A manual of pathological histology / by V. Cornil and L. Ranvier ; translated, with notes and additions, by E.O. Shakespeare and J. Henry C. Simes.

Contributors

Cornil, V. 1837-1908.
Ranvier, L. 1835-1922.
Nimes, J. Henry C., 1841-1907.
Shakespeare, Edward O. 1846-1900.

Publication/Creation

London : H. Kimpton, 1880.

Persistent URL

https://wellcomecollection.org/works/wexfhwrw

License and attribution

This work has been identified as being free of known restrictions under copyright law, including all related and neighbouring rights and is being made available under the Creative Commons, Public Domain Mark.

You can copy, modify, distribute and perform the work, even for commercial purposes, without asking permission.

wellcome collection

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


22101021201



Digitized by the Internet Archive
in 2014

https://archive.org/details/b2041772x

EX LIBR. BIBL. COLL. REG. CHIR. EDIN.

A MANUAL

OF

PATHOLOGICAL HISTOLOGY.

BY

V. CORNIL,

ASSISTANT PROFESSOR IN THE FACULTY OF MEDICINE OF PARIS,

AND

L. RANVIER,

PROFESSOR IN THE COLLEGE OF FRANCE.

TRANSLATED, WITH NOTES AND ADDITIONS,

BY

E. O. SHAKESPEARE, A.M., M.D.,

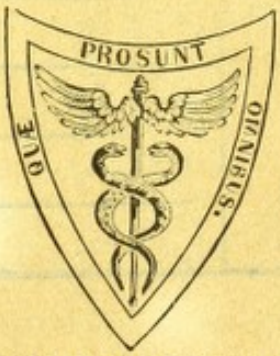
LECTURER ON REFRACTION AND OPERATIVE OPHTHALMIC SURGERY IN THE UNIVERSITY OF PENNSYLVANIA, AND OPHTHALMIC SURGEON AND MICROSCOPIST TO THE PHILADELPHIA HOSPITAL,

AND

J. HENRY C. SIMES, M.D.,

DEMONSTRATOR OF PATHOLOGICAL HISTOLOGY AND LECTURER ON HISTOLOGY IN THE UNIVERSITY OF PENNSYLVANIA.

WITH THREE HUNDRED AND SIXTY ILLUSTRATIONS ON WOOD.



LONDON: HENRY KIMPTON, 82, HIGH HOLBORN.
PHILADELPHIA:
HENRY C. LEA.
1880.

Entered according to Act of Congress, in the year 1880, by
HENRY C. LEA,
in the Office of the Librarian of Congress. All rights reserved.

WELLCOME INSTITUTE LIBRARY
Acc 338161
Call No. QZ4 1869- 1876 C81m3E
M15858

COLLINS, PRINTER.

TRANSLATORS' PREFACE.

THE very high reputation acquired throughout Europe by the Pathological Histology of MM. Cornil and Ranvier as a clear and excellent presentation of this important department of Medical Science would seem to be a sufficient justification of the present effort to make it accessible to the American student.

In France, the work appeared in several portions, at intervals extending from 1869 to 1876. The earlier parts are therefore somewhat behind the existing state of knowledge and opinion. Moreover, the book is very large, and in some portions diffusely written. It has been the endeavor of the Translators, by omitting such passages as are comparatively unimportant or have become obsolete, by condensing others, and by inserting additions where the progress of science has seemed to call for them, to render the American version a more faithful exponent of the subject in its present state, and at the same time to bring it within the compass of a convenient text-book for the student. The additions are scattered throughout the volume, and are generally inclosed within brackets [ ]. The most extensive changes will be found in the sections on Sarcoma, Carcinoma, Tuberculosis, The Bloodvessels, The Mamma, and The Classification of Tumors.

Corresponding alterations have been made in the series of wood-cuts. In this connection, thanks are due to the Surgeon-General of the Army, and to Dr. J. J. Woodward, U.S.A., for their kind permission to use some of the important illustrations in the second part of the medical volume of the Medical and Surgical History of the War.

The foothold which the metrical system of weights and measures is gradually gaining in this country, the wide-spread adoption of that sys-

tem by the scientists of Europe, and the desirability of the employment of scientific terms having a well recognized significance the world over, have led the Translators to retain the metrical values whenever dimensions have been expressed.

PHILADELPHIA, January, 1880.

AUTHORS' PREFACE.

THE absence of a French work upon pathological histology has determined us to publish this book.

The title which we have chosen, *Manual of Pathological Histology*, indicates the object of its publication, viz.: that of presenting a brief, elementary, and succinct explanation of the descriptions, definitions, and classifications of morbid products as seen under the microscope. Our book has not been named *Pathological Anatomy* because it is based entirely upon normal histology—a department of medical science from which we have borrowed both classifications and methods.

This title implies the necessity of paying little attention to naked-eye descriptions, which, indeed, are so complete and satisfactory in the classical works of Cruveilhier, Andral, Bouillaud, and others, that it is impossible to rival them or to successfully abridge them.

The material which has been utilized for the composition of this manual is derived from autopsies and operations in the hospitals of Paris, so rich in this respect that a tenth part of the material daily wasted there would amply suffice for the supply of the most active laboratory. And here we desire to express our acknowledgments to our colleagues, to our friends, and to our chiefs, physicians and surgeons of the hospitals, by whose earnest co-operation most interesting specimens have been placed at our disposal. The examination of this material was made by our pupils and by ourselves in our own *special laboratory*—our manual being the pathological complement to the histological course which we have given for four years.

A knowledge of *normal histology* is indispensable for a comprehension of pathological histology. Although upon that subject the French translation of the treatise of Kölliker and that of Freys' Histology, in course of publication, give full instruction, we have, nevertheless, concluded to offer a brief *résumé* of normal histology before entering upon the study of pathological histology. Hence the first chapter comprises a general examination of the constitution of cells and of normal tissues. Furthermore, the normal histology of each organ is rapidly reviewed before

commencing the study of its pathology. The arrangement of this manual is, consequently, the same as that of a treatise upon normal histology.

General pathology corresponds to *general histology*, and comprises the lesions of cells and of tissues as well as the nature of inflammation and of tumors. This occupies the first part.

To *special histology* corresponds *special pathology*, which is divided into two parts: the one, devoted to the lesions of each of the tissues and systems; the other, to the alterations of each apparatus and particular organ. In this last part our pupil and friend, M. Terrillon, has added his labor to ours.

We disclaim allegiance to any school, belonging neither to the *German* nor to the so-called *French school*. The latter appellation is incongruous, since its real chief, Professor Henle, is a German. We are opposed to such divisions, for they would compromise science itself in the dissensions of savants—science, a unity indivisible as truth. In making our contributions, it behooves us to justly appreciate the labors of others, and to observe our facts with exactness.

But little space has been accorded to *history*, because in writing for beginners, we deemed it necessary above all to state simple facts and interpretations which we believed to be true. The office of a manual is neither to relate nor to criticize every opinion which has been advanced. The omission of the discussion of theories and doctrines has not been because we have considered them useless or barren, but rather because this was not the proper place to examine them.

It had been our desire to head each part of human pathology by introducing a chapter upon *experimental pathology*. But the former will be well understood only when the latter shall have no more mysteries to solve. Notwithstanding the fact that experimental pathology, under the powerful impulse of Cl. Bernard and of Virchow, has already had a vigorous beginning, and that both experimental physiology and histology have tended to stimulate its development, how much remains to be discovered!

PARIS, February 10, 1869.

CONTENTS.

PART I.

GENERAL PATHOLOGICAL ANATOMY

CHAPTER I.

NORMAL HISTOLOGY.—CELLS AND NORMAL TISSUES.

PAGE

SECT. I.—Cell Theory and Structure of Cells 17
SECT. II.—Normal Tissues 22

CHAPTER II.

GENERAL PRINCIPLES.—ALTERATIONS OF CELLS AND OF TISSUES.

SECT. I.—Lesions of Nutrition of Elements and of Tissues . . . 39
A. Lesions Caused by Death of Elements and of Tissues . . 39
B. Lesions Caused by Insufficient Nutrition of the Elements . . 41
C. Serous and Albuminous Infiltrations 42
D. Mucous and Colloid Infiltrations 44
Vitreous Degeneration (Waxy Degeneration of Zenker) . . 45
E. Amyloid Infiltration 46
F. Fatty Infiltration and Fatty Degeneration 47
G. Pigmentation of Elements and of Tissues 49
H. Calcareous Infiltration 51
I. Infiltration of the Urates 52
J. Lesions Caused by an Excess of Nutrition of Cells and of Tissues . 53
SECT. II.—Lesions in the Formation of Cells 53

CHAPTER III.

OF INFLAMMATION.

SECT. I.—Definition of Inflammation 55
SECT. II.—Traumatic Inflammation in Non-vascular Tissues 55
SECT. III.—Artificial Irritation in Vascular Tissues 59
SECT. IV.—Analytical Study of Inflammation in Man . . . 68
SECT. V.—Clinical Forms of Inflammation 73

CHAPTER IV.

OF TUMORS.

PAGE

SECT. I.—Definition of Tumor 74
SECT. II.—Classification and Description of Tumors 75
Sarcoma 76
Myxona 89
Fibroma 91
Lipoma 95
Carcinoma 96
Gumma 107
Tubercles 112
Glanders 126
Enchondroma 126
Osteoma 132
Myoma 134
Neuroma 137
Angioma 139
Lymphangioma. Lymphadenoma 141
Epithelioma 146
Cylindroma 156
Papilloma 157
Adenoma 160
Cysts 164
Mixed Tumors 170
Classification and Condensed Description of Tumors . . . 172
Appendix to Tumors 189
Circumscribed Melanotic Formations 189
Hydatid Cysts 191

PART II.

DISEASES OF ORGANS AND TISSUES.

CHAPTER I.

LESIONS OF BONES.

SECT. I.—Congestion and Hemorrhage of Bone 196
SECT. II.—Osteitis 197
1. Simple Osteitis 200
2. Rarefying Osteitis 200
3. Formative Osteitis 202
4. Diffused Suppurative Osteitis 203
SECT. III.—Necrosis 204
SECT. IV.—Caries 207

PAGE

SECT. V.—Formation of Callus 209
Fractures Complicated with Wounds 210
Fractures not Complicated with Wounds 210
SECT. VI.—Tumors of Bones 212
Varieties of Tumors of Bones 213
Sarcoma 213
Myxoma 214
Lipoma 214
Carcinoma 214
Tubercles 215
Gumma 217
Chondroma 218
Osteoma 218
Lymphadenoma 218
Epithelioma 218
Cysts 218
SECT. VII.—Osteomalacia 219
Osteoporosis 220
SECT. VIII.—Rachitis 220

CHAPTER II.

LESIONS OF CARTILAGE . . . 225

CHAPTER III.

PATHOLOGY OF THE ARTICULATIONS.

SECT. I.—Normal Histology of the Articulations 227
SECT. II.—Acute Arthritis 228
A. Simple Acute Arthritis and Rheumatic Arthritis . . . 228
B. Purulent Arthritis 231
SECT. III.—Chronic Arthritis 233
A. Hydrarthrosis 233
B. Chronic Arthritis by Continuity of Inflammation . . . 233
C. Chronic Rheumatic Arthritis 234
D. Scrofulous Arthritis or White Swelling 238
E. Gouty Arthritis 241
SECT. IV.—Tumors of the Articulations 244

CHAPTER IV.

LESIONS OF CONNECTIVE TISSUE AND SEROUS CAVITIES.

SECT. I.—Normal Histology of the Connective Tissue and Serous Cavities . 247
SECT. II.—Congestion and Hemorrhage of the Connective Tissue . . 248
SECT. III.—Œdema 250
SECT. IV.—Inflammation of Connective Tissue 252
SECT. V.—Purulent Inflammation of the Connective Tissue or Acute Phlegmon 253
SECT. VI.—Chronic Phlegmon 256

PAGE

Sect. VII.—Tumors of the Connective Tissue 257
Sect. VIII.—Hemorrhages of the Serous Membranes . . . 258
Sect. IX.—Inflammation of the Serous Membranes 259
Hemorrhagic 262
Purulent 263
Adhesive 265
Sect. X.—Tumors of the Serous Membranes 265

CHAPTER V.

LESIONS OF THE MUSCULAR TISSUE.

Sect. I.—Normal Histology of Muscular Tissue . . . 269
Sect. II.—Nutritive Lesions of Muscles 270
Atrophy of Muscular Fasciculi 270
Hypertrophy of Muscular Fasciculi 271
Cloudy Swelling of Muscular Fasciculi 271
Fatty Degeneration of Muscular Fasciculi 272
Pigmentation of Muscular Fasciculi 274
Vitreous Degeneration of Muscular Fasciculi 274
Hemorrhage of Muscles 276
Embolic Infarction of Muscles 277
Multiplication of Cellular Elements of the Sarcolemma . . . 278
Inflammation of Muscles or Myositis 278
Suppuration of Muscles 279
Chronic Inflammation of Muscles 279
Rupture of Muscles 280
Sect. III.—Tumors of Muscles 280
Sect. IV.—Parasites of Muscles 282

CHAPTER VI.

LESIONS OF THE BLOOD.

Sect. I.—Normal Histology of the Blood 284
Sect. II.—Pathological Histology of the Blood 287
Hydræmia 287
Leucocytosis 287
Leucocythæmia 288
Melanæmia 288
Parasites 289

CHAPTER VII.

LESIONS OF THE HEART.

Sect. I.—Pericardium 290
Hemorrhages 290
Dropsy of the Pericardium 290
Inflammation, Pericarditis 290
Carcinoma 292

PAGE

SECT. II.—Myocardium 292
Atrophy 292
Hypertrophy 293
Fatty Degeneration 293
Pigmentary Degeneration 294
Congestion, Hemorrhage 294
Aneurisms of the Heart 295
Inflammation or Myocarditis 296
Fibroid Induration of the Heart 297
Abscesses of the Myocardium 297
Tumors of the Myocardium 298
SECT. III.—Endocardium 298
Normal Histology 298
Endocarditis 300
Acute 300
Chronic 302
Valvular Aneurism 302
Formation of Blood Clots in the Heart 304

CHAPTER VIII.

LESIONS OF THE ARTERIES.

SECT. I.—Normal Histology of the Arteries 306
SECT. II.—Pathological Histology of the Arteries 307
Acute Endarteritis 307
Acute Periarteritis 309
Fatty Degeneration of Arteries 310
Chronic Arteritis 311
Atheroma 311
Calcareous Plates 312
Arteritis Deformans 313
Chronic Periarteritis 313
Aneurisms 314
Arterio-Venous Aneurisms 318
Arterial Obliterations 318
by the Ligature 318
by Acupressure or Torsion 325
Spontaneous 325
by Endarteritis and Thrombosis 326
by Embolism 326
Syphilitic Lesions of the Arteries 331
Amyloid Degeneration of Arteries 332
Tumors of the Arteries 333

CHAPTER IX.

LESIONS OF CAPILLARY BLOODVESSELS.

PAGE

SECT. I.—Normal Histology of Capillaries 334
SECT. II.—Pathological Histology of Capillaries 335
Inflammation of Capillaries 335
Nutritive Lesions of Capillaries 336
Calcareous Infiltration, Amyloid Degeneration 337

CHAPTER X.

LESIONS OF VEINS.

SECT. I.—Normal Histology of Veins 338
SECT. II.—Pathological Histology of Veins 339
Phlebitis 339
Venous Thrombosis 340
Varices, Varicose Veins 342
Tumors of Veins 344

CHAPTER XI.

LESIONS OF LYMPHATIC VESSELS.

SECT. I.—Normal Histology 345
SECT. II.—Pathological Histology of Lymphatic Vessels . . . 345
Inflammation or Lymphangitis 345
Dilatation of the Lymphatics or Lymphangiectasis . . . 346
Lesions of Lymph Vessels within Tumors 346

CHAPTER XII.

LESIONS OF LYMPHATIC GLANDS.

SECT. I.—Normal Histology of the Lymph Glands 348
SECT. II.—Pathological Histology of Lymph Glands . . . 351
Pigmentation 351
Inflammation or Acute Adenitis 352
Chronic Adenitis 353
Scrofulous, Caseous, Waxy, and Calcareous Degeneration . . 354
Amyloid Degeneration 355
Colloid Metamorphosis 355
Tumors of Lymph Glands 355
Sarcoma 355
Adeno-sarcoma, Carcinoma 356
Tubercles 356
Gumma, Enchondroma 357
Epithelioma 358

CHAPTER XIII.

LESIONS OF NERVE TISSUE.

PAGE

SECT. I.—Normal Histology of Nerves 359
SECT. II.—Pathological Histology of Nerves 360
Congestion, Hemorrhage, Inflammation 360
Lesions following Division of Nerves 361
Tumors of Nerves 362

CHAPTER XIV.

LESIONS OF THE CENTRAL NERVOUS SYSTEM.

SECT. I.—Alterations of the Meninges 364
Congestion, Cerebral Rheumatism 364
Inflammation, Cerebral, and Cerebro-spinal Meningitis . . . 364
Tuberculous Meningitis 365
Chronic Meningitis 366
Pachymeningitis 367
Tumors of the Meninges 367
SECT. II.—Lesions of the Cerebrum and Cerebellum . . . 368
Cerebral Anæmia, Cerebral Congestion, Œdema of the Brain . . 368
Melanæmia, Cerebral Hemorrhage 369
Miliary Aneurisms of the Brain 371
Cerebral Softening 372
Acute Encephalitis 375
Abscess of the Brain 376
Chronic Encephalitis or Sclerosis 377
Tumors of the Brain 378
Tuberculous, Syphilitic 378
SECT. III.—Lesions of the Spinal Cord 380
Congestion, Hemorrhage, Softening 380
Secondary Degeneration of the Spinal Cord 381
Inflammation of the Spinal Cord 383
Myelitis 383
Acute Suppurative 383
Simple Acute 383
Metastatic Abscesses of the Spinal Cord 383
Interstitial Myelitis or Sclerosis 384
Sclerosis of the Posterior Columns 385
Disseminated Sclerosis or Sclérose en plaques . . . 387
Lateral Sclerosis 387
Tetanus 388
Tumors of the Spinal Cord 388

PART III.

SECTION I.

RESPIRATORY APPARATUS.

CHAPTER I.

PAGE

NORMAL HISTOLOGY OF RESPIRATORY APPARATUS . . 389

CHAPTER II.

PATHOLOGICAL HISTOLOGY OF THE RESPIRATORY APPARATUS.

Sect. I.—Nasal Fossæ 394
Congestion, Hemorrhage 394
Inflammation of the Mucous Membrane of the Nasal Fossæ, Coryza . 394
Tumors of the Nasal Fossæ 395
Sect. II.—Larynx 396
Congestion, Acute Catarrh or Catarrhal Laryngitis . . . 396
Chronic Catarrh, or Chronic Catarrhal Laryngitis . . . 397
Diphtheritic Laryngitis or Croup 397
Erysipelatous Laryngitis, Variolous Laryngitis 398
Laryngitis of Glanders, of Typhoid Fever, of Tuberculosis, of Syphilis 399
Œdematous Laryngitis, Œdema of the Glottis 399
Ulcerous Laryngitis 400
Perichondritis 401
Tumors of the Larynx 401
Sect. III.—Trachea 403
Inflammations, Ulcers, Perforations 403
Carcinoma, Leukæmic Growths 404
Calcifications, Exostoses 404
Sect. IV.—Bronchi 404
Congestion, Hemorrhage 404
Inflammation 404
Intense Bronchitis 404
Diphtheritic Bronchitis 404
Chronic Bronchitis 405
Dilatation of the Bronchi, Bronchiectasis 405
Ulceration of the Bronchi, Calcification 405
Tumors 405
Sect. V.—Lungs 408
Anæmia, Hyperæmia, Œdema 408
Pulmonary Apoplexy 409
Hemorrhagic Infarction 410
Atelectasis, Atrophy 411
Emphysema 412

PAGE

Inflammation, Pneumonia 414
A. Lobular or Catarrhal Pneumonia 414
B. Lobar or Fibrinous Pneumonia, Croupous Pneumonia . . 416
Pneumonia of the New-born, of Adults, of the Aged, of the Emphysematous 419
Abscess of the Lung 419
Inflammation of the Lymphatics of the Lung 420
Gangrene of the Lung 421
Interstitial Pneumonia 423
in the Aged 424
in Chronic Heart Disease 425
Syphilitic Pneumonia 425
Anthracosis, Siderosis 426
Chronic Croupous Pneumonia 426
Tumors of the Lung 427
Tuberculosis of the Lung 429
Tubercle Granulations 430
Tuberculous or Caseous Pneumonia, Phthisis 433
Tuberculous Lobular or Catarrhal Pneumonia . . . 433
Tuberculous Lobar or Croupous Pneumonia 435
Tuberculous Interstitial Pneumonia 437
Sect. VI.—Pleura 438
Congestion, Ecchymoses, Hyperplastic Pleurisy 438
Fibrinous Pleurisy 440
Idiopathic Pleurisy 441
Hemorrhagic Pleurisy 443
Purulent Pleurisy 443
Pyo-pneumothorax 444
Chronic Pleurisy 444
Tumors of the Pleura 445

SECTION II.

DIGESTIVE APPARATUS.

CHAPTER I.

THE MOUTH AND ITS APPENDAGES.

Sect. I.—Normal Histology of the Buccal Mucous Membrane . . 446
Sect. II.—Lesions of the Buccal Mucous Membrane . . . 448
Inflammation, Stomatitis 448
Superficial or Catarrhal Stomatitis 448
Stomatitis of Typhoid Fever 449
The Lead Line, Argyria 450
Stomatitis of Eruptive Fevers, of Cutaneous Diseases, etc. . . 451
Scorbutic Stomatitis 451
Syphilitic Lesions 451
Membranous Ulcerative Stomatitis (Diphtheritic) . . . 452
Superficial Inflammation of the Tonsils or Catarrhal Angina of the Tonsils 452

PAGE

Diphtheritic Inflammation 452
Gangrene of the Mouth (Noma) 453
Tumors 453
Parasites 455

CHAPTER II.

PHARYNX AND ŒSOPHAGUS.

Sect. I.—Normal Histology of the Pharynx and Œsophagus . . 456
Sect. II.—Lesions of the Pharynx and Œsophagus 457
Pharyngitis 457
Retro-pharyngeal Abscess 458
Œsophagitis 459
Foreign Bodies 459
Tumors of the Pharynx and of the Œsophagus 460

CHAPTER III.

THE STOMACH.

Sect. I.—Normal Histology of the Stomach 461
Sect. II.—Pathological Histology of the Stomach. Lesions of Nutrition . 464
Anæmia 464
Congestion 464
Lesions of the Glands 465
Lesions of the Vessels 465
Sect. III.—Inflammation of the Mucous Membrane of the Stomach . 465
Superficial or Catarrhal Inflammation of the Stomach . . . 465
Chronic Catarrh of the Stomach 466
Croupous Gastritis 468
Pemphigus of the Gastric Mucous Membrane 468
Phlegmonous Gastritis 468
Lesions caused by Corrosive or Irritant Agents 469
Gangrenous Gastritis 469
Simple Ulcer of the Stomach 469
Simple or Perforating Ulcer of the Duodenum 471
Sect. IV.—Tumors of the Stomach 472
Syphilitic Tumors of the Stomach 473
Hypertrophy simulating a Tumor 477

CHAPTER IV.

THE INTESTINE.

Sect. I.—Normal Histology of the Intestine 479
Sect. II.—Pathological Histology of the Intestine 483
Post-mortem Changes 483
Congestion 483
Inflammation of the Mucous Membrane, Intestinal Catarrh . . 483
Typhlitis and Perityphlitis 488

PAGE
Acute Dysentery 489
Chronic Dysentery 493
Cholera 499
Uræmic Ulcerations 501
Typhoid Fever 501
Lesions of the Intestine in Hernia 506
Rectal Fistula 507
Tuberculosis of the Intestine 508
Syphilitic Tumors and Ulcers 512
Fibroma, Myoma, Lipoma, Vascular Tumors 513
Adenoma, Lymphadenoma 514
Carcinoma 515
Epithelioma 516

CHAPTER V.

THE LIVER.

Sect. I.—Normal Histology of the Liver 517
Sect. II.—General Pathology of the Liver 521
Changes in the Hepatic Cells 522
Lesions of the Cellulo-vascular System 526
Lesions of the Vessels 527
Sect. III.—Special Pathology of the Liver 527
Post-mortem Changes 527
Congestion 528
Cardiac Liver, Nutmeg Liver 530
Hepatitis 532
A. Parenchymatous Hepatitis 532
B. Purulent Hepatitis 536
Metastatic Abscesses 536
Thrombosis and Phlebitis of Portal Vein . . . 537
Purulent Inflammation of Portal Vein or Suppurative Pylephlebitis 538
Biliary Abscesses 540
Large Abscesses of the Liver 541
Interstitial Hepatitis or Cirrhosis 543
Partial Cirrhosis 543
General Cirrhosis 544
A. Cirrhotic Liver with Smooth Surface 545
B. Granular Liver, Hobnail Liver 547
Cirrhosis with Atrophy 547
Capsule of Glisson in Cirrhosis 548
Condition of Vessels and of the Circulation in the Liver in Cirrhosis 549
Condition of the Biliary Passages in Cirrhosis of the Liver . 550
Condition of the Hepatic Cells in Cirrhosis of the Liver . 553
Degeneration of the Liver 555
Fatty Infiltration 555
Fatty Degeneration 557
Amyloid Degeneration 557

PAGE

Tumors of the Liver 559
Angioma, Tubercle 559
Gumma 560
Lukæmic Tumors 561
Sarcoma 561
Carcinoma 561
Cylindrical-celled Epithelioma 564
Cysts, Hydatid Cysts 565
Biliary Vessels and Gall-Bladder 567
Inflammation 567
Tumors 569

CHAPTER VI.

PERITONEUM.

Sect. I.—Inflammation 571
Acute General Peritonitis 571
Acute Local Peritonitis 573
General Chronic Peritonitis 573
Hemorrhagic Peritonitis 574
Tubercles of the Peritoneum and Tuberculous Peritonitis . . 574
Local Chronic Peritonitis 575
Carcinoma of the Peritoneum and Carcinomatous Peritonitis . . 576
Other Tumors of the Peritoneum 577

CHAPTER VII.

THE PANCREAS.

Sect. I.—Normal Histology of Pancreas 578
Sect. II.—Pathology of Pancreas 578
Parenchymatous Inflammation 578
Suppurative Inflammation 579
Interstitial Inflammation 579
Induration of the Pancreas 579
Fatty Degeneration and Fatty Infiltration 579
Atrophy, Amyloid Degeneration 580
Tumors of the Pancreas 580

SECTION III.

HÆMOPOYETIC ORGANS.

CHAPTER I.

THE SPLEEN.

Sect. I.—Normal Histology of the Spleen 583
Sect. II.—Pathology of the Spleen 584
Atrophy 584
Hyperæmia 585

PAGE
Interstitial Splenitis 587
Suppurative Splenitis 589
Infarction of the Spleen 589
Ruptures of the Spleen 591
Amyloid Degeneration 591
Tumors of the Spleen 593

CHAPTER II.

THE THYROID GLANDS.

SECT. I.—Normal Histology 596
SECT. II.—Pathological Histology 596
Goitre 596
Tubercles 597
Carcinoma 597

CHAPTER III.

THE SUPRA-RENAL CAPSULES.

SECT. I.—Normal Histology 599
SECT. II.—Pathology of the Supra-renal capsules 600
Hyperæmia, Hemorrhages, Thrombosis 600
Fatty and Amyloid Infiltration 600
Inflammation, Tumors 601
Tuberculosis 602

SECTION IV.

GENITO-URINARY APPARATUS.

CHAPTER I.

THE KIDNEYS.

SECT. I.—Normal Histology 604
SECT. II.—General Pathology of the Kidney 609
Alterations of the Epithelium 609
Tube Casts 611
Alterations of the Basement Membrane of the Tubules . . . 613
Lesions of the Renal Connective Tissue 614
Alterations of the Bloodvessels of the Kidney 615
Alterations of the Malpighian Glomeruli 616
SECT. III.—Special Pathology of the Kidney 617
Anæmia 617
Congestion, Hemorrhage 618
Infarction of the Kidney 619
Albuminous Nephritis 619
A. Catarrhal Nephritis 620
B. Parenchymatous Nephritis (Large White Kidney) . . 621

PAGE

C. Albuminous Nephritis with Amyloid Degeneration . . 627
D. Fatty Degeneration 629
Biliary Pigmentation 631
Interstitial Nephritis 631
Albuminuric Interstitial Nephritis 631
Acute 631
Chronic 632
Non-Albuminuric Interstitial Nephritis . . . 641
Suppurative Nephritis 642
1. Diffuse Suppuration 642
2. Limited Suppuration 642
3. Metastatic Abscess 644
Pyelo-Nephritis 645
Catarrhal Pyelo-Nephritis 645
Purulent Pyelo-Nephritis 645
Calculous Pyelo-Nephritis 645
Tuberculosis of the Kidney 647
Gumma 647
Lymphadenoma 648
Sarcoma 648
Carcinoma 650
Cysts 650
Angioma 651
Parasites 651

CHAPTER II.

URINARY PASSAGES.—THE URETERS, BLADDER, AND URETHRA.

Sect. I.—Normal Histology 652
Sect. II.—Pathological Histology 652
Hyperæmia of the Bladder 652
Catarrhal Inflammation of the Bladder 653
Catarrhal Inflammation of the Urethra 654
Tumors of the Bladder 654

CHAPTER III.

THE TESTICLES.

Sect. I.—Normal Histology 657
Sect. II.—Pathological Histology 659
Inflammation 659
Acute Orchitis 659
Suppurative Orchitis 660
Chronic Orchitis 660
Chronic Syphilitic Orchitis 661
Hydrocele 661
Hæmatocele 663
Tumors of the Testicle 663

CHAPTER IV.

THE PROSTATE.

PAGE

Sect. I.—Normal Histology 670
Sect. II.—Pathological Histology 670
Inflammation 670
Abscess 670
Tumors 671

CHAPTER V.

THE OVARIES.

Sect I.—Normal Histology 673
Sect. II.—Pathological Histology 676
Hyperæmia, Hemorrhage 676
Inflammation 677
Tumors 678

CHAPTER VI.

THE FALLOPIAN TUBES AND UTERUS.

Sect. I.—Normal Histology 683
Sect. II.—Pathological Histology 686
Congestion, Hemorrhage of Fallopian Tubes 686
Inflammation of the Fallopian Tubes 687
Tumors of the Fallopian Tube 688
Peri-uterine Hematocele 688
A. Lesions of the Mucous Membrane of the Uterus . . . 689
Congestion, Hemorrhage 689
Catarrhal Inflammation, Endometritis 690
Puerperal Inflammation 692
Phagedenic Ulcer 693
Tumors—Mucous Cysts, Villi, Fibrous Polypi, Mucous Polypi, Tubercles 693
Syphilis, Carcinoma 694
Epithelioma 696
B. Lesions of the Fibro-Muscular Wall 697
Hypertrophy 697
Myoma 698

CHAPTER VII.

MAMMARY GLAND.

Sect. I.—Normal Histology 701
Development 703
Evolution, Involution 704
Colostrum Corpuscles 705

PAGE

Sect. II.—Pathological Histology of the Mammary Gland . . . 706
Acute Inflammation or Mastitis 706
Chronic Inflammation 706
Tumors of the Mammary Gland 707
General Hypertrophy of the Mammary Gland . . . 707
Galactocele 707
Sarcoma 708
Myxoma 709
Fibroma 710
Syphilis 710
Carcinoma, Fibrous or Scirrhous Carcinoma 710
Cancerous Nodules 711
Encephaloid, Colloid, and Villous Carcinoma . . . 713
Enchondroma 714
Adenoma, Melanotic Tumors of the Breast, Epitheliomata . . 715
Cysts—Dermoid and Hydatid 715

SECTION V.

PATHOLOGICAL ANATOMY OF THE SKIN.

CHAPTER I.

