growth returned and proved fatal. It is conceivable that in this instance a secondary streptococcic infection on the influenzal attack may have manufactured a toxin that acted on the hepatic growth, much in the same way as Coley's fluid does on sarcoma.

The only bright side to the prognosis of malignant disease of the liver is the possibility that the diagnosis may be wrong and that the actual condition is gummatous or hydatid disease of the liver.

TREATMENT.—**Medical treatment** is purely palliative, and directed chiefly to the relief of pain and discomfort by morphine, opium, aspirin, and chloral. Hypodermic injection of morphine is preferable to opium by the mouth, inasmuch as it is more surely absorbed, disturbs digestion less, and its effects can be more accurately estimated. From the necessarily fatal nature of the disease morphine may be given without any qualms of conscience as to morphinomania. Measures should be taken to combat the excessive constipation induced by morphine, and it is often advisable to combine the morphine with atropine. Pain over the liver may to some extent be relieved by the local application of a plaster made up of the pharmacopoeial plasters of opium and of belladonna. Hot fomentations or poultices may be given a trial. The application of a belt may give considerable relief. The pain and tenderness are, of course, aggravated by examination, which should, therefore, not be unnecessarily repeated.

For itching, salts of calcium by the mouth, warm alkaline baths, bathing the skin with carbolic acid 1 : 40, or the hypodermic injection of pilocarpine, may give relief; probably morphine will be most generally successful (*vide* p. 567).

Vomiting should be treated by ice, morphine, bismuth, and dilute hydrocyanic acid. Washing out the stomach may be very useful. Flatulence and distension of the intestine should be treated by various carminatives, by minute doses ($\frac{1}{40}$ gr.) of calomel, guaiacol, creosote perles, and by gentle purges. As there may be diminution in the hydrochloric acid of the gastric juice, dilute nitro-hydrochloric acid (♏x) should be given after food. Constipation should be met by saline purges and mild laxatives, such as cascara.

The diet is largely determined by the patient's inclinations; usually there is want of appetite and dislike for meat, so that liquid food, milk, jellies, tea, and coffee are all that he cares to take. Milk has the advantage of being easily digested and giving rise to a minimum of putrefactive products. Stimulants are usually desirable.

If ascites gives rise to abdominal distension and discomfort, tapping should be performed.

Operative Treatment.—Removal of the growth is, of course, the ideal treatment, but is only to be thought of for a primary and single growth. A number of cases have been operated upon and excision of the malignant growth performed.

In a tabular statement of 76 cases in which resection of the liver had been performed for growths or other conditions,[1] Keen gives 18 carcinomas, 5 sarcomas, and 1 endothelioma. Yeoman[2] collected 9 cases of excision of primary carcinoma of the liver.

Excision of a primary malignant growth from the substance of the liver is much more difficult than removal of malignant disease of the gall-bladder. Another practical difficulty is that of arriving with any certainty at a diagnosis of a primary hepatic growth before it has become too extensive for satisfactory removal.

Success is, therefore, more likely to occur in cases in which the exploratory operation was undertaken under the idea that there were conditions other than malignant disease present, such as a hydatid cyst. It is very probable that good results might follow in cases in which a small secondary growth is excised at the same time as a primary carcinoma of the stomach or of the gall-bladder, as in Mayo Robson's case[3] in which complete recovery followed, is removed, or in the rare cases in which a single metastatic growth occurs in the liver after removal of the primary growth elsewhere. But in such cases there is, unfortunately, the danger of the liver being more widely infected than appears to the naked eye.

Cullen[4] reported temporary improvement after removal of a secondary growth, undertaken seventeen months after removal of the left kidney for carcinoma.

Laparotomy, with a view of removing a diagnosed growth, would often be only an exploratory incision, for the extent of the disease and the presence of secondary growths would, in a large number of cases, render any operative treatment impracticable. At the present time, however, the value of resection of the liver for new growths is likely to be more extensively tested. Most of the cases that have been operated upon have died from a recurrence of the growth.

[1] Keen. *Ann. Surg.*, 1899, xxx, 276.
[2] Yeoman. *Journ. Am. Med. Assoc.*, Chicago, 1909, lii, 1741.
[3] Mayo Robson. *Med.-Chir. Trans.*, Lond., 1896, lxxix, 159.
[4] Cullen. *Journ. Am. Med. Assoc.*, Chicago, 1905, xliv, 1239.

JAUNDICE

Definition.—Jaundice is the condition due to the presence of bile-pigment in the blood, and is recognised clinically by staining of the skin, conjunctivae, mucous membranes, blood-serum, and, as a rule, of the urine, by bile-pigment.

Like albuminuria, it is a symptom and not a disease, and may be met with in a number of different conditions, the common and essential factor being obstruction at some point to the passage of bile along the bile capillaries or ducts.

Etymology.—The word jaundice is derived from the French *jaune*, yellow. Wickham Legg[1] gives several possible derivations for icterus, such as ἴκτις, the yellow-breasted marten, which probably was the equivalent in ancient Greek households of our domestic cat; ἴκτερος, the golden oriole, the sight of which was supposed to cure jaundice, whereas the bird died (Pliny); and from ἰκτῖνος, a kite, from the colour of its eyes.

Introduction.—The formation of bile-pigment from haemoglobin is limited to the cells of the liver and cannot be vicariously carried out elsewhere in the body, for, as shewn by experiments on animals, this transformation does not take place when the liver is removed, or—and this comes to the same thing—when all the vessels going to it are ligatured.

Moleschott[2] shewed that after excision of the liver in frogs there was no formation of bile in any part of the body; and by excluding the liver of pigeons from the circulation by ligature of its vessels, Stern[3] and Minkowski and Naunyn,[4] in ducks, proved that the same was true in birds.

It has, however, been argued that since haematoidin, which is chemically identical with bilirubin, is formed in old haemorrhages from haemoglobin, bile-pigment may be similarly manufactured in other parts of the body.

Jaundice, or the presence of bile-pigment in the blood, is due to the passage of bile, manufactured by the liver, into the circulation instead of into the intestines. This miscarriage of the bile may occur either directly the bile-pigment is formed by the liver cells—*i.e.* before the bile enters the bile-ducts—or later, after it has passed into the ducts. It has been suggested by Frerichs, Liebermeister, Szubinski, Minkowski,[5] and Pick[6] that in certain conditions, such as toxaemia, the normal secretion of bile

[1] Legg, J. Wickham. *Bile, Jaundice, and Bilious Diseases*, 1880, p. 225.
[2] Moleschott. *Arch. f. physiol. Heilk.*, 1852, xi, 479.
[3] Stern. *Arch. f. exper. Path. u. Pharmakol.*, 1885, xix, 39.
[4] Minkowski und Naunyn. *Ibid.*, 1886, xxi, 1.
[5] Minkowski. *Verhandl. d. Congr. f. inn. Med.*, Wiesbaden, 1900, xviii, 316.
[6] Pick, A. *Wien. klin. Wchnschr.*, 1903, xvi, 493.

may be so disturbed that the bile passes direct into the lymphatics or blood-vessels of the liver instead of into the bile capillaries (diffusion or acathectic jaundice, jaundice from parapedesis, paracholia). This hypothesis has been employed to explain jaundice in cases in which no obstruction can be found; especially in chronic haemolytic jaundice (*vide* p. 537). There are two views as to the path by which bile passes from the bile-ducts into the circulation in obstructive jaundice; the experiments of Saunders[1] (1803), and later of Fleischl,[2] V. Harley,[3] and Szubinski[4] shewed that the bile enters the lymphatics of the liver, and that jaundice due to ligature of the bile-duct can be removed or prevented by ligature of the thoracic duct. On the other hand, experiments have been brought forward to prove that the bile enters the blood-vessels, and that a fistula of the thoracic duct does not influence jaundice (Mendel and Underhill,[5] Wertheimer and Lapage,[6] Whipple and King[7]).

Obstruction in the ducts leads to a rise in the pressure of the bile, which is normally low, and, as a result, the bile passes into the general circulation. This clearly explains the production of jaundice in cases in which there is a gross mechanical obstruction in the ducts, but it is necessary to consider further the method of causation of jaundice in cases without any manifest obstruction in the larger bile-ducts.

Pathology of Jaundice.—Jaundice was formerly divided into: (i) Hepatogenous or obstructive, due to manifest obstruction in the larger bile-ducts, and (ii) so-called non-obstructive, in which there was no gross obstruction in the course of the bile-ducts. This form included (*a*) jaundice thought to be due to haemolytic changes in the blood, which consisted in the liberation of haemoglobin and its transformation in the circulation into bile-pigment; this was spoken of as *haematogenous jaundice*. (*b*) *Jaundice from polycholia*, in which an excessive secretion of bile was followed by such free absorption of bile by the mucous membrane of the intestine and bile-passages that some of it overflowed into the general circulation. (*c*) *Jaundice by suppression*, in which the cells of the liver were supposed to strike work and no longer form bile. As a result an accumulation of bile-pigments, manufactured in the general circulation, was thought to occur. As in the first-mentioned form (haematogenous jaundice), this explanation was based on the assumption that bile-pigments could be formed elsewhere in the body than in the liver. (*d*) "Urobilin" jaundice.

(*a*) *Haematogenous and Haemolytic Jaundice.*—In various toxic and infective conditions which cause haemolysis slight jaundice is often seen. A good example of this "toxaemic" jaundice is provided in the experi-

[1] Saunders, W. *A Treatise on the Structure, Economy, and Diseases of the Liver*, p. 111, 3rd ed., 1803, Lond.
[2] Fleischl. *Arb. a. d. physiol. Anst. zu Leipz.*, 1874, ix, 24.
[3] Harley, V. *Arch. f. Anat. u. Phys.*, 1893, S. 291.
[4] Szubinski. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1899, xxvi, 446.
[5] Mendel and Underhill. *Am. Journ. Physiol.*, 1905, xiv, 252.
[6] Wertheimer et Lapage. *Arch. de physiol.*, Paris, 1898, 5. s., x, 334.
[7] Whipple and King. *Journ. Exper. Med.*, N.Y., 1911, xiii, 115.

ments of Stadelmann[1] and Hunter[2] with toluylenediamine. This poison destroys the red blood-corpuscles with liberation of haemoglobin (haemolysis) and causes jaundice. After its administration there is at first a more copious flow of bile containing an increased quantity of bile-pigments (polychromia), owing to an augmented amount of free haemoglobin, the antecedent of bile-pigment, reaching the liver. After a time the bile diminishes in amount and becomes more viscid, until finally its flow is almost arrested. This slowing and diminution in the flow of bile depend on inflammation of the smaller intrahepatic bile-ducts, which become swollen and contain thick mucus as a result of the toxic action of the toluylenediamine. The jaundice, therefore, is really due to obstruction, which, being situated in the small intrahepatic ducts, is readily overlooked. This explanation accounts for the comparatively slight jaundice seen in septicaemia, pyaemia, haemoglobinuric fever, pernicious anaemia, phosphorus and other forms of poisoning, and snake-bite. Eppinger[3] finds that in these circumstances the bile capillaries become obstructed by coagulated bile, and that this leads to the passage of bile into the lymphatics. The jaundice is, therefore, toxaemic, and is dependent on changes (inflammation and obstruction) in the small intrahepatic bile-ducts, produced by poisons in the general circulation. It may be appropriately spoken of as intrahepatic or haemo-hepatogenous jaundice, but not, as it formerly was, as "haematogenous" jaundice. Experiment shews that the presence of free haemoglobin in the blood, though it leads to an increased secretion of bile-pigment in the bile (polychromia), does not of itself give rise to jaundice. In practice jaundice is often seen in cases in which extensive haemolysis or destruction of red blood-corpuscles is taking place. The two phenomena are regarded by Hunter as the associated but independent results of infective or toxic factors which destroy the red blood-corpuscles and at the same time excite inflammation of the intrahepatic bile-ducts.

Paroxysmal haemoglobinuria, though usually, is not necessarily, associated with jaundice. In pernicious anaemia haemolysis in the portal area is a very marked feature, but the jaundice is slight and may be practically absent. On careful microscopic examination of the liver in pernicious anaemia catarrhal inflammation of the small bile-ducts may be seen in some instances.[4]

On the other hand, opinion is now inclining to the view that jaundice may in certain conditions be independent of any obstruction in the biliary apparatus and truly haemolytic in origin (*vide* p. 538).

(*b*) *So-called Jaundice from Polycholia.*—When jaundice was found to be associated with bile in the faeces, it was supposed that there was such a profuse secretion of bile (polycholia) that an excessive amount of bile was absorbed from the mucous membrane of the intestines and bile-

[1] Stadelmann. *Der Icterus u. seine verschiedenen Formen*, Stuttgart, 1891.
[2] Hunter, W. *Journ. Path. and Bacteriol.*, 1896, iii, 259.
[3] Eppinger. *Ergebnisse der inneren Medizin und Kinderheilkunde*, 1908, i, 107.
[4] Compare Bret et Cade. *Lyon méd.*, 1902, xcix, 457.

passages and passed through the liver into the general circulation. Bile may be present in the faeces of jaundiced patients under various conditions; thus in obstruction of one hepatic duct icterus results, but the other hepatic duct pours bile into the duodenum. A calculus in the common duct may act like a ball-valve and allow bile to escape into the bowel at intervals; and in biliary cirrhosis bile is usually present in the faeces. In none of these examples is there any suggestion that an excessive secretion of bile exists. In toxaemic jaundice there is in the early stage a secretion of bile rich in bile-pigment (polychromia) and poor in bile acids, the pigment appearing in the excreta; obstruction in the small ducts subsequently occurs, and produces jaundice. This is the explanation of so-called jaundice from polycholia. But it should be pointed out that, strictly speaking, there is not an excessive secretion of normal bile (polycholia), but only of bile-pigment (polychromia), and that the bile-salts, far from being increased, are diminished.

(*c*) *The So-called Jaundice from Suppression of the Bile-secreting Function of the Liver.*—It was formerly supposed that the liver might, from nervous or other influences, cease to secrete bile, and that an accumulation of refuse blood-pigment in the circulation resulted, which became changed, without the intervention of the liver, into bile-pigment.

There is no proof that in jaundice the liver does strike work. In acute yellow atrophy and phosphorus poisoning the jaundice is almost certainly due to obstruction in the small intrahepatic ducts from inflammation, and to the passage of bile into the lymphatics, which results as a natural consequence. In long-continued biliary obstruction the ducts contain clear mucous fluid devoid of bile, and it was formerly thought that the liver ceased to secrete bile under these conditions; but the liver cells, as shewn by the presence of bile-pigment inside them, still manufacture bile, which passes almost directly into the circulation.

(*d*) *"Urobilin" Jaundice.*—(*Synonyms: Haemophaeic Jaundice; Acholuric Jaundice*).—These terms have been applied to cases in which, though the skin is yellow, there is no bile-pigment in the urine. It has been thought that staining of the skin indistinguishable from jaundice may be due to pigments other than those of bile—either urobilin or a hypothetical product of haemoglobin called haemophaein (Gubler). The reason for supposing the pigmentation of the skin to be due to urobilin was that in such cases the urine often contained an excess of urobilin. But in such cases the blood-serum, obtained from a blister or from other sources, is found to contain bile-pigment in small quantities and not urobilin[1]; hence the condition is one of true jaundice, and the terms "urobilin" and "haemophaeic" jaundice are erroneous and misleading. Excessive urobilinuria may occur in cases of toxaemic jaundice in which bile-pigment is temporarily absent from the urine. To this condition the term "acholuric jaundice" has been applied (Gilbert and Herscher[2]). Cases formerly called urobilin jaundice are, therefore, mild cases of jaundice in which a

[1] Compare Thiele. *Trans. Path. Soc.*, Lond., 1903, liv, 62.
[2] Gilbert et Herscher. *Presse méd.*, Paris, 1902, 1239.

sufficient amount of bile-pigment passes into the circulation to stain the skin, but not enough to be present constantly in the urine. The excess of urobilin in the urine is probably due to the action of bacteria on bile-pigment in the intestine, though Gilbert and Herscher[1] consider that the urobilin is manufactured by the kidneys from bile-pigment present in the blood-serum. This form of jaundice is sometimes seen in portal cirrhosis and in gastritis, and may be due to a slight secondary infection of the ducts from the duodenum (Hayem[2]). On the other hand, it may be a mild form of toxaemic jaundice. The condition is closely allied, according to Gilbert and Herscher, to simple family cholaemia (*vide* p. 40), described by Gilbert and Lereboullet,[3] and differs from it in the urine being more concentrated.

Classification.—Jaundice may be divided, therefore, into—(1) *Extra-hepatic or "obstructive,"* in which there is a gross obstruction, usually involving the large, extra-hepatic bile-ducts, to the flow of bile along the bile-ducts. (2) *Toxaemic, intrahepatic,* or *haemo-hepatogenous,* in which there is in most cases obstruction in the small intrahepatic bile-ducts. The obstruction is due to cholangitis or inflammation of the minute ducts, depending on the irritating effect of poisons derived from the blood circulating through the liver. A reservation as to the presence of cholangitis is necessary, for it has recently been urged that in chronic haemolytic jaundice there is no inflammation or obstruction in the bile-ducts (*vide* p. 538).

Jaundice is, therefore, a symptom, not a disease in itself. It may be the result of a purely local condition, namely, a tumour pressing on the large extra-hepatic bile-ducts; or, on the other hand, it may primarily depend on a general infective or toxaemic process.

Toxaemic, Intrahepatic, or Haemo-hepatogenous Jaundice.—This form of jaundice, in which there is no gross obstruction to the flow of bile through the larger bile-ducts, is usually obstructive and due to inflammation of the small intrahepatic bile-ducts (angiocholitis) set up by poisons reaching the liver by the blood-stream. Toxaemic jaundice is met with in numerous conditions which may, for convenience, be divided into three groups: (i) various infections; (ii) as the result of certain poisons or drugs; (iii) chronic splenomegalic haemolytic jaundice.

(i) It may occur in a number of diseases, especially haemic infections, such as pyaemia, septicaemia, relapsing fever, haemoglobinuric fever, and may be seen in pneumonia, typhoid fever, pernicious anaemia. In some instances, as mentioned above, jaundice may be associated with haemolysis, for example, in paroxysmal haemoglobinuria; the jaundice, however, is not a necessary result of haemolysis, but a concomitant effect of a common toxic or infective cause. In the diseases enumerated above jaundice is an incidental, and in most instances not a constant, symptom of a well-recognised disease, but in some instances, as Weil's disease (or infectious

[1] Gilbert et Herscher. *Compt. rend. Soc. Biol.*, Paris, 1902, liv, 795.
[2] Hayem. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1897, 3. s., xiv, 704.
[3] Gilbert et Lereboullet. *Gaz. hebd. de méd.*, Paris, 1902, vii, 889.

jaundice) and acute yellow atrophy, it is one of the most characteristic, if not the most essential, of the clinical features.

(ii) Some of the poisons which give rise to toxaemic jaundice have been already referred to, such as toluylenediamine, phosphorus, snake-bite. In addition, jaundice occasionally follows large doses of chloroform, chloral, coal-tar products such as acetanilide, santonin, filix mas, poisoning by arseniuretted hydrogen, aniline, mushrooms, and even in fatal sulphate of copper poisoning.

(iii) Chronic splenomegalic haemolytic jaundice is described on p. 537.

General Characters and Distinctions from Obstructive Jaundice.—Haemo-hepatogenous or toxaemic jaundice is essentially a sign of some underlying infection or intoxication, and is usually subordinate to the constitutional symptoms. The patient suffers comparatively little from the presence of bile in the general circulation, but is definitely and often severely ill from the primary disease or intoxication. The jaundice is, as a rule, slight, though in acute yellow atrophy and icterus gravis it is bright yellow, and the dark-green tint of chronic obstructive jaundice does not occur. There may be manifest toxaemia, as shewn by cutaneous, nasal, gingival, and gastro-intestinal haemorrhages, and by nervous symptoms. The urine contains less bilirubin than in obstructive jaundice, but, since bile reaches the intestine and is there exposed to putrefactive and fermentative changes, urobilin is formed, absorbed, and excreted in the urine; whereas in obstructive jaundice, when bile is excluded from the bowel, there is no urobilinuria. In both toxaemic and obstructive jaundice bile acids are present in the urine for the first few days, but not after this; the amount of the bile acids found in the urine during these early days is rather less in toxaemic than in obstructive icterus. Hay's sulphur test should be employed in preference to Pettenkofer's test for bile acids. As the result of the general haemic infection or intoxication there are often changes in the renal epithelium leading to albuminuria.

The faeces contain stercobilin, sometimes even in excess; this is due to increased secretion of bile-pigments (polychromia) as a result of the toxaemia augmenting the supply of haemoglobin to the liver cells. The motions in toxaemic jaundice thus differ markedly from the clay-coloured dejecta of cases in which, from complete obstruction of the ducts, bile is excluded from the intestines.

The course of the disease is more acute, as a rule, than in obstructive icterus, and is not accompanied by the itching of the skin, xanthopsia or yellow vision, and slow pulse which may accompany obstructive jaundice. Signs of constitutional disturbance, such as enlarged spleen, fever and albuminuria, are common, and grave symptoms appear sooner and more frequently than in obstructive jaundice, in which they only occur late or at the termination of long-continued jaundice. In severe cases of haemo-hepatogenous jaundice the "typhoid state," with dry tongue, delirium, coma, and multiple haemorrhages, may rapidly develop. The important features, therefore, are the want of proportion between

the slight degree of jaundice and the marked constitutional symptoms, and evidence of haemic infection or intoxication.

Chronic Splenomegalic Haemolytic Jaundice.—*Synonyms*: Haemolytic jaundice with splenomegaly; familial splenomegalic cholaemia; chronic simple jaundice with splenomegaly; chronic infective jaundice (Hayem).

Definition.—Chronic jaundice, moderate though varying in degree, accompanied by enlargement of the spleen, but by little or no enlargement of the liver, urobilinuria, absence of bile from the urine (acholuria), and normally coloured faeces. The red blood-corpuscles are characteristically "fragile," namely, undergo haemolysis in hypotonic salt solutions in an abnormal manner. There is no evidence that the jaundice is obstructive.

Introduction.—The special interest of chronic haemolytic jaundice is that it may prove to be an exception to the general rule that all jaundice is due to obstruction somewhere in the biliary tract; for, as will be seen later, there is some evidence that it is a truly haematogenous jaundice, namely, that the bilirubin is manufactured in the circulation.

History.—In 1885 Murchison[1] described a family, a later generation of which was proved in 1909 to shew this condition (Hutchison and Panton[2]). Wilson[3] (1890, 1893) reported a family in this country with one necropsy, and in 1900 Minkowski[4] gave a detailed description of a family with a necropsy in which there was no evidence of biliary obstruction. Little notice was taken of the condition until Chauffard's[5] discovery (1907, 1908) of the characteristic fragility of the red blood-corpuscles called forth a copious literature in France. In this country Parkes Weber[6] and in America Thayer and Morris,[7] and Tileston and Griffin[8] have paid special attention to the subject. Chronic haemolytic jaundice may be divided into (*a*) the hereditary, familial, and congenital, and (*b*) the acquired forms. The following description will deal with these two forms in common, the differences between them being noted under the "clinical features."

Etiology.—The hereditary, congenital, and familial forms may shew various combinations, thus the condition may be hereditary and congenital, or hereditary but not congenital; in the same family jaundice may come on after birth in one generation and be congenital in subsequent generations (Benjamin and Sluka[9]). This process of "anticipation" suggests that the morbid process becomes intensified.

[1] Murchison. *Diseases of the Liver*, 3rd edit., p. 481, 1885.
[2] Hutchison and Panton. *Quart. Journ. Med.*, Oxford, 1908–9, ii, 452.
[3] Wilson, C. *Trans. Clin. Soc.*, Lond., 1890, xxiii, 162; and (with D. Stanley) *Ibid.* 1893, xxvi, 163.
[4] Minkowski. *Verhandl. d. Congr. f. inn. Med.*, Wiesbaden, 1900, xviii, 316.
[5] Chauffard. *Semaine méd.*, Paris, 1907, xxvii, 25; 1908, xxviii, 48.
[6] Weber. *Internat. Clinics*, Phila., 1909, s. 19, ii, 85; *Amer. Journ. Med. Sc.*, Phila., 1909, cxxxviii, 24; (with Dorner) *Lancet*, Lond., 1910, i, 227.
[7] Thayer and Morris. *Johns Hopkins Hosp. Bull.*, Balt., 1911, xxii, 85.
[8] Tileston and Griffin. *Am. Journ. Med. Sc.*, Phila., 1910, cxxxix, 847.
[9] Benjamin und Sluka. *Berlin. klin. Wchnschr.*, 1907, xliv, 1065.

Chronic haemolytic jaundice presents resemblances to other diseases, such as simple family cholaemia, chronic splenic anaemia of adults, and hypertrophic biliary cirrhosis, especially the metasplenomegalic form, in which the spleen is enlarged first. There are apparently some cases of chronic haemolytic jaundice in which the spleen is not enlarged (A. Pick [1]). In Cade's [2] series there appeared to be some relation between haemolytic jaundice and simple family cholaemia; a man with splenic enlargement and chronic jaundice, whose blood was normal as regards haemolysis, was therefore regarded as the subject of simple family cholaemia; of his seven children three had haemolytic jaundice with splenomegaly, in one this was congenital, in the other two it appeared some years after birth.

Acquired haemolytic jaundice may appear in adult life without apparent cause, or may follow some infection. Brulé [3] divided the cases into primary, which arise without any obvious cause or come on during some transient acute disease and persist indefinitely; and secondary cases, which are transient complications of acute infections or of the action of poisons. Hayem [4] regarded the condition as due to syphilis, but there is no evidence of this in most of the cases, and the Wassermann reaction has been tried in some cases and found to be negative (Weber).

Pathogeny.—The characteristic feature of the blood in chronic haemolytic jaundice is "fragility" of the red blood-corpuscles, which break up with undue facility, and thus provide an increased amount of haemoglobin to form bilirubin. The cause of this fragility is not known, but it has been thought to be due either to inadequacy of the bone marrow or to some "inborn error of metabolism." The haemolysis is not due to a haemolysin in the blood, and has been considered to depend either on the fragility of the corpuscles or on activity of the spleen (Minkowski, Chauffard, Banti). There is little proof that the haemolysis is due to the spleen; the chief arguments are that excessive phagocytic activity in the spleen was described in one case by Vaquez and Giroux,[5] and that cures have followed splenectomy (*vide* p. 540). There is some evidence, which Thayer and Morris have collected, that bile-pigment can be formed in old haemorrhages in parts of the body other than the liver. It has been suggested that haemoglobin is transformed into bilirubin by a tryptic ferment in the presence of a carbohydrate, such as glycogen or dextrose; and that, though these conditions are usually provided by the liver, the change may be carried out in the tissues.

The mechanism by which the jaundice is produced is doubtful; it is not due to inflammation of the small intrahepatic ducts or to viscidity of the bile, for there are no microscopical changes in the minute ducts, and in a patient on whom cholecystotomy had been performed for suspected gall-stone, large quantities of normal and strikingly fluid bile were dis-

[1] Pick, A. *Wien. klin. Wchnschr.*, 1903, xvi, 493.
[2] Cade. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1908, 3. s., xxv, 421.
[3] Brulé. *Thèse de Paris*, 1909, No. 88.
[4] Hayem. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1908, 3. s., xxv, 122.
[5] Vaquez et Giroux. *Ibid.*, 1907, 3. s., xxiv. 1184.

charged. There is thus a want of evidence that the jaundice is hepatic in origin; and, though it cannot be established as proved, it is possible that the jaundice is haematogenous and due to the formation of bilirubin from haemoglobin in the circulation and tissues. It has, however, been thought that there is an increased secretion of bile by the liver and that the excess runs over into the haemic capillaries in the liver (Haus [1]).

Morbid Anatomy.—The bile-ducts both outside and inside the liver are free from any signs of obstruction or inflammation. In 5 out of 6 necropsies on congenital cases small pigment calculi were found in the gall-bladder (Guizzetti [2]); these calculi, which were confined to the gall-bladder, could not account for the jaundice, and must be regarded as a complication. The liver cells shew an iron-containing pigment (haemosiderin), which is usually also seen in the kidneys. The spleen has been found to shew engorgement, siderosis, but no fibrosis. In one case phagocytic activity was described (Vaquez and Giroux).

Clinical Features.—In the hereditary, congenital, and familial cases the blood shews characteristic changes. In 1907 Chauffard discovered that the red blood-corpuscles underwent haemolysis in an abnormal manner when exposed to hypotonic solutions of saline solution; normally haemolysis of the red blood-corpuscles begins in 0·42 per cent NaCl solution and is complete in 0·3 per cent; whilst in haemolytic jaundice it begins at 0·6 per cent and is complete at 0·42 per cent; this is spoken of fragility. The red blood-corpuscles are smaller than normal, 6μ in diameter instead of the normal 7·5μ, and on appropriate staining shew basophil granules, especially at the periphery, and usually well-marked polychromatophilia. There is generally moderate anaemia; but polycythaemia has been described in two cases (Guinon, Rist, and Simon [3]; Mosse [4]); the colour index is less than one; the serum contains bilirubin, but not free haemoglobin, and is hypertonic.

The urine is high-coloured, usually contains urobilin, but is free from bile, though in some cases bile appears temporarily in the urine during exacerbations. The faeces are normal in colour except in the exacerbations, when they are sometimes pale. The jaundice varies and may almost disappear; it becomes more marked after excitement, exposure to cold, and excessive exertion. There is remarkable freedom from the usual symptoms of chronic jaundice, such as itching, slow pulse, and from xanthoma and clubbing of the fingers. The condition is compatible with long life, up to 70, and there is no arrest of growth or development. The only symptom of importance is the occurrence in some cases of attacks of abdominal pain imitating biliary colic, and probably connected with the presence of pigment calculi in the gall-bladder; the attacks are accompanied by a raised temperature, drowsiness, and increase in the jaundice, and are possibly due to infection.

[1] Haus. *Norsk Mag. f. Laegevidensk.*, Christiania, 1910, lxxi, 1277.
[2] Guizzetti. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1912, lii, 15.
[3] Guinon, Rist, et Simon. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1904, 3. s., xxi, 786.
[4] Mosse. *Deutsche med. Wchnschr.*, 1907, xxxiii, 2175.

In *the acquired form* the degree of anaemia is more marked and the jaundice less pronounced than in the congenital form. In fact the blood may resemble that of pernicious anaemia, with a high colour-index and nucleated reds with megaloblasts, but there is leucocytosis with myelocytes and eosinophilia. The fragility of the reds is slight when tested with unwashed corpuscles, and thus contrasts with the congenital form in which the fragility is marked and the anaemia moderate. Another special feature of the blood in the acquired cases is its auto-agglutinative power. In contrast to the congenital form, the patients are definitely ill and suffer from anaemia as well as from attacks of febrile biliary colic. The condition may imitate pernicious anaemia or gall-stones. As the result of febrile attacks the anaemia may advance very rapidly.

Prognosis.—In the hereditary, congenital, and familial forms the outlook as regards life is extremely good, in fact the subjects of the disorder are not ill, but they never become absolutely normal. In the acquired cases, on the other hand, a cure has resulted.

Diagnosis.—The characteristic fragility of the red blood-corpuscles distinguishes the condition from other forms of jaundice, including gall-stones and pernicious anaemia with icterus, in which the resistance of the red blood-corpuscles to haemolysis is increased. By this means the diagnosis of cases in which the jaundice is slight or temporarily absent, from splenic anaemia can also be made.

Treatment.—The subjects of the hereditary, congenital, and familial forms should lead a protected life, so as to avoid cold, over-exertion, and excitement, which lead to exacerbations. The attacks of abdominal pain require symptomatic remedies, but otherwise treatment is hardly necessary. If anaemia is prominent, iron should be given. In the more severe examples of the acquired form rest in bed and iron are indicated; arsenic is not of any use. Simple drainage of the gall-bladder, which would be reasonable if there was any evidence of biliary infection, has seldom been carried out; in one case jaundice returned after closure of the fistula (Chauffard and Troisier[1]). Splenectomy has been reported to have been followed by a cure (Micheli,[2] Banti[3]). The diet should be simple and nourishing. Constipation and intestinal putrefaction should be prevented by purgatives, guaiacol, or calomel $\frac{1}{20}$ gr. t.d.

Obstructive Jaundice

Signs.—*Jaundice* appears first in the conjunctiva, where it can be well seen by drawing the lower eyelid down, then successively on the face, neck, body, and extremities. The "whites" of the eyes are the first part to be stained. The masses of fat (pingueculae) often present under the conjunctiva frequently have a slightly yellow colour and may lead to an erroneous diagnosis of jaundice. Slight icterus is more readily

[1] Chauffard et Troisier. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1908, xxv, 411.
[2] Micheli. *Wien. klin. Wchnschr.*, 1911, xxiv, 1269.
[3] Banti. *Policlin.*, Roma, 1911, xviii (sez. prat.), 1558.

detected in a fair-skinned patient than in one of a dark complexion, in whom the skin is often somewhat sallow. It should also be remembered that jaundice is easily overlooked in artificial light. The mucous membrane of the lips and palate shews the icteric tint almost as soon as in the conjunctiva. In prolonged jaundice in infants the teeth have been found to be green (Thursfield,[1] Langmead [2]). When jaundice has existed for a long time, the bile-pigment in the skin turns of a dark-green colour

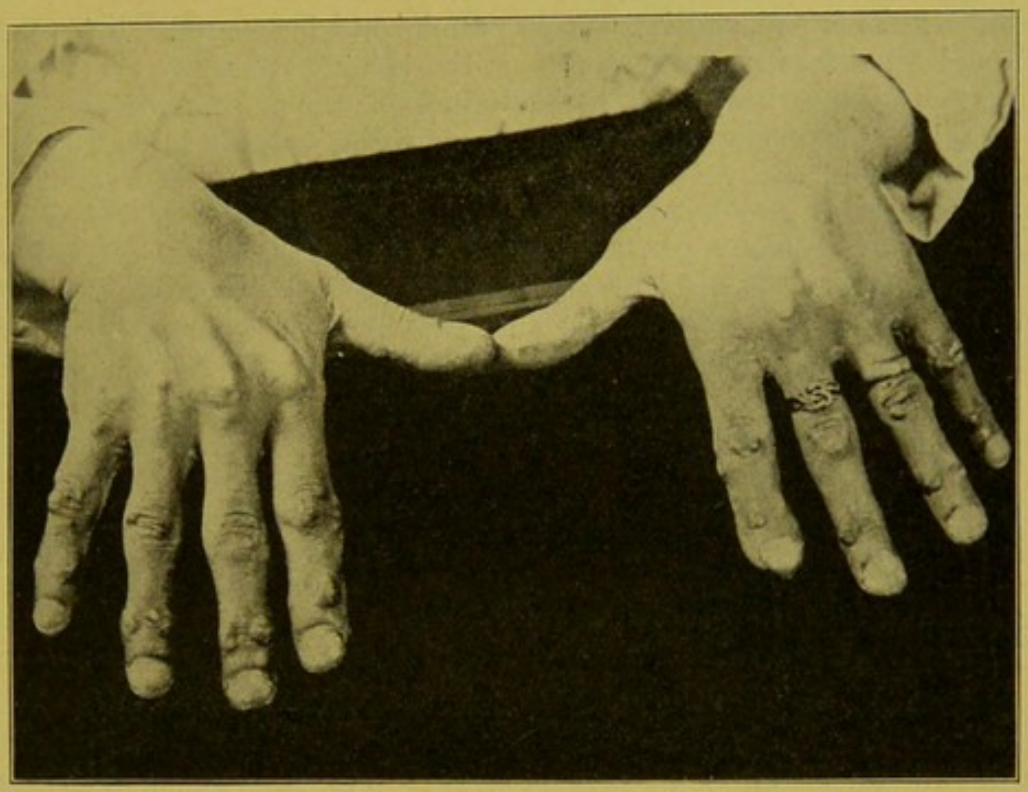


FIG. 78.—Xanthoma tuberosum multiplex in a Jewess who had had jaundice for fourteen years; the liver and spleen were enlarged (Dr. Graham Steell's case).

(biliverdin), and the condition is often spoken of as "black jaundice." In rare instances areas of leucodermia have appeared in jaundice due to malignant disease (Warthin,[3] Rolleston [4]); in Warthin's case the medullas of the suprarenals were infiltrated with growth.

In chronic jaundice, usually of some years' duration, multiple xanthoma, xanthelasma, or vitiligoidea may occur. The relation between chronic icterus and this rare skin disease is uncertain, for xanthoma may occur in the absence of jaundice, and it is seen in a small percentage only of the cases of chronic jaundice. According to Chauffard [5] xanthoma is a local deposit ("tophus") of cholesterin due to excess of cholesterin in the blood. There are two forms: in flat patches and nodular areas. It may be very painful. The plane or flat form may

[1] Thursfield. *Proc. Roy. Soc. Med.*, Lond., 1912, v (Sect. Dis. Child.), 147.
[2] Langmead. *Ibid.*, 148.
[3] Warthin. *Phila. Med. Journ.*, 1900, vi, 38.
[4] Rolleston. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Clin. Sect.), 195.
[5] Chauffard. *Rev. de méd.*, Paris, 1911, xxxi (Jubilé du Prof. R. Lépine), 177.

also occur on mucous membranes. In chronic jaundice there is a tendency to the formation of stigmata, or spider angiomas, on the skin of the face and elsewhere. As the jaundice passes off, the angiomas may also recede (Osler). When, as the result of complete biliary obstruction or from other causes, the protective function of the liver fails, and toxins, manufactured in the alimentary canal, pass into the circulation and give rise to cholaemia, cutaneous and mucous haemorrhages, such as epistaxis and melaena, occur.

The *urine* is acid, and is somewhat diminished in amount. It becomes bile-stained before the conjunctiva or the skin; as much as twenty-four hours may elapse between the appearance of bile in the urine and in the conjunctiva. The colour of the urine varies from an intense yellow, to brown, olive, or a very dark brown. In rare instances in which there is a considerable amount of biliverdin, bilirubin, and other bile-pigments, the urine may appear black (Garrod [1]). When shaken up, the froth becomes yellow. The colour must be distinguished from that in urobilinuria, haematuria, melanuria, and the alterations due to rhubarb, chrysophanic acid, senna, and santonin, by Gmelin's test for bile-pigment.

Occasionally, especially during convalescence, in obstructive jaundice the urine contains no bilirubin, although the skin is still jaundiced. When bile is completely excluded from the bowel, there is no urobilin in the urine; but when the obstruction is incomplete and allows some bile to escape into the duodenum, urobilinuria may appear, urobilin being manufactured from bilirubin in the intestine by microbic activity. Bile salts are present in the urine for the first few days of jaundice, and then disappear; the same holds good in toxaemic jaundice; but the quantity of bile salts in the urine is larger in obstructive than in toxaemic jaundice. The disappearance of bile salts from the urine probably depends on their diminished production in all forms of icterus. In marked jaundice there may be mucus (nucleo-albumin). As a result of the bacterial decomposition of proteins (putrefaction) in the alimentary tract the ethereal sulphates are increased and a considerable amount of indican may be found. It must, however, be remembered that aromatic drugs such as creosote and salol, which are frequently given to control flatulence, are said to increase the ethereal sulphates in the urine (Herter [2]).

When, in the late stages of obstructive jaundice, cholaemia has supervened, the renal epithelium may suffer and albuminuria occur. Casts, if looked for, are almost always present; they depend on the jaundice, and are not necessarily accompanied by albuminuria. Experimental ligature of the bile-duct has been found to give rise to casts in the urine without albuminuria (Wallerstein [3]). In about 40 per cent of urines containing bile there is reduction of Fehling's solution due to the presence of glycuronic acid (Cammidge [4]).

[1] Garrod. *Practitioner*, Lond., 1904, lxxii, 386.
[2] Herter. *Lectures on Chemical Pathology*, p. 205, 1902.
[3] Wallerstein. *Berlin. klin. Wchnschr.*, 1902, xxxix, 310.
[4] Cammidge. *Treatment*, Lond., 1905–6, ix, 649.

The Faeces.—There is usually constipation, and the motions are bulky, of low specific gravity, and often extremely offensive, mainly from the presence of fatty acids. In the absence of bile the faeces are pale and are devoid of hydrobilirubin; the "clay-coloured" appearance being partly due to the absence of the pigment and partly to an excess of finely divided fat and bubbles of gas. The presence of fat in excess probably interferes with absorption of proteins and favours fermentation. When bile is excluded from the bowel the undigested fat may rise from the normal 7 to 10 per cent to 55 or 78·5 per cent (Müller[1]). When obstruction is not complete, bile enters the bowel and the faeces are of a fairly normal colour. This may occur when one of the two hepatic ducts is obstructed, or when a "floating" gall-stone in the common duct allows some bile to escape into the duodenum.

Other Secretions.—There has been a good deal of discussion and discrepancy of opinion about the condition of the various secretions in jaundice. The majority, such as the saliva, the mucus of the mouth and alimentary canal, are not bile-stained. The perspiration is usually free from bile, but it may be present in the secretions of the axilla. Tears and women's milk are more often free from bile than jaundiced. Although the bile-pigments do not appear in the saliva, the salivary glands themselves, like other organs, are deeply bile-stained. The cerebrospinal fluid is free from bile pigment; but in certain pathological conditions it may give Gmelin's test for bilirubin; thus Gilbert and Castaigne[2] obtained a positive reaction in 3 jaundiced patients with nervous diseases; in Mosny and Javal's[3] case there was a sarcomatous growth in the dura mater and the cerebrospinal fluid contained bile, and it is bile-stained in the "Kernicterus" of infants dying with jaundice. In inflammatory conditions the pathological secretions and exudations become icteric, as shewn by pneumonic sputum, pleural and peritoneal effusions, and saliva in mercurial salivation.

Circulatory System.—In the absence of pain and fever the pulse tends to be slow. This is generally true, but in 1902 Mackenzie[4] had never met with a slow pulse in jaundice, and Thomson[5] states that it does not occur in children. It is especially in catarrhal and recent jaundice that slowing of the heart's beat is most marked. It has been ascribed to the inhibitory action of bile salts on the cardiac ganglia, on the myocardium, or to stimulation of the inhibitory fibres of the vagus; for bile acids pass into the blood in the early stage of jaundice, but are produced in very small quantities when jaundice is established. King and Stewart,[6] however, have shewn that the slow pulse is due to the bile-pigments. The pulse is frequently observed to vary very considerably with position; sitting up may increase the pulse-rate by twenty beats. The arterial

[1] Müller. *Ztschr. f. klin. Med.*, Berl., 1887, xii, 45.
[2] Gilbert et Castaigne. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1908, 3. s., xxv, 598.
[3] Mosny et Javal. *Ibid.*, 1909, 3. s., xxviii, 280.
[4] Mackenzie, J. *The Study of the Pulse*, p. 134, 1902.
[5] Thomson, J. *Clinical Examination and Treatment of Sick Children*, p. 235, 1908.
[6] King and Stewart. *Journ. Exper. Med.*, N.Y., 1909, ix, 673.

blood pressure is low. Experimental injection of bile into the jugular vein of rabbits has produced a fall of blood-pressure, and rendered the inhibitory action of the vagus more marked (Meltzer and Salant [1]). From muscular incompetence a mitral systolic murmur may become audible, and from increased pressure in the pulmonary circulation, due to this cause or possibly to reflex constriction of the pulmonary vessels referred from the bile-ducts, the pulmonary second sound becomes accentuated.

The blood-serum is stained of a greenish-yellow tint. The specific gravity of the blood as a whole is increased, but that of the serum is unaffected. The coagulation time is prolonged. The blood may take fifteen to twenty minutes to coagulate instead of the normal four minutes (Osler [2]). In severe cases the alkalinity of the blood has been found to be diminished.

There is very little anaemia except in severe cases; this is rather curious, inasmuch as considerable haemolysis from the action of the bile acids might naturally have been expected. The resistance of the red blood-corpuscles to haemolysis by saponin is greatly diminished (M'Neil [3]), but to hypotonic salt solution it is increased, and, according to Chauffard,[4] the corpuscles are increased in size; whereas in haemolytic jaundice they break up more readily in hypotonic salt solution, and are smaller than in health. The plasma in obstructive jaundice is hypertonic (v. Limbeck [5]). In advanced obstructive jaundice with cholaemia granular degeneration of the red blood-corpuscles is a prominent feature. In cholaemia there is usually leucocytosis. In jaundice of no great intensity and without grave toxaemic symptoms leucocytosis does not occur unless there is some other cause, such as inflammation or suppuration.

A. S. Grünbaum,[6] in 1896, pointed out that the undiluted blood-serum of jaundiced patients in many cases agglutinated typhoid bacilli. But in most cases dilution of the serum is followed by such a marked falling off in the agglutinative power that there is no reason to diagnose typhoidal infection. In some cases of jaundice the serum, even when highly diluted, agglutinates typhoid bacilli in such a manner as to lead to the conclusions that there has been an attack of typhoid fever, that the patients are typhoid carriers, or that bacteria closely related to the *B. typhosus* give rise to a group agglutination reaction (Christian [7]).

The *respiration* is usually normal, but the rate may be slowed. The *temperature*, like the functions of the body generally, is depressed. This is probably due to the action of toxins on the tissues, and also to the diminished intake of food and assimilation. Fever, when present, is either due to the cause responsible for the jaundice, as hepatic abscess,

[1] Meltzer and Salant. *Journ. Exper. Med.*, N.Y., 1905, vii, 280.
[2] Osler, W. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 264.
[3] M'Neil. *Journ. Path. and Bacteriol.*, Cambridge, 1911, xv, 56.
[4] Chauffard. *Semaine méd.*, Paris, 1908, xxviii, 48.
[5] von Limbeck. *Clinical Pathology of the Blood*, p. 316, Engl. Transl., Lond., 1901.
[6] Grünbaum, A. S. *Lancet*, Lond., 1896, ii, 806.
[7] Christian. *Boston Med. and Surg. Journ.*, 1907, clvi, 536.

gumma, or cirrhosis, or is the result of some complication, such as cholangitis in gall-stone obstruction.

The *liver* is often enlarged from damming-up of the bile, and may be tender. In malignant disease and in cirrhosis its surface may be knobby or irregular.

Enlargement of the Gall-bladder.—In chronic jaundice due to gall-stones the gall-bladder is collapsed from previous cholecystitis, whilst in cases of malignant disease pressing on the common bile-duct the gall-bladder forms a tense, pear-shaped tumour. If a calculus be impacted in the cystic duct, the gall-bladder may be distended with mucus, and occasionally contains numerous calculi; these are exceptions to the general rule enunciated by Courvoisier that in jaundice due to gall-stones the gall-bladder is collapsed, and that in jaundice due to malignant disease it is dilated.

The *spleen* is usually not enlarged, but if it is, it points to biliary cirrhosis, some infective or toxic process, such as Weil's disease or infective jaundice, to syphilis, or to that extremely rare condition, alveolar hydatid.

Symptoms.—Apart from the independent effects of underlying diseases, the symptoms accompanying jaundice are due partly to the presence of bile in the circulation, which acts as a depressant, partly to a secondary toxaemia produced by the failure of the liver to perform its important protective functions of stopping poisons brought to it from the alimentary canal, and partly to the absence of bile from the alimentary canal. These distinctions in the causation of the symptoms must not be pressed too far, but it will be convenient to consider the symptoms under the following heads:—

Symptoms due to Bile in the Circulation.—The normal constituents of bile, the bile-salts, bile-pigments, and cholesterin, must be considered from the point of view of their toxic action on the tissues of the body.

The bile-salts exert a well-marked haemolytic action on red blood-corpuscles outside the body, but it is plain that they are not present in the blood in sufficient amounts in jaundice to produce haemolysis. If haemolysis due to this cause occurred, there should be marked anaemia and escape of blood-pigment in the urine in obstructive jaundice. Neither of these events occurs. The absence of anaemia and haemoglobinuria and the fact that bile-salts are only found in the urine during the first few days of jaundice shew that the production of bile-salts by the liver cells is inhibited during jaundice. The toxic effects of the bile-salts are slight compared with what might naturally have been expected. Slowing of the pulse and dilatation of the peripheral vessels have been thought to be thus caused. The headache and mental depression may in part be due to a similar toxic effect on the brain. Experimentally Meltzer and Salant[1] find that bile contains tetanic and depressing elements which usually neutralise each other. Stagnant bile, as in the gall-bladder,

[1] Meltzer and Salant. *Journ. Exper. Med.*, N.Y., 1905, vii, 280.

invariably produces coma and paralysis. Bile-salts contain the tetanic element in less amount than the whole bile.

Bilirubin was thought by Bouchard to be ten times more toxic than bile-salts, and the comparative immunity from severe symptoms in ordinary jaundice was explained by the consideration that much of this pigment was fixed in the skin and other jaundiced tissues. Gilbert and Herscher[1] find that the amount of bilirubin in the blood-serum in obstructive jaundice does not, so long as the kidneys are healthy, exceed the proportion of 1 gram in 900 c.c. of serum. They suggest that there is an excretory mechanism by which accumulation of bilirubin above this point is prevented. It appears, however, that bilirubin is a comparatively feeble poison; the subjective symptoms which have been referred to it are xanthopsia and pruritus.

Yellow vision, or xanthopsia, has been explained as the result of the retina and media having become so infiltrated with bilirubin that the blue and violet rays are absorbed. As a result, the patient suffers from blue blindness. There is a want of relation between the degree of jaundice and yellow vision; it may be absent in advanced icterus and present when it is slight; it is therefore probably due to toxic disturbance of the retina. Yellow vision is seldom a source of sufficient annoyance to lead to a definite complaint on the patient's part, but on inquiry it is not infrequently found. The yellow vision which follows the administration of santonin is more noticeable.

Pruritus, or itching of the skin without any local lesion, was estimated by Frerichs[2] to occur in about 20 per cent of the cases of jaundice. It is often stated that the irritation of the sensory nerves of the skin is due to the constituents of the bile, especially the bile-salts. But sometimes the itching is independent of jaundice, and may appear weeks before icterus, disappear when the jaundice comes out, or persist after jaundice has gone. Graves[3] reported a case of pruritus which began two months before the onset of jaundice and subsided with the onset of jaundice. I have seen a case of most obstinate itching in a woman, without any jaundice, in whom calculi were subsequently removed from the common duct. Riesman[4] refers to the prompt disappearance of pruritus in some cases after drainage of the gall-bladder. Cabot[5] mentions a case with two attacks of jaundice due to gall-stones; one attack was accompanied by severe pruritus, the other was not. The cause of the pruritus is not known, but these considerations suggest that it is a concomitant, rather than a result, of jaundice. It may be due to hepatic inadequacy and to the presence of irritating poisons in the circulation. Robson[6] specially connects pancreatic disease with severe itching. It has also been suggested that it depends on the dry and ill-nourished condition of the skin. Accord-

[1] Gilbert et Herscher. *Compt. rend. Soc. Biol.*, Paris, 1906, lix, 208.
[2] Frerichs. *Diseases of the Liver*, Transl. New Syd. Soc., 1861, ii, 107.
[3] Graves. *Clinical Lectures*, New Syd. Soc., 1884, ii, 296.
[4] Riesman. *Am. Med.*, 1907, N.S., ii, 77.
[5] Cabot. *Differential Diagnosis*, p. 719, 1912.
[6] Robson. *Surg., Gynec., and Obst.*, Chicago, 1908, vi, 29.

ing to Riesman pre-icteric pruritus is suggestive, though not pathognomonic, of malignant disease. Itching is said not to occur in young children. The itching is usually associated with well-developed jaundice. The irritation may be excessive and prevent sleep; the scratching may induce traumatic eczema. Urticaria and lichen are sometimes seen on a jaundiced skin. Urticaria has a very curious appearance, the bile-stained exudation making the bullae look much more jaundiced than the surrounding skin.

Cholesterin was thought by Flint [1] to cause the grave nervous symptoms occurring late in the course of obstructive jaundice, and the term cholesteraemia was employed in the sense that cholaemia often is now. There is no satisfactory evidence that cholesterin is toxic. It is true that experimental injection of cholesterin into the body has been followed by bad results. But these were probably either mechanical and due to obstruction of small blood-vessels, or caused by the glycerin in which the cholesterin was suspended (Herter [2]). Xanthoma and gall-stones have been ascribed to excess of cholesterin in the blood (Chauffard [3]).

Symptoms due to the Presence of Poisons other than Bile in the Circulation.—Owing to the failure of the liver to stop poisons received from the alimentary canal, auto-intoxication results, and if the kidneys do not compensate for this by free diuresis, a toxaemic condition, analogous to that of uraemia, results. The increased fermentation and putrefaction consequent on the exclusion of bile from the bowel render the process of auto-intoxication of considerable importance. In a minor degree mental depression, incapacity for continued mental effort, drowsiness, headache, and general debility are the results of this hepatic toxaemia, while in more marked degrees there may be delirium, somnolence, and coma. A bitter taste in the mouth is common, although the saliva does not contain bile-pigment, and may be due to toxic bodies, which, owing to hepatic insufficiency, have escaped into the general circulation, and so into the saliva. There is often considerable impairment of appetite, especially for fatty food.

The tendency to haemorrhage in chronic obstructive jaundice is of great importance when any surgical operation has to be performed, as fatal haemorrhage may result. Cerebral haemorrhage is very rare; Mayo Robson [4] mentions a case; I have seen one. Haemorrhages into the skin are common, and epistaxis sometimes causes anxiety. The frequent oozing from the gums is accompanied by offensive breath. The coagulation time of the blood in chronic jaundice is much prolonged; instead of four it may be fifteen or twenty minutes (Osler [5]). This blood change may be due to hepatic insufficiency and diminution of the fibrinogen in the blood, or to the failure of the liver to stop poisons and bodies allied to peptones absorbed from the alimentary canal. The

[1] Austin Flint, Jr. *Am. Journ. Med. Sc.*, Phila., 1862, xliii, 305.
[2] Herter. *Lectures on Chemical Pathology*, 1902, p. 331.
[3] Chauffard. *Rev. de méd.*, Paris, 1911, xxxi (Jubilé du Prof. Lépine), 177.
[4] Robson and Cammidge. *The Pancreas, its Surgery and Pathology*, p. 317, 1907.
[5] Osler, W. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 264.

poisons would damage the blood-vessels, while the peptone-like bodies would interfere with the coagulation of the blood. Mayo Robson,[1] however, suggested that the haemorrhagic tendency is pancreatic in origin, and that it may depend on a diminution of lime salts in the blood due to a profuse excretion of lime salts in the urine in pancreatitis.

In experimental obstructive jaundice in dogs it has been found that the calcium content of the blood is not diminished, but that the calcium salts are fixed to the bile-pigment ; this fixation of the calcium salts protects the body against the toxic action of bile-pigment, but it also disturbs the coagulation time of the blood, and plays a part in producing slow pulse (King, Bigelow, Pearce [2]).

Symptoms due to the Absence of Bile from the Intestinal Tract.—Constipation is common, and is usually explained by the absence of the natural purgative, bile. As micro-organisms grow freely in bile, it cannot be regarded as an antiseptic, but flatulence is frequent, and the absorption of the poisonous bodies produced in the intestine may account for headache, mental depression, and other symptoms. The interference with the absorption of fat leads to considerable loss of weight. The finely diffused fat probably favours fermentative changes in the bowel in addition to interfering with absorption of the other food elements.

Diagnosis of Jaundice

As has already been pointed out, jaundice may be overlooked altogether if the patient is seen only by yellow artificial light, such as gas or candle illumination. No serious difficulty should arise in distinguishing jaundice from other pigmentary changes in the skin. The yellow colour of patients with slight icterus is hardly likely to be confused with the bronzing of sunburn, with the natural hue of the yellow-skinned races, or with the tint of the skin in the advanced cachexia of malignant disease ; but should any question arise, examination of the conjunctivae and of the urine, or of blood-serum obtained from a blister, for the presence of bile-pigment will quickly settle the matter. In patients who have absorbed picric acid the skin, conjunctiva, and urine often become yellow, but the urine does not give the reaction of bile-pigment. The dark-green colour of the skin in "black" jaundice of long-continued biliary obstruction might conceivably be confused with the pigmentation of the skin in Addison's disease, haemochromatosis, malarial melanaemia, argyria, etc., but here again examination of the conjunctivae, urine, and blood-serum will prevent error.

The past effects of severe jaundice may cause some difficulty, but further investigation and the history of the case should make matters clear.

[1] Robson, Mayo. *Brit. Med. Journ.*, 1901, i, 1131 ; and *Lancet*, Lond., 1904, i, 770.
[2] King, Bigelow, Pearce. *Journ. Exper. Med.*, N.Y., 1911, xiv, 159.

In a case reported by Cavafy [1] a man aged twenty-nine, who had had syphilis, had abnormal pigmentation and itching of the skin left behind by jaundice eight years previously. A committee reported that it was leucodermia.

Feigned Jaundice.—The skin may be coloured yellow by malingerers in order to escape active work or punishment; saffron and turmeric may be employed for this purpose.[2] The fraud should be readily detected by the absence of bile-pigment from the conjunctivae and urine. If an attempt is made to darken the urine by taking rhubarb or santonin, Gmelin's reaction with nitric acid is absent, and the addition of alkalis turns the urine red instead of brown.

Differential Diagnosis of Jaundice due to various Causes.—Since the distinction between obstructive jaundice and toxaemic (or haemo-hepatogenous) jaundice has already been considered (p. 536), it is now only necessary to refer to the differential diagnosis and the various causes of obstructive jaundice. The numerous causes of obstructive jaundice may be grouped into three classes:—

(1) Where the obstruction is inside the lumen of the bile-ducts, such as a gall-stone or parasites. (2) Where the obstruction depends on changes originating in the walls of the larger bile-ducts, *e.g.* catarrhal cholangitis. (3) Where obstruction is produced by processes arising outside the larger ducts. Thus, tumours or adhesions may mechanically compress the ducts. Malignant tumours may either merely compress or may actually invade the ducts; the former is more frequent.

I. **Jaundice due to Obstruction inside the Lumen of the Ducts.**—These causes of obstructive jaundice are considered elsewhere. (*a*) Gall-stones are described on p. 709. It is possible that inspissated mucus may obstruct the ducts, but the cause of the excessive amount of mucus is inflammation of the ducts and gall-bladder and need not be separately described here. Inflammation of the minute intrahepatic ducts occurs in toxaemic jaundice, in biliary cirrhosis (p. 315), and possibly in simple family cholaemia (*vide* p. 40).

(*b*) *Parasites* may gain access to the ducts and mechanically occlude the lumen. A hydatid cyst may discharge into the ducts, and, as a result, pieces of membrane or daughter cysts may block the ducts and give rise to biliary colic, jaundice, and often to infective cholangitis. The subject is considered at length on p. 418.

Round-worms (*Ascaris lumbricoides*) may enter the common bile-duct from the duodenum and give rise to jaundice. Of this rare condition Mertens [3] collected 48 examples. *Fasciola hepatica* (*Distomum hepaticum*), the liver fluke so fatal to sheep, has been found in the ducts of the human liver, as have, in rare instances, *Opisthorchis sinensis* and *Opisthorchis noverca*. In these cases the diagnosis depends on the recognition of the worms or their ova in the faeces (*vide* p. 682).

(*c*) As pathological curiosities reference may be made to the presence

[1] Cavafy, J. *Trans. Path. Soc.*, Lond., 1881, xxxii, 258.
[2] Legg, Wickham. *Bile, Jaundice, and Bilious Diseases*, p. 375, 1880.
[3] Mertens. *Deutsche med. Wchnschr.*, 1898, xxiv, 358.

of *foreign bodies*, such as fruit-seeds, small cherry-stones, and needles, in the bile-ducts (Graham [1]), but suspicion as to the nature of such foreign bodies must always arise unless the absence of the constituents of gall-stones has been definitely proved.

(*d*) In most exceptional instances *tumours* may extend along the lumen of the common bile-duct and occlude it without necessarily invading the walls of the duct except at the point where they originate or gain entrance into the lumen of the duct. This has been observed in primary malignant disease of the gall-bladder—a cylinder of growth projecting into the common bile-duct (Bohnstedt [2])—and in primary carcinoma of the liver (Gilbert and Claude [3]).

II. Jaundice due to Changes in the Walls of the larger Ducts.—(*a*) *Catarrhal jaundice* due to inflammatory swelling of the mucous membrane of the common bile-duct, either inside the biliary papilla or in the lower part of the duct, is described elsewhere (p. 663). It is preceded by vomiting and diarrhoea, is usually of short duration, and is not accompanied by the splenic enlargement, albuminuria, and fever seen in severe infectious jaundice.

(*b*) *The infective and suppurative forms of cholangitis* are usually associated with gall-stones or rupture of a hydatid cyst into the ducts, but comparatively often complicate the rare condition of malignant disease of the duodenum involving the papilla. Infective cholangitis presents the symptoms of intermittent hepatic fever (*vide* p. 759), while in suppurative cholangitis (*vide* p. 671), in which, however, jaundice is by no means constant, the clinical picture is that of intrahepatic suppuration, and may closely resemble suppurative pylephlebitis. Jaundice in the roseolous stage of syphilis may possibly be due to a change, comparable to the cutaneous rash, in the bile-ducts (*vide* p. 349).

(*c*) *Simple stricture* of the large bile-ducts may be congenital (*vide* p. 649) or acquired (*vide* p. 661). Apart from the cystic duct, stricture of which does not give rise to jaundice, simple stricture of the ducts, such as might conceivably follow cicatrisation of an ulcer set up by a gall-stone, is extremely rare. Hence jaundice occurring some time after biliary colic is more likely to be due either to fresh gall-stone impaction or to malignant disease than to cicatricial stricture.

(*d*) *Primary tumours of the ducts* may be carcinomatous, or in rare instances innocent; the malignant growths (*vide* p. 689) occlude the lumen and give rise to deep, progressive jaundice and usually to enlargement of the gall-bladder. Innocent tumours, such as a papilloma, are really curiosities (*vide* p. 687). Fagge [4] described xanthoma on the mucous membrane of the ducts, but it is doubtful if this is the cause of the jaundice.

(*e*) *Spasm* of the muscular coats of the ducts seems a reasonable

[1] Graham, J. E. Loomis and Thompson's *System of Medicine*, iii, 428.
[2] Bohnstedt, quoted by Devic et Gallavardin. *Rev. de méd.*, Paris, 1901, xxi, 569.
[3] Gilbert et Claude. *Arch. gén. de méd.*, Paris, 1895, clxxv, 53.
[4] Fagge, H. *Principles and Practice of Medicine*, 1886, ii, 280.

explanation of *emotional jaundice*, but it has not received much support. It also explains jaundice in hysterical subjects when there is no evidence of any other causal factor. Jaundice in lead poisoning might, in the absence of any other satisfactory cause, be referred to spasm of the ducts. I have seen recurrent attacks of painful jaundice in a worker in lead, which did not appear to be due to gall-stones.

III. **Jaundice due to Pressure exerted on the Bile-ducts from without.**—*Synopsis.*—(1) By intrahepatic tumours. (2) By enlarged glands in the portal fissure: malignant, tuberculous, syphilitic; gumma in the portal fissure. (3) In lesions of the stomach: carcinoma, gastric ulcer, perigastric adhesions. (4) In duodenal lesions: ulcer, carcinoma. (5) By peritoneal adhesions. (6) By renal and suprarenal tumours: in nephroptosis. (7) Wandering spleen. (8) By retroperitoneal tumours. (9) In pancreatic lesions: carcinoma, cysts, chronic pancreatitis, gumma, calculus. (10) By aneurysm of the aorta, hepatic, mesenteric arteries. (11) In gastroptosis. (12) In hepatoptosis. (13) By uterine conditions and ovarian tumours. (14) Constipation.

(1) *Intrahepatic tumours*, such as carcinoma, may press on the intrahepatic branches of the bile-ducts, and if the obstructed area be large, such an amount of bile stasis may result as to lead to absorption of bile by the lymphatics and so to jaundice. In these cases bile may pass from the other lobe of the liver into the duodenum, so that the faeces retain their normal colour. A hydatid cyst or a gumma in the liver may act in a similar fashion. Primary or secondary malignant tumours of the liver may project into the portal fissure and press upon the hepatic ducts, the common hepatic or common bile-ducts, and so give rise to jaundice. A hydatid cyst or gumma, when projecting from the liver, may exert pressure on the bile-ducts in a similar manner.

In a case recorded by Legg[1] a hydatid cyst projecting from the liver compressed the common hepatic duct and caused persistent jaundice with xanthoma multiplex. Bristowe[2] described obstruction of both hepatic ducts by gummas.

(2) *Enlargement of the glands in the portal fissure* may be due to various causes, such as intrahepatic inflammation, malignant disease, and occasionally to tuberculosis, syphilis, and lymphadenoma. Malignant infiltration of the glands, which is the most frequent cause of jaundice, may be secondary to disease in the liver, gall-bladder, stomach, pancreas, intestine, or peritoneum.

Tuberculous glands in the portal fissure may in rare cases press on the bile-ducts and give rise to obstructive jaundice. Cases have been recorded by Florand,[3] Köster,[4] Knight,[5] Hodenpyl,[6] Lenoble and Attila.[7]

[1] Legg, J. W. *Trans. Path. Soc.*, Lond., 1874, xxv, 155.
[2] Bristowe, J. S. *Ibid.*, 1858, ix, 233.
[3] Florand. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1899, 3. s., xvi, 30.
[4] Köster. *Centralbl. f. inn. Med.*, 1896, xvii, 213.
[5] Knight. *Quart. Med. Journ.*, Sheffield, 1895, iii, 372.
[6] Hodenpyl. *Med. Rec.*, N.Y., 1898, liv, 693.
[7] Lenoble et Attila. *Bull. Soc. Anat. Paris*, 1905, 6. s., vii, 781.

The rarity of tuberculous disease of the glands in the portal fissure depends on the fact that they receive the lymphatics from the liver, and not from the intestine and peritoneum. Tuberculous enteritis and peritonitis, therefore, infect the portal glands in a roundabout manner, viz. by producing tuberculosis of the portal spaces in the liver—the bacilli travelling by the portal vein. The lymphatics of the liver then convey the infection to the portal glands. It is conceivable that tuberculous infection might extend along the lymphatic trunks against the flow of lymph and so spread to the portal fissure from the abdominal cavity. Tuberculous enlargement of the portal glands is, therefore, closely bound up with tuberculosis of the liver (*vide* p. 336), in which, however, jaundice is most exceptional. A tuberculous gland in the portal fissure has been known to open into the common bile-duct (Köster), much in the same way that tuberculous bronchial glands have been found to open into the bronchi. Tuberculous glands may become adherent to the structures in the portal fissure and render any attempt at removal both difficult and dangerous. In Florand's case removal of tuberculous glands compressing the common bile-duct was followed by fatal haemorrhage from the portal vein. Tuberculous retroperitoneal lymphatic glands may compress the common bile-duct near its entrance into the duodenum and give rise to obstructive jaundice. The glands may so indent the pancreas as to look at first like tuberculosis of that organ.

Syphilitic Adenitis.—It has been suggested that enlargement of the glands in the portal fissure may cause the specific jaundice sometimes seen in secondary syphilis, but this is doubtful (*vide* p. 350). It is possible that gummatous change or syphilitic adenitis later in the course of the disease may involve lymphatic glands in the neighbourhood of the bile-ducts, and, by pressure, cause obstructive jaundice. This condition is closely allied to gummatous infiltration about the head of the pancreas (*vide* p. 560).

A man aged thirty-two years under my care with chronic jaundice was explored by Mr. A. M. Sheild, and some hard masses were felt along the course of the common bile-duct. Although there was no manifest evidence of syphilis, he was put on iodides and mercury and became completely cured. The absence of any roseola, or, indeed, of any history of syphilis, made it unlikely that this case was one of jaundice in the early stages of syphilis (*vide* p. 349), and it may have been due to gummatous adenitis.

A *gumma in the portal fissure* may press on or involve the bile-ducts and so give rise to jaundice.

S. West[1] described a large gumma extending from the diaphragm to the neck of the gall-bladder, measuring $4\frac{1}{2} \times 2\frac{1}{2}$ inches. The patient, a girl aged fifteen years with jaundice, was the subject of congenital syphilis. Cases of delayed hereditary syphilis with jaundice due to constriction of the bile-ducts by dense adhesions have been recorded by Mackenzie[2] and Lazarus-Barlow.[3]

[1] West, S. *Trans. Path. Soc.*, Lond., 1890, xli, 155.
[2] Mackenzie, H. W. G. *Ibid.*, 1892, xliii, 84.
[3] Lazarus-Barlow, W. S. *Ibid.*, 1899, l, 158.

(3) *Lesions of the Stomach.*—Jaundice occurs in from 4 to 13 per cent of all cases of *gastric carcinoma.* It occurs more often in cases in which the lesser curvature and the pylorus are affected, and is less frequent when the cardiac end of the stomach is involved.

Jaundice was present in 4 per cent of Osler and McCrae's [1] cases, in 5·5 per cent of Brinton's [2] cases, and in 13·7 per cent of Fenwick's.[3]

Usually jaundice is due to pressure exerted by enlarged lymphatic glands on the ducts, either in the portal fissure or close to the head of the pancreas. In some cases of carcinoma of the pylorus or of the lesser curvature of the stomach the growth spreads by continuity into the lesser omentum and may thus surround the common bile-duct and compress and invade its walls (compare case on p. 510).

This was well shewn in a case of spheroidal-celled carcinoma of the pylorus in a boy aged sixteen years who died in St. George's Hospital with jaundice.

In secondary malignant disease of the liver jaundice is more frequent when the primary growth is in the stomach than when it is in some more distant part of the abdomen, such as the rectum. The explanation of this is that jaundice is less often due to the actual metastases in the liver itself than to glandular infection in the immediate neighbourhood of the ducts or to the direct spread of growth into the lesser omentum.

In Gastric Ulcer and Perigastritis.—Jaundice due to the spread of inflammatory adhesions from a gastric ulcer near the pylorus must be very rare, as it is not mentioned by Murchison, Brinton, or by Dreschfeld.[4] That it may occur is shewn by the following case.[5]

A man aged twenty-seven came under my care in St. George's Hospital with no definite history whatever of gastric ulcer, but with dyspepsia and occasional vomiting of six weeks' duration and jaundice of two weeks' standing. The stomach was dilated and a definite pyloric tumour with what was thought to be thickening of the adjacent curvatures was palpable. The case was regarded as carcinoma of the pylorus, but as unsuitable for gastro-enterostomy. At the necropsy there was no malignant disease, but a cicatrising ulcer at the pylorus giving rise to marked narrowing of that orifice and extensive peripyloric adhesions involving the common duct. The head of the pancreas, which was enlarged from chronic interstitial pancreatitis, had been felt in life and regarded as thickening of the curvatures of the stomach near the pylorus.

A case of jaundice and ascites in a man aged thirty-nine years due to fibrosis spreading from an ulcer near the pylorus to the portal fissure is recorded by James.[6] The common bile-duct was normal, but the two hepatic ducts were compressed by cicatricial tissue which spread into the liver along the portal spaces.

[1] Osler and McCrae. *Cancer of the Stomach*, p. 55, 1900.
[2] Brinton. *Diseases of the Stomach*, p. 212, 1864.
[3] Fenwick, S. *Cancer and Tumours of the Stomach*, p. 69, 1902.
[4] Dreschfeld, J. Allbutt's *System of Medicine*, 1907, iii, 442.
[5] Rolleston. *Practitioner*, Lond., 1897, lix, 465.
[6] James. *Scot. Med. and Surg. Journ.*, 1898, ii, 511.

The converse condition of pyloric obstruction due to pericholecystitic adhesions is much less rare (*vide* p. 758).

(4) *Duodenal Lesions.* — In very rare instances *duodenal ulcer* is associated with jaundice either (i) as a complication or (ii) as an after-result.

(i) Ulceration of the duodenum is almost always confined to the first part of the duodenum and hardly ever extends sufficiently far into the second part to invade the biliary papilla. Concomitant duodenal catarrh, however, may spread to the biliary papilla. Perry and Shaw[1] record several cases of duodenal ulcer with jaundice.

(ii) If, as rarely happens, the ulcer is in the second portion of the duodenum and involves the papilla, cicatricial contraction may cause permanent obstructive jaundice; Moynihan[2] has collected 11 cases of this sequel.

Inflammatory adhesions may spread out from a duodenal ulcer in the first part and compress the common bile-duct as it runs towards the biliary papilla. This mechanism is exactly like that already described in peripyloric adhesions. Moynihan refers to 5 such cases.

Carcinoma of the duodenum is not common, and need not interfere with the outflow of bile unless the growth is in the second part of the duodenum and involves the biliary papilla by extension or starts in the intestinal mucous membrane of the biliary papilla. This latter form of duodenal carcinoma—juxta-ampullary or perivaterian—imitates carcinoma of the head of the pancreas by presenting deep jaundice and distension of the gall-bladder (*vide* p. 557), but in addition it has a special tendency to set up infective cholangitis, multiple foci of suppuration in the liver, and fever. Specimens of this condition are to be found in the museums of St. Bartholomew's, Guy's, St. George's, and St. Thomas's Hospitals. The following case illustrates this sequence.

Carcinoma of Biliary Papilla, Jaundice, Suppurative Cholangitis, Secondary Abscesses in Prostate and Kidneys. — A man aged fifty-two years was in St. George's Hospital with jaundice of ten months' duration, which, however, had disappeared for one month during this period of ten months, loss of strength and flesh, and difficulty in passing water. The liver was much enlarged, but not tender; there was no ascites. The urine contained bile, pus, and indican. He had a greatly enlarged prostate, some diarrhoea, and a hectic temperature during the last five weeks of life. The diagnosis was malignant disease of the prostate with a secondary growth in the portal fissure producing jaundice. The necropsy shewed a carcinomatous growth involving the duodenal surface of the biliary papilla, with great dilatation of the common and of all the bile-ducts in the liver, universal suppurative cholangitis, and empyema of the gall-bladder. The liver was green, not fibrosed, and contained secondary nodules of white growth. The pancreatic duct was dilated. The enlargement of the prostate was due to an abscess; there were numerous abscesses in the kidneys.

[1] Perry and Shaw. *Guy's Hosp. Rep.*, 1893, l, 273.
[2] Moynihan. *Duodenal Ulcer*, p. 223, 1910.

Cases of perivaterian carcinoma of the duodenum without marked jaundice have been recorded by Lannois and Courmont,[1] Mauclaire and Durrieux,[2] and by Descos and Bériel.[3]

Carcinoma of the duodenum may cause jaundice in another way, viz. by inducing gastroptosis, which, if there are adhesions around the ducts, may induce kinking and jaundice (*vide* p. 561).

Mackie Whyte[4] recorded a case in which cancer of the duodenum, not involving the biliary papilla, led to great distension of the stomach and so to kinking of the common bile-duct and jaundice.

(5) *Peritoneal adhesions* around the hepatic or common bile-ducts may produce kinking of the ducts and thus lead to jaundice. Such adhesions may be due to local peritonitis set up in various ways, such as by gall-stones in the gall-bladder, perigastric inflammation (p. 553), adhesions around a duodenal ulcer (p. 554), adhesions to inflamed retroperitoneal glands (B. Robinson[5]), tuberculous peritonitis (Dujon,[6] Berthomier[7]), or possibly by adhesions due to perihepatitis (S. Phillips[8]). It is, however, remarkable how seldom perihepatitis and chronic peritonitis are accompanied by jaundice.

(6) *New growths of the right kidney or suprarenal* very seldom press on the bile-duct and so directly produce jaundice, but secondary growths in the portal fissure may set up jaundice.

In 26 cases of primary malignant disease of the suprarenal bodies jaundice was not present in any (Rolleston and Marks[9]). A *tuberculous right kidney* has been known to compress the common bile-duct and cause jaundice (Tixier[10]).

That *a floating kidney* can exert direct pressure on the bile-ducts and thus lead to jaundice, as suggested by Litten,[11] is regarded as improbable by Macalister.[12] The colic, jaundice, and vomiting induced by a floating kidney on the right side may be explained in the following way: the peritoneum over the kidney being continuous with that covering the duodenum and common bile-duct, undue mobility of the kidney will exert traction on the duodenum and common bile-duct and will lead to narrowing of the bile-duct and duodenum. Nephroptosis may also lead to downward displacement of the duodenum, with stretching of the common bile-duct, displacement of the gall-bladder, with sharp kinking of the cystic duct, torsion of the vertical part of the duodenum, and

[1] Lannois et Courmont. *Rev. de méd.*, Paris, 1894, xiv, 291.
[2] Mauclaire et Durrieux. *Bull. Soc. Anat. Paris*, 1897, lxxii, 721.
[3] Descos et Bériel. *Rev. de méd.*, Paris, 1899, xix, 633.
[4] Whyte, M. *Scot. Med. and Surg. Journ.*, 1897, i, 361.
[5] Byron Robinson. *Am. Med.-Surg. Bull.*, N.Y., 1896, ix, 518.
[6] Dujon. *Procès-verbaux, XIX. Congrès de chir.*, 1906, p. 166.
[7] Berthomier. *Rev. de chir.*, Paris, 1910, xlii, 1179.
[8] Phillips, S. *Lancet*, Lond., 1903, i, 1796.
[9] Rolleston and Marks. *Amer. Journ. Med. Sc.*, Phila., 1898, cxvi, 398.
[10] Tixier. *Rev. de chir.*, Paris, 1910, xli, 443.
[11] Litten. *Charité-Ann.*, Berlin, 1880, v, 10.
[12] Macalister, A. Allbutt's *System of Medicine*, 1897, iv, 346.

perhaps even of the bile-duct (J. Hutchinson, Jr.[1]). A floating kidney may not only cause colic and jaundice, but the displaced kidney may readily be mistaken for a distended gall-bladder (Hutchinson). Cases of jaundice diagnosed as cholelithiasis and proved to be due to floating kidneys have been recorded by Maclagan and Treves[2] (3), Hale White,[3] Cordier,[4] Fenwick,[5] Lawrie,[6] Marwedel,[7] Sherren.[8]

The diagnosis depends on the detection of a floating kidney, for the symptoms, biliary colic and jaundice, are the same as those of cholelithiasis. The attacks of pain are rare at night in floating kidney, common in cholelithiasis (Sherren). If the symptoms persist after the floating kidney has been efficiently and successfully treated, it is probable that there is cholelithiasis in addition.

(7) *Wandering Spleen.*—The traction exerted through the pancreas on the common bile-duct by the elongated pedicle of a wandering spleen has been thought to account for jaundice when it occurs, which is but rarely, in this condition (Bland-Sutton[9]).

(8) *Retroperitoneal tumours* in rare instances press on the common bile-ducts and cause jaundice.

Vander Veer[10] recorded a large retroperitoneal myxosarcoma (weight 6 pounds) arising from the region of the left adrenal, which so interfered with the bile-duct as to produce jaundice. In a male child, aged two and a half years, under my care, with a round-celled retroperitoneal sarcoma near the right suprarenal and numerous secondary growths in the neighbouring lymphatic glands, jaundice, which was not absolutely obstructive, since the faeces were not devoid of pigment, was present for eight weeks before death.

A hydatid cyst arising in the retroperitoneal space near the head of the pancreas may compress the common duct. This is illustrated by a specimen (No. 2256) in St. Bartholomew's Hospital Museum.

(9) *Lesions of the Pancreas.*—Malignant tumours, cysts, chronic interstitial inflammation, gumma, and calculi in Wirsung's duct may all compress the common bile-duct and produce obstructive jaundice, but with the exception of the first named are rarely recognised as acting in this manner.

Malignant tumours of the pancreas may be primary or secondary, but it is almost entirely with primary malignant disease that we are at present concerned. It is practically always carcinoma, and usually attacks the head of the gland—according to Hale White,[11] in 85 per cent of the cases.

[1] Hutchinson, J., Jr. *Practitioner*, 1902, lxviii, 186.
[2] Maclagan and Treves. *Lancet*, Lond., 1900, i, 15.
[3] Hale White. *Brit. Med. Journ.*, 1892, i, 223.
[4] Cordier. *Amer. Journ. Obst.*, 1898, xxxiv, 532.
[5] Fenwick. *Lancet*, Lond., 1899, ii, 1296.
[6] Lawrie. *Brit. Med. Journ.*, 1901, i, 15.
[7] Marwedel. *Beitr. z. klin. Chir.*, 1902, xxxiv, 478.
[8] Sherren. *Lancet*, Lond., 1911, i, 870.
[9] Bland-Sutton. *Gallstones and Diseases of the Bile-ducts*, p. 146, 1907.
[10] Vander Veer. *Amer. Journ. Med. Sc.*, Phila., 1892, ciii, 22.
[11] Hale White. *Guy's Hosp. Rep.*, 1900, liv, 17.

When in this situation, the growth readily compresses the common bile-duct near its termination, but when the growth is limited to the tail or body of the pancreas, jaundice does not result unless a secondary growth compresses the duct or there is some other cause for jaundice, such as a calculus in the common duct. Jaundice occurs in a majority of cases of primary malignant disease of the pancreas.

Mirallié[1] found it in 82 out of 113 cases. Oser gives two-thirds as the proportion of cases in which jaundice occurs. The occurrence or absence of jaundice mainly depends on the anatomical relation of the head of the pancreas to the common bile-duct (*vide* p. 559).

The jaundice may come on gradually and painlessly, or be accompanied by colic. It is permanent and progressive, and becomes intense, so that cholaemia develops comparatively early. The other distinctive features of malignant disease of the head of the pancreas are rapid and extensive wasting, a tumour in the position of the pancreas, which, however, is seldom palpable, and a distended gall-bladder. The association of deep jaundice with a large gall-bladder is sometimes spoken of as the sign of Bard and Pic.[2] It illustrates Courvoisier's law that biliary obstruction due to new growth is accompanied by an enlarged gall-bladder, whereas in gall-stone obstruction of the common duct the gall-bladder is small. As a matter of fact, however, the gall-bladder, even though enlarged as shewn by necropsy, is not always palpable during life. It is practically impossible to distinguish it from primary carcinoma of the common bile-duct, except by means of Cammidge's tests; this point is discussed on p. 699. In primary carcinoma of the ampulla of Vater (*vide* p. 702) and of the duodenal surface of the biliary papilla the jaundice may intermit, which it never does in malignant disease of the pancreas, and fever from infective cholangitis may supervene. From a calculus in the common duct the diagnosis may be easy when the cases are typical, but sometimes it is difficult, as attacks of pseudo-biliary colic may occur about the time of the onset of jaundice in malignant disease of the pancreas, and pain may be absent in some cases of calculus in the common duct. The history of the cases and the course of the disease, especially the character of the jaundice, progressive or intermittent, and the condition of general nutrition will usually clear up a diagnosis which at first was doubtful.

Cammidge's Tests.—By treating the urine, free from sugar, of cases of pancreatitis by a special method, which cannot be described further here except to state that the urine is first boiled with HCl and then with sodium acetate and phenyl-hydrazine hydrochloride, Cammidge[3] obtained crystals which could

[1] Mirallié. *Gaz. des hôp. de Paris*, 1893, lxvi, 889.

[2] Bard et Pic. *Rev. de méd.*, Paris, 1888, viii, 257.

[3] Cammidge. "The Chemistry of the Urine in Diseases of the Pancreas," *Lancet*, Lond., 1904, i, 783; "An Improved Method of performing the 'Pancreatic Reaction' in the Urine," *Brit. Med. Journ.*, 1906, i, 1150; "Urine in Chronic Disease of the Pancreas," *Proc. Roy. Soc.*, Lond., 1909, Ser. B, pp. 81-372; *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Med. Sect.), 163.

not be got from normal urine. The crystals are due to a pentose derived from the pancreatic nucleo-protein which passes into the blood as a result of degeneration of the gland cells. Jaundice due to pancreatitis can thus be distinguished from jaundice due to other causes, and malignant disease of the pancreas, in which "pancreatic reaction C" is not obtained, can be diagnosed from inflammatory affections of the pancreas. From examination of the faeces Cammidge also obtains results important in diagnosis: an acid reaction is in favour of pancreatic disease, for in gall-stone obstruction of the ducts the reaction is usually alkaline. The percentage of unabsorbed fat is higher in carcinoma of the pancreas than in growths of the ducts. The unsaponified fats are in excess of the saponified in diseases of the pancreas, whereas the reverse holds good in obstruction of the common duct by stone or growth when the pancreas is unaffected. These conclusions have been freely criticised.

Carcinoma of the pancreas may be associated with cholelithiasis, and in rare instances with gall-stones in the common duct.

A woman aged fifty-eight, under my care in St. George's Hospital, was thought to be suffering from gall-stone obstruction and was accordingly operated upon; a gall-stone was felt, and on manipulation was displaced, it was thought, into the duodenum. Death occurred on the third day, largely from haemorrhage at the site of operation. At the necropsy it was found that the calculus had been pushed back into the gall-bladder, and that all the ducts were greatly dilated. The gall-bladder was small and contained two round large calculi. The head of the pancreas contained a colloid carcinoma which did not involve the duct, so the jaundice was probably due to the stone in the common duct. Microscopically the growth was a colloid spheroidal-celled carcinoma.

Pancreatic cysts rarely press on the bile-ducts and cause jaundice. Pancreatic and peripancreatic cysts may present in various situations: (i) Above the stomach and below the liver (interhepato-gastric type). (ii) Between the greater curvature of the stomach and the transverse colon; this is the commonest form (subhepato-gastric type). (iii) Below the transverse colon, so that the cyst projects near the umbilicus (subhepato-gastro-colic type). Cysts which pass forwards between the stomach and the transverse colon (subhepato-gastric type) may compress the common bile-duct. Oser[1] collected 15 cases in which jaundice occurred.

A man aged thirty, with jaundice of three months' duration, under my care in St. George's Hospital, was operated upon by Mr. G. R. Turner, and a pancreatic cyst found projecting between the greater curvature of the stomach and the transverse colon.[2] After drainage the jaundice disappeared and the man recovered. Turney and Ballance[3] met with a case of jaundice in a man aged thirty-five in whom the symptoms were ascribed to calculous obstruction of the common bile-duct; laparotomy, however, proved that the jaundice was

[1] Oser. *Nothnagel's Encyclopedia of Practical Medicine*, p. 195, English Transl., 1903.
[2] *Vide* also *Trans. Med. Soc. Lond.*, 1898, xxi, 94.
[3] Turney and Ballance. *St. Thomas's Hosp. Rep.*, 1898, xxvi, 119.

due to the pressure of a pancreatic cyst. Cases have also been described by de Havilland Hall,[1] McPhedran.[2]

A hydatid cyst in the pancreas is a pathological curiosity.

A hydatid cyst in the head of the pancreas caused jaundice of ten months' duration and ascites in a boy aged six years. At the necropsy the gall-bladder was dilated and the bile-duct and portal vein were stretched over the cyst and so compressed that it was impossible to force bile from the distended gall-bladder into the duodenum before the cyst was opened. The liver was enlarged, granular on the surface, and fibrosed.[3]

Acute Pancreatitis.—It has been suggested by Oser and Mayo Robson [4] that the condition ordinarily called catarrhal jaundice is the result of catarrhal inflammation of the head of the pancreas which presses on the common duct (*vide* p. 664). Jaundice is very rare in the graver forms of acute pancreatitis; but haemorrhagic pancreatitis may be associated with jaundice when there is a small stone in the orifice of the biliary papilla (*vide* p. 750).

Chronic Interstitial Pancreatitis.—Mayo Robson [5] and Barling [6] pointed out that chronic inflammation of the head of the pancreas may compress the common bile-duct and produce a train of symptoms—obstructive jaundice, colic, and wasting—strongly suggesting malignant disease or impacted gall-stones. Whether chronic pancreatitis will or will not compress the common bile-duct depends on the anatomical relation of the common bile-duct to the head of the pancreas. In 38 per cent of bodies the duct passes behind the head of the pancreas, and in these cases chronic pancreatitis need not affect the common bile-duct. In 62 per cent of bodies the common bile-duct is embedded in the head of the pancreas (Helley [7]), and in these cases chronic pancreatitis would compress the common duct and cause jaundice. In 62 per cent of cases of chronic pancreatitis associated with gall-stones bile-pigment was present in the urine (Robson and Cammidge [8]). This chronic fibrosis may be directly due to gall-stones in the common duct and may persist after the stone is expelled. The diagnosis is difficult, and the moral is that it is advisable to admit such cases to operation. In some instances the gall-bladder has been drained, either externally or into the small intestine, and in other cases the abdomen has been closed without any more radical measure than manipulation of the parts. Recovery has followed these surgical procedures. It is possible that when the parts have merely been

[1] de Havilland Hall. *Trans. Med. Soc. Lond.*, 1898, xxi, 107.
[2] McPhedran. *Trans. Assoc. Am. Phys.*, 1897, xii, 61.
[3] Guy's Hospital Museum, No. 1475.
[4] Robson, Mayo. *Lancet*, Lond., 1904, i, 770.
[5] *Idem. Ibid.*, 1900, ii, 236.
[6] Barling. *Brit. Med. Journ.*, 1900, ii, 1766.
[7] Helley. *Arch. f. mikr. Anat.*, Bonn, 1898, lii, 773.
[8] Robson and Cammidge. *The Pancreas, its Surgery and Pathology*, p. 319 (W. B. Saunders Co., 1907).

manipulated (Owen,[1] Dalziel[2]) a calculus in the orifice of the biliary papilla has been displaced into the duodenum. It seems highly probable that cases of chronic interstitial pancreatitis have been regarded not only during life, but even after death, as examples of carcinoma of the head of the pancreas. According to Hale White,[3] however, chronic interstitial pancreatitis is rare; for among 20,000 necropsies at Guy's Hospital only 4 cases of this disease were recognised. This conclusion as to its rarity is open to justifiable criticism.

In cases of pancreatitis the secretion of the gland escapes into the surrounding tissues and sets up fat necrosis. As a result of this glycerin and fatty acids are liberated. It was first thought that the tendency to haemorrhage, both in acute and chronic pancreatitis, which is so often accompanied by chronic jaundice, might be due to the action of glycerin (Mayo Robson[4]), but subsequently Mayo Robson[5] referred it to a diminution of the lime salts in the blood depending on increased excretion of oxalates in the urine.

Closely allied to chronic interstitial pancreatitis is the extremely rare condition gummatous infiltration in and around the head of the pancreas.

Gumma.—In a man aged thirty-three who had had syphilis ten years previously, and was suffering from obstructive jaundice, H. B. Robinson[6] opened the abdomen, felt a growth in the situation of the head of the pancreas, and accordingly put the gall-bladder into communication with the hepatic flexure of the colon. Under iodide of potassium the mass disappeared and there was a gain in weight of two stone. A similar case of Da Costa's is mentioned in Gould's *Year-Book of Surgery* for 1902, p. 181. Moynihan[7] has also described this condition.

A large pancreatic calculus in the ampulla of Vater, or in the termination of Wirsung's duct, so that it compresses the end of the common bile-duct, may give rise to jaundice (Pearce Gould,[8] Kinnicutt,[9] Murray[10]).

(10) *Aneurysms of the abdominal aorta* near the coeliac axis may press on the common bile-duct and so cause jaundice and dilatation of the gall-bladder.

In a man aged twenty-eight, who had syphilis when twenty years of age, a sacculated aneurysm involving the origin of the coeliac axis burst into the second part of the duodenum a short distance above the biliary papilla. The common bile-duct was compressed and the gall-bladder distended. Jaundice occurred three days before death, which was preceded by sudden and profuse haematemesis (W. L. Dickinson[11]). Stokes[12] previously reported a case.

1 Owen, *Brit. Med. Journ.*, 1902, ii, 1311; and Hale White, *ibid.*, 1903, ii, 126.
2 Dalziel. *Ibid.*, 1902, ii, 1312.
3 Hale White. *Clin. Journ.*, Lond., 1907, xxx, 278.
4 Robson, Mayo. *Brit. Med. Journ.*, 1901, i, 1131.
5 *Idem. Lancet*, Lond., 1904, i, 770.
6 Robinson, H. B. *Brit. Med. Journ.*, 1900, ii, 1004.
7 Moynihan. *Lancet*, Lond., 1902, ii, 856.
8 Gould, A. P. *Trans. Clin. Soc.*, Lond., 1899, xxxii, 59.
9 Kinnicutt. *Amer. Journ. Med. Sc.*, Phila., 1902, cxxiv, 948.
10 Murray. *Lancet*, Lond., 1912, i, 793.
11 Dickinson, W. L. *Trans. Path. Soc.*, Lond., 1891, xlii, 77.
12 Stokes. *Diseases of the Heart and Aorta*, p. 633, 1854.

Aneurysm of the hepatic artery may compress the bile-ducts above the entrance of the cystic duct, and hence the gall-bladder need not be dilated, as in jaundice due to an aortic aneurysm. Jaundice occurred in 16 out of 41 cases (Rolland [1]).

An *aneurysm of the superior mesenteric artery* near its origin from the aorta has been known to compress the bile-duct and give rise to jaundice (J. A. Wilson,[2] W. T. Gairdner [3]). The majority of aneurysms on this vessel, however, are not associated with jaundice. Those on the peripheral portions of the artery are not in relation with the bile-ducts, and therefore do not compress them.

(11) *Gastroptosis* is not infrequent, but is rarely associated with jaundice. Steele [4] states that gastroptosis alone cannot exert sufficient pressure on the bile-ducts to obstruct the flow of bile; this is based on his observations that after death downward displacement of the pylorus, so as to imitate the conditions present in gastroptosis, though it stretched the gastrohepatic omentum, did not interfere with the passage of bile into the duodenum: If, however, there were any adhesions involving the ducts in the portal fissure, very moderate displacement of the pylorus produced kinking of the ducts and obstruction. It would thus appear that in the presence of adhesions around the ducts, gastroptosis will readily produce jaundice.

(12) *Hepatoptosis.*—In wandering liver jaundice may be due to the presence of gall-stones, to concomitant catarrh of the ducts, to a floating right kidney, or to twisting of the common bile-duct. Dutton Steele [5] collected 15 cases of hepatoptosis in which there were attacks of jaundice without gall-stones. In Crawfurd's [6] case of anteverted liver the bile-duct had apparently been twisted, so as to cause jaundice, at the junction of the common bile and cystic ducts. The descent or dropping of the liver tends to produce this twisting. By injection experiments on the dead body Dutton Steele shewed that the more the liver descends towards the pelvis, the more difficult it is to drive injection from the biliary papilla into the gall-bladder.

(13) *Uterine Conditions, Ovarian Tumours.*—The pressure of a pregnant uterus on the ducts has been regarded as responsible for jaundice (Murchison [7]). This is very doubtful; mild jaundice in pregnant women is usually due to gastro-duodenal catarrh, but may be due to gall-stones, cholangitis, or toxaemic inflammation of the small intrahepatic ducts. The occurrence of acute yellow atrophy is especially favoured by pregnancy (*vide* p. 576).

Ovarian tumours may exceptionally cause jaundice by pressure on the bile-ducts (Poynder [8]). On the other hand, jaundice may be merely

[1] Rolland. *Glasgow Med. Journ.*, 1908, lxix, 342.
[2] Wilson, J. A. *Med.-Chir. Trans.*, Lond., 1841, xxiv, 221.
[3] Gairdner, W. T. *Clinical Medicine*, p. 504, 1862.
[4] Dutton Steele. *Univ. Med. Mag.*, Phila., 1901, xiii, 838.
[5] Idem. *Univ. Penn. Med. Bull.*, Phila., 1903, xv, 424.
[6] Crawfurd, R. P. *Lancet*, Lond., 1897, ii, 1182.
[7] Murchison. *Lectures on Diseases of the Liver*, p. 358, 2nd ed., 1877.
[8] Poynder. *Ind. Med. Gaz.*, 1899, xxxiv, 208.

associated with ovarian cysts and depend on catarrhal inflammation of the papilla, infective cholangitis, or gall-stones. The abdominal distension caused by an ovarian cyst favours stagnation of bile, infection of the ducts, and cholelithiasis. Thus suppurative cholangitis or cholecystitis may complicate ovarian cysts.

(14) *Constipation* may be associated with jaundice. Slight jaundice may possibly be due to absorption of poisons from the intestine producing catarrh of the intrahepatic bile-ducts, or in other cases be due to the spread of associated duodenal catarrh to the common duct. In this way the relief of jaundice after free purgation may be explained. It is improbable that faecal accumulation by direct pressure can give rise to jaundice. But in rare cases in which the colon is firmly united to the under surface of the liver by adhesions, faecal accumulation in the transverse colon may possibly lead to kinking or compression of the common bile-duct.

General Remarks on the Diagnosis of Jaundice.—The large number of conditions which may give rise to jaundice makes it essential that a careful examination should be made for any other evidence of disease. Thus the existence of a tumour in the abdomen, breast, or rectum will suggest malignant disease, and the presence of syphilis, either in the secondary or tertiary stage, should be an indication for specific treatment. The following points have a bearing on the nature of jaundice in a given patient.

Age.—Slight and transient jaundice appearing within a few days of birth is benign or physiological, but if well marked and accompanied by constitutional symptoms and fever, should suggest a grave form of jaundice due either to severe infection of the umbilical cord or to some haemic infection (*vide* p. 571). Persistent jaundice from birth is in favour of congenital obstruction in the larger bile-ducts (*vide* p. 649), which is usually rapidly fatal; in rare instances jaundice may persist from birth into adult life (*vide* p. 573). In childhood and early adult life catarrhal jaundice is common. Between the ages of thirty and forty-five years gall-stones, especially in women, are the most probable cause; later in life malignant disease and cirrhosis must be taken into account.

Sex.—Women are more prone to gall-stones and to malignant disease; men to cirrhosis and perhaps to the infectious forms of jaundice, such as Weil's disease. Pregnant women seem more susceptible than others to acute yellow atrophy. In very rare instances jaundice recurring during pregnancy only has been noted. Benedict[1] reported this in two sisters; in my case three infants of a woman thus affected died with jaundice.[2]

Familial Jaundice.—The occurrence of jaundice in several members of the same family may be due to some acute infection, as in Weil's disease, and is seen in epidemic jaundice. Chronic jaundice in members of the same family is met with in chronic splenomegalic haemolytic jaundice and occasionally in hypertrophic biliary cirrhosis.

[1] Benedict. *Deutsche med. Wchnschr.*, 1902, xxviii, 296.
[2] Rolleston. *Brit. Med. Journ.*, 1910, i, 864.

Onset.—If preceded by gastro-intestinal disturbance, catarrhal jaundice should be thought of; if by severe colic, gall-stones. A gradual onset with no special or striking symptoms should suggest the pressure of a tumour on the ducts. Repeated and transient attacks are in favour of gall-stones. Epidemic jaundice suggests some form of infective jaundice, such as Weil's disease.

Pain.—Constant pain suggests malignant disease; intermittent attacks point to gall-stones. Biliary colic may also occur when hydatid membranes are passed through the ducts and occasionally when malignant disease involves the ducts—pseudo-gall-stone colic. Absence of pain, however, does not exclude malignant disease, though it is the rule in catarrhal jaundice and in cirrhosis.

Duration and Progress.—Jaundice of short duration is most commonly catarrhal or due to gall-stones. If continued for more than six months, malignant disease is unlikely, and biliary cirrhosis or impacted gall-stone should be thought of. Jaundice lasting for years is probably due to haemolytic jaundice or to biliary cirrhosis.

Progressive and black jaundice suggests malignant disease, while chronic jaundice which varies from time to time is more compatible with a stone impacted in the common duct or biliary cirrhosis.

Degree and Intensity of Jaundice.—Slight icterus may be catarrhal, or, if associated with fever and constitutional disturbance, toxaemic. Persistent slight jaundice with splenomegaly suggests chronic haemolytic jaundice. The commonest causes of deep jaundice are malignant disease, impaction of a gall-stone in the common duct, and biliary cirrhosis. Extremely deep jaundice almost postulates malignant disease; that accompanying gall-stone impaction is deeper than that of cirrhosis, but never equals that seen in compression of the common bile-duct by tumours, such as carcinoma of the head of the pancreas or malignant disease of the duct. Jaundice which recurs is in favour of gall-stones.

Outbreaks of jaundice in epidemics suggest some form of toxaemic or infectious jaundice.

Fever suggests toxaemic jaundice or, when associated with considerable splenic enlargement, biliary cirrhosis. Pyrexia, of course, occurs in calculous cholangitis, in hepatic suppuration, such as abscess or pylephlebitis, and occasionally in malignant disease.

The condition of the gall-bladder is of great importance in the diagnosis of the cause of jaundice. It is not enlarged or palpable in toxaemic or intrahepatic jaundice, in biliary cirrhosis, or when there is pressure on the hepatic ducts. Obstruction of the cystic duct usually leads to distension of the gall-bladder with mucus. In obstruction of the common bile-duct by tumours pressing on it from without, or arising in its walls, the gall-bladder is distended; on the other hand, in obstruction by gall-stones the gall-bladder, contrary to what might naturally be expected, is not enlarged. This is known as Courvoisier's law.

In 100 cases of obstruction of the common duct by causes other than calculi the gall-bladder was enlarged in 92, whereas out of 87 cases of calculous obstruction the gall-bladder was shrivelled up and small in 70, or 80 per cent (Courvoisier [1]). Mayo Robson,[2] Tuffier,[3] Tessier,[4] and R. C. Cabot[5] have supported Courvoisier's dictum. Cabot's figures are even more striking than Courvoisier's, and shew that the law is true in 95 per cent of the cases. The shrivelled condition of the gall-bladder in gall-stone obstruction of the common duct is partly the result of past cholecystitis and partly because the obstruction is usually not complete. It has also been suggested that in gall-stone obstruction the spiral valves of Heister in the cystic duct remain competent and prevent regurgitation from the common bile-duct, whereas in obstruction of the common duct by tumours these valves fail.

Condition of the Liver.—Great enlargement occurs in malignant disease, hypertrophic biliary cirrhosis, and in abscess. But in abscess jaundice is slight or absent. In malignant disease the surface is generally nodular and the enlargement is progressive; in hypertrophic biliary cirrhosis the liver is smooth and the spleen is much enlarged.

The association of *ascites* points to malignant disease or cirrhosis, but in cirrhosis jaundice is usually less marked than in malignant disease. Cutaneous haemorrhages in chronic jaundice point to pancreatic disease.

Examination of the *urine* and *faeces* helps to distinguish complete from partial obstructive and toxaemic jaundice. Cammidge's tests are of use in the diagnosis between jaundice due to pancreatitis, gall-stone obstruction, and malignant obstruction of the common bile-duct. Urobilinuria is in favour of inflammation of the ducts.

Prognosis.—The occurrence of jaundice in certain diseases is of importance as shewing that hepatic complications have supervened; thus, when, as very rarely happens, jaundice is met with in typhoid fever, inflammation of the gall-bladder or ducts should be thought of. In puerperal eclampsia jaundice is of extremely bad omen; death usually follows in a few hours or days. The onset of jaundice after phosphorus poisoning is a sign that the liver is affected and must be regarded as of the gravest significance, since very few cases recover when this stage is reached. The onset of jaundice in a patient who has had malaria causes some anxiety at first, as it may be due to the severe haemic infection of haemoglobinuric or "blackwater" fever. Jaundice in relapsing fever makes the prognosis grave (Sandwith [6]). Jaundice in the course of appendicitis makes the outlook bad, as septicaemia is the probable cause; according to Reichel [7] 55 per cent of these cases die.

The ultimate prognosis in any given case of jaundice depends not so much on the degree of jaundice as on the underlying cause. Thus the comparatively slight icteric tint (toxaemic jaundice) in some cases of

[1] Courvoisier. *Path. u. Chir. d. Gallenwegen*, 1890.
[2] Mayo Robson. *Gall-stones and Their Treatment*, 1892.
[3] Tuffier. *Semaine méd.*, Par., 1893, xiii, 55. [4] Tessier. *Ibid.*, 1893, xiii, 7.
[5] Cabot, R. C. *St. Paul Med. Journ.*, Dec. 1901.
[6] Sandwith. *Practitioner*, Lond., 1904, lxxii, 660.
[7] Reichel. *Deutsche Ztschr. f. Chir.*, Leipz., 1907, lxxviii.

pyaemia and the "black" jaundice of complete obstruction of the ducts in malignant disease do not differ very materially in their ultimate prognosis.

Prognosis in Chronic Jaundice.—When gall-stones in the common duct set up chronic jaundice there is a chance, though rather a slender one, that the calculus or calculi may pass and that a spontaneous cure may result. More commonly jaundice may disappear for a time as a result of bile escaping by the side of the gall-stone. Subsequently jaundice may return and may be accompanied by periodic attacks of pain, fever, and increase in jaundice or intermittent hepatic fever. In such cases the prognosis is good if operation for removal of the calculus is undertaken before the patient becomes weak or deeply jaundiced. But when continued fever has developed and there is reason to fear that suppurative cholangitis has supervened, the prognosis is very grave.

In hypertrophic biliary cirrhosis with chronic jaundice, though the chances of ultimate recovery are practically nil, life is often prolonged for years. In such cases the general state of nutrition and the length of the intervals between the exacerbations are points of importance in estimating the probable expectancy of life. Emaciation, weakness, and attacks repeated at short intervals point to death in the near future. When chronic jaundice is associated with splenic enlargement (chronic haemolytic jaundice, *vide* p. 537, and meta-icteric splenomegaly, *vide* p. 680) the prognosis is usually good. In fact, congenital chronic haemolytic jaundice appears to make little or no difference to the subject, for he can hardly be considered a patient.

In deep chronic jaundice, due to whatever cause, the prognosis is unfavourable, since if operation is undertaken, there is considerable danger from haemorrhage, even though large doses of calcium salts are given before the operation. While if the patient is not operated upon, cholaemia will develop sooner or later. In such cases good effects from iodide of potassium point to gummatous obstruction and make the prognosis good.

In chronic jaundice due to malignant disease the prognosis is necessarily fatal, but it is not quite so desperate in cases presumed to be malignant disease of the pancreas as in cases in which new growth is palpable elsewhere. The explanation of this statement is that some cases formerly regarded as slow-growing ("scirrhus") carcinoma of the head of the pancreas are in reality chronic interstitial pancreatitis (Mayo Robson [1]).

In chronic jaundice much depends on the functional activity of the kidneys being well maintained; if the amount of urine falls and waste-products are less freely excreted, biliary toxaemia is likely to result. The presence of albuminuria points to the kidneys being damaged by the toxaemia accompanying the jaundice, and is, therefore, an index of a severe condition. The detection of leucine and tyrosine in the urine of a jaundiced patient makes the prognosis very grave.

When jaundice is accompanied by hepatic insufficiency, so that poisons which should have been destroyed by the liver escape into the general circulation and give rise to a general toxaemia, as shewn by nervous

[1] Mayo Robson. *Lancet*, Lond., 1900, ii, 236.

symptoms, such as delirium, drowsiness, and coma, and by haemorrhages, the prognosis is very grave indeed, since life cannot be long maintained after the onset of cholaemia. Nervous symptoms in jaundice should always arouse anxiety. In some cases, at first quite indistinguishable from simple catarrhal jaundice, nervous symptoms somewhat rapidly appear, and then acute yellow atrophy of the liver supervenes. But in the recently described syndrome characterised by infective jaundice and meningeal symptoms[1] the prognosis is good. The condition which is acute may imitate cerebrospinal meningitis.

When chronic jaundice is accompanied by xanthoma, it may be assumed that the cause of the jaundice is not malignant disease, inasmuch as this would have killed the patient before this change would have had sufficient time to develop.

Treatment.—The radical and the only satisfactory course is the removal or cure of the underlying condition of which jaundice is a result; for this an accurate diagnosis in each case is essential. The methods of treatment in the various conditions giving rise to jaundice are dealt with elsewhere, and will not be repeated here. The necessity for a diagnosis of the cause in order to make successful treatment possible is shewn by the cure of jaundice in the early stage of syphilis by mercury, or when due to the pressure of a gumma on the ducts by iodides; or surgically by the removal of calculi from the common bile-duct in intermittent hepatic fever (p. 759).

Jaundice often depends on catarrhal inflammation of the ducts, which may be removed by medical measures which increase the flow of bile and so flush the bile-ducts, *e.g.* draughts of water containing salts in solution, drinking the waters at Harrogate, Neuenahr, Carlsbad, Vichy, and the administration of urotropin and salicylates. In some cases medical measures fail to remove catarrhal inflammation of the ducts and surgical interference in the form of free drainage may be necessary.

Symptomatic or Palliative Treatment.—Constipation should be prevented by exercises, plenty of water, salines, such as phosphate and sulphate of sodium, sulphate of magnesium, or the natural Carlsbad or other purgative waters, taken on an empty stomach before breakfast. The salts may be made more palatable by the addition of a little infusion of quassia or cinchona. If necessary, a few grains of calomel or of blue pill may be taken the night before. Vigorous purgatives should be avoided, as intestinal catarrh may be thus set up, or, if present, increased. For gastric catarrh careful dieting, bicarbonate of sodium, and for vomiting bismuth, dilute hydrocyanic acid, and warm applications to the abdomen should be ordered. For flatulence minute doses ($\frac{1}{40}$ grain) of calomel or of liquor hydrargyri perchloridi, guaiacol, naphthalene tetrachloride, salicylate of bismuth, creosote, turpentine in capsules, or salol may be given.

Fresh ox or pig's bile contained in capsules or keratin-coated pills,

[1] Guillian et Richet. *Bull. et mem. Soc. méd. des hôp. de Paris*, 1910, 3. s., xxviii, 289. Guillian. *Paris méd.*, 1912, No. 27, p. 9.

so as to pass unaltered through the stomach, are sometimes given to replace the absent bile in the bowel, and may be taken three times a day before food.