Sect. I.—Normal Histology of the Skin 716
A. Epidermis 716
B. Derma, Papillæ 718
C. Vessels and Nerves of the Papillæ and Derma . . . 718
Lymphatic Vessels 719
Termination of Nerves in the Skin 720
D. Glands of the Skin 720
Sebaceous and Sudorific Glands 720
Sect. II.—Œdematous Infiltrations of the Skin 721
A. Simple Œdema 721
A. Œdema of the Lymph Passages 723
Sect. III.—Hemorrhages of the Skin 724
Sect. IV.—Diffuse Inflammation of the Skin 724
A. Acute Dermatitis 724
B. Exudative Inflammation of the Skin 727
a. Suppurative Dermatitis, Simple Phlegmon of Skin . . 727
b. Fibrinous Dermatitis, Diffuse Phlegmon 727
c. Pseudo-Membranous Dermatitis 728
C. Chronic Diffuse Inflammation of Skin 728
1. Fibrous Hypertrophic Dermatitis 728
2. Papillary variety: Diffuse Papilloma of Skin . . . 728
3. Elephantiasis Arabum 729
Scleroderma: Atrophy of Skin 730
Sect. V.—Circumscribed Inflammations of the Skin 730
a. Congestive Localized Inflammation of Skin, Papule . . . 730

PAGE

b. Lesions of the Epidermis: Bullæ, Blisters 731
Vesicles, Pustules 732
Tubercules 734
Circumscribed Peri-glandular Inflammation 735
Sudamina, acne 735
Molluscum Sebaceum, Pityriasis Pilaris 736
SECT. VI.—Tendencies and Evolutions of Cutaneous Inflammations . . 736
1. Hyperplastic Inflammation: Formative Dermatitis . . . 736
a. Syphilitic Papule 736
b. Syphilitic Tubercule 736
c. False Keloid 737
2. Degenerative Inflammation: Specific Ulcers of the Skin . . 737
a. Tuberculous Ulcers 737
b. Dermatitis of Glanders: Farcy Granule 738
c. Leprous Dermatitis: Cutaneous Tubercule of Leprosy . . 738
SECT. VII.—Dystrophies of the Skin 739
A. Tropic Disturbances in the Derma Consecutive to Lesions of the Nervous System 739
B. Dystrophic Alterations of the Epidermis, and Analogous Epidermic Products 740
C. Abnormal Colorations of the Skin 740
SECT. VIII.—Parasitic Affections of the Skin 741
A. Animal Parasites of the Skin of Man 741
a. Acarus Scabiei (Sarcoptes hominis) 741
b. Acarus Folliculorum 742
B. Vegetable Parasites of the Skin of Man 743
a. Tinea Favosa (Achorion Schœnleinii) 743
b. Tricophyton Tonsurans 744
c. Pityriasis Versicolor (Microsporon Furfur) . . . 745
d. Alopecia Circumscripta (Microsporon Audouini) . . . 746
e. Pityriasis Capitis Simplex 747

APPENDIX.—METHODS OF PRESERVING AND HARDENING TISSUES FOR MICROSCOPIC EXAMINATION 749

BIBLIOGRAPHY 753

INDEX 763

LIST OF ILLUSTRATIONS.

FIG.		PAGE
1.	Segmentation of mammalian ovum	18
2.	Division and movements of white corpuscles	19
3.	*a*. Pus cells from a granulating wound	19
	b. Pus cells from an abscess	19
	c. Pus cells from an abscess treated with acetic acid	19
	d. Pus cells from a bone fistula	19
	e. Migrating cells	19
4.	*a*. Reticulum of white blood corpuscles	20
	b. Reticulum of elliptical blood corpuscles	20
5.	*a*. Multinuclear "giant cell" from bone marrow	20
	e, *f*, *g*. Lymph cells from bone marrow	20
	c, *d*, *h*. Lymph cells from bone marrow treated with alcohol	20
	i, *j*. Osteoblasts from bone marrow treated with alcohol	20
6.	Cells from cancer, showing division of nuclei	21
7.	Cells from scirrhus of mamma, showing increase of nuclei	21
8.	Transverse section of tendon	23
9.	Silver-treated tendon of rat	23
10.	Silver-treated cornea of frog	24
11.	Reticulated tissue of lymphoid follicle	24
12.	Proliferating cartilage cells	25
13.	Ossification from cartilage	28
14.	Ossification from fibrous tissue	29
15.	Smooth muscle cells	30
16.	Muscular fibres of heart	31
17.	Muscular fibres, elements of	31
18.	Nerve cells	32
19.	Human nerve fibres (medullated)	33
20.	Nerve fibres of Remak	33
21.	Spinous epithelial cells	34
22.	Villus of intestine of rabbit	34
23.	Silver-treated pericardium	35
24.	Capillary bloodvessel of mesentery, silver treated	36
25.	Papilla from a papilloma	37
26.	Cholesterine crystals	41
27.	Fibrinous degenerated epithelial cells	43
28.	Irritated epithelial cells, showing vacuolation of nucleus	43
29.	Colloid cells from a colloid cancer	44
30.	Mucous transformation of epithelial cells	45
31.	Vitreous degeneration of muscle (waxy degeneration of Zenker)	45
32.	Amyloid degeneration of liver cells	46
33.	Corpora amylaceæ from prostate	46
34.	Fatty infiltration of liver cells	47
35.	*a*. Fatty degenerated cells from cancer	48
	b. Fatty degenerated cells from brain	48
36.	Corpuscles of Gluge from brain	48

FIG.		PAGE
37.	Caries fungosa	49
38.	Cellular structure of melanosis	50
39.	Cells containing pigment	50
40.	Capillary bloodvessel containing pigment and hæmatoidin crystals	51
41.	Cartilage infiltrated with urate of soda	53
42.	Inflamed cartilage	56
43.	Normal omentum, silver treated	57
44, 45, 46.	Artificially inflamed omentum	57
47.	Inflamed capillary of mesentery, showing detachment of an endothelial cell	58
48.	Osteo-malacic rib (bone softening)	60
49.	Inflamed adipose tissue	61
50.	Fibrinous exudation	65
51.	Fibrinous degenerated epithelial cells	66
52.	Pus cells	67
53.	Pus cells treated with various reagents	67
54.	Bloodvessels in granulation tissue	69
55.	Granulation tissue	70
56.	Inflamed adipose tissue	77
57.	Round small-celled sarcoma	79
58.	Spindle-celled sarcoma	80
59.	Large spindle-celled sarcoma	80
60.	Myeloid sarcoma (giant-celled sarcoma)	82
61.	Spindle and giant-celled sarcoma	82
62.	Glioma	83
63.	Alveolar sarcoma	84
64.	Angiolithic sarcoma (Psammoma)	85
65.	Cellular structure of melanosis	87
66.	Cells containing pigment	87
67.	Myxoma	89
68.	Microscopic anatomy of myxoma	90
69.	Silver-treated tendon of rat	92
70.	Transverse section of tendon	92
71.	Fibroma molluscum	93
72.	Papillary fibroma of breast	94
73.	Lipoma	95
74, 75.	Cells from cancer	97
76.	Colloid cells from colloid cancer	98
77.	Stroma of carcinoma	98
78.	Development of carcinoma of mamma	99
79.	Silver-treated carcinoma of mamma	101
80.	Stages of scirrhous carcinoma	102
81.	Encephaloid carcinoma	103
82.	Cells of colloid carcinoma	104
83.	Colloid cancer	104
84.	Cellular infiltration of fatty tissue around carcinomatous lymph glands	105
85.	Syphilitic interstitial pneumonia	108
86.	Gumma of liver	109
87.	Gumma of kidney	109
88.	Indurating hepatitis, first stage	110
89.	Indurating hepatitis, second stage	110
90.	Elements of miliary tubercle	114
91.	Softening of miliary tubercle	116
92.	Miliary tubercle of pia mater	117
93.	Arteriole in the neighborhood of a tubercle	117
94.	Vessel in a tubercle	117
95.	Giant cell from a tubercle	118
96.	Adenoid structure of a tubercle	118
97.	Giant cell from lung in phthisis	118
98.	Tubercle in the submucosa of ileum	119
99.	Lymphatic of ileum affected with tubercle	120
100.	Cartilage of a cephalopod	127

FIG. PAGE
101. Enchondromatous tumor of metacarpus 129
102. Microscopic characters of enchondroma 129
103. Muscle cells from a leio-myoma 135
104. Plexiform neuroma 138
105. Dilated lymph vessels of elephantiasis 141
106. Reticulated tissue of lymphoid follicle 142
107. Lymphadenoma 144
108. Spinous cells from a cancroid epithelioma 146
109. Elements of a lobulated epithelioma 147
110. Irritated epithelial cells 148
111. Variolous pustule 149
112. Epithelioma of a sebaceous gland 150
113. Tubular epithelioma, low power 153
114. Tubular epithelioma, high power 154
115. Cylindrical-celled epithelioma 155
116. Papilla from a papilloma 158
117. Adenoma of mamma 161
118. Adeno-fibroma of mamma 161
119. Egg of Naboth 163
120. Wall of a sebaceous cyst 166
121. Head and neck of tænia solium 191
122. Invaginated echinococcus 192
123. Echinococci 192
124. Osteo-malacic rib (bone softening) 198
125. Rarefying osteitis; canaliculization of osseous tissue . . . 201
126. Syphilitic sclerosis of bone 203
127. Caries fungosa 208
128. Osteo-malacic rib (bone softening) 219
129. Ossification of cartilage 221
130. Cells from fluid of an inflamed knee-joint 229
131. Elements in synovial fluid in acute articular rheumatism . . . 229
132. Splitting of cartilage in acute articular rheumatism . . . 230
133. Arthritis from purulent infection 232
134. Cartilage in nodular rheumatism 236
135. Cartilage in nodular rheumatism 237
136. Cartilage in white swelling, first stage 239
137. Cartilage in white swelling, second stage 240
138. Cartilage infiltrated with urate of soda 242
139. Connective tissue in a wound dusted with vermilion . . . 249
140. Adipose cells in œdema 251
141. Connective tissue in an early stage of suppurative inflammation . 254
142. Silver-treated pericardium 259
143. Gold-treated pericardium, profile view 260
144. Gold-treated pericardium, inflamed, profile view 260
145. Transformed endothelia of inflamed pericardium, two days (parietal) 260
146. Transformed endothelia of inflamed pericardium, six days (visceral) 261
147. Transformed endothelia of inflamed pericardium, six days (parietal) 262
148. Endothelium covering fibrous bands of adhesions, pleura . . 265
149. Heart muscle in typhoid fever, cloudy swelling 272
150. Fatty degeneration of heart 272
151. Vitreous metamorphosis of muscle 275
152. Trichina spiralis in muscle 282
153. Reticulum of blood corpuscles 285
154. Fatty infiltration of heart 292
155. Fatty degeneration of heart muscle 294
156. Pigmentary degeneration of heart muscle 294
157. Acute myocarditis in rheumatism 296
158. Fibroid induration of heart 297
159. Fibroid induration of heart, more advanced 297
160. Valves of heart 299
161. Inflammation of aortic valves 300

FIG.		PAGE
162.	Inflammation of mitral valve	300
163.	Endocarditis due to friction	301
164.	Vegetation from acute endocarditis	301
165.	Small artery and capillary	306
166.	Arteriole and small vein	306
167.	Fatty degeneration of inner coat of aorta	311
168.	Aorta showing middle coat interrupted by embryonal tissue	314
169.	Section of artery 24 hours after ligation, transverse	318
170.	Section of artery 48 hours after ligation, longitudinal	319
171.	Section of artery 48 hours after ligation, transverse	319
172.	Apex of thrombus of fig. 170	320
173.	Section of artery 94 hours after ligation, transverse	320
174.	Section of artery 8 days after ligation, transverse	320
175.	Section of artery 25 days after ligation, longitudinal	321
176.	Section of artery 50 days after ligation, longitudinal	324
177.	Section of artery 3 months after ligation, transverse	324
178.	Section of artery 10 days after modified ligation, longitudinal	325
179.	Artery showing natural hæmostasis	326
180.	Artery containing a septic embolus	328
181.	Hemorrhagic infarction	330
182.	Syphilitic disease of artery	331
183.	Capillary from mesentery, silver treated	334
184.	Inflamed adipose tissue	335
185.	Capillary filled with hæmatoidin crystals and granular pigment	336
186.	Fatty degenerated Malpighian tuft	337
187.	Fatty degenerated renal capillaries	337
188.	Dilated lymph vessels of elephantiasis	346
189.	Silver-treated section of carcinoma of mamma	347
190.	Lymph gland, low power	348
191.	Lymph gland, high power	349
192.	Lymph gland, chronic inflammation of	354
193.	Amyloid degeneration of spleen	355
194.	Cells from lymphatic growth of liver	356
195.	Lymphoma	356
196.	Tuberculosis of lymph gland	357
197.	Silver-treated nerve fasciculus	359
198.	Nerve fibre	359
199.	Nerve ganglion from frog's heart	359
200.	Epithelioma of nerve	363
201.	Miliary tubercle around vessel in pia mater	366
202.	Section of vessel in tubercle	366
203.	Psammoma	367
204.	Capillary filled with hæmatoidin crystals	372
205.	Granular corpuscles in brain softening	373
206.	Tissue change in softening of brain (granular corpuscles)	373
207.	Sarcoma of brain	378
208.	Syphilis of nerve centres	379
209.	Secondary degeneration of spinal cord (lateral columns)	381
210.	Secondary degeneration of spinal cord (posterior columns)	382
211.	Secondary degeneration of spinal cord (posterior columns)	383
212.	Spinal sclerosis (posterior columns)	385
213.	Spinal sclerosis, showing increase of neuroglia	386
214.	Capillary bloodvessel in sclerosis	386
215.	Antero-lateral sclerosis	387
216.	Degenerated ganglionic nerve cells of spinal cord	387
217.	Bronchial tube of pig	390
218.	Reticulated structure of cells	391
219.	Air-cells of human lung, showing epithelium	392
220.	Mucous transformation of epithelial cells in coryza	395
221.	Fibrinous degeneration of epithelial cells in false membranes	398
222.	Cells from sputum of acute bronchitis	405

FIG. PAGE
223. Transverse section of bronchus in acute phthisis 408
224. Lung in interstitial pneumonia and intra-alveolar hemorrhage . . 410
225. Emphysema of lung (macroscopic) 412
226. Emphysema of lung (microscopic) 413
227. Catarrhal pneumonia 415
228. Croupous pneumonia (red hepatization) 416
229. Cellular elements from second stage of pneumonia . . . 417
230. Croupous pneumonia (gray hepatization) 418
231. Fetid pus, showing bacteria among the corpuscles . . . 422
232. Interstitial pneumonia 423
233. Pigmentation of lung 424
234. Syphilitic interstitial pneumonia 425
235. Brown induration of lung 425
236. Vascularization and fibroid development of intra-alveolar exudation of lung (low power) 427
237. Same as fig. 236 (high power) 427
238. Carcinoma of lung 429
239. Bloodvessel of tubercle 430
240. Scrofulous inflammation of bronchus 431
241. Exudation in alveoli of lung in acute phthisis 432
242. Gray tubercle of acute tuberculosis, lung 433
243. Yellow tubercle of acute tuberculosis, lung 434
244. Caseous lobular pneumonia 435
245. Exudation in alveoli of lung in acute phthisis 435
246. Tuberculous interstitial pneumonia of chronic phthisis . . . 437
247. Inflamed pleura, showing fibrinous exudation 440
248. Fibrinous exudation 440
249. Submaxillary gland of dog 447
250. Papillæ of tongue 448
251. Inflammation of conjunctiva 449
252. Silver deposit in gum in argyria 450
253. Section of stomach of child 461
254. Reticulation of epithelial and other cells 462
255. Peptic gastric gland, low power 463
256. Peptic gastric gland, high power 463
257. Commencing formation of cyst in stomach 467
258. Cyst of stomach 467
259. Reticulated tissue of lymphoid follicle 479
260. Villus of intestine, rabbit 480
261. Lymph vessels in vermiform appendix 481
262. Intestinal villi 482
263. Section of colon in acute catarrh 484
264. Vegetable forms in feces 485
265. Enlarged solitary gland in acute diarrhœa 487
266. Colon of child in acute dysentery, showing development of cysts . 489
267. Submucous tissue of colon in acute dysentery . . . 490
268. Colon in chronic dysentery, showing superficial ulcer . . . 493
269. Follicular ulcer of colon in chronic dysentery 494
270. Cyst of colon in chronic dysentery, low power 495
271. Cyst of colon in chronic dysentery, high power 496
272. Histological elements of cyst-wall in chronic dysentery . . . 497
273. Micrococci and bacteria in chronic dysentery 498
274. Lymph follicle in typhoid fever 505
275. Tubercular ulcer of ileum 509
276. Tubercular ulcer of Peyer's patch 510
277. Lymphatic in tuberculosis of ileum 511
278. Submucosa in tuberculosis of ileum 512
279. Cylindrical-celled epithelioma of large intestine 515
280. Liver of a three-months child 517
281. Hepatic cells, isolated 518
282. Hepatic cells, trabecula of 518

FIG.		PAGE
283.	Injected liver of rabbit	519
284.	Injected biliary canaliculi of rabbit	519
285.	Cloudy swelling of liver cells	524
286.	Fatty infiltration of liver cells	525
287.	Amyloid infiltration of liver cells	525
288.	Congested liver of cardiac disease	530
289.	Indurating inflammation of liver, first stage	545
290.	Indurating inflammation of liver, second stage	546
291.	Biliary canaliculi in cirrhosis	552
292.	Cells in cirrhosis of liver	553
293.	Fatty infiltration of liver	555
294.	Fatty infiltration of liver cells	556
295.	Amyloid liver	558
296.	Gumma of liver	560
297.	Silver treated omentum (normal)	571
298, 299.	Inflamed omentum	572
300.	Amyloid spleen	592
301.	Supra-renal capsule (longitudinal section)	599
302.	Supra-renal capsule (transverse section)	599
303.	Diagram of kidney pyramid	604
304.	Henle's loop of kidney (longitudinal)	605
305.	Straight tubes of kidney (longitudinal)	605
306.	Pyramidal substance of pig's kidney	606
307.	Colloid degeneration of epithelial cells in interstitial nephritis	610
308.	Urinary casts	611
309.	Fatty casts from phosphorous poisoning	613
310.	Fatty degeneration of renal capillaries	617
311.	Fatty degeneration of Malpighian tuft	617
312.	Catarrhal nephritis	621
313.	Kidney of Bright's disease	623
314.	Amyloid degeneration of the Malpighian tuft and afferent vessel	627
315.	Uriniferous tubes of cortex in phosphorous poisoning	630
316.	Fatty casts in urine in phosphorous poisoning	630
317.	Interstitial nephritis, earlier stage	632
318.	Granulation of kidney in Bright's disease	633
319.	Malpighian glomerulus of interstitial nephritis	634
320.	Interstitial nephritis, advanced stage	636
321.	Interstitial nephritis, advanced stage	636
322.	Colloid degeneration of epithelial cells in interstitial nephritis	637
323.	Arteries from kidney of chronic Bright's disease	638
324.	Surgical kidney	643
325.	Gumma of kidney	648
326.	Sarcoma of kidney	649
327.	Carcinomatous papilla of bladder	656
328.	Testicle	657
329.	Spermatozoids	658
330.	Ovary of an old bitch	673
331.	Ovule	674
332.	Egg of Naboth	684
333.	Muscular cells from a leio-myoma	699
334.	Mammary gland acinus	702
335.	Mammary gland, involution of	704
336.	Cells of mamma in early stage of involution	705
337.	Elements of human milk	705
338.	Inter-acinus spindle-celled sarcoma of mamma	708
339.	Fibroma of mamma with dilated ducts	709
340.	Fibroma of mamma (papillary)	710
341.	Silver treated section of carcinoma of mamma	711
342.	Development of carcinoma of mamma	712
343.	Scirrhous carcinoma of mamma	712
344.	Adenoma of mamma	715

FIG. PAGE
345. Section of blastoderm of an embryo 716
346. Normal skin 717
347. Tactile corpuscle 719
348. Pacinian corpuscle 719
349. Dilated lymph capillary of the skin in œdema 722
350. Increase of cell elements of the skin in erysipelas . . . 725
351. Vacuolation of the nucleus of spinous cells of epiderm in irritation . 726
352. Variolous vesicle of skin 733
353. Variolous pustule of skin 733
354. Acarus scabiei (female) dorsal surface 742
355. Group of demodex folliculorum 742
356. Achorion Schœnleinii after treatment with liq. potassæ . . . 744
357. Trichophyton tonsurans from herpes carcinatus 745
358. Microsporon furfur 746
359. Hair from case of alopecia (microsporon Audouini) . . . 747
360. Isolated spores from case of alopecia (microsporon Audouini) . . 747

ERRATA.

Page 172, in foot-note, *for* judicial *read* judicious.
" 453, line 6 from bottom, *for* myeloplastic *read* myéloplaxes.
" 468, " 13 " " *omit* seldom.
" 637, " 10 " " *for* Figs. 342 and 343 *read* 321 and 322.

PATHOLOGICAL HISTOLOGY.

PART I.

GENERAL PATHOLOGICAL ANATOMY.

CHAPTER I.

NORMAL HISTOLOGY—CELLS AND NORMAL TISSUES.

Sect. I.—Cell Theory and Structure of Cells.

Before entering upon the study of pathological histology, a summary of our knowledge of normal histology is given, in order that the principles which underlie pathological changes may be understood.

Histology was founded by Bichat. It received its further development by Schwann, who applied to it the discoveries made by Schleiden in the vegetable tissues. It came to be recognized that the *cell*, whether animal or vegetable, is the organic unit, *par excellence*—the simplest body wherein life is individualized. It was then well known that some living beings, possessing the functions of nutrition, movement, reproduction, birth, and death, consist simply of a single cell.

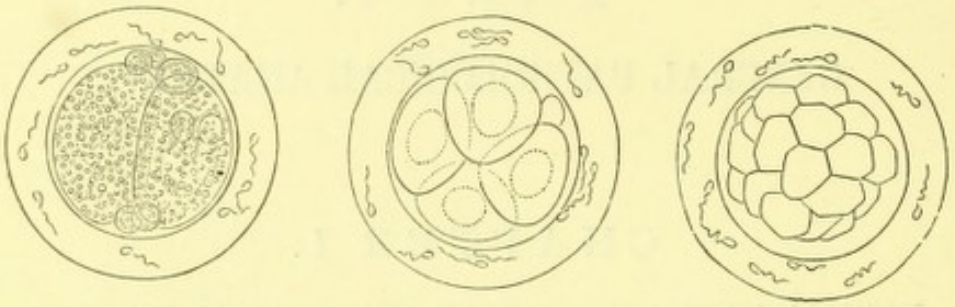
In beings more complex, the cells are surrounded by an intercellular substance to form tissues and organs of which the cells are the essential part, still playing the principal role; but the cells may be so modified, that they can scarcely be recognized, if their metamorphoses are not regarded.

According to Schwann the cell is composed of an enveloping membrane; of contents more or less fluid; of a nucleus; of one or more nucleoli within the nucleus.

In regard to the formation of cells Schwann admitted a *free formation* (spontaneous generation) in a primordial generative fluid, whether the latter be found alone or be placed between pre-existing cells (blastema or cystoblastema). According to him, granules appear in the liquid, rudimentary nucleoli; around these new granules become visible, and surround themselves by a membrane to form the nucleus; the nucleus now acts upon the surrounding blastema, new granules appear and are soon surrounded with a cellular membrane, when at last we have formed the perfect element termed a cell.

Remak, while observing in the ovule the phenomena of development, showed the fallacy of this view. Starting with the idea that the ovule is a true cell, the membrane of which is the vitelline membrane, the contents the vitellus, the nucleus the germinal vesicle, and the nucleolus the germinal spot,—this author considered all the cells of the embryo as derived from this cell, in the following manner. After fecundation, the vitellus by segmentation is divided into two parts, these into two other parts, which process of division continues until there are formed numerous small spherical bodies. These segmentation corpuscles or new cells apply

Fig. 1.



Progresssive stages in the segmentation of the yolk of the mammalian ovum. High power. (*Carpenter.*)

themselves to the internal surface of the vitelline membrane and form a layer (blastoderm), which soon divides into three leaflets formed solely by the cells. It is from the cells of these leaflets, and always by a process of segmentation, that all the cells of the animal are derived. In his investigations upon the origin of tissues, Remak concludes, that all cells arise from pre-existing cells, in one of three ways: by *segmentation* or *division*, by *gemmation* or *budding*, and by *endogenous formation*. According to the present conception of the cell, these three modes are not essentially distinct.

Virchow applied to pathology the physiological facts demonstrated by Remak: he considered that *all new formations of cells or all neoplasms arise by a continuous development from pre-existing cells*, and thus suggested the relation between pathology and physiology. Remak, adopting the definition of the cell given by Schleiden and Schwann, recognized a membrane, contents, nucleus, and nucleolus.

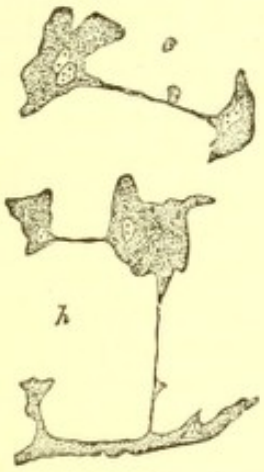
Subsequently through the labors of Max Schultze, von Recklinghausen, Kühne, Beale, etc., the definition of the cell has been much modified.

Dujardin had previously remarked, that inferior beings consisting of a single cell were not always enveloped by a membrane, but that they often consisted of a mass susceptible of change of shape, to such a degree, that very long prolongations might be advanced. To these masses Dujardin gave the name of *sarcode*, and their movements he termed *sarcodic movements*. Max Schultze, investigating more widely these same phenomena, extended his studies not only to unicellular animals called *amœbæ*, but also to the cellular elements of more complex beings. He compared the animal masses susceptible of movement, to the cellular masses of vegetables previously known by the name of *protoplasm;* the funda-

mental substance of animal cells he called protoplasm, and the movements of which they are susceptible he named *amœboid movements*.

Numerous cells of the higher animals and of man, for example the white corpuscles of the blood and embryonic cells, are composed of pro-

Fig. 2.



White corpuscles (or lymph cells) undergoing division, and active movements. (*Carpenter.*)

Fig. 3.



Pus cells: *a*, from a granulating wound; *b*, from an abscess of cellular tissue; *c*, the same treated with dilute acetic acid; *d*, from a bone fistula (necrosis); *e*, migrating cells. (*Rindfleisch.*)

toplasm, possess no membrane, and present amœboid movements. In order that these truly characteristic movements of the protoplasm may be produced, it is necessary that the cells be placed in the conditions of heat and moisture in which they live in the normal state. When colored particles are found near a cell possessing these movements, they become englobed by the amœboid prolongations proceeding from the cell, and penetrate into its interior.

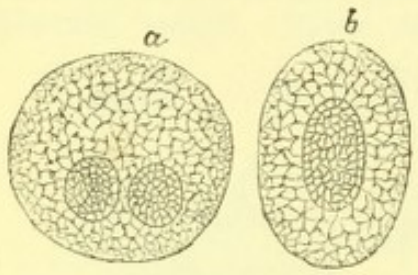
The fusion of the amœboid prolongations, the penetration into the interior of the cell of colored particles, demonstrate that these cells have no membrane and that the definition of the cell given by Schwann is not correct. It should not be concluded from this, however, that all cells are wanting in a membrane, but rather that when it does exist, it constitutes only an accessory. The definition of a cell is therefore reduced to a *mass of protoplasm inclosing a nucleus*. [Even the nucleus is not now considered by some skilled histologists to be essential to a cell. For them the simplest cell consists of a mass of living protoplasm.]

The nucleus of cells appears to be a vesicle, the envelope of which frequently has a double contour; its contents are either clear or finely granular or reticulated. In its interior are found one or more nucleoli, which appear as clear, round, or angular spots. The high refraction of the nucleoli gives them the appearance of fat; but the facility with which they are colored by carmine, their solubility in a solution of potassa, show that they are not fat. The latter is not colored by carmine, and is not dissolved by a cold solution of potassa. Again, the investigations of Balbiani upon the ovule demonstrate that the germinal spot is a vesicle susceptible of change of shape and dimension under the eye of the observer. When considering the epithelial cells of the skin, it will be seen

that their nucleoli are susceptible of becoming vesicular under the slightest irritation.

[In the white corpuscles of the blood, and other cellular elements, a fine reticulum has been lately discovered. The nodal points of this reticulum are slightly larger and more distinct than the minute fibres which form the meshwork. It is these nodal points which give to many cells their granular aspect. This reticulum permeates both the cell body and the nucleus. In the cell body it is termed intra-cellular, in the nucleus intra-nuclear network, the fibrils of the one being continuous with those of the other. In the meshes of this network, besides the gelatiniform substance which naturally fills them, may often be found veritable granules. When such granules are numerous, these cells may be regarded *par excellence* as "granular cells."]

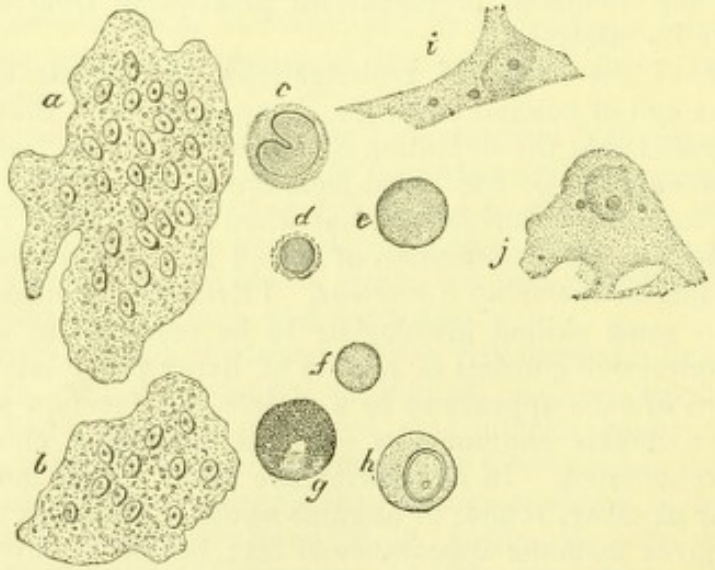
Fig. 4.



a. White blood-corpuscle, showing an intra-cellular and an intra-nuclear reticulum. *b*. Elliptical colored blood-corpuscle, showing similar reticula. High power. (*Klein*.)

At its origin, every cell is composed solely of a mass of protoplasm surrounding a nucleus. Among the cells possessing this original structure, no differences have been found indicating that a given cell will undergo certain ulterior modifications. In the adult these cells are met with only in the blood (white corpuscles), in the lymph, and in the tissues which experience a continuous renewal: such cells constitute the entire embryo; they have therefore been named *embryonic cells*.

Fig. 5.



Cells from the marrow of bone during their period of development. *a*, *b*. Multinuclear "giant cells" (Frey). *e*, *f*, *g*. Lymph cells from the marrow of the tibia of the guinea-pig, examined in the serum of the blood; *c*, *d*, *h*, after the action of alcohol and water 33 per cent. *i*, *j*. So-called osteoblasts from the femur of a new-born dog, after the action of alcohol 33 per cent. High power. (*Ranvier*.)

Cells which do not possess an enveloping membrane, and which present a protoplasm with amœboid movements, are: 1st. The cells of the embryo

before they have acquired a determined shape; 2d. The cells in the developing layer of the marrow of bone; 3d. The mother cells or giant-cells found in the same substance; 4th. The white corpuscles of the blood; 5th. Lymph cells.

Embryonic cells consist of an irregular mass of granular protoplasm, which may be spherical, measuring from .01 mm. to .015 mm. in diameter, are swollen by water and acetic acid, colored brown by a solution of iodine, and faintly by carmine which increases the granular appearance. This protoplasmic mass incloses an oval or spherical nucleus frequently seen only after the action of acetic acid, possessing a double contour and a nucleolus often very small and which is deeply colored by carmine. Instead of one nucleus, if the cell tends to a retrograde change, there are frequently several small and angular nuclei; if the cells tend to growth, the nuclei are spherical and well developed.

In the developing layer of bone from cartilage, cells are met which so closely resemble embryonic cells that there is no characteristic sufficient to distinguish one from the other. In consequence of the changes which these cells undergo they become slightly separated from the primitive type.

The large multinucleated cells, which are found alongside of the foregoing, apart from the multiplicity of their nuclei, from their great irregularity of contour, and from the buds which they present, possess the same general properties as the embryonic cell; the protoplasmic substance which forms them gives the same reactions. Later these elements become flattened, more consistent, and separated from their original type.

Among the white corpuscles of the blood two kinds are recognized: the one incloses a single round or oval nucleus with a distinct nucleolus which resists the action of acetic acid and is colored by carmine; the other contains several small angular nuclei or a single nucleus which breaks into fragments on the addition of acetic acid. We believe the latter to be in a state of retrograde metamorphosis.

Fig. 6.



Cells from a cancer: showing cell-wall, cell-contents, nuclei, and nucleoli; the nuclei dividing. (*Green.*)

Fig. 7.



Cells from a scirrhus of the mamma. ×350. (*Green.*)

All embryonic cells possess the property of giving origin to elements resembling themselves by the following process. The nucleus enlarges, the nucleolus becomes constricted and divides, soon the nuclues divides either

by a fissure, which separates the nucleus into two, or by a kind of constriction which gives it an hour-glass shape. The mass of protoplasm surrounding the two nuclei divides, and two cells are formed. The segmentation of the protoplasm does not always follow that of the nucleus, so that there may be many nuclei in one cell. Frequently a portion of protoplasm is separated inclosing a nucleolus.