For pruritus, which is often extremely troublesome and the cause of sleeplessness, several remedies may have to be tried before relief is obtained, and sometimes nothing but a hypodermic injection of morphine is successful. In the first place the local application of carbolic acid to the skin should be tried; a lotion of 1 in 40 may be dabbed on with a small sponge or applied on strips of lint, or a 2 per cent solution in olive oil may be employed in the same way. These applications should not be used if the skin is excoriated by scratching. Other applications are a 2 per cent solution of ichthyol, menthol in spirit (grs. viiss to the ounce), an ointment composed of equal parts of vaseline, lanoline, and boracic ointment, or the patient may take an alkaline or an acid bath, or warm douches. A bath containing nitrohydrochloric acid is given in a wooden bath, the patient remaining in it for about twenty minutes. Hypodermic injection of pilocarpine, $\frac{1}{6}$ to $\frac{1}{4}$ grain, may be employed with success. Thyroid extract has been found to give relief by Gilbert and Herscher,[1] and has been thought to act by diminishing the formation of bile acids. Nerve sedatives such as antipyrin, chloral, aspirin, and bromides give temporary relief, but their depressing effect renders the patient less able to bear subsequent itching. For itching of the skin and haemorrhages the administration of chloride or lactate of calcium in 15- or 20-grain doses may be tried three times a day for two or three days, but not longer at a stretch, as its effect in promoting coagulation of the blood is lost after a comparatively short time. Before an operation on a jaundiced patient it is well to give calcium lactate and magnesium lactate so as to diminish the risk of bleeding from the jaundiced tissues. Hypodermic injection of fresh blood serum has been employed as a prophylactic against haemorrhage (Leary,[2] Meyer[3]).

Milk is the most satisfactory food in the early stages and as long as jaundice is progressive, since it is easily digested, minimises intestinal putrefaction and fermentation, and acts as a diuretic. The patient's inclination should be consulted, and when appetite returns, rusks, bread, toast, jam, sago, tapioca, boiled rice, potatoes (preferably mashed), pounded fish, kedgeree, pounded chicken, chicken cream, and a little meat may be given. Fatty food, for which jaundiced patients often have a marked distaste, should be avoided. Alcoholic drinks should be forbidden in ordinary jaundice, but are useful in malignant disease.

Even in inoperable malignant disease, such as carcinoma of the head of the pancreas, surgical measures may give some relief by removing the jaundice. Cholecystenterostomy, or uniting the gall-bladder to the small intestine, allows the bile to enter the intestine and thus removes the jaundice, prevents the occurrence of biliary toxaemia or cholaemia, and

[1] Gilbert et Herscher. *Compt. rend. Soc. Biol.*, Paris, 1902, liv, 1087.
[2] Leary. *Boston Med. and Surg. Journ.*, 1908, clix, 73.
[3] Meyer. *Trans. Am. Surg. Assoc.*, 1911, xxix, 442.

greatly improves the patient's condition for a time. The operation must be performed early; if "black jaundice" has already developed, the patient is in a very unfavourable state for this procedure.

JAUNDICE IN THE NEWLY BORN

JAUNDICE occurring within a few days or weeks of birth has such special bearings that it requires separate consideration. The term icterus neonatorum has been specially employed for the simple jaundice so commonly seen within a few days of birth. Various forms of jaundice may attack newly born infants.

As many as nine varieties have been tabulated by Skormin; (i) Benign jaundice; (ii) septic, due to umbilical infection; (iii) infective jaundice; (iv) Winckel's disease; (v) catarrhal jaundice; (vi) toxic jaundice, due to drugs, such as carbolic acid, resorcin; (vii) jaundice following haemorrhages into the skin; (viii) jaundice of acute yellow atrophy; (ix) various forms of obstructive jaundice.

Some of the forms are extremely rare; thus, Skormin[1] could only refer to seven examples of acute yellow atrophy in infants. From a practical point of view jaundice in infants may be conveniently divided into two main groups: (i) Those which are mild and tend to recover; (ii) the severe forms in which the prognosis is grave.

THE MILD FORMS OF JAUNDICE IN THE NEWLY BORN are: (*a*) Idiopathic, simple, or physiological jaundice. (*b*) The mild infective or catarrhal.

(*a*) **Idiopathic, Simple, or Physiological Jaundice.**—*Etiology.*—It is commoner among the poor, and is known under the name of the "yellow gum." It is thought to be more frequent in premature and feeble infants with deficient resistance, and has been said to be commoner in males than in females (J. L. Steven), but this is doubtful. It has been suggested that if the cord is ligatured late, so that the infant obtains a maximum of placental blood, icterus, presumably depending on increased haemolysis, is more likely to result.

Bauzon,[2] however, from a consideration of 240 cases, concluded that, far from favouring the occurrence of jaundice, delayed ligation of the umbilical cord improved the resistance of the infant and thus tended to prevent icterus.

There is no proof that delayed birth or abnormal presentations, such as a breech, are important factors.

Jaundice so soon after birth has naturally been thought to depend on events special to birth and the first few days of independent existence.

[1] Skormin. *Jahrb. f. Kinderh.*, 1902, lvi, 200.
[2] Bauzon. *Méd. inf.*, Paris, 1894, i, 307.

Birch-Hirschfeld thought it might be due to vascular engorgement of the liver causing oedema of the portal spaces, and thus pressure on the bile-ducts. The post-mortem observations of Cohnheim did not support this view. Moreover, oedema of the portal spaces, though it may be associated with jaundice, for example, when there is a tumour pressing on the bile-ducts and lymphatic vessels, does not induce jaundice. Quincke[1] suggested that, owing to patency of the ductus venosus, bile absorbed from the intestine and on its way to the liver passed from the portal vein directly into the inferior vena cava and so into the general circulation.

It is tempting to associate the microbic invasion of the previously sterile intestine with the appearance of jaundice, especially as the bile is often very viscid. There is another factor which, when taken in conjunction with infection of the alimentary canal, may help to account for icterus neonatorum. In the newly born there is an increased number of red blood-corpuscles (polycythaemia) and a correspondingly increased haemolysis. This would normally lead to an increased production of bile, and if, from microbic activity, there was even slight inflammation of the ducts, diffusion of bile into the lymphatics and jaundice would readily result.

Morbid Anatomy.—When such a jaundiced child dies from accident or from other disease, there is widespread staining of the organs and tissues of the body with the exception of the liver, kidneys, and spleen. It is remarkable that the cerebrospinal fluid, parts of the brain, and cartilages which are not stained by bile-pigment in ordinary jaundice are distinctly coloured by the bile. The lenticular and other nuclei in the brain are bile-stained ("Kernicterus") while the cortex escapes. The liver cells contain a good deal of bile-pigment, but there are no other changes; the ducts are normal, and bile can be squeezed from the gall-bladder into the duodenum. The bile is sometimes peculiarly viscid (Still[2]). The pericardial fluid contains bile acids and bile-pigment, shewing that there is true jaundice. The kidneys, as is commonly the case in the newly born, shew masses ("infarcts") of uric acid in the collecting tubules.

Incidence.—It occurs in from 30 to 80 per cent of infants. It is said to be more frequent in lying-in hospitals than in private life. But Holt's[3] figures from the Sloane Maternity Hospital of 900 births with 300 cases of jaundice (intense in 88, mild in 212) give about the lowest incidence. Steven,[4] by adding up various statistics, found that it occurred 1212 times in 2086 children, or in 58·1 per cent. In 248 newly born infants examined by Porak[5] it occurred in 80 per cent.

Clinical Characters.—It comes on within the first four days of life, most commonly on the second or third day, and lasts from one to two

[1] Quincke. *Arch. f. exper. Path. u. Pharmak.*, 1885, xix, 34.
[2] Still, G. F. *Clin. Journ.*, Lond., 1901, xvii, 323.
[3] Holt, E. Quoted by Osler, *Practice of Medicine*, p. 538, 5th ed., 1905.
[4] Steven, J. L. *Glasgow Med. Journ.*, 1897, xlvii, 4.
[5] Porak. *Rev. mens. de méd. et chir.*, Par., 1878, ii, 342.

weeks. In some instances it persists longer, and after arousing a suspicion that there is some more serious factor at work, eventually passes away. After its appearance it increases both in extent and in intensity for about a couple of days and then gradually diminishes. There are no symptoms whatever—the temperature, pulse, appetite, and faeces are normal. The urine is free from bile save in exceptionally marked cases, and there is no albuminuria. The jaundice begins on the face, chest, back, and extends to the abdomen, limbs, and lastly to the hands and feet. The jaundice shews up more prominently because of the general cutaneous engorgement, and is perhaps best seen on the back; it can be distinguished from the normal redness of the infant by pressing the blood out of the cutaneous vessels when the skin remains jaundiced. The gums may be yellow. The sclerotics are not always yellow. A division has been made into the slightest cases, in which the whites of the eyes are unaffected, and those in which the conjunctivae are icteric.

Porak described three classes—(*a*) The staining is slight and passes away in four days, and involves the face, back, and chest, but the conjunctivae are not affected. (*b*) The jaundice extends to the abdomen, arms, and thighs, while the conjunctivae may or may not be affected. (*c*) There is universal jaundice and the conjunctivae are always involved.

It is difficult to explain satisfactorily why the sclerotics are affected later and in a less degree than the skin; exactly the reverse of what occurs in ordinary jaundice. It is possible that it may depend upon the hyperaemic state of the skin and the correspondingly large amount of blood, containing bile, that passes through the vessels of the surface of the body.

Diagnosis.—It is distinguished from the normal reddish-brown tint of the young infant by pressing on the skin and finding that the yellow discoloration remains after the vessels have been obliterated. Its short duration prevents any confusion with congenital obliteration of the ducts; in the rare instances of more prolonged simple jaundice there is an absence of the enlarged and firm liver and spleen seen in the former condition. It must be distinguished from the grave forms of jaundice, such as infection of the umbilical vein, syphilitic disease of the liver, and Winckel's disease, by the healthy condition of the patient, the absence of fever, and, indeed, of every sign or symptom except jaundice. Grave familial jaundice, which begins in the same manner, may be suspected from the history that other infants of the family have died of it.

Prognosis.—In this condition, for it cannot be called a disease, the outlook is perfectly cloudless. But in cases of jaundice in the newly born there is always the question whether the jaundice is "physiological" or whether it is the first sign of some grave organic or infective change. The prognosis of jaundice in the first few days is, therefore, very difficult in the absence of any definite diagnosis. No special form of treatment is required (*vide* also Grave Familial Jaundice, p. 572).

(*b*) **Catarrhal or Mild Infectious Jaundice.**—In the first few days of

life the alimentary canal normally becomes invaded by micro-organisms, and a mild or virulent infection may occur. The mild forms of infectious jaundice are much the same as the catarrhal jaundice of adults, and clinically no trustworthy distinction can be drawn between mild infectious and catarrhal jaundice. Many writers, however, consider that catarrhal jaundice is almost unknown in infants. Skormin [1] refers to but three recorded cases. The disease may occur in epidemics (Lesage and Demelin [2]) or sporadically. It may occur in the first few days of life and in breast-fed infants. It is diagnosed by the presence of gastric symptoms, loss of appetite, vomiting, diarrhoea, slight fever, drowsiness, and jaundice—which is universal. The urine contains bile pigment, but the stools are not necessarily acholic; according to Lesage the faeces are alkaline or neutral instead of acid. These authors also lay stress on the occurrence of cyanosis. Although new-born infants may be very ill with catarrhal jaundice they usually recover (J. Thomson [3]).

Treatment.—The infants should be kept warm, but the room should be well ventilated. Water should be freely given, and fractional doses of calomel or grey powder should be given five or six times daily.

THE SEVERE FORMS OF JAUNDICE IN THE NEW-BORN may be divided into—(1) Those due to definite obstruction or organic change. (2) Virulent infections, either local or general. (3) Grave familial jaundice.

(1) **Jaundice due to Definite Obstruction or Organic Change.**—Congenital obliteration of the ducts (p. 649) and jaundice occurring in hereditary syphilitic disease of the liver (*vide* p. 376) and bile-duct (*vide* p. 658) are dealt with elsewhere.

Gall-stones are very rare in the newly born. Still [4] collected ten cases either in stillborn infants or infants dying within a few weeks of birth. Seven of these were jaundiced. Thomson [5] suggests that the inflammation of the biliary tract which induces cholelithiasis in infants is probably of the same nature as that responsible for congenital obliteration of the ducts (*vide* p. 650).

(2) **Severe Forms of Infective Jaundice.**—*Umbilical Infection.*—A very fatal form of jaundice is associated with infection of the navel in the newly born. There is suppurative phlebitis of the umbilical vein. This form of pyaemia formerly gave rise to a very high mortality among infants born in lying-in hospitals, and has been prevented by cleanliness and antisepsis. According to Cantlie,[6] it is very common in Hong-Kong. The infection may be conveyed from the mother and is streptococcic. At the necropsy there is suppurative phlebitis of the umbilical vein, and the liver is pale, bile-stained, of normal size, and shews areas of small-celled infiltration in the portal spaces. There may be other pyaemic

[1] Skormin. *Jahrb. f. Kinderh.*, 1902, lvi, 200.
[2] Lesage et Demelin. *Rev. de méd.*, Par., 1898, xviii, 14.
[3] Thomson, J. *System of Medicine* (Allbutt and Rolleston), 1908, iv, Part i, 98.
[4] Still, G. F. *Trans. Path. Soc.*, Lond., 1899, l, 151.
[5] Thomson, J. *Edin. Hosp. Rep.*, 1898, v, 1.
[6] Cantlie. *Encyclopaedia Medica*, 1901, vii, 41.

manifestations, such as streptococcic peritonitis, pleurisy, meningitis. There may be septicaemia.

There is jaundice, accompanied by fever and evidence of suppuration at the umbilicus, which is red and swollen. Vomiting and diarrhoea are present; the respiration and pulse are rapid. The child is first restless, and then becomes cyanosed and comatose. Death may be due to umbilical or gastro-intestinal haemorrhage.

Severe Forms of Jaundice due to General Infections. — Septicaemia may give rise to toxaemic jaundice in the newly born as well as haemorrhages and haematuria. It may be sporadic, as in pyaemia secondary to suppurative arthritis or to infected epiphyseal disease in congenital syphilis.

Epidemic Forms of Severe Infective Jaundice.—Epidemics of jaundice in infants accompanied by diarrhoea, haematuria, and attended with great mortality were described by Pollak,[1] Laroyenne,[2] Parrot,[3] and Winckel.[4] Winckel described an epidemic, which proved fatal to 23 out of the 24 infants attacked, under the name of pernicious icteric cyanosis. This disease in the newly born has been called Winckel's disease. It is regarded by Lesage and Demelin as a very severe form of infection of intestinal origin, corresponding to the mild form of infectious or catarrhal jaundice. Thomson[5] also regards this form as of intestinal origin. It is probably a severe form of septicaemia, and closely resembles Buhl's disease, in which there are jaundice, gastro-intestinal haemorrhages, with infarcts and acute fatty degeneration of the organs of the newly born infants.

The clinical features are mainly those of a severe septicaemia occurring in epidemics among newly born infants and accompanied by haematuria and jaundice. The skin has a bronzed appearance, probably due to a combination of jaundice and the cyanotic condition of the skin. An important feature is haematuria: Winckel, however, described haemoglobinuria. The condition is extremely fatal, and treatment is practically useless. The disease differs from umbilical phlebitis in the absence of any signs of local inflammation about the navel, and in the slighter degree of fever. Treatment should be directed to removing the contents of the bowels by purgatives and enemas. Saline solution should be given subcutaneously, and diuresis favoured by giving water by the mouth. Minute doses of calomel should be given every two or three hours until eight or ten doses have been given, so as to disinfect, as far as possible, the intestinal tract.

(3) **Grave Familial Jaundice.**—In some recorded examples successive infants become jaundiced and die. Pfannenstiel[6] considers that the condition is not Winckel's or Buhl's disease, and regards it as an intense

[1] Pollak. *Wien. med. Presse*, 1871, xii, 458.
[2] Laroyenne. *Congrès pour l'avancement des sc.*, Lyon, 1873.
[3] Parrot. *Arch. physiol. norm. et path.*, 1873, v, 512.
[4] Winckel. *Deutsche med. Wchnschr.*, 1879, v, 303, 319.
[5] Thomson. *System of Medicine* (Allbutt and Rolleston), 1908, iv, Part i, 102.
[6] Pfannenstiel. *München. med. Wchnschr.*, 1908, lv, 2233.

form of physiological jaundice of the newly born. Necropsy shews exudations into the serous cavities, enlargement of the liver and spleen, and punctate haemorrhages into the internal organs. All the tissues of the body are bile-stained; and although there are no nervous symptoms, there is selective staining of the lenticular and other nuclei by bile ("Kernicterus"), while the cerebral cortex is unaffected. Busfield [1] noted 9, and Auden [2] 8, in one family. The parents are usually healthy. A woman under my care became jaundiced during each pregnancy and had had three children, who died of jaundice at ages of two weeks, three months, and five months.[3] A similar recurrence of jaundice in the mother and in the infants has been recorded by Nason.[4] In Arkwright's [5] series of 14 cases in a family the mother had had jaundice when four years old. It may be very difficult to separate cases of this kind from congenital obliteration of the ducts in the absence of a necropsy. The treatment is the same as in severe infective jaundice of the new-born; but it may be worth while to treat the mother during pregnancy with urotropin and salicylate of sodium.

Hereditary Jaundice.—Jaundice is hereditary in certain conditions, such as simple family cholaemia (*vide* p. 40), chronic splenomegalic haemolytic jaundice (*vide* p. 537), grave familial jaundice, occasionally in hypertrophic biliary cirrhosis (Boinet,[6] Boix [7]), and in some allied anomalous cases (Lortat-Jacob and Sabaréanu,[8] Barlow and Shaw [9]). In addition, some patients have life-long jaundice without any splenic enlargement; the condition resembles the congenital form of chronic splenomegalic haemolytic jaundice, especially in the remarkable freedom from symptoms (Glaister,[10] Cocking,[11] A. Pick [12]). It has been suggested that such cases may be due to some abnormalities in the bile ducts, or intra-uterine obliterative cholangitis in the liver (Weber [13]), or that there is a congenital communication between the intrahepatic bile-ducts and the lymphatics (Pick).

ICTERUS GRAVIS

ICTERUS GRAVIS, or malignant jaundice, is somewhat loosely used for cases of severe toxaemic jaundice which tend to end fatally and shew

[1] Busfield. *Brit. Med. Journ.*, 1906, i, 20.
[2] Auden. *St. Barth. Hosp. Rep.*, 1905, xli, 139.
[3] Rolleston. *Brit. Med. Journ.*, 1910, i, 864.
[4] Nason. *Ibid.*, 1910, i, 989.
[5] Arkwright. *Edin. Med. Journ.*, 1902, N.S., xii, 156.
[6] Boinet. *Arch. gén. de méd.*, Paris, 1898, clxxxi, 385.
[7] Boix. *Compt. rend. Soc. Biol.*, Paris, 1898, l, 297.
[8] Lortat-Jacob et Sabaréanu. *Rev. de méd.*, Paris, 1904, xxiv, 810.
[9] Barlow and Shaw. *Trans. Clin. Soc.*, Lond., 1902, xxxv, 155.
[10] Glaister. *Lancet*, Lond., 1879, i, 295.
[11] Cocking. *Quart. Med. Journ.*, Sheffield, 1903, xi, 104.
[12] Pick, A. *Wien. klin. Wchnschr.*, 1903, xvi, 493.
[13] Weber. *Edin. Med. Journ.*, 1903, xiv, 111.

extensive degeneration of the liver cells. It thus includes a number of different conditions, such as the most severe cases of febrile jaundice or Weil's disease, acute yellow atrophy of the liver, phosphorus and other forms of mineral poisoning, and other cases in which an acute toxaemic or infective condition of the body falls on the liver and gives rise to widespread acute degenerative and necrotic changes in the liver cells; for example, in yellow fever and in streptococcic and staphylococcic haemic infections. The term icterus gravis may also appropriately be applied to cases in which acute degenerative changes are superimposed on some pre-existing disease of the liver, such as cirrhosis or nutmeg liver. Icterus gravis should, therefore, be regarded not as a specific disease, but as a group of symptoms, due to the rapid development of hepatic insufficiency, eventually becoming absolute, which may be due to many different causes.

Icterus gravis may be divided into—(*a*) Cases in which the liver was previously healthy, in phosphorus poisoning, acute yellow atrophy, and yellow fever. (*b*) Cases in which it supervenes as a terminal lesion on pre-existing hepatic disease—*e.g.* in cirrhosis or chronic venous engorgement. Boix's[1] classification, though based on different grounds, is much the same:

Specific and primary icterus gravis:	In phosphorus poisoning. In yellow fever. Essential (acute yellow atrophy).
Non-specific and always secondary:	In staphylococcic and streptococcic infections. In infection with the colon bacillus.

Acute yellow atrophy is a special form of icterus gravis. The terms icterus gravis and acute yellow atrophy are not absolutely synonymous, for all cases of icterus gravis do not shew the naked-eye appearance of acute yellow atrophy, though the change—acute degeneration in the liver cells—is essentially the same in both. Under the microscope the appearances are so closely allied that from a pathological point of view they may be said to pass into each other. Cases of acute yellow atrophy are often described as icterus gravis, and, conversely, cases of icterus gravis are sometimes reported under the heading of acute yellow atrophy.

Since some of the various conditions, such as acute yellow atrophy, phosphorus poisoning, and Weil's disease, which are or may be included under the generic term icterus gravis, will be separately described, the clinical features of icterus gravis will not require any further description than that found under the heading of acute yellow atrophy. Generally speaking, the liver is somewhat enlarged in icterus gravis and the degenerative changes are not so uniform or so markedly necrotic as in acute yellow atrophy. The morbid changes described under the heading of Acute Hepatitis may be present in icterus gravis, or in some instances very

[1] Boix. *Manuel de médecine*, edited by Debove and Achard, vi, 342.

extensive fatty change (*vide* p. 428). In icterus gravis due to staphylococcic and streptococcic infection the temperature is raised, while in other instances the temperature is, as in phosphorus poisoning, depressed.

Multiple Non-Inflammatory Necrosis of the Liver.—Probably this is the best place to refer to a condition described by Oertel,[1] who could not assign it to any known disease of the liver; subsequently[2] he recorded a case of chronic venous engorgement terminating with this change. Under the title of "*Multiple non-inflammatory necrosis of the liver with jaundice* (Hepar necroticum cum ictero)" he described a peculiar cellular destruction of the hepatic cells, unaccompanied by inflammatory reaction or coagulation-necrosis. The process was most marked in the centre of the lobules, the cells shewing fatty change and infiltration with bile. The liver is not diminished in size to any extent, but appears tough and bile-stained. The process was regarded as due to cytolysis caused by autolytic ferments. Clinically the condition was one of intoxication with stupor, jaundice, delirium, and coma. Curschmann[3] had previously described 2 cases as a "peculiar form of necrosing hepatitis," and Parkes Weber[4] employed the title "disseminated lobular necrosis of the liver with Jaundice." Churchman[5] recorded febrile cases with jaundice resembling intermittent hepatic fever.

ACUTE YELLOW ATROPHY

Synonym: Acute Atrophy of the Liver.

Definition.—An acute, probably autolytic, necrosis of the liver cells with diminution in the size of the liver, accompanied by jaundice, fever, nervous symptoms, and usually a fatal termination.

The history of acute yellow atrophy has been exhaustively investigated by J. Wickham Legg.[6] The earliest case that he has unearthed is one by Baillou (Ballonius), who died in 1616. Bright,[7] in 1836, described the condition as due to acute inflammation, and gave a good coloured drawing of the liver, and Rokitansky gave it the name "acute yellow atrophy" in 1842.

Incidence and Etiology.—That the disease is rare is shewn by the fact that among 21,682 medical cases at the Johns Hopkins Hospital, Baltimore, there were only 3 examples (Thayer[8]). Some observers, however,

[1] Oertel, H. *Journ. Exper. Med.*, N.Y., 1906, viii, 103.
[2] Idem. *Arch. Int. Med.*, Chicago, 1910, vi, 293.
[3] Curschmann. *Deutsche Arch. f. klin. Med.*, Leipz., 1899, lxiv, 564.
[4] Weber, F. P. *Proc. Roy. Soc. Med.*, 1909, ii (Path. Sect.), 109.
[5] Churchman. *Ann. Surg.*, 1911, liii, 783.
[6] Wickham Legg. *Bile, Jaundice, and Bilious Diseases*, p. 416, 1880.
[7] Bright, R. *Guy's Hosp. Rep.*, 1836, i, 613.
[8] Thayer, W. S. *Bull. Johns Hopkins Hosp.*, Balt., 1908, xix, 50 and private letter.

have met with a succession of cases in quite a short time. Reiss saw 5 cases in three months and Arnold 4 in a similar period.

In twenty-seven years I have seen in the post-mortem room or examined the livers of 11 cases.

Up to 1895 W. Hunter [1] was able to refer to only 250 published cases, and in 1903 Best [2] collected 450 cases. In twenty-five years 7 cases occurred at St. Bartholomew's Hospital, which, according to Brunton and Tunnicliffe,[3] is 1 in every 500,000 applications for treatment at that charity. In twenty-seven years there were 11 cases brought to necropsy at Guy's Hospital (Hilton Fagge [4]).

Age.—It is commonest between the ages of twenty and thirty. According to Hunter's figures, half the cases occur in this decade, and four-fifths between the ages of ten and forty. A certain proportion—I have collected 42 such cases—occur within the first ten years of life; while in rare instances it has been seen within the first year or even shortly after birth.

Skormin [5] refers to 7 published instances of acute yellow atrophy in newly born infants.

Subacute atrophy (*vide* p. 583) is relatively more frequent in children, probably from their greater power of repair. In connexion with the occurrence of cases in very early life the resemblance between some cases of icterus gravis and rather rapid intercellular cirrhosis of hereditary syphilis must be borne in mind.

The youngest case in which I have had the opportunity of cutting sections of the liver was in a child aged two years; the liver weighed 11 ounces, and shewed the naked-eye and microscopic appearances of acute yellow atrophy. I am indebted to the late Dr. Schorstein and Dr. O. Grünbaum for the liver of this case.

Sex.—Among adults females are more often attacked than males, the proportion between the two being nearly 2 to 1. In children the incidence appears to be reversed; in 34 cases collected by Phillips [6] there were 25 males and 9 females. The greater incidence of the disease in women seems to depend on a special association between pregnancy and this disease. The influence of *pregnancy* is borne out by the large proportion of the cases in connexion with this event. The liver appears to be peculiarly susceptible to morbid changes during pregnancy, and there is reason to believe that necrotic changes in the peripheral zone of the lobules of the liver play a very important part in the production of puer-

[1] Hunter, W. Allbutt's *System of Medicine*, 1897, iv, 102.
[2] Best. *Thesis*, Chicago, 1903. Quoted by Kelly, *System of Medicine* (Osler and McCrae), 1908, v, 718.
[3] Brunton and Tunnicliffe. *St. Barth. Hosp. Rep.*, 1896, xxxii, 436.
[4] *Principles and Practice of Medicine*, edited by Pye-Smith, vol. ii, p. 544, 4th ed., 1902.
[5] Skormin. *Jahrb. f. Kinderh.*, 1902, lvi, 200.
[6] Phillips. *Amer. Journ. Med. Sc.*, Phila., 1912, cxliii, 177.

peral eclampsia. Williams,[1] who collected 12 cases of the pernicious vomiting of pregnancy shewing acute yellow atrophy, insists on a distinction between eclampsia, in which necrosis occurs in the peripheral zone, and acute yellow atrophy, in which necrosis begins in the intermediate zone of the lobule.[2] Acute yellow atrophy usually occurs in the second half and after the seventh month of pregnancy.

Mental disturbance, shock, or fright has preceded the onset of the disease in a certain number of cases. The mental worry in persons with syphilis or in women that are pregnant, especially if unmarried, may tend further to depress the resistance of the body and to dispose to the disease.

In recording 6 fatal cases of acute yellow atrophy of the liver in Australia Hardie[3] attached importance to the anxiety with which women look forward to parturition in hot climates.

Syphilis.—The secondary stage of syphilis may be accompanied by jaundice, which is usually harmless and yields to specific treatment (*vide* p. 349). In rare instances acute yellow atrophy supervenes. This is more often seen in women than in men. The effect of the syphilitic infection would appear to fall on the liver acutely, just as it sometimes does on the spinal cord, giving rise to acute myelitis. As examination of the liver in 5 cases failed to shew the *Treponema pallidum*, it is probable that the acute atrophy is due to poisons manufactured elsewhere by the *Treponema pallidum* and carried to the liver, and so is analogous to delayed chloroform poisoning (Fischer[4]). M'Donald[5] suggests that syphilis merely reduces the resistance of the organ and thus enables a poison formed in the intestine to set up acute yellow atrophy. Other hypotheses have been put forward (*vide* Weber[6]), such as its dependence on the autolytic action of mercury, which seems unlikely in view of its occurrence in cases in which that drug has not been given.

In 72 cases of acute yellow atrophy syphilis was noted as a causal factor in 7 (Lebert[7]). In 1909 Weber estimated that there were 53 cases of acute yellow atrophy in secondary syphilis on record; out of 50 collected cases there were only 10 males (Fischer). In some cases the jaundice has run a long course, and although the morbid appearances are like those of acute yellow atrophy, it is probable that for a considerable time the jaundice is due to intercellular cirrhosis and that a terminal and acute necrosis of the liver cells supervenes. This would place these cases in the category of icterus gravis.

Hilton Fagge[8] drew attention to the resemblance between the appearances

[1] Williams, J. Whitridge. *Johns Hopkins Hosp. Bull.*, Balt., 1906, xvii, 71.
[2] Compare Opie. *Trans. Assoc. Am. Phys.*, 1904, xix, 132.
[3] Hardie, D. *Austral. Med. Gaz.*, Sydney, 1889–90, ix, 179.
[4] Fischer, W. *Berlin. klin. Wchnschr.*, 1908, xlv, 905.
[5] M'Donald. *Edin. Med. Journ.*, 1908, N.S., i, 83.
[6] Weber, F. P. *Proc. Roy. Soc. Med.*, Lond., 1909, ii (Path. Sect.), 113.
[7] Lebert. *Virchows Arch.*, 1854, vii, 383.
[8] Hilton Fagge. *Trans. Path. Soc.*, Lond., 1867, xviii, 136.

of intercellular cirrhosis and those in a case of acute atrophy supervening on the secondary syphilis.

As already mentioned, the mental anxiety caused by syphilis has been thought to play a part in the production of acute atrophy.

Talamon [1] described a case in which a severe fright in a girl aged seventeen, who had secondary roseola, enlarged glands, and condylomas at the time, was followed within eighteen hours by "emotional jaundice"; this lasted three weeks, and symptoms of acute yellow atrophy, haemorrhages, delirium, and convulsions carried her off on the twenty-ninth day. The liver shewed acute parenchymatous and interstitial inflammation. In this case the emotional jaundice seems to have rendered the liver more susceptible to the syphilitic toxin.

The following case, for which I am indebted to Dr. A. H. Wilson, illustrates some of the features of acute yellow atrophy due to syphilis. A girl aged seventeen, with a sore on the right labium and a roseolous rash, became jaundiced six weeks before death. Three days later she began to vomit and continued to do so until her death; at no time was there blood in the vomit. Three weeks before death jaundice increased, her mental condition was affected, delirium supervened, and the urine and faeces were passed involuntarily. She became extremely hungry and thirsty. She was admitted to the South Devon and East Cornwall Hospital in a state of collapse twenty-four hours before her death. There were bile-pigment, leucine, and tyrosine in the urine. She died comatose. The liver, which I examined microscopically, shewed haemorrhages, intercellular cirrhosis, and acute necrosis of the cells.

Preceding Infective Disease.—The disease has been noticed to supervene very shortly after some infectious disease, such as influenza (Miller and Hayes [2]), enteric fever (George [3]).

Alcoholic excess in a few instances has apparently stood in a causal relation to acute yellow atrophy, since the disease has been noted to come on after recent and undoubted excessive indulgence.

Thierfelder,[4] refers to 6 such cases among his 143 cases of acute atrophy, and cases have been described by Moxon,[5] Cayley,[6] Carrington,[7] Musser.[8]

Acute yellow atrophy may occur in chronic drunkards, and acute atrophy has been described as supervening on existing cirrhosis. Thierfelder quotes 8 cases of this kind. It must, however, be borne in mind that cases of protracted acute atrophy may shew some recent fibrosis. Inasmuch as alcohol is a protoplasmic poison, it is not improbable that the resistance of the liver being diminished by alcoholic excess, other

[1] Talamon. *Méd. mod.*, Paris, 1897, viii, 97.
[2] Miller and Hayes. *Journ. Path. and Bacteriol.*, Cambridge, 1909, xiii, 53.
[3] George. *Inaug. Diss.*, Freiburg, 1899. Quoted by Miller and Hayes.
[4] Thierfelder. v. Ziemssen's *Cyclopaedia of the Practice of Medicine*, 1880, ix, 245.
[5] Moxon. *Trans. Path. Soc.*, Lond., 1872, xxiii, 138.
[6] Cayley. *Ibid.*, 1883, xxxiv, 127.
[7] Carrington. *Ibid.*, 1885, xxxvi, 221.
[8] Musser. *Am. Journ. Med. Sc.*, 1884, lxxxviii, 166.

causes making for acute yellow atrophy are thus enabled to become effective.

Chloroform Narcosis.—Wells [1] recognises two forms of delayed chloroform poisoning—(*a*) with fatty change in the periphery of the lobules, acid intoxication, and no jaundice (*vide* p. 428); (*b*) resembling acute yellow atrophy. The latter is so rare that additional factors, such as infection and diminished resistance of the liver, must be necessary to explain its occurrence. Experimentally a change closely resembling acute yellow atrophy in man has been obtained by the combined action of chloroform and bacteria (*B. coli, Streptococcus pyogenes*) on the liver (Opie [2]).

Max Ballin [3] collected 9 fatal cases of acute yellow atrophy after operations. It has also been reported after narcosis by anaesthol, which consists of chloroform, ethyl chloride, and ether (Torek [4]).

The Influence of Pre-existing Hepatic Disease.—The lesions of acute yellow atrophy may supervene in the course of diseases of the liver, such as cirrhosis, catarrhal jaundice, chronic venous engorgement, or gall-stone obstruction. The onset is, no doubt, favoured by the morbid condition of the organ. In these cases it is more convenient to describe the condition as icterus gravis rather than as acute yellow atrophy. Impaired vitality and resistance on the part of the liver must render it more susceptible to acute infectious or toxic influences, and so to acute atrophy. This very probably accounts for the influence of pregnancy in disposing to acute yellow atrophy. Probably metabolic disturbances may render the liver so susceptible that streptococci are enabled to induce acute atrophy (Opie). The occurrence of such a rare disease in two sisters (Graves [5]), and in a brother and sister (Griffin [6]), suggests that congenital want of resistance may be a factor of importance.

Relation to Phosphorus Poisoning.—Inasmuch as there is a marked resemblance between the clinical features of acute yellow atrophy and phosphorus poisoning, and since the nature of the change in the liver cells is essentially the same, namely, one of acute necrosis with autolysis, it has been thought that all cases of acute yellow atrophy are due to phosphorus poisoning. In support of this it might be urged that examples of what were for a time considered undoubted instances of acute yellow atrophy have on further enquiry turned out to be due to phosphorus poisoning. Poore,[7] who quoted cases of this kind, unhesitatingly believed that clinically and pathologically the two conditions are indistinguishable.

Generally speaking, however, the differences between the two con-

[1] Wells, H. G. *Arch. Int. Med.*, Chicago, 1908, i, 594.
[2] Opie. *Journ. Exper. Med.* N.Y., 1910, xii, 385.
[3] Max Ballin. *Ann. Surg.*, 1903, xxxvii, 362.
[4] Torek. *Ibid.*, 1910, lii, 489.
[5] Graves. *Clinical Medicine*, p. 459, 1843.
[6] Griffin. *London Med. Gaz.*, 1834, xiii, 801.
[7] Poore, G. V. *Nervous Affections of the Hand and Other Clinical Studies*, p. 166, 1897.

ditions are sufficiently definite to separate them, and we are certainly not justified in assuming that all cases of acute yellow atrophy are due to phosphorus poisoning. These differences are—(1) In acute yellow atrophy the diminution in size is practically constant, whereas in phosphorus poisoning enlargement is the rule. (2) In acute yellow atrophy the changes in the liver cells lead to rapid disintegration with but slight increase in the amount of fat; while in phosphorus poisoning there is very extensive fatty metamorphosis of the liver cells, the amount of fat in the organ reaching 30 per cent as against 5 per cent in acute yellow atrophy.

According to Schmaus,[1] however, these differences are merely a matter of time, and as death occurs more rapidly in phosphorus poisoning, there is not time for the absorption and removal of fatty and degenerative products. When life is prolonged, the condition resembles that of acute yellow atrophy.

It may be safely stated that they are closely allied forms of icterus gravis, but at present, for purposes of clinical practice, it is convenient to regard them as distinct.

Morbid Anatomy.—An account will first be given of the changes in the ordinary acute cases, and then the changes in the prolonged cases of subacute atrophy will be described. The liver is diminished in *size*; in fact, cases otherwise resembling acute atrophy, in which the organ is large, belong to the allied condition of icterus gravis, for diminution in size is an essential part of acute yellow atrophy. It may weigh half or a third of its normal weight. Twenty-eight ounces is not uncommonly found instead of the normal (53 ounces in males, 45 ounces in females). Reichmann[2] recorded a weight of 21 oz. (593 grams) in a boy aged seventeen years. The atrophied condition is usually universal, but the left lobe is often in a more advanced state than the remainder, and the change is often thought to begin there.

The surface is smooth, and from atrophy of the liver the capsule is wrinkled and loose, so that it can be picked up by the fingers, like the walls of a half-filled bladder. If a stream of water is turned on to the organ, the capsule is thrown into folds and wrinkles. It can be peeled off quite easily in many cases. Externally the organ has a greenish-yellow colour, often relieved by red splashes. There may be small haemorrhages under the capsule. The liver is flabby and limp, and collapses and bends under its own weight; thus it readily doubles over on itself and is without the rigidity of a normal liver. If kept for some time, the surface of the liver may become covered with a white efflorescence which is composed of crystals of leucine and tyrosine.

On section of the organ the surface is bright yellow usually with reddish-brown areas. As a rule, there is more of the yellowish change, but in some rare examples of what have been called acute red atrophy,

[1] Schmaus. *A Textbook of Pathology and Pathological Anatomy*, p. 396. American translation, 1903.

[2] Reichmann. *München. med. Wchnschr.*, 1908, lv, 959.

diffuse red atrophy greatly predominates or is universal. The yellow areas are softened and swollen, and the red areas firmer and cut like collapsed lung. The yellow colour is due to bile and not to fat. In the red areas the change is older than in the yellow areas. The longer, therefore, the patient lives, the greater will be the extent of the red change found after death. The only exception to this general statement is that in subacute atrophy, in which compensatory hyperplasia has taken place, there are nodular masses composed of proliferating liver cells which may be yellow, green, or white, and contrast with the surrounding red atrophy. In the areas of red atrophy absorption of the necrotic cells and of fat has taken place, and the only tissue left is the fibrous matrix and the capillaries which account for the red colour. Red atrophy is thus a further stage of the yellow atrophy and not an independent change. The areas of red atrophy are sunken and depressed below the level of the yellow areas. It is often more marked in the left than in the right lobe.

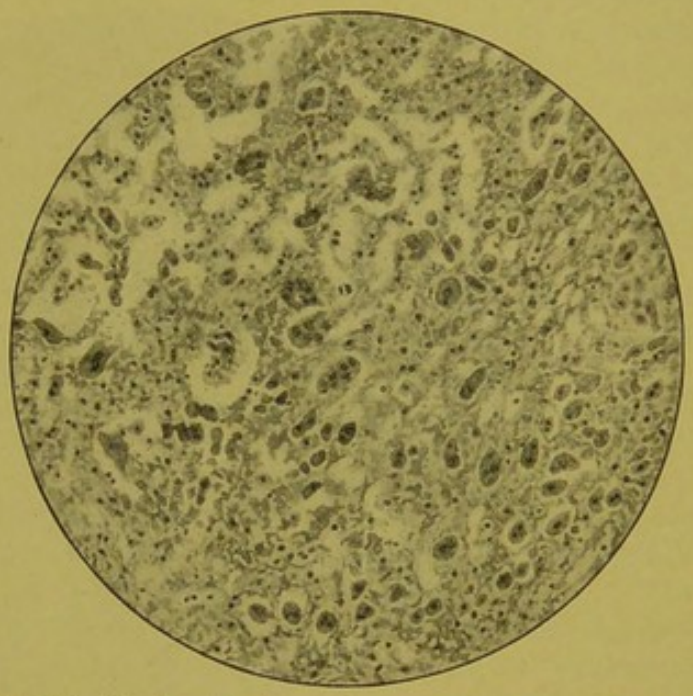


FIG. 79.—Drawing of microscopic section of the liver in acute yellow atrophy. Many of the cells are destroyed, the nuclei of some only remaining in the debris. There are, in addition, groups of liver cells and some with two or three nuclei—evidence of regeneration. × 140.

The outlines of the lobules are lost in the red areas, and with difficulty, if at all, discernible in the yellow areas; if visible, they are much smaller than in health. The gall-bladder contains bile, often thick from mucus, but the larger bile-ducts often contain mucus only. Budd [1] described a case in which the bile was markedly acid.

Analyses of the liver by A. E. Taylor [2] and Wells [3] shew that the amount of fat is not increased, that the amount of water is considerably increased, and that amino-acids due to autolysis are present, viz. histidine, lysine, tyrosine, leucine, glycocoll, alanine, proline, glutaminic and aspartic acids.

A scraping of the fresh section shews under the microscope degenerated liver cells, and crystals of leucine, tyrosine, and xanthine. In

[1] Budd. *Diseases of the Liver*, p. 264, 1857.
[2] Taylor. *Journ. Med. Research*, Boston, 1902, viii, 424.
[3] Wells, H. G. *Journ. Exper. Med.*, N.Y., 1907, ix, 627.

the alcoholic extract of the liver of acute yellow atrophy that had been kept for two years Delépine[1] found Charcot-Leyden crystals. Crystals of leucine and tyrosine may be seen in fresh sections, but for satisfactory examination of the histological condition of the liver properly hardened sections are necessary. Little reliable information can be obtained from fresh sections made by the freezing method, for fresh sections exaggerate existing disorganisation of the liver.

Histologically, the appearances vary greatly in the areas attacked by the yellow and by the red atrophic change respectively, and even in

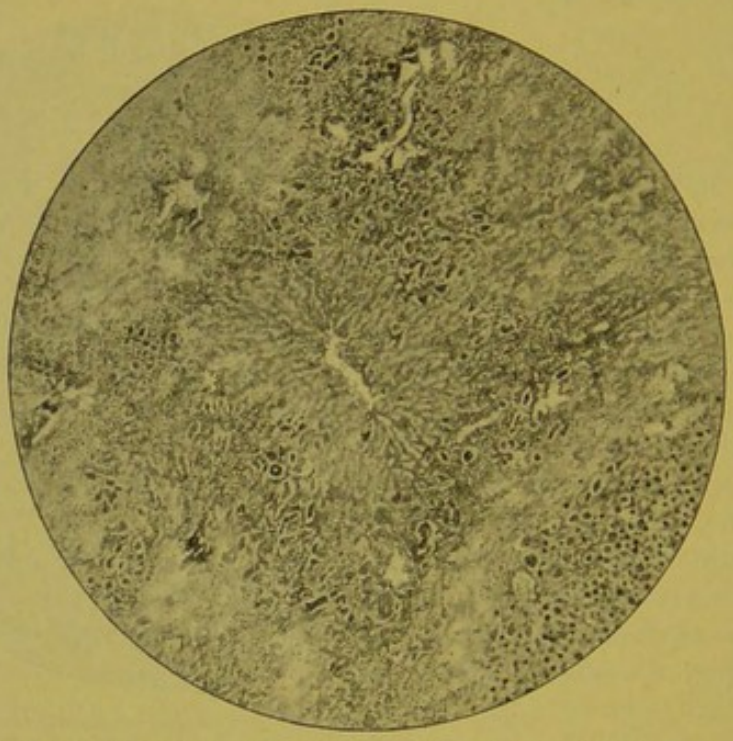


FIG. 80.—Microscopic appearances in acute atrophy of the liver. The liver cells are extensively necrosed. Around the periphery of the lobules there are small-celled infiltration and groups of liver cells. × 30.

different fields of the same microscopic section. In the early stages the liver cells are swollen and may shew some fatty change, but this is not a prominent or essential change. They soon become granular, bile-stained, and shew fragmentary degeneration of the nuclei which stain badly. Haemorrhages occur between the degenerated liver cells, and as the cells begin to undergo a further stage of necrosis, they cease to stain. Necrosis begins in the intermediate zone of the lobules, and extends towards the intralobular vein. The small bile-ducts are in a condition of cholangitis; there is proliferation of the epithelial cells, which are discharged into the lumen of the duct and by obstruction cause jaundice. Later, necrosis of the cells lining the small ducts occurs. Bile-duct-like structures are seen, especially at the margins of the lobules. In some sections the process of regeneration can be seen to be commencing in the liver cells, which are

[1] Delépine, S. *Trans. Path. Soc.*, Lond., 1891, xlii, 458.

collected into solid columns, so as to imitate a primitive tubular liver. These cellular strands are separated from each other by fibrillar tissue, capillaries, or the debris of the degenerated lobule. The liver cells may be much larger than natural, contain several nuclei, and may give the impression of being made up of several liver cells which have run together (*vide* Fig. 79).

In the more advanced stages—that is, in the areas of red atrophy—the cells of the lobules have completely disappeared as the result of very acute necrotic changes, and nothing can be seen except the skeleton of the lobules, formed of the fibrillar vascular connective tissue, enclosing a few nuclei and red blood-corpuscles. Sometimes the necrosis is so complete and widespread that it is difficult to recognise the tissue as liver or to make out the topography of the section. There is often, but not always, evidence of inflammatory reaction in the connective tissue. There may be a small-celled infiltration starting from the portal spaces and spreading into the peripheral parts of the lobules; a similar small-celled infiltration may also be seen around the intralobular vein.

Subacute Atrophy.—Some cases are prolonged and survive for many weeks, months, or even years; thus, in Steinhaus'[1] case the total duration was twenty-two months, and in Stroebe's[2] two years. In these cases, now spoken of as subacute liver atrophy, the naked-eye appearance of the liver is very different from that of the acute cases, and resembles that of nodular parenchymatous hepatitis or cirrhosis.[3] Probably many cases have been described as cirrhosis with adenomas. The relation of this nodular hyperplasia to acute atrophy was probably first recognised and figured by Cayley[4] in 1883. The liver is usually small. The surface shews nodular projections which may be white and caseous-looking, but are generally yellow, green, or brown from bile-staining. They vary in size; in exceptional cases they may be very large; Barbacci[5] recorded one as large as the fetal head, and Milne[6] refers to 2 cases on which laparotomy had been performed for an abdominal tumour. The nodules in the liver substance are surrounded by fibrosis and condensed liver tissue. Microscopically there is fibrosis, often intercellular; and no rigid line can be drawn between subacute atrophy and acute cirrhosis. The changes in the liver cells are described in the next paragraph.

Regenerative Changes.—Cases which do not run a very acute course shew changes in the small bile-ducts and liver cells which are regarded as regenerative and compensatory. These changes have been specially studied by Marchand,[7] Meder,[8] Stroebe, Barbacci, Ibrahim,[9] W. G. Mac-

[1] Steinhaus. *Prag. med. Wchnschr.*, 1903, xxviii, 323.
[2] Stroebe. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1897, xxi, 379.
[3] Compare *Trans. Path. Soc.*, Lond., 1892, xliii, 81.
[4] Cayley, W. *Ibid.*, 1883, xxxiv, 127.
[5] Barbacci. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1901, xxx, 45.
[6] Milne. *Arch. Int. Med.*, Chicago, 1911, viii, 639.
[7] Marchand. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1895, xvii, 206.
[8] Meder. *Ibid.*, 1895, xvii, 143.
[9] Ibrahim. *München. med. Wchnschr.*, 1901, xlviii, 784, 838.

Callum,[1] Muir,[2] Macdonald and Milne.[3] Microscopically it appears that in the early stages of regeneration the surviving liver cells multiply by direct (amitotic) and also by indirect nuclear division, so that columns of liver cells are formed resembling a tubular formation; the liver cells may become much enlarged, especially around the intralobular vein, and may contain several nuclei. Sometimes this compensatory hyperplasia occurs in one-half only of a lobule, the liver cells in the remainder being too necrosed to proliferate; in this event the intralobular vein may appear at the margin of the fresh mass of liver cells. This method of regeneration of the liver cells leads to the production of hyperplastic or "adenomatous" nodules in the liver, which project above the surface of the surrounding parts. According to Macdonald and Milne regeneration of the liver cells is due solely to proliferation of existing liver cells. A number of observers (Meder, Stroebe, Ibrahim, MacCallum, Yamasaki,[4] Adler[5]) believe that when the liver cells have been extensively destroyed, regeneration is brought about in another way. As a result of proliferation of the interlobular bile-ducts blind bile-ducts work their way into the degenerated lobule. The cells forming these projections increase in size and become like liver cells. The terminal cells in the invading masses of cells shew karyokinetic figures and are evidently proliferating. Muir admits that the bile-duct structures may form cells like liver cells, but does not attach much importance to them in compensatory regeneration. To sum up, regeneration occurs as a result of hyperplasia of the surviving liver cells, and possibly from hyperplasia of the interlobular bile-ducts by means of which cells approaching liver cells are produced.

Micro-organisms have been found in some cases, but not in others, and no definite causal connexion can be said to exist between any micro-organism and the changes found.

The colon bacillus, though often found after death, can hardly be regarded as the causal agent, as there may easily be post-mortem invasion of the organ. Streptococci, staphylococci, pneumococci, have also been reported in some cases.

Probably the toxins of various micro-organisms are capable of producing in livers rendered susceptible, for example, by toxaemia, the acute necrotic changes characteristic of acute yellow atrophy.

The *kidneys* are swollen, soft, bile-stained, and shew small haemorrhages. Microscopically the epithelium of the tubules is degenerated. Hewitt[6] recorded 5 cases of acute yellow atrophy with necrosis of the renal epithelium.

The *spleen* is often softened and enlarged.

In 71 cases Wickham Legg found the spleen larger than natural in 43.

[1] MacCallum, W. G. *Johns Hopkins Hosp. Rep.*, Balt., 1902, x, 379.
[2] Muir, R. *Journ. Path. and Bacteriol.*, Cambridge, 1908, xii, 287.
[3] Macdonald and Milne. *Ibid.*, 1909, xiii, 161.
[4] Yamasaki. *Arch. f. Heilk.*, Leipz., 1903, xxiv, 249.
[5] Adler. *Ibid.*, 1903, xxiv, 198.
[6] Hewitt. *Johns Hopkins Hosp. Bull.*, Balt., 1906, xvii, 272.

He quotes Liebermeister's statistics of 87 cases, in 56 of which the spleen was enlarged.

The *lymphatic glands* in the portal fissure and the neighbourhood may be much enlarged.

The *heart* is softened, swollen, and shews cloudy swelling. The blood, as in other toxic and infective conditions, stains the vessels and coagulates imperfectly. Haemorrhages are scattered through the body on the cutaneous, mucous, and serous surfaces. Meningeal and cerebral (Politzer,[1] Lafitte[2]) haemorrhages have been known to occur. Toxic changes in the vessel walls allow extravasation to take place. Brunton and Tunnicliffe point out that viperine poison has the same effect when applied locally to the mesentery of a frog.

The *gastro-intestinal tract* may be inflamed, and patchy haemorrhages or small areas of necrosis may occur. The stomach and intestines may contain altered blood, and slight ascites is not uncommon.

Pancreas.—Degenerative changes in the acini, the islands of Langerhans being unaffected, have been described by Sacquépée,[3] who lays some stress on this since the pancreatic juice has been found to have the power of destroying the toxins of diphtheria, tetanus, etc.

Central Nervous System.—In addition to meningeal and cerebral haemorrhages already referred to, degenerative changes, analogous to the toxic changes seen in a more chronic form in subacute combined sclerosis and in grave anaemia, have been described by Goldscheider and Moxter.[4]

Pathogeny.—The essential factor is a very acute necrosis of the liver cells resembling that produced by bacterial toxins, with evidences of inflammation in the supporting fibrous tissue of the organ. The condition is a very acute hepatitis; subacute or protracted cases pass into acute cirrhosis. It is analogous to, but more advanced than, the toxic changes seen in the liver in phosphorus, iodoform, and arsenic poisoning.

In Germany many sheep die with jaundice, haemorrhages, delirium, and acute yellow atrophy of the liver as a result of eating certain lupins. This disease,—lupinosis,—which is not met with in man, is thought to be due to a poison—ictrogen or lupinotoxin—produced by the agency of fungi in the husks of the seeds.[5]

Flexner[6] suggested that the lesions are due to autolysis. This view that the necrosis is due to a poison which destroys the liver cells, but does not affect their autolytic ferments which then act on the dead cells, has attracted a good deal of support (Wells,[7] White[8]).

[1] Politzer. *Jahrb. f. Kinderh.*, 1860, iii, 40.
[2] Lafitte. *Bull. Soc. Anat.*, Par., 1891, lxvi, 389.
[3] Sacquépée. *Arch. de méd. expér. et d'anat. path.*, Par., 1902, xiv, 485.
[4] Goldscheider und Moxter. *Fortschr. der Med.*, 1897, xv, 529.
[5] *Vide* Brunton and Tunnicliffe. *St. Barth. Hosp. Rep.*, Lond., 1896, xxxii, 425.
[6] Flexner. *Am. Journ. Med. Sc.*, Phila., 1903, cxxvi, 202.
[7] Wells, H. G. *Chemical Pathology*, p. 444, 1907.
[8] White, F. W. *Boston Med. and Surg. Journ.*, 1908, clviii, 729.

Quincke[1] suggested that acute yellow atrophy may be due to obstruction at the biliary papilla, allowing the pancreatic juice to digest the liver. There is as yet no proof of this speculation, which is exactly the converse of Opie's explanation of haemorrhagic pancreatitis as due to the flow of bile into the pancreatic duct (*vide* p. 750). Injection of commercial pancreatin into the common bile-duct of animals has not produced acute yellow atrophy (C. L. Best[2]).

Clinical Picture.—*Course.*—The disease may be divided into two stages. The first, which usually lasts five or six days, but may be prolonged for many weeks, comes on either like catarrhal jaundice with gastro-intestinal disturbance followed by jaundice, or, more gradually, with malaise. In the second stage the patient passes into a "typhoid" state and develops nervous symptoms which are of the gravest significance and should at once suggest the probability of acute yellow atrophy. This stage hardly ever lasts more than a week and is usually limited to three days.

Duration.—More than half the cases, as shewn by Thierfelder and Hunter's statistics, run their course within two weeks. Cases, however, certainly occur in which the disease is spread over many weeks, months, or even up to two years. The cases have been divided into acute and subacute, according to their duration and severity. The prolonged cases may resemble obstinate catarrhal jaundice until the nervous symptoms develop, the long course of the disease being due to prolongation of the earlier or first stage. But in rare instances partial recovery may occur after acute symptoms have appeared, the patient remaining jaundiced.

The *onset* is usually insidious, and may be that of ordinary catarrhal jaundice; in a minority, about one-third, of the cases the patient suffers from indefinite illness and malaise for some time before jaundice appears. As a rule, during the *first stage* there is little or nothing to distinguish the disease from ordinary catarrhal jaundice. Fever, malaise, vomiting, constipation, bilious urine, and not uncommonly muscular pains are present. Vomiting may be very persistent and severe.

Jaundice, which is usually the first definite sign, varies in different cases: it may gradually become more marked, or it may, in prolonged cases, first fade and then become more intense before death. In some instances it may be less marked at the termination than earlier in the disease. It is due to obstruction in the smaller bile-ducts, the result of inflammatory lesions in their walls produced by the same poison that is responsible for the acute degenerative changes in the liver cells. In some exceptional cases there is no jaundice.[3]

This was so in a case, subsequently published by Sir L. Brunton and Dr. Tunnicliffe,[4] which was under my care when I was House Physician at St.

[1] Quincke. In Nothnagel's *Encyclopedia of Practical Medicine*, "Diseases of the Liver," p. 642. American transl., edited by F. A. Packard, 1903.

[2] Best. Quoted by Wells and Bassoe. *Journ. Am. Med. Assoc.*, 1905, xliv, 685.

[3] Bamberger. Quoted by Legg. *Loc. cit.* p. 439. Le Roy. *Lancet*, Lond., 1885, ii, 155.

[4] Brunton and Tunnicliffe. *St. Barth. Hosp. Rep.*, 1896, xxxii, 436.

Bartholomew's Hospital in 1889. Dr. E. T. Wilson kindly sent me the notes and liver of the following case: A woman aged thirty years, never strong, had slight haematemesis two years before, from which she recovered. On December 9, 1897, she suddenly felt pain and subsequently vomited a little blood; next day the liver dulness was diminished; slight haematemesis recurred on December 10 and 11, and melaena on December 12, 13, 14; after this date the motions, always offensive, became clay-coloured. The patient got weaker, drowsy, and died on December 28. There was never any jaundice. The urine was not tested for leucine and tyrosine. The temperature was generally between 99° and 100°, going up on two occasions to 101°, and was often below normal. At the necropsy the liver was very small, pale, firm to the touch and to the knife. The surface was smooth and lightish yellow with patches of slate colour; the edges were remarkably thin. Microscopically there was acute yellow atrophy. Gall-bladder was full of dark bile. Kidneys firm and pale. There were numerous submucous haemorrhages in the stomach, especially at the cardiac end.

The onset of the *second stage* is very definite, and is marked by a pronounced change for the worse in the general condition and especially by the appearance of nervous symptoms. Headache appears, or if present before, becomes intense. Intolerance of light is often complained of; the mental processes are affected; there are restlessness, delirium, and the patient may scream and become extremely violent. Twitching of the muscles and subsultus often occur, and general convulsions may supervene. Transient paralyses, such as squint, are sometimes noted. Apart from jaundice, the clinical manifestations may closely resemble those of meningitis. I have seen an extensor plantar response (Babinski's sign). The nervous manifestations pass into coma, in which the patient dies.

With the onset of the grave nervous symptoms vomiting becomes urgent, and the vomited matters often contain altered blood. The tongue is usually dry, brown, and tremulous, and the teeth become coated with sordes. The amount of sulphocyanide of potassium in the saliva is said to be diminished (Fenwick[1]). Dilatation of the pupils has been regarded as an important sign, and has been so extreme as to suggest belladonna poisoning. The pulse becomes rapid, feeble, and of low tension. The respiratory rate tends to be increased or to become irregular and finally stertorous. The temperature varies, but is more often depressed than raised, but it may rise just before death. In a girl aged twenty under my care the temperature rose to 106° F. before death. The presence or absence of fever was correlated by Hanot[2] with different microbic poisons, infection with the colon bacillus leading, like phosphorus poisoning, to a depressed temperature, while streptococcic and staphylococcic infections are associated with pyrexia; but this is very doubtful. Occasionally a red rash appears, and arthritic swelling has been recorded. Petechiae and haemorrhages occur under the skin, and occasionally epistaxis, haematuria, retinal haemorrhages, and in women

[1] Fenwick. *Saliva as a Test for Diseases of the Liver*, 1889.
[2] Hanot, V. *Arch. gén. de méd.*, Paris, 1896, clxxvii, 77.

metrorrhagia are observed. Pregnant women abort. The faeces may be darkened by blood so as to resemble bile; in the later stage it is improbable that bile passes into the duodenum, inasmuch as after death the bile-ducts contain nothing but mucus. But as constipation exists throughout the disease, some of the faeces may contain bile excreted into the bowel at a very early stage of the disease. The dejecta are often extremely offensive. Diarrhoea is exceptional.

Liver Dulness.—At the onset of grave symptoms the liver may or may not be enlarged. The increased size in the early stages may be due to some old-standing change, but this is not the case in most instances. Whether preliminary hepatic enlargement is made out or not, percussion soon shews diminution of the liver dulness, which may progress until it completely disappears. Entire absence of the liver dulness is due to the atrophied and flabby organ falling away from the abdominal walls and allowing intestinal coils to take its place.

In an exceptional case recorded by Gerhardt[1] the hepatic dulness did not diminish, although the liver (29 ounces) was markedly atrophied. This was explained by the fact that the liver was firmly adherent to the anterior abdominal wall.

Flatulent distension of the intestines occurs and gives rise to difficulty in estimating the size of the liver. As mentioned above, coils of intestine may pass between the abdominal wall and the liver and entirely obliterate the hepatic dulness. The liver is often tender. In 100 cases collected by Legg[2] this was definitely noted in 35. Enlargement of the spleen has been occasionally noted. Ascites, though present in some cases after death, is masked by flatulence and rarely detected during life. Tileston[3] collected 8 cases with ascites. In a case of ascites and intense jaundice recorded by Bryant,[4] the ascites was due to chronic perihepatitis and the jaundice to acute yellow atrophy.

The *blood* shews a delayed coagulation-time, and may contain bile pigment (Neuberg and Richter[5]). The number of red blood-corpuscles is somewhat increased from concentration, and a very moderate leucocytosis has been observed (Cabot, Ewing[6]). Blood cultures have been negative in some instances (Libman,[7] White[8]); in others the colon bacillus has been found (Vincent[9]).

Urine.—The amount is somewhat diminished; it is high-coloured from excess of bile pigment and urobilin. Bile acids are occasionally found. From degeneration of the renal cells albumin and casts are

[1] Gerhardt. *Ztschr. f. klin. Med.*, 1892, xxi, 374.
[2] Legg, W. *Bile, Jaundice, and Bilious Diseases*, p. 465, 1880.
[3] Tileston. *Boston Med. and Surg. Journ.*, 1908, clviii, 510.
[4] Bryant, J. H. *Guy's Hosp. Gaz.*, 1900, N.S., xiv, 147.
[5] Neuberg und Richter. *Deutsche med. Wchnschr.*, 1904, xxx, 499.
[6] Ewing. *Clinical Pathology of the Blood*, p. 341, 1901.
[7] Libman. *Johns Hopkins Hosp. Bull.*, Balt., 1906, xvii, 222.
[8] White. *Boston Med. and Surg. Journ.*, 1908, clviii, 729.
[9] Vincent. *Semaine méd.*, Paris, 1893, xiii, 228.

frequently present. Deutero-proteose, probably from destruction of the liver cells, is sometimes detected. There is no glycosuria. This is remarkable, and shews that glycosuria is not of any value as a sign of hepatic inadequacy (*vide* p. 234).

The total excretion of nitrogen in the urine may be much diminished, normal, or increased. The fall in the total nitrogen may be due to the diminished intake of protein; on the other hand, comparatively considerable excretion of nitrogen in some cases may depend on autolysis of the liver cells. Urea is diminished and the percentage of ammonia increased; normally ammonia accounts for about 5 per cent of the total nitrogen, but in acute yellow atrophy it may account for 20 per cent. This alteration in the relative proportions of urea and ammonia was in the past ascribed to failure of the liver to transform ammonia into urea. But it is probable that the increased ammonia depends on acidosis and fixation of ammonia by organic acids before the liver has a chance of transforming it into urea.

Leucine and tyrosine, to which great importance has been attached as replacing urea, are sometimes present in such quantities that they are spontaneously precipitated. In many cases, however, the urine must be concentrated to demonstrate them. Leucine appears as rounded discs, and tyrosine as needle-shaped crystals. Leucine and tyrosine are not invariably present; they may be absent in cases in which the liver is found to contain them, and one may be found without the other. They have been known to occur in the urine in conditions other than acute yellow atrophy, such as erysipelas, enteric, small-pox, in some obscure febrile conditions, and leukaemia. Their presence, therefore, is not pathognomonic of acute yellow atrophy, and their absence does not exclude that disease. It was formerly assumed that the presence of leucine and tyrosine was due to the degenerated liver cells failing to transform these bodies into urea. This explanation is incorrect, for when the liver has been excluded from the circulation by ligature of the portal vein and the hepatic artery, leucine and tyrosine do not appear in the urine (Minkowski). It appears that the leucine and tyrosine are derived from autolysis of the liver cells. This view is supported by the production of leucine and tyrosine during the autolysis, or the spontaneous digestion by intra-cellular ferments, of other organs, *e.g.* a pneumonic lung or pus.

Uric acid may be present in normal or even in increased quantities; from Jackson and Pearce's [1] experimental work this would appear to be due to hydrolysis of nuclear tissue during the autolysis of the necrotic tissue.

Prolonged or **subacute** cases are those which partially recover but subsequently relapse and die after weeks, months, or even more than a year. The existence of prolonged cases with continuous jaundice is difficult to verify, as the condition merges into acute hepatitis and cirrhosis. Macdonald and Milne [2] collected 19 cases of subacute atrophy, 4 of which occurred in children under ten years of age, and

[1] Jackson and Pearce. *Journ. Exper. Med.*, N.Y., 1907, ix, 577.
[2] Macdonald and Milne. *Journ. Path. and Bacteriol.*, Cambridge, 1909, xiii, 161.

Milne[1] has pointed out that children are specially affected. The morbid changes are described on p. 583.

The following case came under my observation at the Victoria Hospital for Children :—

A boy four and a half years old, whose mother had had one stillborn child and two miscarriages, had had pneumonia and bronchitis a year previously. Jaundice appeared five weeks and ascites two weeks before death. Subsequently haemorrhages developed, paracentesis to 25 ounces of turbid ascitic fluid was performed two days before death, which was preceded by coma. The liver weighed $13\frac{1}{4}$ ounces, the surface was irregular, on the left lobe there was a raised area the size of a florin. On section the liver was somewhat tough, microscopically the appearances were those of acute yellow atrophy with regenerative changes in the adenomatous area in the left lobe. There was acute enteritis.

The clinical course of these cases is vague and variable, and the greater part of the illness resembles cirrhosis with jaundice rather than acute yellow atrophy. The spleen may be enlarged, and ascites appear towards the end.

Termination.—The "typhoid" state deepens into coma and absolute unconsciousness, with stertorous breathing and incontinence of urine and faeces.

Diagnosis.—Jaundice with severe constitutional and cerebral symptoms and diminution in the liver dulness are the main data on which the diagnosis is made.

Differential Diagnosis. — *From Phosphorus and Allied Forms of Poisoning.*—The absence of any evidence that phosphorus or other poison has been taken or vomited is important. The progressive diminution in the hepatic dulness and the fall in the amount of urea in the urine are in favour of acute yellow atrophy. The presence of leucine and tyrosine is not conclusive, as they may be absent in acute atrophy, and be present in phosphorus poisoning and in other conditions, such as typhoid fever, erysipelas, and leukaemia. In phosphorus poisoning there is an interval between the severe irritant symptoms and the onset of jaundice with severe constitutional symptoms; whereas there is no such interval between the first and second stages of acute yellow atrophy. There is more gastric irritation and less cerebral disturbance in phosphorus poisoning.

From *icterus gravis* the chief distinction is the size of the liver—diminished in acute yellow atrophy, increased in icterus gravis. From severe cases of acute infective jaundice the diagnosis is very difficult; in fact, the two conditions run into each other; those that recover are likely to be spoken of as infective jaundice, and those that prove fatal as acute yellow atrophy. Subacute atrophy is difficult to distinguish from acute cirrhosis; in fact there is a transition from acute atrophy to subacute atrophy and to acute cirrhosis. Hypertrophic biliary cirrhosis is not likely to be confused with acute atrophy, as the course of the

[1] Milne. *Arch. Int. Med.*, Chicago, 1911, viii, 638.

disease is very chronic and the liver is greatly enlarged. According to Osler,[1] infective endocarditis has been mistaken for acute yellow atrophy.

Prognosis.—When the disease is fully declared, the prognosis is most gloomy; in fact, some doubt will always arise as to the nature of cases that recover completely. Some cases may have been examples of severe infective jaundice or Weil's disease, or of some other form of acute hepatitis. But the occurrence of subacute cases shewing regenerative changes makes it probable that the disease is not necessarily fatal.

In 1880 Wickham Legg[2] gave a list of 28 cases of reputed recoveries from acute yellow atrophy. In 1892 Wirsing[3] could only collect 15 cases, not associated with syphilis, of recovery.

In a case under my care the diagnosis of acute atrophy and death, the patient being in a condition of coma, seemed equally certain, but recovery followed. In another similar case, seen in consultation, the patient became mentally deranged for several months, but eventually recovered.

Recovery depends on the severity of the attack and on the compensatory power of the body and especially of the liver cells. As nodular hyperplasia of the liver has been described in cases surviving for six months (Marchand[4]), a year and a half (Barbacci[5]), a year and three-quarters (Steinhaus[6]), and two years (Stroebe[7]), the possibility of permanent recovery cannot be denied. But symptoms may recur and prove fatal from degenerative changes attacking the areas of compensatory hyperplasia. Children, probably from their greater power of repair, more often shew the changes of subacute atrophy. The prognosis is therefore better in them than in adults. It is worst in pregnant women.

As in all forms of liver disease, the state of the kidneys is important. If they were previously healthy, the excretion of poisons due to the acute hepatic inadequacy will diminish the intensity of the toxaemia; but even then the outlook is very dismal, since the renal epithelium is affected by the poisons reaching them by the circulation and undergoes acute degeneration.

Treatment.—As the disease is not invariably fatal, it is important to adopt *prophylactic measures* in cases of jaundice in which acute yellow atrophy may possibly follow. Thus, jaundice in pregnant women, cases of catarrhal jaundice presenting much drowsiness or toxaemia, and jaundice during secondary syphilis, should be treated on the lines of diminishing toxaemia. In such circumstances the patients should for a time be kept in bed in a well-ventilated room, and the diet confined to milk and carbohydrates. The milk may be flavoured with coffee, cocoa, or tea, and may be thickened with cornflour. Three to four pints may

[1] Osler, W. *Principles and Practice of Medicine*, p. 704, 3rd ed.
[2] Legg, J. Wickham. *Bile, Jaundice, and Bilious Diseases*, p. 676, 1880.
[3] Wirsing. *Inaug. Diss.*, Würzburg. Quoted by Albu, *Deutsche med. Wchnschr.*, 1901, xxvii, 216.
[4] Marchand. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1895, xvii, 206.
[5] Barbacci. *Ibid.*, 1901, xxx, 49.
[6] Steinhaus. *Prag. med. Wchnschr.*, 1903, xxviii, 323.
[7] Stroebe. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1897, xxi, 379.

be given daily. When digestion is difficult peptonised milk-gruel or Benger's food may be substituted in part or entirely for milk. Sugar and chocolate are of use in preventing acidosis. The patients should drink plenty of water so as to dilute the toxins and increase excretion; for this purpose alkaline mineral waters, such as Vichy or Vals, are suitable. The bowels should be kept freely open by calomel, followed by salts next morning twice a week, with cascara sagrada on the intervening days. The degree of purgation must be regulated by the progress of toxaemic symptoms. If necessary, the urinary excretion may be further stimulated by citrate of caffeine or diuretin combined with digitalis. The jaundice should be met by urotopin (gr. vii.) combined with sodium salicylate (gr. x.), and bicarbonate of sodium (gr. xv.), three times a day before food. Acids should be avoided. Intestinal antiseptics in one of the following forms may be tried: Beta-naphthol (gr. v.), naphthalene tetrachloride (gr. vii.), calomel ($\frac{1}{10}$ gr.), salol (gr. v.), acetozone (1 in 2000 parts of water) sweetened with syrup of lemon (2 oz. to 1 pint), $\frac{1}{2}$ to 1 pint daily, salicylate of bismuth (10 gr.). In the jaundice of secondary syphilis, mercurial treatment is essential.

In cases in which the onset of acute yellow atrophy seems fairly certain the above measures should be pushed, and in addition enemas or subcutaneous or intramuscular transfusions of saline solution should be carried out to obviate the toxaemia. Sodium bicarbonate should be given in larger quantities (1 dram) three or four times daily by the mouth or in the enemas or transfusions (3 drams to 1 pint). As the condition is thought to depend on autolysis of the liver, I gave horse serum, which has an anti-autolytic action, in one case which eventually recovered. Vomiting should be treated by careful feeding, small doses of cocaine, dilute hydrocyanic acid, or small hypodermic injections of morphine. Sleeplessness and delirium should be met by tepid sponging, ice-bags to the head, bromides, morphine, veronal, or trional. Chloral and its allies should be avoided, because the chloroform which is formed exerts a toxic action on the liver cells as shewn by delayed chloroform poisoning. The circulation should be maintained by hypodermic injections of strychnine.

JAUNDICE OF PHOSPHORUS POISONING

Incidence.—Acute phosphorus poisoning is rare in this country; in the ten years ending 1903 there were 152 fatal cases in England and Wales. In Vienna it is commoner, and is used as a means of committing suicide by prostitutes and unmarried girls who are pregnant. When taken with suicidal intent, an emulsion of the heads of lucifer matches or of rat paste has been employed. Accidental poisoning may be due to eating rat paste under the impression that it was something else, or the flesh of animals, especially poultry, which have died from devouring

vermin poisoned by phosphorus (Poore [1]), or even to the application of phosphorescent paste to the skin, and its medicinal use. In the past some writers attributed all cases of acute yellow atrophy to undetected phosphorus poisoning. A condition resembling phosphorus poisoning may be due to iodoform, arsenic, and antimony.

Morbid Anatomy.—The liver is, as a rule, much larger than natural, firm and feeling like a fatty liver, and of a pale yellow colour. In exceptional cases it has presented exactly the features of acute yellow atrophy, but the change in the liver is essentially one of increase in size due to acute fatty metamorphosis, and resembles that of delayed chloroform and of iodoform poisoning. The amount of fat in the liver is greatly increased; normally it contains about 3 per cent of fat, whereas in phosphorus poisoning it may contain 30 per cent. It thus contrasts with acute yellow atrophy in which the amount of fat is not increased. It is said that if life is sufficiently prolonged, the liver diminishes in size from absorption of the fat and so comes to be in the same condition as in acute yellow atrophy. Under the capsule and on section the yellow buff aspect of the liver substance shews here and there reddish spots due to haemorrhage, which stand up against the bile-stained liver substance.

The fat is not produced by changes in the protoplasm of the liver cells, but is brought to the liver from other parts of the body; the degenerated condition of the liver cells allows this fat to be deposited in them in very excessive quantities (Rosenfeld [2]).

Microscopically the liver cells shew cloudy swelling, indistinct outlines, and advanced fatty metamorphosis, especially towards the periphery of the lobules. The cells in parts of the lobules may contain granules of bile-pigment. The cytoplasm is more affected in phosphorus poisoning, whilst in acute atrophy the nucleus suffers most. Glycogen disappears from the cells. Leucine and tyrosine may also be found in the liver. There is sometimes slight proliferation of the connective tissue of the portal spaces, and in cases that recover some cirrhosis probably develops. The small bile-capillaries are blocked and obstructed (Eppinger [3]), thus accounting for the jaundice.

The heart usually shews fatty change, and may be so soft as to be readily perforated by the fingers during its examination. The kidneys shew an apparent fatty increase in the parenchyma, but chemical analysis proves that there is no real increase. The voluntary muscles also undergo fatty change. The spleen may be much enlarged. Haemorrhages are scattered throughout the body.

Pathogeny.—The hepatic changes in phosphorus poisoning are thought to depend on aseptic autolysis due to autolytic ferments, one of which is probably arginase (Wakeman [4]); for Jacoby [5] has shewn that

[1] Poore, G. V. *Nervous Affections of the Hand and Other Studies*, p. 155, 1897.
[2] Rosenfeld. *Verhandl. d. deutsch. path. Gesellsch.*, 1904, vi, 71.
[3] Eppinger. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1903, xxxiii, 123.
[4] Wakeman, A. J. *Journ. Exper. Med.*, N.Y., 1905, vii, 303.
[5] Jacoby. *Beitr. z. chem. Physiol. u. Path.*, Braunschweig, 1903, iii, 446.

the autolytic power of the liver is increased in phosphorus poisoning, and according to Wells [1] phosphorus destroys the liver cells but not their autolytic enzymes. The destruction of the liver cells causes hepatic inadequacy and so toxaemia, poisons which should have been arrested in the liver passing into the general circulation. It is thought that there is an acid intoxication due to sarcolactic acid in the blood.

Clinical Manifestations.—The symptoms due to the irritating effect of phosphorus on the gastric mucous membrane come on a few minutes to three hours after taking the poison. With phosphorated oil or phosphorus in a soluble state the effects appear rapidly, while if the poison was taken in a solid form, the onset is delayed. There is gastric pain, followed by vomiting, which greatly interferes with antidotal treatment and feeding, and may be so constant as to cause dangerous collapse. The vomited matters and eructations may be luminous in the dark, and dark and grumous from the presence of blood. There are usually intense thirst and tenderness over the stomach and liver, but no hepatic enlargement. The patient may die from collapse; if this does not occur and efficient treatment is carried out, permanent recovery may follow; but in a considerable number of cases there is a temporary improvement succeeded by the return of grave symptoms due to the effects of the absorbed poison on the liver and other internal organs. These severe symptoms usually begin about four days after the poison was taken; they may arise sooner, or, on the other hand, be delayed for two, three, or even six weeks (S. West [2]).

The scene reopens with jaundice and recurrence of grumous vomiting, followed by great prostration, coma, and death, usually on the fifth or sixth day from the time the phosphorus was taken, and after a day or two of grave constitutional symptoms. Haemorrhages into the skin and from mucous surfaces are constant and generally larger than in acute yellow atrophy. In one case there were extensive haemorrhages behind the peritoneum, which may have accounted for abdominal pain (Hann and Veale [3]). Jaundice is not always present, and does not bear any relation to the severity of the changes in the liver. The temperature is usually below normal. The liver is enlarged and tender; the spleen is also enlarged, and the abdomen may be distended. The most marked difference between this stage of phosphorus poisoning and acute yellow atrophy is in the size of the liver. But in exceptional cases the liver is not enlarged, and in the early stages of acute yellow atrophy it may be enlarged, so that the clinical resemblance between the two affections is sometimes very close.

In the early stages the number of red blood-corpuscles is often increased (v. Jaksch [4]); this is not necessarily due to concentration of the blood from vomiting, for it may occur in cases without vomiting.

[1] Wells. *Chemical Pathology*, p. 98, 1907.
[2] West, S. *Lancet*, Lond., 1893, i, 245.
[3] Hann and Veale. *Lancet*, Lond., 1910, i, 163.
[4] v. Jaksch. *Deutsche med. Wchnschr.*, 1893, xix, 10.

Occasionally there is a leucocytosis. The blood may become non-coagulable from absence of fibrinogen (Jacoby [1]); its alkalinity is reduced, and it contains an excess of fat.

The *urine* is somewhat diminished in quantity, but never suppressed; it is high coloured and of rather high specific gravity. It may contain albumin, blood, casts, and albumose. Bile pigments and bile acids are generally present. It was formerly said that leucine and tyrosine are absent, and stress was laid on this as diagnostic from acute yellow atrophy; but it is now known that leucine and tyrosine may be present in the urine in phosphorus poisoning. Leucine is less frequently present than tyrosine. Arginine, alanine, and glycocoll have been found in the urine (Wohlgemuth [2]) The presence of leucine and tyrosine in the urine is due, like the albumosuria, to autolytic changes in the liver cells. That it is not, as was formerly thought, due to failure on the part of the liver to transform leucine and tyrosine into urea is shewn by the fact that the experimental exclusion from the circulation of the liver in geese by ligature of the portal vein and hepatic artery does not lead to the appearance of leucine and tyrosine in the urine. The total nitrogen in the urine is increased after the first few days from excessive protein disintegration. Experimentally the rise in the protein metabolism in phosphorus poisoning is only equalled by that in phloridzin diabetes. In the second stage the percentage of urea in the total urinary nitrogen falls from the normal 90 to 70 or 80, and that of ammonia rises from the normal 4-6 to 10-18 per cent. The increased amount of ammonia in the urine can be diminished by the administration of sodium bicarbonate. The explanation of this is that, owing to an increase in organic acids in the body, ammonia is utilised as a base and appears in the urine in combination with organic acids; when sodium bicarbonate is given, the ammonia is no longer utilised in this way, and can therefore be converted into urea.[3] In other words, the presence of ammonia in the urine, though associated with changes in the liver, is not due to any failure in the hepatic cells to form urea out of ammonia, but is evidence of incipient acid intoxication. Acetone, diacetic and sarcolactic acids are frequently present in the urine. Glycosuria is very rare; in 141 cases at Prag it was found in 6 (Walko [4]).

In 19 cases of phosphorus poisoning Frerichs [5] gave large quantities (200 grams) of sugar, but obtained alimentary glycosuria in two only.

Diagnosis.—The history that phosphorus has been swallowed or that symptoms justifying this conclusion have recently occurred is a most important, if not an essential, point. The presence of phosphorus in the vomit or the luminosity of the vomited matters in the dark settles the question. In the diagnosis from acute yellow atrophy the large size

[1] Jacoby. *Ztschr. f. physiol. Chem.*, Strassburg, 1900, xxx, 175.
[2] Wohlgemuth. *Ibid.*, 1905, xliv, 74.
[3] *Vide* Herter. *Lectures on Chemical Pathology*, p. 347, 1902.
[4] Walko. *Ztschr. f. Heilk.*, 1901, ii, 339.
[5] Frerichs, F. T. *Ueber den Diabetes*, 1884. Quoted by Williamson, *Diabetes*, p. 116.

of the liver and the greater prominence of gastro-intestinal symptoms should also be borne in mind. In the absence of a reliable history great difficulty may arise in the differential diagnosis; in fact, Poore [1] considered that clinically and pathologically the two conditions are indistinguishable.

Rapid cirrhosis with a greatly enlarged liver and cholaemia, and sporadic cases of Weil's disease may simulate phosphorus poisoning in the absence of a distinct history.

Prognosis.—In cases with jaundice and enlargement of the liver the outlook is very grave; most cases die.

Treatment.—When the poison has been recently taken, the stomach should be emptied and washed out with warm water containing sulphate of copper or 0·5 to 1 per cent solution of permanganate of potassium. As an antidote, old French or oxidised oil of turpentine should be given every quarter of an hour for the first hour, 40 minims in an emulsion, and afterwards three or four times daily. Mucilaginous drinks should be given, but oils and fats should be avoided, as they render the phosphorus more soluble. Purgatives are advisable. When the grave constitutional symptoms have developed, no special treatment can be relied on. But it would be reasonable to give large doses of sodium bicarbonate by the mouth or by subcutaneous transfusion to counteract acidosis. Enemas of dextrose 5 to 10 per cent may also be given.

INFECTIOUS JAUNDICE

Among the various forms of toxaemic or haemo-hepatogenous jaundice there is a group which, in contradistinction to the malignant forms of toxaemic jaundice or icterus gravis, such as acute atrophy and phosphorus poisoning, is spoken of as benign infectious jaundice or merely infectious jaundice. Of this group, Weil's disease is a well-marked example. The general characters of toxaemic jaundice have already been sketched (*vide* p. 536), and it was there pointed out that the jaundice is subordinate both in degree and in importance to the constitutional symptoms of a general haemic infection or intoxication. In many instances the primary infection constitutes a definite disease, as in the specific fevers, yellow fever, pyaemia, and septicaemia, but in this group of infectious jaundice, although there is a general disorder, its characters are not sufficiently typical to allow of its recognition as a definite disease apart from the febrile condition and jaundice.

There are thus many examples of toxaemic jaundice of undetermined nature grouped under the heading of infectious jaundice. The more severe cases are considered in a special category under the name of Weil's disease. Among the slight forms are some cases often termed catarrhal jaundice, but presenting fever and enlargement of the liver and

[1] Poore, G. V. *Nervous Affections of the Hand and Other Studies*, p. 155, 1897.

spleen; the onset of these cases is the same as that of catarrhal jaundice, but there are the above-mentioned additional features, which shew that there is not a mere local obstruction at the lower end of the bile-duct, but a more widespread infection. No doubt transitional cases between a local infection and obstruction at the lower end of the bile-duct and a more extensive obstruction of the ducts exist, and it is, therefore, convenient to speak of the cases as infectious catarrhal jaundice. It is not infrequent for epidemics of this form of jaundice to occur, and it is not always easy to be certain whether it is a mild infectious jaundice, the infection falling chiefly on the bile-ducts, or whether there is an epidemic form of gastro-intestinal catarrh in which the lower end of the bile-duct is obstructed, while the ducts remain free from more extensive infection.

The epidemic jaundice which occurred in our troops in the South African war (1899–1902) was regarded by some as infectious and by others as due to gastro-intestinal catarrh.[1]

WEIL'S DISEASE

Synonyms: Infective Jaundice; "Bilious Typhoid."

In 1886 Weil[2] described febrile jaundice associated with nephritis and enlargement of the spleen. It occurs in epidemics, one of which had previously been described by Weiss in 1866 as "infective jaundice." The disease was called after Weil, of Heidelberg, by his compatriots, but the French school did not consider that it differed from icterus gravis or infectious jaundice.

Weil's disease is an excellent example of acute infective jaundice due to infection of the body by a proteus bacillus. The jaundice is toxaemic, and has analogies with that induced experimentally by toluylenediamine. Some cases recorded as examples of recovery from acute yellow atrophy may have been examples of Weil's disease. Conversely, fatal cases of Weil's disease are sometimes described as acute yellow atrophy or icterus gravis.

Etiology.—It usually attacks young adults; some estimates give a percentage of 90 in males; it has been very rarely recognised in children.

Brüning[3] reported a case, confirmed bacteriologically, in an infant 4 months of age.

The infection is probably due to eating decomposed meat or drinking water which has been infected by tainted meat or by the bodies of animals dying from a similar disease. Its frequency in the German army has been referred to the consumption of rancid and improperly

[1] Vide *Report of the Imperial Yeomanry Hospitals in South Africa*, 1902, iii, 195.
[2] Weil. *Deutsches Arch. f. klin. Med.*, 1886, xxxix, 209.
[3] Brüning. *Deutsche med. Wchnschr.*, 1904, xxx, 1269.

cooked sausages (H. Brooks [1]). Semmola and Geoffredi [2] quote cases apparently due to inhalation of sewer-gas. It is, therefore, more likely to occur in butchers, soldiers, and sewermen. Most of the cases occur in the summer and in epidemics. It may arise repeatedly in the same place, but does not appear to be contagious.

The disease is rare in England, though some epidemics of catarrhal jaundice have been erroneously described as Weil's disease, and is usually seen in Germany, Russia, and France. Few cases have been recorded in America (Raymond,[3] Lamphear, H. Brooks, Libman,[4] Satterlee,[5] Einhorn). In Smyrna it has been endemic since 1837 and in Alexandria since 1870; Greeks appear to be specially susceptible (Sandwith [6]).

Bacteriology.—Jaeger,[7] Banti,[8] and others described a proteus bacillus as the essential cause. Jaeger found the same organism (*Bacillus proteus fluorescens*) in ducks dying with jaundice, which frequented the water in which his patients had bathed and presumably become infected. Satterlee tabulated the characters of the bacilli found by Weil, Jaeger, Brooks, Libman, and himself. This bacillus is found in the viscera in large numbers, and when cultivated and injected into animals, leads to acute degenerative changes in the liver and kidneys. It appears that bacilli are rarely present in the blood, and that dissemination occurs chiefly by the lymphatics (H. Brooks).

Morbid Anatomy.—The tissues of the body are bile-stained and shew the effect of a general toxic process. The liver is either somewhat increased in size, or of the normal volume. Haemorrhages may be present in the skin and in the mucous and serous membranes. The spleen is swollen, enlarged, and has been seen to contain haemorrhages. The kidneys shew tubal nephritis. There is cloudy swelling of the cells of the kidney, liver, and heart muscle, going on to the further degenerative change of fatty metamorphosis. The changes in the liver may progress further and resemble those in acute yellow atrophy; the mucous membrane of the bile-ducts becomes swollen and degenerated.

Symptoms.—The onset is sudden, and resembles that of influenza. The chief symptoms are malaise, headache, fever, rigors, severe muscular pains, especially in the calves, and often gastro-intestinal disturbance. The pulse-rate is about 120 at first, but becomes slower after the appearance of jaundice. Jaundice appears between the third and fifth days of the illness. In a case under my observation it did not appear until the seventh day. It is generally slight, and lasts about two weeks; the motions may be clay-coloured, but usually contain bile and are often

[1] Brooks, H. *Arch. Neurol. and Psychopath.*, N.Y., 1900, iii, 344.
[2] Semmola and Geoffredi. *Twentieth Century Practice*, 1897, ix, 688.
[3] Raymond. *Med. Age*, Detroit, 1892. Quoted by Brooks.
[4] Libman. *Phila. Med. Journ.*, 1899, iii, 620.
[5] Satterlee. *Med. News*, N.Y., 1903, lxxxii, 1069.
[6] Sandwith. *Brit. Med. Journ.*, 1904, ii, 672.
[7] Jaeger. *Ztschr. f. Hyg.*, 1892, xii, 525.
[8] Banti. *Deutsche med. Wchnschr.*, 1895, xxi, 493.

loose. The liver becomes enlarged and tender. A marked feature of the disease is the splenic enlargement. Fever reaching 103° to 104° F. lasts for about a week; the temperature then falls and becomes normal at about the tenth day.

Max Einhorn[1] has recorded two cases in which small tumours were temporarily palpable on the surface of the liver.

Nervous symptoms are prominent; the muscular pains in the calves are severe, prostration, giddiness and stupor may be marked, so that the patient appears gravely ill, and delirium is usually present. Epistaxis, purpura, and rashes, such as herpes, erythema, and urticaria, may be met with. A relapse may occur a week or so after the temperature has become normal; its occurrence may be suspected if, after the first attack, the spleen remains enlarged. The relapse lasts about a week. Chauffard[2] describes Weil's disease as "relapsing infectious jaundice," but in Germany relapses are comparatively infrequently described; thus, in 84 cases, of which 73 were collected from German literature, Tymowske[3] found relapses mentioned in 19. Quincke[4] says that a relapse occurs in 40 per cent of the cases.

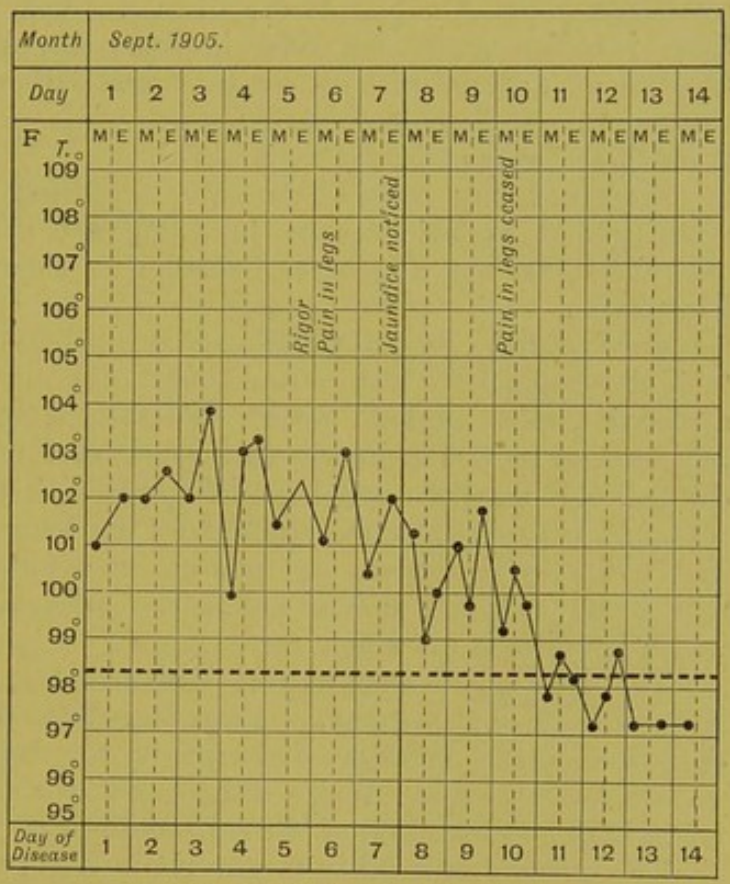


FIG. 81.—Chart of a case of Weil's disease.

The blood is almost always sterile, and the proteus bacillus, described by Jaeger and others, in the viscera, is not to be found in the general circulation. In some cases the blood-serum agglutinates the *Bacillus typhosus* even when diluted (Eckhardt[5]).

[1] Max Einhorn. *Am. Journ. Med. Sc.*, Phila., 1904, cxxviii, 896.
[2] Chauffard. *Traité de médecine* (Bouchard, Brissaud), v, 98.
[3] *Thèse de Paris*, 1889, quoted by Chauffard, *loc. cit.*
[4] Quincke. "Diseases of the Liver," in Nothnagel's *Encyclopedia of Practical Medicine*, English translation, p. 504, 1903.
[5] Eckhardt. *München. med. Wchnschr.*, 1902, xlix, 1129.

The urine is scanty, albuminous, contains bile-pigment, casts, and sometimes blood-corpuscles and bile acids. It shews the proteus bacillus found in the viscera. Bacteriuria may persist for a considerable time; in Satterlee's case, in which it was still present and rendered the urine turbid a month after the disease, it may have been due to local infection of the prostate.

Diagnosis.—Fever, jaundice, enlarged spleen and liver, pains in the calves, and albuminuria occurring in epidemics, running an acute course, and ending in recovery are the characteristics of the special form of infectious jaundice called Weil's disease. Very similar forms of infectious jaundice occur and differ in some clinical features, such as the absence of albuminuria or constant association with gastro-intestinal symptoms. It is, indeed, hardly worth while to separate Weil's disease from these forms of infectious jaundice.

From ordinary *catarrhal jaundice* it is distinguished by its greater severity and by evidence of its being not a local disease limited to the bile-ducts, but a general infection, as shewn by albuminuria and bacteriuria.

From Enteric Fever.—Griesinger originally described the disease as "bilious typhoid." Not uncommonly cases of Weil's disease occur in association with typhoid fever. Further, according to Eckhardt, the blood-serum in Weil's disease may agglutinate typhoid bacilli even when diluted. It has been suggested that Weil's disease is modified typhoid fever, or typhoid infection limited to the biliary tract. The onset of Weil's disease is sudden, and gradual in enteric fever. The duration and course of Weil's disease are shorter than those of enteric fever, in which jaundice is extremely rare.

The more severe examples of Weil's disease approach icterus gravis and acute yellow atrophy. Relapsing fever should be recognised by detection of the *Spirillum obermeieri* in the blood. Dengue and mild yellow fever resemble Weil's disease, but the diagnosis can usually be made from consideration of the surroundings.

The **prognosis** is fairly favourable in Europe, but convalescence may be protracted.

In the 44 cases obtained by adding Weil's, Jaeger's, Haas's, and Wassilieff's figures there were only five deaths. In 300 cases at the Greek Hospital in Alexandria the average mortality was 30 per cent, but at different times it varied from 10 to 60 per cent (Sandwith).

Treatment.—The patient should remain in bed until after the temperature has become normal, and should be restricted to a milk diet. All alcoholic drinks should be interdicted, and the patient should be encouraged to drink freely of water. Intestinal antiseptics, such as calomel ($\frac{1}{20}$ gr.) in minute doses, salol, salicylate of bismuth, or β-naphthol, should be given. Copious enemas of water have been recommended. The treatment is on the same lines as that of catarrhal jaundice (*vide* p. 669).

DISEASES OF THE GALL-BLADDER

ABNORMALITIES.—**Absence** of the gall-bladder is the normal condition in the horse, mule, ass, elephant, and other animals. It is sometimes seen in man, and Gay [1] has collected 19 cases; but some of the older observations, such as those of Cholmeley [2] and Thomas,[3] were evidently cases of obliteration of the gall-bladder due to inflammation during fetal life. I have seen one case at St. George's Hospital in a man aged forty-nine who died from pulmonary tuberculosis (Latham [4]). Congenital absence of the gall-bladder has been associated with imperfect development of the pancreas and imperforate anus (Blakeway [5]). In genuine cases the common bile-duct is sometimes dilated in part of its course. The change has also been described after removal of the gall-bladder (Mayo Robson [6]).

Crucknell's [7] case, in which the common hepatic duct was described as opening into the gall-bladder and the common bile-duct as coming off separately from the gall-bladder, so that all the bile must have passed through the "gall-bladder," was probably a case of absence of the gall-bladder with compensatory dilatation and pouching of the upper end of the common bile-duct.

Two gall-bladders, each with a cystic duct, have been recorded in exceptional instances.

Purser [8] described an example in 1886 and referred to a case recorded in the Philosophical Transactions of 1693–4 in which there was a gall-bladder on the left lobe and another on the right lobe of the liver. Sherren [9] removed two gall-bladders placed side by side, each with a cystic duct, from a woman aged twenty-five.

Bifid Gall-bladder.—A longitudinal septum has been known to divide

[1] Gay. *Trans. Chicago Path. Soc.*, 1902, v, 108.
[2] Cholmeley. *Med. Trans. Roy. Coll. Phys.*, Lond., 1820, vi, 50.
[3] Thomas. *Med. Times*, 1848, xvii, 171.
[4] Latham. *Journ. Anat. and Physiol.*, 1898, xxxii; *Proc. Anat. Soc.*, p. xxxix.
[5] Blakeway. *Lancet*, Lond., 1912, ii, 365.
[6] Mayo Robson. *Brit. Med. Journ.*, 1906, i, 431.
[7] Crucknell. *Trans. Path. Soc.*, Lond., 1871, xxii, 163.
[8] Purser. *Brit. Med. Journ.*, 1886, ii, 1106.
[9] Sherren. *Ann. Surg.*, 1911, liv, 204.

the gall-bladder into two halves. A specimen (No. 1014) from King's College Hospital Museum is figured by Moynihan.[1]

Malposition.—In rare instances the gall-bladder is found to the left of the longitudinal fissure and on the under surface of the left lobe.

There is a specimen in the Anatomical Museum, Cambridge. Dévé[2] figures a case, and Walton[3] records it in a full-time female child.

In cases in which the left lobe is atrophied the gall-bladder appears to be attached to the left margin of the liver (*vide* Fig. 3), and may have its long axis at a right angle to that of the body.

In some instances the fundus of the gall-bladder is embedded in the substance of the liver, and may shew through on the anterior surface like a cyst in the substance of the right lobe. The notch at the anterior margin of the liver is absent in these cases. In exceptional instances the posterior surface of the gall-bladder may be covered over for some distance by a bridge of liver substance and justifies the term intra-hepatic gall-bladder (Dévé, Loughran,[4] Wieder[5]). A gall-bladder so situated would probably not contract so well as a healthy one, and would thus be disposed to infection and cholelithiasis. Lemon[6] recorded a gall-stone in an intrahepatic gall-bladder. Not very rarely there is a kind of mesentery to the gall-bladder so that it is unusually movable. Brewer[7] found that in 5 out of 100 bodies this mesentery was the only attachment of the gall-bladder to the liver. This would favour the occurrence of torsion of the gall-bladder, a very rare event; Nehrkorn[8] and Wendel[9] have recorded gangrene, and Lett,[10] strangulation of the gall-bladder due to torsion.

The gall-bladder has been found in the sac of a femoral hernia.[11]

Abnormalities in Size and Shape of the Gall-bladder.—Quite apart from inflammation or gall-stones the fundus of the gall-bladder, just where it projects beyond the anterior margin of the liver, may shew a constriction which resembles the pathological hour-glass gall-bladder. The projecting portion of the gall-bladder may be twisted like a fish-hook (Dévé). In rare instances fat is found under the peritoneal coat of the gall-bladder; it is of no pathological importance. Subserous oedema is sometimes present in cases of ascites, in the backward pressure of heart-disease, and occasionally when there is no associated pathological change.

[1] Moynihan. *Gall-stones and their Surgical Treatment*, p. 37, 1906.
[2] Dévé. *Bull. Soc. Anat.*, Paris, 1903, lxxviii, 261.
[3] Walton. *Lancet*, Lond., 1912, i, 925.
[4] Loughran. *Ibid.*, 1905, ii, 483.
[5] Wieder. *Univ. Penna. Med. Bull.*, Phila., 1905, xviii, 213.
[6] Lemon. *Lancet*, Lond., 1905, i, 1265.
[7] Brewer. *Ann. Surg.*, 1899, xxix, 721.
[8] Nehrkorn. *Deutsche Ztschr. f. Chir.*, Leipz., 1908, xcvi, 319.
[9] Wendel. *Ann. Surg.*, 1898, xxviii, 199.
[10] Lett. *Lancet*, Lond., 1909, i, 1099.
[11] Battle, *Trans. Clin. Soc.*, Lond., 1904, xxxvii, 245; Waring, *Diseases of the Liver*, 235, 1897.

ACUTE CHOLECYSTITIS

ACUTE CHOLECYSTITIS has various degrees of intensity; it may, like appendicitis, be catarrhal, suppurative, ulcerative, phlegmonous or gangrenous, according to the virulence of the infection and the resistance of the organ. Inflammation which at first is sero-fibrinous may subsequently become purulent, so that what is an acute serous cholecystitis at the outset may eventually present itself as an empyema of the gall-bladder. The causes of acute cholecystitis will first be considered generally, and then a separate description will be given of the acute catarrhal, suppurative, phlegmonous, and gangrenous forms.

Causes.—Acute inflammation of the gall-bladder is very closely bound up with the same process in the ducts, and from the point of view of causation it is rather an artificial distinction to describe these two conditions separately. Acute inflammation may begin in the ducts, as in suppurative cholangitis due to the rupture of an hydatid cyst into the ducts, and spread to the gall-bladder. In some instances an acute cholangitis may infect the gall-bladder, which eventually goes on to suppuration while the primary lesion resolves. On the other hand, acute inflammation may begin in the gall-bladder, as in typhoidal infection, and remain limited to it, or subsequently spread to the ducts. The conditions leading to acute cholecystitis, whether suppurative or not, are: (1) *Disposing*; (2) *exciting*.

I. **Disposing Causes.**—The factors which reduce the resistance of the gall-bladder and render it more liable to infection and inflammation are: (*a*) A previous attack of inflammation of the gall-bladder. Micro-organisms may remain in a latent condition, as in "typhoid carriers," and a relapse may be induced. Further, mild cholecystitis may lead to the formation of calculi.

(*b*) Calculi in the gall-bladder may, by their action, render infection more easy.

(*c*) The rare occurrence of foreign bodies, such as worms or the ova of parasites, in the gall-bladder would have a similar influence to calculi in the gall-bladder.

(*d*) Factors causing biliary obstruction favour the multiplication of any micro-organisms which have gained entrance to the gall-bladder, inasmuch as they are not flushed out, but remain in that viscus. These factors are discussed under the heading of Gall-stones (p. 713), and include sedentary habits, obesity, abdominal tumours, pregnancy, tight lacing, and other conditions which interfere with the descent of the diaphragm.

II. **Direct or Exciting Causes.**—(*a*) Infection of the gall-bladder; this is the cause of almost all the cases. (*b*) Toxins reaching the gall bladder and, in the absence of any micro-organisms, setting up cholecystitis. This is largely theoretical. (*c*) Trauma of the gall-bladder.

(A) Infection.—The infectious diseases which lead to local manifestations in the gall-bladder may be divided into two classes, which, however, to a certain extent, overlap: (1) Haemic infections. (2) Diseases of the alimentary canal.

(1) *In haemic infections*, such as pyaemia and septicaemia, micro-organisms may reach the gall-bladder, being excreted into its cavity and into the bile-ducts from the branches of the hepatic artery. Acute cholecystitis may follow pneumonia and be due to pneumococcic infection. In chronic Bright's disease terminal infections are not uncommon and may involve the gall-bladder. Acute cholecystitis apparently following influenza, but resolving, so that no proof of its nature can be obtained, is probably not very rare. Some of the cases of jaundice following influenza may shew cholecystitis, as well as inflammation of the ducts.

F. A. Packard [1] records a case of influenzal cholecystitis. A man aged forty was admitted under my care with the pains of influenza. He had had a sudden onset of vomiting and intense colic, like that of gall-stones. There was tenderness over the gall-bladder, which could not be felt, and the vermiform appendix, but there was no jaundice and no calculus could be found in the stools. He made a rapid recovery. The case appeared to be one of the gastro-intestinal form of influenza with cholecystitis.

(2) *In diseases of the alimentary canal* infection of the gall-bladder is due to the passage of micro-organisms, especially the colon and typhoid bacilli, from the bowel to the gall-bladder. Infection of the gall-bladder might be due to direct extension up the common bile-duct. In the case of typhoidal cholecystitis there are grounds for doubting this (*vide* p. 607). Under normal conditions the empty duodenum is sterile, or almost so; it is probable that in the absence of duodenal inflammation micro-organisms reach the gall-bladder by the portal vein rather than by direct extension up the common bile and cystic ducts. Influenza, in virtue of its gastro-intestinal form, comes into this group. The relations of appendicitis and cholecystitis with or without gall-stones are interesting. The two conditions may coexist (*vide* also p. 716); this has been frequently noticed in operations (Moynihan [2]). Evidence of this in routine post-mortem work is not striking: among 841 consecutive necropsies at St. George's Hospital Mr. Frankau found 50 cases of cholelithiasis or cholecystitis; in two of these, or 4 per cent, there was appendicitis. It is possible that in some cases both organs are attacked by a simultaneous infection; that in others appendicitis is primary and provides an inlet for micro-organisms which set up cholecystitis (Ochsner,[3] Sheldon [4]), or, lastly, that the cholecystitis is primary and the appendicitis secondary (Dieulafoy [5]). Cholera (Gal-

[1] Packard. *Phila. Med. Journ.*, 1899, iv, 879.
[2] Moynihan. *Lancet*, Lond., 1912, i, 9.
[3] Ochsner. *Phila. Med. Journ.*, 1900, vi, 652.
[4] Sheldon. *Journ. Am. Med. Assoc.*, Chicago, 1906, xlviii, 1458.
[5] Dieulafoy. *Presse méd.*, Paris, 1903, p. 445.

liard [1]), oral sepsis (Daniel [2]), and intestinal kinks (Lane [3]) have been thought to cause cholecystitis.

Cholecystitis due to Infection with Bacillus Coli.—This subject is of great importance in connexion with the production of gall-stones, and is referred to under that heading. Colon bacilli probably reach the gall-bladder mainly by the portal vein, but an ascending infection from the biliary papilla may occur when there is duodenitis. Infection of the gall-bladder may follow intestinal disorders in which the colon bacilli become virulent, or may be due to absorption of bacilli from an intestinal ulcer or an inflamed vermiform appendix.

Cholecystitis due to Typhoidal Infection.—That inflammation of the gall-bladder may complicate typhoid fever has been known since Louis' and Andral's time (1829). Budd,[4] Ayres,[5] and Pepper [6] recorded early cases. For good résumés of the history of typhoidal cholecystitis see A. L. Mason's [7] and Camac's [8] articles. Gilbert and Girode,[9] in 1890, first proved bacteriologically that suppurative cholecystitis may be due to typhoid bacilli. Numerous cases confirming this discovery have since been reported by Chiari [10] and others.

Cholecystitis during or after typhoid fever is not always due to infection with *Bacillus typhosus*. Thus, Cushing [11] met with 5 cases of post-typhoidal cholecystitis in which a pure culture of *B. coli* was obtained. There may be a mixed infection of *B. coli* and *B. typhosus*, as in Marsden's [12] case.

The incidence of cholecystitis in enteric fever is difficult to estimate, inasmuch as the slighter cases often escape detection. Sometimes palpation of the gall-bladder causes pain, but as there are no further symptoms it is impossible to speak with certainty as to the condition of affairs. Murchison [13] and Kelly's [14] observations are in favour of latent cholecystitis in enteric not being uncommon. It probably occurs clinically in less than 1 per cent of the cases. Camac collected 115 cases.

In 620 cases of enteric at Montreal tabulated by Stewart [15] there were 7 examples of cholecystitis, of which 1 (suppurative) was fatal. In 1016 cases of enteric fever admitted into the Imperial Yeomanry Hospitals in South Africa

[1] Galliard. *La Choléra*, Bibliothèque Charcot-Debove, 1894.
[2] Daniel. *Brit. Med. Journ.*, 1910, i, 121.
[3] Lane. *Ibid.*, 1912, i, 991.
[4] Budd. *Diseases of the Liver*, p. 195, 2nd ed., 1852.
[5] Ayres. *New York Journ. Med.*, 1846, vii, 315.
[6] Pepper, W., Sr. *Am. Journ. Med. Sc.*, 1857, N.S., xxxiii, 13.
[7] Mason, A. L. *Trans. Assoc. Am. Phys.*, 1897, xii, 23.
[8] Camac. *Am. Journ. Med. Sc.*, 1899, cxvii, 275.
[9] Gilbert et Girode. *Compt. rend. Soc. Biol.*, Paris, 1890, xlii, 756; *ibid.*, 1893, xlv, 956.
[10] Chiari. *Ztschr. f. Heilk.*, 1894, xv, 199.
[11] Cushing. *Johns Hopkins Hosp. Bull.*, Balt., 1898, ix, 91.
[12] Marsden. *Med. Chron.*, Manchester, 1901, 3. s., iv, 269.
[13] Murchison. *Continued Fevers*, p. 634, 3rd ed., 1884.
[14] Kelly, A. O. J. *Am. Journ. Med. Sc.*, Phila., 1906, cxxxii, 446.
[15] Stewart, J. *Brit. Med. Journ.*, 1901, i, 1465.

during the War 1900–1901, 1 case only of cholecystitis was sufficiently marked to require operation or to be recognised beyond any doubt. Among 2864 patients with enteric in Philadelphia there were 18 cases of cholecystitis, or 0·62 per cent (Ashhurst [1]). Among 1500 cases of enteric fever at the Johns Hopkins Hospital there were 19 cases of cholecystitis, or 1·2 per cent (T. M'Crae [2]). In these 6000 cases there were 45, or 0·8 per cent, cases of cholecystitis.

Typhoidal cholecystitis usually occurs in young adults, but cases in girls of five, six, and ten years old have been recorded (Alexieff,[3] Mason,[4] Armstrong [5]). There is very considerable variation in the interval between the attack of typhoid fever and the cholecystitis. It may complicate the attack or may occur as long as fourteen or twenty years after (Camac). In some instances there is no history of typhoid fever (Cushing,[6] Richardson,[7] Kelly); so that there is primary typhoidal cholecystitis. Cholecystitis complicating typhoid fever is seldom associated with cholelithiasis; among Camac's 115 collected cases of typhoidal cholecystitis there were 4 with gall-stones. The presence of gall-stones would dispose the gall-bladder to inflammation should enteric fever supervene. Acute cholecystitis months or years after typhoid fever is more often associated with cholelithiasis. Typhoid "carriers" not uncommonly have gall-stones which no doubt favour persistence of the bacilli in the gall-bladder; a vicious circle thus results.