Embryonic cells are destroyed or they undergo a series of modifications which characterize their appearance as seen in the different tissues. The simplest example of modification of embryonic elements is that in which there is an elaboration of a new substance in the protoplasm. This is seen in the early development of adipose cells, where the protoplasm contains fat granules; in the formation of coloring material in the white corpuscles of the blood of the embryo during their transition into red corpuscles (Remak and Kölliker). The most important alteration of embryonic cells consists in the formation of a membrane surrounding the protoplasm. This membrane is comparable to the secondary membrane of vegetable cells in which it is formed of cellulose, while in animals it is composed of an albuminoid substance (the cartilage cells, etc.). This membrane has for each variety of cells some notable differences. It is still undecided whether the membrane is a condensation of the superficial layers of the protoplasm or is an excretion of the cell. Whatever it may be, it is entirely distinct from the protoplasm. As soon as a cell is surrounded by a secondary membrane, it becomes [so to speak] permanently fixed and assists in the building up of the tissues. It is impossible to study these fixed elements without considering the tissue which contains them.

Sect. II.—Normal Tissues.

Normal tissues may be divided into three groups.

First Group.—Those in which the substance uniting and separating the cells is characterized by its form, its physical and chemical properties (connective tissues, cartilaginous and osseous tissues). In these tissues, although the cells have special physiological properties, relative to the formation and preservation of the tissue, they have no characteristic form when they are separately considered.

Second Group.—The second group includes those tissues in which the cell has undergone such modifications that it is no longer recognized as a cell, but has assumed certain physical, chemical, and physiological characters. These are the muscular and nervous tissues.

Third Group.—It includes tissues composed of cells having a regular and constant evolution; the cellular elements are intimately held together by a slight amount of uniting substance, the glandular and investing epithelium for example. Frequently their cells have a characteristic shape, and they always elaborate in their interior a definite substance: thus the epidermic cells form the corneous substance; the cells of mucous membrane, the mucine; the cells of glands, their secretions, etc.

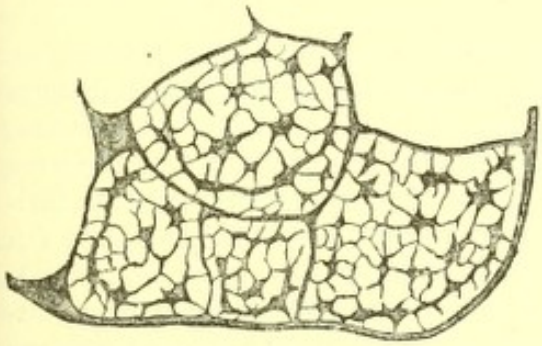
FIRST GROUP.—CONNECTIVE, CARTILAGINOUS, AND OSSEOUS TISSUES.

CONNECTIVE TISSUES.—The connective tissues include *mucous*, *fibrous*, *adipose*, *reticulated*, and *elastic tissues*.

The formation of *mucous tissue* from embryonic tissue is most simple. In the simplest variety of this tissue, as met with in the vitreous humor, there is developed between the cells a hyaline substance containing a large amount of mucin, while the cells remain independent of each other. In another variety, that of the umbilical cord, the cells become fusiform or stellate, anastomose with each other, form a secondary membrane around themselves at the same time that a gelatinous substance is produced between them. In the umbilical cord of a three month's embryo, there are frequently found several cells in one stellate space; each of these cells consists of a distinct mass of protoplasm containing a nucleus. These fusiform or stellate spaces and their contents have been called by Virchow, connective tissue corpuscles, but the term should only be applied to a mass of protoplasm and its nucleus.

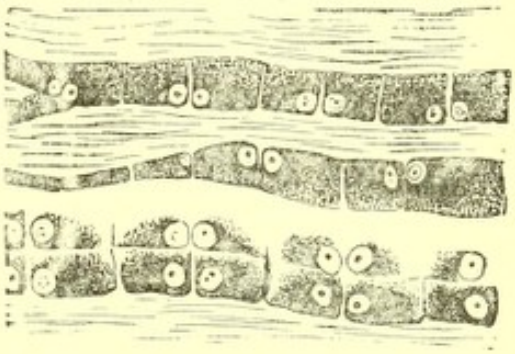
Cells forming *fibrous tissue* are also derived from embryonic cells. Those cells known as "connective tissue corpuscles" consist of a flattened plate of protoplasm inclosing a nucleus, and lie within the fusiform or stellate space containing them. Between the walls of this space and

Fig. 8.



Transverse section of tendon: showing so-called branched corpuscles, inclosing spaces which, left blank, are naturally filled with tendinous fasciculi. High power. (*Carpenter.*)

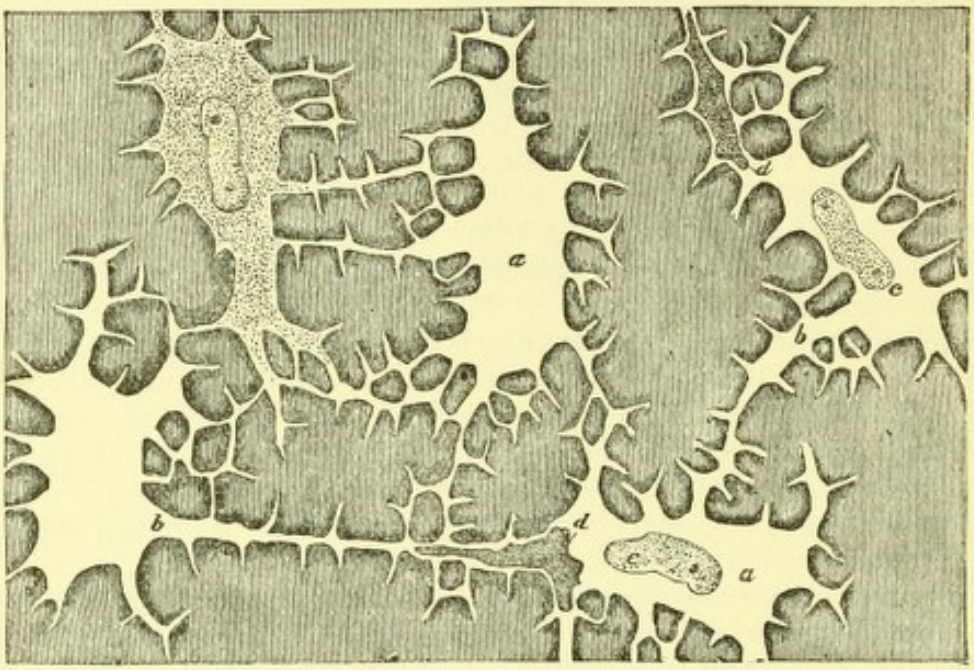
Fig. 9.



Caudal tendon of young rat: showing arrangement and form of the flat endothelial cells, after treatment with silver nitrate. High power. (*Carpenter.*)

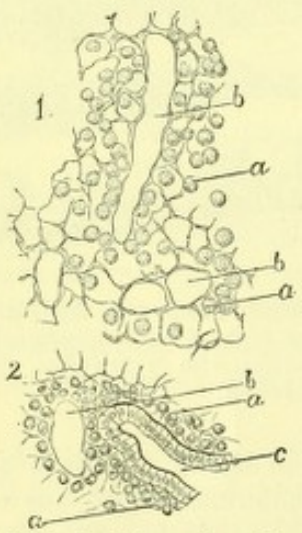
the cell exists a space (lymph lacuna, canalicula) in which circulate the nutritive juices. The lymph canalicular spaces anastomose with one another by their prolongations. Formerly it was believed that the fibres grouped in waving fasciculi in areolar and fibrous connective tissue were derived simply from the cells. But Reichert and Virchow have shown that these fibres are developed in the intercellular substance, which, at first mucous, is afterwards solidified and is finally separated into fibrillæ. From this standpoint fibrous tissue may be considered as a mucous tissue in a more advanced stage of development. So that all tissues which later become fibrous exist in the embryo as mucous tissues. At birth, the umbilical cord and vitreous humor are the only parts which persist as mucous tissue. Once formed, fibrous tissue experiences atrophic changes

Fig. 10.



Cornea of frog, treated with lunar caustic. *a*. Lymph lacunæ. In one place a branched flattened corneal corpuscle is seen with its lengthened nucleus and granular protoplasm. *c*. Nuclei of corneal corpuscles. *b*. Branched canaliculi which connect the lacunæ, and which with the latter constitute the lymph canalicular system. *d*. Migrating or wandering lymph cells, creeping into the branched canals. High power. (*Carpenter.*)

Fig. 11.



1. Reticulated tissue from a lymphoid follicle of the vermiform appendix of the rabbit, with the system of meshes, and remains of the lymph cells *a*. Most of the latter have been removed artificially. *b*. Lymph vessel. 2. Longitudinal section of a Lieberkühn's gland, showing the surrounding reticular tissue, in the meshes of which are seen the lymph cells *a*. *b*. Lumen of a vessel. *c*. Lumen of the gland. (*Frey.*)

of its cellular elements; the protoplasm shrinks, is transformed into a granular mass which surrounds the nucleus also atrophied, and is seen as an irregularly shaped body (in the derm, areolar connective tissue), fusiform (in tendons), or lenticular in shape (in internal membrane of the arteries, etc.). During all these changes the lymph canalicular space preserves its shape and size, as is shown by staining with carmine or, better, by nitrate of silver.

Adipose tissue results from an accumulation of fat in the cells of mucous tissue or areolar connective tissue, which we consider to be a variety of fibrous tissue. The fat is deposited within the cell protoplasm, which it distends by displacing the nucleus and protoplasm to the periphery.

In *reticulated tissue*, the cells send off numerous ramifications, which anastomose one with the other, forming a very complicated network (fig. 11). A cellular body is not found at the nodal points.

The network formed by the cells and their prolongations is occupied by lymph cells

(lymph glands, spleen, Peyer's patches, etc.), or by cells and nerve fibres (neuroglia of the brain and spinal cord).

Elastic tissue has a great resemblance to the preceding, but it differs in having its meshes very irregular, and there is only found a trace of the protoplasm of cells at a few points.

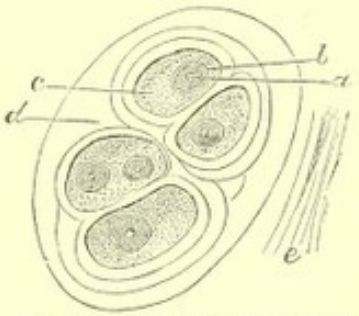
In all these tissues, the embryonic cells and nuclei suffer considerable atrophy, and are represented only by an irregular, round, or elongated mass, which colors red by carmine, and resists the action of acetic acid. Irritation causes all these cells to return to their primitive form.

Cartilaginous Tissue.—Cartilaginous tissue, like connective tissue, occurs in the organism under different forms; but it is always found having as an essential character cells entirely surrounded by a cartilaginous matrix, a transparent substance yielding chondrin by boiling.

The true cartilage cell is a mass of protoplasm containing a nucleus; it varies much in size and form in the same variety of cartilage.

In living cartilage, the shape of the cells is spherical, oval, or lenticular; but when examined in water with acetic acid and in most other reagents, cartilage cells are seen to have a great variety of shapes which are due to distortion. Frequently fatty granules or small drops of fat accumulate in the protoplasm of cartilage cells. When the fat is very abundant, as in adipose cells, the nucleus remains, is well developed, and occupies a position at the side of the cell. The nucleus is always present, is spherical or slightly oval in shape, is limited by a double contour, and its nucleolus is well developed.

Fig. 12.



Proliferating cartilage cells: *c*, protoplasm of the cell; *a*, nucleolus; *b*, nucleus; *d*, primary and secondary cartilage capsules; *e*, ground substance. In one of the cartilage cells are seen two nuclei.

The cartilage cell does not present any characteristic sufficient to distinguish it when isolated, and it is only because it occupies a place in cartilaginous tissue, that the name cartilage cell is given to it. This cell cannot therefore be defined by its physical characters, but only by the property it possesses of forming around it a secondary membrane of cartilaginous substance termed a capsule (fig. 12).

When, in the development of embryonic tissue, cartilaginous tissue appears, the embryonic cells become separated from one another by a substance at first soft, but gradually becoming more consistent, which has all the characters of cartilaginous substance. The formation of this substance is at first slow, it soon increases and condenses as a capsule around the cells. The capsule may also be the result of a new production of the cell itself. This is the *embryonic* variety of cartilage in which cells and capsules are small and spherical. Soon the cellular elements multiply; at this stage there are frequently seen two nuclei in a cell. While dividing, the nucleus at first enlarges, elongates, contracts at the middle, and finally separates into two. The division of the protoplasm occurs after that of the nucleus; consequently we often have cells with two nuclei. Each of the new cellular masses possesses the property of forming around it cartilaginous substance. Thus in the primary capsule

there are developed two secondary capsules. In multiplying, the cells become flattened against each other, and have elongated or prismatic forms. This is *fœtal cartilage*.

When the nutritive activity is very intense, the cells are round and large, as seen in the ossifying layers of cartilage. Permanent cartilage in the adult consists of medium-sized capsules, which frequently contain secondary capsules. Upon the surface of the articulations and under the perichondrium the capsules are lenticular, and are flattened parallel to the surface while they contain no secondary capsules. Cartilage ground substance in the adult is often infiltrated with a calcareous deposit in its deeper parts. This incrustation forms a complete uniform layer in which the cartilage cells are preserved. It is called *calcified cartilage*.

In persons advanced in age, the costal and thyroid cartilages have their cells *infiltrated with fat* and present a *mucous degeneration* of their fundamental substance, causing the formation of anfractuous cavities filled with mucous material and fatty granules. At these same points there also sometimes exists a calcareous infiltration. Finally, Virchow, by the action of a solution of iodine and sulphuric acid, demonstrated the presence of *amyloid degeneration* in the cells. Rapidly proliferating cells in cartilage undergoing ossification present the same reaction. This substance, the true composition of which is still unknown, has no connection with vegetable starch. In the centre of the intervertebral disks and other ligamentous symphyses, there is found a mucous substance in which exist isolated cartilaginous capsules or groups of capsules united together. Each capsule incloses a cartilage cell with its protoplasm and nucleus. This is *mucous cartilage*.

The substance separating the cartilage capsules in some regions, as the fibrous portion of ligamentous symphyses, has all the characters of fibrous tissue. Here the capsules are very distinct from the fundamental substance, and frequently contain secondary capsules. This is *fibro-cartilage*.

In the cartilages of the ear, in the arytenoid cartilages and epiglottis, exists a cartilaginous tissue with very distinct capsules, separated by a felt-like mass of fibrillæ which resemble elastic fibres, although they differ from the latter in their action with acetic acid, which swells the former fibrillæ. This is *reticular cartilage*.

Where cartilage is in contact with the perichondrium, there is found in the embryo a layer of embryonic cells, similar to those under the periosteum, and from which there is a peripheral growth of the cartilage.

Osseous Tissue.—In osseous tissue, we have the *osseous structure*, the *marrow*, and the *periosteum*.

Osseous tissue, which everywhere is the same in composition, consists of parallel lamellæ and bone corpuscles. In a section of dry bone, the osseous corpuscles appear as oval bodies when seen in profile, more round when seen upon their surface; from their bodies proceed numerous canals ramifying and anastomosing with the canals belonging to neighboring corpuscles. Virchow has demonstrated that these corpuscles contain cellular bodies. By decalcifying a lamella of fresh bone with hydrochloric acid and boiling, Virchow separated masses having incomplete branches, and considered them to be osseous cells. In some he was able

to see indistinctly the nucleus. The nuclei, however, are very evident when a piece of decalcified bone is stained with aniline or carmine, and the cellular nature of the osseous corpuscles is plainly demonstrated. The numerous canaliculi proceeding from the corpuscles are channels for carrying the nutritive fluids into the different parts of the osseous substance, which does not possess the property of imbibition or endosmosis in the normal state.

The bone corpuscles are seated in the osseous lamellæ, and lie parallel to their surfaces. A system of parallel lamellæ envelops the surface of a bone, and each medullary cavity is also surrounded by concentric lamellæ, which form secondary systems.

The medullary cavities contain the marrow and bloodvessels. In nearly all long bones these cavities are cylindrical, and parallel to the long axis of the bone. They are known as Haversian canals, and are connected by transverse or oblique canals. Spongy bones do not differ from compact bones except in the size and irregularity of their canals.

The *marrow of bone* is always traversed by bloodvessels. Between these and the bony walls there are found: 1st, small, round, granular cells with a large nucleus (medulla cells of Robin); 2d, large, irregular cells with many nuclei (myéloplaxes of Robin); 3d, adipose vesicles; 4th, stellate and anastomosing connective tissue corpuscles. These different elements exist in varying proportions, in the different bones, and according to the state of development of the osseous tissue. In the bones of the extremities adipose cells predominate; in the bodies of the vertebræ and sternum, the marrow is red, and contains fewer adipose cells. The most important nutritive and pathological phenomena occurring in bone affect the marrow.

The *periosteum* is a fibro-elastic membrane resembling very much the aponeuroses. This membrane surrounds all parts of the bone, stopping at the border of the articular cartilages. It consists of fibrous and elastic tissue, the deeper portion, in contact with the bone, being composed of very fine and dense fibrillæ. The vessels of the periosteum are very numerous, and pass from the deep layer to penetrate directly into the osseous canals.

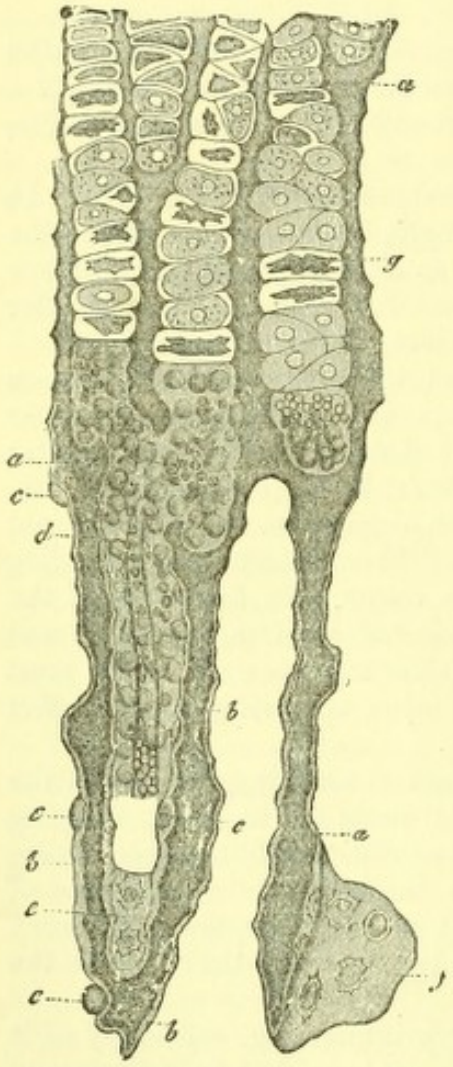
The development of osseous tissue is very interesting, especially as it is not formed directly from the cells of the embryo, but from fibrous or cartilaginous masses which have the form of the bone. Many pathologists base their general views of pathology upon their understanding of *osteo-genesis*.

The formation of a pathological tissue from a healthy tissue which differs from it has been called by Virchow *heteroplasia*. The development of osseous tissue from cartilaginous and fibrous tissues is the physiological type of heteroplasia. Virchow has not so considered it, because he declares that osseous and cartilaginous tissues are the same histologically, and because he believes that osseous tissue arises by nutritive changes of fibrous and cartilaginous tissue, occurring especially in the fundamental substance, which is hardened by calcareous salts. He has applied to the normal development of bone the changes which occur in rachitic bones. But H. Müller, in investigating normal ossification, arrived at a different theory, which we also have verified, that osseous tissue is always de-

veloped according to the same general law, whether from cartilage, or fibrous tissue, or beneath the periosteum.

A. *Ossification from Cartilage.*—The cartilage cells proliferate by the methods previously described; the new cells are surrounded by secondary capsules; the mother capsules, being filled with them, are enlarged and elongated by mutual pressure in such a way as to converge towards the point of ossification.

Fig. 13.



Vertical section from edge of ossifying portion of the diaphysis of a metatarsus, from a fœtal calf. *a*. Ground substance of the cartilage; *b*, of bone. *c*. Newly-formed bone cells in profile, more or less imbedded in intercellular substance. *d*. Medullary canal in process of formation, with vessels and medullary cells. *e*, *f*. Bone cells on their broad aspect. *g*. Cartilage capsules arranged in rows, partly with shrunken cell-bodies. (*Müller.*)

The fundamental substance of the cartilage appears as if fibrillated, and is soon infiltrated with calcareous salts. The secondary capsules are now dissolved, the cartilage cells become free and proliferate, having the characters of embryonic cells, when they may have amœboid movements. The cartilaginous tissue is destroyed, but bony tissue is not yet developed.

This new tissue, which we propose to name *ossiform*, consists of trabeculæ incrusted with calcareous salts, and represents the ground substance of the old cartilage. *In these trabeculæ there are no cellular elements.* They limit alveoli which communicate with one another, forming cavernous spaces filled with marrow.

This tissue does not correspond to the description of *osteoid* tissue of Virchow, nor to *spongoid* tissue of Guérin and Broca. These authors have founded their description upon rachitic bones, where the calcified trabeculæ of osteoid or spongoid tissue of these writers contain cellular elements. In the *ossiform tissue* the vessels coming from the bone [or perichondrium] penetrate into the alveoli and form loops. True ossification now begins. Along the calcified trabeculæ are arranged the cells of the embryonal marrow; these are frequently pressed one against the other, and are angular. Around a few, which have prolongations, is seen a new intercellular substance. Some of these cells may be partly in the osseous substance and partly in the marrow. Soon such cells are completely surrounded by the osseous substance, and become true bone corpuscles. To this first layer of bone are added new layers, always by the same process of formation from the marrow. An irregular

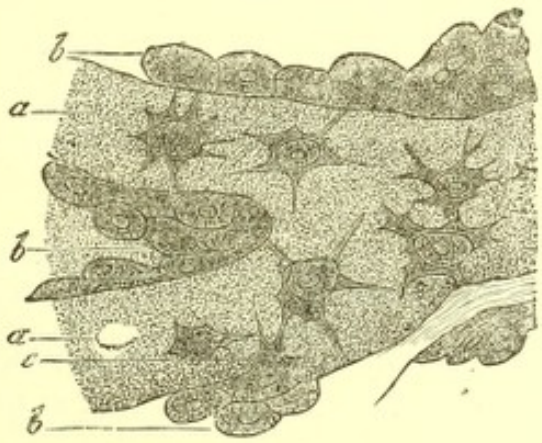
primitive medullary space in the cartilage is thus transformed into a Haversian canal, which contains the marrow and vessels.

B. *Ossification from the Periosteum.*—The preceding description relates to the development of bone from cartilage, but once formed it may grow beneath the periosteum. Under this membrane there is found during this period a layer of round or polygonal cells, with one or more nuclei, not differing from the cells found in embryonal marrow. In this layer, in transverse sections of bone, are seen projecting straight or curved osseous needles, their base being the old bone, and their free extremity directed towards the periosteum. The medulla cells are found ranged along these osseous needles or processes, and some of them are surrounded by osseous substance. Here, also, may the cell be partly in the osseous substance and partly in the marrow; therefore the process of ossification under the periosteum corresponds to that seen in the second phase of ossification from cartilage. The needles, which correspond to vertical sections of laminæ, gradually increase in size, turn inwards, join one with another to form round spaces which correspond to Haversian canals.

C. *Ossification from Fibrous Tissue.*—In the bones of the cranium, the osseous tissue is developed from a fibrous membrane and from trabeculæ, which gradually increase in thickness, turn inwards, and limit medullary spaces.

In a human embryo of two or three months there are found osseous plates corresponding to each of the bones of the cranium. These bones terminate in the fibrous tissue by needles or processes. Along these needles are found one or two layers of embryonic cells, polygonal in shape from mutual pressure, resembling those seen under the periosteum and in the medullary cavities. By the same process these cells become osseous corpuscles.

Fig. 14.



Osteoblasts from the parietal bone of a human embryo thirteen weeks old. *a*. Bony septa, with the cells of the lacunæ. *b*. Layers of osteoblasts. *c*. The latter in transition to bone corpuscles. (*Gegenbauer.*)

The osseous needles terminate in the fibrous tissue by a long filament formed of a refracting and slightly fibrillated substance, not containing cells. These fibres are comparable to the trabeculæ of the fundamental substance of cartilage in the first stage of ossification, and are known as

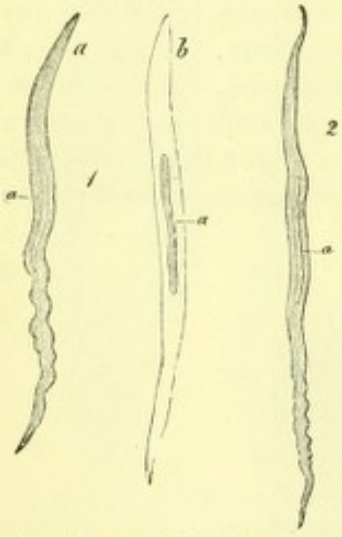
Sharpey's fibres; they appear to be the result of a condensation of the fundamental substance of the connective tissue, and seem to direct the process of ossification.

The embryonic cells which are found along the osseous trabeculæ are very evidently derived from the neighboring fibrous tissue, the cells of which multiply by a process analogous to that described in cartilage, while the wall of the connective tissue corpuscles and the fundamental substance of the connective tissue, analogous to the capsules and cartilaginous substance, are dissolved. Therefore the same general law everywhere presides in the formation of osseous tissue, viz.: *The ground substance of the tissue (capsules of the cartilage cells, fibrous substance) is dissolved; the cells proliferate, become free, and give origin to an embryonic tissue, the elements of which become surrounded by a new fundamental substance, and are thus transformed into osseous corpuscles.*

Second Group.—Muscular and Nerve Tissue.

Muscular Tissue.—This tissue in man presents for consideration three distinct kinds: 1st. Muscles of organic life, consisting of smooth fusiform cells, which contract slowly and involuntarily; 2d. Muscular tissue of the heart, the fasciculi of which are striated and anastomose one with another, and are capable physiologically of a quick and involuntary contraction; 3d. Muscular tissue of the trunk and extremities, consisting of striated fasciculi non-anastomosing, characterized physiologically by a power of quick and voluntary contraction.

Fig. 15.



Smooth muscle fibres from common arteries; *a*, nuclei of fibres. × 300. (*Gray.*)

The elements of organic muscle are fusiform cells greatly varying in length; no enveloping membrane has yet been recognized, they seem to consist of an albuminoid substance (muscular fibrin), transparent, refracting, and amorphous, except in the uterus during gestation, when may be observed a very fine striation which is perhaps related to the new function which the uterus presents, the quick movement necessary to parturition. (Fig. 15.)

Near the centre of the amorphous mass there is seen an elongated rod-shaped nucleus, which is very distinct after coloring with carmine, or treatment with acetic acid which gives it a serpentine shape. The nuclei do not contain nucleoli. The cells are so united as to form fasciculi, or membranes.

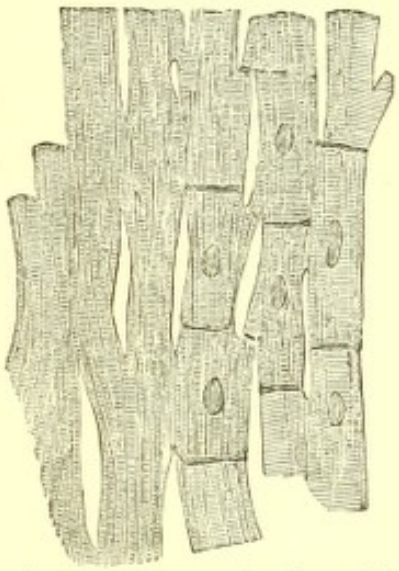
According to most histologists these muscular cells are derived directly from embryonic cells, the protoplasm of which experiences successive changes and is transformed into muscular substance, the nucleus becoming elongated or rod-shaped.

The *muscular fasciculi of the heart* are thus derived from anastomosing embryonic cells; their fundamental substance is always striated, and oval nuclei occupy the centre of the fasciculi. The anastomosis of the muscular

fibres of the heart accounts for the synergia and synchronism of the cardiac muscles. (Fig. 16.)

Striated muscular fibres of voluntary contraction are developed from embryonic cells, which are elongated, the nucleus becomes oval and multiplies, the protoplasm undergoes nutritive changes, which transform it into striated substance, while the membrane of the cell becomes resisting, remains amorphous, and constitutes the sarcolemma. At the beginning of this formation, the protoplasm experiences, only at its peripheral portion, the changes which produce the muscular structure; always around the nucleus there remains some unchanged protoplasm. The nuclei are seen under the sarcolemma constantly surrounded by a small fusiform mass of granular protoplasm.

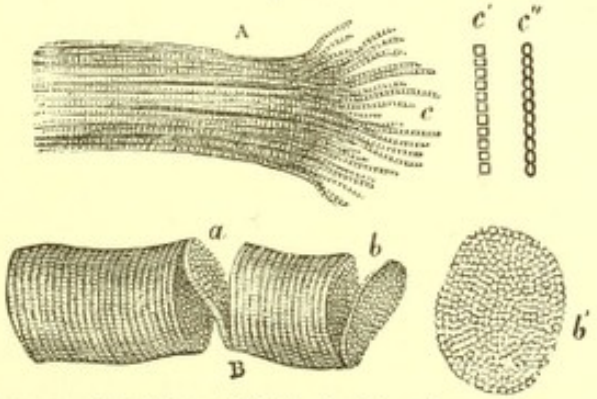
Fig. 16.



Anastomosing muscular fibres of the heart. On the right the limits of the separate cells with their nuclei are exhibited somewhat diagramatically. (*Stricker.*)

The longitudinal and transverse striation divides the muscular substance into small prisms, or *sarcous elements* of Bowman, who compares the striæ to a uniting substance, and the *sarcous elements* to the active part of the muscle. All authors, however, do not agree with this view; several histologists believe in the old opinion, which regards the muscular fibre as composed of fibrillæ; the transverse striation of the fibrillæ being due to successive swellings, or to a spiral-like arrangement. Our observations lead us to admit the existence of *sarcous elements*.

Fig. 17.



Fragments of elementary muscular fibres, striated, showing cleavage in opposite directions. × 300. (*Gray.*)

Nerve Tissue.—The elements of nerve tissue are *cells* and *fibres*. Nerve cells are quite variable in shape and size; they always have simple or ramifying prolongations which connect them with one another or with nerve fibres. They do not possess a membrane; their fundamental substance is finely granular or striated, and always contains a varying amount of pigment. They all have a large nucleus with a large

nucleolus. From the nucleolus, according to Frommann, arise prolongations which pass through the nucleus and body of the cell into its ramifications. Balbiani believes these prolongations to be true canals.

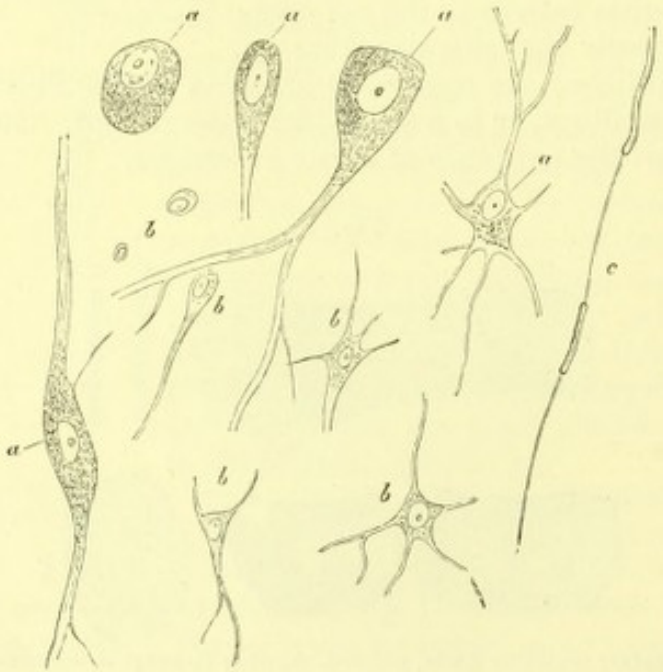
The gray nervous substance contains the nerve cells, which are therefore met with in the convolutions, in the gray masses of the cerebrum, the cerebellum, in the spinal cord, and all the nerve ganglia. They are also found in a few organs upon the peripheral extremities of the nerve fibres.

According to Remak, Kölliker, and Lockhart Clarke, the development of nerve cells is from primitive embryonic cells. According to Beal and Max Schultze, the whole of the protoplasm is not transformed, a portion remaining which surrounds the nucleus of the nerve cell. At the periphery of the nerve cells their substance is striated (arch-like appearance). A weak solution of carmine colors first the nucleolus, then the nucleus, and finally the cell-body, the nucleolus being always most intensely colored.

Nerve fibres are of two varieties, those having a medullary sheath and those which have not. In the embryo only the latter exist; it is during the course of development that the medullary sheath is added.

Medullated nerve fibres are separated into two kinds. One variety, met with particularly in the peripheral nervous system, is uniformly cylindrical, limited by a structureless resisting membrane (membrane of Schwann, neurilemma), in which are seen oval nuclei, similar to those of

Fig. 18.

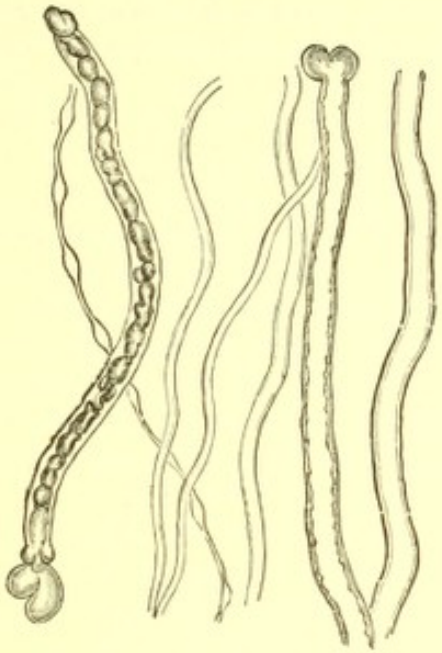


Nerve cells from the inner part of the gray matter of the convolutions of the human brain. × 350.
Nerve cells: *a*, larger; *b*, smaller. *c*. Nerve fibre, with axis-cylinder. (*Gray.*)

the sarcolemma, but only visible after staining with carmine. Beneath this membrane the medullary substance presents a double contour. It consists of *myelin*, an oleaginous substance, which, when the fibre is broken, readily escapes, but it is always limited by a double contour. We know

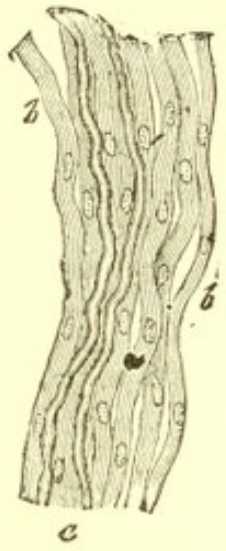
of no explanation of this double contour; neither is the exact chemical composition of myelin accurately known. In the centre of the myelin

Fig. 19.



Human nerve tubes ×350: three of them are fine, one of which is varicose, one of middling thickness and with a simple contour; and three thick, two of which are double contoured, and one with grumous contents. (*Gray.*)

Fig. 20.



Small nerve branch from the sympathetic of a mammal: two dark bordered nerve tubes (*a*) among a number of *Remak's* fibres (*b*). (*Frey.*)

exists a homogeneous, vitreous, slightly longitudinally striated cylinder (*axis cylinder*), varying in diameter, and capable of being colored by carmine when the solution is brought in contact with it.

In the other variety of medullated nerve fibres, obtained by dissecting the white substance of the central nervous system, the fibres are seen as moniliform fibres, very thin in some places, and always having a double contour. The neurilemma of these nerves is so thin that it is difficult of demonstration; and it appears to be devoid of nuclei. The moniliform appearance is due to the escape of myelin by rupture of the neurilemma. It seems to us that, during dissection, the axis cylinder has been separated, and frequently is found floating in the fluid, having a greater diameter than the nerve fibre from which it apparently came. This is an artificial appearance, as sections of hardened brain or spinal cord demonstrate, since there are never found in these preparations nerve fibres having a moniliform arrangement or such a very small diameter.

The *fibres of Remak* are nerve fibres without a medullary sheath. They are composed of an axis cylinder and neurilemma with the numerous nuclei belonging to it.

Nerve fibres are developed from embryonic cells, which enlongate, anastomose, and become surrounded by a membrane to form the neurilemma, while the axis cylinder is developed from the protoplasm of the cells by a process not well understood; the nuclei of the cells remain in the envelope, and do not contribute to the formation of the axis cylinder.

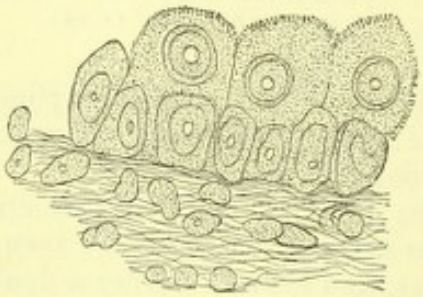
The myeline is subsequently produced, and accumulates between the axis cylinder and the enveloping membrane of the fibre.

Nerve fibres proceed from cells, the prolongations of which are continuous with the axis cylinder. The peripheral terminations of nerve fibres are known only in a few organs and tissues, constituting special apparatuses, such as the corpuscles of Paccini, Meissner, and Krause, terminal plate of muscles, etc.

Third Group.—Epithelial Tissue.

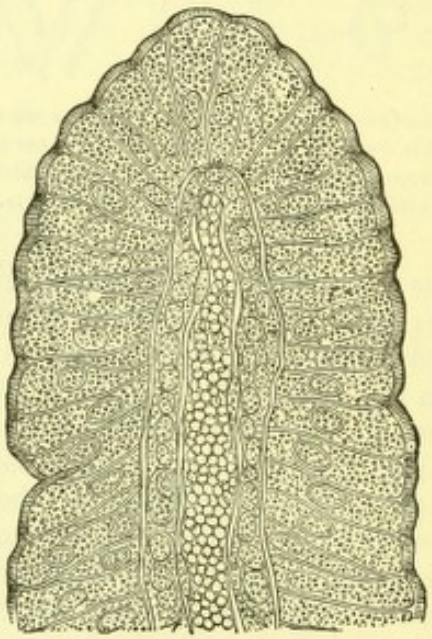
Cells which enter into the composition of epithelial tissues vary much in size and shape. They are polygonal, sometimes very flat (laminated), or their diameters are equal (cubes); others are elongated in the form of cones or cylinders. A few are peculiar in shape, and are with difficulty recognized as epithelial cells when met with isolated: as, the dentated or spinous cells of the middle layer of the rete mucosum of the skin; the ciliated cylindrical cells in the air passages and genitals; the polygonal

Fig. 21.



Spinous epithelial cells of a cancroid epithelioma.

Fig. 22.



Section of a villus of a rabbit. High power. (*Stricker.*)

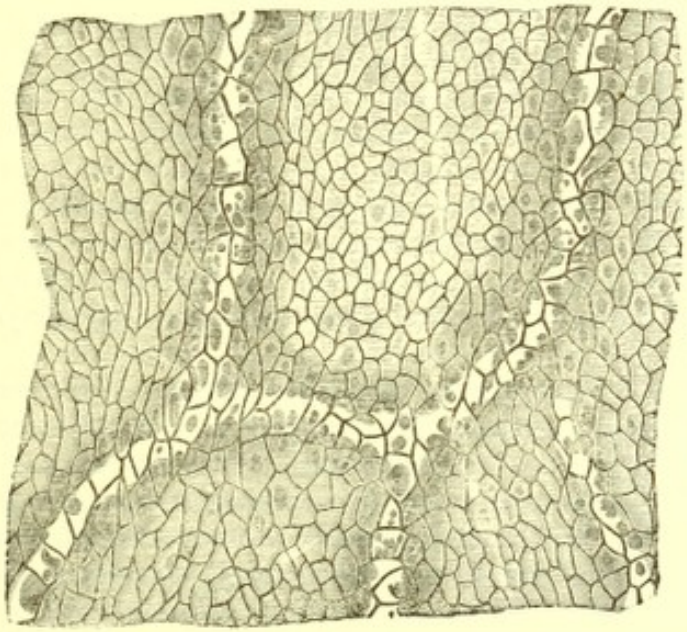
cells in the cerebral ventricles; cells with striated borders, as in the intestine; cylindrical cells with terminal branches, as in the organs of special sense; the cells of the cornea and fibres of the crystalline lens; cells in the form of pyramids, as in the culs-de-sac of racemose glands.

An epithelial cell, however, only takes these characteristic forms during the process of its evolution. Evolution is the chief physiological function of epithelia; all their elements are transitory, they are born, develop, and die, in a variable period of time. For example, in the cutaneous covering, there are found, in the deepest layer of the rete mucosum, in contact with the papillæ, cylindrical cells, which soon be-

come larger, round, with their surface dentated, and gradually increase in size as they approach the surface of the epidermis. Finally, they are flattened into dry lamellæ, and form, by their union, the corneous layer, from which they are detached by physical and chemical agents. The buccal epithelium follows the same evolution, except the corneous transformation. In the mucous membrane of the trachea, the deep cells are oval, and the superficial cells only increase their diameter, assume a distinct cylindrical form, and have cilia upon their free surface. The cells in the glands follow an analogous evolution. It has, however, been demonstrated, that in the glands, the epithelial cells desquamate in order to form part of the excreted substances, and that the contents of the cells constitute an essential part of the secretion.

If epithelial cells, in a few instances only, possess characters by which they may be recognized, there are in the structure of the epithelial tissue itself the elements for an exact definition. The cells which compose it are united together so as to form masses or membranes, which are accurately moulded upon the surfaces to which they adhere. On many of these surfaces, as that belonging to the skin, the mucous membranes, or the glands, there is found a hyaline amorphous layer containing a few nuclei, which is the *basement membrane* of Bowman. Vessels are never found in epithelial tissues.

Fig. 23.



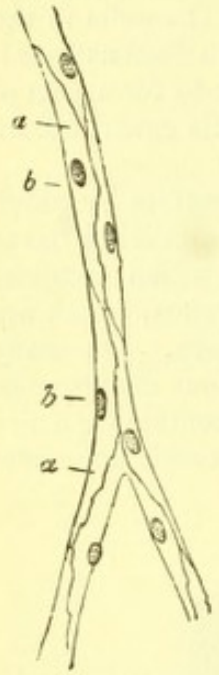
Normal endothelium of the parietal pericardium of a toad, silver treated. Light tracts indicate the course of subjacent bloodvessels. High power. (*Chapman.*)

The majority of epithelial coverings are derived from the external layer of the blastoderm, as, for example, the epidermis and cutaneous glands. The epithelium of the mucous membrane and its glands are developed from the internal layer of the blastoderm.

Some epithelial (endothelial) coverings, those of the vessels, serous membrane, etc., have their origin from the middle layers of the blastoderm. This embryogenic difference has led Rindfleisch, His, and Thiersch

to establish distinct physiological and pathological divisions depending upon the layer from which the epithelium has been developed. His has given them different names; those arising from the external and internal layers he terms epithelium, and those from the middle layer endothelium. He believes the difference of origin always corresponds to a different structure; the endothelia consist of very flat cells united at their borders, and form [almost universally] a single layer, as the epithelium of vessels, serous membranes, articular synovial membranes, serous and mucous bursæ; the epithelia, on the contrary, have one or several layers of cells varying in thickness. But even from this point of view there is great similarity between the two varieties of epithelium. Thus, that lining the pulmonary alveoli, and which is developed from the internal layer, is very thin, and resembles that of serous membranes; while the epithelium covering the synovial fringes, and which is derived from the middle layer, consists of superimposed layers, and it also secretes a liquid containing mucin. The flat form of the cells of the endothelia of His appears to us to be due to mechanical causes, and is explained by the pressure and friction of the blood in the vessels, by pressure and friction of the opposite surfaces of the serous membranes.

Fig. 24.



Capillary from the mesentery of a guinea-pig, after treatment by nitrate of silver: *a*, cell; *b*, nuclei of the same. (*Frey.*)

It will be seen, in the study of pathology, that physical conditions may change the form of the epithelia. Therefore, the distinction made by His is not always correct; moreover, it is founded upon embryogenic facts which are not well established.

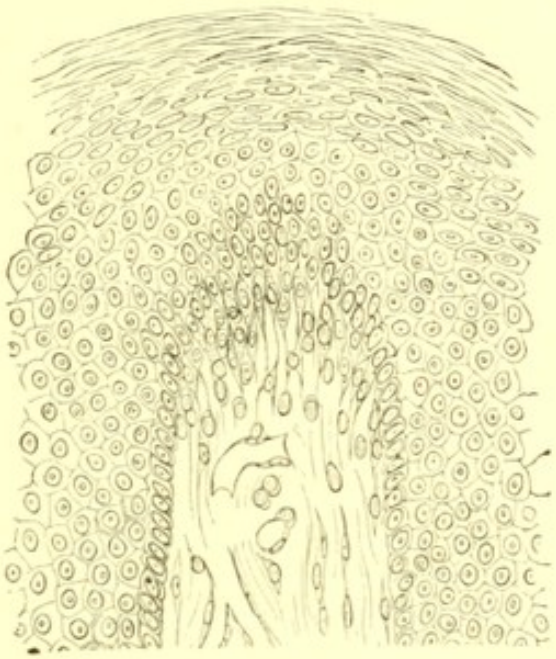
Epithelial tissues are divided into *investing epithelium* and *glandular epithelium*. Investing epithelium consists of stratified layers (laminated) or a single layer (non-laminated).

Laminated epithelium may be separated into two varieties: 1st. Those where the superficial cells are flat, as upon the skin, the buccal mucous membrane, the pharynx, the œsophagus, the conjunctiva, the bladder, the urethra, the vagina, etc. Upon the skin the superficial cells form the corneous layer, nails, or hair, according to the necessities of the case. 2d. Those where the superficial layer is composed of cylindrical and ciliated cells, as in the respiratory mucous membrane.

Non-laminated epithelium is cylindrical or pavement: cylindrical upon the digestive mucous membrane; cylindrical and ciliated upon the uterine mucous membrane, the Fallopian tubes, vas deferens, and seminal vesicles; upon the mucous membrane of the small intestine, the cells terminate at their free border in striations; non-laminated pavement epithelium is met with in the ventricles of the brain, in the pulmonary alveoli, upon the arachnoid, pleura, peritoneum, pericardium, and vessels. Non-laminated pavement epithelial cells are cubical, as in the ventricles of the brain; or flat, as in all the other organs mentioned. In the latter, a satisfactory idea of the epithelium can only be had by staining with

nitrate of silver. When colored with picro-carmine, the nuclei appear beneath the plates, and sometimes a distinct mass of protoplasm surrounds them. The nucleus and protoplasm occupy only a portion of the plates, and are moulded into the subjacent connecting substance. The plate seems to be the result of a secondary exudation from the active portion of the cell.

Fig. 25.



Papilloma: showing a single enlarged papilla, covered by laminated epithelium. (*Rindfleisch.*)

The entire *vascular system* is lined by such an epithelium; it was formerly believed that the capillaries consisted of an amorphous membrane with nuclei. Auerbach, Eberth, and Aeby, employing the process of von Recklinghausen to show delicate epithelia, have been able to demonstrate that the membrane of the capillaries is formed of epithelial cells, each of which corresponds to a nucleus of the capillary wall. If the cells cannot be seen by the usual process, it is because they are so intimately united that their limits cannot be distinguished. But by irritation they become swollen and separated from one another.

By injections of gelatine and nitrate of silver, the endothelial layer in places along the course of the capillaries is elevated, without the injection passing out of the vessels. The capillaries are therefore limited at their periphery. But a double contour of the limiting membrane cannot be seen, so that the demonstration of a true membrane upon which the epithelial cells are placed is not yet complete. It is possible that the capillaries are simply limited by the surrounding condensed connective tissue. This view is founded upon the impossibility of isolating the capillaries when they are not surrounded by a lymphatic sheath. This endothelium is continuous with that of the arteries and veins without any line of demarcation.

Previous to the demonstration of an endothelium of the blood capillaries, von Recklinghausen and His had demonstrated that the lymph capil-

laries were lined by an endothelium formed of flat and lozenge-shaped cells. Von Recklinghausen observed that the lymphatic capillaries inosculated with the branching canals of the connective-tissue corpuscles of Virchow. By staining with nitrate of silver, this author observed that the fundamental substance colored by the deposit was channelled by stellate spaces connected together by a system of canals.

In studying the endothelium of serous membranes the same writer has seen between the cells spaces or stomata, which establish a direct communication between the serous cavities and lymphatic canals. The serous cavities, the lymphatic vessels, and lymph spaces of the connective tissue, therefore, belong to the same system. The larger lymphatic vessels have a much more complex structure, resembling that of veins of the same calibre.

Glandular epithelium, the cells of which may be pavement, cylindrical, in the form of pyramids, etc., also undergoes a constant evolution. Thus in the glands of the stomach, the cells, primarily cylindrical, become spherical, filled with juices, fall into the lumen of the glands, and are destroyed while discharging their contents. Colostrum cells are nothing more than desquamated cells of the mammary acini, and when they are not found in milk it is because they have been destroyed and their fat set free in the fluid. Some cells are not destroyed, but simply empty into the gland their product of secretion. This takes place in the glands of Lieberkühn. The cells in glands are planted upon a limiting, homogeneous, hyaline layer, which does not appear to be formed of cells, but seems to be a condensed layer of the surrounding connective tissue. The structure of this layer is not well determined, but almost always flat nuclei are found in it.

The different varieties of glands are:—

1st. Tubular; that is, consisting of a simple tube, so that the secreting portion of the gland is directly continuous with the excretory duct; they are rectilinear, and lined by cylindrical epithelium (glands of Lieberkühn, of the stomach, of the body of the uterus, etc.), or are rolled into the shape of a ball and lined by pavement epithelium (sudorific glands, kidney).

2d. Acinous; that is, consisting of culs-de-sac, varying in number, which open into an excretory duct. The culs-de-sac and excretory duct are lined by a pavement epithelium, as in the sebaceous and mammary glands; or the culs-de-sac are lined by epithelial cells in the form of a pyramid, while the ducts are paved by a non-laminated cylindrical epithelium, as in the salivary glands, Brunner's glands, tracheal and laryngeal glands, and the pancreas.

In the foregoing brief sketch of normal histology only the essential outlines have been presented. [For a more particular account of the natural structure of the various elements and tissues of which the human organism is composed, the student is referred to the subsequent pages of this work where the different organs and systems are more minutely considered.]

CHAPTER II.

GENERAL PRINCIPLES—ALTERATIONS OF CELLS AND OF TISSUES.

The alterations of cells and of tissues may be divided into two groups; 1st, lesions simply nutritive; 2d, lesions which comprise the formation of new cells.

Sect. I.—Lesions of Nutrition of Elements and of Tissues.

They may be divided into:—

A. Lesions occasioned by death of the elements and of the tissues.

B. Lesions occasioned by insufficient nutrition of the elements (atrophy).

C. Serous and albuminous infiltrations.

D. Mucous and colloid infiltrations.

E. Amyloid infiltration.

F. Fatty infiltration and fatty degeneration.

G. Pigmentation.

H. Calcareous infiltration.

I. Infiltration of urates.

J. Lesions caused by an excess of nutrition.

A. Lesions caused by Death of the Elements and of the Tissues.—The death of certain elements is a physiological fact and sometimes even a necessary ocurrence: for example, almost all the epithelia are subject to an incessant desquamation. It is probable that certain elements, which to us appear permanent, are destroyed at long intervals, to be displaced by younger elements. This is actually seen in the muscle fibres of the frog, where, each winter, a certain number of primary bundles are destroyed (Wittich), only to be reformed in the spring. We may readily believe that analogous phenomena occur in man, notwithstanding the fact that this destruction and new formation of muscles has been observed in the latter only in grave maladies and during convalescence. When in man a large quantity of cells are formed under the influence of an irritation, a certain number of them die because of insufficient nutrition. This always happens when the supply of nutritive fluid is insufficient for the number of new elements. Of all the elements of the human frame, the nerve cells have the greatest longevity; they resist energetically every process of destruction, and, up to the present moment, a physiological destruction of them is not known.

Death supervenes under two conditions: 1st, from arrest of circulation; 2d, as a consequence of initial lesions of cells.

1st. When there is arrest of circulation in a part of the organism, that part dies and determines around it a suppurative inflammation. One says then that there is an *eschar* and *gangrene*; or if a sort of tolerance is established, the necrosed part decomposes, slowly resolves into soluble substances, which little by little are taken up by the circulation—*infarction* and *necrobiosis* of Virchow. The first phenomena which follow necrosis are seen in the most delicate structures. The blood disks give up their coloring matter; their fat of composition escapes in the form of granules, and finally becomes resolved into a granular detritus. Colored granules and rhombohedric crystals of a beautiful orange-red, discovered by Virchow and named hæmatoidin crystals, may be seen in the necrosed parts. Whenever extravasated blood escapes into a natural or artificial cavity, it undergoes similar alterations. The white corpuscles offer a much greater resistance: they shrivel, become granular and angular, contain a few fatty granules, and the nucleus is undistinguishable from the protoplasm. This we regard as a caseous metamorphosis. Having once suffered this metamorphosis, they may remain unaltered for an extremely long time.

Connective tissue, bone, cartilage, tendon, etc., persist almost indefinitely in parts deprived of circulation, if the *gangrene* is *dry*. In this case the preservation even of delicate tissues is due to the fact that the evaporated water of constitution has been replaced by fat, which has escaped from the adipose cells; they are deprived of the oxygen and water necessary for putrefaction. The infiltrated fat gives the dry gangrenous parts the translucence which is seen upon section, while the exposed surface is brown.

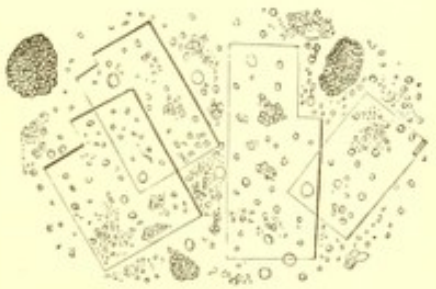
Humid or moist gangrene supervenes when fluids are constantly conveyed to the part, as in gangrene after inflammation or obliteration of the veins. When the parts are deep and cannot dry, the gangrene is, perforce, humid. The fat is reduced to granules, but it cannot infiltrate the tissues which are filled with water. So long as oxygen is not supplied—as in cerebral softening or in splenic infarction—putrefaction is not possible. It takes place very quickly, however, on the surface of the body or in the lungs. Two phases of gangrene should then be distinguished, *mortification* and *putrefaction*. Examples of the first phase are seen in dead embryos which have remained a longer or shorter time in the uterus. Some of these are almost dry, and, after exposure to air, resist putrefaction much better than any other tissue. In these fœtuses it is often still possible to recognize some of the elements of the tissues. The red blood disks are usually destroyed. White corpuscles may still be seen in the vessels, but they have undergone the caseous change. Fatty granules and black melanic granules are also visible. The brain and spinal marrow are reduced to a pulp in which can be recognized bodies consisting of fatty granules as well as crystals of cholesterine and nerve-cells, the nuclei of which are no longer visible. The nerve tubes have completely disappeared. The peripheral nerves are generally very well preserved; the myelin, in small quantity at this age, has merely become precipitated as fine fatty granules. The muscular fasciculi of the trunk and members contain no granules of fat, but solely brown pigment granules derived probably from the coloring matter of the muscles. The

muscle fibres themselves, beautifully striated, may be easily separated into disks or into *sarcous elements*. On the contrary, the muscle fibres of the heart everywhere present fatty granules in abundance. This preservation of muscle is constant.

The cells of the liver are destroyed, and are replaced by accumulations of protein and fatty granules, by fat crystals, and by pigment particles. The uriniferous tubes of the kidney are preserved, but in the place of the lining epithelium exists a granulo-fatty and pigmentary detritus. All of the cartilage cells contain a few fatty granules. The so-called bone corpuscles and the connective-tissue corpuscles also are well preserved.

In *dry gangrene*, the tissues present alterations analogous to those which we have just examined in the macerated fœtus. In *moist gangrene*, however, the modifications which supervene, rapidly induce decomposition of the tissues which are soaked with serum, or infiltrated with pus. Even the toughest fibrous tissue, as the tendons, is separated into its ultimate filaments. The osseous tissue alone preserves its form, and persists for years without alteration. Its surface may be blackened, but this is due to the presence of a combination of sulphur and iron which naturally takes place.

Fig. 26.



Fatty granules with crystals of cholesterine, from atheromatous deposits in the aorta. (*Gross.*)

In moist gangrene, ulterior metamorphoses of the fat give rise to crystals of margarine, of stearic acid, and of cholesterine. The crystals of leucin and tyrosin, almost always present, are derived probably from the proteine substances. Finally brown or black angular granules or crystals, to which the name of melanin has been given, may be met with.

2d. The death of tissues may be due to initial alterations in the cells. This happens in primary fatty degeneration of cells, such as is seen in arterial atheroma, caries, etc., and in degenerations consecutive to a chronic inflammation. A great number of cells being thus destroyed, the tissue whose life depends upon them must also die. Divers phenomena result.

There may be an inflammation of the surrounding tissue, and a genuine elimination of the mortified part, as in caries; the dead tissue may remain in its place, and become infiltrated with calcareous salts, as in the calcareous plates of the aorta; or, as we have seen in the skin and many other parts of a fœtus which had remained for a score of years in the peritoneal cavity, the necrosed part may soften, fall into a granular detritus, and be at last taken up by the circulation.

B. Lesions caused by Insufficient Nutrition of the Elements.—Atrophy from insufficient nutrition has been studied more particularly in its bearing upon organs in gross, rather than in its effects upon the elements and tissues.

Atrophy may be physiological under some circumstances, as in the ductus arteriosus and thymus gland after birth, when the elements undergo

a fatty, colloid, or calcareous degeneration. The genital organs, which, during their periods of activity, have been the seat of a hypertrophy more or less pronounced, usually atrophy in old age. In the atrophy of the uterus, after gestation, there is probably a mixture of simple atrophy of the elements, and atrophy with degeneration. The ovaries, after the menopause, atrophy throughout their whole mass, and the fibrous tissue of the organ condenses. The testicles, in the aged, atrophy through a fatty degeneration of their epithelial elements.

It is thus seen how closely atrophy of organs is connected with the different degenerations of their elements. Atrophy of the mammæ forms an exception to this rule. Here, in effect, after cessation of lactation, it is observed that the retraction of the glandular acini is accompanied by a simple atrophy of the pavement cells which line them. In the aged, certain of the glands atrophy. Some, as the kidney, become shrunken, the uriniferous tubes and their cells are smaller than in the normal state, sometimes cysts are observed and the tubes may be seen to be choked by colloid masses, etc. The liver and the spleen also are smaller, and at the same time their capsule is thickened. The muscles of old people constantly present a certain number of fasciculi which are atrophied and fatty degenerated.

The type of simple pathological atrophy of the elements without degeneration is met with especially in the emaciation following inanition or acute or chronic maladies. The muscular fasciculi lessen in thickness while preserving their structure. The adipose cells give up a part of their fat and contract, or they lose all of their fat while the cell retains its original size and is filled with a serous fluid. The latter condition is seen in œdema of the subcutaneous cellulo-adipose tissue çoincident with emaciation, wherein this tissue becomes gelatiniform and transparent. Irritation of cellulo-adipose tissue also ends in the disappearance of the fat, but then the protoplasm and the nuclei are more swollen and distinct than in the normal state.

Accidental atrophies may be the consequence of compression of the different organs and tissues. Thus in the kidneys, when the pelvis is distended into a cyst by a pyelitis, a hydro-nephrosis, or a tumor, the renal substance flattens while forming the wall of the cyst; the uriniferous tubes are discovered to be extremely narrow, with their epithelia atrophied and generally also fatty degenerated. The same occurs in the hepatic cells compressed by the newly formed tissue of interstitial hepatitis or by tumors of this organ. Every hypertrophy of the interstitial tissue of organs superinduces atrophy of the parenchymatous elements. In such cases, usually interstitial connective tissue and cellulo-adipose tissue take the place of the atrophied parts, fill the void which the atrophy has caused, and it can even happen that there may result, in consequence of a surcharge of fat, an apparent hypertrophy of the organ. This is seen in certain muscular palsies.

C. Serous and Albuminous Infiltrations.—We have seen how, in atrophy of adipose elements, the cells may experience a serous infiltration, and we have discovered that this lesion is met with in emaciation and in cases of irritation. It is probable that the composition of the infiltrate is

not identical in both, notwithstanding the fact that we can distinguish the one from the other solely by the swelling of the nucleus and the protoplasm in inflammation.

Whenever a slight irritation exists, since there is a more abundant supply of nutritive fluid to the epithelial tissues, the epithelial cells swell and become filled with an albuminous liquid containing fine granules which are soluble in acetic acid. This is what has been called *cloudy swelling*. The nuclei and nucleoli may also present similar changes. Thus the nucleus of the cells of the Malpighian layer of the epidermis may fill with liquid and assume a form decidedly vesicular; this condition, although very common, has as yet escaped the attention of observers. (Fig. 28.)

The muscular fasciculi undergo a similar alteration; between this state and that described by Zenker under the name of *waxy degeneration* (see fig. 31), every intermediate stage can be observed. The waxy degeneration of Zenker, perfectly well known in its physical characters, is not sufficiently understood as to its chemistry; for we do not know whether it is simply a serous or albuminous infiltration, or is a colloid transformation, with which, as we shall soon see, it presents certain points in common.

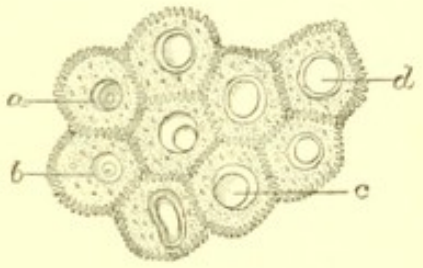
This may also be said of an alteration of the epithelial cells of the mouth, of the pharynx, of the larynx, and of the trachea, described by E. Wagner, which for him constitutes the essential lesion of diphtheritis. (See pp. 45 and 46.) (Fig. 27.)

Fig. 27.



Fibrinous degeneration of pavement epithelial cells. High power. (*E. Wagner.*)

Fig. 28.



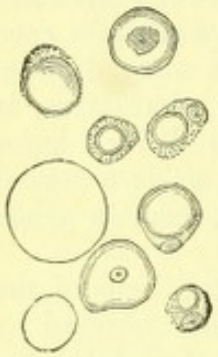
Epithelial cells, from the rete mucosum, during slight irritation. Spinous cells of the epidermis, the nuclei of which have become vesicular by a dilation of the nucleolus; *a*, normal nucleus and nucleolus; *b*, dilated nucleolus; *c*, *d*, a more advanced stage of the same alteration.

In every œdema there is a serous or albuminous infiltration of the areolar connective tissue, when the exudation fills the free spaces between the fasciculi and produces an artificial distension. After desiccation of such a tissue, it retracts and returns to its normal condition and cannot then be distinguished from normal connective tissue. This process is entirely passive. These cases must not be confounded with those where the connective tissue dissolves and is transformed into an albuminous substance, as occurs in many inflammations of the connective tissue.

D. Mucous and Colloid Infiltrations.—When a mucous or synovial membrane is treated with acetic acid, a white filamentous precipitate is obtained which does not dissolve in excess of the acid. Virchow has given the name of *mucin* to the substance which is thus precipitated. The mucin is elaborated by the epithelial cells of the mucous or synovial membranes. We can indeed find in the interior of these cells a fluid presenting the same characters.

There is in the organism a gelatinous *colloid* matter which is more consistent than mucin, and which also results from a physiological metamorphosis of cells. Its type is seen in the thyroid body. This colloid substance colors readily by carmine and preserves the color; although it is not so intensely stained as the nucleus of cells, yet it is more deeply tinged than are the body of the cell and the intercellular substance. Acetic acid only slightly or not at all causes it to swell, and never produces in it a cloudiness. This colloid material is so nearly related to protein substances that latterly Virchow has succeeded in making it artificially. A mucous transformation is often connected with the softening and destruction of the ground-substance of the costal cartilages in the aged. From this single fact some observers, Rindfleisch among others, have supposed that whenever the cells of a tissue become free, it is by means of a mucous transformation of the ground substance, but this opinion very much needs further observation to confirm it. There is no pathological mucous or colloid degeneration which does not find its type somewhere in a physiological evolution of mucous or colloid matter.

Fig. 29.



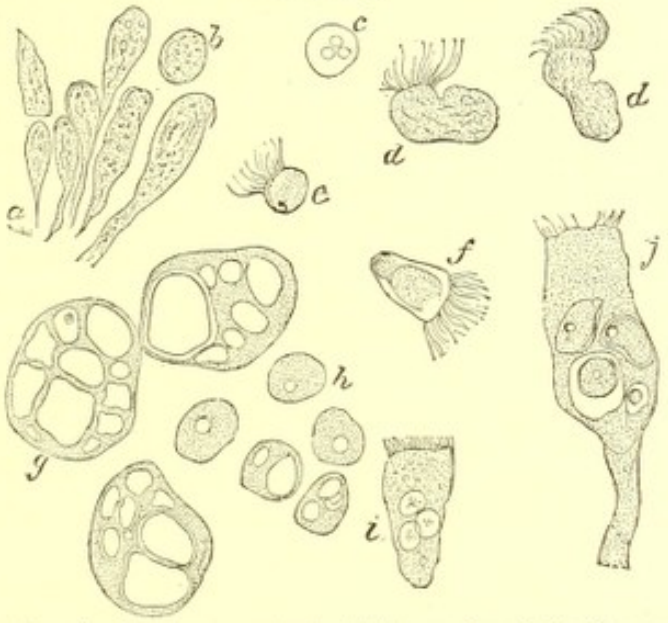
Colloid cells, from a colloid cancer. (*Rindfleisch.*)

The mucous or colloid matter may be diffused throughout the whole cell, as occurs in the epithelium thrown off from mucous membranes affected with catarrh. This lesion of the cell is recognized by a homogeneous, transparent, refractive appearance, and acetic acid occasions a cloudiness. The substance may precipitate and form globular masses enveloping the nuclei. By the accumulation of this material, the nucleus may be pushed to the periphery. The colloid globules may present concentric layers. We shall soon see how they are to be distinguished from calcareous, amyloid, and fatty bodies. The formation of mucus is exaggerated in catarrhs or superficial inflammations of the mucous membranes, and in articular inflammations, particularly in acute rheumatism. It is connected with a greater activity of the old cells, or with the formation of new elements; these cells are rendered turgid by the accumulation of mucus in their interior.