The typhoid bacilli may conceivably reach the gall-bladder by several routes, viz. by the portal vein, the hepatic artery, the common bile-duct, or possibly even through the walls of the bowel.

By the Portal Vein.—The bacilli have but a short way to travel to reach the liver by the portal vein; here they set up focal necroses, and, having thus injured the liver tissue, are able to pass into the bile-ducts. Sherrington [8] shewed that bacilli alone, even though teeming in the blood, cannot pass through normal hepatic tissues, but that some previous damage by their toxins is necessary. Carmichael [9] also found that after injections of typhoid cultures into the portal vein the bile remains sterile. It is, however, not improbable that during typhoid fever the walls of the ducts or of the gall-bladder become damaged by toxins excreted from the blood-stream and so permeable to micro-organisms, and that typhoidal infection from the portal vein may then take place.

From the Hepatic Artery.—Typhoid bacilli are present in the general circulation during the incubation period and there is strong evidence that they pass directly from the circulation into the intrahepatic bile-ducts and so reach the gall-bladder, and may thus set up a descending cholecystitis. Doerr [10] finds

[1] Ashhurst. *Am. Journ. Med. Sc.*, Phila., 1908, cxxxv, 541.
[2] M'Crae, T. *System of Medicine* (Osler and M'Crae), 1907, ii, 137.
[3] Alexieff. Abstract in *Am. Journ. Med. Sc.*, 1897, cxiv, 466.
[4] Mason. *Trans. Assoc. Am. Phys.*, 1897, xii, 23.
[5] Armstrong. *Brit. Med. Journ.*, 1911, ii, 1298.
[6] Cushing. *Bull. Johns Hopkins Hosp.*, Balt., 1898, ix, 92.
[7] Richardson, M. *Am. Journ. Med. Sc.*, Phila., 1898, cxv, 648.
[8] Sherrington. *Journ. Path. and Bacteriol.*, Lond., 1893, i, 258.
[9] Carmichael. *Ibid.*, 1903, viii, 276.
[10] Doerr. *Centralbl. f. Bakt.*, 1905, xxxix, 624 (Orig.).

that experimental injection of typhoid bacilli into the systemic veins is followed by the presence of bacilli in the bile, and as section of the cystic duct prevents the appearance of bacilli in the gall-bladder, and section of the common bile-duct does not have this effect, Doerr concludes that the bacilli enter the bile in the liver.

By Direct Extension up the Common Bile-duct.—The motile typhoid bacilli might readily travel from the duodenum up the common bile-duct and reach the gall-bladder. An ascending infection of the gall-bladder from the duodenum was formerly accepted. Cushing and Livingood,[1] however, in experiments on the bacteriology of the duodenum, find that it is often sterile when empty, while the lower portion of the small intestine contains numerous micro-organisms. This would render an ascending infection of the ducts improbable. Again, if typhoidal cholecystitis were an ascending infection, other micro-organisms, such as the *Bacillus coli* or streptococci, would probably be present, and the pancreas should be as often affected as the bile-duct. On these grounds it is unlikely that the infection in typhoidal cholecystitis is an ascending one.

It has been suggested that *micro-organisms pass directly through the walls of the intestine* into the peritoneal cavity and then through the walls of the gall-bladder. This may take place when both the viscera concerned are inflamed and so allow of the passage of micro-organisms through their walls ; in this way a secondary infection of the gall-bladder when already inflamed may be brought about, but it is highly improbable that the gall-bladder is primarily infected in this way.

The typhoid bacilli are probably derived from the blood in the liver and pass down the ducts into the gall-bladder. The gall-bladder constantly contains typhoid bacilli in fatal cases of typhoid fever, and commonly in pure culture ; this contrasts with the comparative infrequency of cholecystitis. As shewn by Thiroloix and Debré's[2] experiments, some additional factor, such as trauma, previous disease, gall-stones, or extreme stagnation of bile, is necessary to enable the bacilli to set up cholecystitis.

Bacteriology of Cholecystitis.—Besides the colon and typhoid bacilli, paratyphoid bacilli (Cecil[3]), streptococci, staphylococci, pneumococci, Friedländer's pneumobacillus (Clairmont[4]), *Micrococcus melitensis* (Bull and Gram[5]), may give rise to cholecystitis. The *Diplococcus pneumoniae* may attack the gall-bladder primarily, there being no pulmonary or other manifest lesions. Pneumococcic cholecystitis is usually more acute and severe than that due to colon or typhoidal infection. Mignot[6] found that there was no remarkable anatomical difference in experimental cholecystitis due to streptococci, staphylococci, or the colon bacillus. Secondary infections may occur, so that typhoid bacilli, streptococci, staphylococci, etc., may be found together. From operation cases of pyopneumocholecystitis Pende[7] cultivated *Bacillus aerogenes capsulatus* as

[1] Cushing and Livingood. *Johns Hopkins Hosp. Rep.*, Balt., 1900, ix, 543.
[2] Thiroloix et Debré. *Rev. de méd.*, Paris, 1908, xxviii, 401.
[3] Cecil. *Arch. Int. Med.*, Chicago, 1910, v, 510.
[4] Clairmont, P. *Wien. klin. Wchnschr.*, 1899, xii, 1068.
[5] Bull og Gram. *Norsk Mag. f. Laegevidensk.*, Christiania, 1911, lxxii, 1026.
[6] Mignot. *Thèse de Paris*, 1897. [7] Pende. *Policlin.*, Roma, 1907, xiv, 540.

well as other organisms. In primary typhoidal cholecystitis the inflamed gall-bladder may become adherent to adjacent intestinal coils, and the tissues being inflamed, micro-organisms may pass from the bowel into the gall-bladder.

Wunschheim [1] records a case bearing this interpretation. In a fatal case of typhoid fever the gall-bladder contained pus and typhoid bacilli, while the peritoneal lymph on the surface of the gall-bladder shewed the *Staphylococcus pyogenes aureus*, which was regarded as a secondary infection from the intestine.

(B) Toxic Cholecystitis. — Although, practically speaking, acute cholecystitis is always due to bacterial infection of the gall-bladder, it has been shewn by Wakeman's [2] and Claude's [3] experiments that chemical and bacterial poisons are capable of inducing changes allied to inflammation in the gall-bladder.

Wakeman injected strong solutions of perchloride of mercury, carbolic acid, and ricin into the gall-bladders of dogs under antiseptic precautions, and produced considerable epithelial proliferation and desquamation, congestion of the vessels of the submucosa, and thickening of the walls of the gall-bladder. The amount of cholesterin in the bile was increased, but no calculi were formed. In 82 animals poisoned with abrin or with the toxins of diphtheria, tetanus, streptococci, staphylococci, *Bacillus coli*, and *Bacillus pyocyaneus*, Claude found haemorrhages into the gall-bladder in 7.

On the analogy of toluylenediamine, which sets up an inflammation of the small ducts in the liver which may spread down into the duodenum (Hunter [4]), it is reasonable to assume that toxic inflammation of the small bile-ducts in man might extend into the gall-bladder and set up acute cholecystitis. Such a toxic cholecystitis would probably soon become infected with micro-organisms from the blood-stream. As the matter stands, cholecystitis due to poisons, as apart from infection, is a theoretical possibility rather than an established occurrence in practice.

(C) Trauma, such as a fall or blow in the region of the gall-bladder, may so reduce its resistance that any micro-organisms present, which would otherwise be removed or destroyed, are enabled to set up inflammation. It is known, for example, that in typhoid fever the bacilli are always present in the gall-bladder, but that cholecystitis is comparatively infrequent. Trauma in such cases would be an exciting cause of cholecystitis. A blow may set up acute inflammation in cases in which a calculus is latent in the gall-bladder.

Kehr [5] reports the case of a doctor, who after being knocked down by a bicyclist, rapidly developed acute inflammation in a contracted gall-bladder, the

[1] Wunschheim. *Prag. med. Wchnschr.*, 1898, xxxiii, 13.
[2] Wakeman. Quoted by Herter, *Med. News*, N.Y., 1903, lxxxiii, 530.
[3] Claude. *Bull. Soc. Anat.*, Paris, 1896, lxxi, 502; *Med. Week*, Paris, 1897, v, 309.
[4] Hunter, W. *Trans. Path. Soc.*, Lond., 1890, xli, 105.
[5] Kehr. *Gall-Stone Disease*, p. 223, American translation, 1901.

cystic duct of which was blocked by a single calculus. Berger[1] reports two somewhat similar cases.

Forms of Acute Cholecystitis.—There are several forms of acute cholecystitis; the least severe is serous or catarrhal cholecystitis. In suppurative cholecystitis the gall-bladder is the site of an acute purulent inflammation. Midway between these two, and somewhat difficult to include in either, is simple chronic empyema of the gall-bladder, in which a chronic infection of the gall-bladder gives rise to the gradual formation of pus. This chronic suppurative cholecystitis is clinically more allied to dropsy of the gall-bladder, and is referred to again as one of the sequels of acute catarrhal cholecystitis (p. 613). The most severe forms of acute cholecystitis are the phlegmonous and gangrenous.

These three forms—catarrhal, suppurative, and phlegmonous—constitute an ascending series in the severity of the inflammation, but they merge into each other so that a distinction between any two of them may be difficult.

Acute Catarrhal Infective Cholecystitis

Under this heading are included acute inflammations of the gall-bladder which stop short of the production of pus. Different results of inflammation are here grouped together. In some instances there is only a serous exudation; in others it is sero-fibrinous, or ulceration may occur.

The causes of cholecystitis have already been described, and need not be recapitulated, but it may be pointed out that the less severe form (catarrhal) of acute cholecystitis may be produced by the same micro-organisms which, under more favourable conditions or when more virulent, set up suppurative inflammation; thus typhoidal infection of the gall-bladder may give rise to a simple serous cholecystitis or to a severe suppurative inflammation.

Morbid Anatomy.—The gall-bladder is distended and its walls are tense; the serous coat may be congested, dulled from the presence of fibrin, and adherent to adjacent parts. In severe cases the coats of the gall-bladder are swollen from infiltration and softened. The mucous membrane is congested, covered with mucus, and may be ulcerated or shew a deposit of bile on its surface. The cystic duct is often closed by swelling of its mucous membrane, or, as the result of past inflammation and ulceration due to the passage of a calculus, may be permanently obliterated. The cystic duct, however, is not necessarily closed. The contents of the gall-bladder may be practically clear and like serum when the cystic duct has been blocked for some time, or consist of sero-fibrinous or bile-stained turbid fluid. There may be gall-stones or inspissated bile. The lymphatic glands in relation to the cystic and common bile-ducts are enlarged. When recurrent attacks of acute cholecystitis occur the glands may become so hard as to imitate malignant infiltration, when felt during an operation. It has been urged that inflammation commonly

[1] Berger. *Arch. f. klin. Chir.*, 1907, lxxxiii, 7.

spreads from the gall-bladder to the pancreas by means of the lymphatics (Maugeret [1]).

Microscopically the villosities of the mucous membrane are prominent, and the epithelial cells are desquamating and contain myelin granules. The mucous glands in the walls are dilated and inflamed, and the vessels are engorged. The fibro-muscular layers are swollen and may shew small-celled infiltration.

Clinical Features.—Acute catarrhal cholecystitis probably varies a good deal in its severity in different cases and in different infections. Many of the slighter examples never come under observation, while others are entirely overlooked or are regarded as dyspepsia, colic, etc.; in many of these cases the symptoms are not sufficiently marked to allow of accurate diagnosis. Acute cholecystitis is very likely to escape detection when it occurs in typhoid fever. The abdominal signs, pain, etc., may be thought to be due to the original disease, and the patient, from mental torpor, may not complain of pain in the region of the gall-bladder. The frequency with which the gall-bladder is found to be adherent to the stomach or colon without any evidence of chronic inflammation supports the belief that acute cholecystitis is by no means uncommon. Another argument is that gall-stones are usually due to a past attack of cholecystitis and that in many cases of cholelithiasis there is no history of such an acute attack.

The signs and symptoms of acute cholecystitis are by no means constant, and in this respect the clinical picture of acute cholecystitis resembles that of appendicitis.

In a well-marked case the earliest and most prominent symptoms are local pain and tenderness. The character of the pain may vary: in most instances it is paroxysmal and resembles that of gall-stone colic, but is less excruciating. The pain is probably due to spasmodic contractions of the gall-bladder. In a case recorded by Solieri [2] the biliary colic was thought to be due to blood-clot in the gall-bladder. The pain may be continuous from inflammation of the serous coat and dull. It may shoot down into the right iliac fossa and be so definitely localised there as to suggest appendicitis. This has been thought to be due to peritoneal adhesions between the gall-bladder and the appendix (Tripier and Paviot [3]). It is not surprising that cases of cholecystitis are often diagnosed and operated upon as appendicitis. Cholecystitis and appendicitis may coexist (*vide* p. 604).

There is tenderness over the upper right quadrant of the abdomen, which becomes localised and more intense at the so-called biliary point below the tip of the ninth costal cartilage. Cutaneous hyperaesthesia may be present in the eighth and ninth dorsal segments (Head [4]); Elsberg and Neuhof [5] found it in 18 out of 21 cases. There is rigidity

[1] Maugeret. *Thèse de Paris*, 1908. [2] Solieri. *Rev. de chir.*, Paris, 1911, xliii, 482.
[3] Tripier et Paviot. *Semaine méd.*, 1903, xxiii, 29.
[4] Head. *Brain*, Lond., 1893, xvi, 76.
[5] Elsberg and Neuhof. *Am. Journ. Med. Sc.*, Phila., 1908, cxxxvi, 690.

of the upper part of the rectus muscle and of the costal arch on the right side. Monsarrat [1] insists on the shallow jerky respiration in acute cholecystitis. The gall-bladder may be felt and sometimes seen as a pear-shaped tumour, fluctuating or tense, which usually moves with respiration and can be displaced laterally like a pendulum. It may, however, be fixed by old adhesions. The distension of the gall-bladder is due to inflammatory exudation which cannot escape because the cystic duct is occluded by swelling of the mucosa. As the inflammation subsides, the fluid discharges through the cystic duct and the tumour disappears. There may be distinct tenderness, but no palpable tumour, in the position of the gall-bladder, which is concealed by intestines in a condition of paralytic distension due to peritonitis spreading from the gall-bladder. From this tympanitic distension the right hypochondrium and epigastrium may become somewhat prominent.

Halsted [2] recorded a case in which sharply localised paralytic dilatation of the first part of the duodenum and pyloric end of the stomach, corresponding to circumscribed peritonitis, was found at an operation for gall-stones. The paralysed bowel was glued to the gall-bladder by recent exudation. The walls of the gall-bladder were white and thickened, and its cavity contained fluid like white of egg.

Local peritonitis around the gall-bladder often sets up vomiting, and acute intestinal obstruction may arise (Robson,[3] Richardson [4]) from paralysis probably of the hepatic flexure of the colon. The symptoms usually pass off without surgical interference.

The liver is not enlarged unless the inflammation has spread to the ducts, and so into the organ. Elongation of the lower part of the right lobe covering the gall-bladder (Riedel's lobe) is met with as the result of gall-stones and past or chronic cholecystitis, and so might be present when an acute attack supervenes in these conditions. Jaundice is not a necessary accompaniment of cholecystitis; Kehr,[5] indeed, emphasises its rarity. It may depend on an extension of inflammation and spasm to the ducts or on the presence of some obstruction in the ducts. In the mild degrees of serous and catarrhal cholecystitis the temperature is usually normal. But if the inflammation is severe or extends to the ducts or to the peritoneal coat of the gall-bladder, there may be fever, sometimes of such a degree as to suggest suppuration, which, however, as shewn by operation, is not present.

In rare instances micro-organisms absorbed from the gall-bladder may give rise to appendicitis (Dieulafoy [6]), endocarditis (Lorrain [7]), or infection of the urinary tract with *B. coli*.

[1] Monsarrat. *Practitioner*, Lond., 1908, lxxx, 775.
[2] Halsted. *Johns Hopkins Hosp. Bull.*, Balt., 1900, xi, 1.
[3] Mayo Robson. *Med.-Chir. Trans.*, Lond., 1895, lxxviii, 117.
[4] Richardson. *Boston Med. and Surg. Journ.*, 1899, cxli, 662.
[5] Kehr. *Diagnosis of Gall-stone Disease*, p. 39, American translation, 1901.
[6] Dieulafoy. *Presse méd.*, Paris, 1903, p. 445.
[7] Lorrain. *Bull. Soc. Anat. Paris*, 1903, lxxviii, 527.

Diagnosis.—An enlarged gall-bladder must be distinguished from a floating kidney, hydronephrosis, renal tumour, and impacted faeces in the colon. Recurrent attacks of cholecystitis with distension of the gall-bladder may imitate intermittent hydronephrosis with Dietl's crises. The differential diagnosis of a distended gall-bladder from other conditions is given on p. 745.

The diagnosis from *suppurative cholecystitis* may be difficult, as no hard-and-fast line separates the more acute cases of cholecystitis without actual pus formation from the slighter cases of suppurative cholecystitis. Acute cholecystitis may be the early stage of the suppurative form. Clinically the difference between acute catarrhal and suppurative cholecystitis is one of degree, the pain, tenderness, and constitutional symptoms being much more marked in the latter.

From *biliary colic*, which is probably always accompanied by some cholecystitis, the diagnosis may also be very difficult. The pain is more excruciating in gall-stone colic, while the signs of local mischief, such as tenderness, paralytic distension of the intestines, or a palpable gall-bladder, are more prominent in acute cholecystitis.

The milder cases of acute cholecystitis are sometimes secondary to acute cholangitis by extension; in such cases the aspect of the disease is that of catarrhal jaundice, the existence of cholecystitis being determined only by tenderness over the gall-bladder, which may, perhaps, be palpably enlarged.

A mistake which is very easily made is to regard as *appendicitis* a case of cholecystitis, especially when the gall-bladder is dilated or so elongated as to reach the right iliac fossa, or when the right lobe of the liver is prolonged into a Riedel's lobe. Peritoneal adhesions between the two organs, to some extent, explain why in some cases of cholecystitis the pain is referred to the position of the vermiform appendix. A palpable tumour with a rounded edge directed upwards points to appendicitis; a tumour continuous with the liver dulness with a rounded edge below points to cholecystitis. It is much less often that the converse mistake is made, and a case of appendicitis is regarded as cholecystitis. But when the vermiform appendix runs up so as to come into close contact with the right lobe of the liver or even the gall-bladder, appendicitis may imitate cholecystitis very closely. It should also be remembered that acute inflammation of the appendix and of the gall-bladder may coexist (*vide* p. 604).

Acute pyelonephritis on the right side, due to infection with *B. coli*, may exactly imitate acute cholecystitis. The presence of pus in the urine should point to the kidney. But here again there may be infection of both organs by *B. coli*.

Prognosis in the milder cases is good, and the inflammatory process tends to subside rapidly. It is, however, probable that gall-stones will result, and that recurrent attacks of acute cholecystitis and of pain resembling biliary colic may occur subsequently. In the more severe attacks the danger of ulceration and perforation must be faced,

and the prognosis is much the same as in acute suppurative cholecystitis.

Sequels.—Some cases of *serous distension* (hydrops) of the gall-bladder may be due to transient and mild infective cholecystitis, in which a calculus at the neck of the gall-bladder prevents the exit of the inflammatory exudation through the cystic duct (Kehr [1]).

Chronic or Simple Empyema of the Gall-bladder.—Acute cholecystitis may become suppurative rapidly, so that the process is, for all practical purposes, suppurative cholecystitis throughout; or the symptoms of acute inflammation may pass off and be followed by a chronic infection which leads to a collection of pus inside the gall-bladder—simple or chronic empyema of the gall-bladder. These cases might be regarded as suppurative cholecystitis, but their clinical course is much more like hydrops or mucocele of the gall-bladder. They bear the same relation to acute suppurative cholecystitis that a chronic abscess does to an acute one. These cases may have a history of acute cholecystitis. Later there are abdominal pain, a tumour, malaise, loss of appetite, some wasting, and usually absence of fever. Simple empyema of the gall-bladder may intermit, the swelling passing away and then recurring.

In a man under my care gall-stones were associated with early primary carcinoma and chronic empyema of the gall-bladder. The temperature while under observation never rose above 99° F.

Ulceration of the gall-bladder may occur without any suppuration. In rare instances ulceration may lead to extensive haemorrhage.

A man aged thirty-five years, with slight jaundice, died from pneumonia and pericarditis. At the necropsy pressure on the gall-bladder, which was distended, caused practically pure blood to flow from the biliary papilla. The gall-bladder contained 2½ ounces of blood clot, its internal surface was intensely congested, shaggy, and there were some ulcers, one of which had eroded a vessel. Bacteriological examination of the gall-bladder shewed pneumococci. The kidneys weighed 3 ounces each, and were "contracted white." The liver shewed multilobular cirrhosis. The small intestines contained blood.

Acute cholecystitis may lead to *chronic cholecystitis*, which may take one of four forms (*vide* p. 624): (1) The atrophic sclerosing, with great thickening of the walls of the gall-bladder which ultimately contracts and becomes shrivelled up. (2) The catarrhal form, in which there is a distended gall-bladder containing thick, ropy mucus. Calculi are very prone to be produced by this process. (3) Chronic ulcerative. (4) Chronic empyema, described above.

Adhesions may form between the gall-bladder and the colon, pylorus, or duodenum, and give rise to "adhesion dyspepsia," pyloric stenosis, and dilatation of the stomach. These results are described under the morbid results of cholelithiasis (p. 758).

[1] Kehr. *Diagnosis of Gall-stones*, p. 32, American translation, 1901.

Treatment.—The patients should be kept in bed on a nourishing and easily digestible diet, and local pain treated by hot fomentations, dry cupping, or, if severe, by the application of leeches. If the pain is unbearable, morphine hypodermically may be necessary; but it masks the symptoms and should, therefore, be given with reluctance. Sickness should be controlled by effervescing draughts, bismuth, dilute hydrocyanic acid, chloretone (gr. v.) in a cachet, cocaine ($\frac{1}{10}$-grain), or by fractional ($\frac{1}{20}$-grain) hypodermic injections of morphine. In cases in which the temperature is high and there are signs of constitutional disturbance and the area of local peritonitis is increasing, surgical interference will probably be required. In milder cases urotropin and salicylate of sodium, or the combination of these drugs, saliformin, should be given, in order to disinfect the ducts and increase the flow of bile and so prevent extension of inflammation from the gall-bladder to the ducts. Solis-Cohen[1] recommends succinate of sodium, and Reichmann[2] methylene-blue ($\frac{1}{2}$–$1\frac{1}{2}$ grains) in capsules. A mild laxative should be given to keep the bowels open and to favour evacuation of the inflammatory contents of the gall-bladder. Vaccin treatment with *Bacillus coli* gave good results in 2 cases in which sinuses persisted after operations for gall-stones (Wright and Reid[3]). The after-treatment is that of the prophylaxis of gall-stones (*vide* p. 773).

Membranous Cholecystitis

Synonyms: Croupous Cholecystitis; Fibrinous Cholecystitis.

Inflammation of the gall-bladder may give rise to the formation of a cast of its cavity, which to the naked eye resembles the casts in mucous colitis (membranous colitis). As long ago as 1818 Richard Powell[4] described attacks of colic followed by jaundice in patients whose faeces contained membranes, but no calculi. Membranous cholecystitis, of which few cases are on record, is usually associated with gall-stones.

Cases of biliary colic accompanied by membranes in the stools have been described by Mayo Robson[5] and by P. C. Fenwick.[6] In one of Mayo Robson's cases 78 calculi were afterwards removed from the gall-bladder, and Fenwick's patient had almost certainly passed gall-stones previously. In a case operated upon at St. George's Hospital a fibrinous cast of the gall-bladder surrounding a single large calculus was found.[7] In a case operated upon by Moynihan[8]

[1] Solis-Cohen. *Proc. Phila. County Med. Soc.*, xxiii, 36.
[2] Reichmann. *Semaine méd.*, Paris, 1903, xxiii, 140.
[3] Wright and Reid. *Brit. Med. Journ.*, 1906, i, 143.
[4] Powell, R. *Med. Trans. Coll. Physicians*, Lond., 1820, vi, 106.
[5] Robson, Mayo. *Diseases of the Gall-bladder and Bile-ducts*, p. 79, 3rd ed., 1904.
[6] Fenwick, P. C. *Brit. Med. Journ.*, 1898, i, 1072.
[7] Rolleston. *Trans. Path. Soc.*, Lond., 1902, liii, 405.
[8] Moynihan. *Brit. Med. Journ.*, 1903, i, 186.

368 calculi were removed; and Bland-Sutton[1] mentions a case with calculi. In 2 cases mentioned by Walton[2] gall-stones were absent.

Microscopically in the case I examined there was a fibrinous network enclosing bile-pigment and hexagonal and quadrilateral crystals. In the outer layers of the cast there were round-cells, but no trace of the mucous membrane of the gall-bladder was found. The fibrinous structure differs entirely from the microscopic appearances of the casts passed in mucous colitis. Microscopical examination will distinguish it from sloughing of the mucous membrane of the gall-bladder.

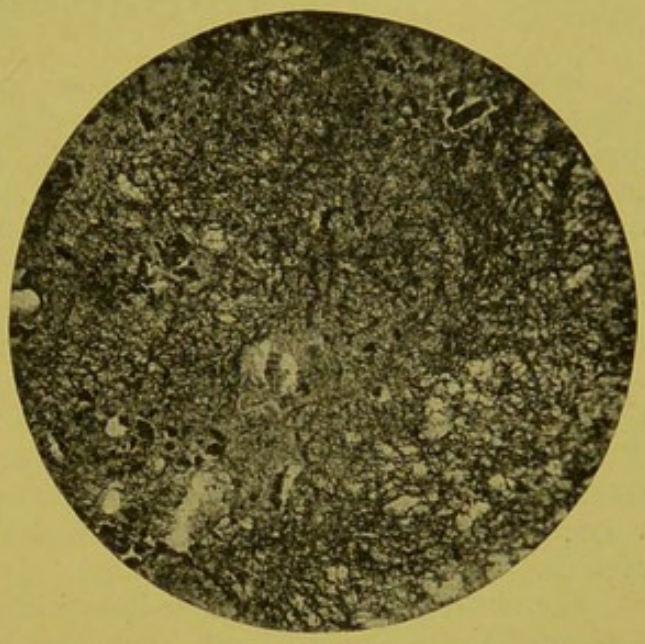


Fig. 82.—Photomicrograph of cast from the gall-bladder, shewing fibrinous network enclosing masses of black bile-pigment. (By Dr. S. G. Penny.)

Clinically the symptoms are those of gall-stone colic, from which it can be distinguished only by finding membranous casts instead of calculi in the motions. The condition may be found only when the gall-bladder is open in the course of an operation, as in the following case:

A woman aged fifty-two, who had never had jaundice or biliary colic, was seized with pain in the right side of the abdomen and vomiting on November 14, 1900. On admission two weeks later a tumour of stony hardness was found in the right iliac fossa, separated by a zone of resonance from the liver dulness. It was thought to be probably carcinoma of the colon. Laparotomy revealed a greatly enlarged gall-bladder with adhesions to adjacent parts. It contained a single gall-stone, rather bigger than a walnut, enclosed in a thick fibrinous sac about $\frac{1}{4}$ inch thick. The calculus and the cast were removed, but the gall-bladder was left. This envelope was quite distinct and easily separable from the lining of the gall-bladder. The microscopical appearances are described above (Fig. 82). The patient made a good recovery.

The *treatment* of an attack is the same as that of gall-stone colic, but if attacks recur, the gall-bladder should be opened and calculi removed. Moynihan considers that the gall-bladder should be removed, but it is doubtful if there are as yet sufficient grounds for this dictum.

Acute Haemorrhagic Cholecystitis is occasionally seen. The condi-

[1] Bland-Sutton. *Gall-stones and Diseases of the Bile-ducts*, p. 30, 1907.
[2] Walton. *Ann. Surg.*, 1911, liv, 176.

tion is one of acute infective inflammation and resembles the more severe forms of acute cholecystitis in its general connections, symptoms, and results.

Suppurative Cholecystitis

In this condition inflammation of the walls of the gall-bladder gives rise to an accumulation of pus in its cavity and may go on to ulceration and perforation. Two conditions have in common the production of pus inside the gall-bladder, but differ in their clinical course and aspects. In one—chronic empyema of the gall-bladder—pus is slowly formed within the gall-bladder, and its features are much the same as those of distension of the gall-bladder with mucous fluid (dropsy of the gall-bladder). In the other there is an acute suppurative inflammation. Except where specially stated, the following description refers to the latter condition. Chronic empyema is referred to on page 613. It is difficult to draw a hard-and-fast line between the less severe cases of acute suppurative cholecystitis and chronic empyema of the gall-bladder. When very acute, suppurative cholecystitis is described as phlegmonous cholecystitis.

The causes of suppurative cholecystitis are much the same as those of cholecystitis in general, and need not be repeated in detail. It is frequently associated with gall-stones. In 55 cases of suppurative cholecystitis collected by Courvoisier 41 were associated with cholelithiasis. Impaction of a calculus in the cystic duct or neck of the gall-bladder favours infection, as any micro-organisms reaching the gall-bladder by the blood-stream are retained and able to multiply. It is possible that in some cases of suppurative cholecystitis a calculus may have been previously expelled, but the presence of gall-stones is no more necessary than are enteroliths in appendicitis. Obstruction of the cystic or common bile-duct may act in a similar manner. Primary carcinoma of the bile-ducts may thus become complicated by suppurative cholecystitis.

Carcinoma of Cystic Duct; Round Worm in Common Bile-duct; Suppurative Cholecystitis.—A woman, aged forty-three, after long-continued and vague pains suggesting biliary colic, became intensely jaundiced, developed a high temperature, and died. There were gall-stones in the gall-bladder and suppurative cholecystitis due to a member of the colon group, primary carcinoma completely obstructing the cystic duct, and a dead lumbricoid worm in the common bile-duct, which, it was thought, had conveyed the infection (Étienne[1]). I have seen acute haemorrhagic cholecystitis associated with early carcinoma of the cystic duct.

Suppuration may spread into the gall-bladder from suppurative cholangitis due to various causes, such as the rupture of a hydatid cyst

[1] Étienne. *Arch. gén. de méd.*, Paris, 1896, clxxviii, 284.

into the ducts. In enteric fever suppurative cholecystitis may occur, but fortunately it is rare, and is not so often seen as catarrhal cholecystitis.

Among 620 cases of enteric fever observed during seven years at Montreal there was 1 case of suppurative cholecystitis.[1] In 2000 fatal cases at Munich tabulated by Hölscher there were 5 of cholecystitis with suppuration.[2] In 1016 cases of enteric fever treated during 1900–1901 in the Imperial Yeomanry Hospitals in South Africa there was 1 case of suppurative cholecystitis. Thus, among 3636 cases of enteric fever there were 7 cases of suppurative cholecystitis, or 0·2 per cent.

Morbid Anatomy.—The gall-bladder is usually enlarged, sometimes very considerably; but suppuration may occur in a gall-bladder shrivelled up and contracted from recurrent cholecystitis. The peritoneal coat is inflamed, granular from adherent lymph, and usually darkish-red or greenish-black in colour. It may be adherent by old fibrous adhesions to the parts around, or glued to them by recent lymph. Inflammation may thus spread to adjacent coils of intestine and cause paralytic distension. The wall of the gall-bladder is swollen from inflammatory exudation, softened, and friable. The mucous membrane is largely destroyed, the free surface shews granulation-tissue and is shaggy, red, and in places has flakes of adherent lymph. Microscopically there is extensive small-celled infiltration of the walls. Ulceration is commoner near the fundus, because calculi are more likely to gravitate there. The contents are bile-stained or sanious pus, and calculi are often present. In chronic empyema the wall of the gall-bladder is thickened from organisation of the inflammatory exudation.

Clinical Picture.—The signs and symptoms vary considerably. They may be local, and at first confined to the region of the gall-bladder, or general, from widespread infection of the peritoneum.

The local manifestations are pain, tenderness, increased resistance of the overlying rectus abdominis muscle and rigidity of the upper part of the right costal arch. In cases in which the abdominal muscles are extremely atrophied there may be no spasm or rigidity. The abdominal reflex may be impaired or absent on the right side (Jamin[3]). The gall-bladder may be palpable as a tense, pear-shaped tumour, in a line between the tip of the ninth rib and a point one inch below the umbilicus in the middle line (Mayo Robson). The gall-bladder varies in shape: when elongated, it may appear to be independent of the liver, since it may be separated from the liver dulness by a zone of resonant intestines. In a case of pyopneumocholecystitis, in which the gall-bladder communicated with the colon, the gall-bladder formed a large tympanitic tumour (Pende[4]). A somewhat similar case in which there was a

[1] Stewart, J. *Brit. Med. Journ.*, 1901, i, 1463.
[2] Hölscher. *München. med. Wchnschr.*, 1891, xxxviii, 43.
[3] Jamin. *Deutsche med. Wchnschr.*, 1904, xxx, 1088.
[4] Pende. *Policlin.*, Roma, 1907, xiv, 540.

communication with the duodenum is mentioned by Mayo Robson.[1] When suppuration occurs in a gall-bladder already considerably distended, the tumour may be palpable in the right iliac fossa and may suggest appendicitis. In such cases the right lobe of the liver is often elongated (Riedel's lobe). In exceptional instances the gall-bladder is found in the middle line of the abdomen. When there is local peritonitis around the gall-bladder, intestinal paralysis and distension may prevent its being felt, but the hypochondrium will be prominent and exquisitely tender. In other cases rigidity of the abdominal muscles prevents the gall-bladder from being made out, unless the examination is made under an anaesthetic. In many instances the gall-bladder is contracted from past inflammation, and though acutely inflamed and containing pus, does not project beyond the margin of the right lobe.

Pain is constant, as a rule; but exacerbations of great severity resembling biliary colic may occur, and its intensity varies considerably in different cases. It is usually felt in the right hypochondrium or pit of the stomach, but may be referred to the right iliac region. The temperature is raised and may be high, and be accompanied by rigors. The pulse is rapid (100–120). An increasing pulse-rate calls for operative interference. There may be vomiting, from the irritation of the peritoneum around the gall-bladder, and the local peritonitis thus produced may spread to neighbouring coils of the small intestines, or to the hepatic flexure of the colon, and lead to paralysis of the bowel and so to the symptoms of intestinal obstruction. Jaundice is very commonly absent, and when present is usually slight. It may be due to extension of inflammation into the common bile or hepatic ducts, or to definite causes of biliary obstruction, such as gall-stones or tumours involving the extra-hepatic bile-ducts. It has been suggested that when the mucous membrane of the gall-bladder is ulcerated, bile may be absorbed from the gall-bladder, and that slight icterus in the early stages of suppurative cholecystitis, before the cavity becomes filled with pus, may be due to this cause, but this is unlikely.

The spleen is occasionally enlarged. Albuminuria may be present in severe cases, and is due to the local action on the renal epithelium of poisons absorbed from the gall-bladder; in very rare cases temporary toxic glycosuria may appear (Mansell Moullin [2]). There is leucocytosis of from 15,000 to 30,000; when the infection is a pure culture of *B. typhosus*, leucocytosis has been said not to occur (Findlay and Buchanan [3]); but M'Crae [4] found a count of from 10,000 to 15,000. According to Libman,[5] blood-cultures are negative unless there is also cholangitis. In rare instances there is pus in the urine from a concomitant infection of the renal pelvis with *B. coli*. In severe cases there may be nothing to indicate that the gall-bladder is the organ at fault, the symptoms being

[1] Robson, Mayo. *System of Medicine* (Allbutt and Rolleston), 1908, iv, part i, 244.
[2] Mansell Moullin. *Lancet*, 1907, i, 1645.
[3] Findlay and Buchanan. *Glasgow Med. Journ.*, 1906, lxv, 189.
[4] M'Crae. *System of Medicine* (Osler and M'Crae), 1907, ii, 137.
[5] Libman. *Am. Journ. Med. Sc.*, Phila., 1908, cxxxvi, 548.

those of general peritonitis or intestinal obstruction, and thus imitating those due to perforation of the intestine or appendix. If operation is delayed, the localising symptoms present in an early stage become masked by general peritonitis.

Complications and Results.—The chief danger is perforation into the general cavity of the peritoneum and fatal peritonitis.

Keen[1] collected 31 examples of perforation due to typhoidal cholecystitis; of these, 26 were not operated upon and all proved fatal; 5 were operated upon, with 3 recoveries.

Perforation of the gall-bladder may lead to a local peritoneal abscess instead of to general peritonitis. The formation of a local abscess is favoured by the presence of previous peritoneal adhesions shutting off the cavity of the general peritoneum. The abscess may imitate other forms of local abdominal suppuration, such as a subdiaphragmatic abscess due to disease of the stomach, duodenum, or pancreas, or malignant disease of the gall-bladder (Tuffier[2]). The abscess may discharge into the stomach, duodenum, colon, or penetrate the diaphragm and cause an empyema or a broncho-biliary fistula; or it may open through the skin close to the costal arch or at the umbilicus. In rare instances the abscess may communicate with the pelvis of the right kidney, or even the bladder or vagina. A suppurating gall-bladder may ulcerate directly into the liver and give rise to an abscess continuous with the cavity of the gall-bladder.

Weir[3] records the case of a woman aged thirty-five whose gall-bladder contained 3 ounces of pus. Ulceration on the anterior wall of the gall-bladder led into an abscess in the liver containing more than an ounce of pus. A woman aged fifty-three died in St. George's Hospital with multiple recurrent growths after removal of the mamma; the cystic duct was blocked by a calculus; the gall-bladder contained pus and communicated by two openings with a small abscess in the liver. Suppuration in a gall-bladder deeply embedded in the liver substance, the so-called intrahepatic gall-bladder (*vide* p. 602), would imitate hepatic abscess.

Concomitant suppurative cholangitis may lead to multiple areas of suppuration in the liver; these readily infect the hepatic veins, induce secondary abscesses in the lungs, which may burst into the pleura and set up empyema. Profuse haemorrhage into the gall-bladder from ulceration of the vessels is very rare; jaundice increases the tendency to haemorrhage.

Appendicitis may complicate suppurative cholecystitis, and in operating on cholecystitis the condition of the appendix should be investigated, as in such a case death may subsequently occur from perforation of the

[1] Keen. *Complications and Sequels of Typhoid Fever*, pp. 249, 325, 1898.
[2] Tuffier. *Bull. et mém. Soc. de chir. de Paris*, 1911, xxxvii, 1343.
[3] Weir. *Med. Rec.*, N.Y., 1900, lvii, 1137.

appendix. The cholecystitis may be secondary to infection from the appendix or *vice versa* (Dieulafoy [1]).

Diagnosis.—Before perforation has occurred suppurative cholecystitis resembles other forms of local peritonitis in the neighbourhood, such as might be set up by a duodenal ulcer before perforation, by a localised subphrenic pneumothorax, or to an abnormally situated appendicitis. In addition to the signs of local peritonitis the presence of a tumour moving with respiration in or near the situation of the gall-bladder is an important indication of cholecystitis. Absence of jaundice does not militate against the existence of cholecystitis, though the history of past attacks of biliary colic with transient jaundice strengthens the diagnosis.

In duodenal ulcer there should be a history of pain about two hours after food, but, unfortunately, the ulcer may remain latent until it perforates and sets up general or localised peritonitis. There may be considerable resemblance between the two conditions; I have seen two cases in which perforating duodenal ulcer was diagnosed as cholecystitis; and adhesions between the gall-bladder and the duodenum, due to an ulcer, may present a very puzzling problem in diagnosis (Hinder [2]).

A localised subphrenic abscess due to perforation of a gastric ulcer hardly ever imitates suppurative cholecystitis, as the abscess is nearly always gaseous (a subphrenic pyopneumothorax); but in the following case the absence of resonance led to an open diagnosis:

A woman aged twenty-eight years had sudden pain on Nov. 14, 1900. She came up to St. George's Hospital on Nov. 16, with a firm mass, tender and dull on percussion, in the position of the gall-bladder. She had no jaundice, and there was no history of gall-stone colic, but she had previously had some dyspeptic pain one hour after food. The pulse was 140, and the patient's face indicated grave abdominal mischief. The diagnosis lay between suppurative cholecystitis and a local abscess due to perforated gastric ulcer. Operation revealed a localised peritoneal abscess due to perforation of a gastric ulcer close to the pylorus.

An elongated and distended gall-bladder may project into the right lower half of the abdomen and simulate appendicitis; as already mentioned, this condition is frequently associated with an elongated right lobe of the liver. Cases of cholecystitis are not infrequently regarded as appendicitis; the converse mistake is much rarer. The differential diagnosis is very difficult, as both these conditions vary so much in their clinical manifestations (*vide* p. 612). As pointed out above, cholecystitis and appendicitis may coexist. Occasionally pneumonia or pleurisy at the right base may imitate acute cholecystitis. The resemblance of a suppurating gall-bladder to a right pyonephrosis may be extremely close.

When perforation of a suppurating gall-bladder sets up general peritonitis, the diagnosis must be made from other forms of peritonitis, especially that due to fulminating appendicitis, which it often closely

[1] Dieulafoy. *Presse méd.*, Paris, 1903, p. 448.
[2] Hinder. *Trans. viii. Australasian Med. Congress*, 1909, i, 317.

resembles inasmuch as the pain may be referred to the right iliac fossa, probably because the contents of the gall-bladder may travel down into the region of the appendix. The history may be of help in forming an opinion, but in either case immediate operation is essential. When the abdomen is opened the character of the exudate may indicate the perforated viscus; thus bile or calculi will direct attention to the gall-bladder; an acid reaction or gas, to perforation of the stomach or duodenum.

Prognosis.—There is little tendency to spontaneous cure by the discharge of the purulent contents through the cystic duct and subsidence of the inflammatory process, since in most cases the cystic duct is blocked or obstructed. This may be due to various factors, such as an impacted calculus, the contraction of cicatricial fibrous tissue, either as the result of past ulceration or from pericholecystic adhesions, or to new growth involving the duct. When the obstruction of the cystic duct depends on swelling of the mucous membrane, due to the spread of inflammation from the gall-bladder, it is possible that the purulent contents may be expelled through the duct. When the progress is less acute, pus may be formed in the gall-bladder and may remain confined there; this is chronic empyema of the gall-bladder. But in acute suppurative cholecystitis the inflammatory process spreads through the walls of the gall-bladder, infects the surrounding peritoneum, and leads to local or general peritonitis. In these circumstances, therefore, the prognosis is grave unless operative interference is invoked before more widespread infection has set in. A local abscess may be treated surgically very successfully, but if general peritonitis has supervened the outlook is very gloomy.

Treatment.—The proper treatment of suppurative cholecystitis and of the more chronic condition, empyema of the gall-bladder, is surgical and consists in opening the gall-bladder and draining it, or, if it appear necessary, removing it. Exploratory puncture through the abdominal walls with a syringe is dangerous, and should never be countenanced. The palliative or medical treatment is the same as in acute cholecystitis.

Phlegmonous Cholecystitis

This is a very acute infective form of cholecystitis, and differs only in degree from the acute suppurative form just described. It passes into gangrenous cholecystitis, from which again it can hardly be separated; in fact, gangrene is merely a result of phlegmonous cholecystitis.

It may supervene on the same conditions as suppurative cholecystitis, such as cholelithiasis, typhoidal cholecystitis (Schlier,[1] Wunschheim,[2]), and is due to a very virulent infection.

Incidence.—Comparatively few cases are on record, but probably many cases described as acute suppurative cholecystitis might be included under this heading. Courvoisier, who first described it as acute pro-

[1] Schlier. *Deutsch. Arch. f. klin. Med.*, 1891, xlviii, 441.
[2] Wunschheim. *Prag. med. Wchnschr.*, 1898, xxiii, 13.

gressive empyema of the gall-bladder, collected 7 cases; Mayo Robson[1] added 5 more; Wright[2] met with 3 cases in a few years.

Morbid Anatomy.—The changes are the same as in acute suppurative cholecystitis, but more extensive and acute. The outside of the gall-bladder is purple, oedematous, and inflamed with adherent lymph. The walls are swollen, friable, and infiltrated with pus and blood; the mucous membrane is swollen, and may be ulcerated, necrosed, or be separated in flakes from the underlying coats. The gall-bladder contains pus and often gall-stones. The cystic duct is closed and may be blocked by a calculus.

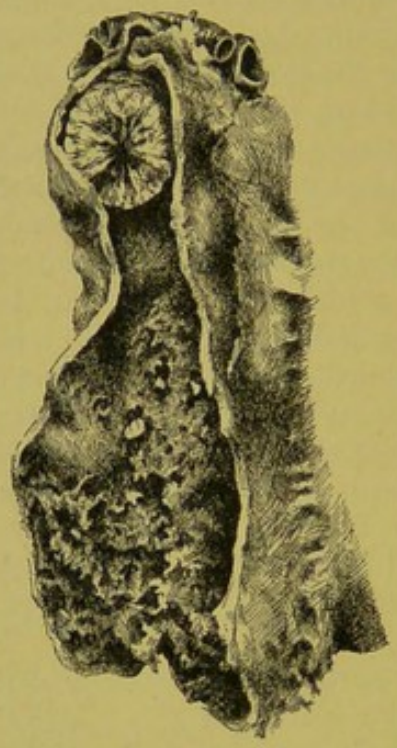


FIG. 83.—Gall-bladder with a large calculus in its neck. Phlegmonous inflammation passing into gangrene. (Drawn by Dr. E. A. Wilson.)

Clinical Features.—Symptoms set in suddenly with pain in the region of the gall-bladder. The peritoneum early becomes involved, at first locally, but soon peritonitis becomes generalised, unless there are firm adhesions around the gall-bladder.

Jaundice may be present from concomitant inflammation of the ducts, but it is inconstant, and therefore of no great diagnostic value. The results are marked toxaemia, peritonitis, ulceration, sloughing, perforation, and gangrene of the gall-bladder, leading to localised or generalised peritonitis.

The **diagnosis** depends on evidence of acute inflammation in the region of the gall-bladder in a patient whose history points to past cholecystitis. In some cases there may only be evidence of general peritonitis with or without the history that it followed localised inflammation in the right upper quadrant of the abdomen. When there is more or less localised inflammation of the peritoneum in the right upper half of the abdomen, the differential diagnosis is the same as in other forms of cholecystitis, to which the reader should refer. It may be very difficult when general peritonitis is established to make out whether it is due to fulminating appendicitis or to cholecystitis. Perforation of a gastric or duodenal ulcer, acute intestinal obstruction, or acute pancreatitis, may be imitated. The accurate diagnosis of phlegmonous cholecystitis is extremely difficult; this is shewn by the following case, in which there was a transition from phlegmonous to gangrenous cholecystitis.

A woman aged sixty-three was admitted into St. George's Hospital with a history of constipation for three days and of more acute symptoms and vomiting

[1] Robson. *Diseases of the Gall-bladder*, p. 90, 1904; *Brit. Med. Journ.*, 1903, i, 189.
[2] Wright, G. A. *Lancet*, Lond., 1906, ii, 795.

for twenty-four hours. The sac of an umbilical hernia which she had had for three years was opened, and was found to contain adherent omentum, coils of small intestine, and a piece of the colon. The bowel, which was not strangulated, was returned. She died thirty hours after the operation. At the necropsy there was general peritonitis. The gall-bladder was adherent to the colon, and contained several gall-stones in the fundus ; its mucous membrane was ulcerated and necrotic, especially on the anterior surface of the gall-bladder. A large calculus, impacted in the neck of the gall-bladder, occluded the commencement of the cystic duct (*vide* Fig. 83).

The **prognosis** is very grave, as the disease may prove fatal in a few days, the process being so virulent that infective peritonitis is rapidly set up. The disease is too acute to allow adhesions capable of localising the infection to be formed.

The **treatment** is generally that of perforative peritonitis, and though the pain may be relieved by hot fomentations and the hypodermic injection of morphine, the only satisfactory measure is laparotomy and removal of the gall-bladder. Morphine should not be given until the diagnosis is made, as it masks the symptoms.

Gangrenous Cholecystitis

Synonym : Gangrene of the Gall-bladder.

In extremely rare instances gangrene of the gall-bladder is due to torsion (Nehrkorn,[1] Wendel[2]). As a rule, it is a further stage, or rather a result, of the very acute infective or phlegmonous inflammation of the gall-bladder just described ; and, as already pointed out, no rigid distinction can be drawn between them. The transitional cases with small areas of necrosis in the gall-bladder may be spoken of as partial gangrene, as in Donoghue's[3] case. It stands in the same relation to cholecystitis that gangrenous appendicitis does to other forms of inflammation of the appendix, but is rare, whereas gangrenous appendicitis is common. It seems probable that the comparative rarity of gangrene of the gall-bladder may in part be explained by its better blood-supply and by the fact that it is not prone, like the appendix, to be twisted on its own axis and its blood-supply thus interfered with. The factors which bear on the production of gangrene are : a highly virulent infection, interference with the blood-supply, such as thrombosis or constriction, and obstruction of the cystic duct whereby drainage is prevented and tension produced.

Incidence.—It is not nearly so rare as was formerly thought, and probably some cases have been described merely as very severe cholecystitis.

[1] Nehrkorn. *Deutsche Ztschr. f. Chir.*, Leipz., 1908, xcvi, 319.
[2] Wendel. *Ann. Surg.*, 1898, xxvii, 199.
[3] Donoghue. *Am. Journ. Med. Sc.*, Phila., 1902, cxxiii, 193.

Cases have been reported by Hotchkiss,[1] Mayo Robson,[2] Mayo,[3] Gibbon,[4] Moynihan,[5] Körte,[6] Elsberg and Neuhof,[7] Lilienthal (7),[8] Bland-Sutton,[9] Waring,[10] and others.

The **morbid anatomy** is the same as in phlegmonous cholecystitis, with the addition of gangrene of the wall of the gall-bladder. The extent of the gall-bladder affected by gangrene varies, but it appears to begin at the fundus and spread towards the neck of the gall-bladder. The gangrenous walls are dark green in colour, extremely soft, and friable. In other cases there are scattered gangrenous patches.

The cystic duct is blocked, and there may be a calculus imbedded in the neck of the gall-bladder. Calculi are present in the gall-bladder in the vast majority of the cases.

The **clinical features** are the same as those of phlegmonous cholecystitis in a late stage—viz. general peritonitis. In fact, as already pointed out, gangrenous cholecystitis is the extreme stage of the phlegmonous form. In Gibbon's case there was a leucocytosis of 37,600, which fell to 12,600 in twenty-four hours after removal of the gall-bladder. In two cases the band of hyperaesthesia in the eighth and ninth dorsal segments was present (Elsberg and Neuhof). In a man with existing renal disease, gangrenous cholecystitis reflexly produced anuria and gave rise to a diagnosis of pyonephrosis (Elsberg and Neuhof).

The **diagnosis** is extremely difficult, and cannot be made from perforative peritonitis due to other lesions of the gall-bladder. It is very likely to be confused with peritonitis due to fulminating appendicitis.

The only **treatment** is surgical, and consists in removal of the gall-bladder (cholecystectomy). There should be no delay in operating on any case thought to be phlegmonous or gangrenous cholecystitis.

Chronic Cholecystitis

Chronic cholecystitis occurs in a number of forms, and there is considerable confusion in the nomenclature. Under the title *chronic catarrhal cholecystitis* Maccarty[11] describes a comparatively slight form in which the principal gross change is erosion of the apices of the papillae of the mucous membrane. The papillae appear as yellow specks, and from their resemblance to strawberry seeds the name "strawberry gall-bladder" has been employed. This condition is obviously different from the form

[1] Hotchkiss. *Ann. Surg.*, 1894, xix, 197.
[2] Mayo Robson. *Brit. Med. Journ.*, 1903, i, 181.
[3] Mayo, quoted by Gibbon.
[4] Gibbon. *Am. Journ. Med. Sc.*, Phila., 1903, cxxv, 592.
[5] Moynihan. *Brit. Med. Journ.*, 1903, i, 186.
[6] Körte. *Beiträge z. Chirurg. der Gallenwege u. der Leber*, S. 108, 1905.
[7] Elsberg and Neuhof. *Am. Journ. Med. Sc.*, Phila., 1908, cxxxvi, 690.
[8] Lilienthal. *Mt. Sinai Hosp. Rep.*, N.Y., 1907, v, 242.
[9] Bland-Sutton. *Gall-stones and Diseases of the Bile-ducts*, p. 29, 1907.
[10] Waring. *Clin. Journ.*, Lond., 1911, xxxviii, 33.
[11] Maccarty. *Ann. Surg.*, Lond., 1910, li, 651.

now to be described, which, however, has often been called chronic catarrhal cholecystitis, and is named chronic cholecystitis by Maccarty.

Causes.—It may be a legacy left by a past attack of acute cholecystitis, and is often associated with gall-stones. In other cases the process is probably chronic from the first, and may be disposed to by sedentary habits, constipation, tight lacing, and the other factors that favour infection of the gall-bladder. Chronic cholecystitis may be part of chronic catarrh of the ducts, and is then quite subordinate to that condition.

Morbid Anatomy.—The gall-bladder is usually somewhat distended with mucus, which may be so thick and tenacious as to resemble grains of boiled sago or aspic. It may or may not contain calculi; occasionally calculi are embedded in the walls of the gall-bladder (parietal calculi). There may be adhesions between the gall-bladder and adjacent organs, but they may be absent even when the gall-bladder contains calculi. The walls of the gall-bladder are thickened, and the inner surface is thrown into folds; but when the gall-bladder is distended as a result of a stone in the cystic duct, its walls are thin and smooth, and have a white, nacreous appearance. From contraction of inflammatory tissue the gall-bladder may become small and shrivelled up (cholecystitis obliterans). Secondary calcification of the walls sometimes occurs (Fig. 84). The cystic duct is often quite pervious. There may be chronic pancreatitis which may be due to infection by the lymphatics (Maugeret[1]).

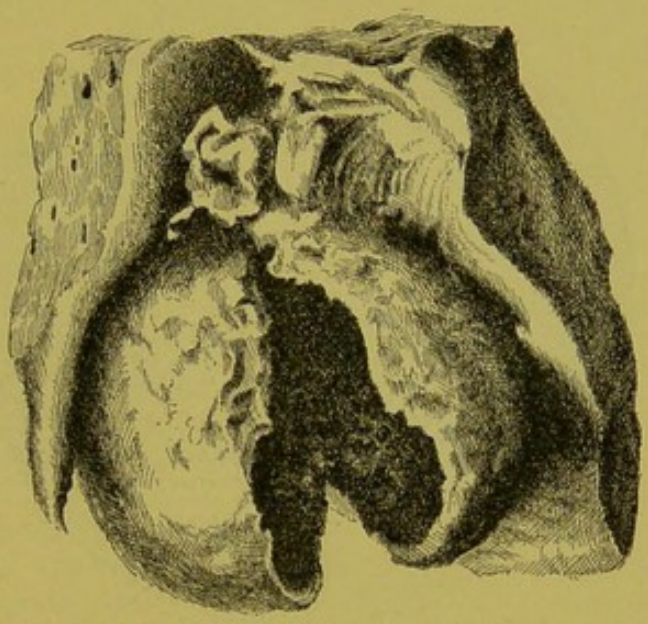


FIG. 84.—Chronic cholecystitis with calcification. From a specimen (Series ix, No. 195 A) in the Museum of St. George's Hospital. (Drawn by Dr. E. A. Wilson.)

Microscopically the thickening of the wall of the gall-bladder is due to fibrosis and proliferation of connective tissue between the muscular and serous coats. There may be much well-formed connective tissue with a little intervening small-celled infiltration. There may also be some oedema and swelling, and sometimes hyaline degeneration of the fibrous tissue. The mucosa may be replaced by scar tissue. I have not observed the elongation of mucous glands through the muscular coat to the serosa described by Ries,[2] and am inclined to consider such a process as evidence of early malignant disease.

[1] Maugeret. *Thèse de Paris*, 1908. [2] Ries. *Ann. Surg.*, 1902, xxxvi, 503.

Clinically, the symptoms are practically those of cholelithiasis. There are attacks of biliary colic from time to time. In the intervals, when the subacute attack of inflammation has subsided, there is no jaundice and no tenderness over the gall-bladder, which can sometimes be felt as a pear-shaped tumour. Elsberg and Neuhof [1] find that cutaneous hyperaesthesia in the eighth and ninth dorsal segments is present in many cases. The distinction between chronic cholelithiasis with periodic attacks of colic and chronic cholecystitis is artificial. From an academic point of view a criterion might be made of the presence or absence of gall-stones; the cases of chronic cholecystitis associated with gall-stones might then be removed to another category and included under cholelithiasis. It is doubtful if a diagnosis between chronic cholecystitis and gall-stones can be made on the ground that the biliary colic is more severe in the case of gall-stones, since, after repeated attacks of biliary colic, the ducts may be so dilated that pain is comparatively slight. When there are no gall-stones, the attacks of colic due to subacute cholecystitis are less likely to be followed by jaundice, and no calculi can be recovered from the stools. Arthritis and phlebitis may be secondary to chronic cholecystitis; and I have known infection of the urinary tract with *B. coli* occur in a patient with cholecystitis. Signs of myocardial insufficiency may occur (Babcock [2]).

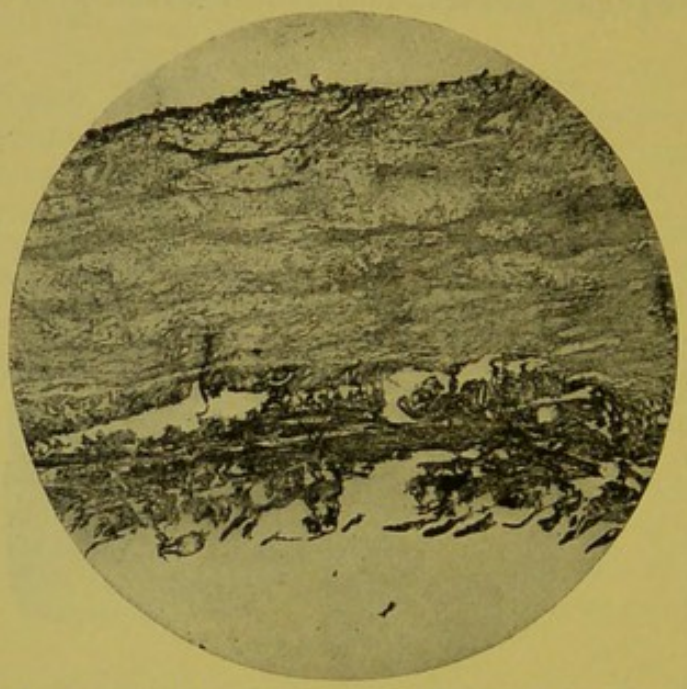


FIG. 85.—Section of wall of gall-bladder in chronic cholecystitis. The villosities of the inner coat are seen, but there is no epithelium left on the surface. The darker longitudinal strands are smooth muscle. The lighter portion, which constitutes two-thirds of the thickness of the wall, is fibrous tissue shewing oedema and some small-celled infiltration. Low power. (Photomicrograph by Dr. H. Spitta.)

Treatment.—The medical treatment is that of cholelithiasis, namely, a careful dietary with plenty of water, salicylate of sodium and urotropin, regular action of the bowels and exercise. These measures are directed to prevent stagnation of bile in the gall-bladder and to increase the flow of bile through the ducts and gall-bladder so as to flush them. Indigestion should be carefully treated so as to prevent further infection of the gall-bladder; Carlsbad salts before breakfast are useful for this purpose.

Surgical drainage of the gall-bladder is followed by good results.

[1] Elsberg and Neuhof. *Am. Journ. Med. Sc.*, Phila., 1908, cxxxvi, 690.
[2] Babcock. *Journ. Amer. Med. Assoc.*, Chicago, 1909, lii, 1904.

Cholecystectomy, according to Ries, is preferable to removing the mucous membrane of the gall-bladder and leaving the rest of the viscus, as practised by Mayo ;[1] and in favour of removal it may be urged that carcinoma may be present although the naked-eye appearances do not suggest it. (*Vide* p. 634.)

Atrophic Sclerosing Cholecystitis.—*Synonym* : Cholecystitis obliterans.—This thickened, retracted condition of the gall-bladder is the result of chronic cholecystitis and is often associated with cholelithiasis of old standing. Rough calculi are probably more likely to be associated with chronic cholecystitis than smooth gall-stones. The gall-bladder is buried in adhesions and firmly contracted on itself, or perhaps on one or more calculi. In such cases the wall of the gall-bladder is often almost inseparable from the calculi. If the calculus is a large one, the gall-bladder may be palpable as a tumour of stony hardness. The walls of the gall-bladder may undergo calcification, and cholesterin may be deposited in the tissues. When extensively calcified, the gall-bladder may be felt through the abdominal wall and will resemble a gall-bladder filled with a large gall-stone. Claude[2] found a calcified gall-bladder the size of a turkey's egg in a woman aged ninety-four.

Chronic ulcerative cholecystitis is usually, but not invariably, associated with calculi. In Norman Moore's[3] case there were multiple ulcers but no real calculi, and in Locke's[4] thirty ulcers without any gall-stones. The gall-bladder may shew pericholecystitic adhesions ; I have seen the omentum completely rolled round the gall-bladder in a case in which a small gall-stone had worked its way through the gall-bladder wall and was adherent externally, the ulcerative passage having become obliterated. Chronic ulcerative cholecystitis may be latent until perforation and acute peritonitis occur.

Chronic Empyema of the Gall-bladder. (*Vide* p. 613.)

Tuberculosis.—Very few cases of tuberculous cholecystitis have been recorded ; Simmonds[5] describes two distinct forms : (i) Chronic ulcerative, of which Latronche[6] collected 7 cases (Riedel, Czerny, Braquehaye, Tédenat[7] (3), and his own), all in women and all with gall-stones. The condition may be responsible for a persistent fistula after cholecystotomy. (ii) Acute tuberculosis with necrosis of the mucous membrane. Lancereaux[8] reported tuberculosis of the gall-bladder, cystic and common bile-ducts in a woman aged thirty-two years.

[1] Mayo. *Ann. Surg.*, 1899, xxx, 490.
[2] Claude, H. *Bull. Soc. Anat. Paris*, 1897, lxxii, 219.
[3] Moore, N. *Trans. Path. Soc.*, Lond., 1891, xlii, 178.
[4] Locke, E. A. *Boston Med. and Surg. Journ.*, 1906, cliv, 703.
[5] Simmonds, M. *Centralbl. f. allg. Path. u. path. Anat.*, Jena, 1908, xix, 225 (Orig.).
[6] Latronche. *Journ. de méd. de Bordeaux*, 1911, xli, 517.
[7] Tédenat. *Rev. de chir.*, Paris, 1910, xlii, 1178.
[8] Lancereaux. *Traité des maladies du foie et du pancréas*, p. 662, 1899.

Actinomycosis.—Mayo Robson[1] operated successfully on a case of this nature, which appears to be unique.

Syphilis.—Fowler[2] reported a rather doubtful case of syphilitic cholecystitis, the gall-bladder being much thickened and contracted.

PARASITIC AFFECTIONS OF THE GALL-BLADDER

Hydatid cysts hardly ever arise in the gall-bladder itself. Cases have been reported by Bowman,[3] J. K. Thornton,[4] F. Page,[5] Langenbuch,[6] Huber,[7] and Barling and Burton.[8] McGavin's[9] specimen was removed from a woman aged thirty-two years during life, but the committee of the Pathological Society, on which I was, reported that the cystic tumour was not the gall-bladder, but a hydatid cyst which had arisen in its neighbourhood and probably displaced it. A number of cases described from clinical evidence, viz. jaundice, a distended gall-bladder, and disappearance of these signs after the passage of hydatid membranes by the bowel, as hydatid disease of the gall-bladder, are open to the criticism that they may have been examples of rupture of a hydatid cyst into the bile-ducts, with subsequent obstruction of the common bile-duct. Cysts have been found loose in the gall-bladder, but this does not prove that the gall-bladder was the primary site of the parasite (Reade[10]). It is conceivable that small daughter cysts which have entered the ducts from rupture of a cyst might pass up a cystic duct which had previously been dilated by a gall-stone, but it would hardly be possible for them to work their way up a normal cystic duct on account of the spiral valves of Heister. A hydatid cyst in the liver may, under conditions such as suppuration, discharge into the gall-bladder; and Bland-Sutton[11] operated upon a hydatid cyst of the omentum which opened into the gall-bladder. The symptoms of hydatids in the gall-bladder are much the same as those of rupture of a hydatid cyst into the bile-ducts.

Fasciola Hepatica.—Budd, in his book on Diseases of the Liver, mentions cases in which liver flukes have been found loose in the gall-bladder.

[1] Robson, Mayo. *Med.-Chir. Trans.*, Lond., 1905, lxxxviii, 225.
[2] Fowler. "Syphilis of the Gall-bladder and Bile-ducts," *New York State Journ. Med.*, 1908, viii, 540.
[3] Bowman. *Lancet*, Lond., 1876, i, 532.
[4] Thornton, J. K. *Ibid.*, 1891, i, 763.
[5] Page, F. *Ibid.*, 1898, i, 995.
[6] Langenbuch. *Deutsche med. Wchnschr.*, 1900, xxvi.
[7] Huber. *Deutsches Arch. f. klin. Med.*, 1891, xlviii, 432. (Multilocular Hydatid.)
[8] Barling and Burton. *Birmingham Med. Rev.*, 1897, xlii, 234.
[9] McGavin. *Lancet*, Lond., 1902, i, 504; *Trans. Path. Soc.*, Lond., 1902, liii, 351.
[10] Reade. *Lancet*, Lond., 1907, i, 882.
[11] Bland-Sutton. *Gall-stones and Diseases of the Bile-ducts*, p. 116, 1907.

INNOCENT TUMOURS OF THE GALL-BLADDER

INNOCENT tumours are rare in the gall-bladder, and are not nearly so often met with as malignant growths.

A **papilloma** of the mucous membrane of the gall-bladder is rather rare—far rarer than carcinoma. I have examined 3 cases. Zenker[1] suggested that papilloma is the early stage of carcinoma; this may be true for some cases of villous carcinoma, but it certainly does not hold good for all cases of carcinoma of the gall-bladder. If it were so, routine examination of the gall-bladder would shew that papillomas are comparatively common.

A papilloma is usually associated with gall-stones; in 8 cases collected by Sand and Mayer[2] calculi were present in 7. It might naturally be expected that the papilloma is secondary to the irritation of calculi; but a papilloma may occur in the absence of any evidence of cholelithiasis. It is possible that some cases regarded as villous carcinoma of the gall-bladder are really large innocent papillomas.

Chappet[3] described a large villous cancer in the gall-bladder attached to the mucosa by two very thin pedicles in a man aged seventy-nine years; there was a calculus in the common bile-duct.

The papilloma is a soft wavy mass which is extremely friable and breaks up on examination so easily that it may, when removed at an operation, suggest material which would later form a gall-stone. After death it is deeply bile-stained. A papilloma may fill up the gall-bladder (Sand and Mayer); or it may become detached and lie loose in the gall-bladder. Microscopically there is a delicate papillomatous growth covered with columnar or subcolumnar cells. In specimens removed during life from the gall-bladder it is impossible, from microscopic examination, to say whether it is a simple papilloma or the superficial part of a villous carcinoma. The structure of the papilloma removed after death is difficult to make out in the microscopic sections I have seen, from the staining and degeneration due to soaking in the bile. A good microscopic drawing is given by Pals-Leusden.[4] V. Schueppel[5] examined microscopic sections of a myxomatous papilloma from a gall-bladder which did not contain any bile. When the papilloma becomes oedematous or undergoes mucoid degeneration, a succulent tumour (myxomatous papilloma) results. No clinical symptoms can be correlated with papilloma of the gall-bladder. The two following examples of

[1] Zenker. *Deutsches Arch. f. klin. Med.*, 1888–9, xliv, 159.
[2] Sand et Mayer. *Arch. de méd. expér. et d'anat. path.*, Paris, 1911, xxiii, 523.
[3] Chappet. *Lyon méd.*, 1894, lxxvi, 146.
[4] Pals-Leusden. *Arch. f. klin. Chir.*, 1906, lxxx, 128.
[5] v. Schueppel. v. Ziemssen's *Cyclopaedia of Practical Medicine*, 1880, ix, 56.

papilloma of the gall-bladder have come under my notice at St. George's Hospital :—

A man aged forty-five died in St. George's with cardiac dilatation secondary to arteriosclerosis. The gall-bladder felt rather like a varicocele, and when opened contained a yellow, bile-stained, papillomatous mass growing from the anterior surface of the gall-bladder close to the fundus. The wall was not thickened or invaded. There were no calculi in the gall-bladder or bile-ducts, but the common duct was dilated, as if by the passage of calculi. In a man who died of pulmonary tuberculosis at the age of thirty-nine the gall-bladder contained a small bile-stained papilloma. There were no calculi in the gall-bladder or ducts, and no dilatation of the ducts. There had been no abdominal symptoms.

A submucous **fibroma** of the gall-bladder has been described.[1] A caution may be thrown out, however, not to regard the early stage of primary carcinoma of the gall-bladder as a fibroma.

Adenoma is extremely rare. It may be cystic.

Stanmore Bishop[2] removed a cystic tumour from the gall-bladder of a woman aged forty-two years who had had bilious attacks accompanied by transient jaundice. The tumour contained a number of separate cavities lined by cylindrical epithelium. I have examined a similar specimen from the fundus of the gall-bladder in a woman aged fifty-nine ; there were no gall-stones. Terrier and Auvray[3] quote a case of Wiedemann's ; Mayo Robson[4] records a case in which the loculi contained cholesterin. A *fibro-adenoma* at the fundus of the gall-bladder is figured by Moynihan[5] from a specimen in the London Hospital Museum. Sutherland[6] recorded a small *adenomyoma*.

Small **cysts** in the mucous membrane of the gall-bladder containing cholesterin are also rare. Terrier and Auvray refer to a case of Adler's in which a gall-bladder presented three such cysts. The cholesterin-containing cysts may develop into parietal calculi embedded in the wall of the gall-bladder. Hydatid cysts are referred to on p. 628.

Oedema under the peritoneal coat of the gall-bladder is sometimes seen in cases of backward pressure due to heart disease or chronic bronchitis and emphysema. When localised it may look like a small cyst ; microscopically it is seen that there is no true cavity, and only oedema of the tissues.

Fatty Tumours.—Local subperitoneal masses of fat are in rare instances seen on the gall-bladder. I have seen this in otherwise perfectly normal gall-bladders. As a result of cholecystitis it is conceivable that an appendix epiploica might become adherent to the gall-bladder and subsequently be detached from the colon.

[1] Albers, quoted in v. Ziemssen's *Cyclopaedia of Practical Medicine*, 1880, ix, 567.
[2] Stanmore Bishop. *Lancet*, Lond., 1901, ii, 72.
[3] Terrier et Auvray. *Chirurgie du foie*, p. 253, 1901.
[4] Mayo Robson. *Med.-Chir. Trans.*, Lond., 1905, lxxxviii, 229.
[5] Moynihan. *Gall-stones and their Surgical Treatment*, p. 135, 1906.
[6] Sutherland. *Glasgow Med. Journ.*, 1898, l, 216.

PRIMARY MALIGNANT TUMOURS OF THE GALL-BLADDER

Frerichs[1] gave an account of the disease in 1861; Villard,[2] in 1870, collected 17 cases; Musser,[3] in 1889, 100 cases; Courvoisier,[4] 103; and in 1901 Fütterer,[5] 268. These tables, of course, deal largely with the same cases. The bibliographies attached to Siegert's,[6] Ames's,[7] and Fütterer's papers shew that the subject has no cause to complain of neglect. This disease has certainly received more attention of late years; of Fütterer's 268 cases, no less than 195 were reported since 1880.

It is remarkable that another annexe of the alimentary canal, the vermiform appendix, in which concretions are comparatively common, is much less often attacked by primary malignant disease. They are both frequently inflamed, and are both very liable to irritation, infection, and calculi.

Morbid Anatomy.—Primary malignant disease of the gall-bladder is practically always carcinoma. I have references to 14 cases of primary sarcoma.

Musser mentions 3 cases of primary sarcoma; Griffon and Segall[8] record a spindle-celled sarcoma, primary in the gall-bladder, which contained two calculi, in a woman aged seventy-six. Czerny (angio-sarcoma), Riedel,[9] Neviadomsky,[10] Landsteiner,[11] Parlavecchio,[12] and Bayer[13] (2) have also met with primary sarcoma of the gall-bladder. Becker[14] described a primary endothelioma, and Bland-Sutton[15] a perithelioma, of the gall-bladder; in Becker's case there were two gall-stones which had almost perforated into the stomach near the pylorus. Wieting and Hamdi[16] described a primary malignant melanotic tumour (melanoblastoma) of the gall-bladder. The growth was a spindle-celled sarcoma in at least 4 cases (Griffon and Segall, Landsteiner, Bayer). I have examined 1 case of primary spindle-celled sarcoma of the gall-bladder. A woman aged fifty-six had a large tumour to the right of the umbilicus which entirely replaced the gall-bladder; it contained a cavity which opened into the transverse colon. The growth had tracked along the cystic and common bile-ducts and projected at the biliary papilla. No gall-stones were found. There were metastases in the aortic

[1] Frerichs. *Diseases of the Liver*, ii, 479. Transl. New Sydenham Soc., 1861.
[2] Villard. *Bull. Soc. Anat. Paris*, 1869, xliv, 217.
[3] Musser, J. H. *Boston Med. and Surg. Journ.*, 1889, cxxi, 525.
[4] Courvoisier. *Pathologie und Chirurgie der Gallenwege*, Leipzig, 1890.
[5] Fütterer, G. *Über die Ätiologie des Carcinoms*, Wiesbaden, 1901.
[6] Siegert. *Virchows Arch.*, 1893, cxxxii, 353.
[7] Ames, D. *Johns Hopkins Hosp. Bull.*, 1894, v, 74.
[8] Griffon et Segall. *Bull. Soc. Anat. Paris*, 1897, lxxii, 586.
[9] Riedel. *Berlin. klin. Wchnschr.*, 1882.
[10] Neviadomsky. *Med. Obozr.*, Mosk., 1900, liii, 190.
[11] Landsteiner. *Wien. klin. Wchnschr.*, 1904, xvii, 162.
[12] Parlavecchio. *Arch. f. klin. Chir.*, Berlin, 1908, lxxxvii, 365.
[13] Bayer. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1909, xlvi, 429.
[14] Becker, W. *Journ. Am. Med. Assoc.*, 1903, xl, 903.
[15] Bland-Sutton. *Lancet*, Lond., 1907, i, 1343.
[16] Wieting und Hamdi. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1907, xlii, 23.

lymphatic glands and in a gland in the right groin. There was no jaundice. Microscopically it was a spindle-celled sarcoma, somewhat alveolar in arrangement, with numerous blood spaces. The patient was in St. George's Hospital in 1891.

The following description will deal with carcinoma of the gall-bladder.

Histology.—Carcinoma of the gall-bladder varies in the form of the cells and in their arrangement; it may be columnar- or spheroidal-celled. The cells may undergo colloid degeneration, or the cavities of the tubes lined by columnar epithelium may become distended by mucoid material without any colloid degeneration of the cells (Fig. 86). Columnar-celled carcinoma may grow into the cavity of the gall-bladder as a villous tumour or papilloma; but the invasion of the deeper layers does not shew a papillomatous arrangement, and is an ordinary columnar-celled carcinoma with a fair amount of fibrous tissue. Frequently a change of type of the carcinoma is visible; parts of the growth may be columnar-, others cubical-, and other parts spheroidal-celled. This transition is seen in columnar-celled carcinoma elsewhere, especially in duct cancer of the breast. In transitional parts, and especially when colloid or allied degenerative changes are present, the large epithelial cells may be so far modified as to appear flattened.[1] Multinuclear cells are also sometimes seen. As the result of metaplasia a squamous-celled carcinoma of the gall-bladder may occur.

Fig. 86.—Microscopic appearances of columnar-celled carcinoma of the gall-bladder. Shews dilated spaces lined by columnar epithelium and containing mucus. (Photomicrograph by Dr. S. G. Penny.)

Deetz (*Virchows Arch.*, 1901, clxiv, 381) described 4 cases and Fütterer (*Journ. Amer. Med. Assoc.*, Chicago, 1904, xliii, 1129) collected 13 examples; to these the cases described by Hebb (*Westminster Hosp. Rep.*, 1895, ix, 316), Mayo Robson (*Med.-Chir. Trans.*, Lond., 1896, lxxix, 159), Speese (*Univ. Penn. med. Bull.*, 1907, xix, 300), Herxheimer, Nicholson (3) (*Journ. Path. and Bacteriol*, 1909, xiii, 41), M'Kenzie (*ibid.*, 1909, xiii, 99), and one at St.

[1] For a discussion of this change see Bret. *Lyon méd.*, 1898, lxxxix, 41.

George's Hospital, should be added, making 22 in all. Deetz, in an examination of 300 gall-bladders, including some with cholelithiasis, never observed transformation of the lining epithelium into squamous epithelium, but he nevertheless believes this change must occur to account for a primary squamous-celled carcinoma of the gall-bladder.

Besides the mucoid and colloid changes already mentioned, fatty and other degenerations of the cells may occur, and parts of the tumour

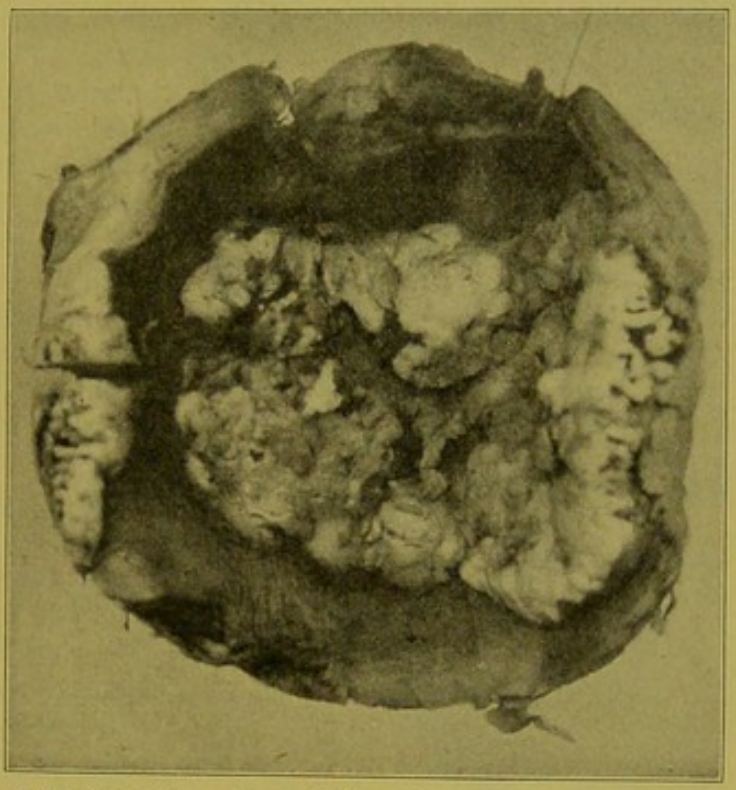


FIG. 87.—Squamous-celled carcinoma of the gall-bladder. Specimen (Series ix, 197D) in St. George's Hospital Museum. (Photograph by Dr. R. S. Trevor.)

may become necrotic. Occasionally haemorrhages take place into the tumour.

Starting-point of the Growth.—It has been thought that spheroidal-celled carcinoma is derived from the mucous glands in the wall of the gall-bladder, and columnar-celled carcinoma from its lining mucous membrane. But the change from a columnar- to a spheroidal-celled carcinoma can be seen in the same specimen, and there is no essential difference between the columnar cells of the surface mucous membrane and of the mucous recesses or "glands" in communication with it. It may be concluded that carcinoma, whatever its form, arises from the mucous membrane as a whole, and no statement that either form of carcinoma arises exclusively from the surface epithelium of the gall-bladder or from the epithelium lining the "glands" is justified.

It has been suggested that carcinoma of the gall-bladder begins as

a papilloma.[1] Although this may be true in some instances, there is certainly no proof that it always holds good. Papilloma of the gall-bladder is rare. Moreover, some cases of carcinoma of the gall-bladder do not shew any villous projection into the lumen of the cavity, but are limited to the infiltration of its wall. Chronic inflammatory changes in the gall-bladder, analogous to pre-cancerous mastitis, appear to play an important part in the development of carcinoma. In five gall-bladders presenting the appearances of universal chronic inflammatory thickening without any naked-eye evidence of growth, Slade[2] found carcinoma. Carcinoma of the gall-bladder may, like carcinoma of the intestine, occur in two forms: (1) That projecting into the cavity of the gall-bladder as a fungating growth; (2) that limited to infiltration of its walls. The fungating form is generally papillomatous, and histologically a columnar-celled growth; the infiltrating form, though it may be columnar-celled, is often a spheroidal-celled carcinoma. The two forms may be combined.

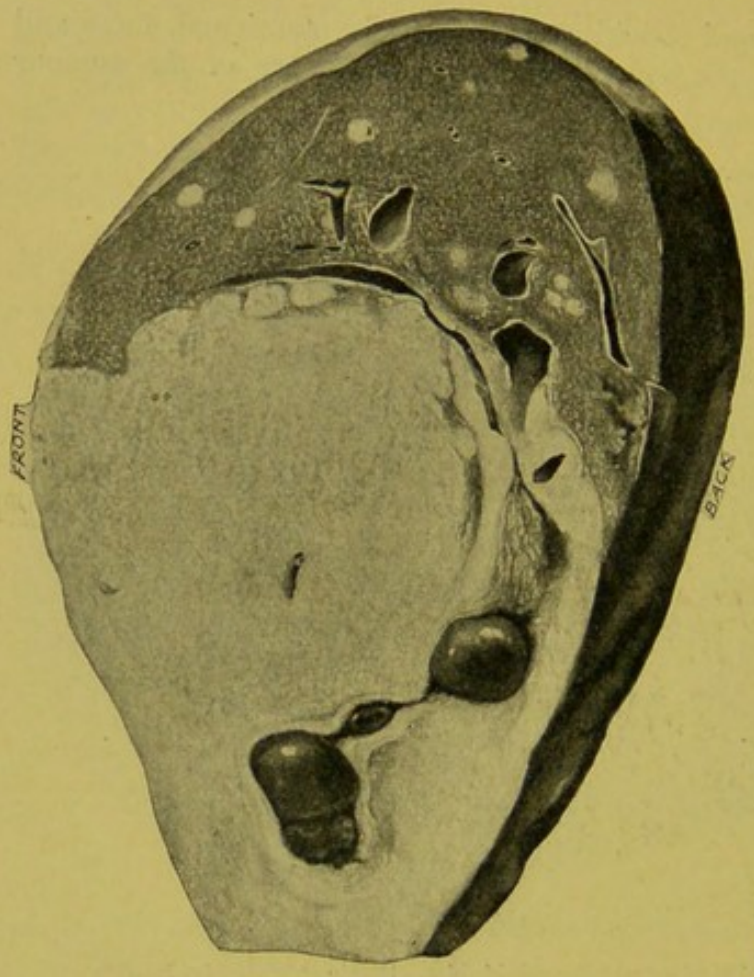


Fig. 88.—Carcinoma in the position of the gall-bladder containing calculi. From a specimen (Series ix, No. 197E) in St. George's Hospital Museum.

Situation of the Tumour.—Carcinoma most commonly starts in the fundus, and the distal compartment of an hour-glass gall-bladder may be the starting-point of the growth. The explanation of this is that the fundus, being the most dependent part, is specially exposed to irritation by calculi. A growth midway between the fundus and the cystic duct may divide the gall-bladder into two compartments or produce an hour-glass gall-bladder (Fig. 89). The growth may begin at the neck of the

[1] Zenker, *Deutsches Arch. f. klin. Med.*, Leipz., 1889, xliv, 159; Aczel, *Virchows Arch.*, 1896, cxliv, 86; Warthin, *Phila. med. Journ.*, 1900, vi, 38.

[2] Slade. *Lancet*, Lond., 1905, i, 1059, and private communication.

gall-bladder, at its junction with the cystic duct, and then give rise to obstruction, either by blocking the lumen or by spreading around the circumference of the narrowed gall-bladder or cystic duct, and producing an annular stricture. As a result the gall-bladder may become distended with fluid. Carcinoma of the cystic duct is much the same as carcinoma of the neck of the gall-bladder, and clinically resembles that condition rather than carcinoma of the other bile-ducts. Carcinoma of the neck of the gall-bladder may appear to depend on the irritation of calculi impacted in that situation.

The growth may, however, involve the whole of the gall-bladder, so that it is difficult or impossible to say in what part—fundus, neck, etc.—it arose. In other cases the place of the gall-bladder is entirely taken by growth; and the condition may be erroneously regarded as primary (massive) carcinoma of the liver. That the growth originated in the gall-bladder is then assumed from the complete absence of that viscus, or from the presence of calculi embedded in the centre of a growth in the position of the gall-bladder (*vide* Fig. 88).

A secondary growth in the gall-bladder may, to the naked eye, resemble a primary neoplasm.

A specimen in St. Bartholomew's Hospital Museum (No. 2216G) looks like a primary tumour, but is really, as shewn by section of the walls of the gall-bladder, a nodule of round-celled sarcoma, secondary to a growth in the lung.

Behaviour and Appearance of the Tumour.—The columnar-celled form may project into the gall-bladder and fill it with a villous growth which easily disintegrates, and then somewhat resembles caseous pus or plaster-like material, imitating both in structure and in appearance psorospermosis of the bile-ducts in a rabbit's liver. But a columnar-celled carcinoma of the gall-bladder may be hard and solid, and not the least villous in arrangement. So, as in the breast, a columnar-celled carcinoma may occur in one of two forms: (i) villous; (ii) like an ordinary columnar-celled carcinoma of the bowel. Generally speaking, the spheroidal-celled carcinoma grows more rapidly and generalises more freely. But the columnar-celled form may spread by continuity into the liver substance, and then shew a transition to the spheroidal-celled type.

Haemorrhage into the gall-bladder from a villous carcinoma is rather rare; it occurred 7 times in Musser's 100 cases. Colloid change is commoner in the more slowly-growing columnar-celled growths than in the spheroidal-celled carcinoma. Carcinoma in an early stage may appear as a localised thickening, like a button, of the wall of the gall-bladder, of a whitish appearance, and may resemble a scar or a gumma. As a rule the tumour is not larger than the closed fist; Michaux[1] records a tumour the size of an adult's head; it was diagnosed as an ovarian cyst.

Extension by Continuity.—As already mentioned, a large tumour in the gall-bladder may directly invade the liver, and thus give rise to consider-

[1] Michaux. *Bull. et mém. Soc. chir. de Paris*, 1907, xxxiii, 1182.

able hepatic enlargement. In these cases the growth may be thought to be a primary carcinoma of the liver.

In one case which I examined, the neoplasm spread from the anterior surface of the gall-bladder into the liver, and projected so little into the cavity of the gall-bladder that it was only on section that it became clear that the tumour started in the gall-bladder. In this instance the primary growth was confined to the surface of the gall-bladder in contact with the liver, and so might have been overlooked, and the numerous secondary growths in the liver might, therefore, have been regarded as multiple primary carcinoma.

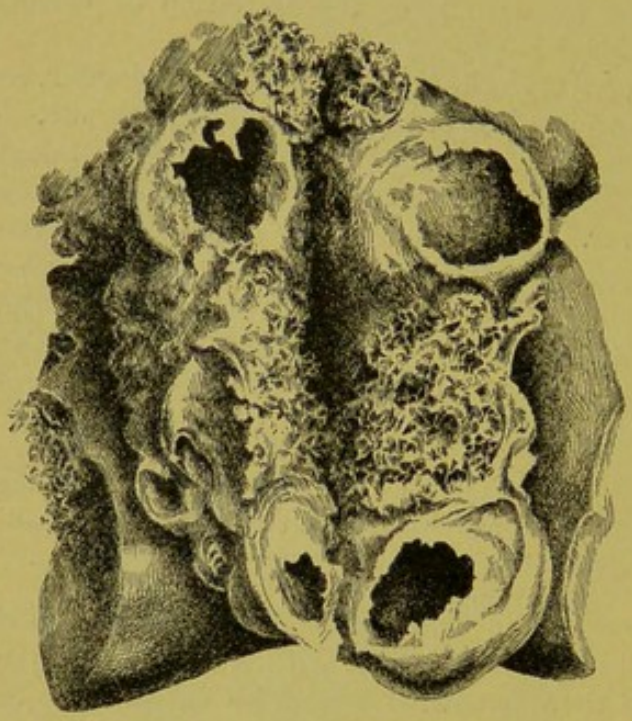


FIG. 89.—Papillomatous form of primary carcinoma of the gall-bladder. The gall-bladder has been opened longitudinally; the growth does not occupy the whole of the gall-bladder, the fundus and neck being unaffected. From a specimen (Series ix, 197A) in St. George's Hospital Museum. (Drawn by Dr. E. A. Wilson.)

Generally, however, when carcinoma of the gall-bladder extends into the liver, its origin is quite clear. The growth may spread in the wall of the cystic duct into the common bile-duct towards the biliary papilla, or along the hepatic ducts into the liver, much in the same way that a growth at the bifurcation of the trachea tracks along the bronchi and their lymphatics into the lung. It may be difficult to decide whether the primary growth started in the bile-ducts and then extended, or originated in the gall-bladder. Carcinoma of the gall-bladder has been known to project as a free process down the cystic duct into the common bile-duct (Bohnstedt [1]), in the same manner that malignant disease of the liver has, in at least one case (Gilbert and Claude [2]), been found projecting into the extra-hepatic bile-ducts.

Fistulae.—When, as is usually the case, carcinoma begins in the fundus of the gall-bladder, it readily becomes adherent to the colon and may open into it. This occurred in 10 of Musser's 100 cases, and in 6 of Riedel's [3] 77 cases. Perforation may occur into the stomach; this was noted in 5 of Riedel's cases. In like manner a carcinomatous gall-bladder may open into the duodenum; this occurred in 10 of Riedel's cases. But this fistula is less often seen in carcinoma than in chole-

[1] Bohnstedt, quoted by Devic et Gallavardin, *Rev. de méd.*, Paris, 1901, xxi, 569.
[2] Gilbert et Claude. *Arch. gen. de méd.*, Paris, 1895, clxxv, 513.
[3] Riedel. *München. med. Wchnschr.*, 1911, lviii. 1337.

lithiasis. The growth may invade the duodenum so widely that it may be difficult to decide in which situation it started.

Coupland [1] described a primary carcinoma of the first part of the duodenum, which grew into and entirely replaced the gall-bladder. Inasmuch as primary carcinoma is much rarer in the first part of the duodenum than in the gall-bladder, it is possible that the growth was primary in the gall-bladder.

The tumour has been known to invade the abdominal wall, then to set up an abscess, and even an external fistula.

In a woman, aged sixty years, who died in St. George's Hospital, carcinoma of the gall-bladder spread to the cystic duct and then ulcerated into the common bile-duct and portal vein; from this fistula extensive haemorrhage into the common duct and duodenum resulted. There was no clot in the portal vein.

Pressure Effects.—When the growth implicates the pylorus, it may cause obstruction, and clinically simulate carcinoma of the pylorus. From their anatomical relations this is more likely to occur when the growth is near the neck of the gall-bladder.

Rabé and Rey [2] found the fundus of a carcinomatous gall-bladder firmly adherent to the first part of the duodenum, which was greatly narrowed, and had led to dilatation of the stomach. The colon was also adherent to the gall-bladder, and the intestinal obstruction in the case was thus partly explained. Lejonne and Milanoff [3] recorded a somewhat similar case.

Thrombosis of the portal vein may be associated with primary carcinoma of the gall-bladder; this occurred in 6 out of 68 cases of pylethrombosis collected by Lissauer.[4]

The gall-bladder may perforate into the peritoneal cavity, or give rise to a localised abscess (compare p. 644). Such a localised abscess may subsequently rupture into the general peritoneal cavity.

In a case reported by Moutier [5] primary carcinoma of the gall-bladder opened into an encysted peritoneal pouch containing bile and imitating, both during life and at the necropsy, a dilated gall-bladder.

Secondary Growths.—The liver is the organ most frequently affected, being involved in about 50 per cent of the cases.

In Musser's [6] 100 cases there were metastases in 55; the liver was involved in 52, the abdominal lymphatic glands in 16, the lungs or pleura in 10, and the peritoneum in 12.

When the growths are numerous, the clinical aspect of the case becomes that of malignant disease of the liver. Secondary growths in

[1] Coupland, S. *Trans. Path. Soc.*, Lond., 1873, xxiv, 103.
[2] Rabé et Rey. *Bull. Soc. Anat. Paris*, 1897, lxxii, 881.
[3] Lejonne et Milanoff. *Ibid.*, 1900, lxxv, 133.
[4] Lissauer. *Virchows Arch.*, 1908, excii, 278.
[5] Moutier. *Arch. gén. de méd.*, Paris, 1905, clxiv, 2001.
[6] Musser. *Boston Med. and Surg. Journ.*, 1889, cxxi, 528.

the portal lymphatic glands may compress the bile-ducts and portal vein, thus setting up jaundice and ascites. Metastases may occur in other abdominal lymphatic glands, in the peritoneum, the ovaries, and the lungs. Infection may travel into the chest along the lymphatic vessels, which pass immediately behind the sternum to the glands in the anterior mediastinum. A tumour may thus project from the chest even before the primary growth has been detected.

Beadles[1] described a case of primary carcinoma of the gall-bladder with a secondary growth as large as a cocoanut near the second rib on the right side. In S. West's[2] case the symptoms were those of mediastinal tumour, which the necropsy shewed to be secondary to a growth in the gall-bladder.

In rare instances the lymphatic glands above the clavicle may be enlarged and readily palpable during life. To this phenomenon the term "Virchow's gland" has been applied. In cases in which acute cholecystitis supervenes in a carcinomatous gall-bladder enlargement of lymphatic glands in the neighbourhood may be inflammatory and not necessarily malignant.

The **liver** may be healthy, but usually it is enlarged, either from distension with bile or from secondary growths. In some cases the growth extends directly into the substance of the right lobe, and, as pointed out elsewhere, the tumour may resemble a primary massive carcinoma of the liver. From infection of the bile-ducts suppurative cholangitis may occur and give rise to miliary abscesses in the liver. Of 60 cases tabulated by Winton[3] 4 shewed miliary abscesses. Rupture of a suppurating bile-duct may give rise to an abscess in the immediate neighbourhood of the liver.

A woman, aged fifty, died under my care with jaundice of two months' duration, fever of a month's duration, and a hard tumour in the position of the gall-bladder. There was primary spheroidal-celled carcinoma of the gall-bladder, secondary growths in the portal glands, liver, and around the pancreas. The intrahepatic ducts were dilated and full of pus, and there was a large abscess under the right lobe of the liver. There was a contracting sinus in the first part of the duodenum which was stenosed and firmly adherent to the gall-bladder. The history was compatible with the view that a gall-stone had ulcerated out of the gall-bladder into the duodenum four years before. At the necropsy there were no calculi in the gall-bladder.

The *pancreas* may shew chronic inflammation due to the previous passage of calculi.

Etiology.—*Relation of Primary Carcinoma of the Gall-bladder and Gall-stones.*—Special interest attaches to the association of gall-stones and carcinoma of the gall-bladder, inasmuch as the calculi are generally thought to be the cause, whether by direct irritation or otherwise, of the neoplasm. Calculi are extremely common in primary carcinoma of

[1] Beadles, C. F. *Trans. Path. Soc.*, Lond., 1897, xlviii, 119.
[2] West, S. *Ibid.*, 1886, xxxvii, 144.
[3] Winton, W. B. Unpublished Thesis for M.D. Cantab., 1902.

the gall-bladder. In Musser's 100 cases they were present in 69, and in only three instances was cholelithiasis definitely stated to be absent. Fütterer[1] and Haberfeld[2] estimated that calculi were present in 70 per cent; Winton in 81 per cent; Zenker[3] in 85 per cent; Courvoisier[4] in 91 per cent; Siegert in 95 per cent. Janowski[5] in 40 cases of malignant disease of the gall-bladder records calculi in all. Possibly in some cases in which calculi are not present at the necropsy, they have been passed at an earlier stage; the case quoted above suggests that this may occur. Conversely, primary carcinoma of the gall-bladder occurs in from 4 to 14 per cent of all cases of cholelithiasis.

Schröder[6] estimated that 14 per cent of persons with cholelithiasis eventually became the subjects of carcinoma of the gall-bladder; in 141 cases of gall-stones there were 20 of primary carcinoma. In 333 cases of gall-stones abstracted from the post-mortem records of Guy's Hospital by Ticehurst[7] there were 45 cases of carcinoma of the gall-bladder or cystic duct, or 13·5 per cent. Riedel[8] estimated the percentage of primary carcinoma in cholelithiasis at from 7 to 8. Among 268 cases of gall-stones at St. George's Hospital there were 12 cases of primary carcinoma of the gall-bladder, or 4·5 per cent; this low percentage is possibly accounted for by the fact that in many instances minute bilirubin-calcium calculi were the only ones present. In 17 gall-bladders shewing chronic inflammatory or other changes associated with gall-stones, and in all but one instance from cases dying from the effects of gall-stones, Slade[9] found carcinoma in 10, or 59 per cent; in 5 of these the condition was only detected microscopically. This is a startling and unusual experience. Among 315 cases of gall-stones in the insane, Candler[10] found 2 cases only of primary carcinoma of the gall-bladder; he considers that hospital statistics shew an unduly high percentage of carcinoma because patients are admitted for that disease. In 24 cases of primary carcinoma of the gall-bladder at St. George's Hospital, 18, or 75 per cent, were associated with gall-stones.

It has, however, been suggested that the calculi are secondary to the growth, and are the result of obstruction to the passage of bile or of other changes set up by carcinoma in the gall-bladder. If calculi were the result of obstruction pure and simple, they would be found more frequently in carcinoma of the bile-ducts, in which biliary obstruction is more constant and prolonged than in malignant disease of the gall-bladder. But they are less frequent, being present in 23 out of my 67 cases, while in carcinoma of the gall-bladder the percentage is about 90. Besides directly obstructing the exit of bile and mucus from the gall-bladder, a tumour in its wall might interfere with its contractions. Both these

[1] Fütterer, G. *Über die Ätiologie des Carcinoms*, Wiesbaden, 1901.
[2] Haberfeld. *Ztschr. f. Krebsforsch.*, Berlin, 1908, vii, 190.
[3] Zenker, H. *Deutsches Arch. f. klin. Med.*, 1888-89, xliv, 159.
[4] Courvoisier. *Path. u. Chirurg. der Gallenwege*, 1890.
[5] Janowski. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1891, x, 449.
[6] Schröder. Quoted by Naunyn, *Cholelithiasis.* Transl. New Sydenham Soc., 1896.
[7] Ticehurst. Quoted by Hale White, *Clin. Journ.*, Lond., 1907, xxx, 275.
[8] Riedel. *Berlin. klin. Wchnschr.*, 1901, xxxviii, 1.
[9] Slade. *Lancet*, Lond., 1905, i, 1059.
[10] Candler. *Proc. Roy. Soc. Med.*, 1911, iv (Path. Sect.), 87.

conditions would cause biliary stagnation and so favour infection, cholecystitis, and the production of calculi. Further, it is conceivable that the presence of a growth or its disintegration might modify the secretion from the mucous membrane of the gall-bladder. In this connexion it is important to bear in mind that the cholesterin in the bile is largely derived from the mucosa of the gall-bladder. Siegert[1] tried to settle the question whether the presence of a growth in the gall-bladder gave rise to the formation of calculi, by a comparison of the incidence of calculi in primary and in secondary carcinoma of that viscus. In 99 cases of primary disease calculi were present in 94; whereas in 13 cases of secondary growths in its walls they were present in only 2. In 19 other cases of secondary growths that I have collected or seen, calculi were present in one; so in these 32 cases of secondary growths in the gall-bladder gall-stones occurred in 3, or 9·4 per cent, or well within the limits, 5 to 12 per cent (Schröder[2]), of the incidence of gall-stones in routine post-mortem work. These figures, as far as they go, do not support the view that a growth in the gall-bladder is a factor of any importance in the production of gall-stones. It must, however, be admitted that the presence of a secondary growth in the gall-bladder is not quite the same as a primary tumour, especially as regards its relation to the mucous membrane. Metastases usually start under the serous coat, and need not invade the mucous coat, which produces cholesterin, whereas a primary carcinoma is due to changes in the mucous membrane.

There is undoubtedly a very definite relation between cholelithiasis and primary carcinoma of the gall-bladder. But gall-stones are so commonly present without carcinoma that some additional factor would seem to be necessary. Rough calculi would be more prone than smooth ones to irritate and set up proliferation of walls of the gall-bladder. Possibly the part played by calculi is that of preparing the soil for the direct cause, whatever it may be, of carcinoma. Gall-stones dispose to fresh attacks of cholecystitis, and in this way a pre-cancerous condition of the gall-bladder may result. The walls of a carcinomatous gall-bladder may shew chronic inflammation, and even calcareous infiltration.[3] On the other hand, gall-stones are due to catarrh of the mucous membrane of the gall-bladder, and it might be suggested that carcinoma and gall-stones are both the results of forms of irritation which have much in common.

To sum up, gall-stones are present in the great majority of cases of primary malignant disease of the gall-bladder, whereas carcinoma occurs in from 14 to 4 per cent of cases of cholelithiasis. It appears that cholelithiasis is the earlier of the two conditions, and that carcinoma *per se*, whether local in the gall-bladder or present elsewhere in the body (*vide* p. 719), does not set up cholelithiasis.

In connexion with the close association between carcinoma of the gall-

[1] Siegert. *Virchows Arch.*, 1893, cxxxii, 353.

[2] Schröder. Quoted by Naunyn, who accepts this estimate, *On Cholelithiasis*, p. 38. Translated by New Sydenham Soc., 1896.

[3] Beadles, C. F. *Trans. Path. Soc.*, Lond., 1896, xlvii, 69.

bladder and cholelithiasis the question of a similar association between renal calculi and tumours of the pelvis of the kidney is of interest. It must be remembered that both renal calculi and new growths of the renal pelvis are less common than gall-stones and carcinoma of the gall-bladder.

Kelynack [1] collected 23 examples of associated renal calculus and malignant renal tumours of various kinds. In 8 cases of papilloma of the pelvis of the kidney collected by Drew [2] calculi were present in 4. It is reasonable to suppose that the irritation of a calculus would give rise to a villous growth of the renal pelvis more readily than to malignant disease of the substance of the kidney.

Sex.—Malignant disease of the gall-bladder is much commoner in women. According to Fütterer's figures (202 females, 52 males), it is four times more often seen in the female sex. Musser's cases included 75 females and 23 males (or 3 to 1); Siegert's, 79 females and 14 males (5½ to 1); Ames gives the proportion of females to males as 4 to 1; Courvoisier, as 5 to 1. In 50 cases of Terrier and Auvray,[3] 40 were women and 10 men. In Winton's 60 cases 43 were females and 17 males (5 to 2). This predominance of females in carcinoma of the gall-bladder corresponds to their greater liability to gall-stones, which is calculated by Schröder in the proportion of 5 to 1, by Murchison and Bouchard 3 to 2, and by myself as 4 to 3 (*vide* p. 723). The overwhelming majority of female patients among the subjects of gall-bladder carcinoma contrasts with the sex incidence in carcinoma of the bile-ducts; thus in 18 cases Musser found the sexes equally represented, and in my 85 cases 50 were males and 35 females.

The pressure of the corset on the liver may, as suggested by Fütterer,[4] increase the friction between calculi and the walls of the gall-bladder, and so may help to explain the great predominance of females in primary carcinoma of the gall-bladder. In this connexion it is remarkable that the bile-ducts, which can hardly be affected in the same way by the wearing of a corset or belt, are more often the site of carcinoma in men than in women. Graham recorded carcinoma of the gall-bladder in a shoemaker whose last pressed upon the liver much as a corset might do, and Fütterer is inclined to think that pressure of this kind may be a factor in the male cases.

While primary carcinoma is much commoner in women, Siegert's statistics of secondary growths in the gall-bladder, though only 13, shewed that the male sex were affected in 10, or 77 per cent, and the female sex in 3, or 23 per cent.

Age.—Frerichs described the disease as one of old age. In 17 cases collected by Villard 9 were over seventy years of age. The average age of Fütterer's large series was fifty-eight years, and was the same in 60

[1] Kelynack, T. N. *Renal Growths*, p. 27, 1898, Edin.
[2] Drew, D. *Trans. Path. Soc.*, Lond., 1897, xlviii, 133.
[3] Terrier et Auvray. *Rev. de chir.*, Paris, 1900, xxi, 143.
[4] Fütterer, G. *Chicago Med. Recorder*, 1897, xii, 325.

cases collected by Winton, many of them from the unpublished records of St. George's and other hospitals. It is very rare before forty years of age. Haas [1] and Chavannaz [2] have described cases in women of twenty-five years. At the other extreme the most advanced age was ninety (Thomas and Noica [3]). The average age of carcinoma of the gall-bladder in the two sexes was almost identical in Fütterer's 194 female and 45 male cases.

Clinical Picture.—The clinical manifestations are roughly divisible into three groups: (i) Symptoms connected with pre-existing cholelithiasis; (ii) the local effects of malignant disease of the gall-bladder; (iii) complications due to invasion of adjacent parts by the tumour and to metastases in the liver, peritoneum, and elsewhere.

The patient, generally a woman between fifty and sixty years of age, may have suffered from symptoms of gall-stones. Biliary colic may closely precede the development of carcinoma, but in some instances there is a very long interval between the first appearance of colic and the development of carcinoma.

Jourdan [4] recorded a case in which the colic began twenty-five years before the growth appeared. Bret [5] describes the case of a woman, who died at the age of thirty-six with carcinoma of the gall-bladder enclosing an oval calculus; she had had biliary colic since the age of twenty.

There is often, however, no history of gall-stone colic in fatal cases of carcinoma of the gall-bladder; the calculi may remain latent in the gall-bladder and never pass into the ducts. Kehr [6] says that clinical evidence of cholelithiasis is wanting in the majority of the patients. In other instances pain really due to inflammation or adhesions around the gall-bladder is regarded as dyspepsia.

Usually the first thing noticed by the patient is a feeling of discomfort and heaviness in the right hypochondrium and parts around. According to Head,[7] the eighth dorsal segment is the visceral area of cutaneous tenderness in connexion with the gall-bladder. There may be loss of appetite, gastro-intestinal disturbance accompanied by definite pain, and even attacks of colic, indistinguishable from biliary paroxysms. A tumour may be felt in more than half the cases in the situation of the gall-bladder, which is at first smooth and oval, and subsequently becomes hard, irregular, and may be tender. Like the liver, it moves with respiration unless fixed by adhesions. It may reach the size of a cocoanut. These may be called the local manifestations, and, on the whole, resemble those of cholelithiasis. As time goes on the growth invades neighbouring parts, and metastases may spring up; additional, or what may be called secondary, symptoms, are thus produced.

[1] Haas. *Prag. Vrtljhrschr.*, 1876, cxxxii, 31. Quoted by Fütterer.
[2] Chavannaz. *Gaz. hebd. de méd.*, Paris, 1901, N.S., vi, 721.
[3] Thomas et Noica. *Bull. Soc. Anat. Paris*, 1896, lxxi, 471.
[4] Jourdan. *Ibid.*, 1891, lxvi, 323.
[5] Bret. *Lyon méd.*, 1898, lxxxix, 35.
[6] Kehr. *Diagnosis of Gall-stone Disease*, p. 92, 1901, American translation.
[7] Head, H. *Brain*, Lond., 1893, xvi, 75.

Carcinoma of the gall-bladder may remain latent and the symptoms may be entirely due to secondary growths (*vide* also p. 637).

A man aged sixty-eight in St. George's Hospital with ascites, but no jaundice, was diagnosed as cirrhosis. At the necropsy there was a primary columnar-celled carcinoma of the gall-bladder which contained gall-stones. The liver was directly invaded by the tumour, and there was a large, broken-down growth in the glands behind the pancreas, which compressed the portal vein. In a case in St. George's Hospital a secondary growth in the spine at first imitated caries. In a case of primary carcinoma of the gall-bladder a secondary growth in the right breast was naturally thought to be primary (Osler [1]).

When the liver becomes infiltrated with secondary growths, the clinical aspect of the case may be that of carcinoma of the liver. Enlargement of the liver can be made out in about half the cases, but it may be obscured by ascites or by flatulent distension. The surface may be smooth when the enlargement is due to distension with bile, nodular from secondary growths, or there may be a definite tumour formed by the cancerous gall-bladder and the adjacent liver substance infiltrated by growth. The bile-ducts may also be invaded by direct extension of the growth or be compressed by secondary growths or by enlarged glands either in the portal fissure or in the neighbourhood of the pancreas. Jaundice is thus set up, and the symptoms are much the same as those of primary carcinoma of the head of the pancreas or of the bile-ducts. Though not a necessary result of carcinoma of the gall-bladder, jaundice is very frequent. In 30 cases collected by Meunier it was absent in only 4. Permanent jaundice occurred in 33, or 55 per cent, of Winton's 60 cases, and in 69 of Musser's 100 cases.

As Mayo Robson [2] points out, jaundice may be due to catarrh of the ducts, but in that event it would not be progressive as in malignant disease, but would vary or even pass away. I have seen several cases of carcinoma of the gall-bladder in which jaundice came on after vomiting and diarrhoea, as in catarrhal jaundice, but persisted until death, and at the necropsy was found to depend on definite obstruction to the ducts. Jaundice may also be due to a gall-stone in the common duct.

Warthin [3] described a case of carcinoma of the gall-bladder in which jaundice, leucodermia, and pigmentation, suggesting Addison's disease, were present. After death secondary growths were found in both adrenals.

Ascites occurs in about one-quarter of the cases. In Winton's 60 cases it was present in 14. It depends not on malignant disease of the gall-bladder itself, but on complications set up by metastases or by extension of the primary growth. It may be associated with, but does not necessarily follow, pressure on the portal vein; but it is most satisfactorily explained by chronic peritonitis set up by secondary growths

[1] Osler. *Brit. Med. Journ.*, 1906, i, 2.
[2] Mayo Robson. *Brit. Med. Journ.*, 1897, i, 710.
[3] Warthin. *Phila. Med. Journ.*, 1900, vi, 38.

on the peritoneum. When there are numerous peritoneal metastases, the effusion may be fatty as the result of cellular degeneration (chyliform or fatty ascites).