The exaggerated formation of colloid matter reaches its greatest intensity in certain tumors of the thyroid body, called goîtres. In some goîtres there is nothing more than an exaggeration of this formation, which ends in the production of cysts more or less voluminous, and possibly communicating with one another. Colloid metamorphosis of cells may be seen in the lymph glands of old people, and numbers of cysts may arise, comparable to the follicles of the thyroid gland in the adult. In the kidney, especially in the old, certain cysts are filled by a colloid substance, which can be seen to come from the epithelium of the tubuli.

The latter dilate and become transformed into cysts, the centres of which are occupied by a colloid substance festooned at its borders and showing cells undergoing this peculiar degeneration, just as in the thyroid gland. The so-called fibrinous casts of Bright's disease appear to be formed of a substance very analogous to that of the cysts.

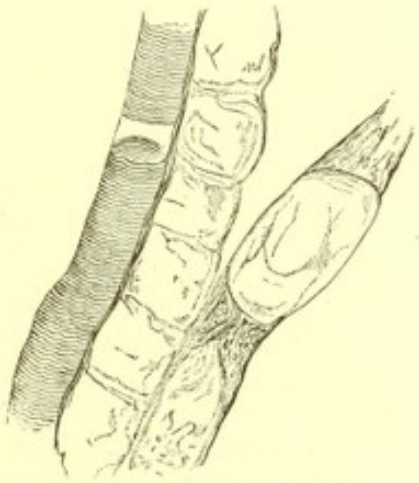
Fig. 30.



Mucous transformation of cells, from a catarrhal inflammation of the air passages. *a*. Degenerated cylindrical cells. *b*. Pus corpuscles; *c*, the same acted upon by acetic acid. *e*, *d*, *f*. Cells coming from the division of a cylindrical cell, showing the cilia. *g*, *h*. Mucous degenerated cells from the nasal fossæ in coryza. *j*. Cylindrical cell, showing endogenous (?) cells. × 450.

We class with colloid metamorphosis the *vitreous degeneration* of muscles (waxy degeneration of Zenker) (fig. 31). In this lesion the muscle

Fig. 31.



A portion of the soleus muscle, from a case of typhoid fever. Preparation teased after treatment with Müller's fluid. × 200; reduced ⅓. (*Green.*)

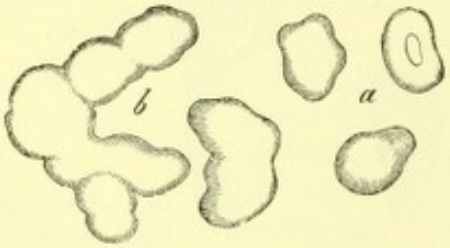
fibres swell and become transparent; they present fractures, transverse and longitudinal; the new substance which determines these physical

changes colors with carmine, and swells slightly in acetic acid, which causes the breaks to disappear. This alteration is seen in typhoid fever and in many affections of the muscles.

In the epithelial cells which have experienced the fibrinous degeneration of Wagner, the essential lesion of the mucous membrane in diphtheritis, we recognize analogous alterations. The cells have a vitreous aspect, are transparent, show prolongations, color very easily in picro-carminate of ammonia, and swell slightly in acetic acid (fig. 27). In tumors the mucous and colloid transformations of cells are very common, and serve for the establishment of varieties in each of them.

E. Amyloid Infiltration.—The name *amyloid substance* is given to an albuminoid material occurring in the form of spheres with concentric layers, or infiltrating the cells and tissues—a matter which possesses the property of staining mahogany-red by iodine (figs. 32 and 33). How-

Fig. 32.



Liver cells infiltrated with amyloid substance: *a*, single cells; *b*, cells which have coalesced. × 300. (*Rindfleisch.*)

Fig. 33.



Corpora amylaceæ from the prostate. (*Virchow.*)

ever feeble the solution of the latter may be, this substance colors deeply, whilst the adjacent tissue is scarcely tinted brown. This substance exists physiologically in the prostate in the form of granules or masses of variable size, with concentric layers. It is seen in the form of spherules in the central nervous system, principally at the periphery of the spinal marrow and at the surface of the brain. Without the use of iodine it would often be impossible to distinguish them from colloid particles.

Pathologically, amyloid matter infiltrates divers elements. In a diffuse manner it invades the cells and destroys them. The cells lose their nuclei, are transformed into amorphous blocks, such as are often seen in the liver and spleen. The smooth muscular tissue of small arteries and the walls of the capillaries are peculiarly susceptible to this degeneration. When the invaded cells limit a canal, the bloodvessels for instance, or the uriniferous tubules, they unite with each other and form an amorphous mass; the wall of the canal is very much thickened by the tumefaction and fusion of the cell-elements, so that the calibre of the vessel or the uriniferous tube is greatly narrowed. The production of amyloid bodies in the brain and spinal marrow takes place in all chronic inflammations of these organs. In most cases of chronic suppuration, especially scrofula, tuberculosis, or syphilis, this substance is observed as a diffuse infiltration in the elements of the liver, the spleen, the kidneys, the lymph glands, the vessels of the intestine, lungs, etc.

F. Fatty Infiltration and Fatty Degeneration.—Fat is met with in the organism in two forms: it may be intimately combined with other substances, as fat of composition, when it cannot be separated except by chemical means; or it may appear under the microscope in the form of granules and globules.

The causes for the visible appearance of the fat of composition are as yet not well known. It has, however, been established that to render the fat apparent in certain elements is to insure the death of the cell. Fatty granules are spherical bodies of variable size, highly refractive, transparent, colorless or slightly yellow, and they are characterized by a very dark border by transmitted light; they are insoluble in acetic acid and in cold potassa (40 parts to 100); they dissolve in a large quantity of ether and in the bisulphide of carbon; they are not colored by carmine, but are colored brown by iodine and black by perosmic acid. When fat, remaining in the organism, is no longer subjected to the nutritive exchanges, it separates into the fatty acids and cholesterine. Stearic acid crystallizes into rhomboidal needles, isolated or radiating from a point. The more important crystals of cholesterine present the form of extremely thin rhomboidal plates (see fig. 26). The latter crystals color red under the action of concentrated sulphuric acid, and blue if they have been previously colored with iodine.

Fat seems always to be deposited in the protoplasm of the cells. In muscles the deposit begins around the nucleus. Free fat among the tissues is an indication that the cells are destroyed or that the examination is made after desiccation; in the latter case, the fat replaces the water which has been evaporated.

Fat may show itself physiologically or pathologically under two different conditions: either it may fill the elements without interfering with their life, *fatty accumulation* or *infiltration*; or the elements invaded by the fat may be destroyed, *fatty degeneration*. It is probable that in the last case the elements at the same time experience inflammatory or other modifications which render life impossible.

Obesity or *fatty accumulation* or *infiltration* is met with physiologically in adipose tissue. The cells of the liver and of the supra-renal capsules also are often the seat of a physiological accumulation of fat globules or granules. In the liver they are met with in much greater numbers after a repast. In nursing women, as well as in all female animals during lactation, the hepatic cells are surcharged with fat, to such a degree that the liver appears to be the magazine of fat intended for the secretion of milk by the mammary gland. The epithelia of the intestinal villi are also loaded with very fine fatty granules during digestion. The cells of permanent cartilages very often contain physiological accumulations of fat in greater or lesser abundance. The presence of fatty infiltration in the liver of phthisical patients appears to be explained by the impediment to the pulmonary circulation and the diminution of respiratory combustion.

Fig. 34.



Liver cells in various stages of fatty infiltration. × 300. (*Rindfleisch.*)

Fatty degeneration as a physiological condition is not rare. It is met with as a normal process in the sebaceous, ceruminous, and mammary glands. In the case of the glands the fat elaborated in the form of granules within the cells is very soon set free by the destruction of these cells. The fatty metamorphosis, after parturition, of the hypertrophied muscle cells of the uterus, that of the cells of the Graafian follicle in the corpus luteum, etc., are also physiological examples.

Fatty degeneration as a pathological state is constantly observed in poisoning from phosphorus, arsenious acid, the salts of antimony, the

Fig. 35.



Fatty degeneration of cells: *a*, from a cancer; *b*, from the brain in chronic softening. The latter show the large "granular corpuscles" (corpuscles of Glüge), and also the manner in which these become disintegrated. × 200. (*Green.*)

Fig. 36.



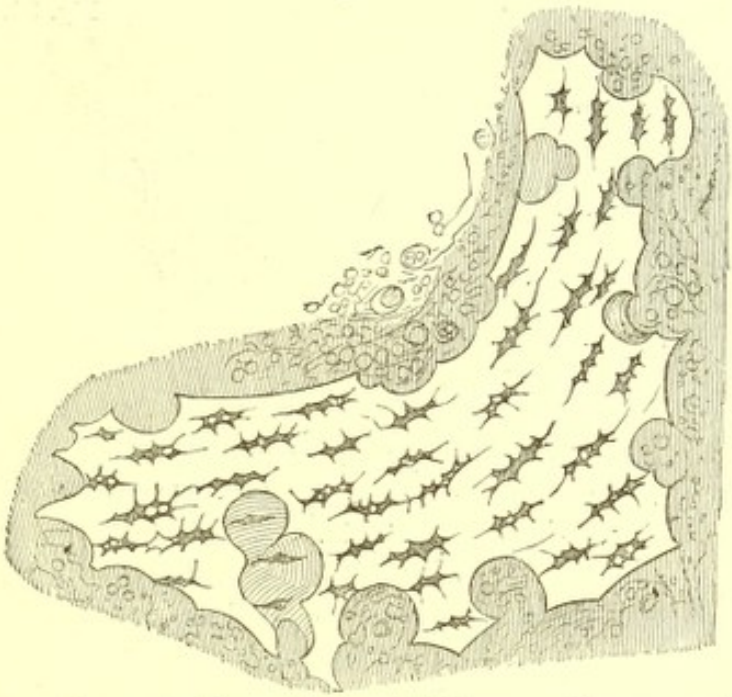
Chronic white softening of the brain: showing the granular corpuscles (corpuscles of Glüge), broken-down nerve fibres, and fat granules, of which the softened substance is composed. One or two nucleated cells (probably nerve-cells) are also visible. × 250. (*Green.*)

mineral acids, the salts of mercury. All the infectious diseases may present analogous lesions in the different viscera. When the circulation of blood is arrested and the part is struck with death, as happens in infarctions and cerebral softening, the elements undergo this same degeneration. (Fig. 36.) In the latter stages of all inflammatory or other neoplasms, when the amount of nutritive supply is not sufficient for the proper nutrition of the new cellular elements which have been formed in great abundance, a part or all of the latter suffer fatty degeneration.

The destruction of the primitive fats, the cause of which we do not know, is seen in the bone corpuscles and in the cells of articular cartilage in caries and in white swellings. (Fig. 37.) This fatty degeneration may be consecutive to a death of the elements caused by arrest of circulation. This alteration once accomplished, the cells no longer undergo changes of nutrition. Similar causes induce fatty degeneration of inflammatory products and of pus. In these cases, it seems very probable that the fat is simply set free in the elements wherein it was masked during their life. This is not so in poisoning or in infectious diseases. Here the quantity of fat is often great, and it seems that an unusual elaboration of it by the elements themselves has occurred. Certain authors think that albuminoid substances may, in the interior of the organism, directly give rise to fat, and they even go so far as to say that a protein granule may become a fat granule. We know no microscopic observation upon which this view is based.

It is seen then that the fat of composition may become apparent under the influence of the following conditions: an impediment or an arrest of nutrition; a superabundant supply of fat by the blood, which always contains it in the physiological state; a more active elaboration of fat by

Fig. 37.



Caries fungosa. A fragment of bone with Howship's lacunæ and bone corpuscles containing fat. × 300. (*Rindfleisch.*)

the elements; the fat in the elements may not be taken up by the circulation with sufficient rapidity.

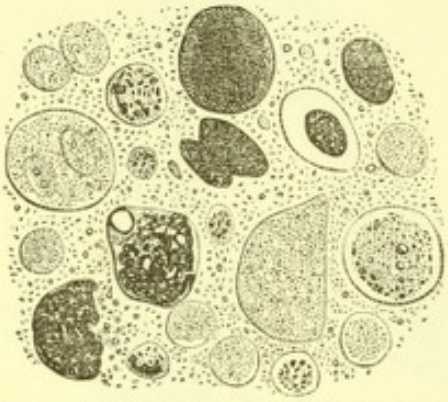
In the cases where the circulation is active the fat, already existing in the cells, disappears very readily, as frequently occurs in inflammation and in the emaciation of fevers.

G. Pigmentation of Elements and of Tissues.—By this phrase are understood extremely varied alterations which consist in the presence in the interior of cells and of tissues of red, yellow, brown, or black granules. They may be derived from without, ready formed, like the particles of vegetable carbon; they may come from the dissolved coloring matter of the blood, by infiltrating a cell and being precipitated there; or the pigment may be elaborated by the cell itself.

The penetration, from without, of minute particles of carbon is readily shown by the black pigmentation of the cells of the sputa when one breathes air charged with the fumes of a lamp. In the physiological conditions under which we live, the cells and the connective tissue of the lungs of every adult contain more or less of carbon. Not only do we see cells which are entirely formed of soft protoplasm containing foreign granules and little fragments, but also even those which are surrounded by a membrane; the penetration of the latter is explained by the extreme minuteness of the particles. The presence of foreign bodies in cells may

oftentimes be accounted for by assuming that they have been enveloped by a cellular formation. It is thus that Kölliker explains the large cells which, in the spleen, contain red blood disks. Foreign particles, for example carbon and the pigments used in tattooing, are usually arrested in the lymph glands belonging to the impregnated region.

Fig. 38.



Cellular structure of melanosis as seen in scrapings. (*Bennett.*)

Fig. 39.



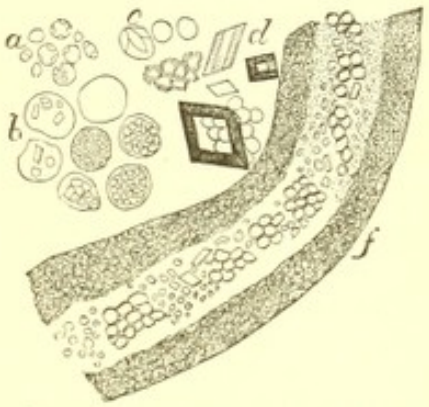
Cells containing pigment. From a melanotic sarcoma of the liver. × 350. (*Green.*)

The physiological pigmentation of cells by the coloring matter of the blood is easily seen in the spleen. Elements containing red, yellow, or black pigment occur normally in the splenic pulp. The coloring matter which enters into the composition of the bile and which is often found in small quantity physiologically in the hepatic cells, also probably comes from the coloring matter of the red blood disks which are destroyed in the liver by the biliary acids. The formation of the corpus luteum in the ovary after the discharge of the ovule and the hemorrhage into the Graafian follicle, is an example of the production of red pigment which may later change to black, when the body usually appears as a small slate-colored cicatrix. Whenever blood is extravasated the connective tissue cells, the epithelium, and usually all the surrounding cell elements are impregnated by a fluid which contains hæmatin in solution—a substance which, by precipitation, gives rise to crystals of hæmatoidin. When the elements die their coloring matter precipitates in a similar manner.

Pathologically, pigmentation was first carefully studied by Virchow, *à propos* of pulmonary hemorrhages. This author saw that the epithelial cells which at first had become spherical and pigmented by a colored fluid, soon showed in their interior yellow or red granules, which afterwards became more and more dark colored, like crystals of hæmatoidin. From this observation he was led to the hypothesis that the coloring matter of the blood, when given up by the corpuscles, first infiltrates the cells as a colored fluid. He admitted, however, the possibility that colored granules formed without the cells may subsequently penetrate into their interior. Pigment granules are well characterized by their color. Crystals of hæmatoidin are rhombohedræ, of a dark orange-red. In certain cases their dimensions are so great that their presence may be appreciated even by the naked eye ; at other times it requires the highest powers of the microscope for their recognition. (Fig. 40.)

In the normal state, the connective-tissue cells of the choroid, of the iris, of the pia mater, the epithelial cells of the choroid, and of the rete mucosum of the skin of the dark races, the muscle fibres of the heart and the nerve cells contain pigment granules which, *ab initio*, are brown, and are by that fact to be distinguished from those granules derived from the blood. They are entirely round, and are evenly diffused throughout the protoplasm of the cell; they may, however, also exist in small number in the nucleus, as may be seen in the mucous layer of the skin of negroes. Pigmentation in the colored races is somehow connected with a certain activity of the skin under the influence of the sun.

Fig. 40.



Crystals of hæmatoidin. *a*. Red disks, becoming granular and losing their color. *b*. Neuroglia cells, a few containing granular pigment and crystals. *d*. Crystals of hæmatoidin. *f*. Occluded vessel; its lumen is seen filled with red granular pigment and crystals. ×300.

As a pathological formation, this pigment seems to be a peculiar elaboration of the cells. It may appear at some distance far from the vessels, and may be black from the first. Its abnormal formation may take place at one time in the stable cells of the connective tissue, simple melanosis; at another, in newly formed cells, as in melanotic tumors, the sarcomata, or carcinomata.

H. Calcareous Infiltration.—The salts which form these infiltrations are the carbonates and the tribasic phosphates of lime. These salts are combined in calcareous deposits everywhere, except in the otoliths, which are solely composed of carbonate of lime. True osseous tissue should not be confounded with tissues infiltrated with lime salts. In the latter there is no real or permanent union with any principal, for when the salts have been removed by acid the original structure of the tissue may be perfectly seen, and there may be no approach to a regular bony tissue. The processes of true ossification, therefore, essentially differ from those of calcareous infiltration. In the latter, the calcareous salts deposited in the tissues are seen as isolated granules, as spherules with concentric layers, or in the form of a genuine petrifaction. The granules are round or angular and highly refractive. When they are minute and in large numbers, they cause a considerable opacity; on the contrary, when a complete petrifaction has occurred, the tissue appears semi-transparent, like aragonite. In the latter case, when a thin lamella is polished and placed under the microscope, the tissue is seen to be transparent and yellowish, and lacunar openings and granules may be demonstrated therein. The openings are the spaces which existed in the primitive structure. All acids more or less completely dissolve the calcareous salts while setting free bubbles of carbonic acid.

Physiologically, in the first phase of ossification calcareous granules are seen in the ground substance of cartilage; concretions or calcareous spheres with concentric layers are found in the choroid plexus of the adult, also often in the thymus gland during its retrogressive state, and in the

meninges of the brain and spinal marrow of the aged; petrifactions sometimes occur in the profound layer of adult cartilage in relation with the osseous tissue, and in the costal and laryngeal cartilages of the aged. Never does the deposit commence in the cell, but always around the latter in the intercellular or ground substance. Subsequently, the cells themselves may become invaded, but they usually escape for a very long time.

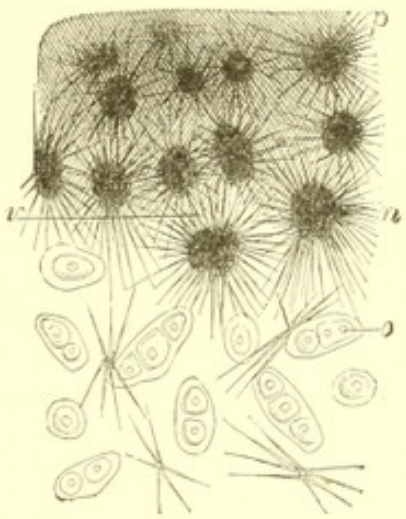
Pathologically, calcareous granules may be met with when a dead part remains for a long time in the midst of living tissue. An extra-uterine abdominal pregnancy of twenty years' standing, old infarctions, caseous masses, especially of the lymph glands, are familiar examples. Calcareous concretions are seen also in the secretions of the salivary glands, the acinous glands of the pharynx, of the pancreas, the follicular crypts of the intestines, in the synovial membranes, as well as in the interior of all cysts, particularly the colloid cysts of the thyroid gland and of the kidneys. In advanced stages of chronic inflammation, especially in endarteritis, often calcareous granules or petrified plaques are to be seen. This metamorphosis supervenes only when the inflammatory process has spent its force, or when the circulation of the fluids is much impeded. The products of chronic inflammations of the serous membranes have a peculiar tendency to calcareous incrustations, which were formerly regarded as true bone. In chronic myocarditis the muscular walls of the heart sometimes present concretions of the same nature. Blood-clots, wherever they may be, may undergo calcareous infiltration. Phleboliths, the concretions occasionally found in varices, have such an origin. In old age, around old fractures, and in the neighborhood of chronic arthritis, the tendons and even the muscles are sometimes the seat of a calcareous deposit of greater or lesser extent. In nearly all the tumors are frequently to be seen calcareous infiltrations, which should always be distinguished from true ossifications, which latter are rare under the same circumstances.

I. Infiltration of the Urates.—The presence of the urates in the solid state, under the form of granules and crystals, is met with physiologically only in the urine. In new-born children, however, very often we find in the straight tubes of the kidneys amorphous urates colored brick-red by the urinary pigment, and visible to the naked eye under the form of minute red lines. Here the deposit occurs in the epithelial cells of the kidney. Under the microscope the urates may appear as very fine granules massed together as a cloud, as refracting spherical grains, or under the form of needle-shaped crystals. The base may be magnesia or lime, but it is usually soda. The urates are decomposed even by the weakest acids, when the free uric acid may precipitate and form crystals which are at first rhombohedric, but which often soon assume the varied forms which uric acid shows by reason of its molecular dyssymmetry. Uric acid and the urates may concrete and form calculi in the urinary passages.

In gout the urates, under the form of granules or crystals, are deposited in the cartilages, the bones, the synovial membranes, the tendons, the skin, and the kidneys. In all cases the deposit first forms in the cells, which serve as centres whence radiate the free crystals. The latter

may penetrate into the neighboring fundamental or ground substance. The primary affection of the cells by the uratic infiltration proves that the cells play an active role here, and indicates that the process is essentially different from that of calcareous infiltration. (Fig. 41.)

Fig. 41.



Vertical section of an articular cartilage infiltrated by urate of soda, from a gouty patient. *p*. Articular surface of the cartilages. *v*, *n*. Amorphous and crystallized urate of soda. *o*. Capsules and cartilage cells. ×200.

J. Lesions Caused by an Excess of Nutrition of Cells and of Tissues.—When a continued and unusually abundant supply of nutritive material, especially in cases of irritation, reaches the cells, the following phenomena may be observed: the nucleus, which in certain cases was atrophied and scarcely visible, hypertrophies; the nucleolus becomes distinct; the protoplasm swells by absorption of fluid; the whole cell, which was lengthened, flat, or very irregular, tends to assume a globular form. This state differs from serous or albuminous infiltrations, which are, in some sort, passive processes, for in it the phenomena of excessive nutrition consist in a natural exaggerated activity of the cells, and they often precede the multiplication of cells.

The cells are physiologically in such a condition during the period of development. The cartilage cells around points of ossification become very voluminous. The muscle cells of the uterus, and muscular fasiculi of the heart hypertrophy during gestation; and the epithelial cells of the mammary gland become much larger towards the end of pregnancy.

The most marked examples of hypertrophy of the elements by excess of nutrition are those drawn from facts observed in the adult connective tissue. This tissue normally contains atrophied cells which, under the influence of a pathological irritation, soon show a voluminous nucleus and a protoplasm, granular and much augmented. Every irritated cell, in whatever tissue it may be located, presents analogous phenomena. Hypertrophy of cells from excess of nutrition leads us directly to the study of their pathological multiplication.

Sect. II.—Lesions in the Formation of Cells.

Cells alone are capable of multiplication; the intercellular or ground substance is not directly concerned in this phenomenon. To Virchow belongs the honor of having been the first to thoroughly appreciate the importance of the multiplication of the cellular elements in pathological processes. He distinguished two kinds of abnormal multiplication of cells: 1st, *simple hyperplasia*, wherein the elements of the new formation differ from their progenitors neither in form nor in function; 2d. *heteroplasia*, in which the elements differ from their progenitors, and

contribute to the formation of a new tissue. Hyperplasia and Heteroplasia, which Virchow regarded only as pathological conditions, may exist in the physiological state, as is seen for example in ossification.

In abnormal hyperplasia the multiplication of the cells is effected always in the same way: the nucleus swells; the nucleolus becomes more voluminous, constricts itself, and divides; the division of the nucleus may be effected by fission or by constriction; the nucleus then presents the form of a wallet, a biscuit, or an hour-glass (see figs. 5, 6), etc.; each newly formed nucleus is surrounded by a part of the protoplasm which itself divides by scission or strangulation. Thus is formed instead of a single cell two or more cellular elements. Never does the ground substance or the cell membrane participate in this division; but most frequently, on the contrary, these may soften or dissolve. At first the cell elements thus formed do not notably differ in appearance from embryonal cells, but they may very soon present characteristic forms. Before leaving this subject perhaps it may be well to reiterate again the general law, that the method of formation of elements of pathological new growths is identically the same as that for physiological formations.

When a cell proliferates, it gives birth to embryonal or indifferent cells. The latter, if the irritation cease or lessen, return to their former condition and form tissue similar to that whence they spring; if the irritation persist, and be intense, the structure of the original tissue is completely destroyed, the embryonal cells become incapable of constituting a definite tissue and form pus, or they organize into a tissue which has deviated from the primitive type.

CHAPTER III.

OF INFLAMMATION.

Sect. I.—Definition of Inflammation.

Redness, pain, heat, and swelling, as primary phenomena, followed by resolution or induration, suppuration or gangrene, have served from the most remote antiquity to specify the complex state understood as inflammation.

Taken singly, none of these signs belong exclusively to inflammation, for redness, pain, and heat may be caused by a passing nervous influence; tumefaction may be due to simple œdema; induration and tumefaction combined appertain also to tumors; gangrene may supervene wherever the vessels are obliterated. Even suppuration is not constant in inflammation; it exists often without any other phenomena, and the conditions of the formation of pus are so far from being understood that it is not yet known if every suppuration is necessarily due to inflammation. It is true that in typical cases where all these characters are found united, as in phlegmon, inflammation is very evident, but a good definition should comprehend every inflammatory state.

It is certain that the inflammation whose symptomatic ensemble we see in the clinic, consists essentially in an exalted nutrition and formation of anatomical elements. Its definition, the study of its intimate phenomena, should be drawn entirely from experimentation, since by the application of the simplest irritants to the tissues of a living animal we can see produced the same chain of symptoms which we recognize in the clinic as inflammatory.

We would define inflammation then, as *the series of phenomena observed in tissues and organs analogous to that which may be produced artificially in the same parts by the action of a physical or chemical irritating agent.*

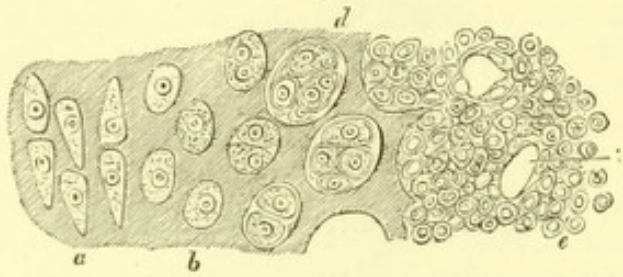
It is by the analysis of inflammation produced experimentally in animals, that we shall commence its study. The principal tissues which we shall pass in review will be, first, the non-vascular; second, the vascular.

Sect. II.—Traumatic Inflammation in Non-vascular Tissues.

If one takes for subject of experiment the permanent cartilages, and exposes a part of their surfaces, in a fortnight the latter will be covered over by a gray, pulpy layer. Let a thin section be made so as to include this layer and the cartilage beneath. The following will be observed. In the layer of cartilage most remote from the wound, the

cartilaginous capsules contain cells whose nuclei are easily rendered visible by a drop of picric acid (fig. 42, *a*). As we advance towards the

Fig. 42.



Section of inflamed cartilage. *a*. The normal cartilage-cells; *b*, the same enlarged. *d*. Multiplication of cells within their capsules; *e*, great increase in the number of the young cells, and destruction of the intercellular substance. × 250.

solution of continuity, the cell nucleus becomes larger, the protoplasm more voluminous. Soon this nutritive irritation is transformed into formative irritation, the nucleus divides and the surrounding protoplasm in its turn also may divide, in order to form around each nucleus a distinct mass. Each cell then excretes around it cartilaginous substance in order to form a new capsule. Up to this point, the irritation has changed neither the structure of the cartilage nor the property which its cells possess, of forming around them cartilaginous substance. This zone (fig. 42, *d*) of proliferation is more or less extensive. Further on, the surface of the cartilaginous substance is broken up into festoons; each of these excavations corresponds to a cartilaginous capsule which has opened; besides the latter, capsules may be seen, still closed, filled with embryonal elements which have lost the property of forming around them cartilaginous substance. The gray pulp which covers the solution of continuity, constitutes an embryonal tissue (fig. 42, *e*); in this tissue bloodvessels may develop (fig. 42, *i*); they come from neighboring parts. The embryonic tissue is formed at the expense of the cartilage, while at the same time it destroys the latter.

The *epithelia* also constitute a non-vascular tissue, usually reposing upon a membrane rich in vessels. The omentum, however, is an exception to this general rule. The fibrous trabeculæ of which the latter is composed vary greatly in thickness. The thickest only, contain adipose cells and vessels. The thinnest have no vessels, and are formed by a single fasciculus of connective tissue. All these trabeculæ are covered with a single layer of large endothelial cells whose form and constitution may be appreciated after the employment of impregnation by nitrate of silver (fig. 43). In the new-born, the omentum is not reticulated as it is in the adult, but forms a continuous membrane. It is in adult animals then, that the epithelium of the trabeculæ should be studied under the influence of irritation.

An artificial irritation is excited by injecting into the peritoneal cavity a few drops of a very weak solution of nitrate of silver or tincture of iodine. Twenty-four hours afterwards, the peritoneal fluid is cloudy and con-

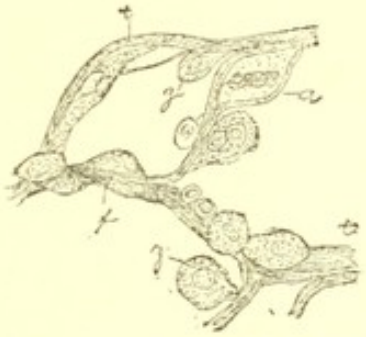
tains cell elements: some resembling pus corpuscles; others larger with one or more oval, sharp bordered nuclei; between these two kinds of cells exist intermediate forms.

Fig. 43.



Normal omentum, stained with nitrate of silver. × 250.

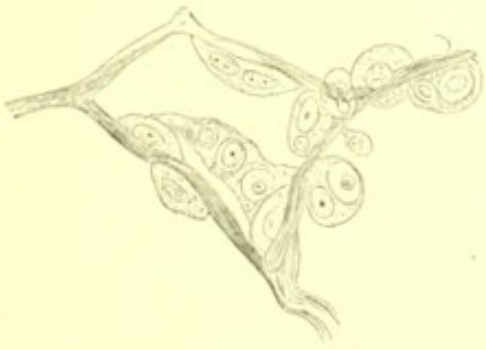
Fig. 44.



Omentum artificially inflamed and silver treated. *a*. Proliferating epithelial cell. *b*. Pus corpuscle. *g*. Endothelial cells, become spherical and prominent in process of detachment from the fibrous trabeculæ *t*. *f*. Swollen but still adherent endothelial cell. × 250.

The nitrate of silver informs us that the epithelial plates no longer entirely cover the trabeculæ of the great omentum. Sticking to these trabeculæ or between them, large, well-formed cells containing nuclei are found (figs. 44, 45). In these elements, all the phenomena of multiplication of cells are seen. Where the hypertrophied cells are adherent, now by a large surface, again only by a point, they form salient projec-

Fig. 45.



Omentum artificially inflamed and silver treated. It shows the epithelial cells in process of proliferation and in the act of detaching themselves from the trabeculæ. Pus cells are imbedded in the fibrin, and thus remain connected with the fibrous trabeculæ. × 250.

Fig. 46.