Oedema of the legs may occur in the late stages of cachexia, and be due to cardiac debility, or possibly to the pressure exerted on the inferior vena cava by a large ascitic effusion or by enlarged glands in the neighbourhood. Thrombosis of the inferior vena cava has been recorded. There is often dyspepsia, which in a few instances is due to pyloric obstruction due to direct invasion by the growth, and may then be associated with a dilated stomach. There may be vomiting, tympanites, and usually constipation, which may alternate with diarrhoea. Extension of the growth to the colon may give rise to chronic or eventually to complete intestinal obstruction. When deep jaundice has developed, the patient gradually passes into the condition of cholaemia. The temperature is normal or subnormal unless there are complications. Muscular wasting and loss of strength steadily progress, and eventually emaciation, exhaustion, and cachexia become extreme; the biliary toxaemia gives rise to haemorrhages, petechiae, epistaxis, and occasionally haematemesis and melaena, mental failure, delirium, coma, and death. Terminal infections may carry the patient off, and this without the temperature being necessarily raised.

Complications.—In rare instances the gall-bladder perforates into the peritoneal cavity and sets up peritonitis. Rixford[1] met with a case in which extensive haemorrhage so distended a carcinomatous gall-bladder that rupture occurred. The growth may perforate into the transverse colon, and, as a result, the gall-bladder may be infected and an abscess, either in the gall-bladder or in its immediate neighbourhood, may result.[2] Suppurative cholangitis may arise and spread into the liver, the gall-bladder or Wirsung's duct, and in the latter event set up acute suppurative pancreatitis. Pus may collect in the gall-bladder, either when the growth is in a very early stage, or when there are numerous metastases.

In a man aged fifty-two, whom I examined after death at St. George's Hospital, a primary carcinoma of the gall-bladder gave rise to numerous secondary growths in the liver, which, with the stomach, weighed 15 pounds. There were calculi and pus in the gall-bladder, and chyliform (fatty) effusions in the left pleura and the peritoneum.

A local peritoneal abscess may form close to a carcinomatous gall-bladder, or there may be circumscribed acute peritonitis in its neighbourhood.

This was present in a woman aged forty-five years upon whom exploratory laparotomy was performed for a large tumour in the hepatic region. A quantity of fibrin was found around a carcinomatous mass, in the position of the gall-bladder, enclosing two calculi.

[1] Rixford. *Trans. Am. Surg. Assoc.*, 1905, xxiii, 219.
[2] Blanc et Leray. *Bull. Soc. Anat. Paris*, 1897, lxxii, 69.

When cholecystitis supervenes in a carcinomatous gall-bladder micro-organisms may be absorbed and infect other parts of the body. Lorrain[1] reported a case of lithiasis and carcinoma of the gall-bladder, with cholecystitis and endocarditis. Pyloric obstruction and obstruction of the transverse colon due to direct extension of growth have been already referred to. Portal thrombosis may occur (*vide* p. 637).

Duration.—It is difficult to determine the duration of the disease, since the early symptoms so closely resemble cholelithiasis, with which it is almost always combined. Probably it remains latent for a considerable time, but when jaundice and cholaemia have set in, the end is near. Some cases die very soon after the onset of definite symptoms. On the whole, the average duration of the disease may be put down as less than six months.

Diagnosis.—The presence of a hard, nodular, progressively increasing tumour in the position of the gall-bladder in a patient about the age of fifty years, especially in a woman, suggests the disease. Dull pain, loss of appetite, and wasting are in favour of growth. The distinct shadow cast by *x*-rays has been found of diagnostic value by Goldmann.[2] When metastases can be felt in the liver or in the supraclavicular fossae, the diagnosis is practically clinched. The only fallacy is, of course, that there is a primary tumour somewhere else which has given rise to generalisation, and that among other places a secondary growth has developed in or close to the gall-bladder. Careful search for a primary neoplasm in the stomach, rectum, oesophagus, breast, and uterus should, therefore, always be made. Jaundice is not an early or essential symptom.

Differential Diagnosis.—*Gall-stones.*—Malignant disease, especially in the earlier stages when the growth is confined to the gall-bladder, is very like cholelithiasis, and since carcinoma in the vast majority of the cases develops subsequently to gall-stones, it is very difficult to say when malignant disease has begun. Enlargement of the gall-bladder is in favour of tumour, especially if it is progressive and nodular. On the other hand, extensive inflammatory thickening of the walls of the gall-bladder may closely simulate carcinoma, even when the parts are exposed during laparotomy, and this impression may be supported when the thick-walled viscus is punctured. An inflamed gall-bladder may clinically appear of stony hardness either from contained calculi, or, more rarely, from calcification of its walls. In addition, the occurrence of dense adhesions to the surrounding parts—colon, stomach, omentum, etc.—and inflammatory enlargement of glands in the portal fissure, lesser omentum, and around the common bile-duct, where it passes into relation with the pancreas, may all suggest, even when the abdomen is opened, that there is malignant disease either of the gall-bladder, pylorus, or colon, and that secondary growths in the glands, by pressure on the ducts, have given rise to jaundice. Gall-stones in the common duct may feel like glands invaded by carcinoma. In any doubtful case the gall-bladder should be

[1] Lorrain. *Bull. Soc. Anat.*, 1903, lxxviii, 527.
[2] Goldmann. *Proc. Roy. Soc. Med.*, Lond., 1908, i (Surg. Sect.), 17.

opened and not merely punctured. As time goes on the cachexia, increasing jaundice, and, most positive evidence of all, secondary growths, may appear and strengthen or decide the diagnosis.

Malignant Disease of the Liver.—In the later stages, when the liver is enlarged and presents either a large tumour or several small ones, the diagnosis from primary or secondary malignant disease is often very difficult or even impossible. The history of gall-stones would suggest that the primary growth might have started in the gall-bladder, and the original appearance of a tumour in that situation would strengthen the diagnosis in the absence of evidence pointing to primary carcinoma of the stomach, colon, or other parts. Unfortunately, a history of gall-stones is often absent, and a tumour in the position of the gall-bladder is felt in about half the cases only.

Syphilitic disease of the liver in rare instances imitates carcinoma of the gall-bladder. From cicatricial contraction and deformity a piece of the right lobe may become elongated and hard and be thought during life to be a carcinomatous gall-bladder (Gerhardt [1]). In such cases the effect of antisyphilitic treatment must be the guide as to the diagnosis.

Carcinoma of the Stomach.—When the cancerous gall-bladder causes pyloric obstruction, it may naturally be regarded as carcinoma of the pylorus. There is an absence of the movable pyloric tumour, but, unfortunately, this may also occur in pyloric cancer. The history of gall-stones and the presence of jaundice point to a biliary origin for the gastric symptoms. A bismuth meal and examination with *x*-rays may give valuable help.

Carcinoma of the transverse colon in the neighbourhood may closely resemble carcinoma of the gall-bladder.

Carcinoma of the bile-ducts and of the head of the pancreas may be simulated by those cases of gall-bladder carcinoma in which jaundice occurs early. In the former conditions the gall-bladder is more often distended and smooth, whereas in the latter the tumour is hard, solid, and may be irregular, and the liver is more likely to be enlarged and shew secondary growths. The question of diagnosis between these two conditions is discussed on page 699. In malignant disease of the pancreas a tumour may sometimes be felt deep in the abdomen and close to the spine.

Tumours arising from the parts around the gall-bladder, such as a hydatid cyst, a floating kidney or renal tumour on the right side, or more rarely a tumour of the right suprarenal, may imitate carcinoma of the gall-bladder; or one of these conditions may be diagnosed when the growth is really in the gall-bladder.

In a man aged seventy-nine years who presented a rounded, tender lump the size of an apple in the right hypochondrium, without jaundice or ascites, the diagnosis lay between a calcified hydatid cyst and carcinoma of the gall-

[1] Gerhardt. *Semaine méd.*, Paris, 1898, xviii, 273.

bladder. At the necropsy there was carcinoma of the gall-bladder with miliary abscesses in the liver.[1]

When a *floating kidney* gives rise to jaundice by traction or pressure on the bile-ducts, the clinical aspect may resemble that of malignant disease of the gall-bladder. The free mobility of a floating kidney and the fact that it can be displaced from continuity with the liver should prevent confusion with malignant disease of the gall-bladder. The lumbar region should be carefully examined, and the abdomen should be palpated in the knee-and-elbow position.

Under certain conditions *faecal accumulation* in the transverse colon may, by the colicky pains and the presence of numerous hard masses in the neighbourhood of the gall-bladder, suggest carcinoma of the gall-bladder with secondary growths around. Examination under an anaesthetic may shew that these masses can be indented by the finger, and subsequent investigation that they vary in position and in number. In such cases the effect of purgatives and massage should be tried.

The **prognosis and treatment** may be considered (1) from a medical, and (2) from a surgical point of view.

(1) The disease being necessarily fatal unless it can be removed, medical treatment is merely palliative, and consists in the relief of pain and discomfort by morphine and opium, of vomiting and nausea by bismuth, hydrocyanic acid and morphine, and of constipation and intestinal fermentation by diet, calomel, salol, or various antiseptic remedies. Under such treatment the prognosis is of the gloomiest.

(2) If the growth be removed and there are no metastases, the prognosis should be more hopeful.

Quénu[2] collected 93 cases of cholecystectomy for carcinoma with an operative mortality of 18 per cent; out of 52 cases in which information was obtained, 14 were alive a year after operation, but only 5 or 6 were really satisfactory. The high mortality from operation mainly depends on haemorrhage; thus, there may be constant oozing from the wound, and after death extensive haemorrhagic infiltration around the ducts and pancreas. This tendency to haemorrhage should always be guarded against by giving large doses of calcium salts to jaundiced patients before operation. Calcium salts do not always prevent haemorrhage in jaundiced patients, and it is possible that degeneration of the vessel-walls is responsible for the haemorrhagic tendency, either alone or in addition to diminished coagulation power of the blood (Berg[3]).

After recovery from operation a biliary fistula is sometimes left. In some instances there is temporary improvement after resection of the gall-bladder, but nearly all cases shew a recurrence, often within six months. The following case illustrates the extreme malignancy of primary carcinoma of the gall-bladder, even when removed in a very early stage and apparently under the most favourable conditions.

[1] Lejonne et Malanoff. *Bull. Soc. Anat. Paris*, 1900, lxxv, 133.
[2] Quénu. *Rev. de chir.*, Paris, 1909, xxxix, 245.
[3] Berg. *Ann. Surg.*, 1903, xxxviii, 356.

Heidenhain,[1] in the course of an operation on the gall-bladder for the removal of six calculi, noticed a small, button-like thickening in its wall and removed the gall-bladder; microscopically it was carcinomatous. Three months later the patient died from growths in the liver, though at the operation it appeared perfectly healthy.

The success of the operation depends on its early performance and on the absence of secondary growths, and this cannot be excluded before laparotomy. The diagnosis being difficult, cases occur in which laparotomy is undertaken with a view of relieving cholelithiasis, and carcinoma of the gall-bladder is found, perhaps in an early stage. Such early cases are the most favourable for cholecystectomy.

According to Carl Beck,[2] 40 per cent of the cases operated upon for cholelithiasis have carcinoma of the gall-bladder.

Secondary Malignant Tumours in the gall-bladder sometimes occur in widespread carcinoma or more rarely sarcoma. The growths are usually either on the peritoneum, as in cases of extensive malignant disease of the peritoneum, or just under the peritoneal covering of the gall-bladder. The growths very rarely invade the mucous coat of the gall-bladder, and, as shewn by Siegert's[3] and my own figures (*vide* p. 640), are not specially related to the presence of gall-stones. Secondary also contrasts with primary malignant disease of the gall-bladder in the sex incidence: whereas primary carcinoma is about four times commoner in women, secondary growths were much more frequent in the male sex in Siegert's figures. As a rule, secondary growths do not obstruct the cystic duct, but this may, of course, occur and give rise to hydrops of the gall-bladder. Growths of the stomach, duodenum, and colon may spread into the gall-bladder.

[1] Heidenhain. *Verhandl. d. deutsch. Ges. f. Chir.*, 1898, p. 126.
[2] Beck, C. *Med. Week*, Paris, 1897, v, 137.
[3] Siegert. *Virchows Arch.*, 1893, cxxxii, 353.

DISEASES OF THE BILE-DUCTS

ABNORMALITIES.—Atresia or complete obliteration of any part of the bile-ducts is pathological, and usually due to inflammatory changes in fetal life. Abnormalities in the ducts chiefly consist in variation in the length of the cystic and common bile-ducts, and in the presence of abnormal communications between the gall-bladder and the liver (hepato-cystic ducts). The left and right hepatic ducts may remain separate for a considerable distance, and only join when the cystic duct unites with them ; in such cases there is no common hepatic duct. The cystic duct may not join the common hepatic duct until close to the duodenum, so that the common bile-duct is very short. A double cystic duct has been recorded (Dreesmann [1]). In congenital absence of the gall-bladder (*vide* p. 601) the common bile-duct may be dilated in part of its course.

Variations in the method of opening of the common bile-duct into the duodenum exist ; Letulle and Nattan-Larrier [2] describe four types of the openings of the common bile- and Wirsung's ducts. In some instances the common bile-duct opens into the duodenum separate from the main pancreatic duct. It very occasionally opens with the accessory pancreatic duct of Santorini, the main pancreatic duct being quite separate and opening alone in the position of the normal biliary papilla. In 104 cases Schirmer [3] found this four times.

The effect of tight lacing on the biliary apparatus is referred to elsewhere (p. 15).

CONGENITAL OBLITERATION OF THE BILE-DUCTS

Nomenclature.—Most of the cases are associated with cirrhosis, and since, as will be seen later, it is probable that the cirrhosis is the primary change and the cholangitis and obstruction of the ducts secondary and later results, the term "congenital hepatic cirrhosis with obliterative cholangitis" describes these cases more accurately. But since congenital obliteration may possibly be brought about in other ways, it is better to

[1] Dreesmann. *Deutsche Ztschr. f. Chir.*, Leipz., 1908, xcii, 411.
[2] Letulle et Nattan-Larrier. *Bull. Soc. Anat. Paris*, 1899, lxxiv, 987.
[3] Schirmer. *Inaug. Diss.*, Basel, 1893.

retain the more familiar and inclusive title of congenital obliteration of the bile-ducts. Our knowledge of this disease is chiefly due to John Thomson.

Incidence.—In 1892 Thomson[1] referred to 50 cases, and in 1911 Howard and Wolbach[2] collected 76 cases with necropsies.

Cases resembling this Condition.—Treves[3] successfully operated upon a girl aged nineteen for jaundice of sixteen years' duration, and found obliteration and absence of the lower end of the bile-duct. It differs so markedly from all the other cases that it can hardly be included in this group. Jaundice did not begin until the age of three years, instead of either at or shortly after birth. Possibly the obliteration of the duct was due to the effects of a calculus lodging in the duct at or about the time of the onset of jaundice. Thomson[4] considers that the same morbid process is at work in cholelithiasis in infants as in congenital obliteration of the bile-ducts, and quotes two cases of infantile cholelithiasis in which the biliary apparatus was abnormal (Cuffer, Bouisson).

Etiology.—*Hereditary Influences.*—In a few instances other members of the same family have died soon after birth with jaundice, and it may be suspected with a similar morbid change (Mathie[5]). In Binz's and Gould's cases (quoted by J. Thomson in 1892) two members of a family were proved to have died from this cause. Arkwright's[6] series of 14 cases of dangerous icterus neonatorum in one family, with 4 survivors, belongs to a different category (*vide* p. 572).

There does not seem to be any real association between *malformations* and this disease. Concomitant deficiencies in the liver must be regarded as part of the disease, and not as true malformations.

Witzel's[7] case of a number of true malformations and obliteration of the ducts was possibly congenital cystic disease of the liver (*vide* p. 448). Congenital obliteration of the bile-ducts has been found in association with hypertrophic stenosis of the pylorus (Barker and Mackey[8]). In a case of complete absence of the biliary apparatus in an infant one month old there was a congenital malformation of the left upper arm (Kirmisson and Hébert[9]).

Syphilis is not an important and certainly not more than an occasional cause of the change in the ducts and liver. This is shewn not only by the histological character of the change in the liver, but by the freedom of the parents and patients from signs of syphilis. Among the parents there is evidence of syphilis in very few instances—less than a twentieth (Thomson). While there is every reason to believe that syphilis plays no part in the usual type of the cases, stricture of the ducts may be due

[1] Thomson, J. *Congenital Obliteration of the Bile-ducts*, 1892, Edin.
[2] Howard and Wolbach. *Arch. Int. Med.*, Chicago, 1911, viii, 559.
[3] Treves. *Practitioner*, Lond., 1899, lxii, 18.
[4] Thomson, J. *Edin. Hosp. Rep.*, 1898, v, 1.
[5] Mathie. *Glasgow Med. Journ.*, 1906, lxvi, 378.
[6] Arkwright, J. A. *Edin. Med. Journ.*, 1902, N.S., xii, 156.
[7] Witzel, O. *Centralbl. f. Gynäk.*, Leipz., 1880, iv, 561.
[8] Barker and Mackey. *Lancet*, Lond., 1910, ii, 459.
[9] Kirmisson et Hébert. *Bull. Soc. Anat. Paris*, 1903, lxxviii, 317.

to fetal peritonitis, which is usually connected with syphilis; and syphilitic inflammation may attack the walls of the ducts (*vide* p. 658).

Sex.—In Thomson's cases the sex was given in 67, and shewed a preponderance of males—41 males, 26 females.

Pathogeny.—There are two explanations: (i) That there is in the first place a developmental aplasia or a narrowing of the duct, which gives rise by obstruction to cirrhosis; (ii) That there is first a mixed cirrhosis of the liver which gives rise to a descending obliterative cholangitis.

(i) John Thomson [1] believes that in the great majority of cases there is, to start with, a congenital malformation of the ducts which relatively narrows the available lumen; with this view Beneke [2] and Milne [3] agree. This obstruction to the free exit of bile disposes to catarrh, blocking, and finally to obliteration of the ducts. Lavenson [4] and Parkes Weber [5] believe that the diverticulum which should form the common bile-duct never becomes pervious. As a result of the obstruction to the passage of bile into the duodenum the bile becomes toxic and biliary cirrhosis is set up.

As a criticism of this view it may be pointed out that cirrhosis of the liver is comparatively rare in association with obstruction of the bile-ducts in adults, and, when present, is usually associated with gall-stones and infection of the ducts which are dilated inside the liver (*vide* p. 331), whereas cirrhosis of quite a different type, and not accompanied by any dilatation of the intrahepatic ducts, is extremely frequent in congenital obliteration of the ducts.

In J. Thomson's 50 cases a microscopical examination was only made in 10 and in all but 1 of these it is stated that cirrhosis was present; in 20 other cases, of which I have notes, cirrhosis was present in 19.

The question therefore arises, is there any evidence that cirrhosis in these cases depends on the obliteration of the larger bile-ducts? If it can be established that the change in the bile-duct is older and more advanced than in the liver, there is fair ground for regarding the hepatic lesion as due to the obstruction in the ducts. Ross [6] described obliteration of the common bile-duct near the duodenum in a female child, aged three months, whose liver shewed small-celled infiltration around the bile-ducts rather than fibrosis. In this instance the evidence points to the change in the bile-duct being the older. On the other hand, in nearly all the other cases, the fibrosis in the liver is quite as old as the lesion in the bile-ducts.

(ii) The following appears to be a reasonable explanation of the pathogeny of so-called congenital obliteration of the bile-ducts: In the first instance, poisons pass from the maternal placenta to the fetus by the umbilical vein; some of this blood at once passes through the liver, and,

[1] Thomson. *Congenital Obliteration of the Bile-ducts*, p. 38, 1892; and *System of Medicine* (Allbutt and Rolleston), 1908, iv, part i, 106.

[2] Beneke. *Die Entstellung der kongenital Atresia der grossen Gallengänge*, Marburg, 1907.

[3] Milne. *Quart. Journ. Med.*, Oxford, 1911–12, v, 409.

[4] Lavenson. *Journ. Med. Res.*, Boston, 1908, xviii, 61.

[5] Weber, P. and Dorner. *Proc. Roy. Soc. Med.*, 1911, iv (Child. Sect.), 41.

[6] Ross, D. *Lancet*, Lond., 1901, i, 102.

in virtue of the contained toxin, induces multilobular cirrhosis of the liver; the rest of the blood in the umbilical vein passes directly into the general circulation of the fetus by the ductus venosus, and subsequently, by means of the hepatic artery, will convey the same poison to the liver. By this means the toxic body, which may be analogous to toluylenediamine, is excreted into the small intrahepatic bile-ducts and sets up cholangitis and unilobular cirrhosis, like that seen in hypertrophic biliary cirrhosis. In this way a mixed cirrhosis (portal and biliary) is induced. The cholangitis descends to the larger ducts, and gives rise to an obliterative cholangitis—a process analogous to obliterative appendicitis. The difference between this condition of congenital (umbilical) cirrhosis with obliterative cholangitis and other forms of cirrhosis in post-natal life consists in the further change in the large bile-ducts and gall-bladder. This additional lesion may be explained as follows: The bile-ducts are extremely small at birth, and any inflammatory change will, from their small size, produce stenosis much more readily than in later life. An analogous effect is seen in the greater incidence of laryngeal obstruction in diphtheria in young subjects than in older patients. The opposed inflamed surfaces of the bile-ducts will also come in contact more readily, and, as in catarrhal appendicitis, obliteration might result.

The following considerations bear on the hypothesis that the disease is primarily a congenital cirrhosis:—

1. The almost constant presence of cirrhosis in these cases of bile-duct obstruction in infants as compared with the infrequency and irregularity with which cirrhosis follows obstruction of the larger bile-ducts in later life.

2. The structural differences between the cirrhosis in congenital obliteration of the ducts, which does not shew any dilatation of the intrahepatic bile-ducts, and the cirrhosis sometimes seen in obstruction of the ducts in later life, in which the intrahepatic ducts are dilated and icteric necrosis of the liver cells is common.

3. The large size of the liver—this resembles hypertrophic biliary cirrhosis. In simple obstruction of the larger bile-ducts in adults the liver, though swollen from retained bile in the early stages, is usually small after death.

4. The large size of the spleen, a phenomenon not met with in uncomplicated biliary obstruction, is best explained as the result of toxic bodies reaching the organ by the splenic artery. In congenital syphilis, in which it is probable that the parasite reaches the liver by the umbilical vein and is derived from the maternal circulation rather than that the ovum is infected by a syphilitic spermatozoon, there is a similar splenic enlargement. The difference between the intercellular cirrhosis of hereditary syphilis and the mixed (unilobular and multilobular) cirrhosis of congenital obliteration of the bile-ducts must depend on a difference in the causes of the two diseases.

5. Against the view that congenital obliteration of the bile-ducts is primarily a form of congenital cirrhosis it might be objected that the poison responsible for the change must pass through the mother, and that she should shew evidence of its influence. In reply it may be suggested that the fetus' liver may be more susceptible than the mother's to poisons tending to produce cirrhosis, just as the effects of syphilis are usually more marked in the child than in its mother.

To sum up, it seems reasonable to believe that the disease is primarily started by poisons derived from the mother and conveyed to the liver of the fetus, and that a mixed cirrhosis and cholangitis are thus set up. The cholangitis accounts for the jaundice, and by descending to the larger extra-hepatic bile-ducts, induces an obliterative cholangitis analogous to obliterating appendicitis. In some cases, especially those fatal early in life, the latter change has not been effected, and cirrhosis alone is found. Possibly in some instances this change never occurs, and in this way some of the cases of cirrhosis in very early life are accounted for. There are probably several conditions at present included under the title congenital obliteration of the ducts, and some, such as D. Ross' case, are due to constriction of the duct by localised peritonitis, and deserve the title better than the cases that are intimately associated with cirrhosis.

Morbid Anatomy.—*The liver* is, in the great majority of the cases, enlarged, and sometimes to a very considerable extent. In my case[1] it weighed twice as much as normal. In only one of Thomson's cases was it definitely stated to have been small. The liver is bile-stained, and often dark green; the surface is usually irregular and has been compared to morocco leather. On section, the organ is tough, firm, and manifestly fibrosed. Cirrhosis was present in nearly all the recorded cases. The lymphatic glands in the portal fissure are usually enlarged.

Microscopically there is well-formed fibrous tissue separating the lobules from each other. The arrangement of the fibrous tissue varies: in parts it is unilobular and separates each individual lobule from its fellows (*vide* Fig. 90); this unilobular fibrosis has been thought to depend in necrosis of the liver cells at the periphery of the lobules (Milne[2]). In other parts a varying number of lobules are enclosed in firm strands of fibrous tissue. There is thus a mixed cirrhosis composed of the unilobular and multilobular forms. The pseudobile canaliculi in the fibrous tissue are prominent, tortuous, and appear to be increased in number. The biliary capillaries between the hepatic cells often contain plugs of inspissated bile. The liver cells are in places well preserved, elsewhere they shew icteric necrosis and do not take the stain.

The Bile-ducts and Gall-bladder.—There is considerable variation both in the situation and the extent of the obliteration of the ducts. Howard and Wolbach describe four groups of cases:—(i) the gall-bladder and cystic duct are patent, but the ducts between the liver and the duodenum are obliterated; (ii) the ducts between the liver and duodenum are patent, but the gall-bladder and cystic duct are absent; (iii) the hepatic and cystic ducts are obliterated; (iv) obliteration at some point in the common duct. They state that by far the commonest situation for obliteration is in the hepatic and cystic ducts; Lavenson found the obliteration most frequent

[1] Rolleston and Hayne. *Brit. Med. Journ.*, 1901, i, 758.
[2] Milne. *Journ. Path. and Bacteriol.*, Cambridge, 1909, xiii, 135.

near the duodenum; and out of 89 collected cases Milne[1] found that the common bile-duct was absent or impervious in 70, the duodenal end being pervious in 5 only; and that in 39 of the 70 the common hepatic duct also was absent or obliterated. The obliterated ducts may be traced in the lesser omentum as fibrous cords which resemble the hepatic artery, and gradually fade off into the surrounding tissues. It is possible that some cases of great cystic dilatation of the ducts (*vide* p. 659) are the outcome of local obliteration of the lower end of the common bile-duct in very early life. The gall-bladder may be collapsed and buried in adhesions, or

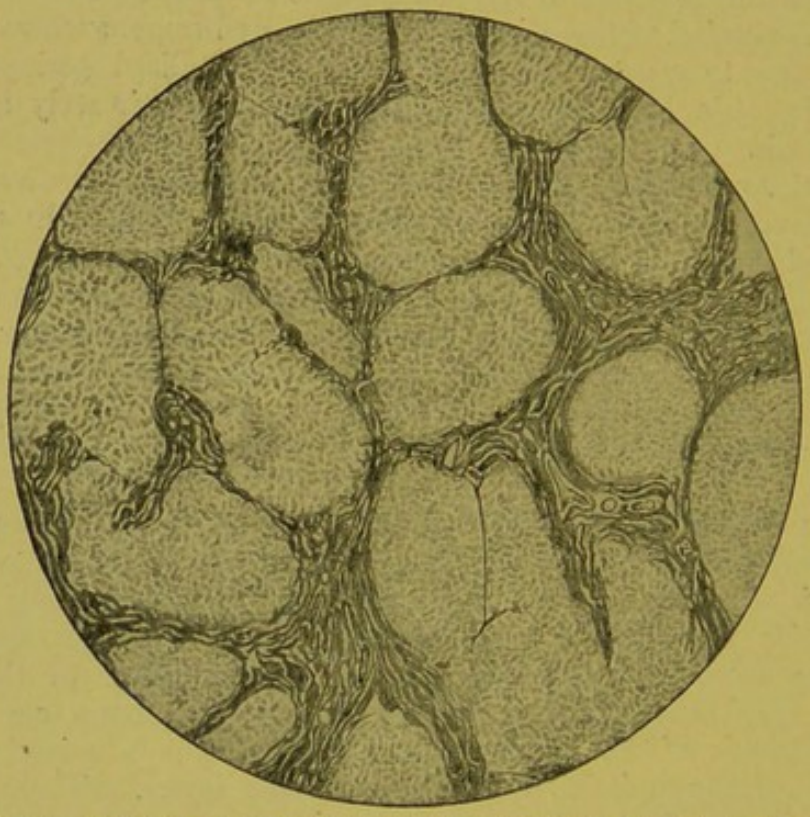


FIG. 90.—Unilobular cirrhosis from a case of congenital obliteration of the bile-ducts in a child aged six months. There is well-formed fibrous tissue, with no sign of recent proliferation, separating the individual lobules. ×18.

thickened and without any cavity. It may contain clear mucus, but rarely bile. In one of Thomson's cases a calculus was found in the gall-bladder.

The Microscopic Appearances of the Ducts.—In my own case the common duct near the point of obliteration shewed great fibrous thickening of its walls, with complete alteration of its normal appearance, its muscular tissue and mucous glands having disappeared. The epithelial lining was lost, and the lumen contained debris and masses of bile-pigment which infiltrated the fibrous walls for a short distance. There was no sign of progressive hyperplasia or inflammation. Thomson (1908) confirms this account. Weber and Dorner described much the same appearances, and in addition embryonic blood-vessels; in the common bile-duct

[1] Milne. *Quart. Journ. Med.*, Oxford, 1911–12, v, 412.

no lumen was found, thus supporting their view that there never had been one.

The gall-bladder in Weber and Dorner's case shewed fibrosis and embryonic blood-vessels; in one of Thomson's cases the walls of the gall-bladder, which was partly obliterated, were thickened and infiltrated with young connective-tissue cells; the lining epithelium, where any cavity remained, was described as normal.

The spleen is usually enlarged, sometimes very greatly. In a child

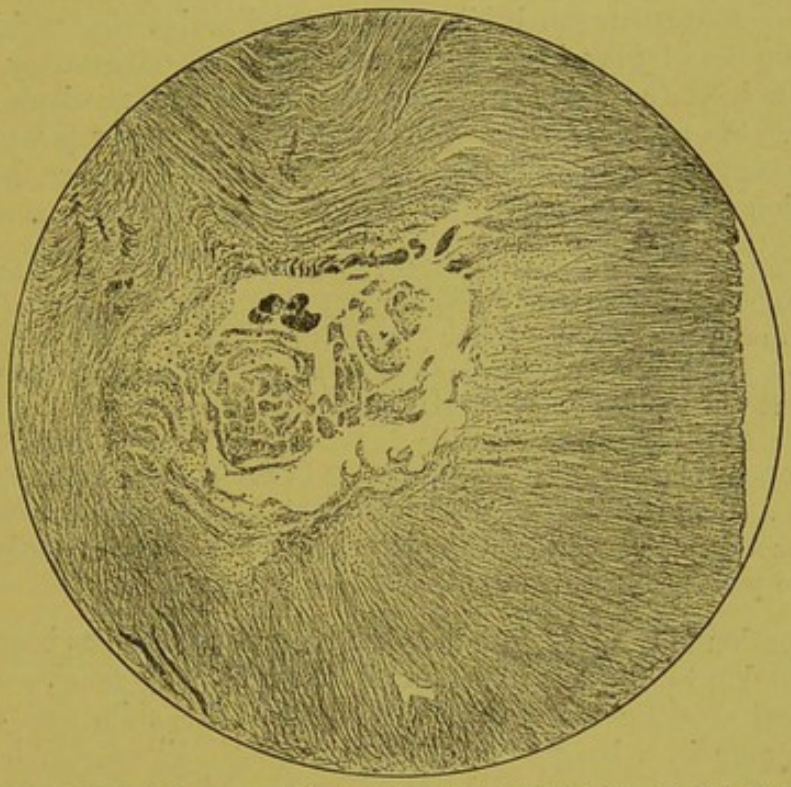


FIG. 91.—Transverse section of common bile-duct close to its obliteration. (×35.) Shews altered and fibrosed walls of duct, and absence of mucous glands and of the lining epithelium. The small black spots infiltrating the walls of the duct are microscopic masses of inspissated bile, not nuclei.

aged six months recorded by Parker[1] it weighed 5 ounces. It may shew fibrosis (Emanuel[2]) and excess of plasma cells (Weber and Dorner).

The Pancreas.—Periductular fibrosis with intact islands of Langerhans has been described (Cattaneo,[3] Emanuel, Thomson). The organ has, however, been found to be normal.

The other organs are deeply bile-stained. Adhesions around the liver or bile-ducts are rare, and probably chiefly occur in cases with a syphilitic taint. A small quantity of ascites is recorded in some of the cases, but is very seldom of clinical importance. The cerebrospinal fluid does not contain bile (Weber).

Clinical Picture.—Jaundice may be present at birth or it may succeed

[1] Parker, G. *Lancet*, Lond., 1901, ii, 520.
[2] Emanuel. *Brit. Med. Journ.*, 1907, ii, 385.
[3] Cattaneo. *Pediatria*, Napoli, 1904, 2. s., ii, 584.

what is regarded as physiological jaundice. In some instances the infant does not become jaundiced until two or more weeks after birth. It is conceivable that the effects of congenital changes in the ducts, like those of congenital morbus cordis, may be delayed, and only appear after an interval of some years. If so, cases like Treves' can be explained as belonging to this category. When once established, the jaundice is progressive and eventually may become dark green, but variations may occur, jaundice becoming less for a time and then darker again. There is never much itching.

The urine contains much bile-pigment and stains the napkins. The meconium passed by the infants is usually normal, and is rarely devoid of bile. In only a few instances have the subsequent motions contained stercobilin. As a rule, normal yellow motions are never passed and the stools are clay-coloured from the first. In some instances, however, a green motion has been described after calomel has been given.

This occurrence has given rise to some discussion; it has been suggested that the green colour may be entirely independent of bile, and due to some chemical combination of mercury and sulphur (Thudichum [1]), or that the green colour is due to chromogenic micro-organisms (Lesage [2]). There seems very slender proof that green stools are due to bacterial pigment alone (Garrod, Kanthack, and Drysdale [3]). It is possible that in the few cases in which the administration of calomel has been followed by a green stool there was biliverdin present and that either there was not complete obstruction of the bile-duct or that the administration of calomel set up ulceration of the intestine and so allowed some bile-stained exudation to pass into the bowel.

Constipation is the rule, but in a few cases diarrhoea has been noticed, and may be due to virulent infection of the alimentary canal.

Haemorrhages from mucous surfaces, into the skin, and from the umbilicus occur in a large number of the cases. Blood may be lost by epistaxis or vomited or passed by the bowel. I have seen fatal haemoptysis. The conjunctivae, which are deeply stained, may shew small haemorrhages. Constant oozing from the umbilicus may occur soon after birth, and is a very grave symptom, since death follows in a few days. In those instances in which more than one child in a family is affected the haemorrhagic tendency is particularly strong (Thomson [4]). Subcutaneous haemorrhages may be scattered all over the body. The haemorrhages, like those seen in other forms of deep obstructive jaundice, in advanced cirrhosis, and in acute atrophy, are due to hepatic insufficiency and the passage of poisons, which should have been stopped by the liver, into the general circulation, to deficiency of fibrinogen and diminished coagulability of the blood, and possibly to degeneration in the vessel walls. Morse and Murphy found the coagulation time of the blood prolonged and a moderate leucocytosis. Weber found the colour-index

[1] Thudichum. *Lancet*, 1889, i, 631.
[2] Lesage. *Arch. physiol. norm. et path.*, Paris, 1888, 4. s., i, 212.
[3] Garrod, Kanthack, and Drysdale. *St. Barth. Hosp. Rep.*, 1897, xxxiii, 13.
[4] Thomson. *System of Medicine* (Allbutt and Rolleston), 1908, iv, part i, 107.

high (1·2), the red blood-corpuscles increased in size (10μ) and more resistant to haemolysis than normal. In Weber and Dorner's case the Wassermann reaction was negative. The liver is enlarged, and may reach the level of the anterior-superior spine, and is firm, very hard, and fairly smooth. The spleen is usually also enlarged and firm.

The infants usually waste if life is sufficiently prolonged, but careful feeding may delay emaciation, which is not an early symptom. Convulsions may come on before death.

Duration and Prognosis.—A certain number of the cases die within the first few days of life from umbilical or other haemorrhages. Of Thomson's 49 cases, 30 lived more than one month, and of these, 16 survived for upwards of four months, 2 living into the eighth month. Of Lavenson's[1] 62 collected cases only 3 survived eight months, 1 of these lived to eleven months. The end may be hastened by streptococcic infection and resulting haemorrhages. It is clear that the prognosis is extremely bad. Possibly cases with only slight changes survive for long periods, as suggested by Treves and Ashby's[2] cases (*vide* p. 660). Moreover, other members of a family in which one child has died of the disease may recover from jaundice in early life.

Diagnosis.—Deep jaundice, haemorrhages, enlargement of the liver and spleen, and the absence of any evidence of acute infection in an infant a few weeks old, point to this disease.

Differential Diagnosis.—Since it is usually manifest that the condition is one of severe jaundice, it is hardly necessary to insist on the distinctions from the slight and common jaundice occurring in the first few days of life, in which the faeces contain bile and the jaundice rapidly fades. Persistent deep jaundice is sometimes followed by recovery; in a case of this kind the cause was thought to be very thick bile (Poynton[3]), a condition which might be due to cholangitis.

From syphilitic disease of the liver, the absence of any history or signs of the disease and the failure of mercurial treatment should distinguish the disease. According to Still,[4] the liver is much harder on palpation during life in congenital obstruction of the ducts than it is in ordinary cases of syphilis.

From infection of the umbilical vein after birth in which haemorrhage from the navel also occurs, the disease should be distinguished by its much slower course, by the absence of any sign of umbilical infection, and by the fact that at first there may be little constitutional disturbance.

In grave familial jaundice (*vide* p. 572) in which there is no gross obstruction, the faeces are not devoid of pigment, and the liver is not always enlarged.

Treatment is chiefly symptomatic. Small doses of grey powder, fractional doses of calomel, salicylates, or salol may be given to minimise

[1] Lavenson. *Journ. Med. Research*, Boston, 1908, xviii, 61.
[2] Ashby. *Med. Chron.*, Manchester, 1898–9, x, 28.
[3] Poynton. *Rep. Soc. Study Dis. Child.*, 1906, vi, 172.
[4] Still. *Clin. Journ.*, Lond., 1901, xvii, 324.

intestinal fermentation, and in the later stages salts of calcium to prevent haemorrhage. It is always well to try antisyphilitic treatment on the chance that the disease is of this nature. Very little can be expected from operative measures, and there is considerable risk of haemorrhage, owing to the patient's jaundiced condition. Since the obstruction may be in the hepatic ducts, opening the abdomen to do a cholecystenterostomy is a speculative or "exploratory" operation. Unsuccessful operations have been performed in some cases (Giese, Putnam, Westerman, Morse and Murphy); Ehrhardt[1] united the intestine with the cut surface of the liver, but the infant died six days later. It is true that success followed in Treves' case (*vide* p. 650), but this belongs to a different category.

Since the disease very probably depends on poisons generated in the mother, it is reasonable to treat the pregnant woman with small doses of calomel ($\frac{1}{40}$ to $\frac{1}{20}$ gr.), salol, and other drugs which inhibit intestinal fermentation, and to pay special attention to her diet and general health during pregnancy.

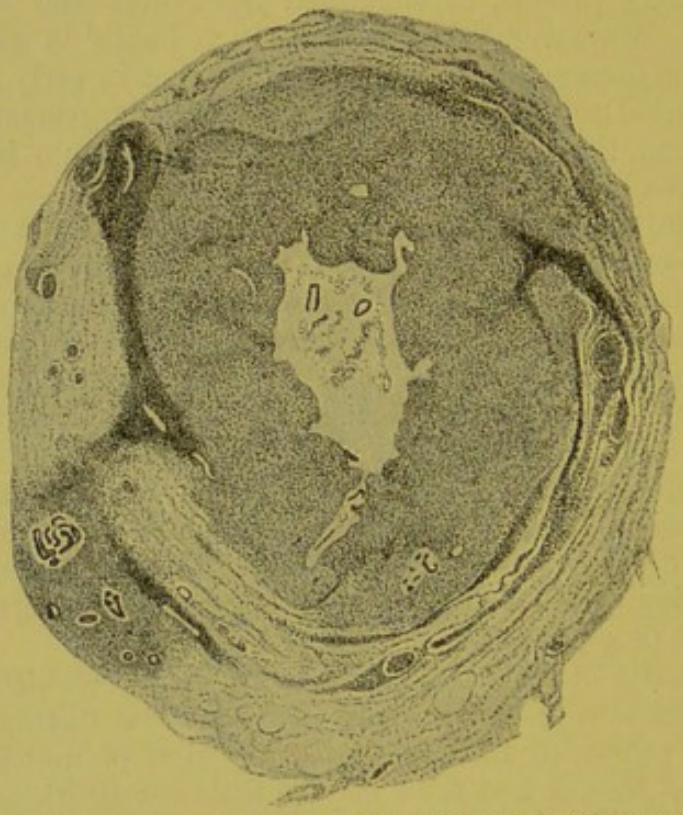


FIG. 92.—Microscopical appearances of congenital syphilitic stricture of the common bile-duct.

Congenital Syphilitic Stricture of the Common Bile-duct.—As the usual form of congenital obliteration of the bile-ducts is not due to syphilis, it is advisable to refer briefly to this rare condition. Beck,[2] Simonini,[3] and others[4] have described cases. Possibly some of

[1] Ehrhardt, O. *Zentralbl. f. Chir.*, Leipz., 1907, xxxiv, 1226 (Orig.).
[2] Beck. *Prag. med. Wchnschr.*, 1884, ix, 257.
[3] Simonini. *Pediatria*, Napoli, 1907, 2. s., v, 356.
[4] *Vide* Milne. *Quart. Journ. Med.*, Oxford, 1911–12, v, 414.

the reported cases of stricture of the common bile-duct in early life, especially those that improved under mercury, may have been of this nature.

My case[1] was a female child three weeks old, deeply jaundiced, emaciated, bleeding from the bowel, and resembled congenital obliteration of the ducts. The liver was much enlarged and hard, and the spleen was palpable. At the necropsy the lower half-inch of the common bile-duct was thickened and formed a white cord about the size of an adult's vas deferens; on transverse section it resembled the cross-section of the stem of a clay pipe, there being a small round hole in the centre. The microscopic appearances are seen in Fig. 92. The liver shewed intercellular cirrhosis. The pancreas was enlarged, firm, and white, and shewed extreme interacinous fibrosis, the islands of Langerhans being prominent and well preserved.

DILATATION

Obstruction in the course of the common bile-duct leads to dilatation of the common and other bile-ducts. Whatever the nature of the obstruction, dilatation will occur, but, generally speaking, it is less when due to a gall-stone in the common duct than when pressure is exerted from without by a tumour, such as carcinoma of the pancreas. The explanation of this is that in cholelithiasis the obstruction is not so complete as in the case of tumours. Mayo Robson[2] and Swain[3] have recorded cases of excessive dilatation of the common duct due to gall-stones. The extent of the dilatation of the biliary duct varies considerably, but it is usually greatest in the common bile-duct above the obstruction; it may be universal, and implicate the intrahepatic bile-ducts widely. Exceptionally a large cyst of the common bile-duct results. The contents of the dilated ducts may be bile or clear mucus; in gall-stone obstruction of the common duct it is very rare to find clear mucus in the ducts. Lenormant[4] could find only two such cases recorded. Colourless mucus in the ducts is usually associated with the pressure of a neoplasm on the common bile-duct.

Cystic Tumours

In rare instances, of which Mathieu[5] collected 20 examples in 1908, and Lavenson[6] 29 in 1909, great dilatation of the common bile-duct, forming a gigantic cyst, occurs; it is usually seen in children. There may not be any obvious obstruction, and the condition has been spoken

[1] Rolleston. *Brit. Med. Journ.*, 1907, ii, 947.
[2] Mayo Robson. *Diseases of the Gall-bladder*, p. 196, ed. iii, 1904.
[3] Swain, W. P. *Lancet*, Lond., 1895, i, 743.
[4] Lenormant. *Rev. de gynéc.*, Paris, 1912, xviii, 175.
[5] Mathieu, P. *Rev. de chir.*, Paris, 1908, xxxvii, 61.
[6] Lavenson. *Am. Journ. Med. Sc.*, Phila., 1909, cxxxvi, 563.

of as "idiopathic" and compared to congenital hydronephrosis (Russell [1]). In some cases there has been a valve-like fold of mucous membrane at the lower end of the common bile-duct; this has been thought to be the cause of the obstruction (Roslowzew [2]); but it may merely be secondary to kinking produced by the cyst. If, as in congenital morbus cordis, changes initiated during fetal life can remain latent for years and then, possibly as the result of slow cicatricial contraction of inflammatory tissue, give rise to obstruction, a satisfactory explanation is obtained of cases (Ashby,[3] Oxley,[4] Lavenson) in which the lower end of the common bile-duct was obliterated.

A girl aged seven had been jaundiced for two and a half years, and more recently had been tapped to the extent of 50 ounces for ascites. She was emaciated and had oedema of the feet. A cyst on the right side of the abdomen was tapped and 16 pints of dark-green mucus came away. In the course of three months it was tapped ten times, and on each occasion 8 to 10 pints were removed. After death the cyst was found to be the dilated common bile and cystic ducts; the common bile-duct was obliterated near the duodenum (Ashby).

Possibly in the following case obstruction in the common duct was due to hereditary syphilis:—

In a deeply jaundiced child aged nine years there was very marked evidence of hereditary syphilis in the body generally, and in the liver in intercellular cirrhosis. The liver and biliary apparatus preserved in the Museum of the College of Medicine, Newcastle-on-Tyne (No. 382–2), shew the common bile-duct dilated to the size of one's fist, the cystic and hepatic ducts being also dilated; the gall-bladder is atrophied and collapsed, and the opening of the common bile-duct into the duodenum cannot be found.

Some of the recorded cysts have been extraordinarily large, and when first seen on opening the abdomen, have resembled ovarian or hydatid cysts. The fluid inside them contains bile-pigment.

In Vater's [5] case of an infant, aged one year, enormous dilatation of the common duct was due to obstruction produced by an indurated pancreas. Todd [6] described a similar case in a girl aged fourteen years. In Wilks and Moxon's [7] case (*vide* p. 687), the common bile-duct of a child aged four years, which was so dilated as to be as big as its head, contained pendulous growths. In a woman aged forty-six years a cystic dilatation, containing 148 ounces of bile, was regarded by Eve as due to valvular obstruction produced by a papilloma growing from the wall of the common bile-duct one inch above the biliary papilla. Papillomatous growths may, however, be secondary to irritation inside a cyst.

[1] Russell. *Ann. Surg.*, 1897, xxvi, 692.
[2] Roslowzew. *Deutsche med. Wchnschr.*, 1902, xxviii, 739.
[3] Ashby. *Med. Chron.*, Manchester, 1898–9, x, 28.
[4] Oxley. *Lancet*, Lond., 1883, ii, 988.
[5] Vater, Abraham. *Diss. de scirrhis viscerum*, Vitemb., 1723. Quoted by Frerichs, *Diseases of Liver*, ii, 468, Transl. New Syd. Soc., 1861.
[6] Todd. *Dublin Hosp. Rep.*, 1817, i.
[7] Wilks and Moxon. *Pathological Anatomy*, p. 485, 3rd ed., 1889.

Out of 20 cases of this condition 18 were in females and 2 only in males. In 22 cases in which the age was given the average age was fifteen years and eight months (Lavenson).

Clinically these cases present themselves as abdominal cysts in connexion with the liver and may be regarded as a dilated gall-bladder, or as pancreatic, hydatid, or ovarian cysts. Jaundice is present, but in a female child aged sixteen months under my observation there was no jaundice. Pressure on the portal vein or inferior cava may explain ascites and oedema of the feet. The **prognosis** and **treatment** are unsatisfactory; out of 22 cases operated upon, 18 died. Drainage of the cyst and exploration of the lower end of the common bile-duct with a probe so as to displace any valvular fold of mucous membrane and allow a free passage of bile into the duodenum have been employed. Eve[1] considered anastomosis of the cyst with the hepatic flexure of the colon the simplest and safest course.

Intra-duodenal Bile-containing Cyst in Communication with the Ampulla of Vater.—R. S. Trevor[2] described a cyst containing bile, the size of a tangerine orange, which projected into the duodenum in the situation of the biliary papilla. It was lined inside and out by mucous membrane and its only communications were with the ampulla of Vater and with the duodenum. It appeared to be due to a congenital fusion in the middle line of two folds of duodenal mucous membrane which are often normally present on either side of the biliary papilla. Normally these folds enclose a fossa, but fusion of the folds would convert the fossa into a cyst; as the fusion was not everywhere complete, a bile-containing cyst communicating both with the biliary papilla and the duodenum resulted. It was found in the body of a man, aged twenty-four years, who died in St. George's Hospital from a perforated duodenal ulcer. There was no jaundice and no gall-stone.

SIMPLE STRICTURE

With the exception of the cystic duct, this is very rare. The cases may be divided into two groups: (i) the congenital cases, described on page 649, and (ii) those acquired in later life, which will be dealt with here. It is possible that in some of these cases a slight congenital change in the ducts might gradually progress so that it would only give rise to bad effects some years after birth (*vide* p. 660).

Incidence.—It is generally assumed that ulceration of the common duct due to gall-stones may, by cicatricial contraction, lead to stenosis, but this sequence is surprisingly rare. The stricture is usually localised, but it may be diffuse (Courvoisier, Mathieu[3]), or there may be more than one stricture. Körte[4] and Moynihan[5] have recorded cases, and a good

[1] Eve. *Trans. Clin. Soc.*, Lond., 1906, xxxix, 144.
[2] Trevor. *Trans. Path. Soc.*, Lond., 1905, lvi, 138.
[3] Mathieu. *Rev. de chir.*, Paris, 1908, xxxvii, 175.
[4] Körte. *Beitr. z. Chir. Gallenweg.*, S. 341, 1905, Berlin.
[5] Moynihan. *Brit. Med. Journ.*, 1905, ii, 1390.

example of a tight stricture of the common duct with a soft calculus just above it, in a woman aged twenty-six, is described in St. Thomas's Hospital Reports.[1] In the cases of simple stricture recorded by Holmes[2] and Moxon[3] the stricture was at the commencement of the common hepatic duct and therefore not much exposed to calculi, except small bilirubin-calcium calculi. In Moxon's, Johnson's,[4] and Phillips's[5] cases there was no history of cholelithiasis. In the following case the termination of the common bile-duct was obliterated, apparently from cicatrisation of an ulcer due to gall-stones :—

A woman aged forty-six years was operated upon for recurrent attacks of biliary colic. The gall-bladder was empty and contracted, but the cystic duct was dilated by five calculi, which were removed. The cystic duct was united to the abdominal wound, and bile was discharged for ten days. The patient then got worse and died suddenly. At the necropsy the common bile-duct was dilated and contained several calculi ; its opening into the duodenum was completely obliterated by cicatrisation of an ulcer.[6]

Stricture and obliteration of the cystic duct in cholelithiasis and cholecystitis are comparatively common, and thus form a marked contrast to the other large bile-ducts.

It is conceivable that in some cases simple stricture is due to ulceration following cholangitis set up by typhoid or influenzal infection. Possibly syphilitic inflammation may account for some of the cases. Lazarus-Barlow[7] recorded a case of stricture in a boy the subject of hereditary syphilis, but in this instance and in that described by H. Mackenzie[8] the cicatricial process probably started outside the ducts and compressed them from without (*vide* p. 380). Mathieu refers to two cases of post-operative stricture of the common bile-duct after choledochotomy. The following is the only case of simple stricture of the common bile-duct which has been detected at St. George's Hospital in the last twenty-four years :—

A man aged sixty years, with chronic jaundice, was admitted with pneumonia which proved fatal. There were a fibrous stricture of the common bile-duct in its lower fourth and great distension of the gall-bladder and bile-ducts. There was no evidence of any malignant disease or of gall-stones.

Some cases of stricture of the bile-ducts in adults may, in the absence of microscopical examination, have been cases of primary carcinoma of the ducts, as a stricture which, to the naked eye, appears merely fibrous, may be carcinomatous.

[1] *St. Thomas's Hosp. Rep.*, 1901, xxix, 169.
[2] Holmes, T. *Trans. Path. Soc.*, Lond., 1858, ix, 130.
[3] Moxon, W. *Ibid.*, 1873, xxiv, 129.
[4] Johnson, G. *Brit. Med. Journ.*, 1880, ii, 200.
[5] Phillips, S. *Trans. Clin. Soc.*, Lond., 1888, xxi, 26.
[6] *St. Barth. Hosp. Rep.*, 1899, xxxv. Surg. Registrar's Report, p. 216.
[7] Lazarus-Barlow, W. S. *Trans. Path. Soc.*, Lond., 1899, l, 158.
[8] Mackenzie, H. *Ibid.*, 1892, xliii, 84.

In a woman aged fifty-seven the lower part of the common bile-duct was much stenosed as if from cicatrisation of an ulcer due to gall-stones, but microscopically it was carcinomatous.[1] Andral[2] described as inflammatory cases which were probably carcinomatous.

The **symptoms** are those of chronic obstructive jaundice and resemble those of malignant disease of the bile-ducts. In Moxon's case, in which jaundice lasted eight months, there was xanthoma multiplex on the hands, back, and scrotum. An accurate diagnosis is impossible before the abdomen is opened and the duct freely exposed.

Treatment.—If there is any suspicion of syphilis, iodides should be given. Failing any improvement from antisyphilitic treatment, an exploratory operation with a view of resecting the stricture, or uniting the gall-bladder with the intestine, if the stricture is in the common bile-duct, should be undertaken.

SYPHILIS.—Stricture of the ducts due to congenital syphilis, the pressure of a gumma, syphilitic adhesions (p. 365), syphilitic adenitis (p. 552) and pancreatitis (p. 560), are referred to elsewhere.

CATARRHAL JAUNDICE OR ACUTE CATARRHAL CHOLANGITIS

CATARRHAL JAUNDICE is usually regarded as due to a local inflammatory swelling of the mucous membrane of the biliary papilla and the termination of the common bile-duct, which leads to biliary obstruction and to the passage of bile into the circulation.

It is essentially due to a local inflammatory obstruction, and must be distinguished from toxaemic and infectious jaundice (Weil's disease) which are the manifestations of a general toxaemia or haemic infection. While giving this view as to the nature of acute catarrhal jaundice, there is room for discussion as to the part played by infection and inflammation spreading from the duodenum. Gastro-duodenal catarrh may be toxic or due to microbic activity, and in the latter case the jaundice might be spoken of as infective. The French school,[3] indeed, includes catarrhal jaundice among the benign forms of infective jaundice. Besides mechanically obstructing the lower end of the bile-duct, the morbid process may extend upwards and involve a greater or lesser extent of the common bile-duct. When a considerable extent of the common bile-duct is inflamed, the condition usually becomes one of chronic cholangitis and clinically presents itself as one of prolonged catarrhal jaundice. The explanation of catarrhal jaundice given above has been often questioned,

[1] Krokiewicz. *Wien. klin. Wchn.*, 1898, xi, 321.
[2] Andral. *Clinique médicale*, Paris, 1831, iv, 500.
[3] Chauffard. *Traité de médecine* (Bouchard, Brissaud), 1902, v, 89.

and it has been thought that the real cause is catarrhal pancreatitis, which compresses the common duct (Oser,[1] Mayo Robson [2]). It is probable that so-called catarrhal jaundice may be of two kinds: (i) due to inflammation of the biliary papilla and lower end of the common bile-duct, or cholangitic jaundice; (ii) due to swelling of the head of the pancreas, pancreatic jaundice.

Causation.—Gastro-duodenal catarrh involving the mucous membrane of the biliary papilla readily spreads into the common channel, or ampulla of Vater, inside the biliary papilla. Comparatively little swelling of the mucous membrane of the narrow orifice of the papilla is sufficient to obstruct the flow of bile through it, and a plug of tenacious mucus may easily form in the lumen of the papilla. Probably this is what happens in the ordinary run of cases, though it is not improbable that inflammatory swelling spreads a varying distance up the common bile-duct or into Wirsung's duct, producing swelling of the head of the pancreas, in more prolonged examples of the disease. Some cases, which apparently begin as catarrhal jaundice, rapidly pass into acute yellow atrophy, and it is possible that inflammation of the lower end of the common duct has extended up to the liver.

The causes of catarrhal jaundice are, therefore, those of gastro-duodenal catarrh; it is a complication of acute gastritis and may be due to alcoholic excess or indiscretions in diet, and follows chills.

Since gastritis is very common in the specific fevers, it is easy to understand that jaundice in the course of enteric fever or pneumonia may depend on purely local obstruction at or near the biliary papilla. On the other hand, jaundice in the course of the specific fevers may be toxaemic, or depend on infection of the bile-ducts and gall-bladder. In enteric fever jaundice is remarkably rare—so much so that Sir W. Jenner [3] never met with it. When it does occur, it may be catarrhal, toxic, or due to infective cholangitis. Catarrhal jaundice may be met with at any period in the course of typhoid fever or in a relapse, and in no way affects the course of the disease.

Da Costa,[4] in a review of 52 cases of jaundice in the course of enteric fever, found 4 due to catarrhal jaundice. Among 1500 cases of enteric fever at the Johns Hopkins Hospital there were 8 cases of jaundice, apart from cholecystitis (T. M'Crae [5]). In 244 cases of enteric, which I analysed, at the Imperial Yeomanry Hospital, Pretoria, there was one case of mild catarrhal jaundice.[6] I have seen similar cases in England.

Catarrhal jaundice may supervene in the course of portal cirrhosis and be due to gastro-duodenal catarrh, which is favoured by chronic

[1] Oser. Nothnagel's *Handbuch*, 1898, xviii, Th. 2, 111.
[2] Robson, Mayo. *Lancet*, Lond., 1904, i, 773; and *Montreal Med. Journ.*, 1904, xxxiii, 741.
[3] Jenner, W. *On Fevers and Diphtheria*, p. 353, 1893.
[4] Da Costa. *Am. Journ. Med. Sc.*, 1898, cxvi, 1.
[5] M'Crae. *System of Medicine* (Osler and M'Crae), 1907, ii, 136.
[6] Rolleston. *Brit. Med. Journ.*, 1901, ii, 976.

portal engorgement and may be lighted up by alcoholic excess. A slight icteric tinge of the skin is very frequent in advanced mitral disease; it is only exceptionally that there is intense jaundice. It may also occur and be perhaps the first symptom in malignant disease involving the liver or bile-ducts.

Thus in two cases under my care in St. George's Hospital at the same time in 1897 jaundice came on suddenly with vomiting and gastro-enteritis: one was a woman with primary carcinoma of the gall-bladder; the other, a man with primary carcinoma of the common bile-duct. In both cases the jaundice lasted until death.

Catarrhal jaundice may also complicate other organic diseases of the liver, such as hydatid. Emotional jaundice has been thought to be catarrhal in origin, but without sufficient grounds. Catarrhal jaundice may be epidemic because gastro-duodenal catarrh is epidemic. Epidemic jaundice, however, is usually due to infection of the ducts. As examples of epidemic infective jaundice, Weil's disease (*vide* p. 597) and jaundice following drain poisoning may be mentioned. It is not always easy to be dogmatic as to the nature of mild epidemic jaundice; probably most cases are infective rather than due to local catarrh of the lower end of the common bile-duct. Probably different micro-organisms may give rise to ordinary catarrhal jaundice; from investigation of the serum reactions in a number of cases Sacquépée and Fras[1] found specific agglutination for *Bacillus typhosus*, *B. paratyphosus* type A, and the colon bacillus. In some instances no specific agglutination was obtained. Jaundice resembling the catarrhal form may be due to infection of the ducts with *B. typhosus* without any symptoms of enteric fever (Étienne and Thiry[2]).

Morbid Anatomy.—Opportunities for investigating the morbid conditions are rare, and only arise when death occurs from some other cause, such as an accident. The mucous membrane of the duodenum, the ampulla of Vater, and adjacent part of the common bile-duct is swollen, injected, and covered by tenacious mucus; a plug of inspissated mucus may be found in the orifice of the biliary papilla. These changes rarely extend further up than the lower end of the common bile-duct. The swelling of the mucous membrane may, however, subside after death, and because it is possible to force bile into the duodenum by pressure on the gall-bladder it does not follow that there was no obstruction during life. The same remark applies, but with more force, to the passage of a probe up the bile-duct from the duodenum. Eppinger[3] found hyperplasia of the lymphoid tissue of the mucosa of the lower end of the bile-duct in a patient who died from an accident on the eighth day of jaundice. He compared the condition to tonsillitis. Catarrhal inflammation and swelling of the head of the pancreas have been found during operations on cases of prolonged catarrhal jaundice (Robson). The liver may be swollen

[1] Sacquépée et Fras. *Compt. rend. Soc. Biol.*, Paris, 1905, lvii, 533.
[2] Étienne et Thiry. *Arch. gén. de méd.*, Paris, 1907, cxcviii, 97.
[3] Eppinger. *Wien. klin. Wchnschr.*, 1908, xxi, 480.

from accumulation of bile and from vascular engorgement. The lining membrane of the heart and vessels is bile-stained.

Clinical Picture.—*Incidence.*—In an analysis of 215 cases of simple catarrhal jaundice Neumann[1] found that 42 per cent occurred in the first ten years of life, but sucklings are rarely attacked. Ten per cent of the cases occurred in the second, and 27 per cent in the third decade. It is commoner in the winter than in the summer.

Premonitory Symptoms.—Before jaundice appears there are usually, though not invariably, signs of gastro-intestinal disturbance which may last for a few days to a week. These are vomiting, loss of appetite, furred tongue, foul breath, bitter taste in the mouth, headache, vertigo, dyspepsia, some general malaise, and occasionally flying pains in the limbs. Diarrhoea from extension of the catarrh to the intestines is often seen. The motions become clay-coloured before the appearance of icterus and markedly offensive. Contrary to what might be anticipated, Cammidge[2] found that stercobilin is constantly present. The faeces may remain pale for a considerable time; this may depend on milk taken as food, and on the faeces containing gas in a finely divided state. Jaundice may not be noticed by the patient until his attention is directed to it by his friends. The conjunctiva is the first part of the body to shew the icteric tint, but the presence of bile-pigment can be detected in the urine even before this. The fatty and often slightly yellow masses (pingueculae) underneath the conjunctivae at the canthi must not be mistaken for icteric tingeing. The face becomes jaundiced soon after the conjunctivae. This is more manifest in blonds than in dark-skinned persons who are often naturally somewhat sallow. The oral mucous membrane, especially under the tongue and on the inner surface of the lips, appears yellow when the blood is pressed out of the superficial vessels. From the face the yellow tint spreads to the trunk and extremities, reaching the legs last; the whole of the body finally becomes jaundiced, and sometimes of a bright yellow colour. The dark green colour seen in obstructive jaundice due to malignant disease is never seen in catarrhal icterus; but the skin may shew the effects of jaundice for a considerable time.

Osler[3] mentions a case in which stigmata or spider angiomas appeared on the face during catarrhal jaundice.

By the time that jaundice has appeared, the gastric symptoms have usually begun to subside. This, however, is by no means universal. Obstinate vomiting may persist if the diet is not carefully restricted and supervised. At the onset there may be fever from the gastro-enteritis, but otherwise the temperature is either normal or below the normal. It is probable that cases which otherwise resemble catarrhal jaundice but shew a raised temperature for more than two or three days are mild cases of toxaemic or infective jaundice.

[1] Neumann. *Deutsche med. Wchnschr.*, 1899, xxv, 574.
[2] Cammidge. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Med. Sect.), 185.
[3] Osler. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 337.

Symptoms when the Disease is Fully Developed.—The pulse is slow ; it is often 60 or less per minute, and is of low tension, soft, and may be dicrotic. The slowing of the heart's action is much less marked in children than in adults. Pruritus is often troublesome, and the scratching may lead to traumatic eczema, or even to an urticarial rash. It is rare in children. Its mechanism is discussed on p. 546. Yellow vision (xanthopsia) is rare ; its existence is seldom a cause of complaint, but the patients may be found to have noticed it on being questioned (*vide* p. 546). The action of the bile constituents on the brain causes mental depression and, sometimes, a melancholic condition. There may be much irritability and incapacity for transacting the ordinary affairs of life efficiently.

The urine contains bile-pigment. On shaking it in a white porringer the foam becomes characteristically yellow. During the first few days and even before jaundice has appeared bile acids as well as bile-pigment may be present in the urine. In 12 cases indican was present in all (Simon [1]). During the period of the disease when the patient feels worst there may be a distinct excess of nitrogen in the urine as compared with that taken in. During this time the patient loses weight. While there is bile in the urine casts may be found, but not albumin. Out of Cammidge's 53 cases of catarrhal jaundice 13 shewed excess of urobilin and 26 calcium oxalate crystals. Cammidge [2] obtained a positive pancreatic reaction in 42 out of 53 cases ; and Garrod [3] recorded an instance of glycosuria during catarrhal jaundice. These observations support the view that in some cases the jaundice may be due to pancreatitis.

The occurrence of bile-pigment in the saliva in cases of jaundice has been recorded by various authors, especially when, as a result of mercurial treatment, inflammatory changes in the mouth are superadded. W. Legg [4] always found the saliva colourless in uncomplicated jaundice. The sweat, especially from the armpits, may contain bile-pigment, but generally the perspiration is colourless. The secretion of the alimentary canal, the tears, nasal mucus, and in women the milk, are, in spite of statements to the contrary, free from bile. In inflammatory conditions the altered secretions and exudations become bile-stained ; this is shewn in pneumonic sputum and in pleural and peritoneal effusions.

The blood-serum contains bile-pigment, but there is no change in the corpuscles. In 27 cases the red count was normal or even above normal in 16, and the leucocyte count was 10,000 or below in 20 (Emerson [5]). Occasionally there is slight leucocytosis at the onset. As has been pointed out above (p. 544), the serum of jaundiced patients has been said to agglutinate typhoid bacilli. Agglutination of paratyphoid bacilli has also been observed (Sacquépée and Fras [6]).

[1] Simon. *Amer. Journ. Med. Sc.*, Phila., 1895, cx, 173.
[2] Cammidge. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Med. Sect.), 171.
[3] Garrod, A. E. *Lancet*, Lond., 1912, i, 560.
[4] Legg, W. *St. Barth. Hosp. Rep.*, 1877, xiii, 12.
[5] Emerson. *Clinical Diagnosis*, p. 586, 1906.
[6] Sacquépée et Fras. *Compt. rend. Soc. Biol.*, Paris, 1905, lvii, 533.

As a rule, there is no hepatic enlargement or tenderness. Many authors state that the liver may be enlarged in simple catarrhal jaundice as the result of distension of the intrahepatic ducts with bile, but if the enlargement is at all marked, it is probable that inflammation of the common bile-duct has spread to the ducts in the liver substance. The gall-bladder is sometimes palpably enlarged, but considerable enlargement should suggest that the disease is cholecystitis with some inflammation of the common bile-duct.

Duration.—The jaundice gradually fades in the course of four to six weeks, but the skin may be tinged for a considerable period. In slight attacks the icteric tint may pass away in a couple of weeks. Occasionally cases, which begin like ordinary catarrhal jaundice and eventually clear up, hang fire and last for months; Chauffard [1] quotes cases lasting from ninety-two to one hundred and fifty-five days. These cases are either examples of chronic catarrhal cholangitis, and allied to the chronic inflammation of the common bile-duct set up by calculi (*vide* p. 759), as is shewn by the occurrence of intermissions, or due to pancreatitis (Robson [2]). Thus, though beginning like catarrhal jaundice, these cases must be regarded as complicated by an extension of the inflammatory process and as belonging to another category. If, in a case regarded as catarrhal jaundice, the disease does not clear up, there is either some complication or the diagnosis is wrong. Relapses of catarrhal jaundice may occur.

Effects.—Considerable loss of weight occurs in well-marked catarrhal jaundice. Loss of appetite and the resulting deficiency in the intake of food partly accounts for this, but the diminished absorption of fats is also an important factor.

Calculi and biliary colic may follow ordinary catarrhal jaundice, but in order to explain cholelithiasis as a sequel of ordinary catarrhal jaundice it must be assumed that mild cholecystitis was present in addition. Cholelithiasis may date from catarrhal jaundice. Dilatation of the lower end of the common bile-duct has been thought to be a result of catarrhal inflammation, but it is probable that when this sequence is noted, the inflammation has been of considerable duration or intensity, or that there has been a gall-stone there. Just as the inflammation of the papilla may spread into the common bile-duct and cause chronic cholangitis, so the catarrhal process may extend into Wirsung's duct and set up acute or chronic pancreatitis. In extremely rare cases acute diabetes may follow what at the time appears to be catarrhal jaundice. Rose Bradford [3] reported a case of this kind. This supports the view that pancreatitis may cause catarrhal jaundice.

In ordinary cases the **prognosis** is extremely good, there being no danger to life and very seldom any after-results of importance. On the other hand, what at first appears to be catarrhal jaundice may be the

[1] Chauffard. *Traité de méd.* (Bouchard, Brissaud), 1902, v, 97.
[2] Robson. *Surg., Gynec., and Obst.*, Chicago, 1908, vi, 29.
[3] Bradford, J. R. *Clin. Journ.*, Lond., 1907-8, xxxi, 76.

initial manifestation of severe organic disease of the liver, such as malignant disease or acute yellow atrophy. It is, therefore, advisable to avoid giving a dogmatic prognosis in the early stages, if this can be done without creating alarm. In the vast majority the result of the case justifies a prognosis of complete and rapid recovery, given at the very outset; but in rare instances the clinical picture radically changes and nervous symptoms rapidly usher in coma and death from acute yellow atrophy, or, in less exceptional cases, the jaundice, instead of gradually disappearing, deepens into that of malignant obstruction of the common bile-duct. When catarrhal jaundice is prolonged, the prognosis alters, as the possibility of some grave cause of obstruction must be considered, but some of these protracted cases recover without any definite developments.

Diagnosis.—The presence of gastro-intestinal disturbance, vomiting, diarrhoea, loss of appetite, and dyspepsia before the onset of jaundice, the absence of severe constitutional disturbance and of pain, and the comparatively mild jaundice fading within a few weeks are the important points in the diagnosis. In some instances gastro-intestinal symptoms are absent and it is then difficult to eliminate at once more serious forms of jaundice; and it must be remembered that catarrhal jaundice may complicate grave hepatic disease. The age of the patient has some bearing, as catarrhal jaundice in late middle life may be the first indication of malignant disease involving the ducts. The duration and character of the jaundice are important; when jaundice lasts more than six weeks, the diagnosis of simple catarrhal jaundice should be seriously questioned, and some other cause sought for. Deep green or "black" jaundice excludes catarrhal jaundice. Several recurrent attacks point to the presence of a calculus in the common duct.

Cases of mild toxaemic jaundice, especially those with only slight fever and enlargement of the liver, are readily confused with catarrhal jaundice. In well-defined toxaemic or infective jaundice there are signs of general infection, such as fever, albuminuria, splenic and hepatic enlargement, but in the milder cases some of these manifestations may be absent and there is a transition to catarrhal jaundice.

The jaundice accompanying the presence of gall-stones in the common duct is much more prolonged than in catarrhal jaundice, and is usually characterised by periodic outbursts of fever, pain, and exacerbations in the degree of jaundice (*vide* p. 761). It may be preceded by biliary colic, but this is by no means always the case, and it may come on quite gradually. It occurs in older persons than catarrhal jaundice, especially in women.

Treatment.—In the early stage, while there is still some gastro-intestinal catarrh, it is important to treat this and to avoid irritation of the stomach by food; gastric disturbance should be allayed by bismuth combined with dilute hydrocyanic acid and bicarbonate of sodium, to which, if vomiting is troublesome, tincture of opium or chlorodyne may be added. The patient should be kept warm in bed, and for the first

day or so may with advantage be starved, but may take a fair amount of Vichy, Vals, Ems, Apollinaris, or hot water containing bicarbonate of sodium. Poultices or warm compresses to the upper part of the abdomen may be employed to relieve epigastric discomfort. Rest to the stomach is most important as a relapse is readily excited by food. Instead of absolute starvation whey may be given. Feeding should begin with peptonised milk or milk containing sodium citrate (grs. x. to the pint), beginning with $1\frac{1}{2}$ pints in the day and increasing it gradually. The bowels should be kept open either by enemas or by a small dose of calomel ($\frac{1}{2}$–1 gr.) given at night and followed next morning by Carlsbad salts; or a pill of grey powder (1 gr.) may be taken three times daily, to which 1 to 2 grains of chalk may be added to prevent diarrhoea. Vigorous purgatives may set up or increase gastro-intestinal catarrh and should therefore be avoided.

When the gastro-intestinal catarrh has subsided, the bland milk diet should be relaxed, and thin clear soup, gruel, Benger's food, toast, soufflés, eggs, pounded fish, kedgeree, chicken cream, and rice pudding given as the patient's condition allows. Fatty food, and especially liquid fat and melted butter, should be avoided. Minute doses ($\frac{1}{40}$–$\frac{1}{20}$ gr.) of calomel, salicylate of bismuth, and salol are useful to inhibit intestinal fermentation; naphthalene tetrachloride, guaiacol, resorcin, and iodoform have been employed with the same object. Salicylate of sodium combined with urotropin should be given to increase the flow of bile and disinfect the bile-ducts. The action of the bowels must be maintained by the purgative waters or by salines, such as Epsom or Carlsbad salts, phosphate of sodium, and, if necessary, by blue pill. Rectal injections of water at 60-70° F. or even ice-cold to stimulate peristaltic action of the gall-bladder and so induce flushing of the bile-ducts by the bile have been recommended (Krull's irrigations). Massage to the liver has been advocated by Gilbert and Lereboullet,[1] and can be carried out at a spa by the liver douche.

During convalescence a tonic containing nux vomica is useful in improving the appetite and digestion. Dilute nitrohydrochloric acid is often given, but I prefer an alkaline medicine. Pruritus should be treated on the lines given on p. 567.

If the jaundice persists and there is no reason to suspect any grave underlying condition, such as malignant disease, the patient will probably receive benefit from a visit to a spa, such as Harrogate, Llandrindod Wells, Vichy, Neuenahr, Ems, Evian, Homburg, Carlsbad, Marienbad, or Bertrich.

[1] Gilbert et Lereboullet. *Gaz. hebd. de méd.*, Paris, 1901, vi, 913.

SUPPURATIVE CHOLANGITIS

Etiology.—The exciting cause of suppurative inflammation of the bile-ducts is a virulent infection; the bacteria which have been found to give rise to this affection are mentioned on p. 673. The conditions and diseases which dispose to suppurative cholangitis are—(i) Local; and (ii) general.

(i) *The local conditions* are: Those which (*a*) diminish the resistance of the ducts, such as tumours, past inflammation, and (*b*) render infection more easy, such as biliary stagnation, gall-stones, rupture of hydatid cysts into the ducts, worms in the ducts. In biliary obstruction and stagnation micro-organisms which have got into the ducts either from the liver and general circulation (descending infection) or from the duodenum (ascending infection) have a better chance of multiplying and setting up inflammatory changes in the ducts, especially since, owing to dilatation, the ducts are probably less resistant than in health.

Cholelithiasis is the commonest antecedent of suppurative cholangitis; this was so in 18 out of 20 cases collected by L. Rogers.[1] The acute suppurative inflammation may supervene on old-standing infective cholangitis (*vide* p. 759) or may occur in a patient who has never had any manifest signs of cholelithiasis. When suppurative cholangitis supervenes on chronic catarrhal inflammation of the ducts, the more virulent infection may be supposed to be favoured by the diminished resistance of the ducts.

Rupture of hydatid cysts into the bile-ducts, though not nearly so frequent a cause of suppurative cholangitis as gall-stones, is a well-established factor. The presence of hydatid membranes in the ducts favours ascending infection from the duodenum, and it is probably to this that suppurative cholangitis is due. The subject of rupture of hydatid cysts into the bile-ducts is considered more fully on p. 418.

In hepatic abscess the inflammation may spread to the bile-ducts, or the abscess may open into the larger bile-ducts. Cholangitis may thus be secondary to hepatic abscess, and by giving rise to multiple foci of suppuration, renders a fatal issue almost certain.

Round worms and liver flukes may pass up the common bile-duct from the duodenum and carry with them micro-organisms. The ducts thus become infected, and suppuration, either diffuse or localised, of the ducts will readily result. When localised, the worm may be found in an abscess cavity in the liver (*vide* p. 683).

A tumour—papilloma or carcinoma—arising on the duodenal surface of the biliary papilla is not common, but is very prone to set up suppurative cholangitis; this depends on the following factors: (1) Obstruction to the outflow of bile and dilatation of the ducts diminish their resistance.

[1] Rogers, L. *Brit. Med. Journ.*, 1903, ii, 706.

Owing to ulceration and necrosis of the growth, the obstruction may intermit, and this intermission very probably favours infection from the duodenum. (2) The growth favours duodenal catarrh and thus renders ascending infection easy. (3) Stagnation of bile in the ducts favours infection.

The growth in the duodenum in the region of the papilla may be a papilloma or a carcinoma; in some instances it appears to the naked eye to be a papilloma, but microscopic examination shews invasion of the duodenal wall and therefore malignancy, as in the specimens in the Museums of Guy's and St. Bartholomew's Hospitals (*vide* p. 554).

Besides malignant disease of the duodenum, carcinoma of the ampulla of Vater and of the lower part of the common bile-duct may lead to suppurative cholangitis (*vide* p. 705). In malignant disease of the liver pressure on the ducts disposes to suppurative cholangitis.

A woman aged forty-four years in St. George's Hospital under the care of Sir I. Owen, with jaundice, was operated upon and found to have multiple growths on the surface of the liver. She had a febrile temperature until her death, one week later. The necropsy revealed primary carcinoma of the splenic flexure and secondary growths in the liver and in the portal fissure. The latter compressed the hepatic ducts. There was intrahepatic suppurative cholangitis. The gall-bladder was collapsed, had a secondary growth in its wall, but was not inflamed or occupied by gall-stones.

In rare instances an aneurysm of the hepatic artery may lead to multiple abscesses in the liver (Osler and Ross[1]). The abscesses may be due to infective emboli, but they may also be the result of suppurative cholangitis. As bearing on the occurrence of suppurative inflammation of the ducts in association with aneurysm of the hepatic artery, it is interesting to note that Dujarier and Castaigne[2] have found that experimental ligature of the hepatic artery leads to stagnation of bile in the ducts and so favours infection.

(ii) *General Diseases Disposing to Suppurative Cholangitis.*—Suppurative cholangitis may occur after infective diseases attacking either the body generally or the alimentary canal.

General blood infections may set up inflammation of the small ducts in the liver in the same way that toluylenediamine, when employed experimentally, gives rise to a descending cholangitis. Micro-organisms or poisons may reach the liver by the blood-stream, and if the bile-ducts are previously damaged, micro-organisms may gain an entrance into the ducts and so set up cholangitis. Influenza and pneumonia have in rare instances been precursors of suppurative cholangitis. In both these diseases it is possible that the cholangitis might be an extension of inflammation from the duodenum, since there is a well-known gastro-intestinal form of influenza, and, in rare instances, pneumococcic gastritis.

[1] Osler and Ross. *Canad. Med. and Surg. Journ.*, 1877, vi, 1.
[2] Dujarier et Castaigne. *Bull. Soc. Anat. Paris*, 1899, lxxiv, 329.

Suppurative cholangitis after influenza has been recorded by Mayo Robson[1] and Rémy[2]; in the latter case cultivations shewed a colon bacillus.

The diseases of the alimentary canal that may be followed by suppurative inflammation of the bile-ducts are typhoid fever and cholera.[3] In typhoid affections of the biliary system the gall-bladder usually bears the brunt of the disease. It is very rare for suppurative cholangitis to occur independently of cholecystitis, though the two are often combined. Experimentally cholangitis has been set up by the injection of cultures of the comma bacillus into the bile-ducts of rabbits (Gilbert and Dominici[4]).

Bacteriology.—Various micro-organisms have been found to be associated with suppurative cholangitis. In some of the cases in which the colon bacillus has grown in the cultures it is not unlikely that other micro-organisms were present, but were crowded out by its vigorous growth. The chief organisms found are *Bacillus coli*, *B. typhosus*, *B. paratyphosus*, streptococci, staphylococci (albus, aureus), pneumococcus, comma bacillus. The colon, typhoid, and comma bacilli being motile, would be able to ascend the ducts from the intestine more readily than the non-motile streptococci and staphylococci. The *Bacillus aerogenes capsulatus*, which usually invades the tissues during the death agony, may, however, be present during life in the circulation, and may even be a primary infection.

In a case of multiple abscesses of the liver in carcinoma of the lower end of the common bile-duct a pure culture of *Bacillus aerogenes capsulatus* was obtained by Pratt and Fulton.[5]

Morbid Anatomy.—The mucous membrane of the ducts is swollen from inflammatory exudation and irregular from ulceration. The outer walls of the duct are also thickened and inflamed, and by extension there may be local peritonitis, which may lead to obliteration of the foramen of Winslow, or to suppurative pylephlebitis. The glands in the portal fissure are enlarged and soft. Possibly some of the areas of suppuration in the liver may arise as pericholangitic abscesses in connexion with the lymphatics. The suppurative process in the ducts may be associated with an empyema of the gall-bladder.

The liver is nearly always greatly enlarged, swollen, and of a greyish colour, with yellowish-green areas around the portal spaces. These foci are softening down into suppuration, and in early stages may, to the naked eye, resemble secondary new growths or even lymphadenoma. When the disease is fully developed, the bile-ducts may be enormously dilated so as to be as large as the small intestine, and have even been opened during laparotomy for supposed suppurative cholecystitis (Rogers[6]).

[1] Mayo Robson. Allbutt's *System of Medicine*, 1897, iv, 251.
[2] Rémy. *Congrès franç. de chir.*, 1896, x, 485.
[3] Galliard. *La Choléra, Bibliothèque Charcot-Debove*, 1894.
[4] Gilbert et Dominici. *Compt. rend. Soc. Biol.*, Paris, 1894, 10. s., i, 38.
[5] Pratt and Fulton. *Boston Med. and Surg. Journ.*, 1900, cxlii, 599.
[6] Rogers, L. *Brit. Med. Journ.*, 1903, ii, 706.

The suppurating ducts may terminate in small abscesses on the surface of the liver, somewhat resembling the condition of the lung in acute bronchiectasis. Numerous biliary abscesses may be scattered throughout

FIG. 93.—Microscopical appearances of the liver in suppurative cholangitis. There are numerous abscess cavities surrounded by condensed fibrous tissue, which appears more darkly stained. It is impossible to distinguish the bile-ducts from the branches of the portal vein, since both are involved. (Photomicrograph by Dr. H. Spitta. Low magnification.)

the liver, both on the surface and in its substance, and adjacent abscesses may run together and form a confluent or areolar abscess which shews fibrous septa. On the other hand, there may be a single localised abscess, or only a few small abscesses formed of ampulla-like dilatations of the

ends of the ducts. The pus is often bile-stained, and may contain soft, calculous matter like brown mud. In the substance of the liver abscesses may form outside the ducts, possibly in the lymphatics, and suppuration may extend into the branches of the portal vein, causing pylephlebitis and diffuse suppuration of the portal spaces.

The suppuration may spread into Wirsung's duct and set up suppurative pancreatitis, and, by further extension of infection to the peritoneum covering the pancreas, a local abscess in the lesser sac of the peritoneum. Pancreatitis due to gall-stones in the common duct is referred to on page 764. Suppuration may spread from the pancreas into the portal vein and set up pylephlebitis.

The suppurating bile-ducts may leak into the peritoneum and cause general peritonitis or a local peritoneal abscess. Abscesses on the convex surface of the liver may perforate the diaphragm and cause an empyema or broncho-biliary fistula; abscesses on the under surface may open into the colon or set up a perinephric abscess (Rogers).

Microscopically the larger portal spaces are dilated, and relics of their fibrous tissue are visible, but it may be difficult to distinguish the remains of the large bile-ducts from those of the portal veins, since both may be involved in the same suppurative process. The walls of the ducts may be destroyed and replaced by small cells which extend into the surrounding liver substance. There may be comparatively well-formed fibrous tissue from chronic pericholangitis, but the chief feature is diffuse small-celled infiltration. In places the liver cells can barely be recognised, and the condition is that of a commencing abscess.

Clinical Picture.—The onset may be insidious. The patient is feverish, has rigors, anorexia, nausea and vomiting, marked prostration, and loss of flesh. The temperature may be only moderately raised and may even be subnormal in the later stages. The liver, which is generally much enlarged and tender, progressively increases in size as the disease goes on; in some instances, however, little or no enlargement can be made out. It is usually smooth but may be irregular. The spleen is enlarged. Jaundice, when present, depends not so much on the cholangitis as on gall-stones, worms in the ducts, rupture of hydatid cysts into the ducts, and new growths of the biliary papilla and the region of the ampulla of Vater. But in the absence of such local conditions suppurative cholangitis may run its course without jaundice.[1] This is difficult to explain; but possibly the absence of jaundice may depend on occlusion of the hepatic lymphatics, which should carry the bile into the general circulation, by the inflammatory changes. In the following case there was very slight jaundice:

A man aged twenty-nine years was admitted to St. George's Hospital in an extremely grave condition, with a large tender liver, an anaemic, sallow complexion, slight ascites, and a history that two weeks ago he had had fever and

[1] *Vide* Gilbert et Lereboullet. "Les Angiocholites anictériques," *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1900, 3. s., xvii, 477.

jaundice. Two and a half years ago he had had appendicitis. The temperature was subnormal. At a consultation various opinions were expressed, such as pylephlebitis secondary to appendicitis, suppurative cholangitis associated with calculi, abscess, and rapid new growth of the liver. The following day an exploratory operation was performed, and a nodule, which might have been either new growth or early inflammatory change, was cut into. Microscopic examination shewed altered liver cells. The patient died two days later. At the necropsy the liver (7 pounds) shewed suppurating areas around the bile-ducts ; the extrahepatic bile-ducts contained mucus. There were no calculi in the gall-bladder. The portal vein and vermiform appendix were normal. The spleen was large and soft, weighing 17 ounces.

Pain may be due to perihepatitis set up by suppuration in the ducts under the capsule, and is worse on respiration and on movement. Colicky pain may be caused by factors underlying the acute infection, such as gall-stones, the rupture of hydatids into the ducts, or worms in the ducts. Pseudo-gall-stone colic may also occur when malignant disease obstructs the ducts. In some instances pain is entirely absent.

Septic absorption which causes the severe constitutional symptoms may lead to diarrhoea and albuminuria. There is leucocytosis, and blood-cultures shew micro-organisms. From local or general peritonitis, secondary to leakage of abscesses on the surface of the liver, abdominal distension may come on before death.

Complications.—In addition to local (such as subphrenic abscess or suppuration in the lesser sac of the peritoneum) or general peritonitis from leakage or rupture of the suppurating areas, general haemic infection may occur. Pus and micro-organisms may pass into the hepatic veins and so reach the lungs and give rise to pyaemic abscesses, pleurisy, and empyema. Empyema, however, may be secondary to subphrenic suppuration and due to the spread of infection through the diaphragm. When the micro-organisms have got into the general circulation, the joints and meninges may be affected, and infective endocarditis may be induced in the same way.

Duration.—As suppurative cholangitis may supervene in chronic catarrhal cholangitis, it is difficult to fix the duration with accuracy. In most cases in which the disease comes on acutely it lasts about three weeks. In exceptional instances in which the suppurating ducts have discharged into the colon or bronchus, the course of the disease is much prolonged. Thus, Rogers[1] describes cases which lasted eighteen and six months respectively. The importance of drainage in the duration of the disease is shewn by the prolonged course of broncho-biliary fistulae, most of which are due to suppurative cholangitis.

Diagnosis.—Fever and grave constitutional disturbance in a patient whose liver progressively increases in size and who has had symptoms pointing to gall-stones are the features of importance. Jaundice is not constant, but its presence is in favour of suppurative cholangitis as against suppurative pylephlebitis and tropical abscess.

[1] Rogers, L. *Brit. Med. Journ.*, 1903, ii, 706.

The **differential diagnosis** must be made from intermittent hepatic fever due to gall-stones, from two other forms of intrahepatic suppuration —pylephlebitis and tropical abscess, from new growth associated with fever, and from acute cirrhosis with jaundice.

In *intermittent hepatic fever* there are periodic attacks of fever, pain, and intensification of jaundice, but in the intervals the patient is comparatively well (*vide* p. 762). In suppurative cholangitis the fever is continuous: jaundice is not so prominent, and the patient's general condition is much graver.

Pylephlebitis is accompanied by the same general symptoms and hepatic enlargement as suppurative cholangitis. Jaundice is more frequent, appears earlier, and is more marked in cholangitis, whilst splenic enlargement is more often prominent in suppurative pylephlebitis. According to Libman [1] blood-cultures are negative in pylephlebitis and positive in cholangitis. It must be remembered that these two conditions may be combined. In *malaria* examination of the blood should shew parasites, and in cholangitis a polymorphonuclear leucocytosis. In *tropical abscess* there is often a history of dysentery and there may be fluctuation or local bulging with oedema of the chest-wall. In cases in which the abscess is deeply situated the diagnosis is difficult. The history of past dysentery or gall-stones is in favour of single abscess or cholangitis respectively; jaundice, if present, makes cholangitis more probable. But in case of doubt, the rarity of suppurative cholangitis and the relative frequency of abscess must have their due weight. Very rapid *new growth* in the liver accompanied by fever and jaundice may closely resemble suppurative cholangitis; in fact some cases of carcinoma involving the ducts shew suppurative cholangitis. In the absence of evidence of new growth, such as a palpable tumour, the diagnosis may be possible only when the liver is freely exposed. In cases of *acute cirrhosis* with fever, jaundice, and enlargement and tenderness of the liver the resemblance to suppurative cholangitis is very considerable. In this form of cirrhosis there are usually a marked alcoholic history, splenic enlargement, and haematemesis, and the constitutional symptoms are less severe than in suppurative cholangitis.

The **prognosis** depends on the course of the disease; if it remains limited to the large ducts or is operated on early, before it has spread to the liver or pancreas, recovery may occur; probably some cases of empyema of the gall-bladder began as suppurative cholangitis, the original lesion having passed away. If it invades the liver and sets up multiple abscesses and diffuse suppuration of the portal spaces, a fatal termination is inevitable; but there may be only a single local area of suppuration in the liver and the outlook is then much better. In addition to its course and complications, much depends on early operation and free drainage. When a broncho-biliary fistula or a communication between the biliary abscess and another hollow viscus, such as the colon or pelvis of the kidney, forms, the free drainage greatly prolongs life and a cure may

[1] Libman. *Am. Journ. Med. Sc.*, Phila., 1908, cxxxvi, 548.

even result. These cases with fistulae in fact differ so much from the rapid course of suppurative cholangitis that they are usually considered as a separate condition.

The proper **treatment** is surgical, and consists in obtaining free drainage for the pus; this may be done by opening the dilated ducts, by cholecystotomy, or by opening biliary abscesses on the surface of the liver.

Medical treatment is only palliative, but it may be combined with surgical treatment and then be of distinct use. Salicylate of sodium combined with urotropin, to wash out and disinfect the ducts, should be given.

Chronic Catarrhal Cholangitis

Chronic infective or catarrhal cholangitis may be divided into two forms: (i) That associated with and largely due to cholelithiasis, and (ii) that due to other causes. The form associated with the presence of a gall-stone in the common bile-duct is so intimately related to cholelithiasis that it is described in connexion with that disease (*vide* p. 759). Non-calculous chronic catarrhal cholangitis will be described under two headings: (A) of the extrahepatic bile-ducts, and (B) of the intrahepatic bile-ducts.

(A) **Non-calculous Chronic Catarrhal Cholangitis of the Extrahepatic Ducts.**—It may depend on chronic gastro-duodenal catarrh, such as is seen in drunkards. It may occur in the course of malignant disease of the liver or of the bile-ducts, and in the latter condition is more likely to supervene when the growth is at the biliary papilla. Suppuration in the liver or the rupture of hydatid cysts into the bile-ducts may set up cholangitis which may be catarrhal at first, but is more likely to become suppurative. Infectious diseases, such as typhoid, influenza, pneumonia, may play some part in the production of chronic catarrh of the bile-ducts. Acute cholangitis may occur in enteric fever and influenza, and probably may leave behind chronic catarrh. How often they may set up slight chronic catarrh without any previous acute inflammation it is difficult to say. In some cases of prolonged catarrhal jaundice [1] which, after hanging fire for weeks and months with intermissions and exacerbations, eventually clear up completely, there may be an underlying chronic inflammation of the common duct.

Clinical Aspect.—When supervening on acute catarrh the jaundice remains and may arouse the suspicion of malignant disease or of an impacted calculus in the common duct. The chronic jaundice leads to some wasting from malnutrition. It varies in intensity from time to time, becoming more marked after attacks of fever and pain. The general features are those of chronic relapsing jaundice, and are in miniature

[1] *Vide* Dieulafoy. *Semaine méd.*, Paris, 1888, viii, 270.

the same as those of intermittent hepatic fever (*vide* p. 759). The inflammation may spread upwards to the liver, and in very rare instances be followed by acute yellow atrophy ; or suppurative cholangitis may develop.

The *diagnosis* of chronic catarrhal inflammation of the larger bile-ducts from hypertrophic biliary cirrhosis with chronic jaundice turns on the absence of the marked hepatic and splenic enlargement.

From a gall-stone in the common duct with chronic infective cholangitis the diagnosis is very difficult, inasmuch as the two conditions are much the same, except for the presence of a gall-stone. I believe that non-calculous cases react much better than calculous cases to urotropin and salicylates. In cholelithiasis with infective cholangitis there is more pain, and the attacks of intermittent hepatic fever are better marked, but not uncommonly there is no history of cholelithiasis, and a differential diagnosis between these two closely allied conditions may not be justified. It is so much commoner to find a gall-stone in the lower end of the common duct in chronic catarrhal or infective cholangitis, that this condition should be diagnosed in any doubtful case.

Treatment.—The diet should be simple, and milk should form a large proportion of the food. Irritating food and alcohol must be forbidden. Calomel and saline purges should be given to prevent constipation and minimise gastro-intestinal catarrh ; for the latter purpose alone calomel should be given in minute doses ($\frac{1}{20}$ gr.) three or four times daily, and urotropin and salicylates and plenty of water so as to disinfect and flush the bile-ducts. Benefit will result from a visit to a spa, such as Harrogate, Llandrindod, Leamington, Bath, Vichy, Neuenahr, Homburg, Carlsbad.

In prolonged cases in which no benefit follows medical and spa treatment, the question of operation with a view to draining the ducts should be considered. This course is also indicated by the difficulty of eliminating the presence of a calculus in the common duct. Lejars [1] and Quénu [2] report cases cured by operation. Some of the cases regarded as hypertrophic biliary cirrhosis, in which cholecystotomy and drainage have been followed by cure may have been examples of chronic infective cholangitis.

Guillot [3] gives a list of 13 cases of chronic hypertrophic biliary cirrhosis or closely allied conditions in which cholecystotomy and drainage were performed, mainly by Delagénière. Recovery followed in 10.

(B) **Non-Calculous Chronic Catarrhal Cholangitis of the Intrahepatic Bile-Ducts.**—Our knowledge of chronic cholangitis of the intrahepatic bile-ducts (or angiocholitis) is very deficient. It may be assumed that bacteria or poisons conveyed to the liver, either by the portal vein or by the hepatic artery, may give rise to inflammation of the intrahepatic

[1] Lejars. *Med. Week*, Paris, 1897, v, 139.
[2] Quénu. *Ibid.*, 1897, v, 163.
[3] Guillot. *Gaz. hebd. de méd.*, Paris, 1902, vii, 49.

ducts ; and that cholangitis complicates diseases of the liver, such as portal cirrhosis, chronic venous engorgement, hepatitis, and malignant growths. Chronic cholangitis occurs in hypertrophic biliary cirrhosis with chronic jaundice, but all cases of chronic catarrh of the intrahepatic ducts do not conform to the type of Hanot's disease, though the conditions are allied. The small ducts shew proliferation of the lining epithelium, which may block up the lumen ; there may be some dilatation of the small bile-ducts, and there is pericholangitic fibrosis.

The following conditions have been ascribed to chronic angiocholitis, but their pathological nature requires confirmation.

Klippel and Vigouroux [1] described a case of chronic cholangitis with hepatic insufficiency, diarrhoea, no jaundice or enlargement of the spleen, in which signs of acromegaly developed. The authors suggest that this was due to hepatic insufficiency in the same way that clubbed fingers develop in hypertrophic biliary cirrhosis. The liver shewed angiocholitis and fibrosis of the portal spaces. Lereboullet [2] described a somewhat similar condition under the name meta-icteric splenomegaly. Jaundice due to cholangitis occurs first, and subsequently as it recedes, the spleen becomes enlarged. The enlargement of the spleen is supposed to be due to passive venous engorgement produced by pressure on the branches of the portal vein by sclerosing cholangitis.

Cases thought to be due to chronic catarrhal inflammation of the small intrahepatic ducts should be treated with plenty of water and occasional courses of salicylate of sodium, combined with urotropin, so as to wash out the ducts and remove catarrh. Minute doses of calomel ($\frac{1}{20}$ gr.) may be given two or three times a day to minimise intestinal fermentation, and the bowels should be kept freely open and the diet should be simple and nourishing. Alcohol should be forbidden. Spa treatment on the same lines as in chronic catarrhal cholangitis of the larger ducts may be adopted.

Pericholangitis

Pericholangitis may be divided into : (*a*) Extrahepatic, affecting the larger bile-ducts ; and (*b*) intrahepatic. Extrahepatic pericholangitis may accompany changes in the larger ducts, but is entirely subordinate to that condition.

Intrahepatic Pericholangitis. — This is chiefly of pathological interest, since it either occurs as part of other morbid lesions or has no definite clinical associations. It is met with under different conditions and may be acute, as in suppurative cholangitis, of which it forms part, or it may be chronic.

[1] Klippel et Vigouroux. *Presse méd.*, Paris, 1903, i, 245.
[2] Lereboullet. *Semaine méd.*, Paris, 1903, xxiii, 180.

Acute pericholangitis cannot be recognised apart from acute inflammation in the portal spaces, such as suppurative cholangitis or pylephlebitis, to which it is, as far as is known, practically always secondary.

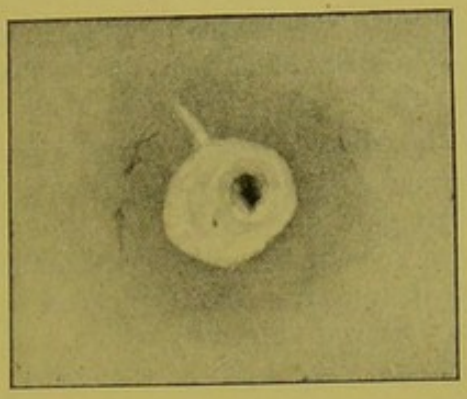


FIG. 94.—Naked-eye appearance of a section of liver with white material due to chronic pericholangitis. There was also secondary pylephlebitis.

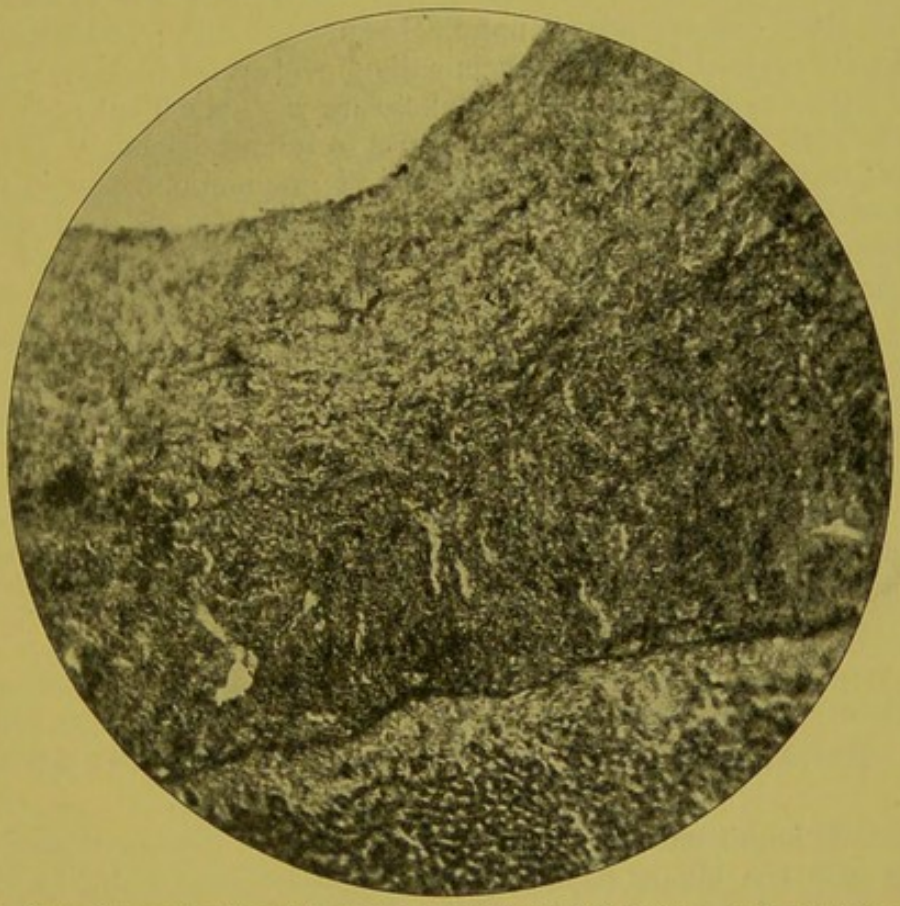


FIG. 95.—Photomicrograph of the white material occupying a portal space. It is composed of granulation tissue. The space at the top represents the remains of the portal vein, which in this instance was destroyed by secondary suppurative pylephlebitis.

It is, however, quite conceivable that an acute inflammation of the lymphatic vessels around the bile-ducts might occur independently of cholangitis. It might be set up by an abscess in the liver.

Chronic pericholangitis occurs in several conditions described elsewhere; thus, in hypertrophic biliary cirrhosis and in gall-stone obstruction with infection of the ducts there is fibrosis around the smaller bile-ducts from extension of inflammation in their interior.

In a case of enormous dilatation of the intrahepatic bile-ducts in which the liver was like a hydronephrotic kidney, there was extensive chronic pericholangitis (Raynaud and Sabourin [1]).

In the condition described as tuberculous cavities in the liver the tuberculous process begins in the loose tissue surrounding the bile-ducts —tuberculous pericholangitis.

Pericholangitis, which is not an entirely subsidiary part of cholangitis, is seen in very rare instances. To the naked eye the portal spaces are occupied by white material (Fig. 94) which has a close resemblance to tubercle. Strangeways Pigg and I [2] described a case, and Morley Fletcher [3] has since given an account of another. In the first it appeared probable that catarrhal cholangitis had set up chronic pericholangitis, but Fletcher took the view that the pericholangitis was primary. In our case there was secondary suppurative pylephlebitis; in Fletcher's the portal vein was healthy. The inflammation involves the portal lymphatics; in our case the glands in the portal fissure were much enlarged, and to the naked eye there was some resemblance to lymphadenoma. The white material in the portal spaces is composed of granulation tissue in various stages of development (Fig. 95), and in these two cases were certainly not tuberculous. It contained numbers of bile-ducts, many of which were proliferating and dilated. According to Amet and Carnot [4] the elastic fibres spreading out from the ducts may be increased in amount.

Clinically, these cases did not present any characteristic features. In Morley Fletcher's case there was bronchiolectasis, and in our case the patient had advanced renal disease and several attacks of haemorrhage from the bowel. In neither was there jaundice; this can to some extent be explained by supposing that blocking of the lymphatics prevented the absorption of bile by the lymph channels.

PARASITIC AFFECTIONS OF THE BILE-DUCTS

Ascaris Lumbricoides.—A round worm in the duodenum may work its way into the biliary papilla and common bile-duct and give rise to biliary obstruction and infection of the ducts. Cases have been described in which jaundice has disappeared after the passage of a bile-stained

[1] Raynaud et Sabourin. *Arch. de physiol. norm. et path.*, Paris, 1879, 2. s., vi, 37.
[2] Rolleston and Strangeways Pigg. *Journ. Path. and Bacteriol.*, 1898, v, 221.
[3] Morley Fletcher. *Trans. Path. Soc.*, Lond., 1901, lii, 193.
[4] Amet et Carnot. *Arch. de méd. expér. et d'anat. path.*, Paris, 1906, xviii, 763.

round worm shewing a constriction (Ebstein,[1] Hilliary [2]); and it has been reasonably assumed that in some instances the head of the worm has temporarily blocked the lower end of the bile-duct. Mertens [3] collected 48 cases of round worms in the bile-ducts, and Sick [4] brought together 64 cases. From the frequency of ascarides in the young it is natural that some of the cases of bile-duct infection are in children. The worms dilate the bile-ducts, carry micro-organisms with them, and, by infecting the bile-passages, give rise either to suppurative cholangitis or to single or multiple abscesses in the liver.

Roud [5] described a case with streptococci and colon bacilli in the hepatic abscesses, which also contained gas.

In 5 of Merten's cases, gall-stones were associated with the presence of round worms. Hanot [6] regards the cholelithiasis as due to the infective agency of the worms. In his own case Mertens believed that the passage of a calculus assisted the entrance of the worm by dilating the passage.

The following case recorded by John Davy [7] is one of the earliest and illustrates the condition well. A Maltese boy aged two years who died from dysentery, was found to have numerous round worms in the stomach, small intestine, colon, and liver. The common and hepatic ducts were distended with worms, and there were several abscesses in the liver containing worms.

A specimen (No. 533) in the Cambridge Pathological Museum shews the bile-duct distended with *Ascaris lumbricoides*. The patient was a child. The duct was so tensely distended that jaundice must have been produced, though there is no history of the case.

The *clinical features* are enlarged liver, jaundice, fever, attacks of biliary colic, and, in a word, those of infective cholangitis with biliary obstruction. In only 2 of 48 cases collected by Mertens was a diagnosis made during life. The diagnosis depends on finding the worms or their ova in the dejecta; otherwise the cases are likely to be regarded as due to gall-stones.

Treatment.—Santonin should be given if the presence of round worms is suspected. In the presence of signs of infection of the common duct the duct should be cut down upon and drained. In a case diagnosed as a calculus in the common duct recovery followed choledochotomy (Neugebauer [8]).

Distomiasis.—Several species of distomidae may be met with in the bile-ducts of the liver in man.

[1] Ebstein. *Deutsches Arch. f. klin. Med.*, 1904, lxxxi, 543.
[2] Hilliary. *Journ. Am. Med. Assoc.*, Chicago, 1905, xlv, 1655.
[3] Mertens. *Deutsche med. Wchnschr.*, 1898, xxiv, 358.
[4] Sick. Inaug. Dissert., Tübingen, 1901. Quoted by Neugebauer. *Arch. f. klin. Chir.*, 1903, lxx, 584.
[5] Roud. *Thèse de Lausanne*, 1896.
[6] Hanot. *Arch. gén. de méd.*, Paris, 1896, clxxvii, 74.
[7] Davy, J. *Diseases of the Army*, p. 423, 1862. This specimen is in the Museum of the Royal Army Medical College, Millbank (Series xxix., No. 131), and is figured in 3rd Fasciculus of Drawings of Specimens in Army Medical Museum, Chatham, Plate II. Printed by Taylor, London, 1838.
[8] Neugebauer. *Arch. f. klin. Chir.*, 1903, lxx, 584.

Fasciola hepatica (*Distomum hepaticum*) or liver-fluke is common in sheep, and gives rise to the disease known as sheep-rot, which has proved so disastrous to so many sheep-farms. In very rare instances men have become infected from taking water or vegetables contaminated with the dejecta of sheep suffering from the disease. Out of 24 reputed cases Ward[1] considers that 14 are authentic. Infection with *Fasciola hepatica* may arise in this country, which is not the case with the other varieties of distoma. Invasion of the ducts by distoma is much commoner in tropical countries, such as China, Japan, and India.

Opisthorchis sinensis (*Distomum sinense*) is found in India, China, Japan, and Tonkin. In Japan 20 per cent of the inhabitants in certain low-lying districts are affected; they suffer from diarrhoea, ascites, cachexia, and eventually die (Baelz[2]). *Dicrocoelium lanceatum* (*Distomum lanceolatum*) and *Opisthorchis noverca* (*Distoma conjunctum*) have in extremely rare instances been met with in the bile-ducts of human beings, but are of no real pathological importance.

Morbid Anatomy.—The distomes cling by their suckers to the mucous membrane of the bile-ducts, which become dilated, shew epithelial proliferation and small papillomas, and contain mucus and the ova of the worms. Cystic dilatations varying from the size of a hazel-nut to a walnut may form in the course of the ducts. There is inflammation with an accumulation of eosinophil cells around the bile-ducts. Suppuration may occur in the dilated bile-ducts. The liver is enlarged and may shew perihepatitis.

Clinical Aspect.—Though sometimes the worms remain latent, some of the following symptoms and signs may be expected: Hepatic pain and enlargement, jaundice, gastro-intestinal disturbance, vomiting, diarrhoea or constipation, fever, enlargement of the spleen, ascites, oedema of the feet, and anaemia. The cases may terminate as suppurative cholangitis or abscess of the liver, and the prognosis is therefore bad. The diagnosis depends on the detection of the ova in the stools. The treatment consists in giving vermicides, such as Filix mas and purgatives. When there are signs of suppurative cholangitis, the common bile-duct should be opened.

Psorospermosis.—The invasion of the bile-ducts of the rabbit by the *Coccidium cuniculi* is extremely common, and leads to the production of papillomatous growths from the mucosa of the dilated ducts. On section, the liver shews white, caseous areas closely resembling tubercles to the naked eye. These appearances have been often described, and reference may be made for a detailed account of the parasite and its effects to Delépine's[3] paper. Sometimes, as the result of secondary infection, acute inflammation is set up in the ducts and the mucous membrane becomes replaced by granulation tissue—psorospermial cholangitis.

Psorospermial invasion is very rare in the human liver, but it has

[1] Ward. *Brit. Med. Journ.*, 1911, i, 930.
[2] Baelz. *Berlin. klin. Wchnschr.*, 1883, xx, 234.
[3] Delépine. *Trans. Path Soc.*, Lond., 1890, xli, 348.

been more often described in the liver than in any other internal organ of the human body. McFarlane[1] collected 20 cases of human psorospermosis, and, omitting supposed psorospermial affections of the skin, such as Darier's disease, found that the liver was affected 11 times, the intestines 5 times, the kidneys twice, and the pleura and spleen once each.

A case of calcification of a psorospermial tumour removed during life from a patient who was thought to have a calcified gall-bladder is put on record by Carrel.[2] In Silcock's[3] case there was considerable enlargement of the liver,

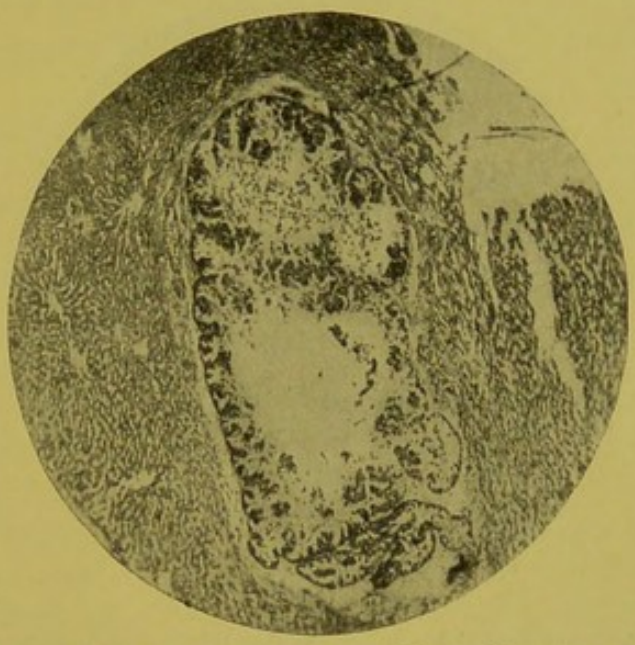


FIG. 96.—Section of rabbit's liver under a low power, with papillomatous growths in the dilated bile-duct due to the irritation of psorosperms. (Photomicrograph by Dr. S. G. Penny.)

which weighed 83 ounces. The spleen and intestines were also affected, and psorosperms were cultivated for two months. Podwyssozki[4] reported 4 cases.

It is, however, not unlikely that some cases have been overlooked and the lesions regarded as caseous tubercle, and that a microscopic examination would have revealed the presence of psorosperms. The coccidia are taken in food, multiply in the stomach, and invade the common bile-duct.

Clinical Aspect.—In the human subject the symptoms are obscure. Some cases have shewn fever, enlargement and tenderness of the liver without jaundice, and prostration. In rabbits eosinophilia has been observed (Federici[5]), and would be anticipated in man.

[1] McFarlane. *Journ. Applied Microscopy*, Rochester, 1898, i, 41.
[2] Carrel. *Lyon méd.*, 1900, xciii, 89.
[3] Silcock. *Trans. Path. Soc.*, Lond., 1890, xli, 320.
[4] Podwyssozki. *Centralbl. f. Bakt. u. Parasit.*, 1889, vi, 41.
[5] Federici. *Riv. crit. di clin. med.*, 1902.

Porocephalus Constrictus.—*Syn.* Pentastomum constrictum.—This parasite gains entrance to the alimentary canal, and, reaching the liver, gives rise to cysts, especially in the neighbourhood of the falciform ligament, which are thought to be dilated bile-ducts. The cysts contain clear fluid and a single coiled-up parasite which may be alive at the time the liver is examined after death. The walls of the cyst are composed of firm fibrous tissue and have a great tendency to undergo calcification. The peritoneum in the neighbourhood of the cysts may shew considerable inflammation, and infection of the lungs may occur. It is remarkable

FIG. 97.—The same section under a higher power, shewing the coccidia loose in the dilated bile-duct. (Photomicrograph by Dr. S. G. Penny.)

that though the parasite gives rise to inflammation of the peritoneum and lungs, it does not appear to irritate the intestines and liver.

Cysts containing the parasite have been observed in the liver by Pruner,[1] Aitken,[2] Giard,[3] Chalmers,[4] and Thiroux.[5] It is said to occur only in negroes, but this is not correct, as there is a specimen of a liver with five cysts containing the parasite, in the museum at the Royal Army Medical College, Millbank (Series xxix. No. 133), taken from an English soldier who died of spinal caries. Fibrosed cysts containing the larvae of *Linguatula rhinaria* have often been found on the surface of the liver.

Balantidium coli.—*Synonym*: Paramoecium coli.—This parasite is very common in the colon of the pig, and has been found in the intestines of man in association with diarrhoea. In the following unique case the parasite was found in the liver of man:

[1] Pruner. *Krankheiten des Orients*, Erlangen, 1847, S. 245.
[2] Aitken. *Science and Practice of Medicine*, Lond., 1868, i, 650.
[3] Giard. *Compt. rend. Soc. Biol.*, Paris, 1896, 10. s., iii, 469.
[4] Chalmers. *Lancet*, 1899, i, 1715, 1729.
[5] Thiroux. *Compt. rend. Soc. Biol.*, Paris, 1905, 10. s., ii, 78.

In the liver of a man aged fifty-nine years Russell and Buzzard [1] found a dozen cysts the size of peas containing living paramoecia. The cysts, which had firm fibrous walls, were probably derived from the bile-ducts and due to the irritation set up by paramoecia which had travelled up the bile-ducts from the duodenum. The cysts did not shew any papillary growths resembling those in psorospermosis of the liver. As the patient died from gastric carcinoma, it is not improbable that absence of HCl in the gastric juice allowed these organisms to develop in the stomach. No proof of this, however, is forthcoming, as the vomit was not examined.

INNOCENT TUMOURS OF THE BILE-DUCTS

Innocent tumours of the bile-ducts are rare.

Papilloma.—Very few examples of papilloma of the larger extrahepatic bile-ducts are on record, but probably the condition is not so exceptional as the number of published cases would suggest. Some of the cases described as malignant, but not examined microscopically, may have been innocent.

Chappet [2] speaks of a case of carcinoma, but states that the growth developed at the expense of the mucosa, which was not ulcerated, and that the other coats of the duct were little or not at all affected, so that it may have been an innocent papilloma.

Extensive mucoid change in papillomas of the bile-ducts might produce a condition such as that described by Wilks and Moxon [3] in a child aged four years whose common bile-duct, dilated to the size of its head, contained pendulous myxomatous growths with muscular fibres in them. The small fatty tumours described by Wardell [4] as obstructing the cystic and common bile-ducts might also be regarded as originally papillomas of the bile-ducts, which subsequently underwent myxomatous degeneration and then, from bile-staining, took on a yellowish tinge, suggesting fat; for no microscopic examination appears to have been made. Devic and Gallavardin [5] quote similar cases of lipomas arising from the mucosa of the bile-ducts recorded by Ehrmann and by Dickmann. As submucous lipomas occasionally occur in the intestines, it is quite possible that they may be found in the bile-ducts.

A papillomatous growth, from the inside of the common bile-duct, was removed by Sir W. Bennett from a woman at St. George's Hospital. It was close to a gall-stone that had been impacted for two months.[6] It was a branching papilloma, composed of a basis of fibrous tissue covered over by columnar

[1] Russell and Buzzard. *Trans. Path. Soc.*, Lond., 1899, l, 149.
[2] Chappet. *Lyon méd.*, 1894, lxxvi, 146.
[3] Wilks and Moxon. *Pathology*, p. 485, 3d ed., 1889.
[4] Wardell. *Lancet*, Lond., 1869, ii, 407.
[5] Devic et Gallavardin. *Rev. de méd.*, Paris, 1901, xxi, 570.
[6] Rolleston. *Trans. Path. Soc.*, Lond., 1894, xlv, 83.

epithelium (Fig. 98). In places the connective tissue had undergone mucoid degeneration. The after-history of the patient, however, rather suggested malignant disease (*vide* p. 690). A papilloma arising from the inside of the common duct one inch above the biliary papilla was considered by Eve [1] to have obstructed the duct in a valvular fashion and so to be responsible for cystic dilatation of the common duct.

The papillomatous growths in rabbits' intrahepatic bile-ducts, due to the irritation of psorosperms, are extremely common, but a similar

FIG. 98.—Papilloma of the common bile-duct. There is some adherent mucus on the surface of the growth. There is myxomatous degeneration of the fibrous core of the papilloma. (From the case referred to in the text, p. 687.) × 40.

lesion in man is a pathological curiosity. A case of cystic tumours of the bile-ducts in man due to the irritation of these coccidia has been recorded by Podwyssozki.[2]

Papillomas or adenomas of the intrahepatic ducts may be multiple and give rise to no symptoms. On the other hand, there may be a single tumour, and in either case they may become cystic (*vide* p. 458).

The simple papillomas occasionally seen around the biliary papilla in the duodenum are growths of the intestinal surface of the papilla and not of the bile-duct. Papilloma may, however, arise in the cavity of the diverticulum of Vater. McPhedran [3] described a case which, like most

[1] Eve. *Trans. Clin. Soc.*, Lond., 1906 xxxix, 144.
[2] Podwyssozki. *Centralbl. f. Bakt. u. Parasit.*, 1889, vi, 41.
[3] McPhedran, A. *Sajous' Annual*, 1899, iv, 422.

of the cases of papillomatous growths around the duodenal orifice of the biliary papilla, gave rise to suppurative cholangitis.

A fibroma the size of a bean obstructing the lumen of the bile-duct has been described.[1]

Volmer[2] reported an *adenomyofibroma* of the wall of the common bile-duct close to the ampulla.

Hydatid Cysts.—Devic and Gallavardin[3] quote 3 cases in which hydatid cysts arose in the walls of the bile-ducts (Cadet de Gassicourt, Ignatieff, Macready).

Xanthoma, xanthelasma, or vitiligoidea has been found on the mucosa of the bile-duct in a few cases of chronic jaundice. It is the result of jaundice and not the cause. Futcher[4] described it in the bile-duct in a case of jaundice of ten years' duration due to calculous obstruction. In 2 cases mentioned by Fagge[5] the lining of the bile-ducts was covered with the flat form of xanthoma.

MALIGNANT TUMOURS OF THE LARGER (EXTRA-HEPATIC) BILE-DUCTS

UNDER this heading primary malignant tumours of the extrahepatic bile-ducts will be dealt with. Carcinoma of the small intrahepatic bile-ducts is, for all practical purposes, primary carcinoma of the liver. Secondary growths are very rare in the bile-ducts, though in multiple malignant growths of the peritoneum they may be invaded from without. Extensions of growth to the bile-ducts from the hilum of the liver, from carcinomatous glands in the neighbourhood, from the lesser omentum, or from the pancreas are referred to elsewhere. Primary carcinoma of the ampulla or diverticulum of Vater is much the same as primary carcinoma of the lower end of the common bile-duct, but a separate description of this condition is given on page 702.

Incidence.—Malignant disease of the large or extrahepatic bile-ducts is probably not so rare as has been thought. The number of cases described has increased rapidly in recent years.

In 1889 Musser[6] collected 18 cases; in 1897 Claisse[7] tabulated 50; in 1901 Devic and Gallavardin,[8] after excluding doubtful cases, analysed 55 examples, and I have notes of 90, about which there seems no doubt.

[1] Albers, quoted in von Ziemssen's *Cyclopaedia of Practical Medicine*, 1880, ix, 569.
[2] Volmer. *Arch. f. klin. Chir.*, Berl., 1908, lxxxvi, 160.
[3] Devic et Gallavardin. *Rev. de méd.*, Paris, 1901, xxi, 571.
[4] Futcher. *Am. Journ. Med. Sc.*, Phila., 1905, cxxx, 949.
[5] Fagge. *Principles and Practice of Medicine*, 1886, ii, 280.
[6] Musser, J. H. *Boston Med. and Surg. Journ.*, 1889, cxxi, 581.
[7] Claisse, P. *Gaz. des hôp. de Paris*, 1897, lxx, 1279.
[8] Devic et Gallavardin. *Rev. de méd.*, Paris, 1901, xxi, 557.

The disease may be overlooked or more probably described as something else. Thus, some of the cases recorded as malignant tumours of the lesser omentum probably originated in the bile-ducts. Again, in some of the cases described as primary malignant disease arising in the portal fissure and involving the bile-ducts the growth may well have started in their walls. In other instances a slow-growing fibrous carcinoma of the bile-ducts has probably been described as a simple cicatricial stricture. In fact, to the naked eye there may be so close a resemblance that a microscopic examination is necessary to settle the question.

Etiology.—According to Zenker[1] primary carcinoma of the gall-bladder begins as an innocent papilloma which subsequently becomes transformed into a carcinoma. I have seen one case which suggests that the same sequence might occur in the bile-duct.

A papilloma removed during a choledochotomy from the bile-duct of a woman was in immediate contact with a gall-stone which had been impacted for about two months. Some months later the patient returned with signs compatible with the view that the growth had recurred in the region of the operation wound, but did not remain under observation. I shewed the specimen to the Pathological Society[2] as an example of a papilloma due to irritation of a gall-stone ; later on, after the patient's return, the question arose whether, supposing the recurrence to be carcinomatous, the growth had been malignant from the first, or whether the growth had subsequently invaded the duct-walls after the manner of a duct carcinoma in the breast. At the operation there was no infiltration of the bile-duct, so that if the recurrent growth was carcinomatous, it would appear that a transformation from a simple to a malignant adenoma had taken place.

It is conceivable that carcinoma may supervene on an ulcer of the bile-duct, as it does on an old gastric ulcer.

In a woman, aged fifty-seven, marked stenosis of the lower end of the bile-duct was thought to be due to cicatrisation of an ulcer set up by a gall-stone. Microscopically there was carcinomatous invasion of the wall (Krokiewicz[3]). On the other hand, there is no proof that it was not a carcinoma from the first which had subsequently ulcerated.

In very rare cases (Necker,[4] Taylor and Teacher[5]) primary carcinoma of the intrahepatic bile-ducts has been found in a liver occupied by independent secondary growths. Taylor and Teacher suggest that the irritation of these secondary growths played a part in the production of the primary growth.

Relation to Gall-stones.—Gall-stones are present in about a third of the cases of primary carcinoma of the bile-ducts ; this contrasts with primary carcinoma of the gall-bladder in which gall-stones are met with in more than 70 per cent of the cases (*vide* p. 638).

[1] Zenker. *Deutsch. Arch. f. klin. Med.*, Leipz., 1889, xliv, 159.
[2] Rolleston. *Trans. Path. Soc.*, Lond., 1894, xlv, 83.
[3] Krokiewicz. *Wien. klin. Wchnschr.*, 1898, xi, 320.
[4] Necker. *Ztschr. f. Heilk.*, Wien u. Leipz., 1905, xxvi (*Abt. path. Anat.*), 351.
[5] Taylor and Teacher. *Journ. Path. and Bacteriol.*, Cambridge, 1908, xii, 441.

In 67 of my cases in which a definite statement as to the presence or absence of gall-stones was made they were present in 23 and absent in 44. It is probable that in a high proportion of the cases in which no statement was made, gall-stones were absent. In 40 cases collected by Devic and Gallavardin [1] gall-stones were present in only nine instances—six times in the gall-bladder and on three occasions in the bile-ducts; in one case only was the growth found to surround the calculus. In Lapointe and Raymond's [2] 69 cases gall-stones were present in a fourth.

Sex.—Males are more often affected than females. In 85 cases, in which the sex is recorded, 50 males and 35 females were affected. This contrasts with carcinoma of the gall-bladder, in which females are attacked four times more frequently than males.

Age.—Primary malignant disease of the bile-ducts usually occurs after fifty years of age. This was so in 58 of my 83 cases. In Musser's 18 cases the average age was 56·6 years, and in 83 of my cases 55·5 years; in my series the average age was practically the same in the two sexes (55·5 in males, 55·4 in females); the extremes were 81 years in a woman and 29 in a man.

Morbid Anatomy.—*Situation of the Growth.*—Carcinoma may arise in any part of the larger bile-ducts, but it is very rarely confined to either of the two hepatic ducts.

In 90 cases the situation of the growth was as follows:

Common bile-duct:	
Lower end	23
Middle part	11
Junction of common bile-duct, cystic, and common hepatic ducts	27
Common hepatic duct	19
Right or left hepatic ducts	3
In cystic duct	6
In cystic duct and in lower end of the common bile-duct	1

The group of cases in which the growth is limited to the common hepatic duct or its two branches, the right and left hepatic ducts, has been called juxta-hepatic (P. Claisse [3]).

Of this form, of which I have collected 22 examples, Ingebrans,[4] in 1902, tabulated 16. When juxta-hepatic carcinoma attacks the lower end of the common hepatic duct, it readily spreads to and occludes the cystic duct, and so becomes carcinoma of the junction of the common, cystic, and hepatic ducts. Devic and Gallavardin [5] adopt a slightly different classification and divide their 54 cases into two groups: (*a*) Those in which the growth was in the common duct, or supra-duodenal, 22 cases; and (*b*) juxta- or sub-hepatic, 32 cases; among this latter category are included 15 cases of growth at the junction of

[1] Devic et Gallavardin. *Rev. de méd.*, Paris, 1901, xxi, 575.
[2] Lapointe et Raymond. *Arch. gén. de chir.*, Paris, 1908, ii, 375.
[3] Claisse, P. *Presse méd.*, Paris, 1897, iv, p. cxxxix.
[4] Ingebrans. *Arch. gén. de méd.*, Paris, 1902, cxc, 268.
[5] Devic et Gallavardin. *Rev. de méd.*, Paris, 1901, xxi, 661.

the common bile, common hepatic, and cystic ducts. Lapointe and Raymond collected 32 cases in which the growth was in the hepatic duct, and 37 in which it was at the junction with the cystic duct.

When the cystic duct alone is affected, the condition is, both anatomically and clinically, much the same as carcinoma of the neck of the gall-bladder, and is, therefore, more conveniently grouped with carcinoma of the gall-bladder. Few cases of carcinoma limited to the cystic duct have been recorded; this is probably because it either begins close to the gall-bladder and so spreads to it, or because it has extended into the junction of the common hepatic and common bile-duct by the time that the anatomical facts can be investigated.

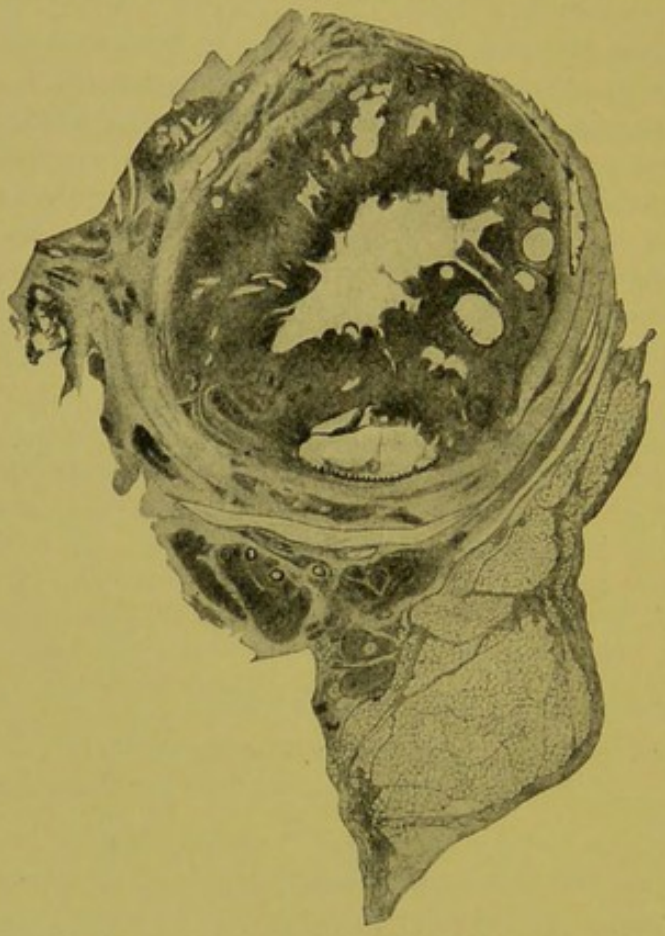


Fig. 99.—Section of common bile-duct with primary carcinoma. The growth projects into the lumen of the duct and narrows it. The muscular walls of the duct are infiltrated with growth. × 6.

Appearance of the Growth.—The growth is firm and white, and nearly always small — often not larger than a cherry. Large tumours are most exceptional; I have seen one as big as an orange. The growth may form a rather diffuse, infiltrating mass around the structures in the portal fissure, as in a case described by Planteau and Cochez,[1] and in 2 cases which I have examined. In these instances it may be difficult to determine the origin of the growth, and the condition is sometimes described as primary carcinoma starting on the portal fissure. The tumour may be villous on its internal surface, but this appearance may be removed by ulceration; in this connexion it is interesting to refer again to the possibility that it may start as an innocent papilloma. Usually carcinoma is localised and infiltrates the walls of the duct, forming a firm annular stricture. Occasionally the growth spreads along the walls of the ducts, and transforms them into thick, rigid tubes. A considerable extent of the common bile-duct or even of the cystic or common hepatic

[1] Planteau et Cochez. *Rev. de méd.*, Paris, 1903, xxiii, 70.

ducts as well may thus be converted into carcinomatous tubes. In some instances the growth projects considerably into the lumen, and may thus produce obstruction rather than by an annular stricture. In one instance two apparently independent growths were found in the extra-hepatic bile-ducts. After death the stricture does not always appear to be absolutely impervious. It is probable that during life muscular spasm increases the obstruction. Haemorrhage occasionally takes place in connexion with the growth. It may be due to cholaemia, to erosion of a blood-vessel, or possibly to acute haemorrhagic pancreatitis.

Behaviour of the Growth.—Usually the growth does not infiltrate adjacent parts widely. It may grow into the substance of the pancreas, liver, or the portal vein. In a specimen (38·25) in the Hunterian Museum, Glasgow, a colloid carcinoma apparently of the common bile-duct invaded the abdominal wall. Carcinoma of the ducts may infiltrate the portal vein and cause thrombosis. As already mentioned, the growth may project into the lumen of the duct and thus obstruct it. It may extend along the walls of the ducts so as to involve widely the mucous membrane of the biliary tract, or it may spread along the lymphatics in the outer coats of the ducts and thus pass into the liver.

In one case in St. George's Hospital, a growth at the junction of the common bile, cystic, and common hepatic ducts spread up along the side of the hepatic ducts into the liver and produced a second stricture of the left hepatic duct inside the transverse fissure. In Planteau and Cochez's case, which was of much the same nature, a growth inside the left lobe of the liver was shewn to be an expansion of a continuous carcinomatous infiltration spreading along the ducts.

Naked-eye Diagnosis of Primary Carcinoma of the Bile-ducts.—Wherever it starts, the growth may spread along the ducts; thus a considerable extent of the common duct, together with the common hepatic duct and its branches, may be affected at the same time, or the gall-bladder, cystic duct, and the common bile-duct may be infiltrated in continuity. In such cases it may be impossible to determine its starting-point. As carcinoma of the lower end of the bile-duct may spread to the pancreas, and so present much the same naked-eye appearances as carcinoma of the head of the pancreas involving the common bile-duct, it is probable that some cases described as carcinoma of the head of the pancreas in reality started in the bile-duct. Microscopically carcinoma of the pancreas is spheroidal-celled, whereas that of the bile-duct is almost always columnar-celled; this provides a criterion for deciding the origin of the growth in any doubtful case.

As pointed out above, carcinoma of the bile-ducts at their exit from the liver merges into primary carcinoma of the liver; carcinoma of the cystic duct resembles malignant disease of the gall-bladder; some cases of carcinoma of the common bile-duct have probably been described as cancer of the gastro-hepatic omentum; and carcinoma of the lower end of the bile-duct may closely resemble disease of the head of the pancreas.

The disease is probably, therefore, less rare than is usually thought. On the other hand, malignant disease of the gall-bladder, or more rarely of the pancreas, may spread for a very considerable distance along the bile-ducts.

Thus in a woman aged fifty-six years, in St. George's Hospital, a spindle-celled sarcoma of the gall-bladder spread down along the cystic and common bile-ducts as far as the biliary papilla. In a case of Rose Bradford's [1] carcinoma extended from the gall-bladder along the cystic duct into the common bile-duct and hepatic duct, the growth terminating abruptly in all directions. When carcinoma arising in the head of the pancreas involves the common bile-duct and spreads along its walls beyond the confines of the pancreas, it may be difficult or impossible to be certain of the starting-point of the growth until a microscopic examination is made. Durante [2] described such a case.

Microscopical Appearances.—Duval[3] described a unique case of primary melanoma of the lower end of the common bile-duct and ampulla of Vater; with this exception primary malignant tumours of the bile-ducts are carcinomas, and in the great majority of instances a columnar-celled growth derived from the surface epithelium.

In 43 cases which I have analysed, the tumour was a columnar-celled carcinoma in 37, spheroidal-celled in 5, and colloid in 1 (Leith [4]). In many cases the description is too vague to base any opinion on, the growth being spoken of as "scirrhus," "encephaloid," or merely as carcinoma.

It is possible that spheroidal-celled carcinoma of the bile-duct may be derived from mucous glands in its wall. Mucoid degeneration of the columnar cells leading to distension of the alveoli is not uncommon. In a certain number of the cases of columnar-celled carcinoma there is a transition to a spheroidal-celled character; this change is commonly seen in carcinoma of other organs, such as the mamma and gall-bladder, and probably depends on increased rate of growth. It is often described as an atypical carcinoma. In rare cases mucoid or allied degenerative changes in the epithelial cells induce a swollen, flattened appearance, and as a result of the invagination of these cells an appearance closely resembling squamous-celled carcinoma is presented. As in the gall-bladder, metaplasia may give rise to a squamous-celled carcinoma (*vide* p. 632).

I am indebted to Dr. W. C. Bosanquet for the section from which Fig. 100 was made. In some parts of this section alveoli formed by flattened epithelial cells contained cholesterin crystals.

The supporting stroma of the tumour consists of well-formed fibrous tissue, shewing that it is slow-growing.

[1] Bradford, J. R. *Brit. Med. Journ.*, 1898, ii, 1555.
[2] Durante. *Bull. Soc. Anat. Paris*, 1893, lxxiv, 342.
[3] Duval. *Journ. Exper. Med.*, N.Y., 1908, x, 465. This case was also recorded by Shepherd, *Ann. Surg.*, 1908, xlvii, 948.
[4] Leith. *Trans. Med.-Chir. Soc. Edin.*, 1896, xv, 59.

Condition of the Bile-ducts.—Below the growth the calibre of the ducts is normal; it is possible that an impacted calculus might be situated below the growth and distend the distal portion of the duct. Above the growth the ducts are dilated, sometimes to such an extreme degree as to allow a finger or a thumb to be introduced. Dilated bile-ducts containing clear mucus, or in the early stages bile, may project on the surface of the liver. In rare instances infective cholangitis is present.

FIG. 100.—Microscopical appearances of carcinoma of the common bile-duct. The growth is columnar-celled in one part, but squamous-celled in others. The latter is an exceptional appearance. (From a specimen lent by Dr. W. C. Bosanquet.)

Condition of the Gall-bladder.—A tumour in the common bile-duct causes distension of the gall-bladder, unless, from former cholelithiasis, the gall-bladder is bound down by adhesions and retracted on itself.

In 18 cases in which the growth was in the common bile-duct the gall-bladder was distended in 17 (Devic and Gallavardin).

When the tumour is in the common hepatic duct, the gall-bladder is nearly always small; in exceptional instances it may be distended with mucus from concomitant obstruction of the cystic duct, or it may be occupied by gall-stones. When the tumour is at the junction of the cystic, common hepatic, and common bile-ducts, the gall-bladder is, as a rule, not enlarged, but from irregularities and variations in the degree of obstruction in the different ducts corresponding differences in the condition of the gall-bladder are met with. Lapointe and Raymond[1]

[1] Lapointe et Raymond. *Arch. gén. de chir.*, Paris, 1908, ii, 375.

state that when growth is at the confluence, the gall-bladder is usually dilated.

Secondary growths are not very common, probably because the primary growth proves fatal from cholaemia before there is sufficient time for extensive metastases. They are most often found in the liver. In 57 cases the liver was affected in 13. Secondary growths may also arise in the adjacent lymphatic glands and in the peritoneum; in the latter situation they may produce ascites. Secondary growths very seldom occur when the primary tumour is in the common hepatic duct or in either of the two hepatic ducts. In 12 cases of this juxta-hepatic form of carcinoma of the bile-ducts analysed by Lecène and Pagniez[1] there was no instance of a secondary growth.

The *liver* shews dilatation of the bile-ducts, first with bile, but later with clear mucoid fluid. It may be either larger or smaller than natural, and is always of a very deep green colour. The liver cells atrophy, and there are areas of icteric necrosis.

According to Fütterer,[2] this icteric necrosis occurs in the central zone of the lobule, the intermediate and the peripheral zones remaining normal. This is explained on the theory that the distension of the interlobular bile-ducts compresses the interlobular channels and reverses the direction of the flow of bile. The bile then flows into the perivascular lymphatics around the central vein, and sets up necrosis of the neighbouring liver cells.

The liver cells contain bile-pigment, which may be regarded as being in the radicles of the bile capillaries. Around the necrosed areas small-celled infiltration and the formation of so-called new bile-ducts are sometimes seen. In the majority of cases there is no cirrhosis or fibrosis as the result of biliary obstruction. The atrophy of the liver cells allows the existing fibrous tissue to appear more prominent, and has led some writers to believe that biliary obstruction produces hepatic fibrosis. What to the naked eye looks like pericholangitic fibrosis may turn out to be new growth extending along the portal spaces. Weber and Michels,[3] and Scagliosi,[4] have insisted on the production of biliary cirrhosis in these cases. In cases in which the ducts have been infected there may be pericholangitic fibrosis. It is conceivable that hepatic cirrhosis may have existed prior to the development of malignant disease of the bile-ducts, or that some fibrosis around the ducts may have been induced by cholangitis due to gall-stones. Infection of the ducts, which is more likely to occur when the tumour is at the lower end of the common bile-duct, may give rise to suppurative cholangitis, empyema of the gall-bladder, and febrile disturbance.

Clinical Picture.—The *onset* is usually insidious, and generally the first thing noticed is jaundice, to which the patient's attention may be

[1] Lecène et Pagniez. *Arch. gén. de méd.*, Paris, 1901, clxxxvii, 176.
[2] Fütterer, G. *Chicago Med. Recorder*, 1897, xii, 325.
[3] Weber and Michels. *Med.-Chir. Trans.*, Lond., 1905, lxxxviii, 261.
[4] Scagliosi. *Riforma med.*, Palermo e Napoli, 1904, xx, 1210.

called by his friends. There may be an acute onset of gastro-intestinal symptoms, followed by jaundice and suggesting ordinary catarrhal jaundice; somewhat vague dyspeptic symptoms may exist for some little time before the appearance of jaundice. In a few cases the sudden onset of pain followed by jaundice imitates the impaction of a gall-stone in the common duct.

Symptoms.—Except when the tumour is in the cystic duct, jaundice is always present; it steadily progresses, and eventually becomes dark-green or black. There are gastro-intestinal symptoms, furred tongue, foul breath, dyspepsia, vomiting, and constipation, which may alternate with diarrhoea. The faeces are pale and to the naked eye quite devoid of pigment, but Cammidge[1] finds that hydrobilirubin can usually be detected; he concludes that the growth allows some bile to pass into the duodenum. There may be occult blood in the stools; in advanced jaundice there may be small gastro-intestinal haemorrhages from cholaemia. There may be distaste for fatty, or indeed for all food. The symptoms are largely those of jaundice combined with progressive loss of strength and flesh. Attacks of biliary colic, usually independent of cholelithiasis, are met with occasionally; this pseudo-gall-stone colic may be due to spasm of the ducts set up by the irritation of the growth, and is sometimes seen in malignant disease of the head of the pancreas. There may be dull pain in the right hypochondrium, but occasionally it is present on both sides. Pain is sometimes felt in the epigastrium, as in carcinoma of the head of the pancreas, and may then be due to invasion of the head of the pancreas by a growth starting in the lower end of the common bile-duct. Pain is not, as a rule, a marked symptom, but it may be so severe as to require the constant use of morphine.

Itching of the skin usually occurs when jaundice is well marked, but occasionally it precedes the appearance of icterus, and there may be little or no itching, even when the jaundice is very deep. The pulse is not slowed. The temperature is normal or subnormal in the absence of complications. I have seen it continuously raised for six weeks in a case in which inflammation was confined to a dilated bile-duct in the liver.

The gall-bladder becomes distended from backward pressure, and is palpable in about half the cases as a uniform smooth tumour. The smooth surface is important in distinguishing it from primary carcinoma of the gall-bladder. The gall-bladder is probably always enlarged, except when the growth involves the common hepatic or hepatic ducts, but it is not necessarily palpable during life. The condition of the liver varies considerably: sometimes it is enlarged and smooth from distension with bile; at other times, though large, it is concealed by tympanitic, or more rarely by ascitic, distension; but it may be normal in size. Secondary growths are very seldom felt during life; in fact, there is hardly time for extensive generalisation, as the disease kills comparatively rapidly by cholaemia. Secondary growths may cause ascites by pressing on the portal vein or by irritating the peritoneum. Ascites is not very

[1] Cammidge. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Med. Sect.), 163.

frequently prominent. It is, however, present in about half the cases examined after death (Devic and Gallavardin [1]), and is often slight in amount and not of any clinical import.

The spleen is rarely palpable. In Devic and Gallavardin's 55 cases it was noted as palpable in 8.

The urine may be, but is not constantly, diminished in quantity, and is always deeply bile-stained. It often contains mucin. Albuminuria has been recorded, but, as a rule, there is no albumin or sugar. Casts may be present without albuminuria. Cammidge's test should give a negative result. This was so in two cases under my care in which the growth was in the common hepatic duct.

The progressive jaundice usually lasts about five or six months. The patient's condition is one of depression, the temperature being subnormal, unless some secondary infection occurs. Xanthopsia, in which everything the patient sees has a yellow tinge, is sometimes present. The usual duration of jaundice—five to six months—is not sufficiently long to allow of the development of xanthoma, which is usually associated with jaundice of considerable standing.[2] Pye-Smith,[3] however, recorded xanthoma in primary carcinoma of the common duct. The symptoms of biliary toxaemia precede death, which may be from exhaustion, coma, or delirium. The biliary toxaemia is due to flooding of the blood by intestinal toxins normally stopped and either destroyed by the liver or excreted into the bile; this is due to a failure of the protective or detoxicating function of the liver. Haemorrhages into the skin and severe itching, when they occur, are due to this toxic condition of the blood. In rare instances death may be due to peritonitis set up by perforation of the gall-bladder. In the case recorded by May [4] there were two gall-stones in the perforated gall-bladder; in Coats and Finlayson's [5] case there was no history or sign of cholelithiasis.

Death may in very exceptional cases be due to haemorrhage in connexion with the growth. This occurred spontaneously in one case which I examined after death, and is a source of danger in cases in which any operative measures—such as cholecystenterostomy—are undertaken. In Huguenin's [6] case the gall-bladder, which was full of blood, ruptured into peritoneal cavity and fatal haemorrhage resulted, 3½ pints of fluid blood being found in the abdomen.

Duration.—Usually death occurs from cholaemia within six months from the onset of jaundice. In one case under my observation jaundice had existed for thirteen months before an exploratory operation revealed carcinoma of the common hepatic duct.

Complications.—Besides haemorrhage around the growth and rupture

[1] Devic et Gallavardin. *Rev. de méd.*, Paris, 1901, xxi, 676.

[2] *Vide* a list of 23 cases of xanthelasma associated with jaundice tabulated in *Trans. Path. Soc.*, Lond., 1882, xxxiii, 381.

[3] Pye-Smith. *Ibid.*, 1877, xxviii, 243.

[4] May. *München. med. Wchnschr.*, 1892, xxxix, 590.

[5] Coats and Finlayson. *Glasgow Med. Journ.*, 1890, xxxiv, 84.

[6] Huguenin. *Virchows Arch.*, 1903, clxxiii, 552.

of the gall-bladder, suppurative cholangitis with or without multiple miliary abscesses has been known to occur. This is more likely to supervene when the growth is near the termination of the common bile-duct. As in cholelithiasis, infective endocarditis has been recorded, deep jaundice favouring infection. Thrombosis of the portal vein was found in Bourgeret and Cossy's [1] case.

Diagnosis.—The painless onset, the steadily progressive character of the obstructive jaundice, eventually becoming dark green, the age of the patient, namely, over fifty, and the absence of definite proof of any other cause are the factors which suggest malignant disease of the bile-ducts. But as it imitates obstructive jaundice due to other conditions, it will be advisable to consider the diagnosis between them seriatim.

Primary carcinoma of the head of the pancreas and primary malignant disease of the ducts are very much alike. In addition to jaundice, both these conditions may or may not shew dilatation of the gall-bladder during life, so this point does not help in the diagnosis. As regards pain, that of pancreatic carcinoma is epigastric, but from extension of the growth to the bile-ducts it may trespass into the hypogastric region. Enlargement of the liver has been thought to be more frequent in bile-duct carcinoma, and secondary growths in the liver are perhaps more often present in pancreatic cancer. In pancreatic disease the primary tumour is seldom, and in carcinoma of the bile-ducts it is almost never, palpable. In both cases the cachexia is rapid,—perhaps more so in cancer of the pancreas,—and death results from cholaemia. Some variation in the condition of the liver and gall-bladder, and in the site of pain, may occur in both. In short, a diagnosis between the two cannot be made on the foregoing grounds; and since pancreatic carcinoma is the commoner, it would, on the score of probabilities, be diagnosed whenever their common symptoms are presented. When carcinoma of the lower end of the bile-duct spreads into the pancreas, it may compress Wirsung's duct as well, and so lead to practically the same morbid condition as primary carcinoma of the head of the pancreas compressing the bile-duct. By his tests Cammidge [2] has found the following distinctive points: In carcinoma of the bile-ducts the saponified fat in the faeces is in excess of the unsaponified fat, whereas in carcinoma of the pancreas the saponified fat is less than or equal to the unsaponified fat. In carcinoma of the ducts the growth usually allows a little bile to enter the intestine, so that the faeces contain some stercobilin; in pancreatic carcinoma there is usually no stercobilin.

The differential diagnosis between primary carcinoma of the common bile-duct and of the ampulla of Vater is also extremely difficult (*vide* p. 706).

Gall-stones, impacted or lying in the common bile-duct, may be indicated by a history of biliary colic immediately preceding the onset of jaundice. But in a patient whose cystic and common bile-ducts are

[1] Bourgeret et Cossy. *Bull. Soc. Anat. Paris*, 1873, xlviii, 347.
[2] Cammidge. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Med. Sect.), 163.

already dilated by the passage of gall-stones, impaction of a calculus may occur, especially near the duodenum, without any satisfactory history of its occurrence. In about a third of the cases of carcinoma of the bile-ducts calculi are found after death in the gall-bladder, and in a small proportion of these biliary colic has occurred in life. Conversely, pseudo-gall-stone colic may possibly occur in cases of malignant disease affecting the bile-ducts in the absence of any calculi. When biliary colic immediately precedes the onset of icterus, the diagnosis of cholelithiasis is more probable, but since gall-stones may enter the common duct without a characteristic history, it is desirable to consider any further points which bear on the diagnosis of gall-stone obstruction from that due to bile-duct carcinoma. The duration of calculous jaundice is very much longer than that of carcinoma of the bile-ducts, and death, when it occurs, is usually due to some complication, such as suppurative cholangitis, rather than to cholaemia. This difference in the course of the two affections is correlated with a difference in the nature of the obstruction in each case. In malignant disease the obstruction becomes more marked as time goes on, whereas with gall-stones the obstruction is complete at first, but subsequently, from the constant pressure exerted from within by the calculus on the wall of the bile-duct, from inflammation, and to some extent from extension of the dilatation of the ducts above the obstruction, the walls of the duct become somewhat separated from the calculus, and the obstruction becomes partial or so slight that eventually the jaundice may almost disappear. In gall-stone obstruction of the common duct periodic attacks of intermittent hepatic fever usually occur (*vide* p. 759) which are quite characteristic of this condition. The course and duration of the diseases, if uninterrupted by surgical treatment, are therefore sufficiently distinct to enable a differential diagnosis to be made, though this may not be possible in the earlier stages.

Courvoisier's law, namely, that in calculous obstruction of the common bile-duct the gall-bladder is not enlarged, whereas in obstruction of that duct by new growth the gall-bladder forms a palpable tumour, should always be borne in mind. But the gall-bladder need not be distended in all cases of carcinoma of the bile-ducts. Thus, in carcinoma of the common hepatic or of either of the hepatic ducts, the gall-bladder is not enlarged, and there may be difficulty in diagnosing the condition from impacted calculus in the common duct. The following points, then, would be in favour of cholelithiasis: The history of colic immediately before the onset of jaundice; intermittent hepatic fever; the chronic nature of the illness; the absence of enlargement of the gall-bladder, and the fact that, although of considerable duration, the jaundice is not very deep or progressive. Cammidge's tests are of use in the diagnosis: in gall-stone obstruction a positive pancreatic reaction is usually present, and there is urobilinuria pointing to cholangitis; in malignant disease of the ducts the pancreatic reaction is absent unless the growth irritates the pancreas.

So long as *primary malignant disease of the gall-bladder* is confined to

the gall-bladder and there is no pressure on the hepatic or common ducts, jaundice is absent, and there is no resemblance to primary carcinoma of the ducts. The jaundice is, therefore, no essential part of the disease, and is due either to extension of the primary growth or to pressure exerted by secondary growths on the bile-ducts. It occurs in the course of more than half the cases—according to Musser, in 69 per cent, which is also the proportion in which gall-stones were present in his 100 cases of carcinoma of the gall-bladder. When jaundice, due to obstruction of the duct, has supervened, the case is for all practical purposes one of malignant disease both of the gall-bladder and of the bile-ducts. Carcinoma of the gall-bladder may form a tumour, which is knobby or irregular, and is not so large as the smooth, dilated gall-bladder frequently met with in carcinoma of the bile-ducts or of the head of the pancreas. In addition to the history, the frequent association (70-95 per cent) of gall-stones with carcinoma of the gall-bladder should be kept in mind.

In *malignant disease of the liver*, whether primary or secondary, with jaundice, the history of the case and the facts that the liver is considerably enlarged and manifestly infiltrated with growth and that the jaundice is not so extreme, or, as a rule, of such long duration, will serve to differentiate it from primary carcinoma of the ducts.

From *hypertrophic biliary cirrhosis* there will seldom be any real difficulty in diagnosis. In some exceptional cases of bile-duct carcinoma the spleen is enlarged, but not to the same extent as in biliary cirrhosis. The latter disease occurs in younger persons, runs a chronic course, measured by years and not by months, and presents much greater enlargement of the liver and spleen.

Catarrhal jaundice is usually ushered in by vomiting and diarrhoea, while the onset of jaundice due to malignant stricture of the bile-duct is usually unobtrusive and unaccompanied by signs of gastro-intestinal catarrh. But the course of the two is so different—the one passing almost spontaneously away in a few weeks, the other getting progressively worse—that even if at first there be difficulty in determining which is the cause at work, little doubt remains after a few weeks have gone by.

There are a number of other causes which may sometimes give rise to chronic jaundice of varying degree, such as secondary malignant disease in the portal fissure, tumours or hydatid cysts in connexion with the liver, inflammatory adhesions, or even possibly gumma implicating the ducts, aneurysms of the hepatic artery or of the abdominal aorta—in short, most of the tumours and many of the morbid conditions to be met with in the abdominal cavity (*vide* p. 551). But the question of diagnosis between them and primary malignant disease of the ducts will seldom arise, inasmuch as there will generally be, either in the history or in the physical signs and symptoms, a clue to the nature of the disease.

Treatment.—The palliative and symptomatic treatment is that of

obstructive jaundice (*vide* p. 566). Pain may require morphine. For the treatment of pruritus see p. 567, but morphine should be given if other means are not successful. Calcium salts may be given both for pruritus and to prevent haemorrhages. Intestinal putrefaction may be combated by guaiacol, naphthalene tetrachloride, acetozone (1 in 2500), minute doses of calomel ($\frac{1}{40}$ – $\frac{1}{20}$ gr.), and by preventing constipation by blue pill and salines. Cholaemia may be obviated temporarily by intravenous or better by subcutaneous transfusion if it is thought to be worth while.

Surgical interference has not been much in vogue, presumably because radical measures are very difficult. The palliative operation of putting the gall-bladder into communication with the small intestine—cholecystenterostomy—will, in favourable cases,—*i.e.* when the obstruction is limited to the common bile-duct,—prevent the bile being dammed up in the liver and absorbed by the lymphatics into the general circulation. In cases in which the obstruction is proximal to the junction of the cystic duct, a biliary fistula has been produced between a dilated duct in the liver and the outside of the abdomen (intrahepatic cholangiostomy) (Weber and Michels [1]). Jaundice and cholaemia, with their attendant symptoms, may thus be obviated, and the patient's general condition greatly improved. As already mentioned, in complete biliary obstruction death is likely to occur from cholaemia, and if this is prevented, life may be greatly prolonged.

Curative Surgical Measures.—The resection of a growth from the bile-duct has been performed in a number of cases. Quénu [2] collected 9 cases—3 of the common bile-duct, 1 of the cystic duct, and 5 of the junction of the common bile, hepatic, and cystic ducts. Since then Littlewood [3] successfully excised a growth of the cystic and common ducts.

A malignant growth of the cystic duct has been removed (Warren [4]), but this operation is more allied to excision of the gall-bladder and is not so difficult as resection of part of the hepatic or common bile-ducts.

MALIGNANT TUMOURS OF THE AMPULLA OF VATER

The common bile-duct, before opening into the duodenum, joins with the main pancreatic duct; this common portion is called the ampulla or diverticulum of Vater. Normally the mucous membrane of the ampulla contains glands and is thrown into folds. It thus appears rougher than the inside of the common bile-duct, but it is not dilated except in definite pathological conditions, such as impaction of a gall-

[1] Weber and Michels. *Med.-Chir. Trans.*, Lond., 1905, lxxxviii, 247.
[2] Quénu. *Rev. de chir.*, Paris, 1909, xxxix, 245.
[3] Littlewood. *Lancet*, Lond., 1910, i, 1341.
[4] Warren. *Boston Med. and Surg. Journ.*, 1900, cxlii, 276.

stone. In 1908 Duval[1] described a melanoma of the lower end of the common bile-duct and of the ampulla of Vater. With this exception the primary malignant tumours of the ampulla of Vater are carcinomas. Carcinoma may start in the mucous membrane of the ampulla, or may spread to it from the lower end of the bile-duct or from the termination of the pancreatic duct.

Busson,[2] in 1890, collected 11 cases, and in 1896 Vincent Georges,[3] a pupil of Hanot's, collected 9 more. Hanot[4] added another later in the same year. Of these 21 cases only about half a dozen are genuine examples of carcinoma of the ampulla of Vater, the others being carcinoma of the lower end of the bile-duct or of the duodenal surface of the biliary papilla.

I have collected 19 cases,[5] 17 of them since the beginning of 1896, which appear to be undoubted examples of carcinoma arising in the mucous membrane lining the ampulla of Vater.

Hanot[6] separated carcinoma of the ampulla of Vater from carcinoma of the lower end of the bile-duct, or, as it is called, juxta-ampullary carcinoma of the common bile-duct. He insisted that the growth is confined to the ampulla of Vater, and does not arise in the common bile-duct or in the duodenum. He spoke of the condition as *cancer du pylore pancréatico-biliaire*. The diagram overleaf shews his views. But the parts are so small that it may be difficult or even impossible to distinguish the form arising in the termination of the bile-duct (*vide* 1, in diagram) from that arising from the lining of the ampulla (*vide* 4, in diagram), away from the opening of the common bile-duct.

Primary carcinoma of the ampulla Vateri, or, as it might more conveniently be called, the choledocho-pancreatic duct, must be distinguished from primary carcinoma—(1) of the termination of the common bile-duct; (2) of the termination of Wirsung's duct. According to Letulle[7] primary carcinoma derived from the mucous membrane or glands of Wirsung's duct is spheroidal and not columnar-celled. This lesion has been very seldom recognised; Carnot and Harvier[8] described a case in a

[1] Duval. *Journ. Exper. Med.*, N.Y., 1908, x, 465; also described by Shepherd, *Ann. Surg.*, 1908, xlvii, 948.

[2] Busson. *Thèse de Paris*, 1890.

[3] Vincent Georges. *Thèse de Paris*, 1896, No. 404.

[4] Hanot. *Arch. gén. de méd.*, Paris, 1896, clxxviii, 547. Previous cases recorded by Hanot are given in Vincent Georges' thesis.

[5] Durand-Fardell, *Presse méd.* 1896, 285; Vincent Georges, *Thèse de Paris*, 1896, No. 404; Rendu, *Soc. méd. des hôp.*, 1896; Hanot, *Arch. gén. de méd.*, 1896, clxxviii, 547; Pilliet, *Bull. Soc. Anat. Paris*, 1889, lxiv, 509; Dominici, *ibid.*, 1896, lxxi, 709; Maury, *Bull. et mém. Soc. méd. des hôp.*, 1902, p. 433; Cornil et Chevassu, *Bull. Soc. Anat. Paris*, 1903, p. 151; May, *München. med. Wchnschr.*, 1892, xxxix, 590; Scheuer, *Berlin. klin. Wchnschr.*, 1902, xxxix, 138; Halsted, *Johns Hopkins Hosp. Bull.*, Balt., 1900, xi, 1; Pratt and Fulton, *Boston Med. and Surg. Journ.*, 1900, cxlii, 599; de Havilland Hall, *Lancet*, 1902, i, 1102; Klotz, *Montreal Med. Journ.*, 1904, xxxiii, 477; Moore, F. C., *Journ. Path. and Bacteriol.*, 1904, x, 76; Riva-Rocci, *Gazz. med. ital.*, 1904; Rolleston, *Lancet*, Lond., 1901, i, 467; and two from St. George's Hospital.

[6] Hanot. *Arch. gén. de méd.*, Paris, 1896, clxxviii, 547.

[7] Letulle. *Presse méd.*, Paris, 1906, p. 256; also Letulle et Verliac, *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1905, xxii, 1063.

[8] Carnot et Harvier. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1906, xxiii, 296.

woman aged sixty-six which was a transitional-celled carcinoma; Luzzatto[1] also recorded a case; and (3) of the mucous membrane covering the duodenal surface of the biliary papilla, or arising in Brunner's glands at this spot (Klotz[2]). This form of duodenal carcinoma is very commonly confused with primary carcinoma of the ampulla. It is not very rare, and there are specimens of it in the museums of St. Bartholomew's, Guy's, and St. Thomas's Hospitals. This lesion seems to be especially prone to lead to infective cholangitis and intrahepatic suppuration. The accompanying diagram illustrates these distinctions. Confusion may also occur between carcinoma of the head of the pancreas and primary carcinoma of the ampulla Vateri. Histologically they differ: carcinoma of the pancreas is spheroidal-celled, while carcinoma of the ampulla Vateri is columnar-celled.

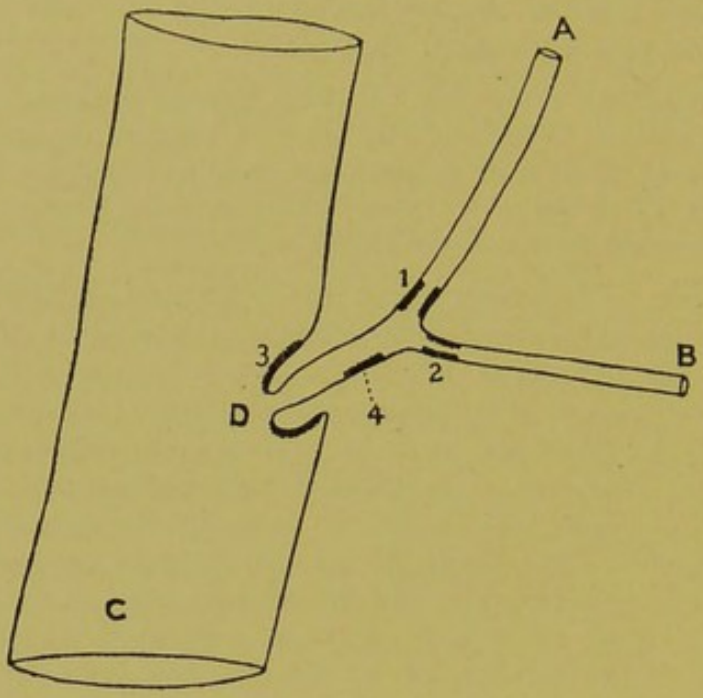


FIG. 101.—Diagram of the ampulla Vateri, shewing the various situations where carcinoma may arise in relation with it and in its neighbourhood.
A, Common bile-duct. B, Wirsung's duct. C, Duodenum. D, Biliary papilla. 1, Carcinoma of the termination of the common bile-duct. 2, Carcinoma of the termination of Wirsung's duct. 3, Carcinoma of the duodenal surface of the biliary papilla. 4, Carcinoma of the ampulla Vateri.

Pic[3] regarded carcinoma of the ampulla as an aberrant form of pancreatic carcinoma corresponding apparently with the excretory type (columnar-celled) of pancreatic carcinoma described by Bard and Pic.[4]

Morbid Anatomy.—The growth begins as a thickening of the mucous membrane of the ampulla and infiltrates its muscular walls. It may form a villous or polypoid tumour, and may then project through the orifice of the biliary papilla, which is dilated or ulcerated, into the duodenum. The growth is white, as a rule, but may be pinkish-white when projecting into the duodenum. It is comparatively small, and is rarely obviously ulcerated. It is probable, from the histological accounts, that some cases described as carcinoma of the Vater were simple

[1] Luzzatto. *Clin. med. ital.*, Milano, 1902, xli, 282.
[2] Klotz. *Montreal Med. Journ.*, 1904, xxxiii, 477.
[3] Pic. *Rev. de méd.*, Paris, 1895, xv, 71.
[4] Bard et Pic. *Ibid.*, 1888, viii, 394.

papillomas. A growth in this situation, whether innocent or malignant, would rapidly give rise to jaundice and to cholaemia. Secondary growths are infrequent; Aynaud [1] estimates that metastases, nearly always in the liver, occur in 20 per cent of the cases. The patient probably often dies from cholaemia before there has been time for secondary growths to occur. If cholaemia is prevented by establishing a biliary fistula, as in the case given on p. 708, life may be sufficiently prolonged for secondary growths to develop.

Histologically it is, like primary carcinoma of the bile-ducts, practically always a columnar-celled carcinoma.

Pathological Results.—A growth in the ampulla of Vater may obstruct the orifice of Wirsung's duct and thus produce dilatation of the intra-pancreatic ducts and chronic interstitial pancreatitis, as in the cases described on pages 707 and 708. As a result of this chronic interstitial pancreatitis diabetes might have been expected. This, however, does not occur. The explanation of this was given by Opie,[2] who shewed that obstruction of the duct is very seldom followed by the intimate fibrosis, which is accompanied by destruction of the islands of Langerhans, necessary to cause glycosuria.

If carcinoma of the ampulla of Vater involved the mucosa and walls of the orifice of the biliary papilla, it might, provided the growth did not obstruct the orifice of Wirsung's duct, convert the common bile-duct and Wirsung's duct into a continuous and closed channel. Bile might then enter the pancreatic duct and set up haemorrhagic pancreatitis. But in 11 cases of carcinoma of the ampulla of Vater collected by Dieulafoy [3] there was no case of haemorrhagic pancreatitis. The production of haemorrhagic pancreatitis by a small calculus impacted in the biliary papilla was described by Halsted and Opie [4] (*vide* p. 750).

An ascending infection of the bile-ducts may induce suppurative cholangitis and multiple hepatic abscesses; this accident is more likely to occur than in primary carcinoma of the bile-ducts.

In a case recorded by Pratt and Fulton,[5] the pus from multiple abscesses in the liver gave a pure culture of the *Bacillus aerogenes capsulatus*, but there was no gas-formation.

Etiology.—The male sex is much more often affected than the female sex, as is the case in primary malignant disease of the larger bile-ducts, whereas primary carcinoma of the gall-bladder is much commoner in females. Of 19 cases 14 were males and 5 females.

It is a disease of advanced life. In 19 cases the average age was 55·2 years, being 56 years in the 14 males, and 52 years in the 5

[1] Aynaud. *Gaz. des hôp. de Paris*, 1907, lxxx, 807.
[2] Opie, E. L. *Journ. Exper. Med.*, N.Y., 1901, v, 397; *Diseases of the Pancreas*, 1903, p. 178.
[3] Dieulafoy. *Presse méd.*, Paris, 1907, p. 657.
[4] Halsted and Opie. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 123.
[5] Pratt and Fulton. *Boston Med. and Surg. Journ.*, 1900, cxlii, 599.

females. The extremes were 34 and 81 years. The average age of 16 cases collected by Aynaud was 62 years.

There is no relation between gall-stones and this form of malignant disease of the biliary system; in only 2 out of 19 cases were calculi present. This is rather remarkable, since gall-stones are not infrequently found in the ampulla of Vater, and may remain there for very considerable periods, so that it might naturally have been assumed, on the analogy of the gall-bladder, that their irritation might give rise to carcinoma.

FIG. 102.—Columnar-celled carcinoma of the ampulla of Vater invading its muscular wall and the duodenum.

The **symptoms, signs,** and **diagnosis** of carcinoma of the ampulla are, in the main, the same as those of cancer of the common bile-duct (*vide* p. 697). The following points of difference bear on the diagnosis between the two conditions, which must be regarded as a very difficult problem:

(i) Jaundice is often intermittent, the faeces becoming normal in colour and the icteric tint of the skin diminishing or even passing off in the earlier stages when the obstruction is possibly valvular, or partly due to spasm of the duct set up by the irritation of the growth. In this connexion it may again be pointed out that confusion is apt to arise in recorded cases between carcinoma of the ampulla and of carcinoma of the duodenal surface of the papilla, in which jaundice is by no means constant. (ii) Intermittent hepatic fever and suppurative cholangitis are apt to occur. (iii) Diarrhoea is more often seen than in carcinoma

of the ducts, in which constipation is the rule. Attacks of diarrhoea may alternate with periods of obstinate constipation.

By his tests Cammidge is unable to differentiate between carcinoma of the ampulla of Vater and a stone in the common duct.[1] The clinical manifestations of the disease are illustrated by the following cases :

Carcinoma of the Ampulla of Vater ; Dilated Bile and Pancreatic Ducts ; Haemorrhage into the Pancreatic Duct.—A man aged sixty-six was admitted into St. George's Hospital under my care on July 22, 1900, with jaundice, pruritus, weakness, and wasting. He had never had any severe illness, and denied alcoholic excess and syphilis. Ten weeks before he had been quite well ; jaundice then appeared quite painlessly. A month later he began to waste, became weaker and drowsy ; two weeks later the skin began to itch. On admission he was deeply jaundiced ; the liver was enlarged and quite smooth ; the gall-bladder could be indistinctly felt ; the spleen could not be made out. The abdomen was somewhat distended, but there was no evidence of ascites. There was tenderness at a spot over the eleventh and twelfth ribs in the right hypochondrium. The urine contained albumin, bile-pigment, and bile acids, but no sugar. A tentative diagnosis of malignant disease of the head of the pancreas was made. On July 25 he had diarrhoea, on July 26 he vomited, had a rigor, and the temperature fell to 96° ; pulse 96, small. Respirations were 36 and the abdomen moved well. The liver seemed larger than on admission. He died eighteen hours after the onset of acute symptoms.

The necropsy shewed a small, hard tumour arising from the mucous membrane of the ampulla of Vater, and not visible from the duodenum. The growth blocked the pancreatic and common bile-ducts. The common bile-duct was as big as one's thumb and contained dark bile and mucus ; when opened and explored in a downward direction with the finger, it was found to end blindly, like a test-tube. The hepatic ducts and the ducts in the left lobe of the liver were widely dilated ; except the main hepatic duct, the bile-ducts in the right lobe were but little dilated. The cystic duct and gall-bladder were greatly dilated ; no calculi were found in the gall-bladder or in the bile-ducts. The liver (4 pounds) was smooth and of a deep green colour. Wirsung's duct was tortuous, dilated throughout its entire length, and near the head of the pancreas it formed a cyst into which recent haemorrhage had taken place. It is probable that the terminal acute symptoms depended on this haemorrhage. Towards the tail of the pancreas the duct contained dark fluid, probably altered blood of older date. The pancreas was attached to the posterior wall of the stomach by old adhesions. No calculi were found in the ducts of the pancreas. The pancreas itself was greatly fibrosed and hard. No secondary growths were found in any part of the body. The abdomen contained two pints of bile-stained fluid. The stomach and intestines shewed recent catarrh. Microscopically the growth was a columnar-celled carcinoma and invaded the muscular coat of the ampulla of Vater (*vide* Fig. 102). The pancreas shewed extensive fibrosis, some recent small-celled infiltration, dilatation of the ducts, which contained minute calculous masses, and widespread atrophy of the glandular tissue. The islands of Langerhans were intact.[2]

[1] Cammidge. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Med. Sect.), 205.

[2] This case was reported in the *Lancet*, Lond., 1901, i, 467.

Carcinoma of the Ampulla Vateri imitating Cholelithiasis.—A woman aged fifty-two was attacked six and a half months before death with colic, shivering, diarrhoea, vomiting, and distension of the abdomen. The pain lasted for two weeks and was succeeded by jaundice. She had several similar attacks resembling biliary colic, and when admitted to St. George's Hospital had lost three stone in weight. She was deeply jaundiced and complained of abdominal tenderness, itching of the skin, and weakness. Cholecystotomy was performed, but no calculi were found. At the operation there was ascites. Before death nodules of growth appeared in the skin around the fistula leading into the gall-bladder. At the necropsy, which I performed, a tumour projected from the gaping lips of the biliary papilla; it arose inside the ampulla of Vater and completely blocked the common bile-duct; the duct of Wirsung was obstructed and presented a cystic dilatation as large as a hen's egg near the tail of the pancreas, which was adherent to the fundus of the stomach. There were numerous secondary growths in the liver, which was small and deeply bile-stained. There was no cirrhosis microscopically, but numerous masses of inspissated bile were present in the minute bile-ducts. The growth was a columnar-celled carcinoma.

The **treatment** has usually been palliative and confined to relief of the symptoms, and on the same lines as in carcinoma of the bile-ducts.

Surgical Treatment.—Quénu[1] collected 9 cases treated by excision with 6 deaths, or 66·6. Oehler[2] has also reviewed the surgical treatment of carcinoma in this region.

Halsted[3] successfully removed a primary carcinoma of the duodenal papilla and ampulla Vateri in a woman aged sixty. The common bile-duct and pancreatic ducts were engrafted into the duodenum; three months later the cystic duct was engrafted into the duodenum to relieve the biliary obstruction which had persisted. Death occurred within a year of the first operation from recurrent carcinoma in the head of the pancreas and duodenum, which had obstructed the openings of the common and cystic ducts into the duodenum. In a somewhat similar case Mayo[4] removed a carcinoma of the terminal part of the common bile-duct by the duodenal route; it recurred in eighteen months.

[1] Quénu. *Rev. de chir.*, Paris, 1909, xxxix, 245.
[2] Oehler. *Beitr. z. klin. Chir.*, 1910, lxix, 726.
[3] Halsted. *Johns Hopkins Hosp. Bull.*, 1900, xi, 1.
[4] Mayo. *Boston Med. and Surg. Journ.*, 1903, cxlviii, 545.

CHOLELITHIASIS[1]

THE formation of gall-stones, whether in the ducts or in the gall-bladder, may be considered under the following two heads—(i) Immediate or exciting causes. (ii) Disposing causes.

Immediate or Exciting Causes.—According to Naunyn[2] the immediate cause of the production of calculi is a mild inflammation of the mucous membrane lining the ducts and gall-bladder. Catarrhal inflammation of the bile-ducts leads to an albuminous exudation which, as is also shewn experimentally by the addition of egg-albumin to bile, precipitates bilirubin in chemical combination with calcium as bilirubin-calcium calculi. This is the form of calculus usually found in the bile-ducts, though under conditions such as impaction of a gall-stone in the common duct, the formation of additional calculous material containing cholesterin, as well as bilirubin-calcium, takes place. Simple stagnation and inspissation of bile do not lead to the precipitation of bilirubin-calcium or to the formation of bilihumin, which is constantly found in these bilirubin-calcium calculi. Something more than inspissation—viz. catarrhal inflammation—is necessary for the formation of these calculi. In catarrhal inflammation of the gall-bladder there is an abnormal formation of cholesterin, or cholesterol, as it has more recently been called, by the mucous cells and glands in its walls. Evidence of this can be seen microscopically in the presence of myelin bodies inside the cells. This excessive and pathological production of cholesterin is responsible for the formation of multiple cholesterin calculi. This differs from the older conception that cholelithiasis was due to a mere precipitation of the cholesterin normally present in bile, brought about by a change in the bile, such as concentration or alteration in its chemical properties or reaction.

It was formerly thought that cholesterin formed elsewhere, and especially in the central nervous system, was picked up from the blood and excreted into the gall-bladder. This explanation was abandoned since its administration by the mouth or under the skin in animals does not increase the amount in the bile. Recently, however, Hürthle has shewn that cholesteryl oleate is constantly present in the blood; and

[1] For historical accounts of this disease the reader is referred to Thudichum's *Treatise on Gall-stones*, 1863, Churchill, London, and to Hoppe-Seyler, "Diseases of the Liver," Nothnagel's *Encyclopedia of Practical Medicine*, American translation, 1903.

[2] Naunyn. *Cholelithiasis*, p. 20. Translated by A. E. Garrod, New Sydenham Soc., 1896.

there is reason to believe that it is excreted into the gall-bladder, and that the oleic radicle is split off and re-absorbed by the epithelium of the gall-bladder (Adami and Aschoff[1]), cholesterin being left in the gall-bladder. Aschoff and Bacmeister[2] believe that single pure (as apart from laminated) cholesterin calculi may be formed without any inflammation of the bile passages, and thus differ from multiple calculi which depend on catarrhal inflammation. The presence of a pure cholesterin calculus may favour infection, and so give rise to multiple gall-stones. For a discussion of the difficult subject of the origin of biliary cholesterin the reader should refer to Adami's *Principles of Pathology* (1910, i. 950).

It will be noticed that the results of catarrh in the small bile-ducts and in the gall-bladder differ both in the mechanism and in the nature of the calculi produced. As the result of catarrh of the small intrahepatic ducts there is a precipitation of bilirubin-calcium, whereas catarrh of the gall-bladder leads, by a perverted metabolism of the mucous membrane, to a pathological formation of cholesterin analogous to that sometimes seen in hydroceles and ovarian cysts.

The catarrh of the ducts and gall-bladder may be spoken of as lithogenic. If the catarrh starts in the ducts, the small calculi of bilirubinate of calcium may possibly find their way into the gall-bladder, and there form the nucleus of cholesterin calculi produced as the result of an extension of the inflammation to the gall-bladder. As catarrhal inflammation plays such an important part in cholelithiasis, it will be necessary to consider what are the exciting and disposing causes of catarrhal cholecystitis and cholangitis. The exciting causes are infection with micro-organisms and possibly the action of poisons excreted into the ducts.

The Microbic Origin of Gall-stones.—Galippe[3] in 1886 first suggested that the formation of calculi depended on bacterial activity. Experimentally it has been shewn that the production of cholecystitis by the typhoid bacillus and the colon bacillus is followed by cholelithiasis. Non-virulent streptococci and staphylococci may also give rise to calculous formation; virulent cultures, however, set up intense cholecystitis without cholelithiasis (Mignot[4]). From Italia's[5] researches it appears that pure cultures of streptococci or staphylococci may lead to the formation of calculi which are composed only of lime salts; cholesterin may be found when there is an admixture with cultures of the *Bacillus coli*. Thus experimental work, like clinical observation, shews that cholelithiasis is due to a comparatively mild cholecystitis, or, expressed in other words, is produced by an attenuated infection; this may depend on the preservation of the cholesterin-producing epithelium in the slighter forms of cholecystitis, and its destruction in more acute inflammations of the gall-bladder. Exner and Heyrovsky[6] find that typhoid and colon bacilli

[1] Adami and Aschoff. *Proc. Roy. Soc.*, Lond., 1906, Ser. B., lxxviii, 359.
[2] Aschoff und Bacmeister. *Die Cholelithiasis*, 1909.
[3] Galippe. *Compt. rend. Soc. Biol.*, Paris, 1886, 8. s., iii, 116.
[4] Mignot. *Arch. gén. de méd.*, Paris, 1898, clxxxii, 129.
[5] Italia. *Riforma med.*, 1901, 830.
[6] Exner und Heyrovsky. *Wien. klin. Wchnschr.*, 1908, xxi, 214.

destroy bile acids and so lead to a precipitation of cholesterin, but that streptococci do not have this action. The important micro-organisms in the production of cholelithiasis are: (1) The colon bacillus. (2) The typhoid bacillus.

(1) The main part in the microbic origin of biliary calculi is usually ascribed to bacilli belonging to the colon group. Mignot produced calculi in a guinea-pig as a result of the action of *Bacillus coli* on the gall-bladder in 1897. The colon bacillus has often been demonstrated inside biliary calculi (Welch,[1] Gilbert and Dominici,[2] Mignot); recent calculi especially shew the presence of bacilli; old calculi usually do not, or at best only the faintly staining shadows of micro-organisms. Droba[3] found typhoid bacilli in a calculus seventeen years after the attack of enteric fever. Chauffard,[4] who rather opposes the bacterial origin of cholelithiasis, has pointed out that the presence of micro-organisms in a calculus does not necessarily prove that they had any part in its formation, since they may invade a calculus from the outside.

It has been thought that the colon bacillus reaches the gall-bladder by an ascending infection of the common bile-duct from the duodenum. But bacteriological examination of the duodenum in health shews that during fasting the mucous membrane may be sterile, and that when micro-organisms are found they are, so to speak, accidental and derived from the ingesta (Cushing and Livingood[5]). Again, if the infection were ascending from the duodenum, the pancreas should be as often affected as the gall-bladder, since both their ducts open into the ampulla of Vater. Probably a condition of catarrhal inflammation of the duodenum would be necessary to render an ascending infection feasible. A factor of importance in the production of an ascending infection is more or less stagnation of the bile; otherwise the micro-organisms would be washed out of the ducts by the bile. On the other hand, it is highly probable that the *B. coli* reaches the liver by the portal vein and is excreted into the ducts.

(2) *Bacillus Typhosus.*—The causal relation between enteric fever and gall-stones was suggested by Bernheim[6] in 1889, on clinical grounds, viz. the occurrence of symptoms in patients shortly after typhoid fever who had not previously had any signs of gall-stones. Calculi have often been found in the gall-bladder shortly after enteric fever in patients who had not previously exhibited any signs of cholelithiasis (Gilbert and Girode,[7] Hanot,[8] Hertz[9]). Dufourt[10] found a history of enteric in 19 cases of cholelithiasis in which no symptoms of gall-stones had appeared

[1] Welch. *Med. News*, N.Y., 1891, lix, 669.
[2] Gilbert et Dominici. *Compt. rend. Soc. Biol.*, Paris, 1894, 10. s., i, 485.
[3] Droba. *Wien. klin. Wchnschr.*, 1899, xii, 1141.
[4] Chauffard. *Rev. de méd.*, Paris, 1897, xvii, 81.
[5] Cushing and Livingood. *Johns Hopkins Hosp. Rep.*, Balt., 1898, ix, 543.
[6] Bernheim. Art. "Ictère," *Dict. encycl. d. sc. méd.*, Paris, 1889.
[7] Gilbert et Girode. *Compt. rend. Soc. Biol.*, 1893, 9. s., v, 958.
[8] Hanot. *Bull. méd.*, Paris, 1896.
[9] Hertz. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Clin. Sect.), 169.
[10] Dufourt. *Rev. de méd.*, Paris, 1893, xiii, 274.

previous to the fever. In 12 of these cases symptoms of gall-stones appeared within six months of the attack of enteric fever. In 42 cases of gall-stones 13 had had enteric fever and had not had any signs of cholelithiasis before the fever (Curschmann [1]).

Typhoid and paratyphoid bacilli (Blumenthal,[2] Cecil [3]) have been found in calculi. Kramer [4] has grown cultures of *B. typhosus* and of *B. coli* in bile and found that a precipitation of material comparable to that of a calculus results; he therefore explains the formation of gall-stones as due to this process and analogous to the formation of a triple phosphate precipitate in urine. In typhoid fever the *Bacillus typhosus* is almost constantly present in the gall-bladder after death, and, as a rule, without any calculous formation. It is, therefore, probable that the production of calculi depends on cholecystitis and not on the presence of micro-organisms alone. Typhoidal cholecystitis is described elsewhere (*vide* p. 605). The agglutination of typhoid bacilli in the bile has been suggested as a nucleus or starting-point for the formation of calculi (Richardson [5]), but this is not supported by experiments outside the body; Cushing [6] added typhoid bacilli to bile and then precipitated them by adding the serum of a typhoid patient, but failed to obtain any precipitation of material from the bile.

Gilbert and Dominici,[7] in 1893, in experimental typhoidal cholecystitis in a rabbit, produced greenish concretions. This was confirmed by Gilbert and Fournier [8] in 1897. The question whether typhoid bacilli reach the gall-bladder by means of the portal vein or directly up the common bile- and cystic ducts has been discussed on p. 606. Here it may be said that it is more probable that the bacilli are carried to the liver by the portal vein and then excreted into the bile-ducts, and so reach the gall-bladder, than that there is an ascending infection from the duodenum.

Cholelithiasis due to other Micro-organisms.—Pearce [9] described cholelithiasis in a man aged fifty-nine years which seemed to depend on leptotrichial infection. The threads of leptothrix were found in the calculi. Cholecystitis and gall-stones due to *Micrococcus melitensis* have been recorded (Bull and Gram [10]).

Question of the Toxic Origin of Gall-stones.—The theoretical production of cholecystitis by poisons, such as perchloride of mercury, ricin, and by bacterial toxins has been referred to on p. 608. It was there stated that Wakeman [11] and Claude's [12] experiments make it probable that cholecystitis

[1] Curschmann. *Die Unterleibstyphus*, S. 355, Wien, 1898.
[2] Blumenthal. *München. med. Wchnschr.*, 1904, li, 1641.
[3] Cecil. *Arch. Int. Med.*, Chicago, 1910, v, 510.
[4] Kramer. *Journ. Exper. Med.*, N.Y., 1907, ix, 319.
[5] Richardson, M. W. *Journ. Boston Soc. Med. Sc.*, 1899, iii, 79.
[6] Cushing, H. *Johns Hopkins Hosp. Bull.*, Balt., 1899, x, 163.
[7] Gilbert et Dominici. *Compt. rend. Soc. Biol.*, Paris, 1893, 9. s., v, 1033.
[8] Gilbert et Fournier. *Ibid.*, 1897, xlix, 936.
[9] Pearce, R. M. *Univ. Penna. Med. Bull.*, Phila., 1902, xiv, 217.
[10] Bull og Gram. *Norsk Mag. f. Laegevidensk.*, Christiania, 1911, lxxii, 1026.
[11] Wakeman. Quoted by Herter, *Med. News*, N.Y., 1903, lxxxiii, 530.
[12] Claude. *Bull. méd.*, Paris, 1896, x, 714.

may be produced by toxins. But though it might reasonably be expected (Gilbert[1]), I am not aware that a toxic lithogenic catarrh of the gall-bladder has been produced experimentally. It may be concluded that although the production of gall-stones from catarrhal inflammation of the gall-bladder set up by poisons, without microbic intervention, is logically possible, it has not been shewn to occur in man.

Disposing Causes.—*Factors which favour the Production of Catarrh of the Gall-bladder and Bile-ducts, and so dispose to Cholelithiasis.*—1. *Stagnation of bile* in the gall-bladder renders infection more easy, since any micro-organisms which get into the bile are not removed. Further, in the absence of stagnation, micro-organisms present in the gall-bladder need not set up cholecystitis; this has been shewn experimentally by Ehret and Stolz,[2] and is supported by the constant presence of typhoid bacilli in the gall-bladder, often without any evidence of cholecystitis, in fatal cases of typhoid fever.

Sedentary habits, want of exercise, obesity, and diseases which necessitate a quiet life dispose to cholelithiasis. Want of exercise carries with it feeble contractions of the abdominal muscles, and as a result bile is not expelled so frequently or efficiently from the gall-bladder. This explains why gall-stones are rare in outdoor labourers and common in women. The influence of a sedentary life is shewn by the occurrence of biliary calculi in pet dogs and by their absence in wild animals. Sitting upright and leaning forwards over a desk keep the fundus of the gall-bladder in a dependent position and prevent, or at any rate inhibit, its proper evacuation. It has, therefore, been considered a disease of literary men, and has also been noticed in prisoners in gaol. The recumbent posture in an easy chair, however, favours the flow of bile out of the gall-bladder.

Tight lacing frequently leads to dilatation of the gall-bladder as the downward displacement of the duodenum strains and kinks the cystic duct, which even under normal conditions requires a spiral valve to keep it open (Keith[3]). Further, downward displacement of the right lobe of the liver makes the fundus of the gall-bladder more dependent than in health, and, since the cystic duct is more fixed at the transverse fissure of the liver, tends to produce kinking of the duct. A wandering liver has much the same effect. A floating kidney on the right side may, by traction on the peritoneum covering the common bile-duct in the lesser omentum, obstruct the outflow of bile from the gall-bladder. Any cause that interferes with diaphragmatic respiration, and therefore with the emptying of the gall-bladder, tends to produce stagnation of bile in the gall-bladder. Among the factors exerting this influence are tight lacing, abdominal distension from pregnancy, ascites, abdominal tumours, and cardiac and pulmonary disease.

2. *Foreign bodies* are exceptional in the gall-bladder. Aseptic foreign

[1] Gilbert. *Arch. gén. de méd.*, Paris, 1898, clxxxii.
[2] Ehret und Stolz. *Berlin. klin. Wchnschr.*, 1902, xxxix, 13.
[3] Keith, A. *Lancet*, Lond., 1903, i, 689.

bodies do not give rise to cholelithiasis; this has been shewn experimentally by Mignot. If, however, cotton wool impregnated with colon bacilli is introduced into the gall-bladder, calculi are formed. Calculi have been found to contain pins or needles (Nauche,[1] Carless,[2] Eastman [3]), hydatid membrane, the ova of bilharzia (Gautrelet [4]), and round worms (Lobstein). Round worms may invade and infect the bile-ducts with micro-organisms from the duodenum, and in very rare instances may get into the gall-bladder. Five of Mertens' [5] 48 cases of round worms in the bile-ducts were complicated by calculi. Hanot [6] considered the worms the cause of the calculi, but Mertens thought the calculi dilated the bile-passages and facilitated the entrance of the worms.

Homans [7] removed 97 calculi from the gall-bladder of a woman; twenty months later he again opened the gall-bladder for similar symptoms, and found 7 calculi crystallised on the sutures which lay free in the gall-bladder. In 3 patients operated on by Kehr [8] recurrent colic was found to depend on calculous formation around sutures introduced at the first operation. Similar cases have been reported by Sinclair White,[9] Malcolm,[10] Drummond,[11] Florcker.[12] Haughton [13] records a case of cholecystitis with gall-stones, in which a bristle and a piece of thread were found in the gall-bladder.

Foreign bodies favour stagnation and so inflammation, if microbes are present; microbes introduced alone may be removed with the bile, but if introduced together with a foreign body, they are enabled, as shewn by Mignot, to induce cholelithiasis.

Relation of Various Factors and Diseases to Cholelithiasis.—The influence of *diet*, except in so far as it causes intestinal catarrh and so favours infection of the gall-bladder, is hard to estimate, and has attracted little interest since Naunyn's conception of a lithogenic cholecystitis became generally accepted. The belief that a saccharine and fatty diet favours cholelithiasis is probably true in virtue of its tendency to cause dyspepsia; but the explanation that a carbohydrate diet leads to a deficiency of bile salts, the solvents of cholesterin, is not of much value in view of the rarity of gall-stones in native Indians who subsist largely on rice. The view that a protein diet is not likely to cause cholelithiasis because it increases the quantity of bile salts may be

[1] Nauche; Lobstein. Quoted by Trousseau, *Clin. Med.* iv, 230. Translated by New Sydenham Soc., 1871.
[2] Carless, A. *King's Coll. Hosp. Rep.*, 1897, iii, 101.
[3] Eastman. *Journ. Am. Med. Assoc.*, Chicago, 1909, lii, 1660.
[4] Gautrelet. *Union méd.*, 1885, Paris, 3. s., xl, 577.
[5] Mertens. *Deutsche med. Wchnschr.*, 1898, xxiv, 358.
[6] Hanot. *Arch. gén. de méd.*, Paris, 1896, clxxvii, 74.
[7] Homans. *Ann. Surg.*, 1897, xxvi, 114 [Plate].
[8] Kehr. *Gall-stone Disease*, p. 105. American transl., 1901.
[9] Sinclair White. *Lancet*, Lond., 1907, ii, 443.
[10] Malcolm. *Proc. Roy. Soc. Med.*, Lond. (Surg. Sect.), 1908, i, 96.
[11] Drummond. *Lancet*, Lond., 1908, i, 1206.
[12] Florcker. *Deutsche Ztschr. f. Chir.*, 1908, xciii, 310.
[13] Haughton. *Med. Press and Circ.*, 1911, cxlii, 474.

met by the argument that it also increases the cholesterin in the bile (Goodman[1]). Chauffard forbids foods, such as eggs, which increase the amount of cholesterin in the blood (*vide* p. 547).

Restriction in the amount of liquid taken by the mouth would tend to diminish the amount of bile and so to impair the freedom with which the ducts are flushed. Inasmuch as the amount of calcium in the bile is not affected by that taken by the mouth, it is very improbable that hard water induces cholelithiasis. Long intervals between meals lead to stagnation of bile in the gall-bladder and so favour infection. Kehr[2] suggests that the greater frequency of gall-stones among German women as compared with men may depend on their going to bed early and therefore fasting for a number of hours, while the late suppers taken by men empty the gall-bladder.

Excessive eating and alcoholism tend to induce gastro-enteritis, and hence cholecystitis and gall-stones are likely to occur in gross feeders, especially when of sedentary habits. Chronic venous engorgement of the portal system, whether from the backward pressure of heart disease, from cirrhosis of the liver or other causes, disposes to gastro-enteritis and so to cholelithiasis.

Anxiety and worry have often been regarded as a cause of gall-stones, and possibly act by inducing dyspepsia and constipation, and so reducing the resistance of the body as a whole, or possibly of the gall-bladder in particular, and so disposing to infection.

Indigestion.—While fully recognising that dyspepsia may be a manifestation of cholelithiasis, there is no doubt that persistent gastro-intestinal catarrh is an important cause of gall-stones. Abnormal bodies manufactured in the intestinal tract will tend to set up catarrh of the biliary tract, and infection of the gall-bladder by the portal vein or up the common duct may also be induced.

Constipation may increase intestinal catarrh and so dispose to infection of the gall-bladder; it may also, by leading to faecal accumulation in the hepatic flexure of the colon, interfere with the flow of bile through the cystic duct and thus produce stagnation in the gall-bladder. Further, intestinal catarrh may be partly due to vigorous purgatives taken to get the bowels open. Kraus[3] found that 80 per cent of his patients with gall-stones at Carlsbad had constipation.

The relation between appendicitis and cholecystitis, and so with cholelithiasis, was mentioned on p. 604. It has been thought that cholecystitis may be due to infection from appendicitis, or from a gastric or duodenal ulcer (Ochsner,[4] Sheldon,[5] Moynihan[6]). Dieulafoy[7] suggested that the appendicitis is secondary to the cholecystitis. There is some variation in the statistics dealing with the combination of cholecystitis and appendicitis.

[1] Goodman. *Beitr. z. chem. Physiol. u. Path.*, 1907, ix, 18, 91 (quoted by Adami).
[2] Kehr. *Gall-stone Disease*, p. 70. American transl., 1901.
[3] Kraus. *On Gall-stones*, p. 20, 1896.
[4] Ochsner. *Phila. Med. Journ.*, 1900, vi, 652.
[5] Sheldon. *Journ. Am. Med. Assoc.*, Chicago, 1906, xlvii, 1458.
[6] Moynihan. *Lancet*, Lond., 1912, i, 9. [7] Dieulafoy. *Presse méd.*, Paris, 1903, p. 445.

Becker[1] collected 34 cases in which the two conditions coexisted. In 46 cases operated upon for gall-stones, Sheldon found appendicitis in 39, or 85 per cent; whereas Kehr[2] in 720 laparotomies for diseases of the biliary tract found appendicitis in 18, or 2·5 per cent. Among 50 cases shewing gall-stones or cholecystitis, abstracted from the post-mortem records of St. George's Hospital, Mr. Frankau found that 2, or 4 per cent, shewed appendicitis; 6, or 12 per cent, gastric ulcer; and 2, or 4 per cent, duodenal ulcer.

Pregnancy.—Gall-stones often develop during or shortly after pregnancy. Naunyn[3] estimated that 90 per cent of women with cholelithiasis had borne children. Pregnancy in many women necessitates a very sedentary life, and is frequently accompanied by considerable constipation. It has been thought that the pregnant uterus impedes the descent of the diaphragm and so leads to failure in the expulsion of bile from the gall-bladder. Mosher,[4] however, finds that pregnancy interferes less with the descent of the diaphragm than has been generally thought, and that respiratory movements tend to become equalised so that diaphragmatic respiration persists as late as the eighth month. It has been supposed that the enlarged uterus may compress the bile-ducts and so favour catarrh of the ducts and cholelithiasis (Körte, Heddaeus[5]). Repeated pregnancies cause a relaxed condition of the muscular abdominal walls and so failure in the expulsion of the contents of the gall-bladder, and may be followed by visceroptosis. During pregnancy the blood contains an excess of cholesterin, which is thought by Chauffard[6] to favour cholelithiasis.

Glénard's disease or *visceroptosis* may dispose to cholelithiasis in several ways. In the general prolapse of the abdominal organs, kinking of or traction on the cystic duct may occur and obstruct the exit of bile. Nephroptosis on the right side may also lead to obstruction of the cystic duct, and so favour inflammation of the gall-bladder. Passive engorgement of the intestines may go on to catarrhal inflammation, and thus tend to lead to the same change in the gall-bladder. Keith[7] states that gall-stones are almost invariably present in Glénard's disease.

Cardiac disease disposes to cholelithiasis in the first place by rendering life more sedentary and thus leading to stagnation of bile in the gall-bladder. Heart disease, in fact, makes the life of a male much the same as regards its sedentary character as that of women. In mitral disease with backward pressure gastric and duodenal catarrh are readily set up, and thus an ascending inflammation is favoured. The walls of the gall-bladder may be chronically engorged, and so more liable to become inflamed should infection be conveyed from the duodenum. The influence of cardiac disease is shewn by statistics from the post-mortem room.

[1] Becker. *Deutsche Ztschr. f. Chir.*, 1903, lxvi, 246.
[2] Kehr. *Die Therapie der Gallenwege*, 1902, iv, 456.
[3] Naunyn. *On Cholelithiasis*, p. 40. Transl. New Sydenham Soc., 1896.
[4] Mosher. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 253.
[5] Heddaeus. *Beitr. z. klin. Chir.*, 1894, xii, 439.
[6] Chauffard. *Rev. de méd.*, Paris, 1911, xxxi (Sabile du Prof. Lépine), 177.
[7] Keith, A. *Lancet*, Lond., 1903, i, 639.

In 1347 successive necropsies at the Manchester Royal Infirmary gall-stones were found by Brockbank[1] in 101, or in 7·4 per cent. Of the 504 cases which shewed gross cardiac lesions biliary calculi were present in 55, or 10·9 per cent—males, 5·2 per cent; females, 22·6 per cent; while in 843 without cardiac disease calculi were met with in 46, or 5·4 per cent—males, 3·2; females, 10·2—so that a gross cardiac lesion seemed to double the incidence of cholelithiasis. This appeared to be almost equally true both for the males and females.

In 533 cases of cardiac disease collected from the post-mortem records of St. George's Hospital (F. A. Mills,[2] D. W. Bull[3]) the incidence of cholelithiasis in 350 males was 33, or 9·4 per cent, while in 183 females there were 31, or 17 per cent.

The statistics from St. George's Hospital also shewed that cardiac disease seems to affect the incidence of cholelithiasis by making it occur rather earlier in life than under ordinary conditions. In Brockbank's statistics mitral stenosis was much the most effective form of heart disease in inducing cholelithiasis; thus, in 87 cases gall-stones were present in 19, or 21·8 per cent, this being twice as high as in any other form of cardiac disease. In 533 cases of cardiac disease at St. George's Hospital the percentage of gall-stones, however, was a little higher in the aortic cases than in the cases of mitral disease.

In 72 cases of aortic aneurysm examined after death at St. George's Hospital (68 males, 4 females) there were no calculi; this shews that the causes of arterial disease and aneurysm, such as syphilis, strain, high tension, hard work, do not dispose to cholelithiasis. In fact, some of them, almost certainly hard work and exercise, tend to prevent it.

Pulmonary diseases, such as emphysema, which interfere with the movements of the diaphragm, or conditions such as chronic interstitial pneumonia, advanced emphysema, pneumoconiosis, which lead to failure of the right side of the heart and so to backward pressure, dispose to gall-stones.

Diabetes.—According to most statistics biliary calculi are rare in the bodies of patients dying with ordinary diabetes mellitus, and it may therefore be concluded that diabetes has no tendency to produce cholelithiasis.

In 220 cases of diabetes collected by Windle[4] there was only one calculus, or 0·45 per cent. In 142 cases of diabetes (including 122 recorded by Seegen) there was only 1 in which a biliary calculus was mentioned.[5] This scarcity Brockbank[6] refers to the nitrogenous diet providing plenty of bile acids which keep the cholesterin in solution. In 50 cases of diabetes examined at St. George's Hospital calculi were found in 6. These figures are in antagonism to those

[1] Brockbank, E. M. *Edin. Med. Journ.*, 1898, iii, 51.
[2] Mills, F. A. Unpublished Thesis for M.B. Cantab., 1898.
[3] Bull, D. W. Ibid., 1908.
[4] Windle. *Dublin Journ. Med. Sc.*, 1883, 3. s., lxxvi, 112.
[5] Williamson. *Diabetes*, p. 119.
[6] Brockbank. *On Cholelithiasis*, 1896.

just quoted, and are possibly explained by the fact, referred to below, that in 2 cases the diabetes was really secondary to chronic interstitial pancreatitis set up by gall-stones in the common bile-duct.

But although diabetes does not lead to the production of gall-stones, the converse does not hold good. Thus, if a calculus becomes lodged near the lower end of the common bile-duct, it may lead to infection and chronic interstitial pancreatitis, which may eventually become so extensive as to set up diabetes mellitus. I have seen at least 2 such cases, which are included among the 6 cases of diabetes at St. George's Hospital which shewed cholelithiasis. The occurrence of transient glycosuria during biliary colic is quite another question and is referred to on page 736.

To sum up, diabetes does not favour the production of gall-stones, but cholelithiasis may indirectly produce pancreatic diabetes.

Renal Disease.—In the arteriosclerotic and granular kidney the incidence of gall-stones is greatly increased, whereas no such influence is exerted by large white and contracted white kidneys. Inasmuch as *arteriosclerosis* and gall-stones both occur about the same period of life, it would be natural to find them often combined. In 115 cases of cholelithiasis Mosher[1] found that 50, or 43 per cent, had arteriosclerosis.

Among 357 cases of various forms of chronic nephritis collected from the post-mortem records of St. George's Hospital by A. W. Moore[2] there were 59, or 16·5 per cent, with gall-stones. Further analysis of these 357 cases yielded the following results:—In 261 cases of granular kidney, with an average age of 56 years, there were gall-stones in 56, or 21·4 per cent (average age, 59 years). In 49 cases of large white kidney, with an average age of 40, there were gall-stones in 2, or 4 per cent, and in 47 cases of small white kidney, with an average age of 34 years, gall-stones were present in 1, or 2 per cent. The greater incidence among the cases of granular kidney does not, as might at first sight appear, depend on the greater average age alone; for among the 261 cases of granular kidney there were 36 between the ages of 32 and 42 (thus including with a margin the average ages of the large white and small white kidneys), in 6 of which, or 16·7 per cent, there were gall-stones. Of these 36 cases, 11 were women, 4 of whom had gall-stones, or 36 per cent, and 25 men, 2 of whom, or 8 per cent, had gall-stones. Of the remaining 225 cases of granular kidney there were 138 men, 21 of whom, or 15·2 per cent, had calculi, and 87 women, 29 of whom, or 33·3 per cent, had calculi. The increased incidence of gall-stones in granular kidney therefore appears to be due to the high incidence of cholelithiasis in women with granular kidney. In the 261 cases of granular kidney the women were to the men as 3 to 5. The incidence of gall-stones in the 98 women was 33 per cent, and in 100 consecutive women over 40, dying in St. George's Hospital from all kinds of diseases, the incidence of gall-stones was 25 per cent. These figures are very small, but appear to shew that granular kidney increases the liability to cholelithiasis in women. It is possible that the increased formation of cholesterin in atheroma associated with granular kidney leads to a larger quantity of cholesteryl oleate in the blood and increased

[1] Mosher. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 253.
[2] Moore, A. W. Unpublished Thesis for M.B. Cantab., 1906.

excretion into the gall-bladder (cf. pp. 547, 709). This hypothesis is supported by the observation that in chronic nephritis the bile contains a high percentage of cholesterin—0·20 as compared with the normal 0·1 (H. Baldwin [1])—and that minute deposits of cholesterin are not uncommon in the gall-bladder (Herter [2]).

Myxoedema.—Many of the conditions favourable to the formation of gall-stones are present in this disease, such as the age (middle life), sex (female), and sedentary habits.[3] According to Lorand [4] cholelithiasis is favoured by ovarian inadequacy as well as by hypothyroidism.

Both in *portal cirrhosis and in biliary cirrhosis* it is rather surprising that biliary calculi are not commoner. In biliary cirrhosis there is catarrh of the small bile-ducts, and microscopic calculi or plugs of inspissated bile are often seen in the minute bile-ducts. In portal cirrhosis a secondary catarrh of the bile-ducts is not infrequent, and is certainly favoured by the condition of the liver.

In 157 cases of cirrhosis examined after death at St. George's Hospital calculi were present in 23, or 14·6 per cent, but in some of these 23 cases there were only small bilirubin-calcium calculi. In 233 cases of gall-stones examined after death in Calcutta there was cirrhosis in 18·2 per cent (Rogers [5]).

Minute bilirubin-calcium calculi are probably more frequent than is generally recognised in portal cirrhosis; they are small, and may easily escape observation.

Malignant Disease.—Musser [6] suggested that the presence of malignant disease anywhere in the body favoured the formation of calculi in the gall-bladder. It would indeed be natural to expect that gall-stones would be found more often in the subjects of malignant disease than in ordinary routine post-mortem work; for carcinoma, which is the most frequent form of malignant disease, occurs, like gall-stones, most often in middle and later life. It is therefore remarkable that the following statistics do not shew a markedly increased incidence of gall-stones in patients dying with carcinoma.

In fifteen years 4616 patients were examined after death at St. George's Hospital. Of these, 268, or 5·8 per cent, had gall-stones. Among the 4616 cases 314 had carcinoma of some part of the body other than the gall-bladder; of these, 21, or 6·6 per cent, had gall-stones (199 males, 7 cases of cholelithiasis, or 3·5 per cent; 115 females, 14 calculi, or 12 per cent). This incidence of cholelithiasis was highest in primary carcinoma of the liver, uterus, and mamma.

Some statistics of malignant disease, such as Colwell's,[7] shew a high incidence of cholelithiasis, but it must be borne in mind that both

[1] Baldwin, H. Quoted by Herter.
[2] Herter, C. A. *Med. News*, N.Y., 1903, lxxxiii, 531.
[3] *Vide* Hertoghe. *Nouv. icon. de la Salpêtr.*, Paris, 1899, xii, 261.
[4] Lorand. *Monthly Cycl. Pract. Med.*, Phila., 1906, N.S., ix, 252.
[5] Rogers. *Ind. Med. Gaz.*, 1908, xliii, 408.
[6] Musser, J. H. *Boston Med. and Surg. Journ.*, 1889, cxxi, 529.
[7] Colwell. *Arch. Middlesex Hosp.*, 1905, v, 142.

malignant disease and gall-stones are commoner in women and in later life, and the influence of sex and age must not be regarded as the effect of malignant disease. Thus, in 44 cases of carcinoma of the mamma gall-stones were present in 16 per cent (Williams[1]). Though this percentage would be high for ordinary routine work, it can easily be explained by the influence of sex and age, the subjects of mammary carcinoma being practically always women and usually over thirty-five years of age.

As is well known, gall-stones are present in from 70 to 95 per cent of cases of primary carcinoma of the gall-bladder, but there can be no doubt that the carcinoma is subsequent to and disposed to by the presence of calculi (*vide* p. 638).

In 13 cases in which secondary growths were present in the gall-bladder Siegert[2] found 2 cases with calculi, and in 19 similar cases, most of which I have examined myself, one only had a calculus. The local action of a secondary growth in the gall-bladder therefore does not favour cholelithiasis.

Uterine fibromyomas do not appear to be a factor in the causation of cholelithiasis.

Among 1224 women operated upon for uterine fibromyomas 7·5 per cent had gall-stones (Mayo[3]). Of 58 cases of gall-stones in women 13, or 22·4 per cent, had fibromyomas (Mosher).

Among the insane the percentage of gall-stones in routine post-mortem work is above the average; thus, at Claybury Asylum Candler[4] found that among 2228 necropsies there were 315 with gall-stones or 14·13 per cent (females 17·85 per cent, males 9·9). Cholelithiasis is commoner in chronic melancholiacs than in acute maniacs; Keay,[5] who quotes figures supporting this statement, believes that the stooping position of melancholiacs plays some part in the production of gall-stones.

Hereditary Influences.—The idea that cholelithiasis is an hereditary condition depending on a constitutional disposition is very old; Morgagni, indeed, insisted on the association of renal and biliary lithiasis, and has been followed by Bouchard, Chauffard,[6] and others who believed that cholelithiasis was a manifestation of the "arthritic" diathesis, which included rheumatism, gout, and "uric acid." Lancereaux[7] in 117 cases of much the same condition, which, however, he called "herpetism," found cholelithiasis in 47. No doubt sedentary habits, overeating, and dyspepsia favour the development of both gout and gall-stones, and the two conditions may occur in the same person; in 166 cases of gall-stones

[1] Williams, R. *Brit. Med. Journ.*, 1893, ii, 490.
[2] Siegert. *Virchows Arch.*, 1893, cxxxii, 353.
[3] Mayo. *Journ. Am. Med. Assoc.*, Chicago, 1911, lvi, 1021.
[4] Candler. *Proc. Roy. Soc. Med.*, 1911, iv (Path. Sect.), 87.
[5] Keay. *Medical Treatment of Gall-stones*, p. 34, 1902.
[6] Chauffard. *Rev. de méd.*, Paris, 1897, xvii, 81.
[7] Lancereaux. *Traité des maladies du foie et du pancréas*, p. 686, 1899.

collected by Senac gout was present in 95. The view that any diathesis plays an important part has not met with so much support since it became clear that local inflammation of the gall-bladder is the immediate cause of gall-stones; Frerichs[1] and Naunyn,[2] in particular, have thrown the weight of their influence against the constitutional factor in cholelithiasis. Gilbert and Lereboullet[3] have laid stress on a family tendency to catarrh of the biliary system (simple family cholaemia) which renders its subjects specially prone to various forms of jaundice, liver disorder, and lithogenic cholecystitis. It is probable that this diathesis, though not the sole or most essential factor, is of importance in the production of cholelithiasis, and it must not be forgotten that conditions of life and disposing factors, such as obesity, may be transmitted from one generation to another. Some statistics shew that gall-stones are hereditary in a large proportion of cases; this was so in 62 per cent of Kraus' Carlsbad patients.

Occupation.—As already pointed out, sedentary occupations dispose to cholecystitis and gall-stones; it therefore occurs more frequently among the idle rich, hard-working literary men, clerks and devoted men of business, shoemakers, and in the poor in workhouses and asylums than in active persons whether well-to-do or tramps. Davy[4] found that it was rare among soldiers, but possibly this is less true in these days of short service than in the first half of the last century. Among 472 patients at Carlsbad more than 50 per cent were professors, teachers, officials, or clergymen (Kraus[5]).

The **incidence** of gall-stones in routine post-mortem work varies somewhat in different countries; it is usually between 10 and 5 per cent.

In 10,866 cases obtained by combining the figures of Roth, Schloth, and Schröder gall-stones were present in 1029, or 9·4 per cent.[6] This agrees with Kehr's[7] estimate that one-tenth of the adult German population are the subjects of cholelithiasis. In America and England the percentage is lower. In 1655 American cases there were 115, or 6·9 per cent, with gall-stones (Mosher[8]). At the Middlesex Hospital Voelcker[9] found gall-stones in 8·5 per cent, and Colwell,[10] for a later period (1900–1904), in 5·4 per cent. Brockbank,[11] at Manchester, found 101 cases of gall-stones in 1347 necropsies, or 7·4 per cent; at St. George's Hospital there were 268 in 4616 or 5·8 per cent.

The percentage found in bodies examined after death is fairly represented by the statistics of a general hospital. The numbers would, of

[1] Frerichs. *Diseases of the Liver*, ii, 511, New Sydenham Soc., 1861.
[2] Naunyn. *Cholelithiasis*, p. 43, New Sydenham Soc., 1896.
[3] Gilbert et Lereboullet. *Gaz. hebd. de méd.*, Paris, 1902, vii, 889.
[4] Davy, J. *Diseases of the Army*, p. 421, 1862.
[5] Kraus. *On Gall-stones*, p. 19, 1896.
[6] Naunyn. *Loc. cit.*, p. 144.
[7] Kehr. *On Gall-stone Disease*, p. 99. American transl., 1901.
[8] Mosher. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 253.
[9] Voelcker, A. F. *Brit. Med. Journ.*, 1898, ii, 1555.
[10] Colwell. *Arch. Middlesex Hosp.*, 1905, v, 145.
[11] Brockbank. *Edin. Med. Journ.*, 1898, iii, 51.

course, be extremely small in a children's hospital and disproportionately high in a workhouse infirmary.

Race and Geographical Distribution.—Gall-stones are rare in warm and tropical countries and are common in cold and damp cities, probably because these conditions tend to induce catarrh of the biliary tract.

Cholelithiasis is common in Germany, Austria, Sweden, Hungary, Russia, and is said to be infrequent in Holland, Finland, Denmark, and Italy. England probably comes about midway between these two groups. In America the percentage incidence is about the same as in England; thus Mosher found it to be 7 per cent.[1] Among 4544 necropsies in India (93 per cent on natives, 7 per cent on Europeans) Rogers[2] found 233 or 5·4 per cent with gall-stones. The natives of Egypt are remarkably free from gall-stones (Day[3]). Gall-stones are rare in negroes, probably from their more active life and possibly from the good state of their teeth, in virtue of which they would not be exposed to infection of the alimentary canal from pyorrhoea alveolaris.

In America cholelithiasis is less common in coloured than in white patients; in 106 cases of gall-stones operated upon in Louisville only 1 was coloured.[4] In routine post-mortem examination at the Johns Hopkins Hospital, Baltimore, however, the percentage incidence of gall-stones among blacks was 5·5 as against 7·9 among whites.

In England many cases come from the east coast, especially Lincolnshire. According to Ralfe[5] the bleak country between Stafford and Wolverhampton and the damp valleys in Wales are responsible for many cases. Keay[6] considers that it is commoner in Lancashire than in London.

Age.—The incidence of gall-stones increases as age advances. The majority of patients with cholelithiasis are over forty years of age, and it is rare before thirty.

G. Harley[7] gave the following estimate: 75 per cent of cases occur in persons over forty; 20 per cent between thirty and forty; 4 per cent between twenty and thirty; 1 per cent under twenty. In Brockbank's[8] 101 cases of cholelithiasis 79 were over and 22 under forty years of age. In 268 cases in which gall-stones were found at St. George's Hospital 222, or 83 per cent, were forty or over. The largest number fell between the ages of fifty and sixty; of the 268 cases, 99, or 37 per cent, were in this decade.

The frequency of calculi in the gall-bladder in old age may possibly be due to senile atrophy of the muscular tissue in the walls of the gall-bladder and bile-ducts (Charcot and Pitres[9]), which, by leading to stagna-

[1] Mosher. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 253.
[2] Rogers. *Ind. Med. Gaz.*, 1908, xliii, 408.
[3] Day. *Lancet*, Lond., 1909, i, 258.
[4] *International Textbook of Surgery*, Gould and Warren, 1900, ii, 741.
[5] Ralfe. *Clin. Journ.*, Lond., 1895, vi, 281.
[6] Keay. *Medical Treatment of Gall-stones*, p. 27, 1902.
[7] Harley, G. *Diseases of the Liver*, p. 577, 1883.
[8] Brockbank, E. M. *Edin. Med. Journ.*, 1898, iii, 51.
[9] Charcot and Pitres. Quoted by Waring, *Diseases of the Liver*, p. 218, 1897.

tion, favours infection and at the same interferes with the expulsion of calculi. Though calculi are very common in the bodies of old persons, especially in asylums and workhouses, symptoms of biliary colic are comparatively rare.

Cholelithiasis in Early Life.—Calculi are rare under twenty years of age. Cholelithiasis in early life may be divided into two classes :—

(i) Cases in which the process begins in intra-uterine life. A striking example of this category is Wendel's[1] case of a child eleven days old in whose gall-bladder there were 90 small cholesterin calculi. Thomson[2] collected 7 cases of jaundice in infants either stillborn or dying within the first month, in which gall-stones were present in the ducts. He suggests that gall-stone formation in infants and congenital obliteration of the ducts depend on the same inflammatory process. Still[3] collected 10 cases, including Thomson's 7, in which small calculi were present in infants dying within a month of their birth.

(ii) Calculi in children. It is difficult to draw a hard-and-fast line between these two categories; and very possibly in cases in which the clinical manifestations are first noticed months or years after birth, the process began in intra-uterine life or depended, as Albu[4] suggested, on some change in the ducts allied to congenital obliteration. Cholecystitis from typhoidal or colon infection may occur in early life; it is, indeed, rather surprising, in the face of the frequency of various forms of gastro-intestinal infection in early life, that cholecystitis is so rare. It has been suggested that the application of a tight binder to a child's abdomen may, by inducing biliary stasis, dispose to the formation of calculi (Wendel). Small bilirubin-calcium calculi may be found in biliary cirrhosis, and are then due to inflammation spreading from the smallest bile-ducts—a descending cholangitis.

Still collected 23 cases under the age of fourteen years, 10 of which were in infants. Cases in children were previously described by Gourdin Servenière[5] Mercat,[6] and Trousseau.[7]

Sex.—Gall-stones are more frequent in women than in men; the ratio has been variously estimated between five to one, and four to three. Schröder[8] found gall-stones five times in females to once in males; Brockbank, four times in females to once in males; Harley,[9] Kraus,[10] and Colwell,[11] twice in females to once in males; Mosher,[12] three times in

[1] Wendel. *Med. Rec.*, N.Y., 1898, liv, 41.
[2] Thomson, J. *Edin. Hosp. Rep.*, 1898, v, 1.
[3] Still, G. F. *Trans. Path. Soc.*, Lond., 1899, l, 154.
[4] Albu. *Deutsche med. Wchnschr.*, 1898, xxiv, 201.
[5] Servenière. *Thèse de Paris*, 1889.
[6] Mercat. *Ibid.*, 1884.
[7] Trousseau. *Clinical Medicine*, vol. iv, p. 228. Transl. New Sydenham Soc., 1871.
[8] Schröder. Quoted by Naunyn, *Cholelithiasis*, p. 40, 1896.
[9] Harley. *Diseases of the Liver*, p. 575, 1883.
[10] Kraus. *On Gall-stones*, English translation, p. 2, 1896.
[11] Colwell. *Arch. Middlesex Hosp.*, 1905, v, 142.
[12] Mosher. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 253.

females to twice in males. In 268 cases in which gall-stones were found after death at St. George's Hospital the number of women (153) was in excess of the males (115) in the ratio of 4 to 3.

The factors determining the greater incidence of gall-stones in women are: (i) A lax condition of the abdominal walls, which favours visceroptosis and so disposes to hepatoptosis. As a result, stagnation of bile in the gall-bladder, a condition facilitating infection, is brought about. (ii) Abdominal tumours, such as uterine myomas and ovarian cysts, and the pregnant uterus produce relaxation of the abdominal wall and interfere with diaphragmatic respiration. (iii) Tight lacing may act in several ways: by displacing the liver it may kink the common or cystic ducts and mechanically obstruct the outflow of bile from the gall-bladder. It also diminishes diaphragmatic breathing and increases costal respiration. The movements of the diaphragm are of importance in emptying the gall-bladder, and hence if they are diminished, stagnation of bile follows. (iv) The sedentary life led by most women. (v) Constipation is common in women and favours infection of the bile-ducts and gall-bladder. (vi) Pregnancy (*vide* p. 716). (vii) The frequency of pelvic infections may be of some importance by serving as a source of infection or by producing peritoneal adhesions which may interfere with the free exit of bile from the gall-bladder (Mosher [1]).

The following **classification of gall-stones**, according to their chemical composition, is based on that given by Naunyn:—

I. *Solitary pure cholesterin calculi* are comparatively uncommon. They are white, yellow, or more rarely brown or greenish, and have a translucent appearance. The surface is nodular, crystalline, or smooth. There is a nucleus of pigment with radiating crystals of cholesterin around it. On section they are crystalline, but not stratified. They are formed in the gall-bladder when the cystic duct is blocked. They are single, and very slow in formation. According to Aschoff and Bacmeister [2] they are formed without any previous inflammation of the gall-bladder.