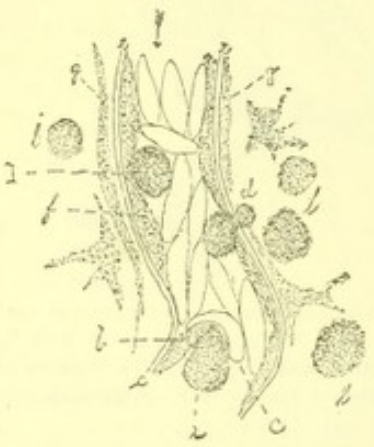
Omentum artificially inflamed and examined the eighth day after the operation: the endothelial cells have again become applied to the fibrous trabeculæ. Their protoplasm is less granular than in the preceding cases, and they form an almost complete epithelial investment. × 250.

tions upon the trabeculæ. They may become detached and continue to live and multiply. They possess no membrane, and have a soft granular protoplasm which is capable of taking the most varied forms and of giving birth to amœboid prolongations. The fibrinogenous substance exuded from the vessels, forms filaments of fibrin which surround the cellular elements and may for a certain time hold them in contact with

the trabeculæ. Pus, however, may be the final product of this new formation.

After five or six days, we may still find clumps of pus corpuscles or of other newly formed cells, floating in the peritoneal fluid; but generally the large swollen cells reapply themselves to the trabeculæ, flatten out, present a protoplasm less granular, and return to their primitive type (fig. 46). At this time one finds in the peritoneal cavity granular elements in a state of fatty degeneration, for these free elements in the peritoneal fluid are placed under conditions not very favorable to their life.

Fig. 47.



A capillary of the mesentery of a frog nine hours inflamed, showing detachment of an endothelial cell which is finally carried off by the blood-current. High power. *e*. Capillary walls. *l*. Leucocytes external to the walls. *f*. Capillary endothelia, granular and swollen with projecting bellies. *g*. Cells of adventitia, also swollen and granular. *a*, *d*, *i*. Colorless corpuscles adherent to the walls; *d* is rather firmly bound to the wall by means of a bud penetrating the latter; *i*, a corpuscle adherent to the point of union of two adjacent endothelial cells; *a*, a white corpuscle adhering tightly to the upper end of an endothelial cell *b*, which is partly pried out from its bed by the action of the red disks. The arrow indicates the direction of the current. (*Shakespeare.*)

We observe in these simple experimental facts two opposite orders of phenomena, due to the inflammatory process. The one consists in an exaggerated nutrition and a formative irritation of cells; the other in the death, by fatty degeneration, of the oldest cells. The first only properly appertains to inflammation, the other is explained by the fact that the cells are placed in conditions unfavorable to life.

Another conclusion follows these experiments. It is that bloodvessels are not necessary to the formation of pus corpuscles, and we may add that in these cases we have vainly sought for pus corpuscles disposed along the vessels in the trabeculæ which contain them.

[From a histogenic point of view, the blood and lymph vessels may be regarded as analogues of the serous cavities. The endothelial cells which line these vessels have a histogenetic origin identical with that of the cells which cover the serous surfaces, and they may be looked upon as transformed connective-tissue corpuscles. Instead, however, of receiving their nutrient supply and discharging their waste products through the mediation of the lymph, as do the connective-tissue cells covering the various serous surfaces and lying in the lymph spaces of the organism, the lining endothelia of the bloodvessels are directly laved by the plasma of the circulating blood. We have already seen that one very considerable source of the embryonal cells, so numerous in the tissues during irritation and inflammation, is to be found in the increased activity and proliferation of the connective-tissue corpuscles and their congeners.

Figure 47 explains an observation recorded by one of us,[1] which shows

[1] Lecture VII. The Toner Lectures. The Nature of Reparatory Inflammation in Arteries after Ligature, Acupressure, and Torsion. By Edward O. Shakespeare, A.M., M.D., delivered June 27, 1879. Washington, Smithsonian Institution.

that the endothelial lining of the capillary bloodvessels may experience alterations during inflammation similar to those above described for the cellular covering of the omentum. In artificially excited inflammation of the arteries the endothelial cells are affected in the same manner. In the paper already cited it was pointed out that the endothelial cells of the vessels should also be regarded as one of the sources of the colorless elements of the blood present during inflammation.

Since what we know of inflammation warrants the belief that the various physiological processes are only faint prototypes of the inflammatory process, it seems justifiable to draw the inference that, like the connective-tissue cells elsewhere, the endothelia of the vessels, particularly those which convey oxygen, may give origin physiologically to some of the white corpuscles of the blood and lymph.

The endothelia of the vessels are probably the main source of the large, granular, colorless cells which have of late years been found occasionally in the blood of typhoid fever, of relapsing fever, etc.]

Sect. III.—Artificial Irritation of Vascular Tissues.

Osseous tissue is very easily studied in inflammation. The osseous trabeculæ limit spaces in which the vascular tissue, the marrow, is the seat of almost every nutritive or formative lesion.

Let us suppose an artificial irritation of a short bone, or the extremity of a long one.

There is at first a formation of embryonal tissue at the expense of the subperiosteal medullary cells and of the cells contained in the medullary spaces. Normally, the medullary cells are free, are not inclosed in a fundamental or ground substance. Some are small (medulla cells); others are large, with one or many ovoid nuclei (myéloplaxes or giant cells). Besides these, there exist large adipose cells and fusiform or stellate elements. It is from all these different elements that the embryonal cells are derived.

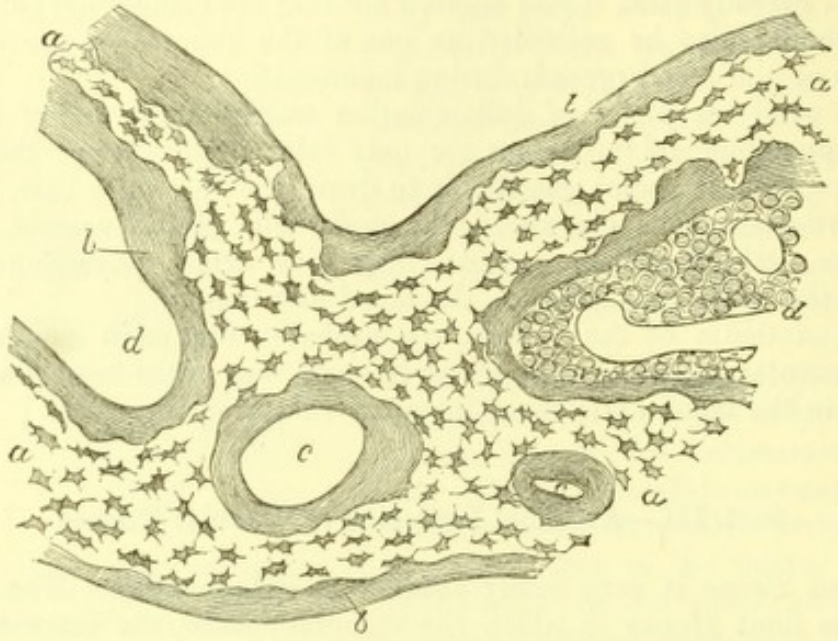
In the adipose vesicles of the irritated bone marrow, the nucleus first hypertrophies, then divides; the swollen protoplasm surrounds each nucleus; at the same time the fat disappears and is replaced by an albuminoid fluid. These new elements multiply and finally completely fill the vesicle; then its membrane is destroyed or ruptured and the contained embryonal cells become free.

The medulla cells assume the character of embryonal cells, to which they are so nearly related, and multiply. If the irritation continues, the osseous lamellæ adjacent to the medullary tissue are absorbed, and each bone cell falls into the medullary cavity. Thus the medullary cavity enlarges and is filled with embryonal cells, and the osseous trabeculæ melt away under the process of absorption. (See fig. 48.)

During this time the capillary vessels undergo very important modifications. The cells which form their walls swell, their nuclei become more apparent, so that on transverse section one might believe the walls to be made of fusiform bodies analogous to the fibro-plastic cells of Lebert; these cells then form projections into the lumen of the vessel

and may impede the circulation (see fig. 49, *f*). The blood is coagulated by chromic or picric acid, used in hardening the tissue, the red and

Fig. 48.



Softening of bone. Spicula of bone from the spongy substance of an osteo-malacic rib. *a*. Normal osseous tissue. *b*. Decalcified osseous tissue. *c*. Haversian canal. *d*. Medullary spaces. The space to the right is filled with red medullary tissue, in which the lumina of the capillaries are open. × 300. (*Rindfleisch.*)

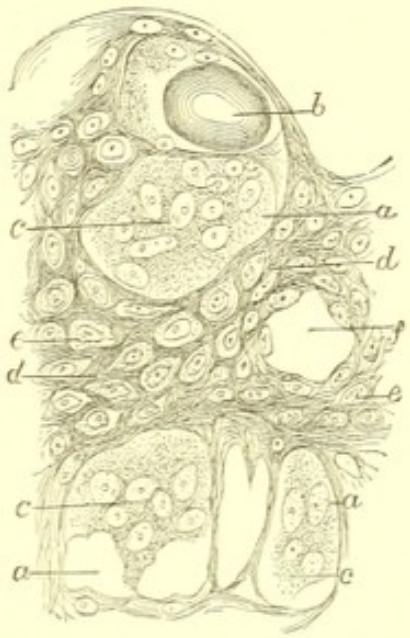
white corpuscles being easily distinguished in the lumen of the vessel. But the white corpuscles do not form a continuous layer, as they should according to the theory of Cohnheim, which will soon be noticed.

In the *subcutaneous cellular tissue* similar phenomena take place under the influence of artificial irritation. This tissue contains plasmatic cells placed in and upon the fasciculi of connective fibres, besides some adipose vesicles and lymph cells. The connective-tissue corpuscles (plasmatic cells) at first hypertrophy to such an extent that the shrunken and thinned nucleus becomes globular, and the protoplasm becomes granular and very apparent (fig. 49, *e*). After a few hours, the nucleus and the protoplasm divide, whence two or more embryonal cells appear in the lymph spaces of the tissue, arranged into elongated islands or chains of cells, pressed against each other, and limited by the parallel fibres. In the adipose vesicles the protoplasm becomes visible, the nucleus divides as in medullary tissue, and the fat disappears. By the continuance of the proliferation each fat vesicle is replaced by a little nest of embryonal cells (fig. 49, *c*). Proliferation of adipose cells is not effected as rapidly as that of the connective-tissue corpuscles. The former may consequently often be seen in the midst of embryonal tissue for some time after the commencement of inflammation.

While the cellular elements are the theatre of the preceding changes, the fundamental fibrous substance of the connective tissue imbibes the fluids, the fibrils become less distinct, and may finally disappear entirely by a complete absorption. According to Rindfleisch, they undergo a

mucous transformation. However this may be, they are converted into a soft and amorphous substance. The secondary membrane of cells of the connective tissue, if it exist, disappears by absorption, and the embryonal cells become free in the midst of an amorphous mass. The elastic fibres experience changes somewhat similar to those of the connective-tissue fibres: they break into fragments and become reduced to fine molecules, which in their turn entirely disappear. The vessels present the same alterations as were seen in the bony marrow; there is an evident multiplication of the nuclei of their cells.

Fig. 49.



Adipose tissue, from a deep wound in a dog, in progress of healing. *a*, Spaces left by the absorption of the fat vesicles *b*; they are found filled with newly formed nuclei *c*, surrounded with granular protoplasm. *e*, Embryonic cells. *f*, Section of a vessel which has embryonic walls.

The different inflammatory phenomena which we have just described are the most important, for they are seen in the non-vascular as well as in the vascular tissues. Nevertheless, for a long time the circulation has been believed to play an immense *rôle* in inflammation, a *rôle* which Cohnheim by his recent experiments has reaffirmed, while adding facts which up to that time had scarcely been suspected.

Kaltenbrünner and Wharton Jones had studied the phenomena of irritation upon the interdigital membranes and the tongue of the frog, and upon the wings of the bat. They saw the vessels first contract, afterwards relax, and subsequently blood stasis take place, but they did not follow inflammation beyond its first stage. We have already seen that proliferation and the formation of embryonal tissue are essential parts of the inflammatory process.

Aug. Waller, of London, in 1846, was the first to publish an observation of the diapedesis of the elements of the blood. His statements were overlooked. Subsequently Cohnheim, apparently without any knowledge of the opinions of Waller, instituted a series of experiments, mainly upon the cornea and mesentery of frogs, which tended to establish in an indubitable manner the emigration of white blood-corpuscles from the lumen of the bloodvessels, and to explain suppuration by their escape in immense numbers into the tissue involved. Cohnheim commenced at first by curarizing the frog, claiming that curara had no action upon the circulation. This claim must be denied, for the poison determines at first a contraction, then a dilatation of the small arteries. This procedure, then, is not entirely free from a first cause of error. The abdominal wall was incised, a loop of intestine withdrawn very gently and spread upon a glass slide, so that the mesentery, when placed under the microscope, showed very distinctly its arteries, veins, and capillaries. The action of the air, the traction, or the contact of needles amply supplied the necessary irritation of the membrane. Cohnheim observed: 1st, a moniliform contraction of the small arteries; 2d, three-quarters of

an hour to an hour after the commencement of the experiment the veins also contract, the circulation is retarded, there is stasis in the capillaries, when the red globules can be distinguished and even counted in their passage along the larger vessels. We know that the inner surface of the small veins is covered by an adhesive layer containing white globules which remain more or less motionless. In inflammation these white cells become more numerous and present amœboid movements. While repeating these experiments, we have been struck by seeing the amœboid prolongations produced only on one side of the globule. The mechanism of this peculiar deformity can be readily observed: when the white corpuscles remain in the adhesive layer, they fix themselves upon the wall of the vessel, while the flowing blood bends them and lengthens them out; if now, under the action of the circulatory movement, they become detached, we see the portion which was adherent present the form of a nipple covered with spines. These corpuscles accumulate in the dilated veins. Up to this point we have ourselves been able to confirm all these phenomena. According to Cohnheim, and many other accurate observers, many of the cells finally pass through the walls and escape into the surrounding tissue.

The manner of escape of the corpuscles of the blood is still doubtful. Cohnheim believes that they go out through stomata between the endothelia. He assimilates the remaining tunics of the vessel to connective tissue in which there are networks of lymph channels and spaces, and he conceives that the escaping cells work their way along these until they pass beyond the wall. The same phenomena appear also in the capillaries.

The red globules also may escape from the vessels. We have observed the passage of the red disks through the walls of the capillaries in the web of the frog's foot. Some authors consider the phenomenon to be physiological. It is a fact that almost all mammiferæ have red disks in their lymph vessels connecting the lymphatic radicles and the lymph glands. These globules have very probably escaped from the bloodvessels. The red globules which have escaped from the bloodvessels are often constricted, mammillated, or fragmented. Their color, their refraction, and their sensibility to reagents, contribute to the determination of their nature. Such altered globules are found in most inflammatory exudations.

The facts advanced by Cohnheim do not conflict in any manner with those which we have described *à propos* of inflammation of cartilage, bone, and connective tissue. The theory of Cohnheim does not appear to us to apply to alterations of inflamed cartilage, because, among other reasons, the phenomena of proliferation therein take place within the interior of each capsule, which, so far as we know, is a closed cavity. Nevertheless, Cohnheim would explain the suppuration even of non-vascular tissues by a migration of the white corpuscles, taking as an example the cornea. In examining the inflamed cornea of frogs in the moist chamber of the microscope, Recklinghausen saw the cells of the lymph spaces increase in number, and slowly move along the canals from one space to another, in order to accumulate as embryonal cells or pus corpuscles at the surface of the cornea.

Cohnheim repeated these experiments, and formed the hypothesis that

these elements come, not from the so-called corneal corpuscles, but from the white corpuscles of the blood. To demonstrate this he injected into the blood of the frog a fluid containing in suspension extremely fine particles of aniline blue; he found that in the cases where the cornea had been already artificially inflamed, the new cellular elements contained blue granules; in these cases a certain number of the white corpuscles within the bloodvessels presented molecules of aniline (these corpuscles are in reality penetrated by granules in a manner similar to the penetration of amœbæ). He concluded from this that the colored white corpuscles found in suppurations were originally nothing else than the white corpuscles of the blood.

This conclusion does not appear to us sufficiently rigorous. After irritation, the cornea may become infiltrated by a large quantity of fluid from the blood. This fluid, holding in suspension the colored particles of aniline, comes in contact with the various cells of the cornea; the granules may then penetrate them directly. Thus, it is possible to set up, in place of the theory of Cohnheim, the hypothesis of the direct penetration of the particles of aniline into pus corpuscles which may be generated in the cornea. Without wishing to deny the theory of Cohnheim, we hold merely that his experiments may be interpreted by another hypothesis, and that upon a question so important it is well to withhold a positive conclusion. Moreover, it has been demonstrated that in irritation of the cornea the plasmatic cells, or so-called corneal corpuscles, proliferate, bud, and multiply by division.

[As early as 1819, the diapedesis of the white corpuscles of the blood had been observed by Döllinger. This observation was subsequently made by at least seven other investigators before Cohnheim's so-called discovery in 1867 of the passage through the walls of the bloodvessels of the white corpuscles of the blood, and the construction of his theory of inflammation and of the formation of pus. Among those who have confirmed Cohnheim's investigations by observations of their own, perhaps Axel Key and Wallis have made the most important studies. On the other hand, the most competent and reliable observers testify in the most positive terms to the multiplication, under irritation, of the nucleus, and finally of the cellular protoplasm of the various so-called fix cells, including the endothelia, the epithelia, the connective-tissue corpuscles, the bone cells, the cartilage cells, the muscle fibres, and the nerve cells. In this category may be mentioned the names of Stricker and Norris, Oser, Kremiansky, Durante, Kundrat, Lang, Rindfleisch, Hutob, Klein and Burdon-Sanderson, Scwergger-Seidel, Flemming, Köster, Baumgarten, Tschausoff, Chapman, etc.]

Now that we have briefly studied the phenomena of inflammation excited experimentally, we may commence the study of inflammation in man.

Sect. IV.—Analytical Examination of Inflammation in Man.

Inflammation offers for study *hyperæmia or inflammatory congestion, exudations, new formations, and inflammatory degenerations.*

1. Hyperæmia or Inflammatory Congestion.—When hyperæmia has been only of short duration, it disappears after death so completely

as to leave no trace behind. But, if it has been intense, if it has lasted a certain time, the capillaries show *post mortem* a fulness. The vessels are distended in the form of cylinders or into fusiform or ampullar dilatations. Inflammatory redness has been explained by the distension of the vessels. This opinion is most generally adopted to-day. It is probable, however, that there should be added to this cause the fact demonstrated by Estor and St. Pierre, that the congested vessels contain a larger proportion of arterial blood, as well as the fact that there is often some diffusion into the tissues of the coloring matter of the blood. The epithelium and connective-tissue cells of the hyperæmic parts often present a color at first yellowish or reddish, and occasionally contain pigment granules which become more and more black. The latter state of the cells is one of the causes of the slaty color of cicatrices of serous membranes.

2. Inflammatory Exudations.—A. *Serous exudations.*—The existence of fluid exudations containing only dissolved albumen has been assumed rather than chemically demonstrated. In reality, these fluids almost always contain variable quantities of fibrinogenous matter, of fibrin, or of mucus, according to the part affected.

B. *Mucous exudations* are met with wherever mucus is produced in the normal state. They contain filaments of precipitated mucin, which acetic acid does not cause to disappear. This reagent at the same time causes the appearance of a granular precipitate. Mucous filaments may form thick layers upon the surface of articular cartilages, notably in the case of white swellings.

C. *Fibrinous exudations* do not escape from the vessels in the shape of coagulated fibrin. Denys de Commercy believes that the fibrinous substance exists in the blood at first in solution, and in exudations in the state of dissolved plasmin, and that this plasmin coagulates into fibrin under the influence of a substance acting as a ferment. Under different terms, Alexander Schmidt has advanced a similar idea. He considers that there exists a substance which he calls *fibrinogen* held in solution, but which possesses the property of coagulating when it comes into contact and combines with another albuminoid substance which he calls *fibrino-plastin.*

The globulin contained in the red blood disks is a fibrino-plastic substance, but all the tissues, the cells in particular, contain it and may consequently effect the coagulation of the fibrinogenous substance.

Under the influence of an intense inflammatory congestion, the fibrinogenous matter escapes from the vessels and coagulates by uniting with the fibrino-plastic substance derived from the cells. The coagulation takes place suddenly and in successive layers, the exudat in contact with the tissues alone coagulating. Exudations in closed cavities, for example the pleural, may almost entirely consist of coagulated fibrin. If these exudations are drawn off, however serous they may be, they soon coagulate, from contact with fibrinoplastic substances. Very thick layers of fibrin covering the thoracic walls are thus often formed. Schmidt assigns to the fibrinogenous substance a very considerable office in inflammation.

Fibrinous exudations have a limited duration. Whether disposed in

filaments or membranous layers they soon undergo a change; first fibrillar, then granular, they finally suffer a complete molecular disintegration. It is not demonstrated that they are susceptible of a higher organization.

D. *Hemorrhagic Exudations.*—Even in the simplest inflammation, for instance coryza, red blood disks escape from the vessels and mix with the exuded fluid, sometimes in considerable quantities, at others in numbers scarcely appreciable by the microscope. In inflammation of the subcutaneous cellular tissue, at the commencement there is always blood mixed with the young cells. Its presence may give to the exuded fluid a color more or less dark. The globules may burst or the coloring matter may otherwise escape into the fluid and be imbibed by the neighboring elements.

E. *Exudations, composed of Fibrin and coagulated Mucin, inclosing Cellular Elements (Croupous Exudation of German authors).*—The phrase "croupous exudation" is applied to exudations deposited upon diseased surfaces in the form of membranes. This exudation consists of cell elements differing according to the part affected, but it also always contains filaments of fibrin, and sometimes mucin and entangled pus corpuscles. These filaments form a network in the meshes of which are found cell elements, epithelium, pus corpuscles. This exudation is met with especially in serous inflammations and in acute croupous pneumonia. German authors still confound these fibrinous exudations with the false membranes of true croup, or the pseudo-diphtheritic membranes of French authors.

Fig. 50.

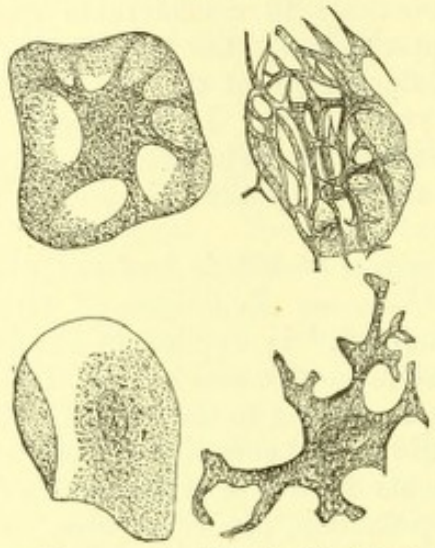


Lymph corpuscles and filaments of fibrin in a fibrinous exudation upon the pleura; *a*, the corpuscles unchanged by acetic acid. (*Gross.*)

F. *Diphtheritic and Pseudo-membranous Exudations.*—Whilst fibrinous exudations persist after death, the false membranes of true croup, on the contrary, have almost entirely disappeared by the time the autopsy is made, or they constitute merely a pultaceous layer very different from that which is seen during life. According to E. Wagner, these false membranes are not composed of fibrin, but of epithelial cells united together, yet easy to separate. After treating these false membranes with a weak solution of carmine, Wagner saw them resolve into blocks, angular and refracting, or into branching elements, interlacing with one another. He has described numerous prolongations of these elements, which he compares to stags' horns, and he has seen all intermediate stages between these and epithelial cells. In acquiring these strange forms the cells become infiltrated with an albuminoid substance, lose little by little their nuclei and their membrane, become transformed into homogeneous masses which present numerous ramifications. Wagner admits the fibrinous degeneration of the cells. These altered epithelial cells, transformed into homogeneous blocks with prolonged ramifications, form in the pharynx whitish layers, thick, opaque, and of a fibrinous appearance, beneath which pus corpuscles and hemorrhagic exudations are often met with. It is the

latter which form the reddish ecchymotic islands seen in the deep layer of these false membranes. In the larynx there are always many superimposed layers of these epithelial membranes (fig. 51). We have veri-

Fig. 51.



Fibrinous degeneration of pavement epithelial cells. High power. (*E. Wagner.*)

fied the exactness of the description given by Wagner, but we would conclude that the cells are filled with a material which approaches mucin rather than fibrin. These exudations of true croup become detached and thrown off in proportion as pus or new epithelial cells form below them.

3. Inflammatory New Formations.—Under the influence of a slight irritation, there occurs a simple *hyperplasia* of the elements. If the inflammation is more intense, the ancient tissue is transformed into embryonic tissue; this is what we call an *inflammatory heteroplasia.*

In man inflammation accords with what we have learned from the experimental study of inflammation in the lower animals. The process evolves in the following order: *hypertrophy of the nucleus; increase, then division of the protoplasm; destruction of the enveloping membrane of the cell; destruction of the fibrous or of the fundamental substance; production of embryonal tissue; formation of new vessels.* At this juncture we shall consider only suppuration, formation of vessels, granulation tissue, cicatrization, and the degenerations consecutive to inflammation. These degenerations take place when the embryonal tissue proliferates with very great activity, and the cells multiply and accumulate, with a corresponding supply of new vessels.

A. *Suppuration. Pus Corpuscles.*—Embryonal cells have a nucleus round or oval. If the division of the nucleus and the nutritive supply is well effected, one cell regularly gives birth to two others; if hyperplasia is active, one finds a few cells with several nuclei. If, however, the nutritive materials cease to be supplied, the division of the nucleus continues to take place, but the cell no longer divides. The cell then contains two to five small nuclei. Such cells are pus corpuscles. They

differ from embryonal cells only by the number and atrophy of their nuclei. In pus recently formed, besides these pus corpuscles, cells are constantly found with only one nucleus. These are embryonal cells. Pus corpuscles are, then, nothing else than embryonal cells with a small amount of vitality. This atrophy of the nuclei is constant in all elements which die or are eliminated. Pus corpuscles may exist in a tissue in large numbers without their presence being revealed to the naked eye by the physical characters of the liquid called pus. Granulation tissue, mucus, and the secretion of serous membranes normally contain them in greater or lesser numbers.

The puriform appearance of a liquid is due to the fact that great numbers of small solid corpuscles float free in it. Thus the cream from milk is opaque like pus, because it holds in suspension many fatty corpuscles: examples could be multiplied. The intestinal mucus may contain in suspension only epithelial cells, and yet to the naked eye absolutely resemble pus.

The following are the physical and chemical characters of pus corpuscles: They present no cellular membrane. When fresh, they appear as a finely granular mass, irregular in outline, often having amœboid movements (fig. 52). Their nuclei are not at first visible, but when a drop of water is added they swell from .008 to .009 mm., which is their normal diameter, to .011 or .012 mm.; they become spherical and show very distinctly, especially after coloration in carmine, from 2 to 4 or 5 nuclei from .002 to .003 mm. in diameter. These nuclei usually have no nucleoli; nevertheless, in some there exists a refracting point, which Foerster calls a punctiform nucleolus. These nuclei resist the action of

Fig. 52.



Pus cells: *a*, from a granulating wound; *b*, from an abscess of cellular tissue; *c*, the same treated with dilute acetic acid; *d*, from a bone fistula (necrosis); *e*, migrating cells. (*Rindfleisch.*)

Fig. 53.



Pus corpuscles: 1, *a*, *b*, in water; *c*, *d*, *e*, after the action of acetic acid; 2, division of nuclei. (*Virchow.*)

acetic acid, whilst, under the influence of this reagent, the cell becomes spherical, pale, and remains for some time limited by a very thin border, which finally disappears in its turn (fig. 53). Pus corpuscles do not differ, then, from certain white corpuscles of the blood.

Theory of the Formation of Pus.—According to an old opinion of Zimmermann, pus escaped directly from the vessels. Cohnheim affirmed this opinion while bringing to its support the experiments which we have previously described. But is pus always thus formed? We have to some extent proved the contrary. The epithelium, for example of the serous or mucous membranes, under irritation divides and forms new cells,

which themselves may divide, and so on *ad infinitum*. When in these smallest cells the nucleus divides without division of the cell following, we have pus corpuscles. So also of the cells of connective tissue (see p. 55 *et seq.*), and of adipose cells. Hence we admit two modes of the formation of pus: 1st, by the proliferation of cellular elements; 2d, by the escape of white blood globules from the bloodvessels.

Pus is very easily changed; it undergoes, according to its age and the influence of the parts with which it is in contact, many modifications.

Fatty degeneration of pus corpuscles occurs whenever the pus is old. In the interior of the corpuscles, then, there exist fine, fatty refracting granules, five to ten in each, and acetic acid does not modify them. When the disintegration is more complete, the corpuscles become distended with granules; they appear as dark masses under a low magnifying power, measuring .015 to .020 mm.; these are what are called the corpuscles of Gluge. These corpuscles of Gluge (see fig. 35, p. 48) do not always come from pus corpuscles; for example, those of the brain in cerebral softening, and those of atheromatous foci of the aorta are considered to be mere agglomerations of fatty granules.

Caseous transformation of pus corpuscles has already been mentioned. In this condition the corpuscles are no longer acted upon either by water or acetic acid.

Pigmentary infiltration of pus corpuscles happens when considerable extravasations of blood accompany the suppuration.

Calcareous transformation of pus corpuscles takes place in very old purulent foci; and in gout the pus corpuscles frequently contain acicular *crystals of urate of soda*.

The *serous acid transformation of pus* is seen in abscesses in bone. The pus then contains lactic acid, under the influence of whichthe corpuscles swell, the protoplasm dissolves, and the nuclei become free. It is this serous appearance, well known among surgeons, by which they recognize at first sight a bone abscess. The same dissolution of pus corpuscles takes place when it contains a large proportion of water.

B. *New Formation of Vessels in Inflammation*.—Whenever inflammation occurs in a vascular tissue morbid phenomena take place in the vessels which may end in the formation of new branches. These inflammatory new formations of vessels serve as a key for the understanding of what happens in tumors, and are so much the more interesting since their mode of production is very uniform.

Under irritation, the cells which constitute the capillary walls swell and soften; if the inflammation continues the nuclei of the capillaries multiply. These phenomena are the same as those already described for the endothelial cells in peritonitis artificially excited. In inflamed tissues the vessels return to their embryonal condition, that is to say, they are formed of embryonal cells disposed in rows, and having at the centre a canal through which the blood circulates (see fig. 49, *f*). The softened wall may easily become distended or ruptured by the blood pressure. How do these altered capillaries become the point of departure of new vessels? There are several types of new formation of vessels: a capillary loop may enlarge and present a more lengthened curve; or the convex part of a capillary loop may send out prolongations which are

channelled by the blood and bounded by embryonal cells, according to the manner suggested by Wiwodzoff. According to Rindfleisch, certain cells in exudations upon serous membranes lengthen and become disposed in parallel rows, between which the blood from a neighboring capillary penetrates. Finally, in this embryonal tissue, as Meyer and Plattner have indicated, we may also see capillaries arising from plasmatic cells following the process described by Kölliker for the embryonal state. These cells and their anastomosing prolongations become hollowed out or channelled, the channels are widened by penetration of the blood globules, and nucleated cells become applied to the wall.

C. *Granulation tissue.*—Granulations which by their union constitute a so-called pyogenic membrane develop most frequently upon wounds or inflamed surfaces communicating with the exterior. It is a general physiological law among the superior animals, that the external and a part of the internal covering everywhere present papillæ which are nothing else than small permanent granulations. Likewise in the pathological state, every new formation projecting upon a surface, takes this papillary form.

The granulations arising from inflammation consist of embryonal tissue; they are of somewhat slow formation, for a considerable mass of embryonal tissue and of newly-formed vessels are necessary for their constitution. Granulations furnish the key of the process of cicatrization of wounds. The size of granulations is extremely variable.

Fig. 54.