II. *Laminated cholesterin calculi* contain from 75 to 90 per cent of cholesterin, with calcium carbonate and traces of bilirubin and biliverdin in combination with calcium. Externally they resemble pure cholesterin calculi, and are also single. On section, there are alternating laminae—white and brown, yellow or green. The coloured layers contain bilirubin-calcium when brown, and biliverdin-calcium and calcium carbonate when green.

III. *The Common Gall-stones* (*Mixed Cholesterin and Bilirubin-calcium*).—They vary in size and colour. There may be a single large barrel-shaped calculus filling the gall-bladder, or they may be multiple, and are then usually faceted, are seldom larger than a cherry, and may be very small and numerous. They are usually yellow, but may be brown or white.

[1] Mosher. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 253.
[2] Aschoff und Bacmeister. *Die Cholelithiasis*, 1909.

When fresh, they are greasy and soft, but when dried, they become hard externally. There may be a central cavity inside.

IV. *Pure Bilirubin-calcium Calculi.*—They vary from the size of a pea to a grain of sand. There are two types: one is solid, brown in colour, rough on the surface, and with a tendency to become welded together. The second type is harder, smooth, black, has a metallic lustre, and internally a spongy structure.

V. *Rarer Forms.*—(*a*) *Amorphous and incompletely crystalline cholesterin gravel:* these small calculi may look like pearls; the nucleus is of different composition—often of bilirubin-calcium. (*b*) *Calcium carbonate calculi* are very rare; these calculi give a shadow with *x*-rays, other gall-stones do not. (*c*) *Calculi containing foreign bodies*, such as fragments of worms, ligatures (*vide* p. 713). (*d*) *Conglomerate calculi*, which are composed of two or more small calculi united under a common sheath. (*e*) *Casts of bile-ducts* are very rare in man; bilirubin-calcium casts are found in cattle.

Mode of Formation of Calculi in the Gall-bladder.—There are two explanations of the formation of gall-stones in the gall-bladder: Naunyn's, that it is due to inflammation of the lining mucosa of the organ, and Aschoff and Bacmeister's view (*vide* p. 710) that solitary pure cholesterin calculi may form independently of inflammation. The latter observers admit that the presence of a pure cholesterin calculus favours infection and inflammation of the gall-bladder, and that as a result multiple calculi containing calcium may result. Naunyn's explanation is as follows: The cholesterin from which the calculi are, in the first instance, largely formed, is not derived from the bile itself, but from the disintegration of the cells lining the gall-bladder, and is the outcome of perverted metabolism induced by catarrh. Cholesterin is formed by other mucous surfaces, but calculus-formation does not result, since there is an absence of the necessary cementing substance. The cementing substance is bilirubin-calcium. Masses of cholesterin mixed with bilirubin-calcium form the earliest stage of a calculus. The further development may proceed in different ways: The mass may become surrounded with a firm crust of bilirubin-calcium, while the cholesterin and bilirubin-calcium crystallise out on the inner surface of the outer crust, thus leaving a central cavity. Or the firm outer layer may be produced by drying, starting in the outer layer of the mass of bilirubin-calcium and cholesterin, after which crystallisation takes place inside the shell with the production of a central cavity as before. So far the formation of an immature calculus has been traced; the further changes leading to the growth and formation of a stratified and more solid calculus are as follows:—

The growth of a calculus is chiefly the result of deposition, on its surface, of concentric layers of cholesterin and of bilirubin-calcium or biliverdin-calcium. The cholesterin forms white laminae, and is deposited, not as crystals, but as a pultaceous mass of myelin bodies supplied by the cells of the gall-bladder. In the formation of pure cholesterin calculi the gall-bladder contents must be free from any bile, as in cases of obstruction of the cystic duct. Bilirubin-calcium forms brown and bili-

verdin green strata; their deposition occurs when the gall-bladder contains bile. The calculus becomes infiltrated from without by cholesterin, exactly in the same way as a calculus in the urinary bladder is invaded by phosphates and other salts. The secondary infiltration of a gall-stone with cholesterin may be derived from the epithelial walls of the gall-bladder, if in contact with it, or from the cholesterin in the bile. The cholesterin tracks along small fissures and canals into the interior of the calculus; it then forms crystals which increase in size. This process begins at the centre, and spreads outwards towards the periphery. The bilirubin-calcium is dissolved out, and the percentage of cholesterin increases; in this way a pure cholesterin calculus may be produced.

Time Required for the Formation of Calculi.—On experimental grounds Mignot[1] believes that it takes five or six months to form a stratified, well-formed biliary calculus. On the basis of gall-stones found after an attack of typhoid fever in a young woman Hertz[2] estimated that calculi may be formed in fifty days. Comparative stagnation of bile is necessary, otherwise the soft, immature calculus would be expelled with the bile from the gall-bladder. Calculi in the gall-bladder may be all of the same age and due to a single attack of cholecystitis. In recurrent attacks,—and these readily take place in a damaged gall-bladder,—fresh calculi may be formed. The formation of calculi in the ducts is described on p. 709.

Size and Number.—There may be one or thousands of calculi in the gall-bladder. A single calculus may be very large and cause great distension of the gall-bladder; it is usually a laminated or pure cholesterin stone.

Meckel recorded a calculus 6½ inches long and 6 inches thick. In Fiedler's[3] case a calculus weighed 1½ ounces, and consisted of three pieces which fitted together to form a cast of the elongated gall-bladder at least 12 inches long. Nehrkorn[4] recorded a gall-stone in the gall-bladder weighing just over 3 ounces. Bartlett[5] removed a calculus weighing 2½ ounces from the common bile-duct of a man aged forty-six; the cavity left in the common duct received the operator's fist. The patient recovered. Richter[6] in 1793 recorded an enormous calculus weighing 3 ounces 5 drams, which is the largest ever described.

Occasionally the number of small calculi in the gall-bladder is very large. Naunyn[7] counted 5000 in a gall-bladder, but this is surpassed by 7802 in Otto's[8] case. The small calculi found in such cases are curiously alike in appearance, and are generally of the mixed cholesterin form.

[1] Mignot, R. *Thèse de Paris*, 1897; and *Arch. gén. de méd.*, Paris, 1898, clxxxii, 129.
[2] Hertz. *Proc. Roy. Soc. Med.*, 1910, iii (Clin. Sect.), 169.
[3] Fiedler. *Jahresb. d. Gesellsch. f. Nat.- u. Heilk. in Dresd.*, 1879.
[4] Nehrkorn. *Deutsche Ztschr. f. Chir.*, Leipz., 1908, xcvi, 319.
[5] Bartlett. *Ann. Surg.*, Lond., 1908 xlviii, 676.
[6] *Vide* Hutchinson's *Arch. Surg.*, Lond., 1892, iii, 6.
[7] Naunyn. *On Cholelithiasis*, p. 6. Transl. New Syd. Soc., 1896.
[8] Otto. Quoted by Thudichum. *A Treatise on Gall-stones*, p. 198, 1863.

Shape.—There is great variation in the shape of biliary calculi; this largely depends on their surroundings. Apart from external influences, calculi tend to be round. The large single stone filling up the gall-bladder is usually somewhat elongated and pear-shaped, and may be conglomerate from the union and welding together of previously separate calculi. A single loose calculus, when composed of pure cholesterin, is often bossed like a mulberry calculus in the kidney. Multiple gall-stones in the gall-bladder are sometimes round, but are more often irregularly square, with facets separated by rounded edges. When impacted in the commencement of the cystic duct, a calculus may be somewhat elongated. Crumbling calculi in the common bile-duct become elongated and moulded to the duct. The small bilirubin-calcium calculi formed in the intrahepatic ducts are elongated and represent the lumen of the duct in which they were formed. Occasionally branching calculi resembling coral are found in the larger intrahepatic ducts.

Small *facets* on the surface of gall-stones shew that there either are or have been more than one calculus in the gall-bladder or ducts. Two or more facets on one calculus are in favour of the number of stones being more than two. Faceting generally indicates that the calculi have been closely packed. Faceting is commoner on medium-sized stones, but may be seen on comparatively large calculi. In small bilirubin-calcium calculi which are freely movable on each other there are no facets as a rule.

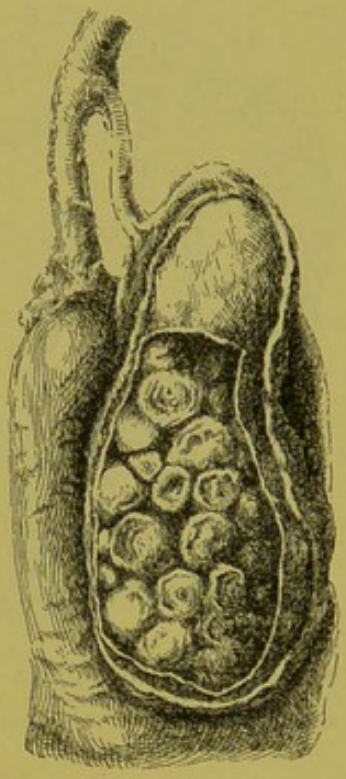


Fig. 103.—Gall-bladder. Distended with faceted gall-stones. In St. George's Hospital Museum, Series ix, 198B. (Drawn by Dr. E. A. Wilson.)

Situation.—Out of 184 cases of cholelithiasis analysed by Kelly,[1] 101 (55·5 per cent) had gall-stones in the gall-bladder alone, 23 (12·5 per cent) in the gall-bladder and cystic duct, 19 (10·5 per cent) in the gall-bladder and common duct, 12 (6·6 per cent) in the common duct alone, and 11 (6 per cent) in the cystic duct alone. Calculi in the gall-bladder are usually loose in the bile, or, when the cystic duct has been permanently blocked for some time, in mucus. In some cases the gall-bladder is firmly contracted on a calculus, or it may contain a large number of calculi closely packed and faceted on each other, there being no bile or mucus in the gall-bladder. When the gall-bladder is thus distended with calculi a crackling sensation may sometimes be felt on palpation. A large number of small stones in inspissated mucus which had acquired the consistency of thick paste and formed a cast

[1] Kelly, A. O. J. *System of Medicine* (Osler and M'Crae), 1908, v, 831.

of the gall-bladder, is figured by Bland-Sutton[1] as "gall-stones in aspic."

A large gall-stone may be adherent to the mucous membrane of the gall-bladder. Calculi in the distal compartment of an hour-glass gall-bladder may be closely united to the mucous membrane. It is comparatively common to find a calculus impacted in the neck of the gall-bladder and thus obstructing the cystic duct. Calculi and masses of cholesterin which hardly deserve the name of calculi are sometimes embedded in the wall of the gall-bladder. Calculi may enter a diverticulum due to ulceration of the gall-bladder, and from subsequent closure of the orifice of the diverticulum become enclosed in the wall of the gall-bladder. Masses of cholesterin may probably be formed from the mucous glands of the gall-bladder.

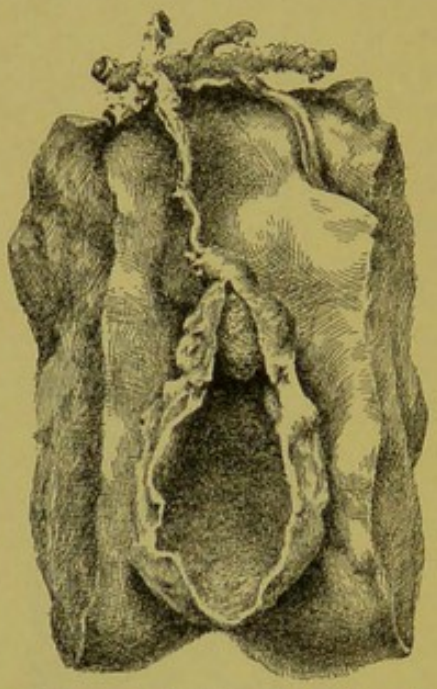


Fig. 104.—A calculus impacted in the neck of the gall-bladder. From a specimen in St. George's Hospital Museum, Series ix, 199A. (Drawn by Dr. E. A. Wilson.)

Peraire[2] recorded a case with a series of parietal gall-stones embedded in the wall of the gall-bladder, and 27 calculi the size of peas in the lumen of the cystic duct, but none in the cavity of the gall-bladder.

A gall-stone may set up ulceration and weakening of the gall-bladder, and may thus form a diverticulum in which it becomes encysted. This is rare, and is more often seen near the fundus or at the neck of the gall-bladder. Under ordinary conditions the calculi are usually found in the fundus of the gall-bladder.

Calculi in the cystic and common bile-duct are referred to elsewhere (*vide* pp. 745 and 747). In rare instances a calculus derived from the gall-bladder passes backwards from the cystic duct into the common hepatic duct.

Carwardine[3] removed gall-stones from the gall-bladder, cystic, common bile, and hepatic ducts of a girl aged seventeen. M. H. Richardson[4] removed 12 gall-stones from the hepatic duct and 3 from the common bile-duct of a patient who had never shewn a trace of jaundice.

Intrahepatic calculi of large size are very rare; the common and hepatic ducts are usually also full of concretions.

[1] Bland-Sutton. *Gall-stones and Diseases of the Bile-ducts*, p. 62, 1907.
[2] Peraire. *Bull. Soc. anat.*, Paris, 1902, lxxvii, 707.
[3] Carwardine. *Brit. Med.-Chir. Journ.*, 1908, xxvi, 39.
[4] Richardson, M. H. *Trans. Am. Surg. Assoc.*, 1905, xxiii, 217.

PLATE VI.

GALL-STONES FROM A CASE IN WHICH FRACTURE WAS SPONTANEOUS.

The largest calculus shews surface where spontaneous fracture has occurred. The calculus below and to the left fitted into it. The other calculi were in the same gall-bladder. From a case of primary carcinoma of the gall-bladder in which spontaneous fracture of the calculi had occurred. Painted by Dr. E. A. Wilson.

Thudichum[1] in 1863 collected six cases including Cruveilhier's plate (livraison xii, Plate V), of large branching intrahepatic calculi like coral. I met with one such case in a man who died with diabetes from secondary chronic pancreatitis[2] (*vide* Fig. 105). There are good specimens of multiple intrahepatic calculi in the museums of the London and Westminster Hospitals (No. 581). In Vachell and Stevens'[3] case there was 520 calculi, the largest being $1\frac{3}{4}$ inches long, in the dilated intrahepatic ducts. Other cases have been reported by M'Arthur,[4] Draper,[5] and Hawkes.[6] In the last case the calculi were successfully removed during life. Major Barry sent me notes about a Hindu cook whose common bile, hepatic and intrahepatic ducts were

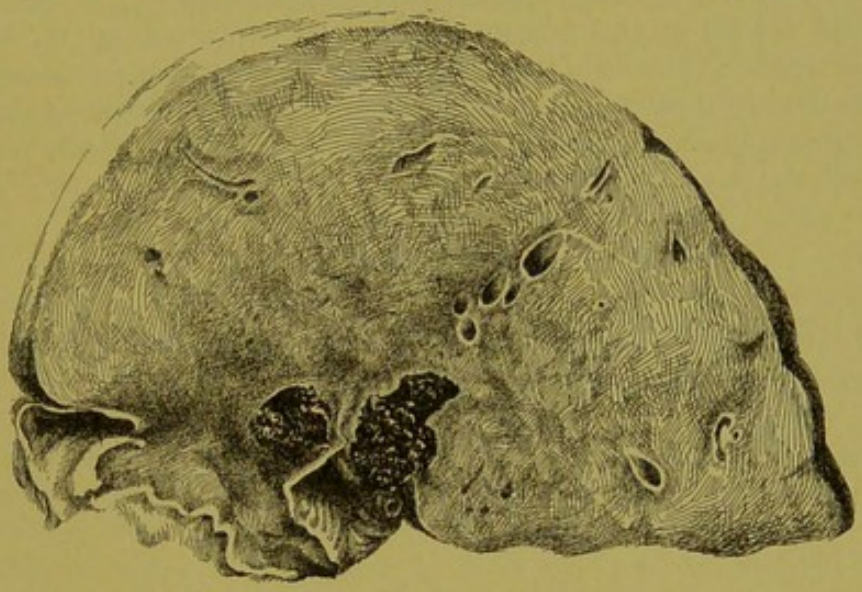


FIG. 105.—Large intrahepatic calculi distending the right and left hepatic ducts. (Drawn by Dr. E. A. Wilson.)

distended with small gall-stones. These calculi usually cause jaundice and a good deal of pericholangitis, which may be suppurative. In Draper's case jaundice was absent. The calculi are chiefly composed of bilirubin-calcium. Smaller calculi are not so rare in the intrahepatic ducts; among 72 cases of cholelithiasis collected by Beer[7] 5 shewed calculi in the intrahepatic ducts. Small black bilirubin-calcium calculi are not uncommon. Occasionally masses of calculous material are found embedded in the substance of the liver in dilated, ampulla-like terminations of bile-ducts which have lost their continuity with the bile-ducts.

Spontaneous Fracture of Gall-stones in the Gall-bladder.—Cases

[1] Thudichum. *A Treatise on Gall-Stones*, p. 176, 1863.
[2] Rolleston. *Trans. Path. Soc.*, Lond., 1898, xlix, 133.
[3] Vachell and Stevens. *Brit. Med. Journ.*, 1906, i, 434.
[4] M'Arthur. *Journ. Amer. Med. Assoc.*, Chicago, 1905, xlv, 1797.
[5] Draper. *Proc. Path. Soc. Phila.*, 1910. N.S., xiii, 16.
[6] Hawkes. *Presbyterian Hosp. Rep.*. N.Y. 1906, vii, 230.
[7] Beer, E. *Arch. f. klin. Chir.*, 1904, lxxiv, 115.

in which a gall-stone has been found to have broken up within the gall-bladder have been reported by Pearce Gould,[1] Hadden,[2] Calvert,[3] and myself.[4] I have seen one case since the one I reported. Trauma during life or in the course of the post-mortem examination appears to have been excluded, and, though conceivable, it does not seem very likely that vigorous contraction of the gall-bladder would fracture even a friable calculus. Calvert suggested that fracture might depend on drying of a calculus. It is conceivable that in some instances the union and subsequent disruption of a number of calculi might imitate spontaneous fracture. Care must also be taken not to regard as examples of spontaneous fracture marked faceting of the surfaces of adjacent calculi. Probably fracture is brought about in much the same way as spontaneous fracture of calculi in the urinary bladder, as explained by W. M. Ord[5] and Plowright.[6] Chauffard[7] and others have shewn that micro-organisms may also pass into calculi, and by forming a deposit between its layers this microbic invasion would tend to loosen and split off the more superficial strata of the calculus.

Clinical Picture

Gall-stones are frequently found in the gall-bladder quite unexpectedly. Kehr[8] states that symptoms occur in only 5 per cent of persons whose gall-bladders contain calculi. But probably this understates the clinical importance of gall-stones, for symptoms really due to cholelithiasis are often regarded as dyspeptic both by the patients and by their medical advisers; further, the presence of gall-stones in the gall-bladder at the necropsy of a patient who has died of some independent disease does not satisfactorily prove that there have never been any symptoms due to gall-stones, as the history may well be deficient. When gall-stones are found during the course of an abdominal operation enquiry will often elicit a history of symptoms pointing to their presence. Moynihan[9] has found this universally. Latency is especially common in old people, in whom the muscular tissue of the gall-bladder and ducts is atrophied, and it has been thought that for this reason the passage of a calculus out of the gall-bladder into the ducts is less likely to occur.

The symptoms produced by gall-stones are extremely numerous and variable. It is difficult to divide the symptoms satisfactorily into water-tight groups, for there is a certain amount of overlapping. I propose to

[1] Pearce Gould. *Trans. Clin. Soc.*, Lond., 1888, xxi, 193.
[2] Hadden, W. B. *Trans. Path. Soc.*, Lond., 1890, xli, 160.
[3] Calvert, J. *Ibid.*, 1898, xlix, 139.
[4] Rolleston, H. D. *Ibid.*, 1898, xlix, 135.
[5] Ord, W. M. *Ibid.*, 1877, xxviii, 170; 1881, xxxii, 304.
[6] Plowright. *Ibid.*, 1896, xlvii, 132.
[7] Chauffard. *Rev. de méd.*, Paris, 1897, xvii, 81.
[8] Kehr, H. *Diagnosis of Gall-stone Disease*, p. 25, American transl., 1901.
[9] Moynihan. *Brit. Med. Journ.*, 1908, ii, 1599.

consider them under the following heads: (I) Masked or inaugural symptoms; (II) biliary colic; (III) the purely mechanical or aseptic effects of gall-stones; (IV) the inflammatory and infective changes set up by cholelithiasis; special descriptions will be given of intestinal obstruction and of fistulae produced by gall-stones, under the headings (III) and (IV) respectively.

I. Masked or Inaugural Symptoms.—The symptoms accompanying the presence of gall-stones may not be characteristic, and it has long been recognised that "dyspepsia" may disappear after removal of gall-stones. These symptoms have been called "inaugural" by Moynihan [1] who insists, contrary to Kehr, that gall-stones always cause symptoms. These early symptoms are flatulence, fulness and dull pain in the epigastrium coming on about half an hour after meals or in the middle of the night, and specially induced by certain forms of food, such as apples and cheese. In these attacks, which are relieved by eructations or vomiting, but not by taking food, there may be pain resembling that of pleurisy due to spasm of the diaphragm. There may also be slight shivering of short duration, drowsiness, and headache. The "goose-skin" sensation is allied to the more pronounced feverish attacks in intermittent hepatic fever (p. 759). There may be chronic pain in the back imitating lumbago, or pain on the top of the right shoulder passing down the outside of the arm which may for years be regarded as neuritis (Mackenzie [2]). It is important to recognise these early manifestations of gall-stones, but Moynihan and Sherren [3] both agree that a diagnosis between these manifestations of gall-stones and ulcer of the stomach and duodenum may be impossible.

II. Biliary colic is generally regarded as the result of spasm excited by the passage of a calculus down the bile-ducts. Attacks of pain of less severity may possibly be due to spasm set up by a stone in the gall-bladder which has not actually entered the cystic duct. Inspissated bile and masses of precipitated cholesterin and bile-pigments in the ducts may also induce biliary colic. Inflammation and spasm extending to the ducts from cholecystitis must also be reckoned with as a cause of biliary colic. In other words, biliary colic may, like the pain of appendicitis, be independent of calculi. Cholecystitis with closure of the cystic duct will cause painful contractions of the gall-bladder; in many cases the factor responsible for closure of the cystic duct is a calculus. According to Lennander [4] spasm of the gall-bladder and bile-ducts is not painful *per se*, but only because it causes traction on the sensitive subperitoneal tissues. Some writers, such as Riedel [5] and Kehr,[6] minimise the mechanical rôle of calculi in biliary colic, and insist on the import-

[1] Moynihan. *Brit. Med. Journ.*, 1908, ii, 1598; *Practitioner*, Lond., 1908, lxxxi, 830.

[2] Mackenzie, J. *Symptoms and their Interpretation*, ed. 2, p. 159, 1912, Lond.

[3] Sherren. *Lancet*, Lond., 1911, ii, 870.

[4] Lennander. *Hygiea*, Stockholm, 1907, 2. f., vii, 657.

[5] Riedel. *Berlin. med. Wchnschr.*, 1901, xxxviii, 1.

[6] Kehr, H. *Diagnosis of Gall-stone Disease*, p. 26, Amer. transl., 1901.

ance of cholecystitis and on the extension of inflammation to the ducts as the cause of pain and jaundice. But though inflammatory obstruction of the cystic duct is quite enough to set up painful contractions of an inflamed gall-bladder, there is no reason to doubt that the mechanical irritation of a calculus in the ducts sets up spasm and colic in the same way that a calculus in the ureter causes renal colic. In other words, biliary colic may be due to inflammatory or to mechanical obstruction, or to both combined.

Cause of the Passage of Calculi out of the Gall-bladder.—As gall-stones are commonly latent in the gall-bladder, some conditions other than those of ordinary life must be responsible for the passage of calculi into the cystic duct, and something more is required than the ordinary contractions of the gall-bladder which suffice to drive out the bile. It has been thought that unusually vigorous contractions of the gall-bladder, such as might be induced by violent emotion, may determine the passage of gall-stones into the cystic duct. The onset of colic at the menstrual periods has been referred to spasmodic contraction of the gall-bladder set up by nervous perturbation and general abdominal hyperaemia (Cornillon [1]). Occasionally jolting, such as riding in a cart without springs, a railway journey, or bicycling, has been thought to determine the passage of calculi into the cystic duct. Keay [2] believes that pain following jolting is due to stretching of adhesions rather than to the passage of gall-stones, and that a stooping posture favours the migration of a calculus out of the gall-bladder. Palpation of the gall-bladder is certainly sometimes followed by colic, but it can be very rarely that the stone is directly forced into the cystic duct. Von Noorden [3] has pointed out that biliary colic may occur in patients immediately after treatment for obesity, and suggests that the removal of fat allows the pressure of corsets to interfere with the flow of bile out of the gall-bladder.

While not denying the possibility that the contractions of the gall-bladder may drive calculi into the cystic and common bile-duct, Kehr [4] believes that the important factor in determining the migration of calculi from the gall-bladder into the ducts is inflammation of the gall-bladder. The mechanism is as follows: Cholecystitis gives rise to an inflammatory exudation which distends the gall-bladder and drives the calculus into the cystic duct. Enlargement of the gall-bladder, tenderness, and fever during biliary colic are in favour of the view that cholecystitis plays an important part in its production. When the calculus is impacted in the duct, it will mechanically set up painful spasm of the ducts and gall-bladder. Acute cholecystitis may be set up by infection either from the intestine or from the general circulation. Diarrhoea, typhoid fever, and influenza, may thus precede an attack of biliary colic. Trauma, such as a fall or blow, may, by reducing the

[1] Cornillon. *Progrès méd.*, Paris, 1897, 3. s., v, 257.
[2] Keay. *Medical Treatment of Gall-stones*, p. 37, 1902.
[3] Von Noorden, C. *Diseases of the Metabolism and Nutrition*, part i, Obesity, p. 31, 1903. E. B. Treat and Co., New York.
[4] Kehr. *Loc. cit.*, p. 26.

resistance of the gall-bladder, allow micro-organisms to set up cholecystitis and so lead to the expulsion of a calculus into the ducts.

The onset of biliary colic may be quite sudden, or may be preceded by symptoms, such as shivering, nausea, and vomiting, compatible with the view that cholecystitis is in progress. Formerly the entrance of a gall-stone into the cystic duct was thought to be due to contractions of the gall-bladder set up reflexly by the passage of food into the duodenum, and three to four hours after a meal was thought to be a specially probable time for the onset of biliary colic. Biliary colic more commonly commences at night.

The onset of the menstrual period has been thought to determine an attack of biliary colic. Biliary colic may occur at any period during pregnancy, but during lactation it is either less frequent or absent. After weaning the child, however, severe attacks may occur. After delivery conditions leading to infection of the gall-bladder are not uncommon, and thus the onset of colic may be determined.

Signs and Symptoms.—The *pain* in biliary colic is due to two factors: in the first instance, there is probably nearly always acute inflammation of the gall-bladder; secondly, the muscular spasm set up by the presence of the calculus in the duct. The pain of acute cholecystitis is felt in the right hypochondrium and epigastrium. The entrance of the calculus into the cystic duct sets up severe muscular spasm and pain in the right loin and back. Keay,[1] from personal experience and from observation of patients, believes that pain due to a calculus in the cystic duct begins to the right of the region between the eighth and eleventh dorsal vertebrae. In this view Keay differs from most authorities, such as Naunyn, who state that the pain begins in the epigastrium or right hypochondrium. This pain is extremely severe, as if the back was being broken. It passes to the right hypochondrium and radiates from this spot in all directions—to the left hypochondrium, the umbilical and hypogastric regions, to the thighs, and even to the arms and neck. The pain may radiate to the right shoulder, but this is less frequent in biliary colic than in hepatic abscess. In rare instances the pain is referred to the left side; two cases of transposition of the viscera have been operated upon for gall-stones (Beck,[2] Billings[3]). Mayo Robson[4] observed left-sided pain in cases in which subsequent operation shewed adhesions between the pylorus and the gall-bladder.

In one case attacks of colic followed by the passage of small calculi, which I examined, were limited to the epigastrium and left side. There was no transposition of the viscera, but more than twenty years ago the patient had had a right-sided empyema drained, with, however, very little thoracic deformity. I have also seen it in a woman who had had much pelvic inflammation on the left side.

[1] Keay. *Medical Treatment of Gall-stones*, p. 75, 1902.
[2] Beck. *Ann. Surg.*, 1899, xxix, 593.
[3] Billings. *Phila. Med. Journ.*, 1900, vi, 670.
[4] Mayo Robson. *System of Medicine* (Allbutt and Rolleston), 1908, iv, part i, 259.

The pain, which is usually paroxysmal, is probably one of the worst that afflict humanity; women speak of it as being much worse than the pains of labour. It may be so intense as to cause hysterical or epileptiform attacks, and in very rare cases the patients have died, apparently simply from shock (*vide* p. 735). The pain is so excruciating that the patient throws himself into various positions to obtain relief, but without any success. He may roll in agony on the floor and scream, cry, or groan in a very distressing manner. The severity of the pain gradually diminishes, and leaves a constant dull aching which is interrupted by acute paroxysms. The first is nearly always much worse than subsequent seizures, and in a first attack a small calculus may give rise to far more pain than larger gall-stones on later occasions. There is thus no absolute relation between the size of the calculi and the severity of the pain. The ducts become dilated by the passage of successive calculi, and eventually a large one may pass almost unnoticed. Pain may suddenly disappear as if by magic; this may be explained as due to sudden relief of tension in the gall-bladder from removal of obstruction, for example the escape of the calculus into the gall-bladder or the duodenum. Keay believes that at the moment when the stone passes into the duodenum there is a peculiar gliding sensation to the right of the tenth and twelfth dorsal vertebrae. The violent pain usually lasts for some hours—three to twelve—if unrelieved by morphine; in rare instances for a few minutes only. Severe pain is sometimes described as lasting for days, but this is probably due to a succession of attacks supervening rapidly, with slighter pain, due to the inflamed or distended and inflamed gall-bladder, in the intervals between the more severe paroxysms. Cutaneous hyperalgesia is described by Head[1] in the eighth dorsal segment and may occur on both sides. After the subsidence of the attack the skin and muscles on the right side of the abdomen may be tender for weeks (Mackenzie[2]).

It has been estimated that the temperature is raised in 60 per cent of the cases. The fever is explained by the concomitant cholecystitis or cholangitis; in some instances a palpable and tender gall-bladder, splenic enlargement, and albuminuria lend support to the theory of infection. The fever was formerly thought to be reflex, and due to the violent nervous stimuli accompanying the colic. This view is to some extent supported by cases in which at operation there is no manifest inflammation of the gall-bladder or ducts. But in such cases it is not unreasonable to believe that there is infection sufficient to induce fever, though not to produce naked-eye changes.

Boix[3] suggested that during biliary colic the detoxicating function of the liver is suspended and that toxins absorbed from the intestinal tract thus pass into the general circulation and give rise to pyrexia.

[1] Head. *Brain*, Lond., 1893, xvi, 73.
[2] Mackenzie. *Symptoms and their Interpretation*, ed. 2, pp. 48, 159, 1912, Lond.
[3] Boix, E. *Arch. gén. de méd.*, Paris, 1901, clxxxviii, 466.

Reflex vomiting accompanies the intense pain, and is often followed by some relief. The contents of the stomach are first brought up, and subsequently those of the duodenum; in very rare instances a calculus has been vomited (*vide* p. 769). There is usually bile in the vomit, which suggests that at this period the common duct is not completely occluded. Dyspepsia and flatulence may accompany or follow the attack. The amount of active hydrochloric acid in the gastric juice is diminished during the attack, but increased in the intervals (Lichty [1]). There is naturally distaste for food, though thirst may be urgent. Constipation is usually present. With well-marked jaundice the faeces may be colourless, but this is far from constant. The abdomen is usually somewhat retracted from vigorous contraction of the abdominal muscles. Occasionally there is considerable tympanitic distension, but, according to Naunyn, this is seen only in persons habitually flatulent. Transient dilatation of the stomach has been described.

The liver is enlarged in some instances, according to Kehr, in from 10 to 20 per cent, but this is difficult to determine, as the hypochondrium is extremely tender and the patient, being in great pain, is naturally far from tolerant of examination, and the recti are rigid. The swelling of the liver may be partly due to inflammation of the bile-ducts and partly to retention of bile from the obstruction. It is often tender without any manifest enlargement. The gall-bladder is probably frequently enlarged, but its examination is far from easy, as there are usually considerable tenderness over the gall-bladder and rigidity of the abdominal muscles. Naunyn estimates that the gall-bladder is only palpable in one-third of the cases of biliary colic.

Enlargement of the spleen is also difficult to estimate, but probably only occurs when severe infective processes or other complications are present. Gilbert and Lereboullet,[2] however, suggest that during biliary colic the pressure of bile in the intrahepatic ducts may compress the branches of the portal vein and give rise to passive engorgement and splenic enlargement.

During a paroxysm the skin is hot and moist or bathed in perspiration, and there may be rigors or shivering. The intense pain leaves considerable prostration for a time after the paroxysm has passed off. Nervous symptoms occasionally accompany biliary colic and are due to the intense visceral pain. Hysterical manifestations,[3] epileptiform convulsions, or even angina pectoris (Douglas Powell [4]) may occur. Sudden death during a paroxysm of pain, due to cardiac inhibition brought on reflexly through the vagus, has been recorded in rare instances.

Naunyn [5] refers to 9 cases of death during severe biliary colic; Clifford

[1] Lichty. *Amer. Journ. Med. Sc.*, Phila., 1911, cxli, 72.
[2] Gilbert et Lereboullet. *Rev. de méd.*, Paris, 1904, xxiv, 908.
[3] Jeanselme et Rabé. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1898, 3. s., xv, 602.
[4] Powell. *System of Medicine* (Allbutt and Rolleston), 1909, vi, 188.
[5] Naunyn. *Cholelithiasis*, p. 89, transl. New Sydenham Soc., 1896.

Allbutt,[1] Osler,[2] Mayo Robson,[3] Calvert,[4] and Périer[5] refer to similar cases.

In exceptional instances temporary hemiplegia, paraplegia, or even tetany has been observed. Sleepiness and drowsiness may follow biliary colic and be due to nervous exhaustion, to the presence of bile in the circulation, or in some degree to the morphine. Extreme drowsiness was a striking feature in a woman aged thirty who had suffered from gall-stone colic for six years (Lévi[6]). Kehr[7] states that the subjects of gall-stone colic frequently have attacks of migraine, which, however, disappear when the calculi are removed by operation. During biliary colic hiccup may occur, and there may be a dry cough due to reflex irritation. Reflex constriction of the vessels in the lungs with rise of blood-pressure in the pulmonary artery, as shewn by accentuation of the pulmonary second sound, has been described, and is supported by the experimental observation that irritation of the bile-duct induces constriction of the pulmonary vessels (François-Franck and Arloing). Signs of congestion of the base of the right lung, and, in very exceptional instances, haemoptysis (Cassoute[8]), have been observed. Dilatation of the right side of the heart has been described, and has been referred by Potain to the rise of pulmonary blood-pressure. It may also be due in some measure to poisons absorbed from the bile-ducts, or in some cases to the effect of bile salts. Temporary dilatation of the left ventricle with a systolic apical murmur may also occur (Gangolphe,[9] Riesman), and has been ascribed to the influence of the high blood-pressure caused by the pains acting on a myocardium weakened by toxaemia. Among 56 gall-stone cases 6, or 10·7 per cent, had transient murmurs (Riesman[10]).

There may be palpitation, disturbed cardiac rhythm, with rapid action, irregularity, or even slowing of the heart. The pulse during a paroxysm becomes small, feeble, and is generally of about the normal rate; in some cases it is even slower than normal. Kraus[11] observed a pulse of 42 in one case.

A moderate degree of leucocytosis in severe biliary colic, to about 15,000, is very common (Emerson[12]). Albuminuria is not infrequent. There is some difference of opinion as to the frequency with which glycosuria occurs. It has been referred to the widespread nervous disturbance, but it is conceivable that it is toxic. True diabetes may be the result of chronic pancreatitis set up by a calculus in the lower part

[1] Allbutt. In *System of Medicine*, 1907, iii, 304.
[2] Osler. *Principles and Practice of Medicine*, p. 551, ed. vi, 1905.
[3] Mayo Robson. *Gall-stones*, p. 77, 1892.
[4] Calvert, J. T. *Ind. Med. Gaz.*, 1903, xxxviii, 413.
[5] Périer. *Normande méd.*, 1904, xix, 396.
[6] Lévi. *Arch. gén. de méd.*, 1896, clxxvii, 63.
[7] Kehr. *Diagnosis of Gall-stone Disease*, p. 56, American transl., 1901.
[8] Cassoute. *Bull. méd.*, Paris, 1897, xi, 821.
[9] Gangolphe. *Thèse de Paris*, 1875.
[10] Riesman. *Amer. Journ. Med. Sc.*, Phila., 1911, cxlii, 655.
[11] Kraus. *On Gall-stones*, p. 36, English translation, 1896.
[12] Emerson. *Clinical Diagnosis*, p. 586, 1906.

of the common bile-duct, but these patients are not often the subjects of typical biliary colic. Conversely in two well-marked cases of diabetes mellitus Gilbert and E. Weil [1] observed that during intercurrent attacks of hepatic colic the glycosuria diminished. Bile-pigment occurs in the urine before there is any manifest jaundice; the presence of bile in the urine may be quite transient and may be succeeded by an excess of urobilin. Indican does not occur in uncomplicated cases; this is a point of importance in distinguishing biliary from appendicular and intestinal colic in which indican may be present.

Jaundice is not an invariable accompaniment of biliary colic. Its incidence has been variously estimated at one-half to three-quarters of all the cases. In the higher estimate cases of very slight and transient icterus are included. Naunyn [2] considers that definite jaundice is present in half the cases. It comes on a varying time after the onset of the pain, and no constant interval can be given. It may vary between a few hours to two or even three days. The occurrence of jaundice after biliary colic is the result of obstruction to the flow of bile through the common bile-duct. The obstruction is generally assumed to be due to the presence of the calculus in the duct, but it may be due to the spread of inflammation and spasm from the gall-bladder to the ducts, and may occur when the calculus is still in the gall-bladder or in the cystic duct. Riedel believes that two-fifths of the cases of jaundice in cholelithiasis are due to this cause. The conjunctivae become yellow before the skin.

During an attack of gall-stone colic not only is no food taken, but the vomiting and fever lead to temporary loss of flesh and weight. When attacks are repeated, nutrition may become very seriously affected.

Complications.—The extremely forcible peristaltic contractions of the intestines, set up reflexly during the height of biliary colic, may cause volvulus of the small intestine and so acute intestinal obstruction (Mayo Robson [3]). Intestinal obstruction produced by gall-stones in other ways, viz. by mechanical obstruction of the lumen of the bowel, by a large calculus, as the result of local peritonitis around the gall-bladder, and by adhesions, is referred to elsewhere (*vide* pp. 751, 758).

Rupture of the gall-bladder or ducts during an attack is fortunately very rare; when it occurs, infection of the peritoneum with fatal results is very prone to occur.

Pauly [4] describes a case in which, after an attack of biliary colic, collapse, abdominal distension, and death occurred. Blood clot was found in the abdomen. There was rupture of the capsule of the liver leading into a cavity containing blood. There were calculi in the gall-bladder and a calculus obstructing the common duct.

The cholecystitis which probably always precedes and gives rise to

[1] Gilbert et Weil. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1898, 3 s., xv, 633.
[2] Naunyn. *Cholelithiasis*, p. 76. Transl. New Sydenham Soc., 1896.
[3] Mayo Robson. *Med.-Chir. Trans.*, Lond., 1895, lxxviii, 117.
[4] Pauly. *Lyon méd.*, 1892, lxx, 430.

biliary colic may become suppurative, or even perforate and set up peritonitis.

Termination.—An attack of biliary colic may terminate suddenly, the pain disappearing in a moment, probably from the calculus dropping back into the gall-bladder or escaping into the duodenum. In other cases the pain may recur at frequent intervals, the calculus, or possibly a succession of calculi, being finally discharged into the duodenum. There is not any convincing evidence that recurring attacks of colic without jaundice are due to a calculus which has once passed into the cystic duct, returning to the gall-bladder and entering the cystic duct again and again. Possibly some of these cases are due to cholecystitis alone, and others to pancreatic lithiasis. The calculus may become impacted close to the biliary papilla and produce intermittent hepatic fever (*vide* p. 759). In rare instances death may occur from various causes. The pain may be so intense that death results from reflex cardiac inhibition (*vide* p. 735). Death from peritonitis due to rupture or ulceration of the ducts or gall-bladder is also described.

Diagnosis.—The extremely severe pain in the right hypochondrium and back, the tenderness over the gall-bladder between the ninth costal cartilage and the umbilicus, vomiting, the subsequent appearance of jaundice, though this is not essential, and the recognition of gall-stones in the stools are the chief points on which a diagnosis of gall-stone colic rests. The presence of calculi in the faeces of course clinches the diagnosis, but calculi are by no means always found; according to Kehr in not more than 25 per cent. The motions should be passed into a solution of carbolic acid 1 : 60, and broken up with the aid of a piece of stick and passed through a sieve.

The patient may be in such agony that it may be very difficult, especially in a first attack or when first seen, to make out what is the matter. In such cases a hypodermic injection of morphine will enable an investigation and a diagnosis to be made. A few whiffs of chloroform remove the widely spread pains and leave a subdued ache in the region of the gall-bladder.

Differential Diagnosis from Cholecystitis.—In acute cholecystitis without gall-stones the pain may be so severe as to imitate colic due to a calculus; Sheldon[1] has collected 32 cases in point. Moreover, it is probable that acute cholecystitis is antecedent to the onset of calculous colic (Kehr,[2] Naunyn[3]). The chief distinction between the two is the greater severity of the pain in gall-stone colic, but this criterion often fails us.

Renal Colic.—Since the pain due to a calculus in the cystic duct is felt to the right of the spine opposite the eighth to eleventh dorsal vertebrae, it is not surprising that cases of biliary colic are from time to time diagnosed as renal colic due to a calculus in the right kidney. In renal colic the pain tends to radiate down the ureter instead of forwards

[1] Sheldon. *New York Med. Journ.*, 1905, lxxxi, 69.
[2] Kehr. *Gall-stone Disease*, p. 26, American transl., 1901.
[3] Naunyn. *On Cholelithiasis*, pp. 113-125. Transl. New Sydenham Soc. 1896.

towards the epigastric and hypochondriac regions, while the kidney is tender on palpation in the loin, and the urine may contain blood, pus, or albumin, and is free from bile. The diagnosis of cholelithiasis in early life is difficult, as it is hardly likely to be thought of in the absence of jaundice. The abdominal pain will probably be referred to intestinal disturbance. In this respect cholelithiasis resembles renal colic in infants, which, as Gibbons [1] has shewn, is very likely to be overlooked.

Floating Kidney.—As described elsewhere (p. 555), a floating kidney on the right side may cause biliary colic and jaundice. The diagnosis depends on the detection of a floating kidney and on disappearance of the symptoms when nephroptosis has been efficiently treated either by a belt and pad or by the operation of nephropexy. If attacks of jaundice and colic still continue, it is probable that there is cholelithiasis in addition; in 13 cases of floating kidney with symptoms suggesting cholelithiasis, 2 were found to have gall-stones (Sherren [2]).

Gastric and Duodenal Ulcer.—The pain due to biliary colic is often regarded not only by the sufferers, but also by their medical advisers, as due to disease of the stomach, such as ulcer, or to a duodenal ulcer. The pain of frank biliary colic is very much more severe than that due to gastric ulcer. In gastric ulcer the pain is chiefly in the epigastrium, and the vomited matters shew excess of hydrochloric acid, whereas in biliary colic the amount of hydrochloric acid is either normal or diminished. Fever, sweating, and prostration are in favour of biliary colic.

Duodenal ulcer is twice as common in men as in women. The pain is relieved by food or by an alkali. Haematemesis may occur or there may be melaena without haematemesis. When the ulcer is in the second part of the duodenum, a rare position, the symptoms may exactly imitate gall-stones (Sherren). The pain of biliary colic is much more severe than that of duodenal ulcer, and is not relieved by taking food or an alkali.

Acute Dyspepsia.—In acute gastritis with flatulent distension of the stomach the symptoms are less urgent than in biliary colic, and there is tenderness over the stomach rather than over the gall-bladder.

Hyperchlorhydria.—In some cases of hyperacidity of the gastric juice attacks of pain may wake the patient up at 3 a.m., and be regarded as due to biliary colic. Examination of the gastric juice and the relief obtained after taking a powder composed of bicarbonate of sodium and carbonate of magnesium should indicate the true nature of these cases.

Appendicitis.—In some cases the pain is referred to the right iliac fossa and the condition resembles appendicitis. A possible explanation of this is that local peritonitis has spread from the gall-bladder to the serous coat of the appendix (Tripier and Paviot [3]). Ordinary cholecystitis is more likely to resemble appendicitis than is typical biliary colic in which the pain is much more severe and higher

[1] Gibbons, R. A. *Med.-Chir. Trans.*, Lond., 1896, lxxix, 41.
[2] Sherren. *Lancet*, Lond., 1911, i, 870.
[3] Tripier et Paviot. *Semaine méd.*, Paris, 1903, xxiii, 29.

up in the abdomen. But appendicitis and cholelithiasis may coexist (*vide* p. 716).

Mucous Colitis.—When the attacks of abdominal pain in mucous colitis are sufficiently severe to suggest biliary colic, examination of the stools should lead to the detection of the characteristic casts of mucous colitis. It is worth while pointing out that membranous cholecystitis with attacks of biliary colic has been reported in patients with mucous colitis (*vide* p. 614). Mucous colitis may be associated with the passage of intestinal sand and with abdominal pain.

Intestinal lithiasis occurs in two forms: (i) The false—or food residues, such as the sclerenchyma of fruits, especially the pips of pears, the vertebrae of sardines, or drugs, such as magnesia or salol. Olive oil taken by the mouth to relieve cholelithiasis, may be passed as saponified masses, which, from a superficial examination, may be regarded as softened calculi.[1] When colic from other causes, such as constipation, is followed by the passage of these food residues, a diagnosis of biliary sand might easily be made unless the masses are chemically or microscopically examined. (ii) True intestinal sand is composed of calcium phosphate, and is probably the result of a "lithogenic catarrh" of the intestine. It may also contain urobilin. The presence of true intestinal sand is often associated with mucous colitis. In some, but not in all, cases of true intestinal sand there are attacks of severe abdominal pain. A chemical examination of the sand is necessary to distinguish the condition from biliary colic due to minute calculi.

Epigastric hernia with adherent omentum in rare cases imitates biliary colic; possibly the traction exerted on the gall-bladder and bile-ducts acts in the same way as a floating kidney. Lothrop[2] refers to 6 cases of this nature.

In *acute pancreatitis* there is more profound collapse; the pain is more in the epigastrium, and is more intense and constant than in biliary colic. Acute pancreatitis may follow on biliary colic, and the haemorrhagic form may be due to bile passing into the pancreatic duct when the orifice of the biliary papilla is blocked by a small calculus (Opie[3]).

Pancreatic colic due to calculi in Wirsung's duct may imitate biliary colic without jaundice. The diagnosis of pancreatic lithiasis is suggested by the discovery in the stools of calculi composed of carbonate and phosphate of lime (*vide* also p. 751).

Hepatic Crises in Tabes, etc.—Crises resembling biliary colic are very rare in tabes, but the resemblance may be very close. Krauss[4] records a case of a woman aged forty-four who was the subject of tabes and had recurring attacks of colic and jaundice. At the necropsy the gall-bladder and ducts were healthy and free from calculi.

The obscure condition *hepatalgia*, or neuralgia of the liver, has been

[1] Compare Delépine, S. *Trans. Path. Soc.*, Lond., 1890, xli, 111.
[2] Lothrop. *Boston Med. and Surg. Journ.*, 1897, cxxxvi, 203.
[3] Opie, E. L. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 179.
[4] Krauss. *Journ. Nerv. and Ment. Dis.*, 1899, xxvi, 107.

described by Clifford Allbutt[1] and Pariser,[2] the latter of whom has reported 7 cases of nervous hepatic colic. The patients are neurotic or neurasthenic, but these conditions of course in no way protect against cholelithiasis. Osler[3] speaks of pseudobiliary colic as not uncommon in nervous women, and as being periodic and often excited by emotion, but not accompanied by jaundice. The abdominal crises of angioneurotic oedema may simulate recurrent biliary colic (Harrington[4]).

From enteralgia, or *neuralgia of the abdominal sympathetic*, the diagnosis is not always easy. According to Clifford Allbutt,[5] the pain of enteralgia often begins at the navel and is more stabbing than in biliary colic. In the early stages of an *aneurysm of the abdominal aorta* near the coeliac axis, before pulsation is manifest, attacks of severe pain may suggest biliary colic. Pseudo-gall-stone colic may occur in malignant disease involving the ducts and in malignant disease of the head of the pancreas, but there is such deep jaundice and the condition of the patient is so grave that little or no difficulty in eliminating ordinary biliary colic is likely to arise.

Lead colic, when severe, superficially resembles gall-stone colic in the great abdominal pain and difficulty in making a thorough examination of the patient. The blue line on the gums, the anaemia, and the absence of any localisation of tenderness near the gall-bladder point to lead colic. I have seen recurrent attacks of colic with slight jaundice in workers in lead, suggesting that spasmodic contraction of the bile-ducts, analogous to intestinal colic, may be set up by lead.

Angina Pectoris.—The severity of the pain may, when it is referred to the cardiac region, imitate angina pectoris.

In a case of de Havilland Hall's[6] there were attacks of pain in the cardiac region, followed by faintness, which resembled angina but were not relieved by nitrites. Subsequently unmistakable biliary colic, followed by a broncho-biliary fistula, developed and the aberrant pain disappeared.

Lumbago.—The pain in the back with which biliary colic may begin may, in some cases, lead to an erroneous diagnosis of lumbago or of spinal disease.

Prognosis.—Under this heading recovery from the actual attack and the prospect as regards the future require consideration.

Death during an attack of biliary colic is extremely rare. It may be due to the intensity of the pain causing cardiac failure (*vide* p. 735), or to rupture of the gall-bladder or bile-ducts during severe spasm, and perforative peritonitis set up by the infected bile. Courvoisier[7] collected 41 examples of this result.

[1] Clifford Allbutt. *Visceral Neuroses*, 1884 ; and his *System of Medicine*, 1897, iii, 481.
[2] Pariser. *Centralbl. f. inn. Med.*, 1896, xvii, 467.
[3] Osler, W. *Practice of Med.*, p. 551, 6th ed., 1905.
[4] Harrington. *Clinical Contributions, Massachusetts General Hosp.*, 1906, i, 94.
[5] Clifford Allbutt. Allbutt's *System of Medicine*, 1897, iii, 482.
[6] de Havilland Hall. *Lancet*, Lond., 1902, i, 593 ; *Trans. Med. Soc. Lond.*, 1902, xxv, 191.
[7] Courvoisier. *Path. u. Chir..d. Gallenwege*, 1890.

In nearly all cases recovery takes place from the actual attack, but it is seldom that the first attack is the last. Usually there are further and less severe bouts. After a series of these attacks the patients may be free from any further trouble. But a calculus is sometimes left in the common bile-duct and the symptoms of intermittent hepatic fever develop, or there is constantly recurring pain from adhesions around the gall-bladder (*vide* p. 758). The prognosis in some degree depends on the presence or absence of facets on a calculus found in the stools. If, after a first attack, a smooth gall-stone without facets is found in the faeces, it may reasonably be hoped that no further attacks will follow. If, on the other hand, the calculus is faceted, there are more calculi in the gall-bladder and the probability of fresh attacks must be faced. The patient's habit of life, his willingness or refusal to avoid conditions which favour catarrhal cholecystitis and the production of fresh gall-stones, bear on the prognosis.

Treatment.—The pain is often so agonising that it will yield to nothing except hypodermic injections of morphine or inhalations of chloroform. After a hypodermic injection has been given, a few whiffs of chloroform will relieve the pain until the effect of the morphine makes the patient comfortable. One-fourth to a half of a grain of morphine combined with $\frac{1}{100}$ grain of atropine may be injected in these cases, and if an inhalation of chloroform is not advisable, 20 minims of chloroform in water may be given by the mouth (Gilman Thompson[1]). A hypodermic injection of morphine is very much better than opium by the mouth, both because it acts more rapidly and because repeated vomiting may lead to rejection of everything taken by the mouth. The hypodermic syringe should, of course, never be entrusted to the patient.

A graphic account of the intense suffering involved in breaking off the morphine habit acquired from repeated biliary colic is given by Keay in his book on the *Medical Treatment of Gall-stones*, p. 105.

The vomiting accompanying the biliary colic hardly requires any special treatment apart from that of the pain, as it will cease with it. Bismuth, soda, dilute hydrocyanic acid, and iced apollinaris or soda-water may be given. Large draughts of water containing bicarbonate of sodium (℥j to Oj), recommended by Prout, relieve purposeless retching by giving the stomach something to bring up. If retching persists and the patient be collapsed, iced champagne may be tried; otherwise it is better to give nothing by the mouth, to apply poultices to the epigastrium, and to keep the patient under the influence of morphine.

In less severe cases the patient may be put in a hot bath (104° F.) and given tincture of belladonna (♏ xx.) in spirits of chloroform to relieve spasm, or the following draught: Turpentine (♏ xv.), spiritus aetheris (♏ xxx.), aquam chloroformi to the ounce. Antipyrin, if given at the beginning of an attack, has been thought to give relief, but Kraus[2] considers that it

[1] Gilman Thompson. *Med. News*, N.Y., 1897, lxx, 516.
[2] Kraus. *On Gall-stones*, p. 83. English transl., 1896.

does good chiefly by inducing profuse perspiration, and insists on its futility when the attack has lasted two to three hours. Robson [1] recommends aspirin 5–10 grs., and exalgin in 1 gr. doses every half-hour for three or four doses. Naunyn [2] has had favourable results with a single dose of salicylate of sodium (30–45 grains) given at the beginning of an attack. Some observers recommend several ounces of olive oil; possibly relief of pain may be due to the oil inhibiting the secretion of HCl in cases with hyperchlorhydria. Washing out the stomach has been thought to alleviate the pain (Baruch [3]). Hot fomentations or poultices may be tried over the liver.

The external application of salicylate of methyl over the liver has been recommended in hepatic colic: 1 to 2 drams may be painted on daily and covered with gutta-percha to favour absorption. Chambart-Hénon [4] says it gives relief in half an hour.

Surgical Treatment.—During an attack of biliary colic operation is justified only in the presence of severe complications which would otherwise prove fatal. These complications are (i) rupture of the gall-bladder or bile-ducts, with severe collapse and signs of perforative peritonitis; (ii) widespread peritonitis due to acute infective inflammation of the gall-bladder, and (iii) signs of acute intestinal obstruction due to volvulus of the intestine from exaggerated peristalsis.

When, in spite of medical treatment, attacks of colic continually recur and the patient becomes incapacitated and is in danger of contracting the morphine habit, surgical measures must be considered. The gall-bladder should be opened, calculi removed, and, if necessary, the gall-bladder excised. Some difference of opinion has, perhaps naturally, existed between physicians and surgeons as to the recurrence of cholelithiasis after the operative removal of calculi from the gall-bladder. Reference has been made on p. 714 to 8 cases in which fresh calculi formed around sutures introduced into the wall of the gall-bladder during an operation for the removal of calculi. On the other hand, recurrence is very rare; for in 1500 operations on the gall-bladder and bile-ducts gall-stones re-formed in the gall-bladder in one case only (Mayo [5]). Many supposed examples of recurrence are due to incomplete removal of calculi from the ducts.

It might appear that when operation is required in recurrent biliary colic, the gall-bladder should either be removed or so treated that no fresh formation of gall-stones in it is possible. Mayo, however, considers that cholecystectomy should not be done as a routine course, because it is not necessary from the point of view of recurrence and because it renders subsequent drainage or cholecyst-enterostomy impossible. The treatment during the intervals is the general treatment of cholelithiasis described on page 774.

[1] Robson. *System of Medicine* (Allbutt and Rolleston), 1908, iv, part i, 263.
[2] Naunyn. *Cholelithiasis*, p. 178. Transl. New Sydenham Soc., 1896.
[3] Baruch. *Principles and Practice of Hydrotherapy*, p. 235, 1900, Lond.
[4] Chambart-Hénon. *Gaz. méd. de Paris*, 1898, 11. s., i, 408.
[5] Mayo. *Ann. Surg.*, 1906, xliv, 209.

III. The mechanical effects of gall-stones will be considered under the following heads, according as the stones are: (1) in the gall-bladder; (2) in the cystic duct; (3) in the common bile-duct; (4) in the ampulla of Vater; and (5) intestinal obstruction.

(1) **Mechanical Effects of Gall-stones in the Gall-bladder.**—The mechanical effects pure and simple of calculi in the gall-bladder are not very frequent, or, as a rule, very important. A large calculous gall-bladder may give rise to a feeling of dragging or heaviness and discomfort in the region of the liver. The gall-bladder, when full of tightly packed calculi or containing a large single gall-stone, may press on the pylorus or duodenum, and by producing pyloric obstruction and dilatation of the stomach, may imitate carcinoma of the pylorus (Naunyn,[1] Potherat[2]). In these cases examination of the gastric contents may be of use in settling the diagnosis: free hydrochloric acid should be present in cholelithiasis, whereas in gastric carcinoma it should be absent; but I have seen gall-stones in the gall-bladder necessitate operation in a case of carcinoma of the stomach with a normal amount of HCl in the gastric juice. Unless the calculi contain lime salts no shadow is thrown by *x*-rays. Gall-stones in the gall-bladder do not, as a rule, obstruct the outflow of food from the stomach simply and solely in a mechanical way, but set up spasm or adhesions between the pylorus and the gall-bladder which contract and slowly lead to pyloric obstruction (*vide* p. 758). A large single calculus ulcerating out of the gall-bladder into the duodenum may mechanically obstruct the pylorus (*vide* p. 769). There may be a combination of cholecysto-gastric fistula, adhesions around the pylorus, and mechanical obstruction of the lumen of the pylorus by a calculus.

From the pressure of a large calculous gall-bladder the common bile-duct might be compressed and jaundice set up. Thrombosis of the portal vein from this cause has been reported.[3] From traction exerted by a gall-bladder containing calculi the right lobe of the liver may be elongated into a Riedel's lobe. Axial rotation of a long cystic duct of a calculous gall-bladder has been observed (Wendel[4]).

The gall-bladder filled with calculi may be felt as a hard tumour through the abdominal wall, sometimes just below the costal arch; in other cases, owing to the presence of a Riedel's lobe, the gall-bladder is considerably depressed and may be found in the neighbourhood of the right iliac fossa. Unless fixed by adhesions, the calculous gall-bladder moves with respiration and can be displaced in a lateral direction. When there are numerous calculi, crepitus may be detected on palpation over the tumour, but this is often absent.

When the gall-bladder is filled with gall-stones and its walls are much atrophied, spontaneous rupture may possibly occur; but in most cases ulceration and softening due to inflammation are responsible for

[1] Naunyn. *On Cholelithiasis*, p. 151. Transl. New Sydenham Soc., 1896.
[2] Potherat. *Bull. et mém. Soc. de chir.*, Paris, 1903, n.s., xxix, 669.
[3] Donkin. *Med. Times and Gaz.*, 1868, ii, 396.
[4] Wendel. *Ann. Surg.*, 1898, xxvii, 199.

rupture of a gall-bladder containing calculi (*vide* p. 773). The presence of calculi in the gall-bladder disposes to primary carcinoma; this is discussed elswehere (*vide* p. 638).

(2) **Mechanical Effects of Calculi in the Cystic Duct.**—When a calculus passes into the cystic duct, it stretches the walls and sets up spasm and biliary colic (*vide* p. 731). A calculus may remain impacted in the cystic duct for long periods; sometimes no definite history of past colic is forthcoming in such cases to mark the time of impaction. The calculus is nearly always fixed close to the neck of the gall-bladder. It may completely obstruct the flow of bile into the gall-bladder, which then becomes distended with mucus, at first mixed with bile, but later quite clear. Its walls may become extremely thin, or may be thickened from inflammation. This is hydrops vesicae felleae, or mucocele of the gall-bladder. Infection and cholecystitis are very prone to occur under these conditions. The distended gall-bladder may be the site of painful spasmodic contractions resembling biliary colic, except that jaundice is usually absent; in these cases the condition is very likely to be regarded as indigestion. Nausea and persistent vomiting may be very troublesome. I have seen fatal vomiting in a woman in whom the presence of small calculi in the cystic duct was the only morbid condition at the necropsy. Jaundice may, however, be brought about by extension of spasm to, or by concomitant inflammation of, the common bile-duct. According to Riedel,[1] jaundice is present in from 10 to 15 per cent of the cases in which a calculus is impacted at the neck of the gall-bladder. Attacks of painful spasm with intermittent distension of the gall-bladder have been explained as depending on the valvular action of a calculus in the neck of the gall-bladder which allows bile to enter the gall-bladder but not to leave it. It is, however, more probable that the distension of the gall-bladder is due to inflammation of the mucosa of the cystic duct, which also accounts for some of the pain. Conversely it has been stated that the valvular action of the calculus may only allow mucus to pass out of the gall-bladder.

A *distended gall-bladder* appears as an abdominal tumour in the right half of the abdomen; in very rare instances it is so large as to occupy the greater part of the abdomen, and has been mistaken for ascites and tapped.

In a case of Lawson Tait's[2] it contained 11, in Collinson's[3] 25, and in Terrier's[4] 42 pints of fluid. Large cystic gall-bladders occur almost always in women.

Usually it is not larger than the closed fist; it is pear-shaped at first, and as it grows becomes cucumber-shaped (Doran[5]). The dilated gall-bladder may be associated with a Riedel's linguiform lobe, and as a result

[1] Riedel. *Berlin. klin. Wchnschr.*, 1901, xxxviii, 78.
[2] Tait, L. *Lancet*, Lond., 1889, i, 1294.
[3] Collinson. *Brit. Med. Journ.*, 1909, i, 1294.
[4] Terrier. *Bull. Acad. de méd.*, Paris, 1890, 3. s., xxiv, 831.
[5] Doran. *Brit. Med. Journ.*, 1905, i, 1316.

the gall-bladder may form a tumour in the right iliac fossa and imitate appendicitis. H. J. Waring[1] figures a gall-bladder which entered into a right femoral hernia. It forms a smooth, tense, pear-shaped tumour with the apex upwards and the base downwards. It usually moves with respiration and can be displaced laterally, but not downwards. It is separated from the liver by a groove or depression, is immediately under the abdominal walls, and in thin patients may be visible as a raised surface. It is not tender unless there is concomitant inflammation. It may be resonant on percussion. A gall-bladder distended with mucus from obstruction of the cystic duct may subsequently shrivel up.

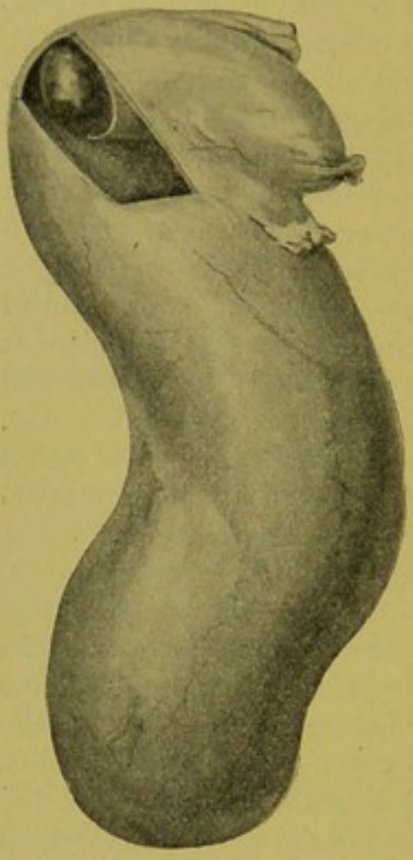


FIG. 106.—Calculus impacted in the cystic duct; cholecystitis with distension of the gall-bladder, mucocele. St. George's Hospital Museum, Series ix, 199g.

A distended gall-bladder must be distinguished from a floating kidney, a renal tumour or hydronephrosis, a tumour of the pylorus, a growth in the transverse colon, an ovarian cyst fixed by adhesions. Confusion is most likely to arise between a distended gall-bladder and a floating kidney on the right side, since both are commoner in women and may be accompanied by attacks of severe pain followed by jaundice. An enlarged gall-bladder forms a tumour which is much more constant and does not disappear or vary in position in the same way as a floating kidney. A gall-bladder is usually movable, but is limited by its attachment to the liver and cannot be displaced into the false pelvis like a floating kidney. If displaced backwards towards the loin, it returns to its former position directly the pressure is removed, whereas a floating kidney tends to remain there as long as the patient is recumbent. A distended gall-bladder does not escape from one's grasp in the same way that a floating kidney does. A careful bimanual examination should always be made. Distension of the colon with air (Ziemssen's test) may be useful, as it should press the gall-bladder forwards and displace a floating kidney backwards; but it is not infallible. Mayo Robson met with a case in which it pushed a growth of the right suprarenal forwards. Kehr also distrusts this test, as the colon may pass in front of the gall-bladder. In a fat person it may be very difficult to distinguish between a floating kidney and a distended gall-bladder. In some cases a floating kidney and a distended gall-bladder may both be present, and may be adherent to each other (Reymond[2]).

[1] Waring. *Diseases of the Liver*, p. 235, 1897.
[2] Reymond. *Rev. de chir.*, Paris, 1900, xxi, 749.

Chance[1] described a dilated gall-bladder containing 200 calculi which exactly imitated a tuberculous kidney.

A tumour of the pylorus lies in a plane, roughly speaking, at right angles to that of the gall-bladder and is hard and tender. In gall-bladder cases there may be gastric symptoms and some dilatation of the stomach from pyloric obstruction, but the gastric symptoms are not so prominent as in pyloric new-growth. A tumour of the transverse colon is less sharply defined than a dilated gall-bladder, and, like the pyloric tumour, tends to have its long axis at right angles to that of a distended gall-bladder. Faecal impaction in the transverse colon will usually be accompanied by faecal masses elsewhere in the abdomen, and the condition will be cleared up or altered by the use of enemas. It may be impossible to distinguish between a small dependent hydatid cyst and a dilated gall-bladder until the abdomen is opened (*vide* p. 628). Aspiration would settle the matter, but this is too dangerous a method to be recommended.

In a woman aged forty a dilated gall-bladder containing 11 pints of liquid, due to a calculus impacted in the cystic duct, imitated a parovarian cyst (L. Tait[2]).

Naunyn[3] quotes two cases in which a calculus in the cystic duct exerted direct pressure—on the portal vein in one instance, and on one of its branches in the other—and set up pylethrombosis. Haematemesis may thus be an indirect result of cholelithiasis. A calculus in the cystic duct may possibly exert pressure on the common hepatic duct and so give rise to jaundice.

The passage of calculi along the cystic duct dilates and straightens out the tortuous lumen of the duct, and so facilitates the subsequent passage of calculi from the gall-bladder. The valves of Heister, which under ordinary conditions obstruct the return of a calculus from the duct into the gall-bladder, become almost obliterated and only appear as slight elevations of the mucous membrane; when thus altered, they may allow a calculus to travel towards the gall-bladder.

In a case under my care a large gall-stone in the common duct was displaced at a laparotomy, undertaken for its removal, by manipulation, and was thought to have passed into the duodenum. At the necropsy, however, it was in the gall-bladder (*vide* p. 558).

(3) **Mechanical Effects of Gall-stones in the Common Bile-duct.**—The passage of a calculus through the common bile-duct sets up biliary colic (*vide* p. 731). A calculus may, however, pass into the common duct and become permanently lodged there without giving rise to the symptoms of colic. While in the common duct the calculus increases in size from deposit on its outer surface.

[1] Chance. *Med. Chron.*, Manchester, 1902, xxxvii, 120.
[2] Tait. *Lancet*, Lond., 1889, i. 1294.
[3] Naunyn. *Cholelithiasis*, p. 123. Transl. New Sydenham Soc., 1896.

Situation of the Calculi in the Common Duct.—Though statistics are not unanimous, the commonest site for calculi appears to be the lower end of the common duct and the ampulla Vateri.

In Courvoisier's 123 cases the calculi were found to occupy the whole of the common bile-duct in 26 ; the upper segment in 17 ; the middle segment in 19 ; to be close to the duodenum in 20 ; in the orifice of the biliary papilla in 41 ; so that in almost exactly half the cases the calculus was close to the lower end of the duct. In 380 operation cases Mayo Robson [1] found the calculus in the duodenal end in 67 per cent ; in the middle portion in 18 per cent ; and at the upper end in 15 per cent. From a smaller number of cases Vautrin [2] came to the opposite conclusion : number of cases, 47 ; calculi in part of the duct above the duodenum, 27 ; in part of duct in contact with the duodenum, 18 ; in the ampulla Vateri, 2. This distribution he explained by the fact that the duct is readily dilatable above the duodenum, but resists dilatation where it is supported by the pancreas. The passage of a calculus from the lower end of the common duct into the ampulla is probably a matter of time.

Number of Calculi in the Common Duct.—In the great majority of cases there is a single calculus ; thus, in 149 observations Courvoisier [3] found that in 95 there was a single calculus, in 36 instances there were from two to six calculi, and in the remaining 18 a dozen or more calculi in the duct. A single calculus is usually firm, but there may be a soft, crumbling mass which fills the whole of the dilated duct and may extend into the common hepatic duct. Several soft crumbling calculi may be found. Mayo Robson once removed 88 calculi from the common duct.

Results and Clinical Features.—A calculus in the common duct often sets up inflammation, the manifestations of which are fully described on p. 759. Here we are only concerned with the purely mechanical effects. Reflex irritation of calculi in the common duct may give rise to vomiting. Leclerc [4] reports a case in which vomiting persisted for forty days until two calculi were removed from the common duct ; there was no other cause, such as adhesions or pyloric obstruction, for the vomiting.

A calculus may completely obstruct the common duct, partially occlude the lumen so that some bile can run past it into the duodenum, or be floating in the common duct and exert a ball-valve action (Osler,[5] Fenger [6]). A calculus which at first is firmly impacted and completely occludes the common duct may subsequently become loose. This is due to several factors ; the obstruction dilates the ducts above and thus leads to widening of the duct at the point of impaction ; the constant pressure of the calculus produces atrophy of the walls of the common duct, while inflammatory softening and ulceration are extremely likely to occur. It

[1] Mayo Robson. *Diseases of the Gall-bladder and Bile-ducts*, p. 278, 1904.
[2] Vautrin. *Rev. de chir.*, Paris, 1896, xvi, 454.
[3] Courvoisier. *Path. u. Chir. d. Gallenwege*, 1890.
[4] Leclerc. *Lyon méd.*, 1903, c, 737.
[5] Osler, W. *Med. Times and Gaz.*, 1881, ii, 111.
[6] Fenger, C. *Am. Journ. Med. Sc.*, Phila., 1896, cxi, 125.

is, therefore, rare for absolute biliary obstruction to persist for a long time, but jaundice may be kept up both by intermittent obstruction depending on the ball-valve action of a calculus and also by concomitant inflammation of the bile-ducts (*vide* p. 759). Jaundice which has been marked early in the course of the impaction may wane and finally disappear, and after death a loose calculus may be found in the duct. Griffon[1] records four cases of this kind in which the calculus was found just above the biliary papilla. In exceptional instances there may never at any time be jaundice although the common duct contains calculi.

Chronic obstruction of the bile-duct with calculi may, however, induce long-standing jaundice. In these cases there may be a large crumbling calculous mass occupying a considerable extent of the common bile-duct. A calculous accumulation of this kind grows from deposit of bilirubin-calcium and is accompanied by infective cholangitis. When the duct contains a single calculus, jaundice, though present for a time, usually passes away. The occurrence of malignant disease of the duct at the site of a calculus is very rare.

As the result of obstruction of the common duct by calculi there may be (i) cylindrical or (ii) saccular dilatation of the duct. (i) *Cylindrical dilatation* is the commoner. The duct is often the size of a chemical test-tube, and may be larger and resemble a piece of intestine. The cylindrical dilatation may spread through the common and hepatic ducts into the intrahepatic bile-ducts. The dilatation is more marked on the surface of the organ, and is often more prominent in the left lobe, probably because there is less resistance on the surface of the liver and especially in the smaller left lobe. Local saccular dilatation of the varicose bile-ducts on the surface of the liver may occur.

(ii) *Saccular Dilatation.*—In rare instances the common bile-duct may form a large cyst which may be diagnosed as a dilated gall-bladder, a pancreatic cyst, a hydatid cyst, etc. The condition is like that described on p. 659. Occasionally there are local cystic dilatations in the intrahepatic branches of the bile-ducts on the surface of the liver; this local dilatation may be superimposed on a widespread cylindrical dilatation.

Simply from distension with bile *the liver* becomes at first enlarged. Subsequently atrophy of the liver cells occurs, with prominence of the existing fibrous tissue. The question whether mere stasis of the bile can lead to genuine hepatic cirrhosis has given rise to considerable discussion and experimental investigation (*vide* p. 327). The conclusions from human morbid anatomy are that biliary obstruction alone does not induce real cirrhosis, but if infection of the bile-ducts occurs, pericholangitic fibrosis will result. In obstruction of the ducts with calculi infective cholangitis is readily produced, and thus fibrosis of the liver may result.

In very rare instances a calculus in the common bile-duct may

[1] Griffon. *Bull. Soc. Anat. Paris*, 1896, lxxi, 513.

mechanically compress the portal vein and give rise to thrombosis (Naunyn,[1] Westenhoffer,[2] Körte [3]).

Diagnosis.—In cases in which a stone has entered the common duct without any symptoms of colic, the painless and gradual onset of jaundice may suggest carcinoma of the head of the pancreas. The differential diagnosis is considered on p. 762.

(4) **The Mechanical Effects of a Calculus in the Ampulla of Vater.**—A calculus may bulge the papilla into the duodenum, and prolapse of the terminal portion of the duct comparable to prolapse of the ureter into the urinary bladder has been described (Bland-Sutton [4]). A difference between the mechanical effects of a calculus in the ampulla and of one in the lower end of the bile-duct is that a calculus in the ampulla of Vater may in addition obstruct Wirsung's duct. The accessory duct of Santorini may, however, carry off the secretion into the duodenum, and so prevent any accumulation of the pancreatic juice in the ducts. In about one-third of the cases, however, there is no communication between the two ducts (Schirmer [5]), and in these cases obstruction of the orifice of Wirsung's duct would lead to its distension with pancreatic secretion.

As a matter of fact, however, there is nearly always some additional inflammatory change when a calculus is in the ampulla of Vater. This sets up pancreatitis and leads to enlargement and fibrosis of the pancreas, dilatation of Wirsung's duct, and in some instances to the formation of pancreatic calculi. The chronic interstitial pancreatitis due to obstruction of the ducts is hardly ever so extensive as to destroy the islands of Langerhans, or to cause glycosuria or diabetes (Opie [6]).

When a small calculus is impacted in the ampulla of Vater close to the biliary papilla and is not sufficiently large to obstruct the opening of the main duct of the pancreas into the ampulla Vateri, the direct mechanical obstruction to the flow of bile into the duodenum results in the passage of bile into the pancreatic duct. This has been shewn by Halsted and Opie [7] and by Bunting [8] to have occurred in fatal haemorrhagic pancreatitis. Opie, moreover, proved by experiments on dogs that the passage of bile into the pancreatic duct induces haemorrhagic pancreatitis; and Flexner [9] has shewn that the bile salts are the active factor in producing pancreatitis, whilst the colloid constituents of the bile exert a protective action. He suggests that bile containing a large amount of mucilaginous (or colloidal) constituents, as in biliary obstruction, or of albuminous products, as in inflammatory conditions, provides exactly the theoretical requirements for subacute or chronic lesions of the pancreas,

[1] Naunyn. *Cholelithiasis*, p. 133. Transl. New Sydenham Soc., 1896.
[2] Westenhoffer. *Semaine méd.*, Paris, 1903, xxiii, 33.
[3] Körte. *Ibid.*
[4] Bland-Sutton. *Gall-stones and Diseases of the Bile-ducts*, p. 87, 1907.
[5] Schirmer. *Inaug. Dissert.*, Basel. Quoted by Opie. *Am. Journ. Med. Sc.*, Phila., 1901, cxxi, 30.
[6] Opie, E. L. *Journ. Exper. Med.*, N.Y., 1901, v, 397.
[7] Halsted and Opie. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 179.
[8] Bunting. *Ibid.*, 1906, xvii, 265.
[9] Flexner. *Journ. Exper. Med.*, N.Y., 1906, viii, 167.

should such bile enter the pancreatic duct. The reason why impacted calculi in the ampulla of Vater only rarely induce haemorrhagic pancreatitis is that usually the calculi are sufficiently large to obstruct the orifice of Wirsung's duct and to interfere with the entrance of bile into the pancreatic duct. Williams and Busch,[1] however, suggest that the passage of gall-stones may so dilate the opening of papilla that intestinal contents are able to pass into the pancreatic duct and produce inflammation and necrosis of the pancreas. A pancreatic calculus which passes into the ampulla of Vater would differ from a gall-stone in giving a shadow with *x*-rays and causing distension of the gall-bladder (Murray [2]).

(5) **Mechanical Obstruction of the Intestines by Gall-stones.**—*Incidence.*—When a large gall-stone ulcerates out of the gall-bladder into the duodenum, or in rare instances into the colon, it may produce mechanical obstruction of the bowel. This is decidedly rare; thus at the Leeds Infirmary, where a large number of gall-stone operations are done, only one case occurred in ten years,[3] and there were three cases at St. George's Hospital in twenty-one years. But from the interest attaching to such rare and striking cases a large number have been reported, and Morestin,[4] in 1900, was able to refer to as many as 242 cases. The relative frequency of this cause to other causes of intestinal obstruction has been variously estimated at from 1 to 13 to 1 to 45.

In 295 cases of intestinal obstruction Fitz found 23 due to gall-stones, or 1 in 13; Gibson,[5] 40 in 696, or 1 in 17; Leichtenstein, 41 in 1152, or 1 in 28; in 669 consecutive cases of intestinal obstruction in thirteen years at the London Hospital, Barnard [6] found 15, or 1 in 45, due to gall-stones.

Entrance of the Calculus into the Intestine.—It is probably very seldom that a calculus which passes down the bile-duct into the duodenum is of sufficient size to occlude mechanically the ileo-caecal valve. In some instances a large calculus is found projecting from the lower end of the bile-duct, and it is conceivable that such a calculus, after squeezing through the biliary papilla into the duodenum, would be large enough to obstruct the ileo-caecal valve. It is probable that a comparatively small calculus, after passing into the intestine, may increase in size from addition of phosphates to its surface, as in Eve's case,[7] and so become large enough to obstruct the ileum or ileo-caecal valve. Treves [8] removed a calculus, with a diameter in its long axis of 1½ inches, from the ileum of an old lady who for years had taken carbonate of magnesium daily. Its nucleus was a small gall-stone, and its large size was due to layers of magnesia and faecal material. In very rare instances intestinal

[1] Williams and Busch. *Journ. Med. Research*, Boston, 1907, xvii, 35.
[2] Murray. *Proc. Roy. Soc. Med.*, 1912, v (Surg. Sect.), 131.
[3] *Vide* Moynihan. *Med. Chron.*, Manchester, 1903, xxxviii, 277.
[4] Morestin. *Bull. Soc. Anat. Paris*, 1900, lxxv, 196.
[5] Gibson, C. L. *Ann. Surg.*, 1900, xxxii, 506.
[6] Barnard, H. L. *System of Medicine* (Allbutt and Rolleston), 1907, iii, 744.
[7] Eve, F. *Trans. Clin. Soc.*, Lond., 1895, xxviii, 91.
[8] Treves, F. *Intestinal Obstruction*, p. 193, 2nd ed., 1899.

obstruction may be due to impaction of a congeries of small calculi in the intestine (Cantlie [1]). A calculus not sufficiently large to obstruct the normal small intestine may, if the intestine is narrowed from some other cause, completely obstruct the stricture.

Thus Mayo Robson [2] found a calculus entangled in a pouch between two tuberculous strictures of the ileum. Garrett [3] found a gall-stone arrested where the small intestine passed under an omental cord; the bowel was thus completely occluded. Moynihan [4] found a large gall-stone fitted as tightly as a cork in the lumen of a malignant mass at the ileo-caecal valve. Bush [5] found a gall-stone completely occluding the intestine in a hernial sac.

A comparatively small calculus may, especially if it is angular, set up spasm of the intestinal wall around the calculus, and so lead to closure of the lumen of the bowel; this explains why in some fatal cases of gall-stone obstruction the calculus has been found loose in the bowel. Another method by which a comparatively small calculus may cause intestinal obstruction is by setting up localised inflammation of the mucous membrane of the bowel in its immediate neighbourhood. The resulting swelling and spasm of the wall of the bowel may then lead to impaction of the calculus.

In the vast majority of cases mechanical obstruction of the intestine by gall-stones is due to a large calculus which has ulcerated out of the gall-bladder into the duodenum, or less commonly into the transverse colon. Intestinal obstruction is much more likely to follow the passage of a calculus into the duodenum, as it has then to pass through the jejunum and the narrowed lower part of the ileum, than in cases in which a calculus ulcerates directly from the gall-bladder into the colon.

It is stated that a calculus may enter the intestine and remain there comparatively quietly for days, months, or even years, and yet eventually give rise to intestinal obstruction. Ulceration and thickening of the lower part of the ileum have been found in association with a number of calculi in that position (N. Ward [6]). When a calculus is in the intestine, it may set up repeated attacks of colic, vomiting, and pain, suggesting mild obstruction, and finally bring about acute obstruction.

In Anderson and Smith's [7] case the calculus was thought to have entered the intestine fifteen and in Eve's case ten years before acute obstruction was produced.

As there may be two calculi in the intestine, attacks of transient obstruction may recur even after a calculus has been passed by the bowel.

It is probable that all large calculi spontaneously passed by the bowel

[1] Cantlie, J. *Brit. Med. Journ.*, 1904, i, 181.
[2] Mayo Robson. *Trans. Clin. Soc.*, Lond., 1902, xxxv, 58.
[3] Garrett. *Brit. Med. Journ.*, 1902, ii, 789.
[4] Moynihan. *Clin. Journ.*, Lond., 1906–7, xxix, 411.
[5] Bush. *Bristol Med.-Chir. Journ.*, 1903, xxi, 301.
[6] Ward, N. *Trans. Path. Soc.*, Lond., 1850–52, iii, 365.
[7] Anderson and Smith. *Lancet*, 1887, ii, 1103.

have entered the transverse colon from the gall-bladder by a cholecysto-colic fistula, for a calculus with a diameter of an inch or more would almost certainly become impacted at the ileo-caecal valve. Among Gibson's[1] 40 cases the largest gall-stone weighed three and a half ounces.

Site of the Obstruction.—The obstruction is most frequent in the lower end of the ileum near the ileo-caecal valve. When a large calculus ulcerates from the gall-bladder into the duodenum, the site of the obstruction may be in the duodenum itself, at its junction with the jejunum, or in the ileum. When a calculus ulcerates into the colon, the obstruction may occur in the sigmoid flexure or close to the anus. As seen at operation the contraction of the empty intestine immediately below the calculus produces a septum on which the calculus rests (Barnard).

In 104 cases Lesk[2] found the site of obstruction to be in the duodenum in 5, in the jejunum in 17, in the ileum in 36, in the ileum near the ileo-caecal valve in 26, in the small intestine (not further specified) in 13, in the colon in 6, and in the rectum in 1. In 40 cases collected by Gibson the calculus was impacted in the large intestine in one case only; in the ileo-caecal valve in one instance, and in all the other cases in the small intestine. The larger the gall-stone, the higher up in the small intestine will it be arrested (Barnard).

Sex.—Intestinal obstruction due to gall-stones is very much commoner in women than in men. This is a natural result of the great frequency of cholelithiasis in women.

In Lesk's 148 cases 39 were men and 109 women. In 50 cases which I have collected there were 42 females and 8 males.

The *average age* is over 50 years of age. In 50 recent cases the average age was 62·7 years, and many cases between 70 and 80 years of age have been reported. In Lesk's 148 patients there were 6 under 40 years of age.

Clinical Picture.—The onset is sudden. In some cases it has been preceded by attacks of vomiting and pain, but usually signs suggesting that the calculus has been for some time in the bowel are absent, and there may be no evidence of former gall-bladder trouble or of cholelithiasis. In 41 out of 120 cases the onset was preceded by symptoms which could be referred to ulceration of the calculus into the intestine (Naunyn). Although the bowel is obstructed, it is not strangulated, and as the circulation through its walls is not interfered with, they do not become paralysed and hence tympanites is usually absent, and flatus and faeces are often passed by the bowel. A calculus has been known to ulcerate out of the bowel and set up peritonitis.[3] At first pain and collapse are not marked. When the calculus is entering the duodenum the pain is referred to the epigastrium, later when it has passed into the

[1] Gibson. *Ann. Surg.*, 1900, xxxii, 506.
[2] Lesk. *Deutsche Ztschr. f. Chir.*, Leipz., 1908, xcix, 47.
[3] Jeaffreson. *Brit. Med. Journ.*, 1868, i, 531.

small intestine the pain is more diffuse and referred to the umbilicus. Vomiting is an early symptom and extremely profuse, and when the calculus is impacted in the duodenum or in the upper part of the small intestine, the vomited matter is bilious and may become stercoraceous. It may contain blood from haemorrhage produced in the ulceration of the calculus into the duodenum.

As the calculus passes down the small intestine the vomiting becomes less copious; this remission usually occurs on the third day (Barnard). After this the calculus may become impacted, so that unless relieved by operation death occurs from acute obstruction. In about 50 per cent the symptoms are spontaneously relieved, sometimes quite suddenly, so that the patient at once knows that his condition has improved. In some instances, even though the patient has been relieved from the acute symptoms of obstruction, the wall of the bowel is so damaged that perforation or leakage from an ulcer occurs and sets up peritonitis.

Duration and Prognosis.—In fatal cases death from collapse usually occurs within five to ten days after the onset. In Sands' case [1] recovery took place after the condition had lasted for twenty-eight days; this is the longest case on record. About 50 per cent of the cases die if not operated upon. The statistics of cases operated upon shew a high mortality; thus, in Schüller's 82 cases 56 per cent, in Sir J. Hutchinson's 50 per cent, and in Courvoisier's 125 cases of operation, 44 per cent, died. The advanced age of the patients is, no doubt, partly responsible for this high mortality; but operation after the fourth day of obstruction is hardly ever followed by recovery (Barnard).

Diagnosis.—When there is a definite history of gall-stones in the past and acute obstruction comes on suddenly with the disappearance of a tumour in the position of the gall-bladder, and the presence of a hard lump elsewhere in the abdomen, the diagnosis would appear to be fairly clear. But, unfortunately, in a number of the cases there is no history of cholelithiasis, and the gall-stone is hardly ever felt in the abdomen before the operation. In two cases reported by Barnard [2] the calculus was felt before operation. It is possible that examination under an anaesthetic might enable a calculus to be felt in a certain number of cases. But as a matter of fact, the condition is very seldom correctly diagnosed before the abdomen is opened or the calculus is spontaneously passed by the rectum.

Treatment.—As the symptoms are those of intestinal obstruction and it is seldom possible to make a certain diagnosis of mechanical obstruction due to a gall-stone, the safest course is to open the abdomen and remove the stone by incising the bowel. In cases in which the stone is comparatively small and is impacted at the lower end of the ileum, it might be pressed on into the colon. It is important that if an operation is necessary, it should be undertaken as soon as possible, for the patients are usually elderly and are often wanting in vitality.

[1] Quoted by Treves. *Intestinal Obstruction*, p. 388, 2nd ed., 1899.
[2] Barnard, H. L. *Ann. Surg.*, 1902, xxxvi, 161.

Medical treatment has been successful in a certain number of cases. The most reasonable method seems to be to give belladonna or atropine in order to relieve spasm, and so to allow of the onward passage of the calculus; this method should be adopted in less severe cases in which there is any reason to suspect or believe that the cause of obstruction is an impacted calculus in the intestine, and at an early stage. In such cases Mayo Robson[1] advises morphine to relieve the pain, and extract of belladonna ($\frac{1}{4}$ gr.) every four hours. Under chloroform anaesthesia a thorough examination of the abdomen can be made, by which the diagnosis may be cleared up if it is doubtful, and if a calculus is felt it may be pressed on. If these measures fail, operation should be undertaken without further delay.

J. Hutchinson[2] advocated a policy of non-interference in gall-stone obstruction, and urged the use of anaesthetics, opium, and rectal injections with air or fluid to diminish spasm and assist in the passage of the calculus. Massage has been followed by cure.

In Martin and Brouardel's[3] case massage was employed on the sixth day of obstruction and on the next day a large gall-stone and ten smaller stones were evacuated.

IV. The Inflammatory and Infective Changes set up by Gall-stones include a large number of irregular manifestations and results, and will be conveniently described under the various headings of changes in connexion with—(A) The gall-bladder; (B) the cystic duct, (C) the common bile-duct; (D) the ampulla of Vater; and (E) the various fistulae.

Synopsis

(A) Gall-bladder: cholecystitis; ulceration; haemorrhage; scars, hour-glass contraction; perforation; pericholecystitic adhesions.

(B) Cystic duct: swelling; obliteration; diverticulum.

(C) Common bile-duct: intermittent hepatic fever; extension to pancreatic duct—pancreatitis, cysts; extension to portal vein—pylephlebitis.

(D) Ampulla of Vater.

(E) Fistulae.

(A) **Inflammatory and Infective Changes in the Gall-bladder.**—The presence of gall-stones, which are due to comparatively mild inflammation of the gall-bladder, disposes to fresh infection and thus to cholecystitis and to a vicious circle. No doubt gall-stones also favour persistence of the original infection, and thus are important in connexion with typhoid "carriers."

[1] Mayo Robson. *Diseases of the Gall-bladder and Bile-ducts*, p. 157, 1904.
[2] Hutchinson, J. *Arch. Surg.*, Lond., 1890–91, ii, 4.
[3] Martin et Brouardel. *Bull. Soc. Anat. Paris*, 1875, l, 570.

Mieczkowski,[1] from examination of the bile of 15 patients whose gall-bladders were healthy and were aspirated during laparotomy for other conditions, concludes that human bile is sterile. In 23 cases of cholelithiasis investigated by him the bile was infected in 18. Gall-bladders containing gall-stones, therefore, are usually infected and are thus prone to fresh attacks of cholecystitis.

Cholecystitis.—Inflammation of various degrees of severity may supervene in a gall-bladder containing gall-stones. There may be acute infective cholecystitis, serous, sero-fibrinous, or purulent, which may go on to ulceration and perforation or gangrene; or there may be chronic serous or purulent cholecystitis, the latter condition being often spoken of as empyema of the gall-bladder. Descriptions of these various forms of cholecystitis are given elsewhere (*vide* p. 609). Acute cholecystitis may set up local peritonitis, and by paralysing the peristaltic movements of the intestines, may imitate acute intestinal obstruction.

Ulceration of the mucous membrane of the gall-bladder may give rise to: (1) Changes in the gall-bladder—(*a*) haemorrhage; (*b*) scars; (*c*) hour-glass contraction and diverticula. (2) Perforation of the gall-bladder—(*a*) into the general cavity of the peritoneum; (*b*) into part of the peritoneum shut off by adhesions; (*c*) into the liver; (*d*) into other adjacent structures, such as bile-ducts, portal vein, hepatic artery; (*e*) into the duodenum, colon, etc. (*vide* Fistulae, p. 766).

(1) *Changes in the Gall-bladder.*—(*a*) *Haemorrhage.*—An ulcer due to cholecystitis may cause haemorrhage into the gall-bladder. This may depend on erosion of a small vessel in the wall of the gall-bladder, but in rare instances ulceration of the gall-bladder may involve the hepatic artery and give rise to an aneurysm (*vide* p. 45) which may subsequently rupture.

(*b*) *Scars.*—As a result of the healing of an ulcer in the mucous membrane of the gall-bladder a scar results. In 343 cases of cholelithiasis tabulated by Schloth[2] there were 14 with cicatrices. These are usually in the fundus or close to the origin of the cystic duct. Their site depends to some extent on the mechanical irritation of the calculus. It may be pointed out, however, that what looks like a scar on the surface of the gall-bladder may in reality be a very early stage of primary carcinoma.

(*c*) *Hour-glass Contraction.*—Cicatrisation following inflammation and ulceration may lead to hour-glass contraction. The gall-bladder may thus become divided into two compartments communicating by a narrow orifice, one or both of which may contain calculi. The orifice between the two may become closed, so that the fundus no longer communicates with the cystic duct.

Kehr[3] records such a case in which one compartment contained pus, the

[1] Mieczkowski. *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1900, vi, 307; Abstract in *Am. Journ. Med. Sc.*, 1902, cxxiii, 372.

[2] Schloth. *Diss.*, Würzburg, 1887. Quoted by Naunyn.

[3] Kehr. *Diagnosis of Gall-stone Disease.* American transl., p. 48, 1901.

other clear bile. In Donald's[1] case the peripheral part contained mucus only.

Courvoisier collected 15 examples of hour-glass gall-bladder, and others have been recorded since his monograph was published in 1890. Much the same appearance is seen in cases in which a number of septa from the walls of the gall-bladder form ridges between a succession of calculi. In this way the gall-bladder may become divided into several compartments communicating by narrow orifices. Barnard[2] described a gall-bladder containing four such compartments, one of which opened into the duodenum.

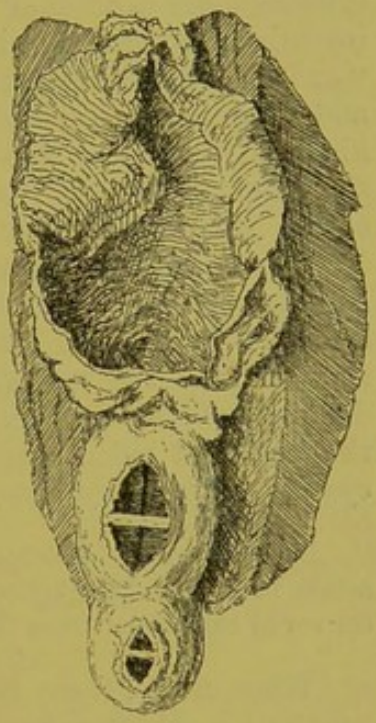


Fig. 107.—Hour-glass contraction of gall-bladder. The fundus, which communicates with the remainder of the gall-bladder through a minute orifice admitting a bristle, contains two calculi, one above the other, partially separated from each other by a septum from the wall of the gall-bladder. (Drawn by Dr. G. H. Goldsmith.)

(2) *Perforation of the Gall-bladder.*—(*a*) *Into the General Cavity of the Peritoneum.*—Perforation or rupture of an inflamed gall-bladder allows bile and even gall-stones to escape into the general cavity of the peritoneum and sets up severe and usually fatal peritonitis. This is especially seen in phlegmonous and gangrenous cholecystitis (*vide* pp. 621 and 623).

(*b*) *Into a Localised Part of the Peritoneum cut off by Adhesions.*—A local abscess formed in connexion with perforation of a calculous gall-bladder into part of the peritoneum previously cut off by adhesions may contain gall-stones, and may open in one or more of a number of different situations, such as the duodenum, stomach, on the surface of the abdomen, etc. (*vide* Biliary Fistulae), or present as a subphrenic abscess, or give rise to an empyema on the right side.

(*c*) *Ulceration of the Gall-bladder into the Substance of the Liver.*—Ulceration of the gall-bladder may extend directly into the liver; it may then give rise to an abscess cavity in the liver communicating with the gall-bladder, or to haemorrhage into the gall-bladder. This, however, is very rare.

Arbuthnot Lane[3] described a case in which the liver shewed an encysted cavity, containing calculi and opening into the gall-bladder; and a second case[4] in which the gall-bladder, probably containing a calculus, exhibiting on its anterior surface a rupture extending into the liver and giving rise to profuse haemorrhage into the gall-bladder.

[1] Donald. *Glasgow Med. Journ.*, 1898, N.S., xlix, 348.
[2] Barnard, H. L. *Ann. Surg.*, 1902, xxxvi, 161.
[3] Lane. *Lancet*, Lond., 1893, ii, 874.
[4] Idem. *Trans. Clin. Soc.*, Lond., 1895, xxviii, 160.

(*d*) Ulceration of the gall-bladder may extend into the common bile-ducts, portal vein, and hepatic artery in the lesser omentum. These extremely rare events are also referred to under the head of biliary fistulae (*vide* p. 772). Ulceration of the hepatic artery may give rise to an aneurysm (*vide* p. 45).

Pericholecystitic Adhesions.—Inflammation of a calculous gall-bladder readily gives rise to adhesions which unite it to adjacent organs, especially the pyloric end of the stomach and the duodenum. According to the thickness and density of the adhesions symptoms of a varying degree of intensity are induced. In the slighter cases there is pain after food, or "adhesion dyspepsia," due to interference with the gastric movements and to dragging on adhesions. Dense adhesions may so constrict or kink the pylorus or duodenum that pyloric obstruction is induced, and the case may closely resemble carcinoma of the pylorus with dilatation of the stomach (Mayo Robson,[1] Tuffier and Marchais,[2] Thomas,[3] Page,[4] Villard[5]). In many cases the symptoms come on very gradually, and a considerable time after definite symptoms of gall-stones, so that their causation is obscure. In a few cases haematemesis has been recorded, thus making the resemblance to primary gastric disorder even more definite. When dieting and thorough medical treatment fail to relieve these cases of pyloric stenosis due to adhesions set up by calculous cholecystitis, exploratory laparotomy is justified.

Dr. Fütterer, of Chicago, kindly sent me photographs of the gall-bladder in a case in which old adhesions between a calculous gall-bladder and the pylorus conveyed carcinoma from the pylorus to the gall-bladder.

When a gall-stone has ulcerated into the duodenum the cicatricial contraction which follows may give rise to stricture of the duodenum and so to obstruction.[6] Bland-Sutton[7] mentions a case of hour-glass stomach which may have been produced in this manner. In some instances adhesions due to past cholecystitis may form bands which constrict the colon or the small intestine and so produce acute intestinal obstruction.

Niles[8] reported a case of stenosis of the hepatic flexure by pericholecystitic adhesions which was cured by dividing the adhesions and removing 60 small calculi from the gall-bladder.

Adhesions may be formed between the gall-bladder and the vermiform appendix as the result of inflammation of the gall-bladder. This may explain why cholelithiasis often gives rise to pain suggesting appendicitis.

[1] Mayo Robson. *Trans. Clin. Soc.*, Lond., 1894, xxvii, 1.
[2] Tuffier et Marchais. *Rev. de chir.*, Paris, 1897, xvii, 100.
[3] Thomas. *Rev. méd. de la Suisse Rom.*, Genève, 1897, xvii, 5.
[4] Page, F. *Brit. Med. Journ.*, 1897, i, 205.
[5] Villard. *Lyon méd.*, 1902, xcix, 737.
[6] Labadie-Lagrave et Magdelaine. *Rev. gén. de clin. et de thérap.*, Par., 1898, xii, 401.
[7] Bland-Sutton. *Clin. Journ.*, Lond., 1906-7, xxix, 18.
[8] Niles, H. D. *Ann. Surg.*, 1902, xxxv, 344.

(B) **Results of Inflammation in the Cystic Duct.**—The impaction or passage of a calculus, especially an angular one, along the cystic duct may set up severe inflammatory changes, ulceration, and subsequently cicatricial contraction of the duct. In some cases inflammatory adhesions around the cystic duct may constrict the neighbouring common hepatic and common bile-ducts. A calculus when impacted may lead to ulceration and bulging of the walls of the duct, so that it becomes encysted in a diverticulum.

In a woman who died of bronchitis in St. George's Hospital the liver was very freely movable and shewed evidence of tight lacing. The neck of the gall-bladder was long, and just at the commencement of the cystic duct there was a recess containing a gall-stone (*vide* Fig. 108). The gall-bladder was not dilated, and bile could easily be driven from the gall-bladder into the duodenum.

Fig. 108.—Gall-bladder with elongated neck and diverticulum at the commencement of cystic duct containing a calculus.

A calculus in such a diverticulum may press on the cystic duct (W. W. Cheyne[1]), or possibly on the common hepatic duct.

A calculus may ulcerate out of the duct and give rise to a localised abscess in the immediate neighbourhood. A calculus in the cystic duct may set up inflammation which spreads into the common duct and so causes jaundice.

(C) **Inflammation and Infective Changes in the Common Bile-duct.**—The inflammation of the common bile-duct associated with the presence of a gall-stone may possibly be an extension of the cholecystitis which originally drove the calculus out of the gall-bladder, but probably in most cases the presence of the calculus favours an ascending infection of the common bile-duct from the duodenum. Calculi in the common duct frequently set up the infective condition described below as intermittent hepatic fever. It may also give rise to ulceration of the duct and to perforation and the formation of a local abscess, or to suppurative cholangitis (*vide* p. 671) and multiple abscesses in the liver.

Intermittent Hepatic Fever.—A characteristic result of calculi in the common bile-duct is a group of symptoms collectively described as intermittent hepatic fever. Its clinical features, first noted by Charcot,[2] and especially insisted upon by Osler,[3] are now well recognised.

Anatomically the calculus "floats" near the lower end of the common bile-duct, which is often greatly dilated. The calculus is movable, and is said to exert a ball-valve action (Osler,[4] C. Fenger[5]). In many cases the

[1] Cheyne, W. W. *King's Coll. Hosp. Rep.*, 1897, iii, 94.
[2] Charcot. *Leçons sur les maladies du foie et des voies biliaires*, p. 178, 1877.
[3] Osler. *Johns Hopkins Hosp. Rep.*, Balt., 1891, ii, 3. *Lancet*, Lond., 1897, i, 1319.
[4] Idem. *Med. Times and Gaz.*, 1881, ii, 111.
[5] Fenger, C. *Am. Journ. Med. Sc.*, 1896, cxi, 125.

dilatation of the duct around and above the gall-stone, which often lies in a pathologically dilated ampulla of Vater, allows bile to trickle past into the duodenum. The gall-stone may make the biliary papilla project into the duodenum. The common and other bile-ducts are dilated, often greatly, and their walls are thickened, but the mucous membrane, though inflamed, is usually free from ulceration. Adhesions over the convexity of the liver, due to past attacks of perihepatitis, are common. The intra-hepatic bile-ducts may be dilated, and from pericholangitis there is increased fibrosis around them with some atrophy of the liver substance; this constitutes the condition often described as obstructive biliary cirrhosis (*vide* p. 331).

The gall-bladder is usually small, thickened, and contracted from past cholecystitis in accordance with Courvoisier's [1] well-known law that in jaundice due to gall-stones the gall-bladder is small, whereas in icterus due to the pressure of a tumour on the ducts the gall-bladder is distended. There are frequently adhesions between the gall-bladder and the adjacent viscera, especially the omentum, stomach, and the transverse colon. There may, or may not, be gall-stones in the gall-bladder. The head of the pancreas is commonly enlarged from chronic interstitial pancreatitis.

Charcot regarded the fever as due to absorption of poisons from the bile-ducts. Netter and Martha,[2] Abbott, and Pick [3] found micro-organisms, especially the colon bacillus, in the ducts. Budd [4] drew an analogy between urethral fever following catheterisation and intermittent hepatic fever. Murchison and Ord [5] regarded the fever as the reflex result of irritation exerted by the calculus.

The striking intermissions in the symptoms may possibly depend on the micro-organisms which have set up acute swelling of the mucous membrane of the duct and biliary obstruction, passing away into the duodenum. Or, on the other hand, periodic intervals of immunity may be developed with the result that the symptoms disappear, only to re-appear when, immunity being exhausted, the micro-organisms, which in the interval, though present, have remained latent, set up a fresh and acute cholangitis.

Clinical Picture.—The symptoms may come on many years after the original attack of cholecystitis which gave rise to the gall-stone, or there may be recurrent attacks of biliary colic eventually terminating in intermittent hepatic fever.

W. Moore [6] reported a case in a woman aged fifty-four who first had jaundice when nineteen years old. For twenty-five years she had had yearly attacks of biliary colic, which recently had been accompanied by jaundice and shivering. Recovery followed removal of a calculus from the common bile-duct and 21 calculi from the gall-bladder.

[1] Courvoisier. *Pathologie u. Chir. d. Gallenwege*, 1890.
[2] Netter et Martha. *Arch. de physiol. norm. et path.*, Paris, 1886, 3. s., viii, 7.
[3] Pick, *F. Verhandl. d. XV. Congr. f. inn. Med.*, Berl., 1897, xv, 468.
[4] Budd. *Diseases of the Liver*, p. 376, 3rd ed., 1857.
[5] Ord, W. M. *Brit. Med. Journ.*, 1887, i, 496.
[6] Moore, W. *Intercolon. Med. Journ. Australas.*, 1899, iv, 407.

There may not be any history of colic from which to date the passage of the calculus into the common duct, so that, especially in old people, the onset of jaundice may be gradual and painless, as in malignant disease. The clinical aspect of these cases may be summed up in the occurrence of ague-like attacks of fever, pain, rigors, and increase in the jaundice, while in the intervals the patients are fairly well and even able to live their ordinary lives. The disease may continue for years, but eventually may terminate in suppurative inflammation of the ducts, the liver, or in the neighbourhood of the calculus.

The attacks, which sometimes closely resemble ague in their periodicity, are accompanied by fever, the temperature going up as high as 103°, rigors, and sweating. The pain is felt in the region of the liver and epigastrium, and may be as severe as that of ordinary biliary colic and necessitate relief by hypodermic injection of morphine. There may be tenderness in the back, close to the tenth dorsal spine on the right side. Jaundice may be transient, intermittent, or disappear after being distinct, or be entirely absent; it was absent in 25 per cent of Moynihan's[1] cases. It is commonly slight during the intervals, but during the attacks it becomes more intense and may be accompanied by itching of the skin; but I have seen most intense pruritus in the absence of jaundice. Vomiting is often present during the attack, and dyspepsia and gastric pain are frequently troublesome. These symptoms are often the most prominent and sometimes the only ones; many cases indeed are regarded as purely gastric. There may be so much pyloric obstruction as to suggest organic stricture due to pericholecystic adhesions; in some instances no adhesions are found on exploration and the pyloric obstruction may be assumed to be due to spasm. I have seen sprue-like diarrhoea associated with attacks of colic and cured by removal of a calculus from the common bile-duct. The liver may be somewhat enlarged and tender during an attack, but the gall-bladder cannot be felt. The spleen is usually palpable during the attacks. There is a leucocytosis during the attack, but not in the intervals (Pick). Temporary glycosuria has been thought to be due to the action of poisons, absorbed from the duct, on the islands of Langerhans, and has been known to disappear when thorough drainage was established (Mansell Moullin[2]). There is excess of urobilin in the urine.

Complications.—Inflammation and ulceration of the common bile-duct in rare instances lead to cicatricial contraction of the duct. Examples of this curiously infrequent sequel are given on p. 661.

Kehr[3] records complete obliteration of the common bile-duct at its junction with the cystic duct due to this cause.

Suppurative cholangitis may supervene, and spread widely into the liver, and into the pancreas (*vide* p. 675).

Diagnosis.—The periodicity of the febrile attacks may closely imitate

[1] Moynihan. *Brit. Med. Journ.*, 1912, i, 347.
[2] Mansell Moullin. *Lancet*, Lond., 1907, i, 1645.
[3] Kehr. *Diagnosis of Gall-stone Disease*, American transl., p. 48, 1901.

malaria, but there is no reaction to quinine and the malarial parasite is not found in the blood. The presence of jaundice in the intervals and its intensification during the attacks should always suggest cholelithiasis. The diagnosis of gall-stones by *x*-rays cannot be relied upon, as no shadow is given unless the calculi contain lime salts. A negative result is therefore of no value.

It is important to distinguish the condition from suppuration of the bile-ducts, which, as has been pointed out, may supervene on intermittent hepatic fever. In suppurative cholangitis the fever is continuous, the paroxysms are more frequent, and there are no intervals of comparatively good health; the patient is much worse, the liver is more enlarged, the gall-bladder may be palpable, and the jaundice is not so marked.

In hepatic abscess the fever is continuous, the liver is more enlarged, and leucocytosis, if present, is constant and does not pass away as it does in intermittent hepatic fever.

In malignant disease the liver is more enlarged and often irregular; the course of the disease is more rapid, and, though there may be fever, it is not periodic. In malignant disease pressing on the ducts, as in carcinoma of the head of the pancreas, the jaundice is deep and the motions are devoid of stercobilin. The gall-bladder is generally distended and the temperature is not raised. Cammidge's [1] tests are of value in the differential diagnosis between stone in the common duct and malignant disease of the head of the pancreas:—

	Stone in Common Duct.	Carcinoma of Pancreas.
Pancreatic reaction.	Positive in 66 per cent.	Negative in 66 per cent.
Urobilinuria.	Present.	Rare.
Crystals of calcium oxalate.	Present.	Rare.
Fat in the faeces.	Proportion of saponified exceeds that of unsaponified fat.	Proportion of saponified less than, or equal to, that of unsaponified fat.

From chronic cholangitis due to infection of the ducts with micro-organisms of no great virulence the diagnosis is difficult; but the pain and intermittent fever are more severe and prominent in the cases complicated by cholelithiasis; and the non-calculous cases react better to urotropin.

Hypertrophic biliary cirrhosis in rare instances comes on acutely and might imitate a calculus passing into the duct; the periodic attacks of

[1] Cammidge. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Med. Sect.), 163.

fever, pain, and increased jaundice are much less severe in biliary cirrhosis; further, splenic enlargement is prominent in biliary cirrhosis, and is absent in the intervals between the attacks in intermittent hepatic fever.

The prognosis is rather bad on medical or expectant treatment, as suppuration may supervene in the bile-ducts, the liver itself, or in the neighbourhood. In 10 cases tabulated by Osler,[1] spontaneous recovery occurred in 5. The outlook is much better if the cases are submitted to operation and the stone or stones removed from the common bile-duct. I have, however, seen persistent diarrhoea like sprue prove fatal a considerable time after successful operation. This case shewed chronic pancreatitis and two ulcers in the duodenum.

Treatment.—In cases in which the attacks occur at considerable intervals medical treatment should be tried. The patient should take a light, digestible diet, avoid stimulants, and keep the bowels open. The dieting of cases with gastric pain is often very disappointing, a result which can hardly be wondered at since the pain and dyspepsia are largely reflex and depend on the presence of the calculus in the duct, or possibly on adhesions around the pylorus. Carlsbad water at home, or better a cure there or at one of the spas mentioned on p. 779 is advisable, and it is well to increase the flow of bile over the calculus in the hope of dissolving its surface sufficiently to allow it to slip into the duodenum. Urotropin combined with salicylate and bicarbonate of sodium should be given to increase the flow of bile and to inhibit bacterial activity; if there is itching, much jaundice, or haemorrhages calcium salts should be given. For the treatment of pruritus see p. 567.

For the pain hot applications, fomentations, or poultices may be tried, but in many cases morphine is required and there is the danger that the habit may be acquired. Antipyrin and phenacetin may be tried, or a mixture containing belladonna and spiritus chloroformi to allay spasm. Turpentine and ether have been given with the same object. With the exception of morphine, these measures often fail. Massage is unsafe, and olive oil by the mouth of no real use so far as removal or solution of the calculus is concerned. In cases in which the patient cannot be operated upon, some prolongation of the intervals between the attacks may follow injection of autogenous vaccines of *B. coli*, isolated from the faeces and proved by the agglutination reaction or the opsonic index to be the infecting agent. I have seen a good effect in one case.

If no improvement follows medical treatment, *operative measures* should be advised before the patient loses too much flesh or gets deeply jaundiced, as these conditions render operation dangerous. Further, from continued infection of the ducts the liver becomes damaged (pericholangitic fibrosis and atrophy); the irritation of other calculi in the gall-bladder favours primary carcinoma; suppurative cholangitis may supervene; and in long-standing cases dense adhesions may form around the gall-bladder and ducts and make operation both more difficult and dangerous. Generally

[1] Osler. *Lancet*, Lond., 1897, i, 1319.

speaking, the time devoted to unsuccessful medical treatment should not exceed two months, but each case must be considered on its merits. The most radical and effective treatment is laparotomy and removal of the stone from the common duct. Probably in some cases operation short of this has done good; mere manipulation of the ducts may drive a softened stone into the duodenum and effectually remove it.

A woman aged fifty-four who had had about 20 attacks within the year came under my care in 1896 in St. George's Hospital. During an attack the temperature went up to 104°, jaundice became more marked, bile appeared in the urine, and there was marked tenderness over the common bile-duct. Mr. Sheild explored the abdomen, broke down adhesions around the common bile-duct, which felt thickened, but did not open the duct, as no calculi were palpable. After this the patient remained free from any further attacks.

Extension of Inflammation and Infection to the Pancreas.—Gall-stones in the common duct, especially when in their usual situation, viz. the lower end, readily give rise to inflammation of Wirsung's duct of the pancreas and pancreatitis. The inflammation may spread (1) from the bile-duct into Wirsung's duct, (2) from the duct by continuity into the pancreas, (3) by the lymphatics (Maugeret[1]).

Thirty-two cases of acute pancreatic lesions, such as haemorrhage, suppuration, acute pancreatitis, have been collected by Opie[2] in which gall-stones were present. Of 105 cases of acute pancreatitis collected by Egdahl[3] 44 were associated with gall-stones. I had previously called attention, though on a much smaller number of cases, to the production of pancreatitis by cholelithiasis.[4]

The following list of changes in the pancreas, due to cholelithiasis, is based on Mayo Robson's[5] classification: (*a*) Changes in the ducts: catarrh, suppuration, lithogenic inflammation. (*b*) Changes in the pancreas: (i) acute; catarrhal, haemorrhagic, gangrenous, suppurative inflammation; (ii) subacute; localised abscess; (iii) chronic, interstitial pancreatitis.

The production of suppuration in the pancreas by calculi in the common bile-duct was described in 1882 by Norman Moore.[6] The following case illustrates this point:—

A man, aged sixty-three, who had had an attack of jaundice and abdominal pain five years before, was seized with abdominal pain a week before his death. He was admitted to St. George's Hospital in a jaundiced, drowsy, and exhausted condition. His temperature was 101°, there was tenderness in the upper part of the abdomen, and he sweated profusely, without any shivering. He died from exhaustion within twenty-four hours of admission. At the necropsy there were three large crumbling calculi in the common bile-duct, which was dilated to the size of one's thumb and had a granular, thickened condition of its mucous

[1] Maugeret. *Thèse de Paris*, 1908.
[2] Opie. *Am. Journ. Med. Sc.*, Phila., 1901, cxxi, 27.
[3] Egdahl. *Johns Hopkins Hosp. Bull.*, Balt., 1907, xviii, 130.
[4] Rolleston. *Trans. Path. Soc.*, Lond., 1898, xlix, 149.
[5] Mayo Robson. *Lancet*, Lond., 1904, i, 770.
[6] Moore, N. *Trans. Path. Soc.*, Lond., 1882, xxxiii, 186.

membrane. The cystic duct was dilated, there was an ulcer in the fundus of the gall-bladder, which contained bile-stained mucopus but no calculi. The intrahepatic ducts were slightly dilated and shewed pericholangitic fibrosis, but there was no suppuration. The pancreatic duct contained discoloured pus, and there were spots of suppuration in the pancreas.

Pancreatitis may cause inflammation of the peritoneum of the lesser sac and so lead to closure of the foramen of Winslow and to an inflammatory exudate. Cholelithiasis may thus set up a peripancreatic effusion in the lesser sac, the contents being either serous or purulent. Many so-called pancreatic cysts are of this nature. The following case is of interest in this connexion :—

A man, aged twenty-five, was seized two weeks before his death with pain, never very acute, in the lower abdomen, and vomiting, which persisted until his death. He had never had jaundice, a blow on the abdomen, or any serious illness. An indistinct tumour was felt in the left hypochondrium, with the stomach resonance above it. At the necropsy there were 59 small calculi in the gall-bladder and one in the cystic duct, which was very long and joined the common hepatic duct $\frac{3}{4}$ inch above the biliary papilla. The cystic duct was inflamed, and it seemed possible that inflammation had spread from it to the pancreas. There was a localised effusion distending the lesser sac of the peritoneum into a cyst as large as one's head, the foramen of Winslow being closed. The pancreas shewed acute pancreatitis under the microscope. This peripancreatic cyst was evidently secondary, just as pleurisy is to pneumonia, to acute inflammation of the pancreas, which in its turn was associated with cholelithiasis.[1]

Chronic pancreatitis from extension of inflammation from the common bile-duct *via* Wirsung's duct is a frequent accompaniment of calculi in the lower part of the common bile-duct. Chronic pancreatitis does not occur in every case in which a calculus occupies the lower end of the common bile-duct; the determining factors are the anatomical relations (*a*) of the common bile-duct and Wirsung's duct, and (*b*) of the common bile-duct to the head of the pancreas (*vide* also p. 559). In some cases the common bile-duct and Wirsung's duct open separately into the duodenum, and in these circumstances inflammation is not likely to spread from the bile-duct to the pancreas. In 62 per cent of bodies the common bile-duct is embedded in the head of the pancreas, and in these cases inflammation readily extends from the duct into the head of the pancreas; in the cases in which the anatomical relation of the two is not so intimate, the duct running behind the head of the pancreas in 38 per cent of bodies (Helley [2]), chronic pancreatitis is not so likely to supervene (*vide* Robson and Cammidge [3]). The head of the pancreas may become so hard that when felt during the course of an operation for gall-stones the surgeon may assume that there is malignant disease of the head of the pancreas and abandon the operation.

[1] Rolleston. *Trans. Path. Soc.*, Lond., 1898, xlix, 145.
[2] Helley. *Arch. f. mikr. Anat.*, Bonn, 1898, lii, 773.
[3] Robson and Cammidge. *The Pancreas, its Surgery and Pathology*, p. 365, 1907.

The inflammatory changes thus started may progress, even though the calculi which caused it have passed into the duodenum (Mayo Robson,[1] Barling [2]). Subsequently the enlarged head of the gland undergoes atrophy from cicatricial contraction of the newly formed fibrous tissue, and imitates a hard, slowly growing carcinoma of the head of the pancreas by compressing the common bile-duct and producing chronic jaundice.

The treatment of such cases is to establish free drainage for the gall-bladder; if this is kept up for some time, the condition of the pancreas will improve. It seems safer to drain the gall-bladder externally and not to do cholecystenterostomy.

Pylephlebitis.—Inflammation of the bile-ducts may give rise to suppurative pylephlebitis. The inflammation may spread to the main trunk of the portal vein or to its intrahepatic branches. In some instances the infection may spread to the portal vein by the lymphatics or by the small veins of the bile-ducts which open into the branches of the portal vein. This subject is fully discussed elsewhere (*vide* p. 72).

(D) **Inflammatory Effects of a Calculus in the Ampulla of Vater.**—A calculus in the ampulla Vateri often obstructs the main pancreatic duct, but as the latter usually communicates in the pancreas with the accessory or Santorini's duct, the pancreatic secretion is not prevented from entering the duodenum. But the presence of a calculus in the ampulla of Vater favours the spread of infection into the pancreas and very commonly causes chronic pancreatitis. As the result of continued chronic pancreatitis, cicatricial contraction may result and compress both the ducts, giving rise to retention of the secretion, dilatation of the ducts, and sometimes to the formation of cysts in the gland. The chronic interstitial pancreatitis very seldom causes glycosuria or diabetes.

(E) **Biliary Fistulae.**—Abnormal passages between the gall-bladder and bile-ducts and other viscera or the outside of the body are in the great majority of instances due to gall-stones and inflammatory processes accompanying them. External fistulae may result from other causes, such as operations on the gall-bladder and ducts, or on hepatic abscesses and hydatid cysts. The following remarks on biliary fistulae refer to those associated with calculi.

External or Cutaneous Biliary Fistulae.—Suppuration in the gall-bladder may eventually discharge through the abdominal walls. This form of biliary fistula has been most frequently reported.

Naunyn [3] collected 184 examples out of a total of 384 biliary fistulae due to cholelithiasis, the next most frequent form of fistula being that between the gall-bladder and duodenum (108).

The communication between the gall-bladder and the opening in the abdominal wall is often by a long fistulous tract which may be tortuous and difficult to follow. The fistula may be the opening of an abscess in

[1] Mayo Robson. *Lancet*, Lond., 1900, ii, 236.
[2] Barling, G. *Brit. Med. Journ.*, 1900, ii, 1766.
[3] Naunyn. *On Cholelithiasis*, p. 143. Transl. New Sydenham Soc., 1896.

the neighbourhood of the gall-bladder or may lead directly into the suppurating gall-bladder.

External biliary fistulae usually open near the umbilicus; this depends partly on the vicinity of the gall-bladder and partly on the fact that the falciform ligament seems to guide the pus in this direction. Not uncommonly the opening is in the right hypochondrium. In rare instances there may be a discharging abscess in the right iliac fossa which imitates an appendicular abscess.

Gibbon[1] explored a spontaneous sinus in the right iliac fossa, $\frac{3}{4}$ inch below and $2\frac{1}{2}$ inches internal to the anterior-superior spine of the ilium, and removed 52 calculi, after which the fistula healed.

In very rare instances a biliary fistula may be established in the thigh. Porges[2] has recorded the discharge of gall-stones from such a fistula.

Fistulae between the Biliary and Gastro-intestinal Tracts.—Often, when this condition is found after death, there have been no clinical manifestations of the process, such as intestinal obstruction from a large gall-stone, or the passage of a calculus in the faeces, and its existence has not been suspected during life. A fistula may be suspected when a large calculus is passed by the bowel, but this often occurs when no absolute proof of a fistula is forthcoming.

In 111 cases in which a large calculus, viz. one the size of a nut, was passed by the bowel, the method by which it gained entrance into the bowels was quite unknown in 69 (Le Roy[3]).

Duodenal fistulae are the most frequent. In Naunyn's list of 384 biliary fistulae due to cholelithiasis the duodenum was involved in 108. As a rule the communication is between the fundus of the gall-bladder and the duodenum, but in a certain number of cases a calculus ulcerates through the walls of the common bile-duct into the first part of the duodenum, above the biliary papilla.

Cholecysto-duodenal Fistulae.—This form was present in 93 out of the 108 cases mentioned above. The fundus of the gall-bladder communicates with the first part of the duodenum. The process of ulceration may cause severe gastro-intestinal haemorrhage. Such cases may easily be misinterpreted and regarded as simple gastric or duodenal ulcer. Jaundice is absent as a rule, and if present is due to some complication.

A patient with impaction of a gall-stone in the common duct and a cholecysto-duodenal fistula had transient jaundice two months before death. The passage of a gall-stone into the common duct was thought to have both caused the jaundice and, by raising the pressure of bile in the gall-bladder, to have driven another calculus in the gall-bladder through a commencing cholecysto-duodenal

[1] Gibbon, J. H. *Phila. Med. Journ.*, 1901, vii, 128.
[2] Porges. *Wien. klin. Wchnschr.*, 1900, xiii, 597.
[3] Le Roy, C. *Thèse de Paris*, 1902, No. 474.

fistula, and by thus providing an outlet for the bile to have removed the jaundice (Barnard [1]).

In some instances cicatrisation of the fistulous communication may lead to stricture of the duodenum and to symptoms of pyloric obstruction. Dense adhesions between the gall-bladder and the duodenum may imitate malignant disease even when the parts are exposed during an exploratory laparotomy. Primary carcinoma may occur in the gall-bladder after the formation of the fistula (*vide* case on p. 638). The mucous membrane around the fistulous opening in the duodenum may become extensively ulcerated and set up persistent vomiting; this may occur without any cicatricial stenosis of the duodenum or pylorus.

A calculus may ulcerate out of the gall-bladder, but fail to pass into the duodenum; the end of the calculus which projects into the intestine may be white, the pigment having been removed by the action of the acid contents of the duodenum (Barnard). So much cicatricial contraction may be set up around the duodenum that obstruction results. A case of this kind is reported by Labadie-Lagrave and Magdelaine.[2] Occasionally an abscess, formed around a gall-stone which is ulcerating out of the gall-bladder or common bile-duct, discharges in several directions and a complicated fistula results, with openings into the duodenum, stomach, and gall-bladder.

A woman aged fifty-four years died in St. George's Hospital after removal of the right big toe. She had diabetes of pancreatic origin and was jaundiced. The gall-bladder was shrivelled up on a gall-stone, and communicated by a fistula with the first part of the duodenum. There was a soft, crumbling calculus the size of a pigeon's egg in the lower part of the common bile-duct. Near this calculus, but not in actual continuity, there was an abscess, partly in the head of the pancreas and partly in the lesser omentum and left lobe of the liver. This abscess communicated by two small openings with the duodenum, and by two more fistulae with the stomach on its posterior wall. The pancreas was markedly fibrotic.

Choledocho-duodenal Fistula.—A communication between the common bile-duct and the first part of the duodenum is probably commoner than is believed. Naunyn points out that in some cases in which the calculus is seen projecting into the duodenum the orifice is not the biliary papilla, as is often assumed merely because there is an opening there, but a fistulous passage. Naunyn thinks it not improbable that fistulae between the duodenum and the common bile-duct are as common as those between the duodenum and gall-bladder. But of his 108 collected cases of duodenal fistulae 15 only were between the common duct and the duodenum, and the remaining 93 between the gall-bladder and the duodenum.

Biliary Gastric Fistulae.—Communications between the stomach and biliary tract are very rare, and when they do occur, are in some instances

[1] Barnard. *Ann. Surg.*, 1902, xxxvi, 161.

[2] Labadie-Lagrave et Magdelaine. *Journ. des praticiens*, June 25, 1890.

due to an abscess, arising in connexion with the gall-bladder or ducts, opening into the stomach and also into the duodenum or colon, or both, as in a case reported by Voelcker.[1]

Naunyn[2] quotes 12 gastrobiliary fistulae, 8 of which were between the gall-bladder and 4 between the ducts and the stomach. In Nicholls' case[3] the patient was a woman aged eighty-five. In a complicated case reported by Lejonne and Milanoff[4] there was a communication between the stomach and the gall-bladder, and a second fistula between the common bile-duct, which contained a calculus, and the first part of the duodenum. The gall-bladder shewed primary carcinoma, but the fistulae probably depended on cholelithiasis. The patient was a woman aged eighty-seven years. Cholecystogastric fistulae due to gall-stones have also been recorded by Ochsner[5] and Snively.[6] In a case recorded by Carter[7] a calculus was wedged in the pylorus like a cork.

A cholecystogastric fistula may be brought to light in separating dense adhesions during operations on cases without any symptoms of such a fistula.

In a woman aged sixty who had had attacks of gall-stone pain for fifteen months, lately very frequently, followed by slight jaundice and constant dyspepsia with frequent vomiting and loss of flesh, Mayo Robson[8] found the stomach and gall-bladder firmly adherent. On separating the adhesions a fistula between the gall-bladder and stomach was found. The gall-bladder contained calculi.

Vomiting of gall-stones has been thought to be good evidence of a gastrobiliary fistula; but this is not convincing, for since bile is commonly regurgitated into the stomach in vomiting, small calculi should be too. When, as rarely happens, a large calculus is vomited, a gastrobiliary fistula probably exists.

Thompson[9] recorded the case of a woman aged ninety-four who vomited a calculus the size of a nutmeg. Jeaffreson[10] quoted a case in which a large calculus was vomited, and after death the stomach was found adherent to the gall-bladder. In 12 cases in which gall-stones were vomited there was only 1 in which a gastrocholecystic fistula was proved to exist (Murchison[11]). Mayo Robson,[12] Nicholls, Kellett Smith and Bailey,[13] Crooke,[14] Johnson,[15] Pfeiffenberger,[16] and others have reported more recent cases in which gall-stones were vomited.

[1] Voelcker. *Trans. Path. Soc.*, Lond., 1895, xlvi, 78.
[2] Naunyn. *On Cholelithiasis*, p. 143. Transl. New Sydenham Soc., 1896.
[3] Nicholls, A. G. *Montreal Med. Journ.*, 1898, xxvii, 829.
[4] Lejonne et Milanoff. *Bull. Soc. Anat. Paris*, 1900, lxxv, 33.
[5] Ochsner. *Ann. Surg.*, 1902, xxxv, 712.
[6] Snively. *Journ. Am. Med. Assoc.*, Chicago, 1903, xl, 963.
[7] Carter. *Brit. Med. Journ.*, 1911, i, 307.
[8] Mayo Robson. *Ibid.*, 1903, i, 185.
[9] Thompson. *Trans. Path. Soc.*, Lond., 1861, xii, 129.
[10] Jeaffreson. *Brit. Med. Journ.*, 1868, i, 531.
[11] Murchison. *Diseases of the Liver*, p. 548, 1885.
[12] Mayo Robson. *Lancet*, Lond., 1897, i, 1526.
[13] Kellett Smith and Bailey. *Liverpool Med.-Chir. Journ.*, 1902, xxii, 74.
[14] Crooke. *Ibid.*, p. 76.
[15] Johnson. *Montreal Med. Journ.*, 1909, xxxviii, 315.
[16] Pfeiffenberger. *Journ. Am. Med. Assoc.*, 1910, lv, 1024.

Cholecystocolic Fistulae.—A fistulous communication between the biliary tract and the colon is less frequent than one involving the duodenum as the result of cholelithiasis.

Naunyn gives 49 examples of fistulae between the gall-bladder and the colon and one between the common bile-duct and the colon.

An indirect result of gall-stones, namely, carcinoma of the gall-bladder, may cause a fistulous opening into the colon. Out of 9 cases of cholecystocolic fistulae mentioned by Murchison 6 were associated with carcinoma of the gall-bladder. Faeces may pass through a cholecystocolic fistula into the gall-bladder and set up suppuration in the liver.

This is exemplified in the following case in St. George's Hospital. A woman aged thirty-one years had had jaundice, without any definite biliary colic, for one and a half years before her death; the jaundice varied from time to time but became very dark before death. She was thought to have malignant disease, and an exploratory operation was performed, but it was impossible to do anything. At the necropsy the gall-bladder had ulcerated into the colon, and the parts around were firmly matted together by dense adhesions. There were gall-stones and faeces in the gall-bladder, the right hepatic duct contained faecal material, and there were multiple abscesses in the liver (*vide* Plate VII).

Fistulae between the Biliary Tract and the Small Intestine.—A direct communication between the gall-bladder or ducts and any part of the small intestine except the duodenum is most exceptional, and hardly any cases are on record. The small intestine is, from its position and free mobility, less likely to become adherent to the gall-bladder. Naunyn[1] refers to 1 case in which the jejunum (Gaston), and another in which the ileum, communicated with the gall-bladder.

Results of the Passage of Calculi into the Intestines.—In addition to causing mechanical obstruction of the bowel, which is described on p. 751, a calculus may damage the wall of the intestine and lead to the formation of a diverticulum containing the calculus, or even to gangrene. In exceptional instances a small gall-stone has passed into the vermiform appendix, and been found on removal of the inflamed appendix; the presence of calculi would favour infection and inflammation. Undoubted examples have been recorded by Kelly and Hurdon[2] (2), Mayo Robson,[3] Lediard,[4] Wynne and Sturm.[5] Gall-stones have also been found in a Meckel's diverticulum (Sherren[6]). As the result of ulceration between the gall-bladder and duodenum or colon cicatricial contraction and stricture of the bowel may occur. Cicatrisation of a fistula is, however, rare (Naunyn) or is rarely recognised at the necropsy.

[1] Naunyn. *On Cholelithiasis*, p. 148.
[2] Kelly and Hurdon. *The Vermiform Appendix and its Diseases*, p. 363, 1905.
[3] Mayo Robson. *Lancet*, Lond., 1906, ii, 1768.
[4] Lediard. *Ibid.*, 1907, i, 83.
[5] Wynne and Sturm. *Brit. Med. Journ.*, 1909, ii, 515.
[6] Sherren. *Proc. Roy. Soc. Med.*, 1910, iii (Clin. Sect.), 11.

PLATE VII.

Section of Liver Shewing Abscesses due to Infection of the Bile-ducts in a Case of Cholecystocolic Fistula from Cholelithiasis.

Broncho-biliary Fistulae.—In 49 cases of this condition collected by Ido and Yasuda,[1] 26, or 58 per cent, were due to cholelithiasis. As cholelithiasis is the most frequent cause of broncho-biliary fistulae, a general account of the condition will be given here. Gall-stones may give rise to a broncho-biliary fistula in several ways: (*a*) Gall-stones in the common duct set up infective cholangitis and an abscess in the liver which perforates the diaphragm and, after setting up adhesions between the diaphragm and the base of the lung, ruptures into the latter; or the liver abscess may perforate first into the pleura and subsequently into the lung. (*b*) Intrahepatic calculi may give rise to a similar sequence of events. (*c*) A calculus may ulcerate out of the gall-bladder or ducts, and set up an intra-peritoneal abscess which perforates the diaphragm and either opens into the lung direct or first into the pleura and subsequently into the lung. (*d*) A suppurating gall-bladder associated with cholelithiasis may set up a subphrenic abscess which perforates the diaphragm and eventually opens into the lung. (*e*) In very rare cases, as in Mandard's,[2] the gall-bladder may perforate directly through the diaphragm into the lung.

Symptoms.—Irritating cough may be accompanied by orthopnoea and the expectoration of large quantities of bile, sometimes almost pure; Graham[3] speaks of expectoration of as much as 700 c.cm. of bile in the twenty-four hours. A few patients have coughed up biliary calculi.

Signs.—There may be dullness in the right inframammary and axillary regions, extending back for a variable extent, the breath-sounds over this area being coarse and accompanied by rales. On the other hand, there may be no dullness on percussion, and merely bronchitis. When the discharge of bile is free, there may be no jaundice and no bile in the urine, as in Smith and Rigby's[4] case.

The diagnosis depends on the copious expectoration of bile. In jaundiced patients with bronchitis or pneumonia the sputum is bile-stained, but the amount of bile is much less. Fragments of liver tissue may also be found in the sputum. The cause of a broncho-biliary fistula may be obscure; other signs of cholelithiasis, or in rare cases the expectoration of biliary calculi, hydatid membrane, or round worms, would settle the diagnosis.

Prognosis.—Recovery may occur spontaneously or after operative interference on the biliary apparatus. When spontaneous recovery occurs, there is, generally speaking, no liability to return of the fistula; a relapse has, however, been known to occur.

A patient, after expectorating bile, was free for ten years from any symptoms; they then recurred and proved fatal (J. E. Graham).

Treatment.—If the condition does not tend to pass away and undergo spontaneous cure, laparotomy, with the view of removing the obstruction

[1] Ido und Yasuda. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1912, lii, 567.
[2] Mandard. *Thèse de Paris*, 1854. Quoted by Naunyn.
[3] Graham, J. E. *Trans. Assoc. Am. Phys.*, Phila., 1897, xii, 247.
[4] Smith and Rigby. *Brit. Med. Journ.*, 1903, ii, 313.

to the passage of bile into the intestine, should be undertaken; when the gall-stones are removed from the common duct, the fistulous channel into the lung should heal up.

Other and rare forms of Fistulae.—Fistulae between the bile-ducts themselves.—Naunyn,[1] who quotes 8 cases, adds that they are merely of anatomical interest.

Fistulae between the gall-bladder and the portal vein are very rare; Naunyn quotes 3 cases, but does not admit Bristowe's[2] case. According to tradition there were three calculi in the portal vein of Ignatius Loyola, but Thudichum[3] emphatically states they were phleboliths; possibly the calculi were really in the common bile-duct, which was mistaken for the portal vein. Ulceration of a calculus into the portal vein would, of course, tend to set up suppurative pylephlebitis.

Ulceration of the Hepatic Artery.—A communication between the gall-bladder or the bile-ducts and the hepatic artery or its branches leads to profuse or even fatal haemorrhage which runs down the ducts into the alimentary canal. These cases may be regarded as examples of aneurysms of the hepatic artery or its branches, rupturing into the biliary tract. But it must be remembered that ulceration of the gall-bladder or bile-ducts in cholelithiasis may erode the walls of the hepatic artery or its branches and first give rise to an aneurysmal bulging and subsequently to rupture of the vessel into the biliary tract (*vide* also p. 45).

According to Naunyn,[4] Lebert's case of hepatic aneurysm rupturing into the gall-bladder was probably of this nature; M. B. Schmidt recorded a case of ulceration of a bile-duct, due to a calculus, producing hepatic aneurysm.

Fistulae between the gall-bladder and the kidneys are also very rare. Courvoisier[5] quoted 5 cases. The fistulous passage is usually between the gall-bladder and the pelvis of the right kidney. An abscess formed after perforation of the gall-bladder may open into the pelvis of the right kidney and enable biliary calculi to escape from the body by the urinary tract (Jones[6]). Elsner[7] reported another case with a gall-stone in the pelvis of the right kidney.

Fistulae between the Gall-bladder and Urinary Bladder, etc.—Barnard[8] refers to a number of cases. H. Faber, in 1839, wrote an octavo volume on the subject. Köstlin and Wucherer have described fistulae, and Abt, Güterbock,[9] Hahn, and Michel[10] biliary calculi in the urinary bladder. In fistulae between the urinary and biliary tracts bile may appear in the urine without jaundice.

[1] Naunyn. *On Cholelithiasis*, p. 149. Transl. New Sydenham Soc., 1896.
[2] Bristowe. *Trans. Path. Soc.*, Lond., 1858, ix, 285.
[3] Thudichum. *A Treatise on Gall-stones*, p. 11, 1863.
[4] Naunyn. *Loc. cit.*, p. 141.
[5] Courvoisier. *Pathologie u. Chirurgie der Gallenwege*, 1890.
[6] Jones, T. C. L. *Lancet*, Lond., 1907, i, 1085.
[7] Elsner. *Med. News*, N.Y., 1898, lxxii, 164.
[8] Barnard, H. L. *Ann. Surg.*, 1902, xxxvi, 161.
[9] Güterbock. *Virchows Arch.*, 1876, lxvi, 273.
[10] Michel. *Zentralbl. f. Gynäk.*, Leipz., 1909, xxxiii, 25.

A case of cholecysto-vaginal fistula has been reported. It is quite conceivable that an elongated gall-bladder with an abscess in connexion with it may track into the pelvis.

A communication between the *pericardium and the biliary tract* is one of the rarest fistulae. In 1892 Naunyn only knew of 1 case. An abscess on the surface of the left lobe of the liver, secondary to intrahepatic cholangitis set up by a calculus in the common bile-duct, opened in a case of Legg's [1] into the pericardium.

Rupture and Perforation of the Gall-bladder into the Peritoneum.—It is most unlikely that a healthy gall-bladder would rupture merely from the weight of contained gall-stones, but, as a matter of fact, the gall-bladder is seldom healthy in cholelithiasis. It may be thinned from distension, and rupture may then take place from trauma, or as the result of sudden pressure brought to bear on the gall-bladder by contraction of the abdominal walls in violent straining, coughing, etc., or in the vigorous abdominal contractions of delivery. In such cases there may be no active inflammation or previous ulceration of the gall-bladder. If the bile is sterile, the peritoneum may suffer little. Cases have occurred in which large quantities of bile have been removed from the abdominal cavity, but this chiefly occurs when a hydatid cyst in communication with a bile-duct ruptures into the peritoneum (*vide* p. 416). Usually rupture of the gall-bladder is disposed to by recent inflammation of its walls or by definite ulceration, and the infective contents of the gall-bladder readily set up generalised peritonitis.

In some instances, as the result of adhesions around the gall-bladder, the rupture or perforation sets up a localised peritoneal abscess, which may contain calculi, in communication with the gall-bladder. An abscess of this kind may open either on the surface of the body or into one, or even into several, of the abdominal or thoracic viscera, and thus give rise to fistulae, which may be multiple and extremely complicated. In rare instances a localised abscess forms behind the peritoneum, the gall-bladder having become adherent to the posterior abdominal wall. In other cases calculi may ulcerate out of the gall-bladder and be found surrounded by adhesions.

Moynihan [2] described a case in which three gall-stones, each the size of a Barcelona nut, had ulcerated almost through the walls of a gall-bladder with chronic sclerosing cholecystitis. Two of these calculi lay in pockets in the omentum and the third was almost hidden in a cavity in the liver. In a lunatic numerous calculi were found firmly adherent to the peritoneum in various parts of the abdomen (Gillespie [3]).

Treatment.—*Prophylaxis.*—In fat people, especially women, and after enteric fever, influenza, malaria, and pregnancy, it may sometimes be within the medical man's power to advise a change in the patient's mode of life which will tend to prevent, or diminish the liability to, catarrhal

[1] Legg, J. W. *Trans. Path. Soc.*, Lond., 1874, xxv, 133.
[2] Moynihan. *Brit. Med. Journ.*, 1903, i, 186.
[3] Gillespie. *Ibid.*, 1905, i, 990.

inflammation of the gall-bladder and bile-ducts and stagnation of bile. These measures are, in the main, on the same lines as those for the general hygienic treatment of cholelithiasis in the intervals between the attacks. Thus gentle exercise, in the fresh air if possible, short of fatigue, so as to favour the passage of bile into the intestine, is advisable. When this is not practicable, breathing exercises to increase the movements of the diaphragm and liver should be instituted. Stooping over desks and working in a cramped position must be corrected, and the use of tight corsets and belts should be discontinued. The patient should be warmly clad, so as to avoid chills. In enteric fever the bile constantly contains the pathogenetic organism, and it is therefore reasonable during the course of the fever and in convalescence to give short courses of urotropin. A visit to one of the spas mentioned on page 779 is a valuable precautionary measure.

The General Medical Treatment of cholelithiasis and its various manifestations may be considered under the following heads: (1) To prevent stagnation of bile. (2) To prevent the occurrence of catarrhal inflammation of the gall-bladder and bile-ducts. (3) To remove catarrhal inflammation when it has appeared. (4) Attempts to dissolve calculi. (5) Attempts to remove calculi. (6) Spa treatment. (7) Diet.

(1) **To Prevent Stagnation of Bile.**—Exercise leads to increased movements of the diaphragm and liver and so to an increased flow of bile into the duodenum. In comparatively young and vigorous persons active exercise, rather than a "constitutional" walk, is needed. Horse exercise is perhaps the best, but bicycling, climbing, tennis, and rowing are excellent. In cases in which active open-air exercise is not possible, deep respirations should be practised so as to induce vigorous movements of the diaphragm and liver, and in some cases abdominal massage is useful in increasing the tone of the abdominal muscles and the flow of bile. After pregnancy the lax condition of the abdominal wall, which favours enteroptosis, hepatoptosis, and stagnation of bile, may be met by massage to the abdominal muscles, care being taken not to bring direct pressure to bear on the gall-bladder, since cholecystitis may thus be set up.

The factor of dress, especially the corset, tight waist-bands, and heavy skirts, in constricting the lower part of the chest and preventing free diaphragmatic respiration, has been referred to in the consideration of the greater incidence of gall-stones in women (*vide* p. 723). These causes should be obviated, and the wearing of tight belts in men discontinued.

By the Administration of Food and Drink.—When food passes into the duodenum, bile is driven out of the gall-bladder into the duodenum. Meals at short intervals, therefore, are effective in preventing biliary stagnation. In addition to meals at comparatively short intervals some supper should be eaten before going to bed, and it is a good plan to have light food available, so that in case the individual wakes, a small meal

may be taken during the night. The subject of the diet will be referred to later (*vide* p. 779).

Though experimental results shew that water cannot be considered a cholagogue, good results undoubtedly follow the taking of large draughts of hot water. Carlsbad, Harrogate old sulphur, Vichy, and Contrexéville waters have a good effect, or hot water containing some sulphate or phosphate of sodium. The action of an increased amount of water is probably complex: the bile is diluted and rendered more copious, while catarrh of the ducts and intestine is relieved. In order to get the maximum effect from water it should be taken before meals, when the stomach is empty. Thus it may be taken the last thing at night or, as is more frequently done, early in the morning. It should then be sipped in the intervals of dressing, or later in the day while walking about in a garden.

The water should, of course, not be taken in excessive quantities or too hot, otherwise dilatation of the stomach may occur. Dr. Whittick has told me of a patient who, having a little knowledge of medicine, treated himself for gall-stones by copious draughts of water as hot as he could bear, and as a result developed very acute dilatation of the stomach which nearly proved fatal.

Copious enemas of hot water have been recommended and have been thought to induce muscular contraction of the gall-bladder and expulsion of the contained bile.

Cholagogues.—Although a number of drugs have been credited with the power of increasing the secretion and flow of bile, it is probable that salicylate of sodium and bile itself are the only drugs which really increase the secretion of bile. Mercury, podophyllin, iridin, rhubarb, senna, aloes, turpentine, and other drugs may excite peristaltic contraction of the ducts and so lead to a temporary increase in the amount of bile discharged into the duodenum, but do not really augment the secretion of bile (Rutherford and Vignal,[1] Mayo Robson [2]). Toluylenediamine at first increases the flow of bile, but later the bile becomes more viscid from a larger quantity of mucus in it. This body has only very occasionally been employed in medicine, and is dangerous from its haemolytic or destructive action on the red blood-corpuscles and its tendency to produce inflammation of the small bile-ducts and jaundice (*vide* p. 533).

Secretin, which, as Starling and Bayliss [3] have shewn, is manufactured in the duodenal mucous membrane and stimulates the secretion of the pancreas, also increases the secretion of bile.

Ox or pig's bile is sometimes given in capsules, but it is better to give the salts of the bile acids alone, since the bile-pigments are themselves somewhat poisonous.

[1] Rutherford and Vignal. *Journ. Anat. and Physiol.*, 1876, x, 253.
[2] Mayo Robson. *Proc. Roy. Soc.*, Lond., 1890, xlvii, 21.
[3] Starling and Bayliss. *Ibid.*, 1902, lxix, 352.

Gautier[1] met with complete relief from attacks of biliary colic, which had extended over five years, after a prolonged course of ox bile.

Salicylate of sodium has the advantage that it not only increases the secretion of bile, but that it acts as an intestinal antiseptic and so tends to diminish intestinal catarrh. It may be given in 10-grain doses twice or three times daily with an equal quantity of bicarbonate of sodium. The most satisfactory treatment from the point of view of inducing an increased flow of bile is to give salicylate of sodium combined with plenty of alkaline waters. Aspirin (salicylacetic acid) may also be given, but is incompatible with bicarbonate of sodium. Salicylate of sodium may advantageously be combined with urotropin, which is excreted into the biliary tract (Crowe[2]) and may exert an antiseptic influence; calcium chloride may be added to counteract haemorrhage or itching.

Chauffard[3] combines salicylate of sodium (gr. x) with benzoate of sodium (gr. iii) three times daily for periods of twenty, fifteen, or ten days in every month for a year or two, the duration of the course diminishing as time goes on. Iodide of potassium has been stated to check frequent attacks of colic. Its method of action is doubtful; possibly it may increase the mucous secretion from the walls of the biliary tract and so augment the flow of fluid through the ducts and thus relieve catarrh. It is also conceivable that, like chloroform and ether, it may diminish spasm.

(2) **To Prevent Catarrhal Inflammation.**—Indigestion and gastritis, which, by leading to gastro-duodenal catarrh, might set up catarrhal inflammation of the bile-ducts, must be treated by careful dieting, drugs, and the prevention of constipation. The food should be bland, nutritious, and eaten slowly. The condition of the teeth should be seen to, so that the food can be properly masticated, and further that there is no oral sepsis to set up gastritis. Worry and anxiety frequently cause dyspepsia, and in this way favour infection of the ducts and gall-bladder. Constipation and the attendant liability to indigestion and gastro-intestinal fermentation and putrefaction should be prevented by gentle purgatives; vigorous purges must be avoided, as enteritis may thus be induced. Salines such as half a tumbler of natural Carlsbad water with a little hot water before breakfast, or one or two drams of Carlsbad salts dissolved in hot water are useful. Phosphate of sodium in dram doses may also be given in water early in the morning. The Carlsbad salts are better borne by the stomach if a little infusion of quassia or cinchona is added to the draught. While sipping the salts the patient should walk about, or better, practise systematic exercises with deep inspiratory movements so as to favour the descent of the diaphragm, and should not have any food until an hour after the draught has been taken.

[1] Gautier. *Rev. méd. de la Suisse Rom.*, Genève, 1898, xviii, 318.
[2] Crowe. *Johns Hopkins Hosp. Bull.*, Balt., 1908, xix, 109.
[3] Chauffard. *Traité de méd.* (Bouchard, Brissaud), 1902, v, 85.

(3) **To Remove Catarrhal Inflammation of the Biliary and Intestinal Tracts.**—It is important to remove inflammation of the gall-bladder, because calculi are formed as a result of catarrhal cholecystitis and are not likely to be dissolved so long as the gall-bladder is inflamed. Harley and Barratt[1] and Bain,[2] experimenting with dogs, have shewn that calculi are dissolved by the bile in healthy gall-bladders, but not in the presence of cholecystitis. As the gall-bladder of patients with calculi is usually affected, there is little chance that calculi will be dissolved.

The methods already referred to, by which the flow of bile is increased and the bile-passages washed down, are of use in removing catarrhal inflammation of the gall-bladder and bile-ducts. Urotropin is of great use for its disinfecting action. Carlsbad salts, phosphate of sodium, Epsom salts in hot water, or table waters, such as Contrexéville and Homburg, should be taken so as to remove catarrhal inflammation of the intestines and to keep the bowels loose. Vigorous purgatives should be avoided, as they tend to set up inflammation of the mucous membrane.

The abdomen should be kept warm; and when there is tenderness over the gall-bladder poultices, hot packs, or fomentations, or heat by means of the thermophore, may be applied over the right hypochondrium.

A. E. Wright[3] suggested that patients should be immunised against the colon bacillus, so as to arrest cholecystitis due to infection with *B. coli*, so that the calculi might gradually dissolve in the bile. Cholecystitis with a persistent fistula after operations for gall-stones has been benefited by vaccines of *B. coli* (Wright and Reid[4]).

(4) **Attempts to Dissolve Calculi.**—Numerous drugs have been tried and recommended with a view to dissolving calculi, but with very little, if any, success. Naunyn estimated that this is effected in about 1 per cent of the cases. A very famous, ancient remedy was Durande's, which consisted of a mixture of ether (℥ xv) and turpentine (℥ x) in a capsule. Although this remedy may do good by virtue of the antispasmodic action of ether or of the expulsive action of turpentine—radically opposed as these actions are—there is no reason to believe that the calculi in the gall-bladder are acted upon directly by the drugs. Chloroform, which has been employed as a solvent, probably acts chiefly as an antispasmodic.

Olive oil has been widely used to relieve the symptoms of cholelithiasis. It has been proved to dissolve calculi in a test-tube (Brockbank,[5] L. Scott[6]), but there is no evidence that olive oil given by the mouth, much less when injected per rectum, can act on calculi in the gall-bladder. In fact, there is a well-known fallacy about some of the good effects ascribed to its use, namely, that the oil itself may be so

[1] Harley and Barratt. *Journ. Physiol.*, 1903, xxix, 341.
[2] Bain. *Brit. Med. Journ.*, 1905, ii, 269.
[3] Wright, A. E. *Ibid.*, 1903, i, 1073.
[4] Wright and Reid. *Ibid.*, 1906, i, 143.
[5] Brockbank. *Med. Chron.*, Manchester, 1893–4, xix, 155.
[6] Lindley Scott. *Brit. Med. Journ.*, 1897, ii, 798.

digested and altered as to imitate softened calculi when passed by the bowel.

Delépine [1] described the case of a patient who took olive oil for cholelithiasis and passed 40 round or oval bodies which were at first regarded as biliary calculi and as evidence of the success of the treatment. They turned out to be masses of crystals of fatty acids derived from the oil.

It is conceivable, however, that olive oil might exert a solvent action on a calculus impacted in the actual orifice of the biliary papilla. It has also been thought that fatty acids and glycerin absorbed from the bowel may reach the liver and lead to an increased flow of bile into the gall-bladder. Bile acids dissolve cholesterin, hence the more bile passes over a calculus, the better the chance of some absorption taking place. Some of the good effects of oil may be due to its power of inhibiting hyperchlorhydria and to its soothing and antispasmodic action on the intestine. Olive oil is given in quantities of from 6 to 12 ounces a day by the mouth, but is far from a pleasant thing to take. Some writers, however, speak highly of the good effects of olive oil in cholelithiasis. Pure olive acid (Merck) and eunatrol, or pure oleate of sodium, and glycerin, have been recommended instead of the oil. Fat and cream may also be taken in place of the oil, unless they disturb digestion.

Since the bile acids dissolve cholesterin, any increase in the secretion of bile, such as is induced by salicylates or by the administration of bile by the mouth, may be regarded as a means of dissolving calculi. Since protein food increases the percentage of bile acids in the bile, meat has been regarded as an important element in the diet of patients suffering from gall-stones; but, as it has recently been shewn that a protein diet also increases the amount of cholesterin in the bile, this argument is not of much weight. As already pointed out, V. Harley and Barratt's experiments shew that calculi are dissolved by the bile provided cholecystitis is absent. It is, therefore, important to prevent or remove inflammation of the gall-bladder, and for this purpose urotropin and salicylate of sodium, or their combination in the form of saliformin, are advisable. Partly on experimental grounds and partly on clinical observation, Bain [2] recommends Harrogate old sulphur water and urotropin combined with iridin as solvents of gall-stones.

(5) **Attempts to Remove Gall-stones.**—Measures, such as massage, and drugs, such as turpentine and purgatives, which lead to muscular contraction of the gall-bladder and bile-ducts, have been employed to favour the expulsion of calculi. At the commencement of a course at Carlsbad it not uncommonly happens that a patient experiences an attack of biliary colic and passes calculi. Increasing the flow of bile by salicylates and ox bile cannot be regarded as likely to drive calculi out of the gall-bladder, though their good effects in reducing catarrh of the ducts and the possibility that calculi may, as already pointed out, be dissolved,

[1] Delépine, S. *Trans. Path. Soc.*, Lond., 1890, xli, 111.
[2] Bain. *Brit. Med. Journ.*, 1905, ii, 269.

must not be forgotten. Measures intended to lead to the expulsion of gall-stones are uncertain in their action. Massage of the gall-bladder and bile-ducts in order to effect "the extrusion of gall-stones by digital manipulation" was advocated by George Harley[1] in 1888, and has been condemned as a dangerous method of working in the dark. No doubt it might lead to the expulsion of soft calculous masses lying in the common bile-duct, but in many cases it would be quite powerless to do any good and might easily do harm by leading to rupture of an ulcerated gall-bladder or duct. If it were possible to recognise with certainty cases with soft calculous material in the common duct, gentle massage might be recommended, but, unfortunately, our methods of diagnosis are not sufficiently sure to enable us to do so.

(6) **Spa Treatment.**—Mineral waters dilute and increase the flow of bile and may thus lead to some degree of solution of calculi in the ducts and gall-bladder and to their ultimate discharge into the duodenum. The increased flow of bile flushes the bile-ducts and thus tends to remove infective catarrh, and so to prevent the further formation of calculi and possibly to favour absorption of calculi. It is not absolutely necessary to go to a spa in order to undergo the treatment, for it can be carried out under medical advice at home; but the patient probably gains by going to the original source, from the change of scene and from the influence exerted by the regular life, the régime, and the freedom from business cares and worries. Hot Carlsbad water should be sipped while walking up and down an hour before breakfast and in the afternoon, about ¾ pint being taken on each occasion and three-quarters of an hour being devoted to the process. The taste of the salts is less disagreeable if some infusion of quassia or cinchona is added. No food should be taken until an hour after the last dose of water is taken.

Carlsbad, Vichy, Marienbad, Kissingen, Homburg, Neuenahr, Ems, Bertrich, Brides, are appropriate spas on the Continent. In England Harrogate, Llandrindod Wells, enjoy some reputation, while in America Bedford, Pa., Las Vegas Hot Springs, Sharon, White Sulphur, are recommended for the treatment of gall-stones. At Carlsbad and Vichy calculi are not infrequently passed after the treatment has begun; patients should, therefore, be warned that they may have a return of colic with jaundice. Neuenahr and Bertrich are less depressing than Carlsbad; the waters at Salzschlirf, Wiesbaden, Nauheim, and Soden are sometimes recommended.

(7) **Diet.**—Food should be taken at comparatively short intervals and the amount at each meal should not be large; overeating must, of course, be prevented. As to the kind of food most suitable for patients with gall-stones, considerable divergence of opinion has been expressed. It is unnecessary to insist that the food should be digestible and not too bulky. The amount of starchy food should be much restricted, and bread should be taken sparingly and preferably as toast, sugar in small quantities only, and porridge and rice in moderation. It is particularly

[1] Harley, G. *Illust. Med. News*, Lond., 1888–9, i, 73.

with regard to fatty food that contradictory statements have been made. Some writers believe that fat favours the production of calculi; others that fats are indicated as solvents of gall-stones. It is probable that fatty food has no particular action in dissolving calculi in the bile-ducts or gall-bladder, and that it only does harm indirectly, viz. when it gives rise to acid dyspepsia. As a general rule, fatty food should be taken in small quantities and carefully watched; when any signs of dyspepsia or fermentation appear, it should be diminished in amount, or, if need be, discontinued. Protein food may be taken with greater freedom in the form of mutton, beef, game in small quantities, and vegetables containing a good deal of albumin. Alcohol is best avoided, and if required for other reasons, should be well diluted. Light claret, still Moselle, or a little whisky may be taken in this way. Beer, stout, champagne, and especially liqueurs should be forbidden. The importance of taking plenty of water before meals has already been insisted on.

Surgical Treatment.—It has already been pointed out that in acute biliary colic operative interference is justifiable only when life is threatened by some extremely grave complication, such as rupture of the gall-bladder or bile-ducts with resulting peritonitis, or when, as rarely happens, concomitant acute infective cholecystitis sets up widespread peritonitis, or when signs of acute intestinal obstruction appear. There is naturally considerable difference of opinion as to the indications for operative interference in gall-stones. Moynihan[1] is of opinion that as soon as gall-stones are known to be present in the gall-bladder the safest, the speediest, and the only proper course is to remove them, and that the only contraindication is the presence of some morbid condition which would render operation dangerous.

The effects of cholelithiasis which require surgical interference may be arranged as follows:

(i) When there is acute inflammation in the region of the gall-bladder with the signs of severe localised peritonitis.

(ii) When, in a case with a history of gall-stones, there are symptoms pointing to acute perforative peritonitis, such as might be set up by perforation of the gall-bladder.

(iii) When, from the presence of fever, pain, jaundice, etc., there is evidence that severe infective inflammation of the bile-ducts has developed. Under these conditions the gall-bladder and ducts should be freely drained.

(iv) When acute intestinal obstruction occurs in patients with a history of gall-stones.

(v) When there is a large tumour constantly present in the position of the gall-bladder, such as might be due to distension of the gall-bladder by serous or mucous fluid (dropsy of the gall-bladder), by pus (empyema), or by a collection of calculi.

(vi) When jaundice in a patient with a history of gall-stones becomes chronic. The period which should be allowed to elapse after the onset

[1] Moynihan. *Practitioner*, Lond., 1908, lxxxi, 835.

of permanent jaundice varies very considerably. Hanot fixed the period at three months; Boix[1] shortened it to six weeks; and C. Beck[2] argued in favour of four weeks. If medical measures are quite ineffectual and the patient loses ground, the chance of relief from operation is certainly diminished by delay, as the liver cells are further damaged by the prolonged stagnation of the bile in the intrahepatic bile-ducts. There is also the danger that suppuration may supervene in the dilated bile-ducts or in the liver. Further, the marked tendency to haemorrhage which exists in so many deeply jaundiced patients makes operative interference difficult and dangerous. No rigid rule can be laid down as to the time which should be allowed to elapse before a patient with chronic jaundice is operated upon. The patient's condition, general nutrition, presence or absence of symptoms, and response to treatment must all be considered. If improvement occurs under medical treatment, it would obviously be unwise to adopt operative measures. As a general rule, operation should be advised earlier in poor patients whose livelihood depends on their ability to work than in well-to-do patients who can afford a cure at Carlsbad, Neuenahr, and other spas.

(vii) In intermittent hepatic fever, in which there is a calculus in the common bile-duct which sets up recurrent attacks of fever, pain, and jaundice, medical treatment should always be given a good trial, and if the attacks become less frequent and severe and gradually disappear, there is, of course, no need for operation. On the other hand, if the attacks become more frequent or no improvement occurs, operation should be considered and should be carried out before the patient becomes too run down in strength and resistance.

(vii) In recurrent biliary colic, without the passage of calculi in the stools, which leads to serious impairment of the patient's health and threatens to induce a condition of chronic invalidism, the question of operative interference must be considered. A poor man who cannot afford the loss of time and expense involved by a cure at Carlsbad, Neuenahr, Harrogate, etc., should be advised to submit to operation. A rich patient should be given the chance of a course of spa treatment under careful medical supervision before an operation is undertaken. An additional reason for operating in some cases is that carcinoma of the gall-bladder occurs in from 14 to 4 per cent of all the persons with gall-stones, and that removal of the gall-stones and, if necessary, of the gall-bladder may prevent this sequel. In a case of recurrent attacks of biliary colic it would probably be safer to advise operative interference at any earlier date in patients who have a family history of carcinoma than in other patients. The patient's condition, strength, and power of resistance must be considered in deciding on operative interference.

(ix) When, from adhesions between the gall-bladder and pyloric end of the stomach, continued and severe gastric symptoms are produced (*vide* p. 758).

[1] Boix. *Arch. gén. de méd.*, Paris, 1901, clxxxviii, 470.
[2] Carl Beck. *Med. Week*, Paris, 1897, v. 137.

(x) In patients who are acquiring the morphine habit as the result of prolonged suffering operative interference is necessary to prevent the establishment of this pernicious habit.

(xi) In some cases of fistulae, both external and internal.

For the details of the operations the reader must consult the text-books on operative surgery. The question of recurrence after operation is dealt with on p. 743.

INDEX

Abdomen, the, disease of and displacement of the liver, 19-22 ; in malignant disease of the liver, 508 ; pain in, and Riedel's lobe, 14 ; strapping of, in ascites, 259 ; tumour of, and Riedel's lobe, 14

Abrin poisoning, and acute cholecystitis, 608 ; and portal cirrhosis, 192

Abscess, actinomycotic, of the liver, 385 (Fig. 50) ; areolar hepatic, 75, 123 (Fig. 21) ; biliary, 674 (Fig. 93) ; cerebral, due to single hepatic abscess, 144 ; gummatous, of the liver, 356 ; localised peritoneal biliary, 773

Abscess, multiple of the liver, 154-157 ; and appendicitis, 155 ; and dysentery, 155 ; and large single hepatic abscess, 157 ; diagnosis from single hepatic abscess, 147 ; in portal vein infection, 155 ; in pyaemia, 154 ; in suppurative cholangitis, 619, 674 ; in suppurative pylephlebitis, 74

Abscess, pericholangitic, 673 ; porto-pyaemic of the liver, 68-82 ; round the gall-bladder, 619 ; secondary pyo-septicaemic hepatic, 157

Abscess, single or tropical, of the liver, 117-153 (Figs. 20, 21) ; abdomen in, 138 ; age and, 126 ; alcoholism and, 125 ; altitude and, 124 ; amoebae in, 130-132 ; and appendicitis, 123 ; and enteric fever, 121 ; and extension of inflammation, 121 ; and hepatic aneurysm, 44 ; and influenza, 122 ; and pyaemia, 123 ; and suppurative pylephlebitis, 68 ; and yellow fever, 126 ; arthritis in, 135 ; bacteriology, 131-132 ; blood-changes in, 136 ; capsule round, 129 ; climate and, 124 ; clinical picture, 133-135 ; complications, 144-145 ; cough in, 134 ; course and duration, 140 ; decubitus in, 135 ; diagnosis, 145 - 151 ; diagnosis from hydatid cyst, 407, from pylephlebitis, 80, from suppurative cholangitis, 677 ; diarrhoea in, 140 ; diet and, 125 ; disposing factors, 124-127 ; due to ulceration of the gall - bladder, 757 ; empyema due to, 137 ; etiology, 117-124 ; fever in, 133 ; geographical distribution, 124 ; imitated by acute leukaemia, 443 ; imitated by gumma, 365 ; in England, 125 ; jaundice in, 136 ; latent, 133, 140 ; leucocytosis in, 145 ; liver dulness in, 139 ; liver in, 128-130 ; malaria and, 125 ; morbid anatomy, 127-131 ; nervous symptoms in, 135 ; number of, 128 ; onset, 133 ; pain in, 134 ; painful succussion in, 138 ; perihepatitis in, 139 ; physical signs, 135 - 140 ; prognosis, 151 ; prophylaxis, 152 ; pus in, 130-132 ; race and, 124-125 ; recurrence of, 143, 152 ; rigors in, 134 ; rupture of, 140-144 ; sex and, 126 ; shape and size of, 128 ; spleen in, 139 ; sweating in, 133 ; tenderness in, 134 ; termination, 140-144 ; trauma and, 120-121 ; treatment, 152-153 ; urine in, 139 ; wasting in, 135

Abscess, subphrenic, and bronchobiliary fistula, 771 ; and hepatic abscess, 121, 142 ; and hepatoptosis, 33 ; and suppurative pylephlebitis, 80 ; diagnosed in cholecystitis, 620 ; diagnosis from hepatic abscess, 146-147, from hydatid cyst, 407, 410 ; due to hydatid cysts, 422 ; in suppurative pylephlebitis, 76 ; liver displaced in, 20

Abscess, suprahepatic, 127 ; tropical, *see* Abscess, single ; tuberculous hepatic, 345

Accessory livers, 4

Acholia, 38

Acholuric jaundice, 534

Acid, chondroitin sulphuric, in lardaceous disease, 434 ; glycerophosphoric, in fatty liver, 432 ; organic, and portal cirrhosis, 183, 184

Acidosis, in acute yellow atrophy, 589, 592 ; in phosphorus poisoning, 595 ; in portal cirrhosis, 233

Acromegaly with chronic cholangitis, 680

Actinomycosis of the gall-bladder, 628

Actinomycosis of the liver, 383-388 (Fig. 50) ; and hepatic abscess, 122 ; and hepatic tuberculosis, 342, 345 ; clinical picture, 386 ; diagnosis, 387 ; method of

infection, 384 ; prognosis, 387 ; sex and, 383 ; treatment, 387
Acupuncture of hydatid cysts, 412
Acute yellow atrophy of the liver, 575-592 ; *see* Liver, acute yellow atrophy of the
Addison's disease, and biliary cirrhosis, 320 ; and haemochromatosis, 307
Addison's pill, 95 ; in ascites, 264
Adenoma of the gall-bladder, 630
Adenoma of the liver, 455-463 (Plate V ; Fig. 59) ; acinous, 455 ; and cirrhosis, 225 ; and thrombosis of hepatic veins, 48 ; clinical aspect, 463 ; cystic degeneration of, 445 ; cystic solitary, 453, 458 ; derived from the bile-ducts, 457-458 ; fetal origin of, 456 ; histology, 462 ; imitating carcinoma, 470 ; in subacute atrophy, 583-584; in portal cirrhosis, 198, 207, 292, 459 ; morbid anatomy, 457, 462 ; single, 455-459 ; solitary, 455
Adenomyofibroma of the common duct, 689
Adhesion-dyspepsia, 613, 758
Adhesions, pericholecystitic, 758 ; peritoneal, liver displaced by, 20
Adrenalin, injection of after paracentesis, 260 ; in haematemesis, 273
Ague (*see* Malaria) and intermittent hepatic fever, 761
Alanine, urinary, in acute yellow atrophy, 581 ; in phosphorus poisoning, 595
Albumin, presence of, in hydatid fluid, 393, 395
Albuminuria, hepatogenic, 514 ; in acute hepatitis, 115 ; in acute congestion of the liver, 109 ; in biliary cirrhosis, 322 ; in biliary colic, 736 ; in lardaceous disease, 363-364 ; in obstructive jaundice, 542 ; in portal cirrhosis, 233 ; in suppurative pylephlebitis, 79
Albumosuria, in hydatid disease of the liver, 404 ; in portal cirrhosis, 234 ; in single hepatic abscess, 139-140
Alcaptonuria, and haemochromatosis, 307 ; distinction from melanuria, 516
Alcohol, use of, in acute congestion of the liver, 111 ; in functional liver disease, 43 ; in portal cirrhosis, 296-297
Alcoholism, and acute congestion of the liver, 108 ; and acute yellow atrophy, 578 ; and biliary cirrhosis, 312 ; and catarrhal jaundice, 664-665 ; and cholelithiasis, 715 ; and chronic simple peritonitis, 223 ; and perihepatitis, 166 ; and portal cirrhosis, 181-183, 286 ; and portal cirrhosis in children, 334 ; and single hepatic abscess, 125 ; fatty liver in, 426
Aluminium poisoning and cirrhosis, 184
Ammonia, urinary, in acute congestion of the liver, 109 ; in acute yellow atrophy, 589 ; in cirrhosis, 109 ; in phosphorus poisoning, 595 ; in portal cirrhosis, 233
Ammonium chloride, use of, in acute congestion of the liver, 109 ; in acute hepatitis, 117 ; in hepatic abscess, 152 ; in lardaceous liver, 438 ; in portal cirrhosis, 300
Ammonium salts, conversion into urea, 37
Amoeba buccalis, 131
Amoeba coli Lösch, 131, 141
Ampulla of Vater, the, malignant tumours of, 702-708 (Figs. 101, 102) ; and papilloma, 704-705 ; carcinoma, 703 ; cholelithiasis and, 706 ; diagnosis, 706 ; etiology, 705 ; illustrative cases of, 707-708 ; jaundice in, 706 ; melanoma of, 703 ; metastases in, 705 ; morbid anatomy, 704 ; pathological results, 705 ; treatment, 709
Ampulla of Vater, the, mechanical effects of gall-stones in, 750, 766
Amyl alcohol and portal cirrhosis, 182
Amyl nitrite, use of, in haematemesis, 273
Anaemia, after haematemesis, 267 ; fatty liver in, 428 ; pernicious, imitated by chronic splenomegalic haemolytic jaundice, 540
Anaemia, splenic, and haemochromatosis, 307 ; and portal thrombosis, 66 ; ascites in, 256 ; diagnosis, from cirrhosis, 272, 290, from gumma of the liver, 365, from portal thrombosis, 64
Anastomosis, venous, in portal cirrhosis, 209-215 ; hepatopetal, 60
Aneurysm, abdominal, and biliary colic, 741 ; and cholelithiasis, 717 ; and jaundice, 560 ; liver displaced by, 21
Angina pectoris and biliary colic, 735, 741
Angiocholitis, 535, 679, 680
Angiofibroma, hepatic, 465
Angioma, cavernous biliary, 453 ; cutaneous, in portal cirrhosis, 228-229 ; encysted, 464 ; melanotic, 465 ; of the liver, 463-467 (Fig. 60), cyst-formation by, 445 ; pharyngeal, and haematemesis in portal cirrhosis, 271
Angioma, spider, in catarrhal jaundice, 666 ; in chronic jaundice, 542 ; in portal cirrhosis in children, 334
Angiosarcoma, of the gall-bladder, 631 ; of the liver, 483
Ankylostomiasis and cirrhosis, 176, 190
Anthracosis, hepatic, 302 ; of the lungs, 302
Antipyrin in biliary colic, 742
Antiseptics, intestinal, 592 ; in biliary cirrhosis, 326
Anuria, reflex, in cholecystitis, 624
Anxiety and cholelithiasis, 715
Apocynum, use of, in ascites, 265
Appendices epiploicae, the, adherent to the gall-bladder, 630 ; and lipomas of the liver, 468
Appendicitis, and cholecystitis, 604 ; and cholelithiasis, 715 ; and multiple hepatic abscess, 155-156 ; and portal cirrhosis, 187 ; and single hepatic abscess, 123 ;

and subphrenic abscess, 147 ; and suppurative pylephlebitis, 69 ; diagnosis, from acute cholecystitis, 612, from biliary colic, 739 ; due to cholecystitis, 758 ; due to gall-stones, 770 ; obliterative, 652
Arginine, urinary, in phosphorus poisoning, 595
Argyria, and portal cirrhosis, 184 ; imitated in haemochromatosis, 306 ; imitated in melanotic sarcoma, 511 ; of the liver cells, 440
Arm, pain in the, in cholelithiasis, 731
Arsenic poisoning, and portal cirrhosis, 184
Arsenic, use of, in portal cirrhosis, 301
Arteriosclerosis, and portal cirrhosis, 214, 223 ; of the hepatic artery, 47
Artery, hepatic, the, 44-48 ; and typhoidal cholecystitis, 606 ; and tuberculosis of the liver, 337
Artery, hepatic, the, aneurysm of, 44-46 (Fig. 10), 758 ; and cholelithiasis, 772 ; and hydatid cyst, 407 ; and jaundice, 561 ; and portal thrombosis, 58 ; and suppurative cholangitis, 672
Artery, hepatic, the, arteriosclerosis of, 47 ; embolism of, 47, and infarction, 105 ; in congenital syphilis of the liver, 374 ; in portal cirrhosis, 215 ; ligature of, 47 ; thrombosis of, 47
Artery, pulmonary, the, amoebae in, 141
Arthritis, in biliary cirrhosis, 321 ; in single hepatic abscess, 135
Arthritism, 26, 40 ; and portal cirrhosis, 186
Ascaris lumbricoides, cholelithiasis due to, 713 ; cholangitis due to, 671 ; jaundice due to, 549 ; in the bile-ducts, 682 ; in the common bile-duct, 616
Ascites, acute, 246 ; bilious, 416
Ascites, chylous or chyliform, in carcinoma of the gall-bladder, 644 ; in chronic venous engorgement of the liver, 94 ; in lymphadenoma, 390 ; in malignant disease of the liver, 513 ; in portal cirrhosis, 247-248
Ascites, compression of inferior vena cava by, 212 ; diagnosis of, from distended gall-bladder, 745, from hydatid cysts in the liver, 410 ; encysted, 250 ; haemorrhagic, 248, 480, 485, 491 ; in actinomycosis of the liver, 387 ; in acute yellow atrophy, 585, 588 ; in alveolar hydatid, 425 ; in bilharziasis, 190 ; in carcinoma of the gall-bladder, 643 ; in chronic venous engorgement of the liver, 93 ; in cirrhosis maligna, 476 ; in congenital obliteration of the bile-ducts, 655 ; in congenital syphilis, 377 ; in delayed congenital syphilis, 380 ; in gumma of the liver, 361-362 ; in hepatic angioma, 466 ; in hydatid cysts of the liver, 403 ; in lardaceous liver, 436-437 ; in leukaemic infiltration of the liver, 443 ; in local perihepatitis, 161 ; in lymphadenoma, 390 ; in malignant disease of the bile-ducts, 697 ; in malignant disease of the liver, 510, 512-513
Ascites in portal cirrhosis, 226-227, 242-266 ; and collateral hepatic circulation, 243 ; and Eck's fistula, 262 ; and heart-failure, 245 ; and perihepatitis, 245 ; and peritonitis, 244 ; and portal obstruction, 243 ; and portal thrombosis, 244 ; and toxaemia, 244 ; bacteriology, 248 ; bad effects of, 258 ; causes of, 243-246 ; chyliform, 247 ; chylous, 247 ; connexion with portal blood-pressure, 262 ; continuous drainage of, 260 ; cytology of, 243, 247, 254 ; diagnosis, 251 - 256 ; diaphragm raised by, 249 ; diet in, 265 ; dilated abdominal veins in, 249 ; diuretics in, 264 ; effects, 251 ; encysted, 250 ; fluid in, 246-249 ; haemorrhagic, 248 ; heart displaced by, 249 ; lactescent, 247 ; liver dulness in, 249 ; onset, 246 ; paracentesis in, 257-260 ; physical signs, 249-251 ; prognosis, 256 - 257 ; prognostic value of, 295 ; purgatives in, 265 ; symptoms, 251 ; tension of fluid in, 248; thrill in, 250 ; treatment, 257-266 ; umbilicus in, 249, 251 ; weight of liver in, 243
Ascites in portal cirrhosis in children, 334
Ascites, in portal thrombosis, 64 ; in sarcoma with cirrhosis, 485 ; in single hepatic abscess, 138 ; in suppurative pylephlebitis, 79 ; lactescent, 247 ; milky, 248 ; opalescent, 248 ; pseudochylous, in chronic venous engorgement of the liver, 94 ; purulent, in malignant disease of the liver, 513 ; recurrent, in pericarditic pseudocirrhosis, 96-97 ; wrongly diagnosed, in hepatic abscess, 150, in single hepatic abscess, 138
Aspiration, *see* Paracentesis
Aspirin as a cholagogue, 776
Asthma in hepatoptosis, 32
Asystole, hepatic, 85-96
Atrophy, acute yellow of the liver, 575 ; *see* Liver, the, acute yellow atrophy of ; pericholangitic, 763 ; red, of the liver, 580-581, 583 ; subacute, 583, 589
Australia, hydatid disease in, 398
Auto-intoxication, in chronic venous engorgement of the liver, 94 - 95 ; in obstructive jaundice, 547
Autolysis, in acute yellow atrophy, 579, 581, 589, 592 ; in phosphorus poisoning, 593

Babinski's sign in acute yellow atrophy, 587
Bacillus aerogenes capsulatus, in acute cholecystitis, 607 ; in foaming liver, 6-7 (Fig. 4) ; in suppurative cholangitis, 673, 705 ; in suppurating hydatid cysts, 402, 422
Bacillus coli communis, in acute cholecystitis, 605 ; in acute yellow atrophy, 579,

588 ; in ascitic fluid, 248 ; in biliary cirrhosis, 312, 313 ; in cholelithiasis, 710-711 ; in chronic perihepatitis, 166 ; in congenital syphilis, 377 ; in portal cirrhosis, 189, 193 ; in single hepatic abscess, 131, 132 ; in suppurating hydatid cysts, 422 ; in suppurative cholangitis, 673 ; in suppurative pylephlebitis, 75 ; infection with, in cirrhosis, 278
Bacillus comma in suppurative cholangitis, 673
Bacillus fragilis in suppurating hydatid cysts, 422
Bacillus influenzae similis in multiple hepatic abscess, 157
Bacillus moniliformis in suppurating hydatid cysts, 422
Bacillus mucosus capsulatus, in foaming liver, 6 ; in single hepatic abscess, 132 ; in suppuration of the hepatic veins, 53
Bacillus paratyphosus, in acute cholecystitis, 607 ; in catarrhal jaundice, 665 ; in cholelithiasis, 712 ; in suppurative cholangitis, 673
Bacillus proteus in congenital syphilis, 377
Bacillus proteus fluorescens and Weil's disease, 597, 598
Bacillus pseudodiphtheriae in portal cirrhosis, 190, 193
Bacillus pyocyaneus, and portal cirrhosis, 185, 192, 193 ; in single hepatic abscess, 132
Bacillus tuberculosis, in lobulation of the liver, 1, 346 ; in chronic perihepatitis, 166 ; in portal cirrhosis, 190
Bacillus typhosus, in acute cholecystitis, 605 ; in biliary cirrhosis, 312 ; in catarrhal jaundice, 664, 665 ; in cholelithiasis, 710-712 ; in chronic perihepatitis, 166 ; in single hepatic abscess, 122, 132 ; in suppurative cholangitis, 673 ; in suppurative pylephlebitis, 75
Backward pressure, diagnosis from perihepatitis, 171
Bacteriuria in Weil's disease, 600
Baillie's pill, 95 ; in ascites, 264
Balantidium coli in the bile-ducts, 686
Ball-valve action of gall-stones, 748, 759
Ballottement in single hepatic abscess, 139
Banti's disease, and arsenical poisoning, 184 ; and portal cirrhosis, 188 ; and splenic anaemia, 273 ; diagnosis, from ascites and cirrhosis, 256, from biliary cirrhosis, 325, from portal cirrhosis, 290 ; distinguished from chronic splenic anaemia, 216 ; relation to biliary cirrhosis, 316 ; terminal cirrhosis in, 83
Baths, use of, in functional liver disease, 43
Belladonna, use of, in cholelithiasis, 755
Belt, abdominal, in hepatoptosis, 34-36
Bile, the, absent in cysts of cystic disease, 450 ; action on hydatid cysts, 395 ; and cholagogues, 775, 777 ; bitter taste of, 41 ; effects of water-drinking on, 775 ; expectoration of, 142, 771 ; inspissation of, 709 ; stagnation of, treatment, 774 ; sterility of, 756, 773
Bile-ducts, congenital obliteration of the, 188, 649-659 (Figs. 90-92) ; cases resembling, 650 ; cirrhosis in, 330 ; clinical picture, 655-657 ; diagnosis, 657 ; duration, 657 ; etiology, 650 ; haemorrhages in, 656 ; heredity and, 650 ; incidence, 650 ; liver in, 652, 653 ; malformations and, 650 ; nomenclature, 649 ; pathogeny, 651-653 ; prognosis, 657 ; sex and, 651 ; site of obliteration, 653-654 ; spleen in, 652, 655 ; syphilis and, 650, 657-659 (Fig. 92) ; treatment, 657 ; urine in, 656 ; wasting in, 657
Bile-ducts, malignant tumours of the larger, 689-708 (Figs. 99-102) ; age and, 691 ; and carcinoma of the pancreas, 693-694 ; and papilloma, 690 ; appearances, 692 ; ascites in, 697 ; bile-ducts in, 695 ; cholelithiasis and, 690 ; clinical picture, 696-698 ; complications, 698 ; diagnosis, 699-701 ; diagnosis from carcinoma of the gall-bladder, 646 ; due to invasion, 694 ; duration, 698 ; etiology, 690 ; gall-bladder in, 695 ; incidence, 689 ; jaundice in, 696-698 ; juxta-hepatic, 691 ; metaplasia in, 694 ; morbid anatomy, 691-696 ; naked-eye diagnosis of, 693 ; not diagnosed, 689-690 ; onset, 696 ; pain in, 697 ; pseudobiliary colic in, 741 ; secondary growths in, 696 ; sex and, 691 ; situation of the growth, 691 ; spread of, 693 ; symptoms, 697 ; treatment, 701 ; tubular, 692
Bile-ducts, the, diseases of, 649-708 (Figs. 90-102), *see also* Duct ; aberrant, in cystic disease, 453, 454 ; abnormalities of, 649 ; adenomas derived from, 457-458 ; and primary carcinoma of the liver, 480 ; atresia of, 649 ; carcinoma of, 689-708 ; carcinoma of, and portal thrombosis, 57 ; casts of, 725 ; cystic papilloma of, 688 ; cystic tumours of, 659-661 ; cysts of, 444-446 ; dilatation of, 659 ; distomiasis of, 683-684 ; experimental ligature of, 327-329 ; fistulae between, 772 ; fistulae of, 647, 766-774 ; foreign bodies in, and jaundice, 549-550 ; growth of hepatic malignant disease into, 482, 492, 511 ; hydatid cysts of, 689 ; in carcinoma, 695 ; in chronic splenomegalic haemolytic jaundice, 539 ; in congenital obliteration of the bile-ducts, 653 ; in cystic disease of the liver, 452 ; in portal cirrhosis, 208 ; in secondary syphilis, 349-350 ; in suppurative cholangitis, 673 ; innocent tumours of, 687-689 (Fig. 98) ; lipoma of, 687 ; lithogenic catarrh of, 710 ; myxomatous tumours of, 689 ; newly

formed, in portal cirrhosis, 205-206 (Fig. 32), *see also* Canaliculi, pseudobile ; occluded by secondary malignant growths in the liver, 492 ; papilloma of, 457, 687-689 (Fig. 98) ; carcinomatous, 690 ; parasitic affections of, 682-687 (Figs. 96, 97) ; rupture of hepatic abscess into, 143 ; rupture of hydatid cysts into, 411, 418-420 (Fig. 53) ; simple stricture of, 661-663 ; spasm of, 706, 731 ; spasm of, and colic, 697 ; stricture of, and carcinoma, 662 ; tuberculosis of, 340-343 ; tumours inside the, and jaundice, 550 ; ulceration of, and carcinoma, 690 ; vitiligoidea of, 689 ; xanthelasma of, 689 ; xanthoma of, 689
Bile-pigments, the, effects on the heart, 543 ; formation of, 531, 538 ; in obstructive jaundice, 542
Bile-salts, the, and pancreatitis, 750 ; as cholagogues, 775 ; effects of, in jaundice, 545-547 ; urinary, in jaundice, 542
Bilharziasis and portal cirrhosis, 190
Biliary colic, 731 ; *see* Colic, biliary
Biliary mask, the, 40
Bilihumin, 709
Biliousness, 41
Bilirubin, in gall-stones, 724-725 ; in hydatid cysts, 395 ; toxicity of, 546 ; urinary, in jaundice, 542
Bilirubin-calcium, 709-710
Biliverdin in jaundice, 541
Biliverdin-calcium, in gall-stones, 725
Birds, hepatic tuberculosis in, 337, 343
Bladder, gall-, the, *see* Gall-bladder, 601
Bladder, the urinary, biliary fistula into, 772
Blood, the, in acute yellow atrophy, 588 ; in biliary cirrhosis, 321-322 ; in catarrhal jaundice, 667 ; in chronic splenomegalic haemolytic jaundice, 537-540 ; in congenital obliteration of the bile-ducts, 656 ; in malignant disease of the liver, 514 ; in obstructive jaundice, 544 ; in phosphorus poisoning, 594 ; in single hepatic abscess, 136 ; in suppurative pylephlebitis, 79
Blood-pressure, in portal cirrhosis, 236 ; intrahepatic, 24
Bradycardia in obstructive jaundice, 543
Breast, the, carcinoma of, and secondary growths in the liver, 500
Bright's disease and cholelithiasis, 718
Bronchitis in portal cirrhosis, 284
Brood-capsule, hydatid, 391-392
Brunner's glands, carcinoma of, 704
Budd's cirrhosis, 186
Buhl's disease, 572
Butyric acid and portal cirrhosis, 184, 186

Calcification, in gumma of the liver, 355-356 (Fig. 44) ; in hepatic angiomas, 464 ; in the liver cells, 440 ; of a psorospermial tumour, 685 ; of the gall-bladder, 627 ; of the portal vein, 83
Calcium carbonate crystals in hydatid cysts, 391, 393
Calcium salts, and jaundice, 548, 567, 776 ; in haematemesis, 273
Calculus, biliary, *see* Gall-stones ; cholesterin, 710 ; pancreatic, and biliary colic, 738 ; pancreatic, and jaundice, 560
Calomel, use of, in biliary cirrhosis, 326 ; in chronic catarrhal cholangitis, 679 ; in congenital syphilis, 383 ; in functional liver disease, 42 ; in jaundice, 540, 566 ; in malignant disease of the bile-ducts, 702 ; in portal cirrhosis, 299
Cammidge's tests, 557 ; in carcinoma of the bile-ducts, 699 ; in carcinoma of the pancreas, 762 ; in catarrhal jaundice, 667 ; in gall-stone in the common duct, 762 ; in malignant disease of the bile-ducts, 698
Canaliculi, pseudobile, in acute yellow atrophy, 582-584 ; in biliary cirrhosis, 315-316 ; in carcinoma with cirrhosis, 477, 479 ; in congenital obliteration of the bile-ducts, 653 ; in congenital syphilis, 374 (Fig. 48) ; in gumma of the liver, 354 ; in hepatic adenomas, 461, 462 ; in lymphadenoma, 388 (Fig. 51) ; in multiple adenomas, 461 ; in obstructive biliary cirrhosis, 331 ; in portal cirrhosis, 205-206 (Fig. 32) ; in single hepatic abscess, 129 ; round hydatid cysts, 393
Cancer du pylore pancréatico-biliaire, 703
Cancer en amande, 472
Caput Medusae, in hydatid cysts of the liver, 401 ; in portal cirrhosis, 211-212, 229 ; in portal thrombosis, 65
Carbamic acid poisoning and Eck's fistula, 214
Carcinoma, and cholelithiasis, 719 ; atypical, of the bile-ducts, 694 ; duodenal, 704 ; juxta-ampullary, 702 ; juxta-hepatic, 691 ; mammary, and cholelithiasis, 720 ; mammary, method of spread to the liver, 497 ; of Brunner's glands, 704 ; of the gall-bladder, 631-648 (Figs. 86-89) ; of the larger bile-ducts, 689-708
Carcinoma of the liver, primary, 469-486 (Figs. 61-66), 505-530 ; acute, 518 ; ascites in, 512 ; degenerative changes in, 481 ; diagnosis from secondary new growth, 526-528 ; diffuse, 473 ; duration, 518 ; forms of, 472 ; gall-stones and, 482 ; general diagnosis, 519-526 ; histology, 472-474, 477-479 ; imitated by adenoma and cirrhosis, 470 ; incidence, 469 ; infiltrating, 473 ; injury and, 471 ; massive, 472 ; melanotic, 480 ; multiple or nodular, 473 ; operative treatment, 529 ; origin of, 480 ; physical signs, 505-516 ; secondary growths due to, 481 ; sex and, 469 ; situation of growth, 471 ; symptoms, 516-518 ;

termination, 519 ; trabecular, 477, 480 ; treatment, 529 ; with cirrhosis, 474-479 (Figs. 63-66)
Carcinoma of the liver, secondary, 481, 487-530 (Plate I ; Figs. 70, 73, 74) ; and tuberculosis of the liver, 496 ; colloid, 491 ; degenerative changes in, 490 ; diagnosis from primary tumours, 526-528 ; duration, 518 ; general diagnosis, 519-526 ; histology, 493 ; local fibrosis in, 494 ; operative treatment, 529 ; perihepatitis due to, 492 ; physical signs, 505-516 ; prognosis, 528 ; pseudocysts in, 491 ; remainder of liver in, 494-497 ; resembling gumma, 353 ; situation of primary growth, 498-504 ; symptoms, 516-518 ; termination, 519 ; treatment, 429 ; umbilication in, 489, 492 ; without a primary focus, 474
Carcinoma, of the stomach, jaundice in, 553 ; of Wirsung's duct, 703 ; perivaterian duodenal, 508 ; spheroidal-celled of the bile-ducts, 694 ; subhepatic, 691 ; supraduodenal of the bile-duct, 691 ; suprarenal, 504
Cardiac liver, 85-96
Carlsbad water, in cholelithiasis, 775, 776, 779
Carriers, typhoid, and cholecystitis, 603, 606
Caseation, in adenomas of the liver, 460, 461 ; in congenital syphilis, 371 ; in gumma of the liver, 353 ; in tuberculosis of the liver, 343-345
Catarrh, lithogenic, of the gall-bladder and bile-ducts, 710 ; of the intestine, 740
Cavernoma of the liver, 463-467 (Fig. 60)
Cerebrospinal fluid, the, in congenital obliteration of the bile-ducts, 655 ; in obstructive jaundice, 543
Charcot's intermittent hepatic fever, 759-764
Charcot-Leyden crystals, in acute yellow atrophy, 582 ; in hydatid cysts, 396
Children, hepatic cirrhosis in, 333-336
Chill on the liver, 107
Chitin, in hydatid cysts, 393
Chloroform poisoning, and acute yellow atrophy, 579 ; and portal cirrhosis, 185 ; fatty liver in, 428, 432, 433 ; jaundice in, 536
Chloroform, use of, in biliary colic, 738, 742
Chloroma, 504 ; liver in, 442
Cholaemia, in carcinoma of the ampulla of Vater, 705 ; in carcinoma of the bile-ducts, 698 ; in carcinoma of the gall-bladder, 644 ; in carcinoma of the pancreas, 557 ; in hepatism, 40 ; in obstructive jaundice, 542 ; leucocytosis in, 544 ; prognosis, 566
Cholaemia, familial splenomegalic, 537-540
Cholaemia, simple family, 40 ; and chronic splenomegalic haemolytic jaundice, 538 ; and urobilin jaundice, 535
Cholagogues, 775
Cholangitis, acute catarrhal, 663-670 ; associated with pericholangitis, 682 ; bacteriology, 665 ; blood in, 667 ; catarrhal pancreatitis and, 664, 668 ; causation, 664 ; clinical picture, 666 ; diagnosis, 669 ; diet in, 670 ; duration, 668 ; effects, 668 ; gastroduodenal catarrh and, 663 ; in carcinoma of the gall-bladder, 638, 644 ; incidence, 666 ; liver in, 668 ; morbid anatomy, 665 ; premonitory symptoms, 666 ; prognosis, 668 ; pulse-rate in, 666 ; treatment, 669-670 ; urine in, 667
Cholangitis, and biliary cirrhosis, 312, 315 ; and congenital obliteration of the bile-ducts, 651-653 ; and suppurative pylephlebitis, 72-73 ; ascending, 711
Cholangitis, chronic catarrhal, 678-680 ; and intermittent hepatic fever, 762 ; diagnosis from suppurative cholangitis, 677 ; extrahepatic, 678 ; intrahepatic, 679
Cholangitis, descending, 711 ; due to hydatid disease, 418 ; due to ruptured hydatid cyst, 411 ; fetal, and cystic disease, 452, 454 ; in acute yellow atrophy, 582 ; in acute congestion of the liver, 108 ; in malignant disease of the liver, 507-508 ; in obstructive biliary cirrhosis, 331 ; jaundice in, 550 ; obliterative, 652 ; obliterative congenital, 330
Cholangitis, suppurative, 671-678 (Fig. 93) ; abscess-formation in, 619, 674 ; and pylephlebitis, 80 ; bacteriology, 673 ; cholelithiasis and, 671 ; clinical picture, 675 ; complications, 676 ; diagnosis, 676-677 ; duration, 676 ; etiology, 671 ; histology, 675 ; hydatid cysts and, 671 ; imitated by cholangitis, 673 ; in carcinoma of the ampulla of Vater, 705 ; in intermittent hepatic fever, 761-762 ; infectious diseases and, 672 ; jaundice in, 675 ; morbid anatomy, 673 ; prognosis, 677 ; tuberculous, 338, 340-343
Cholecystectomy, 624, 627, 647, 743
Cholecystenterostomy, in congenital obliteration of the bile-ducts, 658 ; in jaundice, 567 ; in malignant disease of the bile-ducts, 702 ; in pancreatitis, 766
Cholecystitis, acute, 603-624 (Figs. 82, 83) ; acute haemorrhagic, 615 ; adhesions in, 610, 613, 620 ; albuminuria in, 618 ; and gall-stones, 616 ; appendicitis and, 604, 610, 612, 715 ; bacteriology, 604-608 ; calculi and, 603 ; catarrhal infective, 609-614 ; causes, 603 ; clinical features, 610, 615, 617-619, 622 ; colic in, 618 ; complications and results, 619 ; diagnosed as appendicitis, 620 ; diagnosis, 612, 620, 622 ; diagnosis from biliary colic, 738 ; empyema of gall-bladder in, 613 ; typhoidal with gall-stones, 606 ; foreign bodies and, 603 ; forms of, 609 ; gangrenous, 623 ; histology, 610, 615, 617 ; in carcinoma of the gall-bladder, 645 ; incidence, 621 ;

infection and, 604 ; influenzal, 604 ; intestinal infection and, 604 ; jaundice in, 618 ; lymphatic glands in, 609 ; membranous, 614 ; morbid anatomy, 609, 617, 622, 624 ; pain in, 610, 618, 622 ; peritonitis in, 611 ; phlegmonous, 621-623 (Fig. 83) ; prognosis, 612, 621, 623 ; respiration in, 611 ; sequels, 613 ; serous, 609 ; signs and symptoms, 626 ; suppurative, 612-621 ; toxic, 608 ; trauma and, 608 ; treatment, 614 ; ulceration of gall-bladder in, 613 ; vomiting in, 611, 614, 618

Cholecystitis, chronic, 624-628 (Figs. 84, 85) ; as a cause of biliary colic, 732 ; association with gall-stones and carcinoma of the gall-bladder, 638-641 ; biliary colic in, 626, 731 ; catarrhal, 624 ; diagnosis from hydatid cyst, 406 ; due to acute cholecystitis, 613 ; due to gall-stones, 756 ; histology, 625 ; in portal cirrhosis, 208 ; morbid anatomy, 625 ; treatment, 626

Cholecystitis, chronic ulcerative, 627 ; croupous, 614 ; experimental typhoidal, 712 ; fibrinous, 614 (Fig. 82) ; lithogenic, 710-714 ; membranous, 614 ; obliterative, 625, 627 ; phlegmonous, 621-623 ; sclerosing atrophic, 627 ; suppurative, 616-621 ; tuberculous, 627 ; ulcerative, in cholelithiasis, 756

Cholecystotomy, in biliary colic, 743 ; in chronic catarrhal cholangitis, 679

Choledochotomy, 683, 764 ; stricture after, 662

Cholelithiasis, 709-782 (Figs. 103-108) ; age and, 722 ; and aneurysm of the hepatic artery, 45 ; and appendicitis, 715 ; and atrophy of the left hepatic lobe, 3 ; and bronchobiliary fistula, 771 ; and carcinoma of the bile-ducts, 690-691 ; and cholangitis, 671 ; and chronic cholecystitis, 626 ; and dyspepsia, 730, 731 ; and floating kidney, 556 ; and foreign bodies in the gall-bladder, 713 ; and malignant disease of the ampulla of Vater, 706 ; and portal thrombosis, 58 ; and pregnancy, 716 ; and sedentary life, 713 ; and stagnation of the bile, 713 ; and suppurative cholecystitis, 616 ; and tight lacing, 8, 11 ; anxiety and, 715 ; association with *Ascaris*, 683 ; association with carcinoma of the gall-bladder, 638-641 ; biliary colic in, 731-737 ; Bright's disease and, 718 ; carcinoma and, 719 ; causes of passage of stones from gall-bladder, 732 ; cholagogues in, 775 ; cholecystitis and, 709-713 ; clinical picture, 730-737 ; constipation and, 715 ; diabetes mellitus and, 717 ; diagnosis, 738-741 ; diagnosis from carcinoma of the bile-ducts, 699, from carcinoma of the gall-bladder, 645, from hepatoptosis, 34 ; diet and, 713 ; diet in, 779 ; dilatation of the bile-ducts in, 659 ; disposing causes of, 713 ; effects of, on the gall-bladder, 745-747 ; geographical distribution, 722 ; heart disease and, 716-717 ; heredity and, 720 ; immediate or exciting causes of, 709-713 ; in early life, 723 ; in infants, 650 ; in the newly born, 571 ; incidence, 721 ; indications for surgical interference, 780-782 ; indigestion and, 715 ; inflammatory changes in, 755-773 ; intermittent hepatic fever in, 759-764 ; intestinal obstruction in, 737, 751-755 ; jaundice in, 669, 737, 780-781 ; latent, 730 ; masked or inaugural symptoms, 731 ; massage in, 774, 778-779 ; myxoedema and, 719 ; number of stones in, 726 ; occupation and, 713, 721 ; olive oil in, 777-778 ; pancreatic affections in, 764-766 ; prophylaxis, 773 ; pylephlebitis in, 766 ; race and, 722 ; sex and, 723-724 ; shape and situation of stones in, 727 ; spa treatment of, 779 ; stricture of bile-ducts in, 661-663 ; treatment, medical, 774-780, surgical, 780-782 ; visceroptosis and, 716 ; water-drinking in, 775

Choleperitoneum after rupture of a hydatid cyst, 416

Cholera, and portal cirrhosis, 187 ; and suppurative cholangitis, 673

Cholesterin, biliary, increased in cholecystitis, 608 ; in calculi, 724-725 ; in hydatid cysts, 396 ; in the gall-bladder, 709 ; percentage of, in the bile, 719 ; poisoning by, in jaundice, 547 ; solution of, by olive oil, 777-778 ; tophus of, in xanthoma, 541 ; urinary, in single hepatic abscess, 140

Cholesterinaemia, 547

Cholesterol, 709, *see* Cholesterin

Cholesteryl oleate, 709

Chorea, tetanoid, 281, 335

Chorion-epithelioma of the liver, 473, 481

Cicatrice à filtration in ascites, 260

Cicatrices, syphilitic hepatic, 357 (Fig. 45)

Circulation, collateral, the, hepatopetal in the omentum, 60 ; in portal cirrhosis, 209-215, 291-292, bad effects of, 213-214 ; porto-caval, in portal cirrhosis, 210

Cirrhose biliaire anictérique, 310

Cirrhosis, acute, 677 ; and subacute diffuse hepatitis, 116 ; diagnosis from subacute atrophy, 590

Cirrhosis, and functional liver disease, 43 ; annular, 177 ; anthracotic, 184, 302, 440, pigmentation in, 204 ; arteriosclerotic, 173 ; ascites in, 175-176 ; atrophic, 177 ; atrophic biliary, 310, 314 ; biliary, 173, 309-336 (Figs. 39, 40), *see* Cirrhosis, hypertrophic biliary ; biliary types of, 173, 176 ; Budd's, 89, 186 ; carcinomatosa, 474-479 (Figs. 63-66) ; cardiac, 88 ; cardiotuberculous, 101, 346 ; centrilobular, in nutmeg liver, 91 ; classifications of, 172-176

Adami's anatomical, 173, Chauffard's etiological, 172, Rolleston's anatomical, 174, Rolleston's clinical, 175, Senator's clinical, 175; comparison with diseases of the kidneys, 176, 310; congenital hepatic, 333; congenital hepatic with obliterative cholangitis, 649, 651-653; dyspeptic, 89, 183, 347; epithelial, 452; Glissonian, 167, 168; haematemesis in, 175-266; hepatomegalic biliary, 175; hepatomegalic hypertrophic biliary, 310; hypersplenomegalic hypertrophic biliary, 175, 310, 316, 319; hypertrophic, 309; hypertrophic alcoholic, 196

Cirrhosis, hypertrophic biliary, 309-327 (Fig. 39); age and, 311; alcoholism and, 312; and cholelithiasis, 719; arthritis in, 321; bacteriology, 313; blood in, 321-322; cholangitis and, 312; cholecystotomy in, 679; clinical picture, 317; clubbing of the fingers in, 320-321; comparison with renal diseases, 310; course, 318; definition, 309; diagnosis, 323-325; diagnosis from intermittent hepatic fever, 762, from malignant disease of the bile-ducts, 701, from malignant disease of the liver, 520, from portal cirrhosis, 288; diet in, 326; different forms of, 310-311; duration, 325; etiology, 311; gall-stones in, 330; haemorrhages in, 320; heart in, 321; hepatomegalic, 175; history, 309; hypersplenomegalic, 175; imitated by gumma of the liver, 366; in children, 335; in congenital obliteration of the bile-ducts, 651-653; in malignant disease of the bile-ducts, 696; incidence, 311; jaundice in, 318, 320; juvenile type of, 310; larval forms of, 311; liver in, 314-316, 319; metasplenomegalic hypertrophic, 175, 189; morbid anatomy, 314-317; nervous system in, 321; onset, 317; pancreas in, 313, 317; pathogeny, 312; portal lymphatic glands in, 317; prognosis, 325; relation to Banti's disease, 316; respiratory system in, 322; sex and, 311; signs, 319; spleen in, 316, 319; splenomegalic, 175; symptoms, 318; termination, 323; treatment, 325-326; urine in, 322

Cirrhosis, hypertrophic fatty, 346

Cirrhosis, in children, 333-336; in congenital obliteration of the bile-ducts, 653; in congenital syphilis, 372-375 (Figs. 46, 48); in constriction lobes, 9, 11; insular, 327; intercellular, 174; intercellular, in congenital syphilis, 373; jaundice in, 173-176; Laennec's, 177; maligna, 474-479 (Figs. 63-66); metasplenomegalic hypertrophic biliary, 175, 189, 310, 320; microsplenic biliary, 319; mixed type, 174; multilobular, varieties of, 174; nodular, 461, and portal thrombosis, 56, in malaria, 195; nodular parenchymatous, and subacute atrophy, 583

Cirrhosis, obstructive biliary, 327-332 (Fig. 40); bacterial infection in, 328, 330; clinical features, 332; experimental evidence for, 327-329; gall-stones in, 330; history, 327; in intermittent hepatic fever, 760; incidence, 329; ligature of bile-ducts in, 327-329; morbid anatomy, 331-332; pancreas in, 332; spleen in, 331; treatment, 332

Cirrhosis, ordinary, common, or portal, 175; parasyphilitic, 180, 188; parasyphilitic multilobular, 369, 370, 381-383, and arteritis, 223; Pick's pericarditic pseudo-, 96-101; pigmented, 203, 302-308 (Fig. 38)

Cirrhosis, portal, abdominal haematoma in, 214-215; absent in pericarditic pseudo-cirrhosis, 98; acute, 677; acute infections in, 282; adhesions in, 198; age and, 177, 196, 293; albuminuria in, 233; alcohol in, 265, 274; alcoholism and, 181-183; and acute hepatitis, 113, 189; and arsenic poisoning, 184; and bacterial infection, 187, 189, 192; and carcinoma of the liver, 225; and cholelithiasis, 719; and cholera, 187; and Eck's fistula, 214; and enteric fever, 187; and fetal disease, 187-188; and gout, 185; and lead poisoning, 185; and mitral disease, 186; and sarcoma of the liver, 484; and secondary malignant disease of the liver, 495; and syphilis, 333; and the spleen, 188-189; and thrombosis of hepatic veins, 48, 50; and toxins, 190-192; arteriosclerosis in, 223; ascites in, 242-266, 295; association with congenital obliteration of the bile-ducts, 649, 651-653; association with syphilis of the liver, 358; bile-ducts in, 208; blood-changes in, 236-237; blood-pressure in, 236; bronchitis in, 284; chronic peritonitis in, 286; clinical features, 226-283; clubbing of the fingers in, 229; collateral circulation in, 209-215, 291-292; coma in, 227, 279-280; combined with biliary cirrhosis, 188, with primary carcinoma, 474-479 (Figs. 63-66); complications, 283-288, 296; constipation in, 299; convulsions in, 280; cyanosis in, 236; cystic formations in, 444; debility in, 230; definition, 177; delirium in, 280, 283; delirium tremens in, 280; diagnosis, 288-291; diagnosis from biliary cirrhosis, 323, from gumma of the liver, 361-363, from lardaceous disease, 437, from malignant disease, 520; diarrhoea in, 231; diet in, 265, 274, 297; diuretics in, 264; drugs in, 298; due to hepatic adenomas, 460; due to parasites in the portal vein, 84; due to portal thrombosis, 62; duration, 281; dyspepsia in, 231, 299; early stage of, 226; epi-

plopexy in, 261 ; epistaxis in, 226, 277 ; etiology, 177-180 ; facial aspect in, 228 ; fatty heart in, 283 ; fatty liver in, 195 ; fever in, 296 ; fibrosis in, 193-195 ; gall-bladder in, 208 ; general haemorrhages in, 278 ; general nutrition in, 293 ; generalised tuberculosis in, 282 ; geographical distribution, 179 ; glycosuria in, 234 ; gout in, 287 ; haematemesis in, 226, 266-274, prognostic value of, 294 ; haematuria in, 215, 277 ; haemochromatosis in, 207 ; haemoptysis in, 276 ; heart in, 224 ; hepatic abscess rare in, 130 ; hepatic artery in, 215 ; hepatic pain in, 239 ; heredity and, 179 ; histology, 201-208 ; history, 177 ; hyperplasia of liver-cells in, 205-207 ; in children, 333 ; infective endocarditis in, 288 ; jaundice in, 229 ; kidneys in, 221 ; late or ascitic stage of, 226-228 ; latent, 178, 196, 227, compensatory hyperplasia of the liver in, 461, spleen in, 215-216 ; liver in, 237-240 ; liver-cells in, 206-208 ; malarial pigmentation in, 307-308 ; melaena in, 267, 274-276 ; menorrhagia and metrorrhagia in, 278 ; method of death in, 281-283 ; milk in, 297-298 ; morbid anatomy, 195-201 ; multiple adenomas of the liver in, 459 ; nervous symptoms in, 279-281 ; non-alcoholic, 185 ; occupation and, 179 ; oedema in, 241-242, 295 ; oesophagus in, 219 ; offensive breath in, 230 ; operative treatment of, 260-264 ; pain in, 300 ; pancreas in, 219, 221 ; paracentesis abdominis in, 257-260, 283 ; paralysis in, 280 ; pathogeny, 180-195 ; perihepatitis in, 198, 239 ; peripheral neuritis in, 286 ; pigmentation in, 228 ; pleurisy with effusion in, 285 ; portal engorgement in, 300 ; portal lymphatic glands in, 215 ; portal vein in, 208 ; prognosis, 291-296 ; pruritus in, 279 ; pseudobile canaliculi in, 205-206 ; pulse-rate in, 235 ; purgatives in, 265 ; relation to primary carcinoma, 475 ; renal disease in, 224, 287 ; respiration in, 237 ; sex and, 178, 197 ; size of liver in, 294 ; size of spleen in, 294 ; skin in, 228 ; small intestine in, 220 ; spa treatment of, 299 ; spleen in, 215-219 (Fig. 36), 240-241 ; stomach in, 220 ; sudden death in, 235 ; temperature in, 237 (Fig. 37) ; terminal infections in, 287 ; terminal stages of, 286 ; termination, 281-283 ; thrombosis in, 288 ; treatment, 296-301 ; tuberculosis in, 222-223, 283-284, 345-348 ; tympanites in, 238 ; uraemia in, 282 ; urine in, 232 ; urotoxic coefficient in, 235 ; vascular system in, 235-236 ; venous anastomoses in, 209-215 ; venous bruits in, 229, 239, 241 ; vomiting in, 299 ; wasting in, 230 ; with nervous symptoms, 281

Cirrhosis, presplenomegalic hypertrophic biliary, 310, 320 ; splenogenous, 188, 314 ; splenomegalic hypertrophic biliary, 310 ; splenomegalic biliary, 175 ; sporadic fibrosis in, 174 ; syphilitic, so-called, 357 ; syphilitic, and thrombosis of the hepatic veins, 50 ; tuberculous, 347 ; umbilical vein, 187, 652 ; unilobular, 174 ; unilobular, in congenital obliteration of the bile-ducts, 653 ; venous, 177

Cirsomphalos, 249 ; in portal cirrhosis, 229

Climate and single hepatic abscess, 124, 153

Clubbing of the fingers, in biliary cirrhosis, 320-321 ; in delayed congenital syphilis, 380 (Fig. 49) ; in hydatid disease of the liver, 405 ; with lardaceous liver, 437 ; in portal cirrhosis, 229

Coagulability of the blood, the, in acute yellow atrophy, 588 ; in jaundice, 547 ; in obstructive jaundice, 544 ; in portal thrombosis, 67

Coccidium cuniculi in the bile-ducts, 684 (Figs. 96, 97)

Colic, biliary, 731-737 ; and pancreatic calculus, 738 ; caused by palpation, 732 ; complications, 737 ; connexion with carcinoma of the gall-bladder, 642 ; diagnosis, 738-741 ; diagnosis from acute cholecystitis, 612 ; fever in, 734 ; gall-bladder in, 735 ; haemoptysis in, 736 ; imitated by malignant disease of the liver, 517 ; in chronic cholecystitis, 626 ; in chronic splenomegalic haemolytic jaundice, 539 ; in hepatic abscess, 144 ; in intermittent hepatic fever, 761 ; in malignant disease of the bile-ducts, 697 ; in suppurative cholangitis, 676 ; in tuberculosis of the bile-ducts, 342 ; independent of calculi, 731 ; jaundice in, 737 ; left-sided pain in, 733 ; liver in, 735 ; onset, 733 ; pain in, 733-735 ; prognosis, 741 ; recurrent, 738, 781 ; signs and symptoms, 733-737 ; termination, 738 ; treatment, 742, 781 ; urine in, 736 ; vomiting in, 735, 742

Colic, intestinal, due to gall-stones, 752 ; lead, and biliary colic, 741 ; pancreatic, 740 ; pseudobiliary, 45, 697, 700, 741 ; renal, diagnosis from biliary colic, 738

Colitis, mucous, diagnosis from biliary colic, 615, 740 ; ulcerative, and abscess of the liver, 119

Colon, the, carcinoma of, and secondary growths in the liver, 499 ; scybala in, mistaken for malignant disease of the liver, 525

Coma, in portal cirrhosis, 227, 279-280 ; treatment, 298, 300 ; treatment by transfusion, 280

Concato's disease and perihepatitis, 162

Condyloma of the common bile-duct, 350

Congestion of the liver, 39

Conjunctiva, the, in catarrhal jaundice, 666 ; in congenital obliteration of the bile-

ducts, 656 ; in jaundice, 540 ; in jaundice in the newly born, 570
Constipation and cholelithiasis, 715 ; after paracentesis abdominis, 259 ; diagnosis from carcinoma of the gall-bladder, 647 ; in acute congestion of the liver, 108, 111 ; in congenital obliteration of the bile-ducts, 656 ; in portal cirrhosis, 231, 299 ; in single hepatic abscess, 135 ; jaundice in, 562
Constriction lobe of the liver, 8 (Fig. 5)
Convulsions in portal cirrhosis, 280
Copaiba resin in ascites, 265
Corsets, use of, and carcinoma of the gall-bladder, 641 ; and hepatoptosis, 25 ; suitable for hepatoptosis, 34
Cough in bronchobiliary fistula, 771 ; in hepatoptosis, 32-33 ; in single or tropical abscess, 134
Courvoisier's law, 557, 563-564, 700, 760 ; exceptions to, 545
Crackling, gall-stone, 727, 744
Creatinuria in malignant disease of the liver, 515
Crisis, hepatic, in tabes dorsalis, 740
Cryoscopy, urinary, in biliary cirrhosis, 322
Curries and portal cirrhosis, 183, 185-186
Cyanosis, in single hepatic abscess, 136 ; pernicious icteric, 572
Cyanotic atrophy of the liver, 85-96
Cyst, abdominal, simulating ascites, 252 ; allantoic, simulating ascites, 252 ; biliary, 444 ; carcinomatous, 490 (Fig. 70) ; hydatid, *see* Hydatid cysts
Cysts in the liver, 444-447 ; containing *Porocephalus*, 686 ; in hepatic tuberculosis, 342 ; in secondary malignant growths of the liver, 491 ; simple, 445 ; of the bile-ducts, 659-661 ; of the gall-bladder, 630; ovarian, diagnosis from ascites, 251, 255 ; ovarian, diagnosis from hydatid cysts in the liver, 410 ; ovarian, liver displaced by, 20 ; pancreatic, and jaundice, 558 ; pancreatic, diagnosis from hepatic abscess, 148 ; pancreatic, diagnosis from hydatid cysts of the liver, 409 ; pancreatic, due to cholelithiasis, 765 ; pancreatic, imitated by sarcoma of the liver, 483 ; parovarian, diagnosis from ascites, 251, 255 ; parovarian, imitated by a distended gall-bladder, 747 ; peripancreatic, diagnosis from hydatid cysts of the liver, 409-410
Cystadenoma of the liver, 458

Daughter cysts, hydatid, 392
Death, sudden, in biliary colic, 735 ; in portal cirrhosis, 235
Degeneration, fatty, of the liver, 426, 429
Degeneration, progressive lenticular, 335 ; and cirrhosis, 281
Delirium tremens in portal cirrhosis, 280
Dementia choreo-asthenica, 335
Dermoid cyst, abdominal, 504
Diabète bronzé, 303-307 ; and haemochromatosis, 221
Diabetes mellitus, and carcinoma of the ampulla of Vater, 705 ; and cholelithiasis, 717-718 ; biliary colic in, 737 ; following catarrhal jaundice, 668 ; in haemochromatosis, 303, 307 ; rare in obstructive biliary cirrhosis, 332
Diaceturia in portal cirrhosis, 232-233, 296
Diaphragm, the, in acute hepatitis, 115 ; in ascites, 249 ; in portal cirrhosis, 221-222 ; perforated by hepatic abscess, 141-142
Diaphragmatic hernia, liver in, 17
Diarrhoea, in acute congestion of the liver, 108 ; in carcinoma of the ampulla of Vater, 706 ; in fatty liver, 427-428, 432 ; in intermittent hepatic fever, 761 ; in lardaceous liver, 438 ; in portal cirrhosis, 231, 300 ; in portal thrombosis, 65 ; in single hepatic abscess, 135, 140
Diathesis and cholelithiasis, 720-721
Dicrocoelium lanceatum in the bile-ducts, 684
Digitalis, the administration of, in ascites, 264 ; in chronic venous engorgement of the liver, 95 ; in haematemesis, 273
Diphtheria and portal cirrhosis, 191, 192
Diplococcus pneumoniae, and acute cholecystitis, 607 ; in biliary cirrhosis, 313, 314 ; in single hepatic abscess, 132
Dipping for the liver, 250
Displaced liver, 16-22
Distoma conjunctum in the bile-ducts, 684 ; *D. sinense* in the bile-ducts, 684
Distomiasis of the bile-ducts, 683-684
Distomum hepaticum in the bile-ducts, 684 ; jaundice due to, 549 ; *D. lanceolatum* in the bile-ducts, 684
Diuretics in ascites, 264
Diverticulum of the gall-bladder, in cholelithiasis, 728, 757 ; of cystic duct, 759
Diverticulum of Vater, *see* Ampulla, 702
Dogs and hydatid disease, 391, 398, 415
Drainage, continuous abdominal, in ascites, 260 ; in chronic perihepatitis, 172
Drowsiness due to biliary colic, 736
Ducks, infectious jaundice in, 598
Duct, choledochopancreatic, 703
Duct, common bile, the, abnormalities of, 649 ; and enteric cholecystitis, 607 ; and tuberculosis of the liver, 338 ; carcinoma of, distinction from carcinoma of the ampulla of Vater, 703 (Fig. 100) ; cicatricial contraction of, 761 ; condyloma of, 350 ; cylindrical dilatation of, 749 ; diagnosis of gall-stone in, 750 ; extension of carcinoma into, 482 ; gall-stone in, 748 ; gall-stone in, diagnosis from malignant disease, 524 ; impaction of gall-stones in, 748 ; inflammation of, due to gall-stones, 759-764 ; intraduodenal cyst of, 661 ; malignant tumours of, 691 ; mechanical effects of gall-stones in, 747 ; papilloma

of, 688 ; primary melanoma of, 694 ; prolapse of, 750 ; relation to Wirsung's duct, 765 ; results of gall-stones in, 748 ; round worm in, 616 ; saccular dilatation of, 749 ; situation of gall-stones in, 748 ; stricture of, after choledochotomy, 662
Duct, common hepatic, the, malignant tumours of, 691
Duct, cystic, the, abnormalities of, 649 ; carcinoma of, 635 ; double, 601 ; filled by carcinomatous outgrowth from the gall-bladder, 636 ; gall-stone in, 745 ; in catarrhal cholecystitis, 609 ; in cholecystitis, 616, 622, 624 ; in secondary carcinoma of the gall-bladder, 648 ; malignant tumours of, 691, 692 ; mechanical effects of gall-stones in, 745-747 (Fig. 106) ; results of inflammation of, 759
Duct, hepatic, the, malignant tumours of, 691
Duct, Santorini's, 649, 750, 766
Duct, Wirsung's, 649 ; carcinoma of, 703 ; in cholelithiasis, 764
Ducts, bile, the, *see also* Bile-ducts ; carcinoma of, 698-708 (Figs. 99-102) ; congenital obliteration of, 649-659 (Figs. 90-92) ; diseases of, 649-708
Ductus venosus, persistent, 212
Duodenum, the, biliary fistulae into, 767-768 ; carcinoma of, and jaundice, 554 ; juxta-ampullary carcinoma of, 554 ; malignant disease of, and suppurative cholangitis, 671-672 ; obstruction of, by a gall-stone, 753 ; obstruction of, by calculous cicatrisation, 768 ; perivaterian carcinoma of, 554 ; rupture of hepatic abscess into, 143 ; rupture of hepatic hydatid cyst into, 420 ; ulcer of, diagnosed as cholecystitis, 620 ; ulcer of, and biliary colic, 739, and haematemesis in cirrhosis, 269, and jaundice, 554, and suppurative pylephlebitis, 70
Durande's remedy for gall-stones, 777
Dysentery, and acute hepatitis, 112 ; and portal thrombosis, 66 ; and suppurative pylephlebitis, 71
Dysentery, amoebic, and multiple hepatic abscess, 155 ; and tropical hepatic abscess, 117-120
Dysentery, asylum, and abscess of the liver, 119
Dysentery, bacillary, and abscess of the liver, 118, 120 ; and multiple hepatic abscess, 155
Dyspepsia, and acute congestion of the liver, 107 ; and cholelithiasis, 715 ; diagnosed in cholelithiasis, 730, 731, 739 ; in acute hepatitis, 115 ; in carcinoma of the gall-bladder, 642, 644 ; in hepatoptosis, 31 ; in malignant disease of the liver, 517 ; in portal cirrhosis, 183, 185, 186, 231 ; in single hepatic abscess, 134 ; the liver and, 38
Dyspepsia, adhesion-, 159, 758 ; after acute cholecystitis, 613
Dysphagia in single hepatic abscess, 134