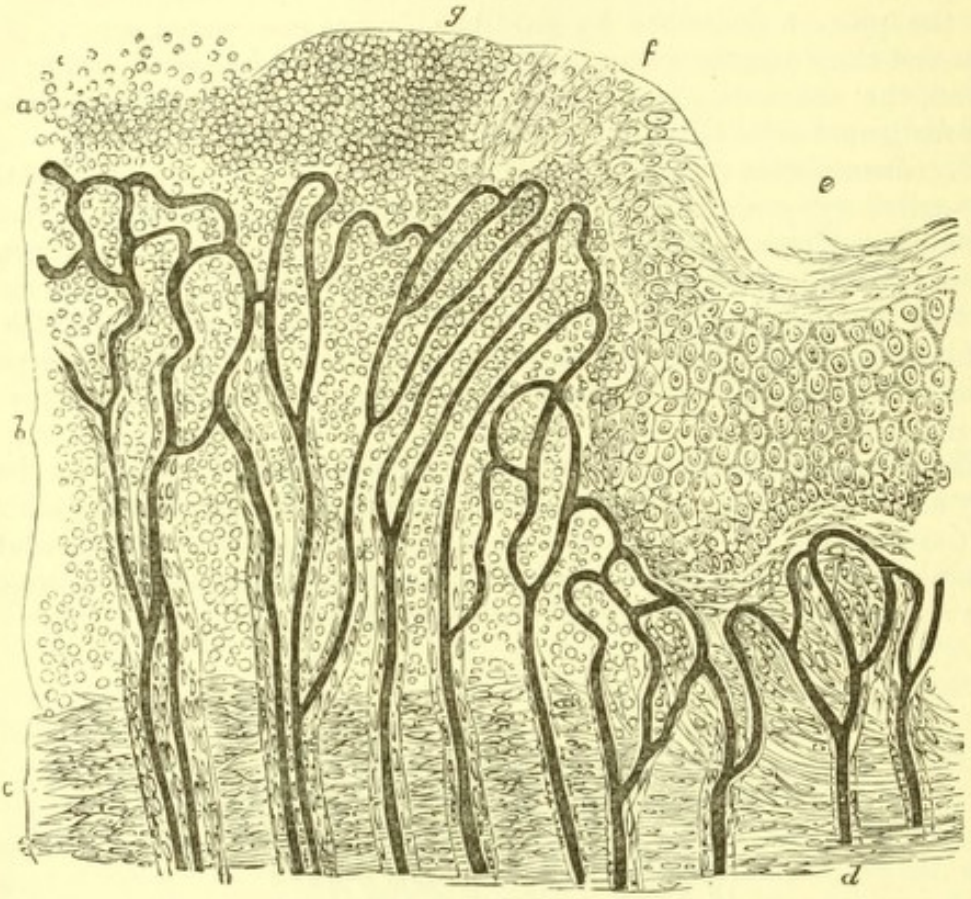
Blood-vessels in granulations. × 40. (*Billroth.*)

They are generally simple, but they may be compound; the latter, much the more voluminous, present at their surface a series of secondary granulations. The structure of simple granulations consists at first of spherical or polygonal embryonal cells, some of which have a very distinct nucleus of .005 to .006 mm., others have several very small nuclei. Among these elements capillaries are formed in an embryonal condition. This initial stage does not usually last long. Soon a certain number of the embryonal cells change their form, become angular, send out prolongations, and unite by anastomoses of the latter, thus constituting a network of plasmatic cells. The meshes of this network are filled with amorphous fundamental substance in the midst of which remain imprisoned the round cells which are distinct from the network of the connective tissue cells.

Of the cells embedded in the fundamental or so-called cement substance, some are embryonal cells with a single nucleus, others are cells with

several nuclei or pus corpuscles. In bones, granulations contain in addition some giant cells with multiple nuclei (see fig. 5). In many of the elements which are obtained by scraping granulation tissue, amœboid movements are visible. The quantity of pus corpuscles is variable,

Fig. 55.



Section through the border of a healing surface of granulations. *a*. Secretion of pus. *b*. Granulation tissue, with capillary loops, whose walls consist of a longitudinal layer of cells decreasing in thickness from within outwards. *c*. Beginning of the cicatricial formation in the deep layers (spindle-cell tissue). *d*. Cicatricial tissue. *e*. Complete epithelial covering; the central layer of cells consist of serrated cells. *f*. Young epithelial cells. *g*. Zone of differentiation. × 300. (*Rindfleisch.*)

being generally greatest at the beginning. It also varies according to the general and local pathological condition of the patient. Generally when the granulations are healthy they are reddish and contain few pus corpuscles, when they are unhealthy they are usually puffy and gray and inclose a large number of pus corpuscles. In the proportion that the granulations contain pus, to make use of an old expression, they secrete it on the surface. How do the pus corpuscles reach the surface? Are they simply produced there, or have they wandered from the depths of the tissue? Up to the present time we have no direct proof of this migration; but the pus is sometimes so abundant in a short time as to lead to the supposition that at least very many of the elements come from the interior, either by aid of their amœboid movements, or by the influence of a current in the fluid which tends toward the surface and which the capillaries may possibly establish in the granulation. As evidence of the possibility of the latter, we know that after actively

irritating a flesh wound we may see some colored drops exude from the surface; in this fluid numbers of pus corpuscles exist which have evidently been washed out of the tissue. Neighboring granulations unite and their vessels communicate. As cicatrization advances pus is no longer formed in the interior of the granulation. The cement substance of the granulation tissue condenses, the embryonal cells become spindle form, fibres of connective tissue are developed, finally the newly-formed fibrous tissue by virtue of its continued contraction gradually lessens and almost disappears.

D. *Cicatrization or Healing of Wounds.*—A wound may heal by first or second or even by the third intention. Cicatrization consists essentially in all cases, in the formation between the lips of the wound of an embryonal tissue which subsequently becomes converted into adult tissue. A solution of continuity gives rise to hemorrhage from the divided vessels, which is soon arrested. The extravasated blood coagulates as does also the blood in the capillaries opening upon the solution of continuity. The coagulation in the latter extends as far as the first collateral capillaries. The blood continues to circulate in that part of the vascular net which remains permeable. The borders of the wound undergo a formative irritation which ends in the filling up of the loss of substance with embryonal tissue. The permeable capillaries in the neighborhood of the cut surface present the changes which we have already indicated for these inflammations, proliferation of their cells and softening of their walls. New capillary loops coming from the old modified vessels advance their convexities toward similar loops from the opposite side. If the surfaces of the wound are maintained in contact a vascular communication is established by the union of loops from opposite sides. Then the solution of continuity is filled up by a small quantity of embryonal tissue, the cells become stellate, anastomose and form a network; the cement or intercellular substance soft at first soon becomes fibrillar and as resistant as the old tissues. Such is union by first intention. However rapid the union may be, it is not so simple as some authors have thought.

In union by second intention, granulations begin to vegetate upon the surfaces which cannot be kept united. From the sixth to the eighth day they constitute a membrane composed of granulation tissue, the vessels of one granulation anastomosing with those of the neighboring bud. As cicatrization progresses the embryonal tissue becomes transformed into connective tissue, as in the previous case. The mode of healing is really the same in the two cases, only, in the second, cicatrization is slower, and the tissue may experience the divers accidents incident to suppurating wounds.

Union by third intention differs from the preceding only in the depth to which the tissues are divided, in the greater difficulty and slowness of union. Cicatrices of inflammatory tissues have very diverse issues. In the skin the cicatrix is composed of fibrous tissue in which fat vesicles soon appear in the deep layers, but never in such numbers as in the normal state, moreover the fibrous tissue is always very dense. The fibrous and elastic tissues of the skin are reformed and the papillæ may be more or less perfectly reconstructed, but never so the glands. In many cases of destruction of the derm, as in variolous pustules and syphi-

litic ulcers, where the papillæ have been destroyed by the suppuration, they are not perfectly regenerated, and the resulting cicatrix remains smooth and depressed. The epidermis reforms. Do its cells come from the neighboring epiderm, or do they form independently at the surface of the granulation? Both modes appear to us to be proved, for, if in a wound undergoing repair, the new epithelial covering most frequently starts from the old epidermis and is developed from the periphery towards the centre, nevertheless islands of epithelium also form without any direct connection with the old epidermis. [According to Billroth, it is only when a remnant of the rete Malpighii remains that islands of epithelium form upon granulating surfaces.] These new epidermal cells may be the transformed embryonal cells of the superficial layer of the granulative tissue. The epiderm of cicatrices is always thinner and more subject to desquamation than is that of the neighboring tissues.

Bony cicatrices will be studied *à propos* of bone. Cicatrization of nerves will be discussed with the diseases of the peripheral nervous system. To formulate the general law which presides over the ulterior transformations of inflamed tissue: *Whenever artificial or pathological irritation has determined a growth of embryonal elements, if the irritation cease this new growth always tends to return to the original form of the tissue which served as a matrix.* This tendency is especially noticeable in irritation of osseous tissue, when very frequently hyperostoses and exostoses result. Another still more important law has relation to the seat of the new embryonal tissue at the time of its alteration into a permanent tissue. *Whatever may be the origin of the embryonal tissue it has a tendency to reproduce the tissue of the region where it is seated.* Thus when a bone of a young person is extirpated the embryonal tissue which replaces it helps to build up a piece of bone similar to that which is removed; *vice versâ*, there are cases where fragments of cartilage or of bone introduced under the skin disappear after several months. They are transformed at first into embryonal tissue, then into fibrous tissue. There is not a simple absorption, for, as we shall see when we come to study necrosis of bone, an osseous fragment does not become absorbed. Instead of absorption by necrosis there has been, on the contrary, a superabundant formation of elements which first determine the metamorphosis of the bone into embryonal then into fibrous tissue.

4. Degeneration Consecutive to Inflammation.—A. *Fatty Degeneration.*—We have already seen that the disappearance of fat from the adipose vesicles is a result of inflammation at its beginning. Per contra, fatty granules appear in cells developed under the influence of irritation whenever these elements are more numerous than necessary for the reformation of the primitive tissue, and when they are in too large numbers relative to the nutritive supply.

In irritations affecting the parenchymatous cells in the so-called parenchymatous inflammations of Virchow, the elements, after presenting some phenomena of proliferation, become infiltrated with fatty granules. So also of the proliferated elements of connective tissue.

B. *Gangrene.*—It presents *two* essential *forms*. In the *first*, the gangrenous parts are large, and are eliminated entire as eschars. This

form is seen when stasis in the inflamed part, subsequent to coagulation of the blood in the vessels, occurs, from arrest of circulation caused by pressure due to the accumulation of the exudation around the vessels. Such conditions are common in very acute inflammations of osseous tissue. In all such cases of gangrene the mortified part acts as a foreign body. The irritated surrounding parts give birth to embryonal tissue, granulations and pus. By this means the necrosed part is isolated and removed. A *second form* is that of secondary molecular gangrene. It is met with in the ulceration of phagedenic chancres, in hospital gangrene, etc., also in the diphtheritic inflammation of German authors. It is considered to be the result of an infiltration of the tissues by pus and fibrin, which, by compression of the vessels, prevent a sufficient afflux of blood to the affected parts.

Sect. V.—Clinical Forms of Inflammation.

A useful, and an anatomical classification of the different forms of inflammation is based upon the form of the lesions themselves, upon their seat, their degree of intensity, and their cause.

I. Congestive Inflammations.—Such are hyperæmias, cutaneous erythemas, erysipelas, every acute catarrhal inflammation of the mucous membranes, rheumatic inflammation of the joints, etc. In all these lesions we always find with the congestion, which predominates, proliferations and mucous exudations.

II. Exudative Inflammations.—We have already considered them. As many forms should be recognized as there are distinct exudations. Almost all these exudations are mixed in character, and contain fibrin, albumen, mucus, and pus; almost all enter into what the German physicians call croupous exudations, such as acute pneumonia, pleurisy, pericarditis, peritonitis, etc.

III. Purulent Inflammations.—Appertaining to this variety are purulent infectious diseases, etc. In these cases pus shows itself everywhere with an extraordinary facility and in abundance. The phenomena of congestion are much less prominent.

IV. Hyperplastic or Interstitial Inflammations.—Such are cirrhosis of the liver, of the kidney, interstitial pneumonia, sclerosis, etc.

V. Gangrenous Inflammations.—See above, page 72.

VI. Tuberculous and Caseous Inflammations.—(Foerster.)

VII. Pseudo-Membranous Inflammations.—Such are the lesions of true croup, etc.

CHAPTER IV.

TUMORS.

Tumors differ from inflammatory products by their tendency to persist and enlarge, while inflammatory new formations tend always to disappear or to reproduce the tissue of their matrix.

Sect. I.—Definition of Tumor.

The word *tumor*, swelling, from the most remote antiquity has been applied in medicine to the most diverse productions. This definition underwent a modification at the hands of the pathological anatomists, who applied the term only to every abnormal tumefaction which could be demonstrated at the autopsy. In proportion as the histological structure of tumors has become better known, the group of tumors has been circumscribed.

The following is the definition and classification which we have adopted:—

We would designate as a tumor *every mass constituted by a new formation (neoplasm) having a tendency to persist or to increase.* This definition comprehends two terms which we ought to analyze; the neoplasm, its persistence and increase.

Neoplasms are subject to two general laws. The first was announced by J. Müller: *The tissue which forms a tumor has its type in a tissue of the organism, either when the latter is in an embryonal condition or in a state of complete development.* The second is from Virchow: *The cellular elements of a tumor are derived from the pre-existing cells of the organism.* Virchow adds that *they are derived from the cells of the connective tissue.*

Histologists to-day are inclined to admit the law of Müller. The law of Virchow is true in its first proposition, but the second proposition is not tenable, for the cells may be developed from epithelial or other cellular elements.

The word *neoplasm*, which we have made use of in the definition of tumors, should neither include effusions such as escape into cavities, nor the retained products of secretion, etc., which Virchow wrongly, as we think, looks upon as tumors.

The *second term* of our definition, the *persistence* and *increase* of tumors, completely separates these neoplasms from inflammations. In the latter, when the neoplasm forms it organizes and reproduces tissue similar to that whence it sprang, or it disappears little by little, by suppuration or caseous metamorphosis, etc. This is a fact so important that we insist upon it.

Tumors obey in a general way the laws which regulate living tissues. Nevertheless, to some extent, they live an independent life. They possess their own proper circulation, they extend, they grow at the expense of the tissue upon which they are implanted, so as to constitute an entity within an organism more complete. For example, the patient with a lipoma becomes emaciated without seeing his tumor diminish. A malignant tumor grows rapidly, while the patient falls away and sinks into an incurable cachexia.

It is not known that tumors possess nerves, unless they may be constituted by nervous tissue of new formation (neuroma); they want, consequently, those regulators of the nutritive functions which connect the different parts of the same living organism with a common centre. This absence of nerves impressed Schrœder van der Kolk and prompted him to make the following experiments: he cut the nerves of a dog's paw, then produced a fracture of it; the callus became exuberant and formed a veritable tumor of granulation tissue. This fact would suggest the importance of a series of researches for the purpose of learning if the exaggerated nutrition of a part of the organism, separated from its regulating centre by interruption of the nerve tubes, could determine the production of a tumor.

Sect. II.—Classification and Description of Tumors.

The law of Müller suggests to us a classification of tumors. Our classification will be based solely upon the analogy of tumors with the normal tissues, either in their adult or embryonal state. Thus we will admit those which are analogous to embryonal tissue, to fibrous tissue, to cartilaginous tissue, to osseous tissue, etc. We will employ, as often as possible, words formed by the radical of the normal tissue, to which the termination *oma*, *omata* will be added. We will study successively the following groups:—

First Group.—It comprehends tumors whose constitution is analogous to embryonal tissue. To them we will apply the word *sarcoma*.

Second Group.—It includes tumors constituted by a tissue, the type of which is found in connective tissue. This tissue may be mucous, the tumor is then called a *myxoma;* it may be fibrous, it is then called a *fibroma* or an *innoma;* it may be adipose, it is then called a *lipoma*. In certain cases the tissue undergoes a hypertrophic aberration, which mainly affects the volume and number of its cells, this is *carcinoma*, which should be better named *alveolar fibroma;* in other cases the cells atrophy, as in *tubercle*, *syphilitic gummata*, *glanders*.

Third Group.—It comprehends tumors constituted by cartilaginous tissue: *enchondromata*.

Fourth Group.—These tumors are formed of osseous tissues: *osteomata*.

Fifth Group.—Tumors formed of muscular tissues are divided into two kinds according as they are composed of striated or unstriated fibres: *myoma strio-cellulare*, and *myoma leio-cellulare*.

Sixth Group.—Tumors consisting of nervous tissue comprise two varieties: *neuroma medullare*, which contain nerve cells; and *neuroma fasciculata*, which contain nerve tubes.

Seventh Group.—In this group are included tumors formed of blood-vessels: *angiomata*.

Eighth Group.—Comprehends tumors constituted by lymph vessels: *angio-lymphomata*, and those which reproduce the structure of lymphatic glands, *adeno-lymphomata*.

Ninth Group.—Tumors formed of new epithelium, divided according as the cells are in irregular masses, upon papillæ, in culs-de-sac, or in newly formed cavities, into four kinds: *epithelioma*, *papilloma*, *adenoma*, and *cysts*.

Tenth Group.—*Mixed tumors;* they contain a great variety of tissues.

The foregoing is purely an anatomical classification, and does not respond to the legitimate desire of the clinician; in fact no anatomical classification can do so at present. The malignancy of a tumor depends upon the continued formation of a great quantity of embryonal elements, by which the tumors very rapidly increase.

TUMORS CONSTITUTED BY EMBRYONAL TISSUE.

Sarcoma.

We will at first study the generic characteristics of tumors analogous to embryonal tissue, then we will discuss the characters which appertain particularly to each species and variety.

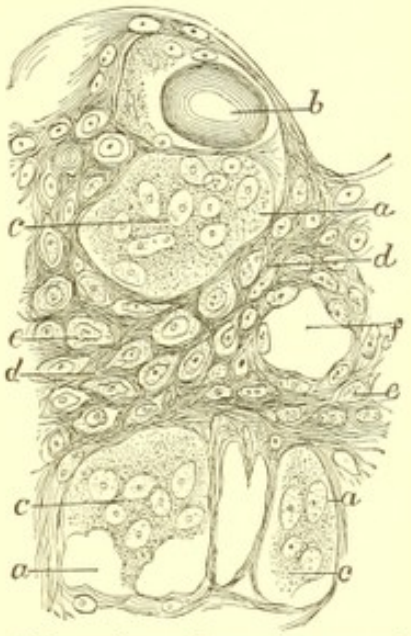
Synonyms.—There are no tumors which have received more different denominations than the sarcomata. J. Müller termed them *fibro-albuminoid*, Lebert called them *fibro-plastic*. Chas. Robin thought that fibro-plastic tumors should be separated from certain ones which had, with the former, numerous analogies, but which differed by the round form of their cells; he named them *embryoplastic tumors*. Paget gave to the fibro-plastic tumors the name of *recurring fibroid*, and classed with them certain tumors having a structure similar to the marrow of bones, which he named *myeloid tumors*. The latter were called by Chas. Robin *tumors with medulla cells* and *tumors with myéloplaxes*. Finally, Virchow separated from sarcoma some tumors which, till then, were classified with them, and to which he gave the name of *glioma* and *psammoma*.

Definition.—We define sarcomata as, *tumors constituted by embryonal tissue, simple or undergoing one of the first modifications through which it passes in order to become adult tissue*. Thus, as embryonal tissue is transformed into fibrous tissue, the spherical cells lengthen and become fusiform, and an intercellular amorphous substance is formed. Tumors presenting an analogous constitution are *sarcomata*. If sarcomatous tissue has its type in a physiological state we should find its analogue also in a pathological condition during inflammation. In cicatrizing granulation tissue, we meet with all the phases of connective tissue. Certain sarcomata have a similar structure. In inflammatory tissue arising in the bony marrow, cells like those of the bony marrow show

themselves, and often even bony trabeculæ in course of development are seen; identical appearances are met with in the tissue of certain sarcomatous tumors (see fig. 5). The only difference between the sarcomatous and inflammatory tissue is that we may recognize a different beginning and end for each.

While as a general rule, both in inflammatory tissue and in sarcoma, when the processes are slow or chronic the elements are large, and when they are active the cells are small, the elements are usually larger in sarcoma than in simple inflammation. Moreover, the form of the cells in sarcoma, is not very rigidly dependent upon its seat; thus, sarcoma springing from the skin or a gland may show large giant cells similar to those which are developed usually under the influence of inflammation in bone. The cellular eléments constitute almost the entire mass of sarcoma.

Fig. 56.



Adipose tissue from a deep wound in a dog in progress of healing. *a*. Spaces left by the absorption of the fat vesicles *b*; they are found filled with newly formed nuclei *c*, surrounded with granular protoplasm; *e*, embryonic cells; *f*, section of a vessel which has embryonic walls.

General Description of Sarcoma.—The cells of sarcoma include the most varied forms. Some are spherical, others are irregular, with multiple processes, which sometimes anastomose. They possess one or more large round nuclei; many of the latter are fusiform (the fibroplastic element of Lebert). In cranial tumors the cells are often flat and extremely thin; they frequently are large in size and possess a central lenticular nucleus; seen in profile they appear as a fibre, showing at its centre a lengthened nucleus (see Psammoma).

We see then that the morphology of the cells of sarcoma is very complex; the size of the elements may vary from .005 or .006 mm. up to .05 mm. The structure of these cells is very simple. They possess one or several nuclei, either spherical or oval, varying in size from .005 to .003 mm., and in number up to fifty. The nucleoli are usually shining and small, but they may exceptionally acquire a diameter of .005 mm. Nuclei are particularly numerous in the large giant cells or myéloplaxes. Around the nucleus exists a granular substance. Examined in a neutral medium the nuclei are always distinct, but when examined simply in water, or in water slightly acidulated with acetic acid, they become much more sharply defined. These cells have no membrane. In certain cases the albuminoid granules of the cells so arrange themselves as to produce an appearance of striation. As in embryonal tissue, the cells of sarcoma are very sensible to the action of reagents. Because of their friability, when the surface of fresh tumors is scraped, the elements are often ruptured and the nuclei set free. It is this presence of free nuclei in the scrapings

which has led certain histologists to admit the existence of free nuclei in the tumor itself. On account of the variety in form and dimension of the elements of sarcoma, and their non-characteristic appearance, the anatomical diagnosis of the tumor cannot safely be made by examination only of the scrapings.

It is the arrangement of the elements and their relation to each other and to the vessels, which furnish distinctive characters. The cells are placed close together, they are in contact or are separated only by an extremely small amount of intercellular or cement substance, which is amorphous and very soft or, perhaps, indistinctly fibrillar. Bloodvessels always exist in great numbers in sarcoma; they are in direct relation with the cells, or they are surrounded by fasciculated connective tissue, as is occasionally the case with some of the large vessels. (See fig. 57.) The bloodvessels are not regularly disposed. Their arrangement, and the structure of their walls are very similar to those of inflammatory tissue. They are, therefore, difficult to separate from the mass of the tumor. When, after having hardened one of these tumors, thin sections are made, the lumen of the vessels is seen to be limited by round or fusiform cells, but rarely does one discover proper walls appertaining to these blood channels. This is an essential point, for joined to the general disposition of the elements it distinguishes sarcoma, and explains the rupture of the bloodvessels, the extravasations, and the blood cysts observed in these tumors.

[In his excellent lectures on sarcoma of the long bones, Dr. S. W. Gross[1] well expresses what is now almost universally regarded as a characteristic of the relation between the cellular and other elements in sarcoma. According to him the cells are contained in an intercellular substance which is hyaline, granular, fibrillated, or alveolar, and which, along with the various degenerations to which these tumors are liable, furnish a basis for subdivisions. Moreover, in accordance with the dimensions of the cells, the sarcomata should be separated into small-celled and large-celled, a distinction which is most useful, not only because the size of the cells influences the consistence of tumors, but particularly because it has a special bearing upon the prognosis.]

Species and Varieties of Sarcoma.—These are based upon the form of the cells, their cement substance, the vessels and the ultimate tendency of the tissue. A sarcoma does not always consist of a single variety of cells; all the forms previously indicated may be met with. In regarding the characters of the elements for the purpose of classification, we must not only demonstrate the presence of certain cell forms, but we should also take account of the relative proportion in which they are found. The intercellular substance is sometimes semi-fluid, in this case the cells are generally round, at other times it is solid, the cells may then, from mutual pressure, assume varied forms. If the cells are compressed laterally in every direction, they become fusiform; if they are compressed in a single direction they are flattened. Upon the foregoing basis the following is the classification which we propose:—

[1] American Journal of the Medical Sciences, Philadelphia, July, 1879.

1*st species*, *encephaloid* [*or round-celled*] *sarcoma.*
2*d species*, *fasciculated* [*or spindle-celled*] *sarcoma.*
3*d species*, *myeloid* [*or giant-celled*] *sarcoma.*
4*th species*, *ossifying sarcoma.*
5*th species*, *glio-sarcoma* [*glioma*].
[6*th species*, *alveolar sarcoma.*]
7*th species*, *angiolithic sarcoma* (psammoma of Virchow).

To the foregoing we ought also to add, as distinct species, the three following forms:—

8*th species*, *myxo-sarcoma.*
9*th species*, *lipomatous sarcoma.*
10*th species*, *melano-sarcoma.*

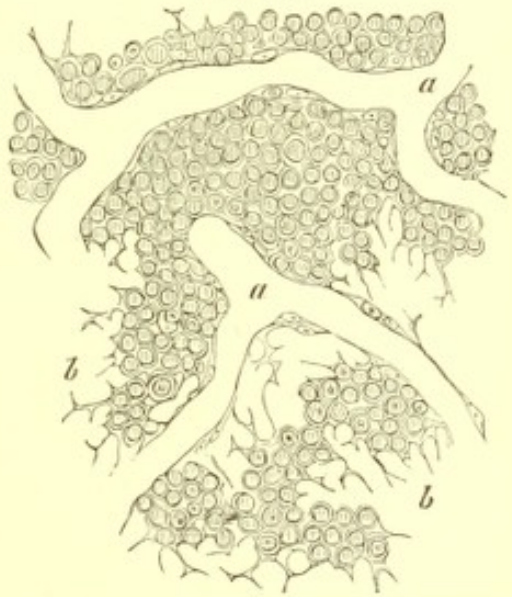
These different tumors may recur at the place of their location, or they may be propagated to remote parts of the organism, the recurring or secondary growths reproducing the structure and nature of the original tumor. In each of these principal species of sarcoma, lesions of nutrition may give rise to varieties. Such lesions are:—

a. *Fatty degeneration.*
b. *Infarction.*
c. *Calcareous transformation.*
d. *Formation of blood-cysts.*
e. *Inflammatory phenomena.*

We shall now study in detail each of the preceding species.

Round-celled Sarcoma.—Formerly it was confounded with carcinoma under the name of encephaloid cancer. In France it was often spoken of as an embryoplastic tumor. Its encephaloid or pulpy appearance is commonly well marked; its color is usually gray, and it is more or less translucent. The primary tumor often very quickly attains an enormous size. There may be metastasis to the different organs, especially the lungs. The vessels are voluminous, often dilated, and varicose or aneurismal; these then appear to the naked eye as little red points; finally, they may rupture and form little cysts filled with fluid or clotted blood or with mucus holding in suspension degenerated elements; the rupture may also give rise to ecchymoses or diffuse hemorrhages. Most frequently, when these hemorrhages occur the red globules are preserved and there is no pigmentation of the neighboring elements. When perfectly fresh, the tumor contains a juice which is perfectly transparent. Twenty-four, or forty-eight hours after death or ablation, however, an

Fig. 57.



Round small-celled sarcoma: *a*, vascular lumina; *b*, parenchyma partly brushed out, so that the hardened basis or intercellular substance appears as an elegant network. × 350. (*Rindfleisch.*)

abundant juice of white color, and resembling that of cancer is obtained by scraping, which circumstance is due to the cadaveric liquefaction of the intercellular substance and to the fluid thus formed holding in suspension many cellular elements.

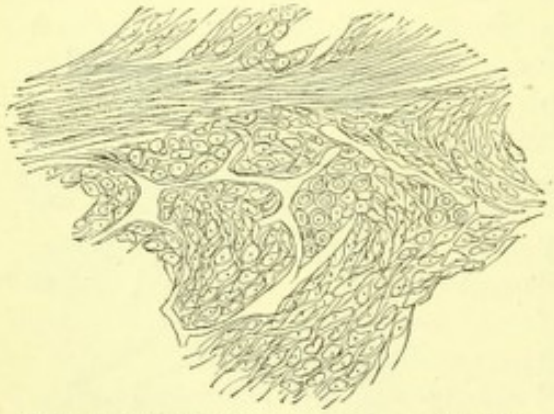
The cells of encephaloid sarcoma are generally small and round, or more or less irregular. Their nuclei are large and inclose from one to three nucleoli, which may be vesicular. They seldom have the diversity of form of cells of carcinoma. In these tumors there often is to be found a certain quantity of old pre-existent connective tissue.

Beside alterations in nutrition, these tumors often present in their oldest portions granular corpuscles and an infiltration of the elements by fine fatty granules. Sometimes portions of the tumor have undergone mucous or calcareous degeneration, or they may have become infiltrated with red or black pigment. In these cases, to the term encephaloid sarcoma, which represents the species, a term which would indicate this partial degeneration should be added. One might say, for example, *encephaloid sarcoma with partial mucous degeneration.*

The seat of encephaloid sarcoma is very variable: it is seen in the skin, subcutaneous cellular tissue, bone, muscles, in the glands—particularly the breast and testicle. Of all the sarcomata [except the alveolar], this species is the most malignant; it recurs very frequently, and by metastasis invades a great number of organs.

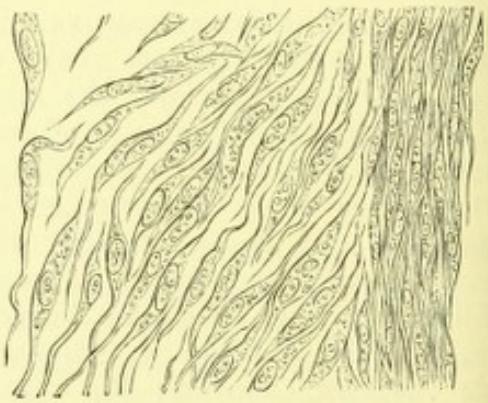
Spindle-celled Sarcoma.—In this species the structure of the embryonal tissue is more nearly related to connective tissue. It is the fibro-plastic tumor of Lebert. Tumors of this class are so common that they have been regarded as the type of sarcoma. From their trans-

Fig. 58.



Thin section of a fasciculated sarcoma (spindle-celled sarcoma). The section has taken some of the spindles longitudinally and some transversly. The vessels are gaping. × 200. (*Virchow.*)

Fig. 59.



Large spindle-celled sarcoma. To the left, the cells have been separated by teasing, so that their individual forms are apparent; to the right, they are in their natural state of apposition, such as would be seen in a thin section of the tumor. (*Virchow.*)

lucency and their fasciculated aspect they have been compared with muscular tissue, whence comes the name sarcoma (flesh).

The cells which constitute fasciculated sarcoma are fusiform, and are terminated by two lengthened extremities which sometimes ramify. They

are of variable size, their mean length being from .015 to .03 mm.; but they may acquire colossal dimensions, reaching even .1 mm.

The tissue of fasciculated sarcoma is very simple; the cells are quite or nearly in contact with each other in such a manner that the spindle extremities of one cell are applied along the bellies of another; these interdigitating cells form real fasciculi, which may be parallel with each other or may intercross. The direction of the vessels is the same as that of the cells. (Figs. 58, 59.)

The peripheral limit of these tumors is sometimes sharp, sometimes diffuse and continuous with the neighboring tissues. Their increase takes place at the periphery, at one time irregularly, at another by the formation of distinct and spherical lobules. Their volume is variable, but they are usually smaller than encephaloid sarcomata. Nevertheless, in the limbs they often grow from the periosteum until they reach the size of an adult head. These tumors contain no juice in the fresh state; but the day after the operation or later, after cadaveric changes, a small quantity may be observed. Very often, fasciculated sarcomata are seated under the periosteum; they exist in bone, connective tissue, and muscle, in the breast, the testicle, etc. By secondary deposits they may invade all the organs.

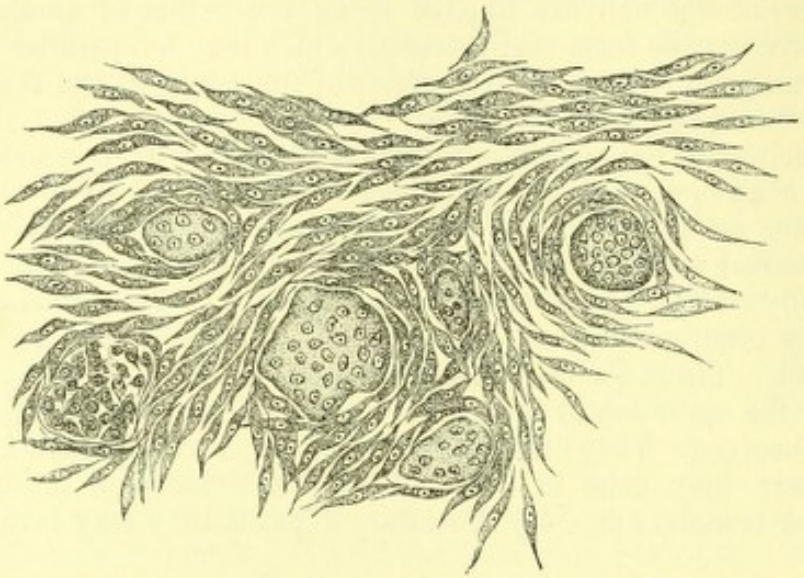
In the mammæ these tumors and those of the preceding species are accompanied by a proliferation of the cells of the glandular acini to such an extent that Billroth has recognized them as a separate variety under the name of adeno-sarcoma. In France the latter are often called adenomata of the breast. Many tumors of different species have been confounded in the breast under the name *adenoma!*

Sarcomata of the mammæ present two forms: they constitute a mass through which the acini are regularly disseminated; or the sarcomatous tissue, through pressure upon the walls of the ducts and culs-de-sac, forms projections into their lumen. These projecting vegetations are covered with epithelial cells. The lacunar cysts thus formed have varying dimensions and present, upon section, irregular, stellate, or semilunar openings, the epithelial cells which cover the opposite walls often being in contact. These cavities may appear as large spaces which separate the tumor into as many lobes. By scraping the cut surface of these tumors of the mammæ an abundant milky fluid is obtained. In sarcoma of the mammæ and of other regions there is never true adipose tissue in the midst of the morbid mass. We shall see later that this furnishes an excellent characteristic for their differentiation, by the naked eye, from carcinoma, in which, on the contrary, adipose tissue is preserved.