Eck's fistula and portal cirrhosis, 214, 292 ; effects of, 262
Eclampsia, and acute yellow atrophy, 577 ; and portal thrombosis, 59 ; the liver in, 39
Ectocyst, hydatid, 391-392
Ectopia, congenital, of the liver, 16
Effusion, pleural, diagnosis from hydatid cyst, 407-408
Elastic tissue, in biliary cirrhosis, 315 ; in carcinoma with cirrhosis, 479 ; in chronic perihepatitis, 168 ; in portal cirrhosis, 203 ; in pseudo-cirrhosis, 98
Electrolysis of hydatid cysts, 395, 412-413
Emaciation in malignant disease of the liver, 505
Embolism, and infarcts of the liver, 103 ; fatty, of the lungs, in fatty liver, 432 ; in secondary malignant disease of the liver, 497 ; of hepatic veins, 53 ; of the portal vein, 82 ; pulmonary, by hydatid cysts, 420-421
Embolism, retrograde, and infarct of the liver, 105 ; in multiple hepatic abscess, 154-155 ; in the hepatic lymphatics, 497 ; in the hepatic veins, 53, 498
Embryoma of the liver, 468 ; malignant, 504
Emphysema, and cholelithiasis, 717 ; and furrowed liver, 10-11 ; interstitial, in the liver, 7 ; liver in, 19
Empyema of the gall-bladder, 613, 621-623, 627
Empyema of the lung, and hepatic abscess, 121 ; in single hepatic abscess, 133, 137, 144 ; in actinomycosis of the liver, 386 ; simulated by hepatic abscess, 151
Endarteritis obliterans, hepatic, and infarction, 105 ; in congenital syphilis of the liver, 374 ; in gumma of the liver, 354 ; in portal cirrhosis, 200
Endocarditis, infective, diagnosed as acute yellow atrophy, 591 ; diagnosis from pylephlebitis, 81 ; in portal cirrhosis, 224, 288 ; in cholecystitis, 611
Endocyst, hydatid, 391-392
Endophlebitis, hepatic, 50-52 ; portal, 83 ; splenic, and portal cirrhosis, 188
Endothelioma of the liver, and carcinoma, 480 ; and sarcoma, 469, 486 ; derived from angioma, 465 ; melanotic secondary, 504 ; of the gall-bladder, 631 ; pigmented, 501 ; suprarenal, 504
Enemas in cholelithiasis, 775 ; Krull's, 670
Entamoeba histolytica of Schaudinn, 131 ; in suppurative pylephlebitis, 75
Enteralgia and biliary colic, 741
Enteric fever, acute cholecystitis in, 605, 617 ; acute cholecystitis and cholelithiasis in, 606 ; and biliary cirrhosis, 312 ; and catarrhal

jaundice, 664 ; and cholelithiasis, 711-712 ; and multiple hepatic abscess, 156 ; and portal cirrhosis, 187, 192 ; and suppurative cholangitis, 673 ; and suppurative pylephlebitis, 80 ; diagnosis, from hepatic abscess, 149, from portal cirrhosis, 291, from Weil's disease, 600 ; imitated by pylephlebitis, 80 ; portal thrombosis rare in, 59 ; pylephlebitis rare in, 70 ; suppuration in rectus muscle after, 148 ; suppurative cholecystitis in, 617
Eosinophilia, after rupture of a hydatid cyst, 416 ; in alveolar hydatid, 425 ; in chronic splenomegalic haemolytic jaundice, 540 ; in hydatid disease, 393, 404 ; in psorospermosis, 685
Epilepsy due to biliary colic, 734
Epiplopexy in ascites, 261
Epistaxis, in acute congestion of the liver, 108 ; in portal cirrhosis, 226, 277
Epithéliome trabéculaire, 477
Epithelium, ciliated, carcinomatous, 473 ; in hepatic cysts, 451 ; in solitary hepatic adenoma, 458
Erasistratus on ascites, 242
Erythroblastic foci in congenital syphilis, 372
Eunatrol in cholelithiasis, 778
Euonymin in liver disease, 42
Exercises, use of, in acute congestion of the liver, 111 ; in cholelithiasis, 774 ; in functional liver disease, 43 ; in hepatoptosis, 35
Eye, the, melanotic tumours of, 480, 485, 501

Facies, the, in portal cirrhosis, 228
Faeces, the, causes of green, 656 ; in acute yellow atrophy, 588 ; in catarrhal jaundice, 666 ; in congenital obliteration of the bile-ducts, 656 ; in haemohepatogenous jaundice, 536 ; in liver disorders, 38 ; in malignant disease of the bile-ducts, 697 ; in obstructive jaundice, 543
Falciform ligament, the, accessory livers in, 4 ; secondary new growths in, 509 ; veins of enlarged, in cirrhosis, 211
Familial character, in acute yellow atrophy, 579 ; in cholelithiasis, 721 ; in chronic splenomegalic haemolytic jaundice, 537 ; in hepatic cirrhosis in children, 333 ; in jaundice, 562 ; in jaundice in the newly born, 572
Farre's tubercles, 489
Fasciola hepatica, comparison with alveolar hydatid, 424 ; in the bile-ducts, 684 ; in the gall-bladder, 628 ; in the portal vein, 84 ; jaundice due to, 549
Fat-necrosis in pancreatitis, 560
Fats, consumption of, in cholelithiasis, 777-778, 780
Fatty change in the liver, 426-433 ; in acute yellow atrophy, 580 ; in phosphorus poisoning, 593 ; in Weil's disease, 598
Fever, in acute yellow atrophy, 587 ; in biliary colic, 734 ; in hepatic gumma, 364 ; in lymphadenoma, 390 ; in malignant disease of the liver, 506, 523 (Fig. 77) ; in portal cirrhosis, 237 (Fig. 37) ; in portal cirrhosis in children, 334
Fever, intermittent hepatic, 679, 759-764 ; diagnosis, from hepatic abscess, 147-148, from malignant disease, 524 ; surgical treatment in, 781
Fibro-adenoma, of the bile-ducts, 458 ; cystic, of the liver, 453
Fibroma, of the liver, 467 ; submucous, of the gall-bladder, 630 ; syphilitic, of the liver, 373-374
Fibrosarcoma of the liver, 467
Fibrosis of the liver (*see also* Cirrhosis), and tuberculosis, 1, 346; cardiac, of the liver, 88-89 ; in cirrhosis, 193-195 ; in cystic disease, 450 ; in infarcts, 102 ; in pericarditic pseudo-cirrhosis, 98
Fibrosis, replacement, 430
Fingers, clubbing of the, in portal cirrhosis, 229-230 ; in biliary cirrhosis, 320 ; *see also* clubbing of the fingers
Fissure, the portal, aneurysm and new growth in, 46 ; case of adhesions in, 166, 167 ; gumma in, producing jaundice, 365 ; gumma of, and portal thrombosis, 59 ; hydatid cyst in, 403 ; lymphatic glands in, 85 ; lymphatic glands in, in acute yellow atrophy, 585, in biliary cirrhosis, 317, in congenital obliteration of the bile-ducts, 653, in portal cirrhosis, 215, in secondary syphilis, 350 ; malignant disease in, and portal thrombosis, 57 ; primary carcinoma of, 692 ; syphilitic cicatrices in, 357 ; syphilitic glands in, 551 ; tuberculous glands in, 337, 341, 343, 550-551 ; tumours in, and jaundice, 551-552
Fistula, between the bile-ducts, 772 ; between the gall-bladder and portal vein, 772
Fistula, biliary, 647, 766-774 ; and hepatic abscess, 145 ; biliary gastric, 768 ; biliary jejunal, 770 ; biliary ileal, 770 ; cutaneous biliary, 766 ; in carcinoma of the gall-bladder, 636 ; in hydatid cysts, 420 ; pericardial, 773
Fistula, bronchobiliary, 419, 619, 677, 771-772 ; in gumma, 353 ; in hydatid disease, 417 ; in suppurative cholecystitis, 619
Fistula, cholecystocolic, 753, 770 (Plate VII.); cholecystoduodenal, 767-768; cholecystogastric, 744, 769 ; cholecystonephric, 772 ; cholecystovaginal, 773 ; choledochoduodenal, 768 ; duodenal biliary, 767-768 ; Eck's, and portal cirrhosis, 214 ; enterocholecystic, 617-618, 619 ; external biliary, 766 ; gastrobiliary, 769 ; gastrocholecystic, 769 ; in localised peritoneal biliary abscess,

773 ; pericardial, 773 ; pleuroperitoneal, 285 ; umbilical biliary, 767
Floating abdominal organs, 22
Fluid, the, in alveolar hydatid, 424 ; in cystic disease of the liver, 450 ; in cystic sarcoma, 483 ; in hydatid cysts, 393-396, 405, 411, 413, 415 ; in simple cysts of the liver, 445, 446
Foie cordé, 27
Foie en gourde de pèlerin, 27
Foie silex, 371

Gall-bladder, the, diseases of, 601-648 (Figs. 82-89) ; abnormalities of, 601-602 ; absence of, 601 ; adenoma of, 630 ; and accessory livers, 4 ; and fistula into the portal vein, 772 ; angiosarcoma of, 631 ; actinomycosis of, 628 ; acute progressive empyema of, 621-623 ; bifid, 601 ; calcification of, 627
Gall-bladder, the, carcinoma of, 631-648 (Figs. 86-89) ; age and, 641 ; and cholecystocolic fistula, 770 ; and secondary growths in the liver, 500 ; ascites in, 643 ; association with gall-stones, 638-641 ; cachexia in, 644 ; cholangitis in, 644 ; clinical picture, 642-644 ; complications, 644 ; degenerative changes in, 632 ; diagnosis, 645-647 ; diagnosis from carcinoma of the bile-ducts, 700 ; duration, 645 ; early cases of, 634 ; etiology, 638-642 ; extension by continuity, 635 ; fistulae in, 636 ; growth down the cystic duct, 636 ; haemorrhage in, 635 ; histology, 632 ; jaundice in, 643 ; latent, 643, 645 ; liver in, 637-638, 643 ; morbid anatomy, 631-635 ; mucous glands in, 633 ; oedema in, 644 ; pressure effects of, 637 ; prognosis, 647 ; secondary deposits from, 635, 637 ; secondary malignant tumours of, 648 ; sex and, 641 ; situation of the tumour in, 634 ; starting-point of growth in, 633 ; transitional forms of, 632 ; treatment, 647-648 ; villous, 635 ; Virchow's gland in, 638
Gall-bladder, the, chronic or simple empyema of, 613, 621-623, 627 ; dilated, mistaken for hepatic abscess, 150 ; double, 601 ; endothelioma of, 631 ; fistulae of, 766-774 ; foreign bodies in, 713 ; gangrene of, 623 ; greatly distended, 745 ; haemorrhage into, 756 ; hour-glass, 756 (Fig. 107) ; hydatid cysts of, 628 ; hydrops of, 648, 745 ; in acute yellow atrophy, 581 ; in atrophy of the left lobe of the liver, 3 ; in biliary cirrhosis, 313 ; in biliary colic, 735 ; in carcinoma of the bile-ducts, 695, 697 ; in catarrhal cholecystitis, 609 ; in chronic cholecystitis, 625 (Figs. 84, 85) ; in chronic perihepatitis, 167 ; in congenital obliteration of the bile-ducts, 653 ; in intermittent hepatic fever, 760 ; in membranous cholecystitis, 615 ; in obstructive jaundice, 545 ; in portal cirrhosis, 208 ; in suppurative cholecystitis, 617 ; inflammation of, *see* Cholecystitis ; innocent tumours of, 629-630 ; intrahepatic, 602, 619 ; lipoma of, 630 ; lithogenic catarrh of, 710 ; malposition of, 602 ; mechanical effects of gall-stones in, 744 ; melanoblastoma of, 631 ; mesentery of, 602 ; mucocele of, 745 ; mucous glands of, in chronic cholecystitis, 625 ; oedema of, 630 ; parasitic affections of, 628 ; perforation of, in cholelithiasis, 757-758 ; perithelioma of, 631 ; rupture of hepatic abscess into, 143 ; rupture of hepatic aneurysm into, 772 ; rupture into the peritoneum, 773 ; rupture of, in cholelithiasis, 744 ; sarcoma of, 631 ; scars on, 756 ; secondary malignant tumours of, 648 ; size and shape, 602 ; spasm of, 731 ; strawberry, 624 ; submucous fibroma of, 630 ; syphilis of, 628 ; torsion of, 623 ; tuberculosis of, 627 ; two, 601
Gall-stones (*see also* Cholelithiasis), adherent, 728 ; and catarrh of the gall-bladder, 725 ; and Riedel's lobe, 8, 15 ; and suppurative pylephlebitis, 72-73 ; association with carcinoma of the gall-bladder, 638-641 ; attempts to dissolve, 777 ; bacterial origin of, 710 ; bilirubin-calcium, 725 ; calcium carbonate, 725 ; causes of passage from the gall-bladder, 732 ; causing appendicitis, 770 ; cholesterin, 724 ; classification of, 724 ; conglomerate, 725 ; coral, 727, 729 ; encysted, 728, 759 (Fig. 108) ; expectoration of, 771 ; faceted, 727 (Fig. 103), prognostic value of, 742 ; formation of, on sutures, 714, 743 ; foreign bodies and, 713 ; growth of, in the intestine, 751 ; imitated by hepatic gumma, 365 ; in biliary cirrhosis, 314 ; in portal cirrhosis, 208 ; in primary carcinoma of the liver, 482 ; in the common bile-duct, 747-750 ; in the cystic duct, 745-747 ; indence, 721 ; large intrahepatic, 728-729 (Fig. 105) ; mechanical effects of, 744-755 ; mixed, 724 ; mode of formation, 725 ; parietal, 625 ; shape, 727 ; situation, 727 ; size and number in cholelithiasis, 726 ; spontaneous fracture of, 729 (Plate VI). ; time required for formation of, 726 ; toxic origin of, 712 ; vomiting of, 735 ; vomiting of, and gastrobiliary fistula, 769
Gangrene of the gall-bladder, 623-624
Gastrectasis due to cholelithiasis, 744
Gastritis, and catarrhal jaundice, 664 ; and cholelithiasis, 776 ; and haematemesis in cirrhosis, 268
Gastro-enteritis and portal cirrhosis, 183, 185-187
Gastroptosis and jaundice, 555, 561
Gastrosuccorrhoea in portal cirrhosis, 231
General paralysis of the insane, imitated by

carcinoma of the liver, 481, 519 ; hepatic endarteritis in, 48
Gerhardt's reaction in portal cirrhosis, 232-233
Giant cells, carcinomatous, 472 ; in acute yellow atrophy, 583 ; in carcinoma of the gall-bladder, 632 ; in carcinoma with cirrhosis, 477 ; in congenital syphilis of the liver, 374 ; in hydatid disease, 393 ; in primary sarcoma of the liver, 482, 484
Gin-drinker's liver, 177
Ginger and portal cirrhosis, 185-186
Glisson's capsule in congenital syphilis, 373
Glycocoll, urinary, in acute yellow atrophy, 581 ; in phosphorus poisoning, 595
Glycogen in hydatid cysts, 393, 405
Glycosuria, absent in acute yellow atrophy, 589 ; and the hepatic functions, 39 ; in biliary cirrhosis, 322 ; in biliary colic, 736 ; in carcinoma of the ampulla of Vater, 705 ; in catarrhal jaundice, 667 ; in intermittent hepatic fever, 761 ; in malignant disease of the liver, 514 ; in phosphorus poisoning, 595 ; in portal cirrhosis, 234
Glycosuria, alimentary, in biliary cirrhosis, 322 ; in chronic venous engorgement of the liver, 94 ; in portal cirrhosis, 234-235 ; in portal thrombosis, 65
Gmelin's reaction in jaundice, 542, 549
Gout, and acute congestion of the liver, 110 ; and cholelithiasis, 720-721 ; and liver disease, 40 ; in portal cirrhosis, 287
Granuloma, infective, and alveolar hydatid, 423 ; syphilitic, 371
Grocco's triangle of dulness, absent in hepatic abscess, 150-151
Gumma of the liver, 351-369 (Figs. 41-45), 373 ; abscess formation in, 356 ; age and, 360 ; and tabes dorsalis, 360, 369 ; ascites in, 361-362 ; associated with malignant disease, 495 ; caseation in, 353 ; causing dyspepsia, 364 ; cicatrisation of, 357 (Fig. 45) ; clinical manifestations, 360-366 ; diagnosis, 366-367 ; diagnosis from chronic splenic anaemia, 365, from gall-stones, 365, from hepatic suppuration, 364, from hypertrophic biliary cirrhosis, 366, from lardaceous disease, 363, from other hepatic tumours, 363-364, from portal cirrhosis, 361, from secondary malignant growths, 490 ; endarteritis in, 354 ; fever in, 364 ; gastro-intestinal symptoms in, 361 ; in congenital syphilis, 371, 373 ; in the portal fissure, 552 ; incidence, 359 ; injury and, 359 ; lardaceous change in, 358 ; method of formation, 351 ; microscopic appearances, 354 ; miliary, of the liver, 371, 373 ; pain in, 361 ; perihepatitis in, 165, 353, 361 ; predisposing causes, 359 ; prognosis, 367 ; resembling carcinoma, 353 ; retrogressive changes in, 355 ; sclero-gummatous form of, 358 ; structure, 352 ; treatment, 367
Gumma, pancreatic, and jaundice, 560

Haemangioma, of the liver, 465 ; primary, of the portal vein, 60
Haematemesis, due to cholelithiasis, 747 ; in adhesion-dyspepsia, 758 ; in hepatoptosis, 32 ; in pericholecystitic adhesion-dyspepsia, 758 ; in portal thrombosis, 63, 67
Haematemesis in portal cirrhosis, 213, 226, 240, 266-274 ; diet in, 274 ; diagnosis, 271-273 ; etiology, 268-271 ; fatal, 267, 268, 270 ; gastric and duodenal ulcers and, 269 ; ice in, 273, 274 ; in portal cirrhosis in children, 334 ; incidence, 266 ; minute erosions and, 268 ; pharynx and, 271 ; prognosis, 273 ; quantity, 267 ; recurrent, 267, 270, 273 ; temperature after, 267-268 ; treatment, 273
Haematoidin, and bilirubin, 531 ; in hydatid cysts, 395 ; in nutmeg liver, 90 ; in the liver cells, 440
Haematoma of abdominal wall in cirrhosis, 214, 278
Haematoporphyrinuria, in chronic venous engorgement of the liver, 94 ; in fatty liver, 432 ; in leukaemia, 443
Haematuria, and jaundice in the newly born, 571, 572 ; in portal cirrhosis, 215, 234, 277 ; in malignant disease of the liver, 514
Haemochromatosis, 174, 175, 303-307 ; and endarteritis, 223 ; associated with carcinoma, 479 ; diagnosis, 307 ; diagnosis from biliary cirrhosis, 324 ; glycosuria in, 234 ; haemolysis in, 303 ; hepatic arteritis in, 48 ; in portal cirrhosis, 207 ; liver in, 203, 306 ; morbid anatomy, 305 ; pancreatitis in, 221 ; pigmentation in, 304 ; prognosis, 307 ; sex and, 305 ; symptoms, 306 ; treatment, 307
Haemofuscin, 439 ; in cirrhosis, 304 ; of haemochromatosis, 305
Haemoglobin, formation of bile-pigment from, 531, 538
Haemoglobinuria, and jaundice in the newly born, 572 ; paroxysmal, with jaundice, 533, 535
Haemolysis, and jaundice, 532, 535, 544 ; by bile-salts, 545 ; in chronic splenomegalic haemolytic jaundice, 538 ; in haemochromatosis, 303 ; in jaundice of secondary syphilis, 350
Haemoperitoneum in portal cirrhosis, 215
Haemophaeic jaundice, 534
Haemophaein, 534
Haemoptysis, due to ascites, 251 ; due to biliary colic, 736 ; in hepatic abscess, 142 ; in hydatid disease, 408 ; in portal cirrhosis, 276
Haemorrhage, local, due to hydatid cysts,

401 ; in hepatic angioma, 466 ; in simple cysts of the liver, 446
Haemorrhage, occult, 697 ; in cirrhosis, 275
Haemorrhages, general, in acute yellow atrophy, 587 ; in biliary cirrhosis, 320 ; in carcinoma of the bile-ducts, 693 ; in carcinoma of the gall-bladder, 635, 644, 647, 698 ; in chronic jaundice, 542 ; in congenital obliteration of the bile-ducts, 656 ; in malignant disease of the liver, 509 ; in pancreatic disease, 560 ; in phosphorus poisoning, 594 ; in portal cirrhosis, 213, 294 ; in Weil's disease, 598
Haemorrhoids, *see* Piles
Haemosiderin, in leukaemic liver, 442 ; in malarial liver, 113 ; in pigmented cirrhosis, 302, 304 ; in primary sarcoma of the liver, 486 ; in the liver cells, 439
Hamartoma fibrocanaliculare of the liver, 467
Hanot's disease, 309, 319, 680
Head's areas, in acute cholecystitis, 610 ; in biliary colic, 734 ; in carcinoma of the gall-bladder, 642 ; in chronic cholecystitis, 626
Heart, the, displaced in ascites, 249
Heart-disease, and cholelithiasis, 716-717 ; and cirrhosis in children, 336 ; and nutmeg liver, 85 ; ascites in, 93
Heart-failure, and ascites in portal cirrhosis, 245 ; ascites in, diagnosis from cirrhosis, 256 ; due to biliary colic, 736 ; in acute yellow atrophy, 585 ; in phosphorus poisoning, 593 ; in portal cirrhosis, 224
Heister, the valves of, 747
Hemiplegia due to biliary colic, 736
Hepar necroticum cum ictero, 575
Hepatalgia, 740
Hepatic artery, *see* Artery, hepatic
Hepatic asystole, 85-96
Hepatic veins, *see* Veins, hepatic
Hepatism (Glénard's), 26, 40
Hepatitis, acute, 111-117 (Figs. 18, 19) ; acute parenchymatous, 112 ; and portal cirrhosis, 189 ; clinical picture, 115 ; diagnosis, 115-116 ; diagnosis from hepatic abscess, 149, from malignant disease, 522 ; dysentery and, 112 ; fever in, 115 ; *hyperémique phlegmasique*, 112 ; in acute yellow atrophy, 585 ; in dyspepsia, 39 ; in malaria, 307-308 ; jaundice in, 115 ; morbid anatomy, 111 - 114 ; nodular parenchymatous, 112 ; parenchymatous hyperplastic, 113 ; treatment, 116
Hepatitis, chronic interstitial, 177 ; gummatous, in congenital syphilis, 375 ; hypertrophic fatty tuberculous, 346 ; influenzal, 522 ; necrosing, 575 ; nodular, 459 ; nodular parenchymatous, and subacute atrophy, 583 ; subacute diffuse, 113 ; syphilitic, 350 ; tropical, imitated by gumma, 365
Hepatocele, 16
Hepatolysins in portal cirrhosis, 237
Hepatoma, 459, 460 ; term for primary carcinoma of the liver, 474
Hepatomphalos, 16
Hepatopexy, in constriction lobes, 12 ; in hepatoptosis, 35-36 ; in Riedel's lobe, 15
Hepatoptosis, 22-36 (Fig. 9) ; abdominal belt for, 34-36 ; and cholelithiasis, 713 ; and jaundice, 561 ; causation, 25 ; colic in, 30-31 ; diagnosis, 33-34 ; diagnosis from malignant disease of the liver, 525 ; forms of, 27 ; frequency, 23 ; haematemesis in, 32 ; history, 22 ; jaundice in, 32 ; onset, 30 ; pain in, 31 ; partial, 8, 12-15 ; physical signs, 29-30 ; prophylaxis, 36 ; symptoms, 30-33 ; total, 23 ; treatment, 34-36
Heredity, in biliary cirrhosis, 311 ; in cholelithiasis, 720-721 ; in chronic splenomegalic haemolytic jaundice, 537 ; in congenital obliteration of the bile-ducts, 650 ; in jaundice in the newly born, 573
Hernia, gall-stones in, 752 ; diaphragmatic, liver in, 17 ; epigastric, imitating biliary colic, 740 ; femoral, gall-bladder in, 746
Herpetism and cholelithiasis, 720
Hiccup in perihepatitis, 159
Histidine, urinary, in acute yellow atrophy, 581
Hobnail liver and abnormal lobulation, 1
Hobnails, hepatic, 460 ; carcinomatous, 474 ; in portal cirrhosis, 177, 198 (Fig. 26)
Hodgkin's disease, in the liver, 388-390 (Fig. 51)
Hour-glass gall-bladder, 756 (Fig. 107)
Hour-glass stomach due to pericholecystitic adhesions, 758
Hyaloserositis, multiple progressive, and perihepatitis, 162, 168
Hydatid, alveolar, 392, 422-426 ; clinical features, 425 ; course, 425 ; diagnosis, 425 ; diagnosis from malignant disease, 521 ; exogenous cyst-formation in, 423-424 ; incidence, 423 ; morbid anatomy, 424 ; nature, 423 ; prognosis, 426
Hydatid cysts, of the bile-ducts, 689 ; of the gall-bladder, 628
Hydatid cysts of the liver, 391-426 (Figs. 52-53) ; age and, 400 ; and hepatic abscess, 122 ; and portal cirrhosis, 225 ; associated with other hepatic diseases, 397 ; associated with secondary malignant disease, 495 ; calcification of, 396 ; capsule of, 392-393, 396 ; colic in, 418-419 ; complications, 415-422 ; daughter cysts, 416-417 ; diagnosis, 405-410 ; diagnosis from biliary cirrhosis, 324, from gumma, 364, from hepatic abscess, 146, from hepatoptosis, 34, from malignant disease, 521, from portal cirrhosis, 290, from simple cysts, 446 ; duration, 394, 410 ; dyspnoea due to, 400 ; ectocyst of, 393 ; endocyst of, 393 ; endogenous, 392 ; eosinophilia

in, 393, 404 ; etiology, 398-400 ; exogenous, 392 ; fluid in, 393, 405 ; gas in, 402, 417, 422 ; geographical distribution, 398 ; glycogen in, 405 ; intestinal obstruction due to, 400 ; latent, 400 ; life history, 391-392 ; liver displaced in, 20 ; liver in, 396 ; method of infection, 399 ; number, 394 ; pain in, 400 ; pedunculated, 392 ; physical signs, 401-405 ; precipitin reaction in, 404 ; prognosis, 411 ; prophylaxis, 414 ; pseudotuberculosis in, 417 ; relation to alveolar hydatids, 392 ; relative frequency of, 397 ; rupture of, 411, 415-421 ; secondary in the peritoneum, 416-417 ; sex and, 399 ; situation in the liver, 393 ; size, 394 ; spontaneous death of, 394-395 ; sterile, 392 ; structure, 392 ; suppurating, 146, 411, 421 ; suppurative cholangitis due to, 671 ; surgery of, 414 ; symptoms, 400 ; thrill in, 402 ; toxin in, 395, 405, 413-414 ; trauma and, 391 ; treatment, 412-415 ; urine in, 404
Hydatid cysts, of the lung, 408 ; of the pancreas, 559 ; of the peritoneum, 416-417 ; of the pleural cavity, 408
Hydatid, multilocular, 422
Hydramnios, in congenital syphilis, 377 ; simulating ascites, 253
Hydrobilirubin in malignant disease of the bile-ducts, 697
Hydronephrosis, diagnosis from distended gall-bladder, 746, from hepatoptosis 33, from hydatid cysts of the liver, 409
Hydrops vesicae felleae, 745
Hyperchlorhydria, diagnosis from biliary colic, 739 ; in portal cirrhosis, 231
Hyperplasia of the liver, compensatory, in acute yellow atrophy, 583-584 ; in cirrhosis, 459-461 ; in hydatid disease, 396-397 ; in portal cirrhosis, 301 ; in sarcoma of the liver, 486 ; in secondary malignant disease of the liver, 494 ; in syphilis, 358
Hypochondriasis and hepatoptosis, 33
Hysteria, and hepatoptosis, 33 ; jaundice in, 551

Ice, use of, in haematemesis, 273, 274
Iced liver, 86, 97-98 (Fig. 15), 161-172
Iceland, hydatid disease in, 398
Icterus, *see* Jaundice, 531-575 ; etymology, 531
Icterus gravis, 573-575 ; and acute hepatitis, 111 ; and Weil's disease, 600 ; classification of, 574 ; diagnosis, from acute yellow atrophy, 590 ; in biliary cirrhosis, 323 ; in portal cirrhosis, 229, 287 ; relation to phosphorus poisoning, 579-580
Icterus neonatorum, 568-573
Ictrogen in lupinosis, 585
Ignatius Loyola, 772
ἴκτερος, 531
ἰκτῖνος, 531
ἴκτις, 531
Ileocaecal valve, the, obstruction of, by gall-stones, 751, 753
Ileum, the, obstruction by a gall-stone, 753
India, abscess in, 118 ; hepatic cirrhosis in, 333, 335; hydatid in, 399; portal cirrhosis in, 185-186
Indicanuria, distinction from melanuria, 516; in biliary colic, 737 ; in jaundice, 542 ; in portal cirrhosis, 232
Infancy, cystic disease of the liver in, 447-455 (Figs. 57, 58) ; jaundice in, 568-573; renal colic in, 739
Infantilism, in delayed congenital syphilis, 380 ; in hypertrophic biliary cirrhosis, 320, 335
Infarction, hepatic, common in portal thrombosis, 61 ; in secondary malignant disease of the liver, 495
Infarction, renal, in jaundice in the newly born, 569
Infarcts of the liver, 101-107 (Figs. 16, 17) ; anaemic, in hepatic embolism, 47 ; and retrograde embolism, 105 ; embolism and, 103 ; etiology, 103 ; haemorrhagic, 89 ; in the liver, 82 ; morbid anatomy, 102 ; pathogeny, 106 ; traumatic anaemic, 106 ; traumatic haemorrhagic, 105
Infiltration, degenerative fatty, of the liver, 430
Infiltration, fatty, of the liver, 426, 429-430
Influenza, and acute yellow atrophy, 578 ; and hepatic abscess, 122 ; and hepatitis, 111 ; and suppurative cholangitis, 672 ; hepatic enlargement in, 149
Inoscopy, in ascites, 248, 254
Insanity, alcoholism, and portal cirrhosis, 181 ; and cholelithiasis, 720
Insomnia, in single tropical abscess, 135
Intermittent hepatic fever, 759-764
Intestines, the, haemorrhage from, in cirrhosis, 274-276 ; in biliary cirrhosis, 317 ; in haemochromatosis, 305 ; in portal cirrhosis, 220 ; lithiasis of, 740 ; obstruction of, in cholelithiasis, 737, 751-755, diagnosis from portal cirrhosis, 291 ; rupture of hepatic abscess into, 143 ; rupture of hepatic hydatid cyst into, 420 ; ulceration of, and suppurative pylephlebitis, 70
Inunction, mercurial, in congenital syphilis, 378
Iodine stain, the, in lardaceous disease, 435
Iodoform poisoning, fatty liver in, 429
Iodophilia in single hepatic abscess, 137
Ipecacuanha in hepatic abscess, 152
Iridin, as a cholagogue, 775 ; in liver disease, 42
Iron iodide in delayed congenital syphilis, 383
Itching, *see* Pruritus

Jaundice, 531-575 (Fig. 78) ; absent in

bilious ascites, 416 ; absent in haemochromatosis, 304 ; absent in leukaemic infiltration of the liver, 443 ; acathectic, 532 ; acholuric, 534 ; acholuric, in portal cirrhosis, 229, 232 ; age and, 562 ; bilirubinuria in, 542 ; black, 541, 548, 565, 669 ; catarrhal, *see below* ; chronic infective, of Hayem, 537-540 ; chronic simple, with splenomegaly, 537 - 540 ; chronic splenomegalic haemolytic, *see below* ; classification of, 535 ; conjunctiva in, 540 ; constipation in, 566 ; course and duration, 563 ; definition, 531 ; degree of, 563 ; diagnosis, 548 ; diet in, 567 ; diffusion, 532 ; due to *Ascaris*, 682-683 ; due to gummatous cicatrix in the portal fissure, 357 ; emotional, 551, 578, 665 ; epidemic, 563, 597, 598 ; etymology, 531 ; extrahepatic, 535, 540 ; familial, 562, 657 ; feigned, 549 ; fever in, 563 ; gall-bladder in, 563 ; general diagnosis of, 562-566 ; haematogenous, 532-535 ; haemohepatogenous, 533, 535-540 ; haemolytic, 532-533 ; haemolytic, with splenomegaly, 537-540 ; haemophaeic, 534 ; hepatogenous, 532-535 ; in actinomycosis of the liver, 387 ; in acute congestion of the liver, 108 ; in acute hepatitis, 115 ; in acute parenchymatous hyperplasia of the liver, 113 ; in acute yellow atrophy, 586 ; in alveolar hydatid, 425 ; in aortic aneurysm, 560 ; in appendicitis, 564 ; in biliary cirrhosis, 318, 320 ; in biliary colic, 737 ; in carcinoma of the ampulla of Vater, 706; in carcinoma of the gall-bladder, 643 ; in carcinoma of the stomach, 553 ; in carcinoma with cirrhosis, 480 ; in chronic catarrhal cholangitis, 678 ; in chronic venous engorgement of the liver, 92, 94 ; in congenital obliteration of the bile-ducts, 653, 655-656 ; in congenital syphilis, 376-377 ; in constipation, 562 ; in delayed congenital syphilitis, 380 ; in duodenal carcinoma, 554 ; in duodenal ulcer, 554 ; in fatty liver, 431 ; in gall-stone in the cystic duct, 745 ; in gastric ulcer, 553 ; in gastroptosis, 561 ; in hepatic aneurysm, 560 ; in hepatoptosis, 32, 561 ; in hydatid cysts, 403, 418-420 ; in lymphadenoma, 390 ; in malaria, 564 ; in malignant disease of the bile-ducts, 696-698 ; in malignant disease of the liver, 510-511 ; in miliary tuberculosis of the liver, 340 ; in ovarian tumour, 561 ; in pancreatic cyst, 558 ; in pancreatic disease, 556-560 ; in pericholangitis, 682 ; in perigastritis, 553 ; in perihepatitis, 170 ; in peritoneal adhesions, 555 ; in phlegmonous cholecystitis, 622 ; in phosphorus poisoning, 592-596 ; in portal cirrhosis, 229 ; in portal thrombosis, 65 ; in pregnancy, 561, 562 ; in secondary syphilis, 349-351 ; in single hepatic abscess, 136 ; in superior mesenteric aneurysm, 561 ; in suppurative cholangitis, 675 ; in suppurative cholecystitis, 618 ; in suppurative pylephlebitis, 78 ; in the newly born, *see below* ; in tuberculosis of the bile-ducts, 342, 344 ; infectious, 596 ; infective, *see* Weil's disease, 597-600 ; intrahepatic, 533, 535-540 ; introduction, 531 ; leucocytosis in, 544 ; leucodermia in, 541 ; liver in, 564 ; non-obstructive, 532 ; obstructive, *see below* ; onset, 563 ; pain in, 563 ; pathology, 532 - 535 ; physiological, 656 ; polycholic, 532-534 ; prognosis, 564-566 ; relapsing infectious, 599 ; sex and, 562 ; suppressive, 532 ; toxaemic, 532, 535-540, 596 ; toxaemic, diagnosis of, 669 ; treatment, 566, 592 ; urobilin, 232, 534 ; urobilinuria in, 542 ; with meningitis, 566 ; xanthopsia in, 546

Jaundice, catarrhal, 550, 596, 663-670 ; alcoholism and, 664-665 ; bacteriology, 665 ; blood in, 667 ; catarrhal pancreatitis and, 664, 668 ; causation, 664 ; clinical picture, 666 ; diagnosis, 669 ; diagnosis from malignant disease of the bile-ducts, 701 ; diet in, 670 ; duration, 668 ; effects, 668 ; gastroduodenal catarrh and, 663-664 ; in infancy, 571 ; incidence, 666 ; liver in, 668 ; morbid anatomy, 665 ; premonitory symptoms, 666 ; prognosis, 668 ; pulse-rate in, 666 ; treatment, 669-670 ; urine in, 667

Jaundice, chronic splenomegalic haemolytic, 324, 532, 535, 537-540 ; acquired form, 538, 540 ; and biliary cirrhosis, 311 ; clinical features, 539 ; definition, 537 ; diagnosis, 540 ; etiology, 537 ; history, 537 ; pathogeny, 538 ; treatment, 540 ; urine in, 539

Jaundice in the newly born, 568-573 ; catarrhal or mild infectious, 570 ; duration, 569 ; epidemic, 572 ; etiology, 568 ; general infections and, 572 ; grave familial, 572 ; hereditary, 573 ; idiopathic, simple, or physiological, 568 ; morbid anatomy, 569 ; nine varieties of, 568 ; obstructive, 571 ; severe forms of, 571 ; umbilical infection and, 571

Jaundice, obstructive, 540-568 ; bile-salts in, 545-547 ; constipation in, 548 ; diagnosis, 548-562, from non-obstructive jaundice, 536 ; faeces in, 543 ; fever in, 544 ; gall-bladder in, 545 ; glandular secretions in, 543 ; haemorrhagic tendency in, 547-548 ; heart in, 543 ; liver in, 545 ; respiration in, 544 ; spleen in, 545 ; symptoms, 545-548 ; urine in, 542

Jejunum, the, obstruction of, by a gall-stone, 753

Juxta-ampullary carcinoma, 554, 702

Juxtahepatic carcinoma, 691

Kala azar, and cirrhosis in children, 336 ;

and portal cirrhosis, 192 ; diagnosis from portal cirrhosis, 290
Kernicterus, 335, 569, 573 ; cerebrospinal fluid in, 543
Kidneys, the, association of renal calculus with malignant renal tumours, 641 ; biliary fistula into, 772 ; cystic, associated with cystic disease of the liver, 448 ; disease of, and cholelithiasis, 718, and jaundice, 555, and portal cirrhosis, 214 ; diseases of, compared with cirrhosis of the liver, 176, 194 ; floating, and biliary colic, 713, 739 ; floating, diagnosis, from the distended gall-bladder, 746, from hepatoptosis, 33 ; formation of urobilin in, 535 ; growths of, diagnosis from hydatid cysts of the liver, 409 ; in acute yellow atrophy, 584, 591 ; in biliary cirrhosis, 317 ; in chronic perihepatitis, 169 ; in congenital syphilis, 375 ; in melanuria, 515 ; in portal cirrhosis, 221, 224-225, 287 ; in Weil's disease, 598 ; lobulated, and lobulation of the liver, 1 ; rupture of hepatic abscess into, 144
Korsakoff's syndrome in portal cirrhosis, 286
Krull's irrigations, 670
Kumiss, in portal cirrhosis, 297
Kupffer's cells, 113 ; haemosiderin in, 439 ; in congenital syphilis, 372 ; in haemochromatosis, 305

Laennec's cirrhosis of the liver, 177
Laevulosuria, alimentary, in portal cirrhosis, 235
Lardaceous disease of the liver, 433-439 ; imitated by gumma of the liver, 363 ; in gumma of the liver, 354, 358 ; in hepatic abscess, 145 ; in tuberculosis of the liver, 345
Lead colic and biliary colic, 741 ; spasm of the bile-ducts in, 551, 741
Lead poisoning and portal cirrhosis, 185
Leeches, in acute congestion of the liver, 109
Leptotrichosis and cholelithiasis, 712
Leucine, urinary, in acute yellow atrophy, 580, 582, 589 ; in phosphorus poisoning, 595 ; in single hepatic abscess, 140
Leucocytosis, in actinomycosis of the liver, 387 ; in acute hepatitis, 116 ; in biliary colic, 736 ; in catarrhal jaundice, 667 ; in cholaemia, 544 ; in congenital obliteration of the bile-ducts, 656 ; in gangrenous cholecystitis, 624 ; in intermittent hepatic fever, 761 ; in portal cirrhosis, 236 ; in single hepatic abscess, 136-137, 145 ; in suppurative cholangitis, 676 ; in suppurative cholecystitis, 618
Leucocythaemia, liver in, 441-443 (Fig. 56)
Leucodermia in jaundice, 541, 549
Leucopenia in Banti's disease, 325
Leukaemia, acute, and chloroma, 504 ; diagnosis, from hepatic abscess, 150 ; enlargement of the liver in, 289 ; liver in, 441-443 (Fig. 56) ; myeloid, liver in, 441
Lichen in jaundice, 547
Lineae albicantes in ascites, 249
Linguatula rhinaria, calcified, in the liver, 441, 686
Lipoma, of the bile-ducts, 687 ; of the gall-bladder, 630 ; of the liver, 468
Liqueur de van Swieten, 378
Lithaemia (Murchison's), 26, 39-41 ; and acute congestion of the liver, 108
Lithogenic catarrh, 710, 740
Littré's hernia in ascites, 249
"Liver" attacks, 38
Liver, the, abnormal lobulation of, 1-5 (Figs. 1-3) ; acquired deformities of, 8-16 (Figs. 5-8) ; acquired displacements of, 17-22
Liver, the, acute congestion of, 107-111 ; causes, 107 ; clinical picture, 108 ; morbid anatomy, 108 ; prophylaxis, 110 ; treatment, 109-111
Liver, the, acute yellow atrophy of, 85, 575-592 (Figs. 79, 80) ; age and, 576 ; alcoholism and, 578 ; and icterus gravis, 574 ; and secondary syphilis, 349 ; autolysis in, 585, treatment, 592 ; bacteria and, 579, 584 ; blood in, 588 ; clinical picture, 586-590 ; course, 586 ; definition, 575 ; diagnosis, 590 ; duration, 586 ; etiology, 575-580 ; faeces in, 588 ; fever in, 587 ; haemorrhages in, 587 ; histology, 582-583 ; in infants, 568 ; incidence, 575 ; influenza and, 578 ; jaundice in, 586 ; kidneys in, 584, 591 ; liver dulness in, 588 ; lupinosis and, 585 ; mental disturbance and, 577, 578, 587 ; morbid anatomy, 580-584 ; onset, 586 ; pancreas in, 585, 586 ; pathogeny, 585 ; pre-existing hepatic disease of, 579 ; pregnancy and, 576 ; prognosis, 591 ; prolonged cases of, 589 ; prophylaxis, 591 ; pupils in, 587 ; recovery from, 591 ; regenerative changes in, 583 ; relation to phosphorus poisoning, 579-580 ; second stage of, 587 ; sex and, 576 ; subacute, 576, 583, 589 ; syphilis and, 577 ; termination, 590 ; treatment, 591 ; urine in, 588 ; vomiting in, 586, 587 ; with syphilis, 350
Liver, the, adhesions of, 159 ; amyloid, 433-439 ; angioma of, 463-467 (Fig. 60) ; angiosarcoma of, 483 ; anthracosis of, 302 ; antitoxic functions of, 37 ; appendicular, 156 ; calcification in, 440-441 ; carcinoma of, *see* Carcinoma of the liver, ; carcinoma of, and multiple adenomas, 460 ; cavernoma of, 463-467 (Fig. 60) ; chief functions of, 36-42 ; chondroid, 433-439 ; chorion-epithelioma of, 473, 481
Liver, the, chronic venous engorgement of, 85-96 (Fig. 13), 289 ; and growths in the liver, 86 ; and mediastinitis, 86 ; cirrhosis in, 88-89 ; course, 95 ;

diagnosis, 95, from malignant disease, 523; in pericarditic pseudo-cirrhosis, 97; jaundice in, 92; microscopic appearances, 89 (Fig. 13); morbid anatomy, 86-88; pancreas in, 91; pleurisy in, 94; spleen not enlarged in, 91; symptoms and signs, 91-94; termination, 95; treatment, 95-96; urine in, 94
Liver, the, cloudy swelling of, 5; compensatory hyperplasia of, in cirrhosis, 459-461, in syphilis, 358; congenital malposition of, 16-17; congenital syphilis of (*q.v.*), 370-383 (Figs. 46-49); corset liver, 8-12 (Figs. 5-6); cystadenoma of, 458
Liver, the, cystic disease of, 447-455 (Figs. 57, 58); age and, 447, 449; and obliteration of the bile-ducts, 650; association with cystic kidneys, 448; clinical picture, 454; degenerative hypothesis of, 453; developmental hypothesis of, 453; diagnosis from malignant disease, 521; histology, 450-452; incidence, 447; inflammation and, 452; inheritance of, 449; morbid anatomy, 449; pathogeny, 452; sex and, 449; tumour formation and, 453
Liver, the, cysts of, 444-447; cysts of, containing *Porocephalus*, 686; detoxicating function of, 37; direct invasion of by new growths, 498; disseminated lobular necrosis of, with jaundice, 575; embryoma of, 468; encysted angioma of, 464; enlargement of, causes, 289-291
Liver, the, fatty change in, 426-433 (Figs. 54, 55); diagnosis, 432; fibrosis in, 430; in portal thrombosis, 62; in tuberculosis, 345; morbid anatomy, 428-430; prognosis, 433; signs, 430-432; toxins and, 426-428; treatment, 433
Liver, the, fibroma of, 467; fibroma, syphilitic, of, 373-374; fibrosarcoma of, 467; foaming, 6-8 (Fig. 4); formation of bile-pigment in, 531; functional disease of, 36-43; furrows on the, 5; granulated, 177; gumma of, *see* Gumma; gumma of and portal cirrhosis, 225; haemangioma of, 465; haemosiderosis of, 439; hamartoma fibrocanaliculare of, 467; hyperplasia of, in portal cirrhosis, 292; iced, 86, 97-98 (Fig. 15), 161-172
Liver, the, in acute cholecystitis, 611; in acute congestion, 108; in acute hepatitis, 115; in acute yellow atrophy, 580-584; in alcoholism, 181-183; in alveolar hydatid, 425; in biliary cirrhosis, 314-316 (Fig. 39); in biliary colic, 735, 749; in carcinoma of the gall-bladder, 637-638; in catarrhal jaundice, 668; in chloroma, 442; in chronic perihepatitis, 167; in cirrhosis maligna, 476; in cloudy swelling, 5; in congenital obliteration of the bile-ducts, 652, 653; in congenital syphilis, 371-375 (Figs. 46-48); in delayed congenital syphilis, 379; in haemochromatosis, 306; in hydatid cysts, 396-397, 401-403; in lardaceous disease, 435; in lymphadenoma, 388 (Fig. 51); in malignant tumours of the bile-ducts, 696; in malignant tumours of the liver, 508; in multiple adenomas, 462; in obstructive biliary cirrhosis, 331; in phosphorus poisoning, 593; in portal cirrhosis, 195-208 (Figs. 26-33), 237-240, 294; in portal thrombosis, 61-62; in secondary malignant disease, 494-497; in secondary melanotic sarcoma, 502-503; in single hepatic abscess, 128-130 (Figs. 20, 21); in suppurative cholangitis, 673-675; in suppurative pylephlebitis, 74; in Talma-Morison operation, 261; in Weil's disease, 598
Liver, the, inadequacy of, and glycosuria, 589
Liver, the, infarcts of, 101-107 (Figs. 16, 17); anaemic, 102 (Fig. 16); haemorrhagic, 102; pseudo-infarcts, 101-102; true, 101 (Fig. 17)
Liver, the, inflammation of, *see* Hepatitis
Liver, the, lardaceous disease of, 433-439; acute onset of, 434; diagnosis, 437, from cirrhosis, 255, from malignant disease, 521; etiology, 433; histology, 435-436; incidence, 433; morbid anatomy, 435; pathogeny, 434; prognosis, 438; signs, 437; symptoms, 436; suppuration and, 434; treatment, 438
Liver, the, leucocythaemic infiltration of, 441-443 (Fig. 56); leukaemic infiltration of, 441-443 (Fig. 56); lipoma of, 468; lymphangioma of, 466, 467; lymphatics of, 84-85; malignant adenoma of, 474-479 (Figs. 63-66)
Liver, the, malignant tumours of, 469-530 (Figs. 61-77); abdomen in, 508 (Fig. 76); age and, 470, 488; albuminuria in, 514; and suppurative cholangitis, 672; ascites in, 512-513; blood in, 514; cachexia in, 506; chyliform ascites in, 513; chylous ascites in, 513; cirrhosis and, 474-479 (Figs. 63-66); clinical aspects, 479, 505-518; degenerative changes in, 481, 490; diagnosis, 519-526; diagnosis between primary and secondary, 526-528; diagnosis from ascites, 254, from carcinoma of the gall-bladder, 646, from hepatic abscess, 149, from hydatid cyst, 406, 407, from portal cirrhosis, 289; duration, 518; etiology, 471; Farre's tubercles in, 489; fever in, 506, 523 (Fig. 77); formation of pseudo-cysts in, 491; forms of, carcinoma, 472, sarcoma, 482; gall-stones and, 469, 482, 524; gastric disturbance in, 517; haemorrhages in, 509; histology, 472-476, 493-497; in malignant disease of the bile-ducts, 696; incidence, 469, 487; jaundice in, 510-511, 551; liver in, 494, 508;

melanuria in, 515 ; methods of metastasis in, 497 ; morbid anatomy, 471-479, 488-493 ; oedema in, 516 ; operative treatment of, 529-530 ; origin of, carcinoma, 480, sarcoma, 486 ; pain in, 517 ; peripheral neuritis in, 517 ; physical signs, 505-516 ; primary, 469-486 ; prognosis, 528 ; pruritus in, 517 ; rapid progress of, 506 ; secondary, 481, 487-530 ; secondary, situation of primary growth in, 498-504 ; sex and, 469, 487 ; situation of growth in, 471, 498-504 ; spontaneous recovery from, 528 ; symptoms, 516-518 ; termination, 519 ; thoracic signs in, 516 ; treatment, 529 ; umbilication in, 484, 489, 492 ; urine in, 514-516

Liver, the, melanotic angioma of, 465 ; metasyphilitic affections of, 369 ; multiple non-inflammatory necrosis of, 575 ; myxoma of, 467 ; myxosarcoma of, 467 ; naevus of, 463-467 (Fig. 60) ; necrosis of, *see* Necrosis ; neuralgia of, 740 ; nodular hyperplasia of, 459 ; normal position of, 24 ; parasyphilitic affections of, 369 ; perithelioma of, 526 ; pigment in cells of, 439-440 ; post-mortem appearances of, 5-8 (Fig. 4) ; pseudocysts in, 491 ; pseudo-infarcts of, 101-102 ; pulsation of, in chronic venous engorgement, 92-93 ; puncture of, in portal cirrhosis, 300-301 ; red atrophy of, 85, 580-583 ; rupture of, in biliary colic, 737 ; sarcoma of, *see* Sarcoma of Liver ; scirrhus of, 470, 484 ; scrofulous disease of, 433 ; silicosis of, 302 ; simple cysts of, 445 ; subacute atrophy of, 576, 583 ; substance of, administration in ascites, 265, in portal cirrhosis, 301 ; suppression of bile-secretion by, 534 ; suppuration in, and pylephlebitis, 72, diagnosis from portal cirrhosis, 291

Liver, the, syphilis of (acquired), 348-369 (Figs. 42-45) ; calcification in, 441 ; cirrhosis due to, 348-349 ; clinical features, 350 ; diagnosis, 351 ; diagnosis from ascites, 255, from biliary cirrhosis, 324, from malignant disease of the gall-bladder, 646 ; from malignant disease of the liver, 520, history, 348 ; jaundice in, 349-351 ; lardaceous disease in, 369 ; metasyphilis of, 369 ; onset, 350 ; parasyphilis of, 369 ; secondary, 348-351 ; sex and, 350 ; syphilitic fibroma of, 373-374 ; tertiary, 351-369 (Figs. 41, 45), *see* Gumma

Liver, the, telangiectasis of, 466 ; tenderness of, in chronic venous engorgement, 91 ; teratoma of, 468 ; tight-laced, 8-12 (Figs. 5, 6), secondary malignant growths in, 495 (Fig. 73) ; tropical, 109 ; tuberculated, 177

Liver, the, tuberculosis of, 336-348 (Plates III, IV) ; abscess in, 345 ; and actinomycosis, 342, 345 ; and multiple adenomas, 459, 461 ; and the portal vein, 338 ; caseating, 343-345 ; clinical features, 340, 342, 344 ; confluent miliary, 340 ; congenital, 337 ; forms of, 338 ; histology, 340, 342 ; imitated by nutmeg liver, 91 ; introduction, 336 ; jaundice in, 340, 342 ; local, 340-345 ; miliary, 339 ; morbid anatomy, 339, 341, 343 ; paths of infection in, 337-338 ; solitary, 343 ; umbilical vein and, 337

Liver, the, ulceration of the gall-bladder into, 757 ; waxy, 433-439

Liver-fluke, the, 684

Lobes of the liver, accessory, 3 ; appendicular, 12-15 ; constriction, cirrhosis in, 9 (Fig. 6) ; diagnosis, 11 ; floating lobe, hepatic, 12-15 ; infarction and, 103 ; linguiform, 12-15 ; potential Riedel's, 12 ; Riedel's, 8, 12-15 (Figs. 7, 8) ; Spigelian, 3, *see* Spigelian lobe

Lumbago in cholelithiasis, 731, 741

Lungs, the, collapse of, in fatty liver, 432 ; disease of, and nutmeg liver, 85-86 ; in single hepatic abscess, 133, 137-138 ; in suppurative pylephlebitis, 76 ; malignant disease of, liver in, 19 ; rupture of hepatic abscess into, 141-142, 153 ; rupture of hydatid cyst into, 417

Lungs, the, tuberculosis of, and haemoptysis in cirrhosis, 276 ; and nutmeg liver, 86 ; and tuberculosis of the liver, 337-338, 339, 347 ; diagnosed as hepatic abscess, 151 ; fatty liver in, 427 ; in biliary cirrhosis, 322 ; in portal cirrhosis, 222, 283-284

Lupinosis and acute yellow atrophy, 585

Lymphadenoma, in the liver, 388-390 (Fig. 51) ; diagnosis from hepatic abscess, 150 ; imitated by pericholangitis, 682 ; imitated by suppurative cholangitis, 673

Lymphadenoma cells, 389

Lymphangioma of the liver, 466, 467

Lymphangitis in the liver, 84-85

Lymphatics, the, and the metastasis of new growths, 497 ; and tuberculosis of the liver, 338, 343 ; in portal cirrhosis, 203 ; of the liver, 84-85 ; of the portal fissure in cirrhosis, 215

Lymphomata, hepatic, in enteric fever, 187

Lymphomatosis granulomatosa in the liver, 388-390 (Fig. 51)

Lysine, urinary, in acute yellow atrophy, 581

Malaria, and acute hepatitis, 112, 113 ; and biliary cirrhosis, 312 ; and intermittent hepatic fever, 761-762 ; and nodular cirrhosis, 195 ; and portal cirrhosis, 188, 192 ; and single hepatic abscess, 125 ; chronic, lardaceous disease in, 434 ; diagnosis from hepatic abscess, 149, from pylephlebitis, 81 ; enlargement of the liver in, 289 ; hepatitis in, 307-308 ;

jaundice in, 564 ; liver disease due to, 107, 109 ; liver enlarged in, 81 ; pigmentation of cirrhotic liver in, 204, 307-308
Malta fever, and acute cholecystitis, 607 ; and single hepatic abscess, 126
Mania, acute, and cholelithiasis, 720
Massage in cholelithiasis, 774, 778-779
Match-heads and phosphorus poisoning, 592
Meals in cholelithiasis, 779-780 ; time of, 774
Mediastinitis and nutmeg liver, 86
Mediastino-pericarditis and perihepatitis, 162
Melaena, after haematemesis, 267, 274-276 ; in cirrhosis, treatment, 276 ; in portal thrombosis, 64-65 ; in single hepatic abscess, 135 ; without haematemesis, 275
Melancholia, and cholelithiasis, 720 ; in catarrhal jaundice, 667
Melanin, 501, 515 ; in ascitic fluid, 512
Melanoblastoma of the gall-bladder, 631
Melanogen, 513, 515
Melanoma, 480, 485, 489, 496, 500-504, 703 ; of the common bile-duct, 694
Melanosis, cutaneous, 502
Melanuria, 515 ; distinction from indicanuria, 516
Meningitis, imitated by acute yellow atrophy, 587 ; with jaundice, 566
Menorrhagia in portal cirrhosis, 278
Menstruation, and biliary colic, 732 ; suppressed, and acute congestion of the liver, 108
Mercury, and acute yellow atrophy of the liver, 577 ; as a cholagogue, 775 ; in congenital syphilis, 378, 383 ; in gumma of the liver, 367-368 ; jaundice due to use of, 350
Mesenteric veins, trauma of, and pylephlebitis, 71
Mesentery, disease of, and pylephlebitis, 71
Mesohepar, extreme rarity of, 25
Mesonephros, the, and cystic disease, 453
Metaplasia, in carcinoma of the bile-ducts, 694 ; of the gall-bladder, 632
Metastasis, in melanotic sarcoma, 503 ; in primary carcinoma of the liver, 481 ; in secondary malignant disease of the liver, 497-498 ; in secondary sarcoma, 487
Metatoluylenediamine poisoning, 317
Methyl-salicylate in biliary colic, 743
Methylene-blue test, the, in portal cirrhosis, 232
Methyl-violet stain for lardaceous disease, 436
Metrorrhagia in portal cirrhosis, 278
Micrococcus foetidus in suppurative pylephlebitis, 75
Micrococcus melitensis and acute cholecystitis, 607, in single hepatic abscess, 132
Middeldorff's diagnostic method, 148
Migraine, and cholelithiasis, 736 ; and liver disease, 41
Milk, the, in jaundice, 543
Milk, use of, in portal cirrhosis, 297-298
Milk-spots, cardiac, and perihepatitis, 160
Mitral disease and portal cirrhosis, 186
Moles, pigmented, and secondary growths in the liver, 485, 501-503
Morphine, use of, in biliary colic, 738, 742, 782 ; in calculous intestinal obstruction, 755
Morphine habit, the, in biliary colic, 742, 743
Movable liver, reposition of, 29
Mucocele of the gall-bladder, 745 (Fig. 106)
Mucous membranes and cholesterin, 725, 728
Multiple cystic disease and foaming liver, 8
Murmurs, cardiac, in biliary colic, 736
Mussel poisoning, and portal cirrhosis, 184 ; compensatory hyperplasia of the liver in, 459
Mydriasis in acute yellow atrophy, 587
Mytilotoxin and portal cirrhosis, 184
Myxoedema, and cholelithiasis, 719 ; and chronic perihepatitis, 165
Myxoma of the liver, 467
Myxosarcoma of the liver, 467

Naevus of the liver, 463-467 (Fig. 60)
Naphthol poisoning and portal cirrhosis, 185
Necrosis, focal hepatic, and acute hepatitis, 111 ; absent in haemorrhagic hepatic infarcts, 102 ; disseminated lobular, of the liver, 575 ; due to tuberculosis, 345 ; in anaemic hepatic infarcts, 105, 106 ; in enteric fever, 187 ; in hydatid cysts, 413 ; in the specific fevers, 191
Necrosis, icteric, 330, 696 ; multiple non-inflammatory, of the liver, 575
Nephritis and cholelithiasis, 718
Nephroptosis, and biliary colic, 739 ; diagnosis from carcinoma of the gall-bladder, 647 ; producing jaundice, 555-556
Nervous symptoms, in acute yellow atrophy, 587 ; in portal cirrhosis, 279-281 ; in Weil's disease, 599
Neurasthenia, and hepatoptosis, 27 ; and liver disease, 40 ; and pseudobiliary colic, 741
Neuritis, peripheral, in malignant disease of the liver, 517 ; in portal cirrhosis, 286
Nodule, regeneration-, 462, *see* Adenoma
Nutmeg liver, 85-96 ; and pericarditic pseudocirrhosis, 101

Obesity simulating ascites, 253
Obesity-cures and biliary colic, 732
Obstruction, intestinal, by gall-stones, 737, 751-755 ; age and, 753 ; clinical picture, 753 ; diagnosis, 754 ; in cholelithiasis, 737, 751-755 ; incidence, 751 ; pain in, 753-754 ; prognosis, 754 ; sex and, 753 ; site of obstruction, 753

Obstruction, pyloric, due to cholelithiasis, 744
Ochronosis and haemochromatosis, 307
Oedema, absent in pericarditic pseudocirrhosis, 100 ; in alveolar hydatid, 425 ; in carcinoma of the gall-bladder, 644 ; in chronic perihepatitis, 169, 170 ; in fatty liver, 431 ; in hydatid cysts of the liver, 403 ; in malignant disease of the liver, 516 ; in portal cirrhosis, 241-242, prognostic value of, 257, 295 ; in single hepatic abscess, 138, 139, 145 ; of the gall-bladder, 630 ; pre-ascitic, in portal cirrhosis, 241
Oedema, angioneurotic, and biliary colic, 741
Oesophagoscope, the, in portal cirrhosis, 270
Oesophagus, the, carcinoma of, and secondary growths in the liver, 498, 500 ; disease of, and suppurative pylephlebitis, 70 ; in portal cirrhosis, 219 ; varix of, and haematemesis in cirrhosis, 269-271
Offal and hydatid disease in dogs, 399, 415
Olive oil, in biliary colic, 743 ; in cholelithiasis, 777-778
Omentum, the, in Talma-Morison's operation, 261 ; carcinoma of, 693 ; gall-stones in, 773 ; in chronic perihepatitis, 170
Omentum, the lesser, hepatopetal circulation in, 60 ; malignant tumours of, 690, diagnosis from hepatoptosis, 34
Opisthorchis noverca, jaundice due to, 549 ; in the bile-ducts, 684 ; *sinensis*, jaundice due to, 549 ; in the bile-ducts, 684
Opium in haematemesis, 273
Opsiuria, 94 ; in portal cirrhosis, 232
Osteo-arthropathy in biliary cirrhosis, 321 ; in portal cirrhosis, 230
Otitis media and multiple hepatic abscess, 154
Ovary, the, tumours of, and jaundice, 561
Overeating and acute congestion of the liver, 107
Ox bile, as a cholagogue, 775-776
Oxybutyric acid, urinary, in portal cirrhosis, 233

Pain, the, in biliary colic, 733 ; in malignant disease of the liver, 517, 529
Pancreas, the, affections of, in cholelithiasis, 764-766 ; and acute yellow atrophy, 586 ; and pruritus in jaundice, 546 ; calculus of, and biliary colic, 738 ; cystic, association with cystic disease of the liver, 449 ; diagnosis of pancreatic cyst from hepatic abscess, 148 ; disease of, and jaundice, 556-560 ; in biliary cirrhosis, 313, 317 ; in carcinoma of the gall-bladder, 638 ; in congenital obliteration of the bile-ducts, 655 ; in haemochromatosis, 304, 305 ; in nutmeg liver, 91 ; in portal cirrhosis, 219, 221, 234-235 ; in suppurative pylephlebitis, 76
Pancreas, the, infection of, in cholecystitis, 610
Pancreas, the, carcinoma of, and carcinoma of the bile-ducts, 693-694 ; and jaundice, 556 ; and malignant disease of the larger bile-ducts, 699 ; and portal thrombosis, 57 ; biliary obstruction in, 329 ; cirrhosis of the liver rare in, 329-330 ; diagnosis from carcinoma of the gall-bladder, 646
Pancreatitis, and acute yellow atrophy, 586
Pancreatitis, acute, and jaundice, 559 ; and pylephlebitis, 71 ; diagnosis from biliary colic, 740 ; from hepatic abscess, 148 ; in cholelithiasis, 764
Pancreatitis, chronic interstitial, and carcinoma of the ampulla of Vater, 705 ; and jaundice, 559 ; and portal thrombosis, 58 ; in cholelithiasis, 750, 765 ; in chronic cholecystitis, 625 ; in haemochromatosis, 221 ; in intermittent hepatic fever, 760 ; in portal cirrhosis, 221
Pancreatitis, haemorrhagic, and cholelithiasis, 705, 750 ; suppurative, in suppurative cholangitis, 675
Papilloma, of the ampulla of Vater, 704-705 ; of the bile-ducts, 457, 660, 687-689 (Fig. 98) ; cystic, 688 ; development of carcinoma in, 690
Papilloma of the gall-bladder, 629 ; and carcinoma of the gall-bladder, 633-634 ; myxomatous, 629
Papilloma, ovarian, ascites in, 255-256
Paracentesis abdominis, fatal haemorrhage after, 257 ; in ascites, 257-260 ; in chronic perihepatitis, 166, 170 ; in pericarditic pseudocirrhosis, 100 ; in portal cirrhosis, 227 ; in suppurative cholecystitis, 621
Paracentesis, of hydatid cysts, 405, 412-414, accidents due to, 413 ; of the gall-bladder, 745
Paracentesis of the liver, in acute congestion, 110 ; in acute hepatitis, 117 ; in single or tropical abscess, 146, 152-153
Paracholia, 532
Paramoecium coli in the bile-ducts, 686
Parapedesis, jaundice from, 532
Paraplegia due to biliary colic, 736
Pentastomum constrictum in the bile-ducts, 686
Pepper, black, and cirrhosis in children, 335-336
Periarteritis nodosa and hepatic aneurysms, 45
Pericarditis, adherent, and pseudocirrhosis of the liver, 96-101 ; action on the liver, 100 ; and perihepatitis, 163 ; cirrhosis of the liver in, 168
Pericardium, the, biliary fistula into, 773 ; calcified, liver cirrhotic in, 98 ; rupture of hepatic abscess into, 142 ; rupture of hydatid cyst into, 411, 418
Pericholangitis, 680-682 (Figs. 94, 95) ; acute, 681 ; chronic, 342, 452, 682 ; fetal, and cystic disease, 452, 454 ; from intrahepatic gall-stones, 729 ; gummatous,

355 ; in malignant disease of the bile-ducts, 696 ; in obstructive biliary cirrhosis, 330, 331 ; in portal cirrhosis, 208 (Fig. 34) ; tuberculous, 338, 340-343, 682
Pericholecystitis and portal thrombosis, 58
Perigastritis, jaundice in, 553
Perihepatitis, and ascites in portal cirrhosis, 245 ; and secondary malignant growths in the liver, 492 ; chronic deforming, 161-172 ; chronic hyaline, 161-172 ; chronic local, 160-161 ; diagnosed in gumma of the liver, 362-363 ; diffuse chronic hyperplastic, 161-172 ; in delayed congenital syphilis, 379 ; in gumma of the liver, 353, 361 ; in intermittent hepatic fever, 760 ; in malaria, 308 ; in malignant disease of the liver, 509 ; in pericarditic pseudocirrhosis, 97 (Fig. 15) ; in suppurative cholangitis, 676 ; rarely latent, 227 ; syphilitic, treatment, 368 ; treatment of pain due to, 109 ; tuberculous, 339
Perihepatitis, acute, 157-160 (Fig. 22) ; causation, 157 ; diagnosis, 159 ; in acute hepatitis, 115 ; morbid anatomy, 158 ; pain in, 159, 160 ; primary or secondary, 158 ; signs and symptoms, 159 ; treatment, 160
Perihepatitis, chronic universal, 161-172 (Figs. 23, 24) ; and alcoholism, 166 ; and arteriosclerosis, 163-165 ; and bacterial infection, 166-167 ; and cirrhosis of the stomach, 166 ; and granular kidney, 163-165 ; and syphilis, 165 ; and tuberculosis, 166 ; ascites in, 167, 170 ; classification of cases, 162 ; course, 169 ; diagnosis, 171 ; gall-bladder in, 167 ; jaundice rare in, 167 ; liver in, 167 ; morbid anatomy, 167-169 ; onset, 169 ; pathogeny, 162-167 ; prognosis, 171 ; sex and, 169 ; signs and symptoms, 170-171 ; treatment, 172
Periostitis, acute, and multiple hepatic abscess, 154
Periphlebitis, hepatic, chronic, 52
Perisplenitis, and local perihepatitis, 160 ; in biliary cirrhosis, 317 ; in portal cirrhosis, 216
Perithelioma, of the gall-bladder, 631 ; of the liver, 526
Peritoneum, the, carcinoma of diagnosed as ascites, 252, 254 ; gall-stones adherent to, 773 ; in chronic perihepatitis, 169 ; in pericarditic pseudocirrhosis, 97 ; in portal cirrhosis, 210 ; pseudotuberculosis of, in hydatid disease, 417 ; rupture of hepatic abscess into, 143 ; rupture of hydatid cysts into, 411, 415-417 ; rupture of the gall-bladder into, 773 ; systematic hypertrophic cirrhosis of, 166
Peritonismus, after paracentesis of hydatid cysts, 413 ; due to ruptured hydatid cyst, 416
Peritonitis, acute, and perihepatitis, 158 ; diagnosis from ascites, 253 ; due to rupture of an hepatic abscess, 143 ; in acute cholecystitis, 611 ; in carcinoma of the gall-bladder, 643-644 ; in cholecystitis, 619-621 ; in miliary tuberculosis of the liver, 339 ; in suppurative cholecystitis, 619 ; in suppurative pylephlebitis, 76 ; perforative, in cholelithiasis, 741, 756
Peritonitis, chronic, adhesions due to, and jaundice, 555 ; and ascites, 93-94 ; and lobulation of the liver, 1 ; and portal cirrhosis, 244-245, 286-287 ; and portal thrombosis, 58 ; diagnosed in gumma of the liver, 362 ; diagnosis from ascites, 253 ; fetal, and congenital stricture of the bile-ducts, 650-651 ; fetal, and lobulation of the liver, 1
Peritonitis, simple chronic, in portal cirrhosis, 223
Peritonitis, tuberculous, diagnosis from ascites, 253-254, from chronic perihepatitis, 171 ; in portal cirrhosis, 223, 283
Peritonitis fibrosa, case of, 165
Perivaterian carcinoma, 508, 554
Periviscerits and arteriosclerosis, 163 ; and granular kidney, 163
Perl's test for iron, 439 ; in haemochromatosis, 305 ; in nutmeg liver, 90 ; in the spleen in cirrhosis, 216
Phantom tumours, and hydatid cysts of the liver, 406 ; diagnosis from hepatic abscess, 148
Pharynx, the, and haematemesis in cirrhosis, 271
Phlebitis, hepatic, adhesive, 50 ; suppurative, 52
Phleboliths, 772
Phlebosclerosis, in portal thrombosis, 55, 60 ; in nutmeg liver, 87
Phosphorus poisoning, jaundice in, 592-596 ; clinical manifestations, 594 ; diagnosis, 595 ; diagnosis from acute yellow atrophy, 590 ; incidence, 592 ; morbid anatomy, 593 ; pathogeny, 593 ; relation to acute yellow atrophy, 579-580 ; treatment, 496 ; urine in, 595 ; vomiting in, 594
Pick's pericarditic pseudocirrhosis, 96-101 ; and perihepatitis, 163
Pictou cattle disease, 189
Pigmentation, cutaneous, in biliary cirrhosis, 320 ; in haemochromatosis, 303-307 ; in portal cirrhosis, 228
Piles, haemorrhage from in cirrhosis, 276 ; occurrence in cirrhosis, 213, 220 ; oesophageal, in cirrhosis, 212
Pilgrim's bottle liver, 27
Pilocarpine in pruritus, 567
Pingueculae and jaundice, 540, 666
Pins in the appendix and suppurative pylephlebitis, 70
Pleura, the, in suppurative pylephlebitis, 76 ; rupture of hepatic abscess into, 142 ; rupture of hydatid cyst into, 417

Pleurisy with effusion, diagnosis from hepatic abscess, 150-151 ; liver in, 18
Pleurisy, and acute hepatitis, 137 ; and acute perihepatitis, 159 ; due to hydatid cyst, 401 ; in chronic venous engorgement of the liver, 94 ; in portal cirrhosis, 285 ; in single hepatic abscess, 132, 137
Pleurisy, haemorrhagic, in portal cirrhosis, 285
Pneumobacillus, Friedländer's, and acute cholecystitis, 607
Pneumonia, and suppurative cholangitis, 672 ; in patients with fatty liver, 433 ; liver displaced in, 19
Pneumothorax, liver displaced in, 19
Podophyllin as a cholagogue, 775
Polyarteritis acuta nodosa and hepatic aneurysm, 45
Polycholia, jaundice from, 532
Polychromia, biliary, 534 ; in haemohepatogenous jaundice, 536
Polycythaemia in chronic splenomegalic haemolytic jaundice, 539
Polydactyly, in cystic disease of the liver, 447-448, 454
Polyorrhymenitis and perihepatitis, 162, 164
Porocephalus constrictus in the bile-ducts, 686
Potassium iodide, in actinomycosis, 387 ; in cholelithiasis, 776 ; in chronic perihepatitis, 172 ; in gumma of the liver, 356, 362-365, 367-368 ; in lardaceous disease, 438 ; in portal cirrhosis, 298 ; mode of action of, 368
Potassium sulphate and portal cirrhosis, 182
Portal pyaemia, *see* Pylephlebitis, suppurative, 62-68
Portal thrombosis, *see* Pylethrombosis, 53
Portal vein, *see* Vein, portal
Porto-pyaemic liver abscess, 68-82
Precipitin reaction in hydatid disease, 404
Pregnancy, and acute yellow atrophy of the liver, 576, 588 ; and cholelithiasis, 716, 774 ; and jaundice, 561, 562 ; diagnosis from malignant disease of the liver, 525 ; liver in, 39
Prolin in acute yellow atrophy, 581
Protease in secondary malignant growths, 490
Protein metabolism in phosphorus poisoning, 595 ; the liver and, 37
Pruritus, in catarrhal jaundice, 667 ; in hydatid disease of the liver, 403 ; in intermittent hepatic fever, 761 ; in jaundice, 546, 697 ; in malignant disease of the liver, 517 ; in portal cirrhosis, 279 ; in syphilis of the liver, 350 ; preicteric, 546-547 ; treatment, 567
Pseudo-actinomycosis of the liver, 385
Pseudobile canaliculi, *see* Canaliculi, pseudobile
Pseudobiliary colic, 45
Pseudocirrhosis, Pick's pericarditic, 96-101 ; morbid anatomy, 98 (Figs. 14, 15)
Pseudocysts in secondary malignant growths of the liver, 491 (Fig. 70)
Pseudo-infarcts of the liver, 101-102
Pseudotuberculosis, of the liver, 343 ; peritoneal, in hydatid disease, 417
Psorospermosis of the liver, 342, calcification in, 441 ; of the bile-ducts, 684-685 (Figs. 96, 97), 688
Puerperal eclampsia, the liver in, 39
Pulse, the, in biliary colic, 736 ; in catarrhal jaundice, 666 ; in jaundice, 543
Purgatives, use of, in acute congestion of the liver, 109 ; in acute hepatitis, 116 ; in catarrhal jaundice, 670 ; in chronic venous engorgement of the liver, 96 ; in functional disease of the liver, 42 ; in portal cirrhosis, 299-300
Pyaemia, and cholecystitis, 604
Pyaemia and single hepatic abscess, 123 ; multiple hepatic abscess in, 154 ; portal, 68-82, *see* Pylephlebitis, suppurative ; umbilical, and jaundice in the newly born, 571-572
Pyelonephritis, diagnosis from acute cholecystitis, 612
Pylephlebitis adhaesiva, 53-68 (Fig. 11)
Pylephlebitis, suppurative, 68-82 (Fig. 12) ; age and, 73 ; and tropical abscess, 68 ; ascites rare in, 79 ; bacteriology, 75 ; blood in, 79 ; course, 76 ; diagnosis, 79-81 ; diagnosis, from hepatic abscess, 147 ; from suppurative cholangitis, 677 ; etiology, 68 ; gall-stones and, 72 ; histology, 75 ; in cholelithiasis, 766 ; in suppurative cholangitis, 673, 675 ; jaundice in, 78 ; liver in, 74, 78 ; morbid anatomy, 73 ; onset, 76 ; prognosis, 81 ; prophylaxis, 82 ; sex and, 73 ; signs, 77 ; spleen in, 75, 78 ; thoracic signs in, 79 ; treatment, 82 ; tuberculous, 341 ; vomiting in, 78
Pylethrombosis, 53-68 (Fig. 11) ; due to cholelithiasis, 747 ; due to gall-stones in the common duct, 750
Pylorus, the, disease of, and jaundice, 553-554 ; tumour of, diagnosis from a distended gall-bladder, 747
Pyonephrosis imitated in cholecystitis, 621
Pyoperihepatitis, 158
Pyopneumocholecystitis, 607, 617
Pyopneumohydatid, 422
Pyopneumoperihepatitis, 158
Pyorrhoea alveolaris and gastritis, 268
Pyrexia, *see* Fever

Quinine in single hepatic abscess, 153

Rabbits, biliary psorospermosis in, 684 (Figs. 96, 97), 688
Rash, hydatid, 403, 413, 414
Rat paste and phosphorus poisoning, 592
Rectum, the, carcinoma of and secondary

growths in the liver, 499-500 ; haemorrhage from in cirrhosis, 275
Rectus muscle, the, suppuration in, 148, 406
Regeneration, hepatic, in nutmeg liver, 90
Regeneration-nodule, the hepatic, and carcinoma, 476
Rests, duodenal, and primary carcinoma of the liver, 480 ; hepatic, 4 ; pancreatic, and primary carcinoma of the liver, 481 ; splenic, in the liver, 464 ; suprarenal, and adenoma of the liver, 458-459
Retrograde infection in the lymphatics, 84, 85 ; embolism, 105
Retroperitoneal tumours and jaundice, 556
Retzius, subperitoneal venous plexus of, 210
Rheumatism and pericarditic pseudo-cirrhosis, 96
Ricin-poisoning, and acute cholecystitis, 608 ; and portal cirrhosis, 192
Rickets, cirrhosis in, 336 ; displaced liver in, 18
Riedel's lobe, hepatic, 8 ; and diagnosis of appendicitis, 612 ; and dilated gall-bladder, 745 ; and suppurative cholecystitis, 618 ; gumma in, 14, 15 ; potential, 12 (Fig. 7)
Rigors, occurrence of, in biliary colic, 733 ; in intermittent hepatic fever, 761 ; in single hepatic abscess, 134 ; in suppurative cholecystitis, 618 ; in suppurative pylephlebitis, 76 (Fig. 12), 78
Round ligament, the, cyst of, 445, 447 ; in portal cirrhosis, 211-212
Routte's operation in ascites, 260
Ruspini's styptic in haematemesis, 273

Saliformin, 614, 774
Saliva, the, in acute yellow atrophy, 587 ; in catarrhal jaundice, 667 ; in jaundice, 543, 547 ; in portal cirrhosis, 230-231
Salvarsan, in congenital syphilis, 378 ; in gumma of the liver, 368
Sand, intestinal, 740
Santorini, accessory pancreatic duct of, 750, 766
Sarcoma of the liver, melanotic, 480, 485, 489, 496 ; age and, 502 ; and hepatic embolism, 47 ; ascites in, 512 ; histology, 503 ; pigmented moles and, 485, 501 ; secondary growths of in the liver, 500-504
Sarcoma of the liver, primary, 469-486 (Figs. 67-69, 76), 505-530 ; age and, 470 ; alveolar, 486 ; angioplastic, 481 ; combined with suprarenal sarcoma, 471 ; diagnosis from secondary new growth, 526-528 ; diffuse or infiltrating, 484 ; duration, 518 ; forms of, 482 ; general diagnosis, 519-526 ; incidence, 469 ; injury and, 471 ; liver in, 486 ; massive, 482 ; multiple or nodular, 483 ; operative treatment, 529 ; origin of, 486 ; physical signs, 505-516 ; prognosis, 528 ; sex and, 469 ; situation of growth, 471 ; suppuration in, 486 ; symptoms, 516-518 ; termination, 519 ; treatment, 529 ; with cirrhosis, 484
Sarcoma of the liver, secondary, 487-530 (Fig. 75) ; degenerative changes in, 490 ; diagnosis from primary new growth, 526-528 ; duration, 518 ; general diagnosis, 519-526 ; histology, 493 ; incidence, 487 ; local fibrosis in, 494 ; operative treatment, 529 ; perihepatitis due to, 492 ; physical signs, 505-516 ; pseudocysts in, 491 ; remainder of liver in, 494-497 ; sex and, 487 ; situation of primary growth, 498-504 ; symptoms, 516-518 ; termination, 519 ; treatment, 529 ; umbilication in, 489, 492 ; sarcoma of the suprarenals, 504 ; of the gall-bladder, 631 ; secondary, of the gall-bladder, 648
Sausages and Weil's disease, 597
Scarlet fever and portal cirrhosis, 191
Schistosomiasis associated with primary carcinoma of the liver, 479
Schistosomum haematobium in the portal vein, 83 ; *S. japonicum* and portal cirrhosis, 190
Schnurleber, 27
Scirrhus of the liver, 470, 484
Sclérose hépatopancréatique hypertrophique avec hypersplénomegalie, 313
Sclerotics, the, in jaundice in the newly born, 570
Scolex, hydatid, 391
Secretin as a cholagogue, 775
Sedentary life and cholelithiasis, 713
Septicaemia and cholecystitis, 604 ; and hepatic abscess, 149 ; and hepatic infarction, 106-107 ; and jaundice in the newly born, 572
Serositis, multiple, 97 ; and perihepatitis, 162, 163
Sewer-gas and Weil's disease, 598
Sheep and hydatid disease, 398
Sheep-rot, 684
Shoulder, pain in the, absent in perihepatitis, 159 ; in acute hepatitis, 115 ; in cholelithiasis, 731, 733 ; in single hepatic abscess, 135
Siderosis in portal cirrhosis, 207
Sigmoid flexure, the, obstruction of by a gall-stone, 753
Silicosis of the liver, 302
Silicosis, pulmonary, and portal cirrhosis, 184
Silver poisoning and portal cirrhosis, 184
Situs transversus and lobulation of the liver, 1
Skin, the, in biliary cirrhosis, 320 ; in fatty liver, 431
Snake-bite, jaundice due to, 536
Sodium benzoate in cholelithiasis, 776
Sodium salicylate, as a cholagogue, 776 ;

in biliary colic, 743, 778 ; in catarrhal jaundice, 670 ; in chronic catarrhal cholangitis, 679 ; in intermittent heptic fever, 763 ; in suppurative cholangitis, 678
Soot in the lever cells, 440
Spa treatment, in acute congestion of the liver, 110 ; in acute hepatitis, 117 ; in biliary cirrhosis, 326 ; in cholelithiasis, 779 ; in catarrhal jaundice, 670 ; in chronic catarrhal cholangitis, 679 ; in chronic venous engorgement of the liver, 96 ; in functional liver disease, 43 ; in intermittent hepatic fever, 763 ; in jaundice, 566 ; in portal cirrhosis, 299
Spasm, intestinal, due to gall-stones, 752
Spiced foods and acute congestion of the liver, 108 ; and portal cirrhosis, 183, 185-186
Spigelian lobe, the, case of enlarged, 199 ; enlarged in hepatic endophlebitis, 52 ; hydatid cyst in, 403 ; in hydatid disease, 397 ; pedunculated, 3, 5
Spinal curvature, the liver in, 18
Spleen, the, abscess of, and suppurative pylephlebitis, 72; calcification in, 216, 441 ; cardiac, 217 ; hepatic, 217 ; in acute yellow atrophy, 584 ; in alveolar hydatid, 425 ; in biliary cirrhosis, 316-317 ; in biliary colic, 735 ; in carcinoma with cirrhosis, 477 ; in chronic perihepatitis, 169 ; in chronic splenomegalic haemolytic jaundice, 538 ; in congenital obliteration of the bile-ducts, 652, 655 ; in congenital syphilis, 375, 376 ; in delayed congenital syphilis, 380 ; in haemochromatosis, 305 ; in malignant disease of the bile-ducts, 698 ; in nutmeg liver, 91 ; in obstructive biliary cirrhosis, 331 ; in obstructive jaundice, 545 ; in parasyphilitic multilobular cirrhosis, 382 ; in portal cirrhosis, 215-219 (Fig. 36), 240-241, 294 ; in portal thrombosis, 62 ; in suppurative pylephlebitis, 75 ; in syphilis of the liver, 364 ; in the Talma-Morison operation, 261; in tuberculosis of the liver, 344 ; in Weil's disease, 598 ; puncture of in portal cirrhosis, 301 ; rests of, in the liver, 464 ; wandering, and jaundice, 556
Splenectomy, in chronic splenomegalic haemolytic jaundice, 538 ; in portal and splenic thrombosis, 67 ; in portal cirrhosis, 299 ; in splenic anaemia, 272
Splenic anaemia, lymphatics in, 84 ; portal calcification in, 83
Splenomegaly, meta-icteric, 565
Sputum, the, in catarrhal jaundice, 667
Stagnation of the bile and cholelithiasis, 713
Staphylococcus pyogenes, and acute cholecystitis, 607, 608 ; and portal cirrhosis, 185, 193 ; in single hepatic abscess, 132 ; in suppurating hydatid cysts, 422
Status epilepticus, fatty liver in, 428
Stercobilin, in carcinoma of the bile-ducts, 699 ; in carcinoma of the pancreas, 699 ; in haemohepatogenous jaundice, 536
Stigmata, venous, in catarrhal jaundice, 666 ; in chronic jaundice, 542 ; in portal cirrhosis, 228, 293
Stomach, the, carcinoma of, and haematemesis, 272 ; and hepatic abscess, 121 ; and portal thrombosis, 57 ; and secondary growths in the liver, 499, 527 ; and suppurative pylephlebitis, 70 ; diagnosis from carcinoma of the gall-bladder, 646 ; invading the liver, 498 ; jaundice in, 553
Stomach, the, cirrhosis of, and perihepatitis, 166 ; dilatation of, simulating ascites, 252 ; erosions of and haematemesis in cirrhosis, 268, 272 ; in portal cirrhosis, 220 ; rupture of an hepatic abscess into, 143 ; rupture of hepatic hydatid cyst into, 420
Stomach, the, ulcer of, and biliary colic, 739 ; and haematemesis in portal cirrhosis, 269, 271 ; and multiple hepatic abscess, 156 ; jaundice in, 553 ; in portal thrombosis, 63 ; in suppurative pylephlebitis, 70, 78
Strawberry gall-bladder, 624
Streptococcus pyogenes, and acute yellow atrophy, 579 ; in single hepatic abscess, 132 ; in suppurating hydatid cysts, 422
Streptotrichosis of the liver, 385
Sub-infarcts of the liver, 101-102
Sugar-iced liver, 161, 167
Sulci, diaphragmatic hepatic, 5, 10-11
Suppuration in hydatid cysts, 411, 421-422 ; in malignant disease of the liver, 486, 507
Suprarenal glands, accessory, adenoma of the liver due to, 458-459
Suprarenal glands, the, and haemochromatosis, 304-305 ; disease of, and jaundice, 555 ; growths of, diagnosis from hydatid cysts of the liver, 409 ; in congenital syphilis, 376 ; in leucodermia, 541 ; sarcoma of, with sarcoma of the liver, 471 ; secondary carcinoma in, 643
Suprarenal rests and primary carcinoma of the liver, 481
Surgical treatment, in acute cholecystitis, 621, 623 ; in biliary cirrhosis, 326 ; in biliary colic, 743 ; in bronchobiliary fistula, 771 ; in calculous intestinal obstruction, 754-755 ; in carcinoma of the gall-bladder, 647 ; in cholelithiasis, 780-782 ; in chronic catarrhal cholangitis, 679 ; in chronic splenomegalic haemolytic jaundice, 540 ; in gumma of the liver, 368-369 ; in hepatic angioma, 467 ; in hydatid disease of the liver, 414 ; in intermittent hepatic fever, 763 ; in malignant disease of the bile-ducts, 702 ; in malignant disease of the liver, 529 ; in suppurative cholecystitis, 678 ; in tuberculosis of the liver, 345
Suspensory ligaments, the hepatic, 24-25
Sustentacular formation, hepatic, 8

Sweat, the, in jaundice, 543, 667
Sweating in single hepatic abscess, 133
Sweeps' cancer, 474
Sympathetic, the abdominal, neuralgia of, 741
Symphyse péricardio-périhépatique, 163
Syphilis, acquired, of the liver, 348-383 (Figs. 42-45); and acute yellow atrophy of the liver, 577; and chronic splenomegalic haemolytic jaundice, 538; and furrowed liver, 11; and hepatic endophlebitis, 51; and lobulation of the liver, 1; and perihepatitis, 165; and portal cirrhosis, 333; and portal endophlebitis, 83; and portal thrombosis, 56; and stricture of the bile-ducts, 662-663; and stricture of the hepatic veins, 50; diagnosis, from perihepatitis, 171, from portal cirrhosis, 290; hepatic enlargement in, 150; jaundice due to enlarged portal glands in, 552; of the gall-bladder, 628; roseola of, and jaundice, 550
Syphilis, congenital, of the liver, 370-383 (Figs. 46-49); and congenital obliteration of the bile-ducts, 650, 657 (Fig. 92); and cysts of the bile-ducts, 660; and hepatic cirrhosis in children, 333, 335; and portal cirrhosis, 187; ascites in, 377; clinical features, 376-377; diagnosis, 377; jaundice in, 376-377; lardaceous disease in, 434; liver in, 371-376; mistaken for malignant disease, 470-471; prognosis, 378; spleen in, 376; treatment, 378
Syphilis, delayed congenital, of the liver, 378-381 (Fig. 49); clinical features, 379; diagnosis, 381; incidence, 379; morbid anatomy, 379
Syphilis, hereditary, 370; *see* Syphilis, congenital
Syphiloma, in congenital syphilis, 371, 373; use of the term, 351

Tabes dorsalis and gumma of the liver, 360, 369; hepatic crises in, 740
Taenia echinococcus, 391, 399; and alveolar hydatid, 423
Talma-Morison operation, 210, 260-264; contra-indications, 264; early performance advised, 263; in chronic perihepatitis, 172; results, 264
Tapping, *see* Paracentesis
Teeth, green, in jaundice, 541
Telangiectasis, hepatic, 466
Teratoma of the liver, 468; malignant, 504
Tetanoid chorea and cirrhosis, 281, 335
Tetany due to biliary colic, 736
Thigh, biliary fistula in the, 767
Thrill, hydatid, 402
Thrombophlebitis, hepatic, 51
Thrombosis, venous, due to secondary malignant growths in the liver, 492; in portal cirrhosis, 288; marantic, and microbes, 55; multiple, in cirrhosis, 278; of hepatic veins (*q.v.*), 48; of hepatic angiomas, 466; of inferior vena cava and of the hepatic veins, 49; of the portal vein, 53-68 (Fig. 11), in portal cirrhosis, 208, without infarction, 106
Thyroid extract in pruritus, 567
Tight-laced liver, 8-12 (Figs. 5-6); and cholelithiasis, 713, 723; and hepatoptosis, 25-26; and Riedel's lobe, 13; effect on gall-bladder, 15; in cystic liver, 449; liver in, 18
Tissue fibrinogen, infarction of liver by, 106
Toluylenediamine poisoning, cholangitis in, 313; effects of, 775; jaundice due to, 533
Tophus of cholesterin and xanthoma, 541
Torpid liver, 39, 41-42
Torsion of the gall-bladder, 623
Toxaemia, action in producing ascites, 262; and acute congestion of the liver, 107; and ascites in portal cirrhosis, 244; and hepatic infarction, 106; in obstructive biliary cirrhosis, 332; in portal cirrhosis, 233-234, 293, 300; in portal thrombosis, 65-66; splenic enlargement and, 218
Toxins and fatty change in the liver, 426-428; and portal cirrhosis, 185; in hydatid fluid, 413-414
Trauma and ascites in portal cirrhosis, 246
Treponema pallidum, in congenital syphilis, 370; in gumma of the liver, 354
Trocar, use of in paracentesis, 258, 260
Tropical liver, 109; and acute hepatitis, 115
Tubera circumscripta, 489; diffusa, 489
Tuberculin reaction, the, in actinomycosis, 387, 388
Tuberculoma, multiple hepatic, 344; solitary hepatic, 344
Tuberculosis, avian, and cirrhosis in guinea-pigs, 346
Tuberculosis, bovine, and perihepatitis, 167
Tuberculosis, human, and portal cirrhosis, 89, 191; and pseudo-cirrhosis, 100, 101; and secondary carcinoma, 496; effects of on the liver, 346-348; in portal cirrhosis, 222-223, 282-284; in portal cirrhosis in children, 334-335; miliary of the liver, 339-340; of glands in the portal fissure, 551-552; of the gall-bladder, 627; of the liver, 336-348, *see* Liver, the, tuberculosis of; pericholangitic, 682; solitary hepatic, 343
Tumours, abdominal, simulating ascites, 252
Turpentine, in cholelithiasis, 775, 777; in phosphorus poisoning, 596
Turpeth, in ascites, 265
Tympanites in portal cirrhosis, 231, 238
Typhoid, bilious, 597-600
Typhoid carriers and cholelithiasis, 755
Typhoid fever, *see* Enteric Fever
Typhoid state, the, in acute yellow atrophy,

590 ; in haemohepatogenous jaundice, 536
Tyrosine, urinary, in acute yellow atrophy, 580, 582, 589 ; in phosphorus poisoning, 595 ; in single hepatic abscess, 140

Ulcer of the stomach, and pylethrombosis, 54 ; and suppurative pylephlebitis, 70
Umbilical cord, liver in, 17
Umbilication in malignant growths of the liver, 484, 489, 492, 508-509
Umbilicus, the, biliary fistula at, 767 ; everted in ascites, 253 ; infection of, and jaundice in the newly born, 571 ; secondary new growths at, 509
Uraemia, and portal thrombosis, 65 ; in cystic disease of the liver, 455
Urea, administration of in ascites, 265 ; excretion of in portal cirrhosis, 233 ; in acute yellow atrophy, 589, in phosphorus poisoning, 595
Uric acid, and cholelithiasis, 720 ; formation of, 40-41 ; in acute yellow atrophy, 589 ; metabolism of, 40-41
Uricaemia in hepatism, 40
Urine, the, bile in, without jaundice, 772 ; bile-salts in, in jaundice, 542 ; in acute catarrhal cholangitis, 667 ; in acute congestion of the liver, 109 ; in acute yellow atrophy, 588-589 ; in alveolar hydatid, 425 ; in biliary cirrhosis, 322 ; in biliary colic, 736-737 ; in catarrhal jaundice, 667 ; in chronic splenomegalic haemolytic jaundice, 539 ; in chronic venous engorgement of the liver, 94 ; in congenital obliteration of the bile-ducts, 656 ; in fatty liver, 432 ; in functional hepatic disorders, 39 ; in haemohepatogenous jaundice, 536 ; in hydatid disease of the liver, 404 ; in intermittent hepatic fever, 761 ; in leukaemia, 443 ; in malignant disease of the bile-ducts, 698 ; in malignant disease of the liver, 514 ; in melanotic sarcoma, 515 ; in obstructive jaundice, 542 ; in phosphorus poisoning, 595 ; in portal cirrhosis, 232-235 ; in portal thrombosis, 65 ; in single hepatic abscess, 139-140 ; in suppurative cholecystitis, 618 ; in suppurative pylephlebitis, 79 ; in Weil's disease, 600 ; leucine and tyrosine in, 589, 590
Urobilin, excretion of, in portal cirrhosis, 232 ; formation of in the kidneys, 535
Urobilin-jaundice, 534
Urobilinuria, 564 ; in catarrhal jaundice, 667 ; in intermittent hepatic fever, 761 ; in jaundice, 542
Uro-erythrin in portal cirrhosis, 232
Urohaematoporphyrin in portal cirrhosis, 232
Urotropin, administration of, in acute cholecystitis, 614 ; in catarrhal jaundice, 670 ; in cholelithiasis, 776, 778 ; in chronic catarrhal cholecystitis, 679 ; in chronic cholecystitis, 626 ; in intermittent hepatic fever, 763 ; in suppurative cholangitis, 678
Urticaria, in catarrhal jaundice, 667 ; in hydatid disease of the liver, 403, 413, 414 ; in jaundice, 547 ; in Weil's disease, 599
Uterus, the, carcinoma of and secondary growths of the liver, 500 ; fibromyoma of, and cholelithiasis, 720 ; prolapse of in ascites, 250
Uvea, the, malignant growths of, 480, 485, 489, 496, 501

Vaccine treatment, in cholelithiasis, 777 ; in intermittent hepatic fever, 763 ; in suppurative pylephlebitis, 82
Vagina, biliary fistula into the, 773
Varicocele in portal cirrhosis, 210
Varix, oesophageal, in cirrhosis, 212-214 ; haemorrhage from, 213
Vater, ampulla *or* diverticulum of, *see* Ampulla, 702
Vegetable trocar, the, 265
Vein, coronary gastric, in cirrhosis, 213 ; deep epigastric, wounded in paracentesis, 259
Vein, mesenteric, trauma of and pylephlebitis, 71 ; parumbilical, enlarged in cirrhosis, 211 (Fig. 35)
Vein, portal, and typhoidal cholecystitis, 606 ; and fistula into the gall-bladder, 772 ; and tuberculosis of the liver, 338 ; calcification of, 83 ; embolism of, and infarction, 103 ; extension of carcinoma into, 482 ; in portal cirrhosis, 208 ; obstruction of, and infarcts, 104 ; parasites in, 83 ; primary haemangioma of, 60 ; rupture of an hepatic abscess into, 144
Vein, portal, thrombosis of the, 53-68 (Fig. 11) ; abscess of the liver and, 54 ; age and, 60 ; and chronic pancreatitis, 58 ; and chronic peritonitis, 58 ; and infarction, 104 ; ascites in, 64 ; association with multiple adenomas of the liver, 460 ; causation, 53 ; cirrhosis and, 55 (Fig. 11), 56 ; clot in, 61 ; diagnosis, 66 ; diagnosis from cirrhosis and ascites, 255 ; distribution of, 60 ; gall-stones and, 54 ; gastro-intestinal symptoms, 64 ; in adenoma, 462 ; in carcinoma of the gall-bladder, 637 ; in carcinoma of the pancreas, 57 ; in carcinoma of the stomach, 57 ; in malignant disease, 56 ; in malignant disease of the bile-ducts, 699 ; in portal cirrhosis, 244 ; inflammation and, 53 ; intestines in, 63 ; jaundice in, 65 ; liver in, 61 ; morbid anatomy, 60 ; onset, 63 ; phlebosclerosis and, 55 ; pleural effusion and, 286 ; primary, 59 ; prognosis, 66 ; sex and, 59 ; spleen in, 62, 64 ; symptoms and signs, 63-66 ; syphilis and, 56 ;

trauma and, 59 ; treatment, 67 ; ulcer of the stomach and, 54
Vein, splenic, the, and portal cirrhosis, 188-189 ; thrombosis of, 218 ; thrombosis of, spleen in, 63
Vein, sublobular hepatic, in portal cirrhosis, 201 ; superior haemorrhoidal, in cirrhosis, 213
Vein, umbilical, and tuberculosis of the liver, 337 ; in congenital obliteration of the bile-ducts, 651, 657 ; in portal cirrhosis, 211
Veins, hepatic, diseases of the, 48-53 ; extension of carcinoma into, 482 ; occlusion of, 48-52 ; rupture of hepatic hydatid cyst into, 420 ; rupture of hepatic abscess into, 144 ; stenosed by syphilitic cicatrix, 358 ; thrombosis of, 48-49, 462 ; thrombosis of, and infarcts, 105 ; stricture of, 49-52
Veins, varicose gastric, and haematemesis in cirrhosis, 271 ; varicose oesophageal, and haematemesis in cirrhosis, 269-271
Vena cava inferior, the, compressed in ascites, 212 ; obliterated by syphilitic cicatrix, 358 ; rupture of hepatic abscess into, 144 ; rupture of hepatic hydatid cyst into, 420-421 ; thrombosis of due to hepatic abscess, 145 ; thrombosis of in cirrhosis, 212
Venous hum, in angioma of the liver, 466 ; in portal cirrhosis, 239, 241 ; in malignant disease of the liver, 509
Venules, enlargement of the thoracic, 212, 229
Villous carcinoma of the gall-bladder, 635
Vinegar and portal cirrhosis, 180, 334
Virchow's gland, 290, 516, 527, 638
Visceroptosis, and cholelithiasis, 716 ; and hepatoptosis, 25, 26 ; and jaundice, 561
Vitiligoidea, in jaundice, 541 ; of the bile-ducts, 689
Volvulus and portal thrombosis, 59
Vomicae, tuberculous hepatic, 341, 345
Vomiting, coffee-ground, in portal cirrhosis, 267 ; fatal, in cholelithiasis, 745 ; in acute cholecystitis, 611 ; in acute yellow atrophy, 586 ; in biliary colic, 742 ; in calculous obstruction of the intestine, 754 ; in catarrhal jaundice, 666 ; in intermittent hepatic fever, 761 ; in phosphorus poisoning, 594 ; in portal cirrhosis, 299 ; of gall-stones, 769 ; persistent, in cholelithiasis, 748 ; reflex, in biliary colic, 735
Vomiting, morning, in portal cirrhosis, 231

Wandering liver, 16, 22-36
Wassermann's reaction, in gumma of the liver, 362-367
Watercress and hydatid disease, 399
Water-drinking, in cholelithiasis, 775
Weather, hot, and foaming liver, 6
Weil's disease, 535, 597-600 (Fig. 81) ; and acute hepatitis, 115 ; bacteriology, 598 ; diagnosis, 600, from biliary cirrhosis, 324 ; morbid anatomy, 598 ; relapse in, 599 ; symptoms, 598 ; treatment, 600 ; urine in, 600
Whisky-drinker's liver, 177
Widal's reaction, in catarrhal jaundice, 665, 667 ; in jaundice, 544 ; in Weil's disease, 599
Winckel's disease, 572
Wirsung's duct, 649, carcinoma of, 703, in cholelithiasis, 764

x-ray examination, in acute hepatitis, 115 ; in clubbing of the fingers 320 ; in gall-stones, 725, 744, 751, 762 ; in haemochromatosis, 305 ; in hydatid cysts of the liver, 408 ; in pancreatic calculus, 751 ; in single hepatic abscess, 127
x-ray treatment, cirrhosis of the liver after, 442 ; in actinomycosis, 387
Xanthelasma, multiple, in jaundice, 541 (Fig. 78) ; of the bile-ducts, 689
Xanthine, in acute yellow atrophy, 581 ; metabolism of in the liver, 41
Xanthoma, in jaundice, 541 (Fig. 78) ; in malignant disease of the bile-ducts, 698 ; of the bile-ducts, 689 ; prognostic value of, 566
Xanthopsia, in catarrhal jaundice, 667 ; in jaundice, 546, 698

Yellow atrophy of the liver, acute, 575-592 (Figs. 79, 80)
Yellow fever and single hepatic abscess, 126 ; and Weil's disease, 600
Yellow gum, 568
Yellow vision, 546, 667, 698

Ziemssen's test, 746
Zuckergussleber, 97-98, 161-172 (Figs. 23, 24)

THE END

Printed by R. & R. Clark, Limited, *Edinburgh.*

A SYSTEM OF MEDICINE

BY MANY WRITERS

Medium 8vo.

SECOND EDITION

EDITED BY

SIR CLIFFORD ALLBUTT, K.C.B., M.D., F.R.S.

AND

HUMPHRY DAVY ROLLESTON, M.D., F.R.C.P.

Vol. I. Prolegomena and Infectious Diseases. 25s. net.

II. Part I. Infectious Diseases (*continued*), Intoxications. 25s. net.

II. Part II. Tropical Diseases and Animal Parasites. 25s. net.

III. Certain General Diseases, Diseases of the Alimentary Canal and Peritoneum. 25s. net.

IV. Part I. Diseases of the Liver, Pancreas, Ductless Glands, and Kidneys. 25s. net.

IV. Part II. Diseases of the Nose, Pharynx, Larynx, Trachea, and Ear. 25s. net.

V. Diseases of the Respiratory System, Disorders of the Blood. 25s. net.

VI. Diseases of the Heart and Blood-Vessels. 25s. net.

VII. Diseases of the Muscles, The Trophoneuroses, Diseases of the Nerves, Vertebral Column, and Spinal Cord. 25s. net.

VIII. Diseases of the Brain and Mental Diseases. 25s. net.

IX. Diseases of the Skin. General Index (99 pages). 25s. net.

MACMILLAN AND CO., LTD., LONDON.

PRESS NOTICES OF
THE SECOND EDITION OF
A SYSTEM OF MEDICINE

VOLUME I

LANCET.—"As a whole, the work is one of which the profession of medicine in this country may well be proud, and one which, like its predecessor, will be of great value to the investigator and the practitioner who desires to keep himself informed of the advances in medical knowledge and to have the current state of that knowledge conveniently summarised."

NATURE.—"Altogether this volume commands admiration, and if its high standard be maintained, as it doubtless will be, in the succeeding volumes, this *System of Medicine* will form a lasting monument of the high place which British medicine holds at the present time."

VOLUME II.—PART I

BRITISH MEDICAL JOURNAL.—"The new instalment of the *System* will thus be seen to be as full and complete a work of reference as the most expert writers and the most discriminating of editors can make it. . . . A work which presents a trustworthy compendium of all that is really known upon the subjects with which it deals."

SCOTTISH MEDICAL AND SURGICAL JOURNAL.—"It is impossible in the short limits of this review to attempt to do justice to the great value of Dr. Allbutt's *System*. Every article which it contains is worthy of a prolonged consideration. We can only conclude by wishing the second edition the same success which has been so signally attained by the first, and by suggesting that even those who possess the first edition will do well to secure the second, which, as we have endeavoured to show, is to all intents and purposes a new book."

VOLUME II.—PART II

BRITISH MEDICAL JOURNAL.—"It is sufficient to say that the hope of the editors that the volume will serve as a complete work on tropical medicine has been realised; it should, in fact, become the standard of the subject in the English language, both as a book of reference and for study."

EDINBURGH MEDICAL JOURNAL.—"As the subjects are treated in the exhaustive manner characteristic of this system of medicine, with the matter thoroughly up to date, it will be eagerly welcomed by all interested in these branches of medicine. . . . The editors are to be congratulated on the production of an excellent work, which, containing in a compact form such a mass of information with copious references to the literature on the various subjects, should prove invaluable not only to students of tropical medicine, but to practitioners at home and abroad."

PRESS NOTICES—*continued.*

VOLUME III

LANCET.—"The present volume well maintains the credit gained by those which have previously appeared, and there is every indication that the new *System* will retain the place secured by the former edition as the most popular standard medical text-book in this country."

BRITISH MEDICAL JOURNAL.—"The volume in every way maintains the high standard which has characterised this publication throughout."

VOLUME IV.—PART I

LANCET.—"We once more congratulate the editors on the success of their labours. The present volume is a valuable addition to the *System of Medicine*. It contains much new matter, and will serve as a most excellent work of reference."

BRITISH MEDICAL JOURNAL.—"Limits of space prevent our mentioning all the new articles, but we would refer our readers to this volume with great satisfaction as being a perfectly adequate presentment of all the subjects with which it deals."

VOLUME IV.—PART II

LANCET.—"An extremely creditable volume. . . . Well up to the high standard set by the rest of the work."

VOLUME V

LANCET.—"The whole volume maintains the high standard which we are accustomed to expect in our leading medical text-books. In almost all instances a careful and thorough survey of medical literature, both of our own and of foreign countries, has been made, and valuable bibliographies are appended to the articles."

BRITISH MEDICAL JOURNAL.—"A volume which cannot but enhance the high reputation deservedly earned by the previously-issued portions of the new edition of the *System*."

VOLUME VI

BRITISH MEDICAL JOURNAL.—"A volume which is in all respects representative of the latest knowledge and experience at home and abroad."

LANCET.—"The present volume contains a vast amount of information in connection with diseases of the heart and blood-vessels. As a separate work of reference it is one of great value, while it forms a worthy addition to the *System*, which now holds a high place in medical literature upon which Sir Clifford Allbutt and Dr. Rolleston may be heartily congratulated."

VOLUME VII

MEDICAL TIMES.—"With such an array of contributors, all of the front rank in their several spheres of work, it goes without saying that the volume before us worthily represents this particular branch of British Medicine."

MEDICAL PRESS AND CIRCULAR.—"The accounts of the various diseases treated of in the present volume have been brought up to date in the most thorough manner, and no step has been omitted by the Editors or by their contributors to make the book a true reflection of modern teachings on these subjects."

PRESS NOTICES—*continued.*

VOLUME VIII

BRITISH MEDICAL JOURNAL.—"The whole bears constant witness to the thorough and careful revision demanded by a department of medicine the progress of which, by the expansion of its confines, the development of its resources and changing terminology and conceptions, is unsurpassed by that of any other. . . . Varying naturally in accord with the subject as to length and individual method of treatment, the separate articles are at one in their animating spirit of thoroughness, lucidity of utterance, and discriminating judgment."

EDINBURGH MEDICAL JOURNAL.—"It should be read by all alienists, and as a book of reference should prove most valuable in the library of the general practitioner."

VOLUME IX

BRITISH MEDICAL JOURNAL.—"The field of dermatology has been divided up among a number of contributors, who have dealt with the numerous morbid conditions in an able and thorough manner. Where the quality is so good and sustained throughout, it would be invidious to select any one article for particular examination. In all the sections the subjects have been brought up to date, and useful bibliographies appended, which cannot fail to be of great help to those consulting the book."

SECOND EDITION

A SYSTEM OF GYNÆCOLOGY. By many Writers.

Edited by Sir CLIFFORD ALLBUTT, K.C.B., M.D., F.R.S., W. S. PLAYFAIR, M.D., F.R.C.P., and THOMAS WATTS EDEN, M.D., F.R.C.P. Medium 8vo. 25s. net.

BRITISH MEDICAL JOURNAL.—"The editors have taken full advantage of their opportunities to make the second edition a distinct improvement on the first, a popular, widely read and fully quoted textbook."

JOURNAL OF OBSTETRICS AND GYNÆCOLOGY OF THE BRITISH EMPIRE.—"The appearance of a new edition of Allbutt and Playfair's System is an event of the first importance in the gynæcological world. . . . The present edition shows a marked improvement."

MACMILLAN AND CO., LTD., LONDON.