Myeloid Sarcoma.—These are soft tumors, the cells of which are nearly in contact and are very similar to those of the preceding species; a certain number of them, however, tend toward a more stable organization by surrounding themselves with a membrane, and their contour is more regular and more distinct. Some elements are round and spherical like the cells of embryonal bony marrow; others are fusiform; large, flat, irregular, giant cells are seen, which are filled with ovoid nuclei (see fig. 5). We should remark, however, that the latter cells are not peculiar

to myeloid sarcoma. They are found in small numbers in other sarcomatous tumors. Finally, some cells in these tumors resemble the angular

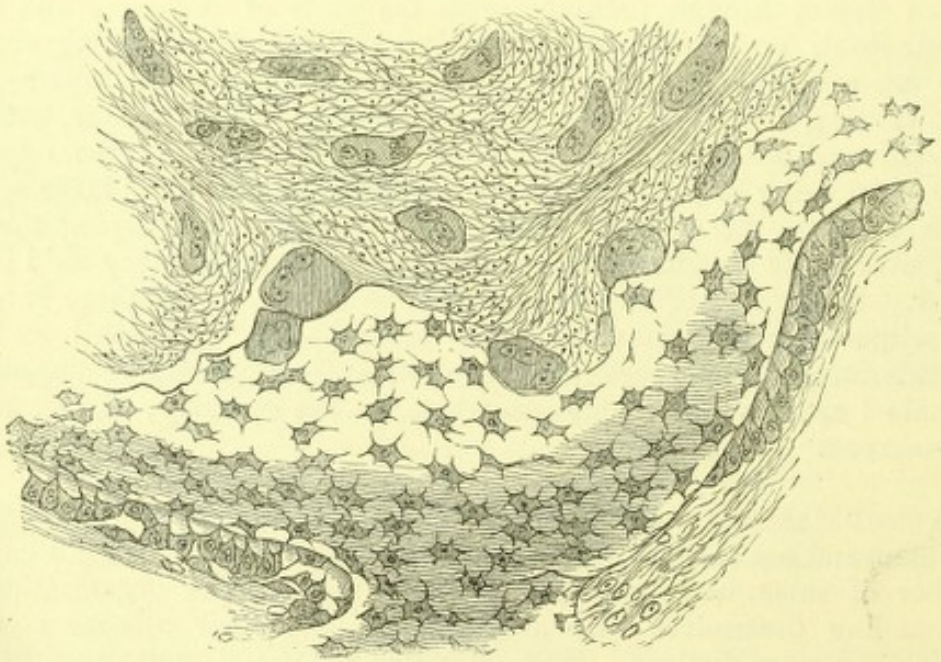
Fig. 60.



Myeloid sarcoma: showing spindle and giant cells. High power. (Drawn by Dr. Shakespeare for Dr. S. W. Gross. See *Amer. Journ. Med. Sciences*, July, 1879.)

elements which result from reciprocal pressure, and which Gegenbauer has improperly called osteoblasts. Myeloid sarcomata are nearly always located in the bones. They are usually limited to a single bone, which they may destroy completely.

Fig. 61.



Portion of a section from the border of a spindle- and giant-celled sarcoma of the lower maxilla, showing an osseous trabecula, which disappears at the one side by absorption, and grows at the other by apposition. The cells applied to the lower border of the trabecula are osteoblasts, and are forming new bone, while the giant cells applied to the upper edge of the bony trabecula occupy the position of Howship's lacunæ and are eating away the bone. They might, therefore, be well termed osteoclasts. × 500. (*Rindfleisch.*)

Ossifying Sarcoma.—This species differs from the preceding tumors only in the tendency of the elements to produce osseous tissue. In this osseous tissue it is rare to find bony lamellæ and Haversian canals.

The small tumors of the dental arches, which are called epules, are sometimes myeloid, sometimes ossifying sarcomata (fig. 61). It may be asked whether these epules are osteomata or sarcomata; we have classified them as sarcomata, because they have only a tendency to ossification, their ossification is never complete and permanent.

The little tumors which are called subungual exostoses are identical in structure and nature to that of epulis. Both may return.

The tumors of this species are seated, by preference, in the short spongy bones. When they are on the long bones, they are almost always located in their epiphyseal extremities. They should be carefully distinguished from growths simply incrusted or permeated by calcareous deposits. The latter have only the form of needles, disposed like osseous trabeculæ, and cannot, with the naked eye, be differentiated from bone; but under the microscope, it is seen that the intercellular substance is incrusted with calcareous salts, that it is opaque, and presents small round or ovoid cavities without processes which serve to lodge the cells of the sarcoma. [Many authors make no distinction between ossifying and calcifying sarcomata, and regard both as highly malignant.]

Glioma.—Virchow has given to these tumors the name gliomata, because their consistence resembles that of glue, and as he found their tissue similar to that of the neuroglia, he has separated them from sarcoma.

Fig. 62.



Glioma. High power. (*Hamilton.*)

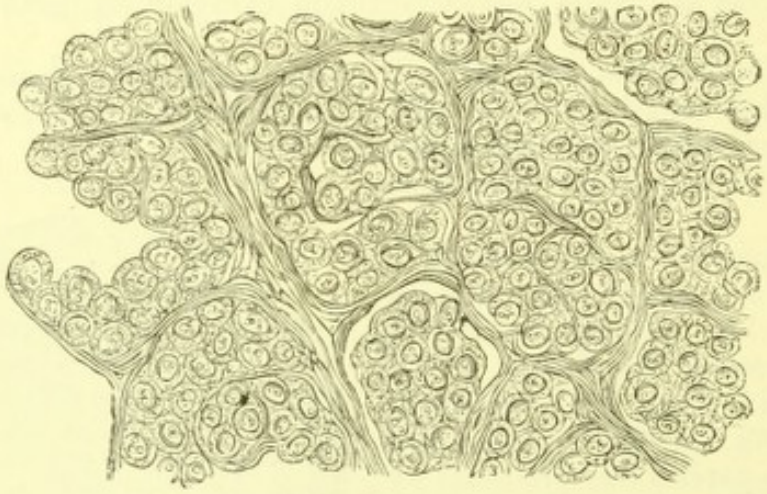
These tumors contain cells from .006 to .012 mm. in diameter, consisting of a nucleus and a very small mass of protoplasm surrounding it. After the growth is hardened in alcohol or chromic acid, certain of these cells are seen to possess fine processes by which they anastomose and form a reticulum similar to that of neuroglia. This reticulum can seldom be seen in the fresh state, and is, at least in part, probably artificial. We may add that similar forms of cells may be seen in other species of sarcoma, after thorough hardening. It is then not characteristic. In the meshes of this network exist small free cells which, by their characters and reciprocal relations, recall those of encephaloid sarcoma. Besides, it is rare that one of these tumors is constituted throughout its entire mass by such a reticulated tissue; very frequently islands are observed which have the structure of encephaloid or fasciculated sarcoma. We recognize, then, in the gliomata only sarcomata whose tissue has a tendency to organization into neuroglia. The centre of these tumors is generally in such a state of fatty degeneration that, at first sight, one might hesitate between voluminous cerebral tu-

bercles or sarcomata. The vessels of a glio-sarcoma often possess lymph sheaths.

Glio-sarcomata are found in the brain and spinal marrow, both in the gray and in the white substance; they may develop along the cranial nerves and in the retina. Virchow reports an observation of a glioma in the cortical substance of the kidney.

[Alveolar Sarcoma (*Sarcoma carcinomatodes of Rindfleisch*).—This species of sarcoma appears, both in a clinical and histological point of view, to occupy a middle ground or connecting link, as it were, between the sarcomata and the carcinomata. These tumors possess an alveolar structure. Their alveoli may be large or small. In proportion to their size, the alveoli are occupied by one, two, or three large cells, or they contain large numbers of small cells. The cells are usually of the type of embryonal cells, although Rindfleisch declares that in some cases they are epithelioid. According to Billroth, from the size and arrangement of the cells, it is often extremely difficult to distinguish the growth from a carcinoma. According to S. W. Gross, roundish heaps of

Fig. 63.



Alveolar sarcoma from the tibia. × 400. (*Billroth.*)

small cells are seen contained in the alveoli or spaces of a connective-tissue meshwork. At certain points, the masses of cells are intersected by delicate bands of connective tissue, which are given off from the alveolar walls, and which divide the larger cell clusters into smaller ones. Tumors which possess this structure are excessively vascular, and are often the seat of pulsation and a bellows murmur, which have sometimes caused them to be confounded with aneurism during life. Jaffé considers that in the very vascular tumors of this kind the walls of the alveoli are formed by the capillaries. Weber believes that in the vascular tumors the stroma is due to the obliteration of the blood channels and their conversion into solid fibres. According to Gross, and in this he agrees with Billroth and ourselves, the points which distinguish this form of sarcoma from carcinoma are: firstly, that the cells are intimately connected with the walls of the alveoli or the vessels which form them; secondly, that, by pencilling, an intercellular substance like that met with

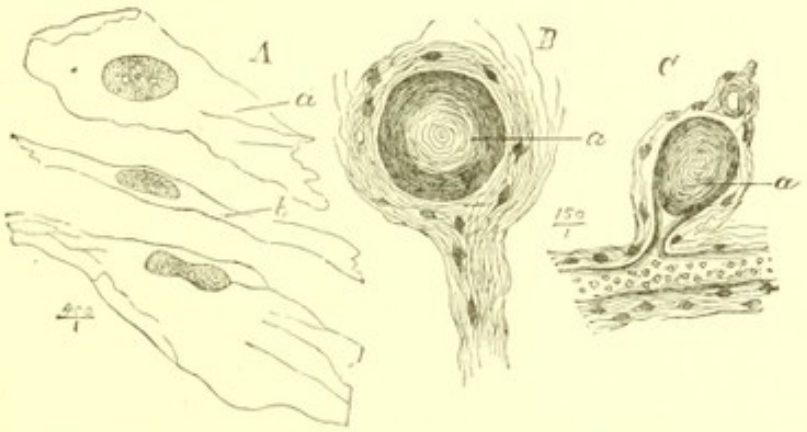
in the lymphadenoid form of tumor is disclosed, the fibres of which arise from the alveolar walls which inclose the groups of cells. In other words, in alveolar sarcoma, the stroma and cells are intimately interwoven into a single tissue, whereas, in carcinoma, the cells and stroma are easily separable into two distinct tissues.

This form of tumor is rare. It has been found in the skin, in muscles, in bone, in the lymph glands, and in the dural covering of the spinal cord. It is second in malignancy only to the carcinomata, and, like the latter, it, as a rule, secondarily involves the lymph glands. Metastases are frequent.]

Angiolithic Sarcoma (*Psammoma of Virchow*).—In the form of its cells, this very curious growth does not essentially differ from the preceding species. These tumors contain "cerebral sand," and the physiological type of their structure is met with in the choroid plexus. They are seen only within the cranial vault, in the arachnoid, and in the pia and dura mater.

Such sarcomata are soft, easily crushed, and contain no juice. Their color is gray, and they are more or less opaque; they are often surrounded by a fibrous capsule. The cells comprising them are flat and

Fig. 64.



Angiolithic sarcoma (Psammoma). A. Isolated cells, seen in surface at *a*, in profile at *b*. × 400. B. Vascular bud, containing a calcareous globe, *a*. C. Vessel infiltrated with calcareous salts, and presenting at *a* a calcareous concretion upon one of its branches. × 150.

thin, of colossal dimensions, and of irregular form. Viewed in face, their border is so thin that it is difficult to follow, and the nucleus at the centre appears lenticular; seen in profile, they look like a fibre or an extremely long fusiform cell, the centre of which is occupied by the nucleus. The cells resemble the endothelium of the veins, but they are not united at their edges. These neoplasms are distinguished from all epithelial tumors by the fact that the vessels are in direct connection with the cells. This relation never exists in epithelial growths.

The bloodvessels are numerous and are easily isolated. No matter what may be the size of the vessel, the wall is entirely formed of cells similar to those which constitute the morbid mass. These cells are only loosely united; they easily allow the blood to ooze out between them. Hollow buds (or diverticula) are constantly seen, which communicate with the lumen of a vessel. These little buds grow and become pedun-

culated; the flattened and concentrically disposed cells which compose them become incrusted with calcareous salts. This process of infiltration is identical with the physiological modifications of the vessels of the choroid plexus. When the calcified buds have not broken their connection with the vessels, the peduncle and a part of the vessel-wall are often incrusted with calcareous salts, and have become homogeneous and vitreous. (Fig. 64, C.) After separation from their attachment, these little knobs may somewhat resemble a "cell nest" of epithelioma. They may or may not be calcified, and the tendency of infiltration by calcareous salts separates them from the epidermic globes or "cell nests" of epithelioma. In other parts of the body, particularly in the thymus gland, we meet with concentric spheres which may be calcified or not, and which also are appendages of the vessel-walls and have a similar origin.

Myxo-sarcoma.—The mucoid degeneration of the cells of sarcoma, associated or not with fatty degeneration, ends in the destruction of the cells and the formation of cavities more or less large, filled with transparent gelatiniform matter. These cavities have a variable volume. The whole tumor may be riddled by them, and some authors in this case call the growth a cysto-sarcoma. It is only when the degeneration is very marked, extends almost throughout the whole tumor, even the most recent portions, and particularly when the secondary tumors present the same appearance, that we would name the tumor a myxo-sarcoma.

Lipomatous Sarcoma.—In this form, which is not uncommon, the cells are infiltrated with globules of fat without being destroyed and without ceasing to function, a capital distinction which differentiates this form of sarcoma from that in which the cells are undergoing fatty degeneration and consequent destruction. Those cells which contain many oil globules may be much enlarged, with their nuclei crowded to the periphery. The cement or intercellular substance is very slight, and the cells are close together. The tumor is sometimes soft, and the surgeon, when examining it by the naked eye, may be disposed to call it an encephaloid cancer. It is usually very large, and it may occasion secondary formations with identical characters.

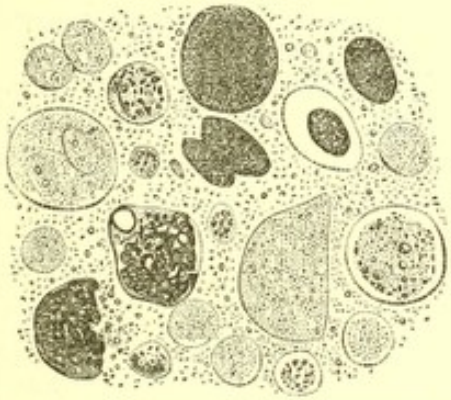
Melano-sarcoma.—Melanotic sarcoma has its usual point of departure in the eye or skin; but it may also primarily appear in the lymph-glands. In the developing tumor, all of the cells are not equally pigmented; variously colored zones may be seen, white, gray, often semi-transparent in the youngest points, black in the oldest points, of sepia or slate-color in intermediate spots. Sarcomata of this species may be black throughout their entire mass from the commencement.

The cells of these tumors are round or fusiform, their disposition and that of the intercellular substance is variable, but they correspond in a general way with the structure of a fasciculated sarcoma. (See figs. 65, 66.)

What constitutes the specific character of these tumors is the presence of black granules in the interior of the cells. The granules are black from the first, and this forms a distinction between dark melanotic pigment and the black pigment which follows blood extravasations. When these black melanotic granules are round, they may at first be confounded with very fine fatty granules; when they are angular, they are more

readily recognized. These pigment-granules often unite into small round clumps surrounded by a brilliant zone, which is nothing else than a deposit around them of albuminoid material.

Fig. 65.



Cellular structure of melanosis as seen in scrapings. (*Bennett.*)

Fig. 66.



Cells containing pigment. From a melanotic sarcoma of the liver. × 350. (*Green.*)

The melanotic granules are first formed in the protoplasm around the nucleus; afterwards they may invade the nucleus itself.

This morbid growth has a great tendency to occasion secondary invasion of the distant tissues by similar growths. The name of melano-sarcoma should not be applied to those sarcomata in which only blood extravasations and their sequelæ are found.

Papillary Sarcoma.—This does not constitute a species, but a form which any sarcoma may assume when it grows upon a mucous or cutaneous surface. We have already indicated that sarcoma of the mamma has a tendency to send buds into the lumina of the acini and galactophorous canals. Sarcoma of the skin, which is the type of this variety, at one time presents rugæ upon the surface, at another papillæ. Through proliferation of their elements, the papillæ of the skin undergo a considerable hypertrophy and even give off lateral buds. They are covered with epidermis, the cells of which are more pigmented than in the normal state. In certain cases, even the cells of the sarcomatous papillæ are also slightly pigmented; it is possible that such may be the commencement of a melano-sarcoma, but in the most of these cases the pigment appears to be due to ecchymoses. These tumors generally increase slowly, but at any moment they may take on a rapid growth and cause secondary formations.

Development, Extension, and Generalization of Sarcoma.—The development of sarcoma, like that of most tumors, comprehends three terms: 1st. the development of the primary tumor; 2d. the extension of the primary tumor; 3d. the formation of secondary tumors.

1st. The manner of the development of the primary tumor is very simple. It should be studied, by preference, in tissue of which the structure is very different from that of sarcoma. In bones, the development of sarcoma is exactly the same as that of inflammatory tissue (p. 60). In tendons the endothelial cells, so atrophied in the normal state, swell-their nuclei divide and surround themselves with distinct masses of pro-

toplasm; the embryonal cells, thus formed, become disposed in long rows, while the intercellular substance disappears. [To these proliferated endothelial cells, the white blood corpuscles and their derivations should perhaps be added to form the neoplasm.] Thus results an embryonal tissue which is similar to that of encephaloid sarcoma, but which may become by modification of cells and intracellular substance, a fasciculated sarcoma, etc.

2d. Increase of the primary tumor takes place: a. *By the proliferation of its own elements.* b. *By continuous invasion of the neighboring tissue.* A smooth, regular, peripheral outline is an indication that the tumor is no longer extending by an invasion of the neighboring tissue. If it is not sharply limited from the parts which surround it, the invasion is still continuing. When the growth is extending, we see, under the microscope, masses of embryonal elements in process of formation at the expense of the normal elements of the surrounding tissue. This mode of invasion should suggest a grave prognosis, but less grave, however, than when morbid masses isolated from the principal tumor are to be found in the tissue around the growth: the latter mode is what is termed interrupted or *discontinuous invasion.*

3d. When new tumors of the same nature as the primary growth are developed in distant organs, we say that they have become *generalized;* we call this *metastasis.*

It is precisely upon this property of metastasis that we have based our classification. Sarcomata as a general rule do not invade the lymph glands by secondary metastasis, they become generalized through other channels than their lymphatics, probably through their bloodvessels which are often in an embryonal condition and easily ruptured.

Prognosis of Sarcoma.—The gravity or malignancy of sarcoma, aside from the seat and the volume of the growth, is dependent upon its tendency to extension and metastasis. *Sarcoma is more or less grave in proportion as its organization is more or less lowered.*

According to their malignancy the sarcomata might be classified as follows, beginning with the most malignant:—alveolar, encephaloid, melanic, colloid or mucous, lipomatous, then fasciculated, ossifying, etc. Sarcomata which present true osseous trabeculæ are less to be feared than those which have simply undergone calcification. The more pronounced the tendency of sarcomata to produce perfect tissue, the more the organization of the latter will be elevated, and the less grave they will be. Thus among the myeloid sarcomata those which actually resemble bony masses will be more benign than those in which we will find parts representing the tissue of encephaloid or fasciculated sarcoma. It is important to take account of these complications and of their prognostic value; they explain why, for example, the tumors which some authors still call myelo-plastic cannot always be regarded as benign.

Virchow, who has not made a distinction between ossifying and calcifying sarcomata, says, in a general way, that they are very grave. In making this distinction we are led to say, on the contrary, that ossifying sarcomata, as epules and subungual tumors, are, as everybody knows, benign; while fasciculated sarcomata incrusted with calcareous salts are

grave, the gravity resulting not particularly from this calcification but from the fact that they are fasciculated sarcomata.

Glio-sarcoma is grave solely by reason of its seat and extension by continuous or discontinuous invasion; it rarely if ever occasions metastases. We would say the same of psammoma or angiolithic sarcoma.

[Alveolar sarcoma possesses a great tendency to metastasis, and of all the sarcomata, it most frequently invades the neighboring lymph glands.]

II.—TUMORS OF WHICH THE TYPE IS FOUND IN THE DIFFERENT VARIETIES OF CONNECTIVE TISSUE.

1st Class.—**Myxoma.**

Definition.—Myxoma is a tumor formed of mucous tissue. Its definition is involved in that of mucous tissue. This tissue forms the umbilical cord; it persists after birth in the vitreous humor of the eye, but in the embryo it is met with in various parts of the body. Mucous tissue in the embryo is observed as one of the first phases of development of the embryonal into fibrous and adipose tissue. The tumors constituted by it ought, therefore, to be described between those formed of embryonal tissue and those constituted by fibrous tissue.

Physiologically, mucous tissue presents two forms: 1st. Round cells isolated in the midst of a mucous intercellular substance; 2d. Stellate and anastomosing cells, suspended in a similar intercellular substance. It is rare that myxoma presents one of these two forms alone.

Description of Myxoma.—Myxomata are trembling, gelatiniform tumors permeated by vsssels which are readily seen and isolated; when one scrapes them, no milky juice is obtained, but, on the contrary, a fluid similar in appearance to a solution of gum arabic. In this fluid, red blood disks which have been forced from the torn vessels are seen, together with cells of various forms, round, angular, fusiform, sometimes possessing processes. The cells may contain one or more nuclei; they are pale, and their contours are not distinct, because they are seen in a substance whose index of refraction nearly equals their own.

Freshly examined, a large meshed capillary network is seen, in the walls of which the nuclei and the outline of the endothelial cells can be readily made out. Between the vascular meshes is mucous tissue, in which are suspended large pale fusiform or stellate cells, which anastomose with each other by their processes. (Fig. 67.)

Besides this net of plasmatic cells, the mucous fluid contains round and small cells [leucocytes] which have no connection with their neighbors. The presence of the cell-net is rendered very apparent by the

Fig. 67.



Myxoma. A minute piece of a myxoma of the arm, showing the characteristic branched anastomosing cells. There are also a few leucocytes, and one or two spindle-shaped elements. ×200. (*Green.*)

addition of a solution of iodine or picro-carminate of ammonia. Besides these elements, the morbid mass often contains elastic fibres and adipose cells. Such are the general characters of tumors of this group. (See fig. 68.)

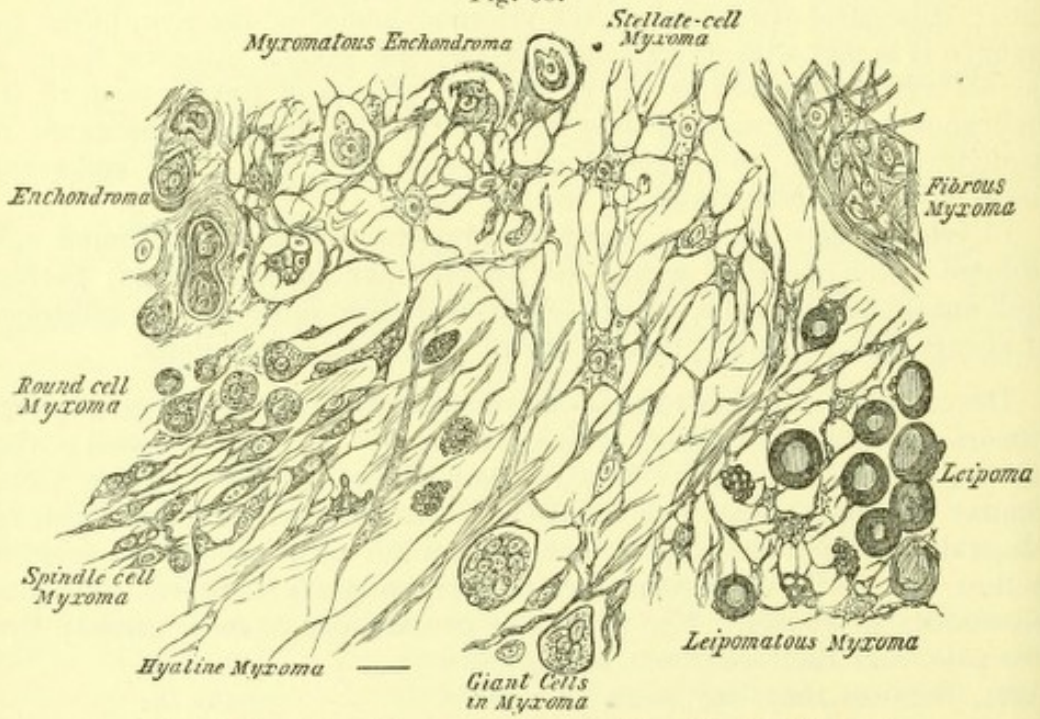
Species and Varieties of Myxoma.

1st species: Pure myxoma.—It is composed of mucous intercellular substance, through which are scattered vessels, and round fusiform and stellate anastomosing cells.

2d species: Myxoma containing a considerable quantity of elastic fibres.

3d species: Lipomatous myxoma.—The adipose tissue which characterizes this species may be so abundant that it will be difficult to determine whether we have to do with a myxoma or a lipoma.

Fig. 68.



Microscopic anatomy of myxoma. [A composition picture.] (*Bryant.*)

Besides these three species which may present the appearances above indicated, myxoma may undergo the following alterations in nutrition:—

a. The vessels may rupture, an accident which does not occur so frequently as in sarcoma, because the vessel walls are not softened; we have then *hemorrhagic myxoma*.

b. The elements of the tumor may undergo mucous metamorphosis. The cells are subject to alterations somewhat similar to those of the cells in other tissues.

The elements, so degenerated, disintegrate and form a detritus; there thus result cystic cavities filled with mucous masses, and it is particularly from the surface of these cysts that the hemorrhages occur. Generally, fatty degeneration complicates these lesions, and a part of the tumor may thus become transformed into a cystic cavity. This variety might be termed a *cystic myxoma*.

c. Myxomata are papillary, pedunculated, and, when they spring from a mucous membrane and are located in a mucous cavity, are also polypoid. These polypi, growing from the cellular tissue of the mucous membrane of the nasal fossæ, are covered by ciliated cylindrical cells, and often contain hypertrophied glandular tubes which the mucous membrane contains.

d. Mucous polypi may *inflame* and even *ulcerate*, especially when they project externally. In the foci of inflammation there is a transformation of the mucous tissue into *embryonal tissue*.

e. Myxoma may be the seat of *gangrene*, either limited or general.

The SEAT of myxoma is variable. They are encountered in the placenta, and analogous productions occur along the umbilical cord of the fœtus and of the new-born child.

Myxomata occur by preference in locations where cellulo-adipose tissue exists; they are frequent in the subcutaneous tissue and in the muscles. In nerves, they are often multiple, developing from point to point along the course of a peripheral nerve. Ascending along such a nerve, they may even reach the cranial cavity.

It is remarkable to note the power of resistance which the peripheral nerves offer to the compression and invasion of these tumors. The nerve tubes usually undergo no appreciable nutritive alteration. In the brain myxomata often form greenish tumors. The various glands may also be their seat. They are occasionally found under the periosteum, and are met with also in the bones, usually in the short bones, where they are generally connected with the periosteum. In the skin they may often assume the papillary form.

ANATOMICAL DIAGNOSIS OF MYXOMA.—The differential diagnosis is very difficult only when we attempt to determine whether a tumor is a sarcoma with mucous metamorphosis, or a myxoma with islands of embryonal tissue. We may be guided by the fact that in parts of a sarcoma which have suffered colloid metamorphosis, the cells are destroyed; in the remainder of the sarcomatous tumor the proper structure can be recognized. The presence of elastic fibres or of genuine adipose cells immediately suggests a myxoma.

PROGNOSIS OF MYXOMA.—Myxomata are generally non-malignant. Entirely removed, they very rarely return. They almost never cause secondary formations, except in the case of multiple myxoma of nerves. When incompletely removed, they redevelop with a new vigor, like every tumor irritated by surgical interference which is not effectual. Myxoma may increase in size at the expense of the neighboring connective tissue which has first become embryonal, or it may enlarge by the proliferation of its own proper mass. Virchow has several times seen these tumors form metastatic formations.

It is probable that their gravity or benignancy is proportional respectively to the amount of embryonal tissue and of elastic or adipose tissue which they contain.

2D CLASS.—Fibrous Tumors. Fibroma.

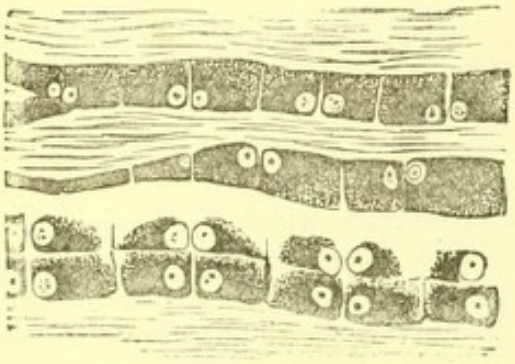
SYNONYMS.—These tumors have received the name of *fibroid* and *desmoid*. When the tumor was very hard, J. Muller called it a steatoma.

Verneuil proposed the name of *fibroma*, which is now generally employed, and which defines the tissue as well perhaps as the word *innoma*, given by Paget.

Definition.—The definition of fibroma is supplied by that of fibrous tissue.

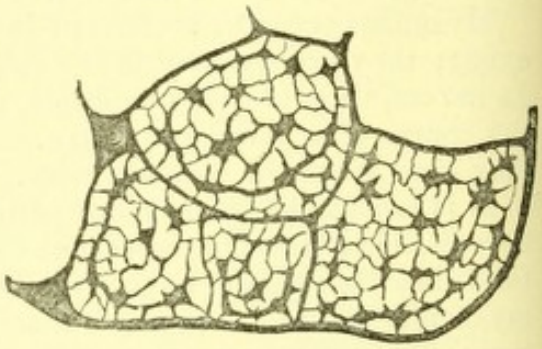
Two varieties of fibrous tissue, that known as dense white fibrous tissue, and that seen in the inner membrane of arteries, will serve as a basis for the description of two corresponding varieties of fibroma.

Fig. 69.



Caudal tendon of young rat: showing arrangement and form of the flat endothelial cells, after treatment with silver nitrate. High power. (*Carpenter.*)

Fig. 70.



Transverse section of tendon: showing so-called branched corpuscles, inclosing spaces which, left blank, are naturally filled with tendinous fasciculi. High power. (*Carpenter.*)

In order that a tumor may be called a fibroma, it is not sufficient that it contain connective tissue and vessels; it is necessary that it contain nothing else.

Description of Fibroma.—Fibromata are tumors which are dry, hard, firm, and pearly, pink, or white. When they are scraped with a razor, the edge of the instrument detaches small distinct fragments. In a thin section of a fibroma, one will see bundles of fibres which intercross in every direction, as in the skin; some of the fasciculi will be seen lengthwise, others in cross-section, still others obliquely. It will be impossible to misconstrue this disposition, especially if the sections are colored with carmine and treated with acetic acid. One will then see very distinctly a network of plasmatic cells among the bands of fibrous tissue. These bands are to be distinguished from bundles of spindle-cells or smooth muscular tissue by the fact that the nuclei of the fibres are not in their interior, but are upon them.

Generally there are no elastic fibres in this tissue, and this is one important point. Vessels are not very abundant; they are found especially in those parts of the tumor which possess a loose connective tissue, and they consist of arteries, capillaries, and veins.

We will describe two species of fibroma.

1st species: Fibroma with flat cells and an amorphous fundamental substance.—We often see upon serous membranes—especially the peritoneum which covers the liver, and, above all, the spleen—hard

tumors, usually small, disposed in plates, in villosities, or small globular masses, which certain authors have described *à propos* of perihepatitis and perisplenitis. These tumors are at times flattened upon the convex surface of the organ; otherwise they form prominences, consisting of one or more lobules closely united by intermediate tissue, or scattered over the surface some distance apart. To the naked eye, they have a great resemblance to cartilage; they are translucent and slightly yellow; they cut with difficulty, but do not creak under the knife like cartilage. They are so hard that thin sections can readily be made in the fresh condition. The latter examined in water, without recourse to any reagent, show parallel lamellæ separated by openings. After staining with carmine, cells can be very distinctly seen in these open spaces. The cells are flat, have an elongated nucleus, and processes which anastamose with neighboring cells. These preparations very much resemble those of the cornea, and, on this account, Rindfleisch called them corneal fibromata. But their fundamental substance is different from that of the cornea, for it is amorphous. It probably consists of gelatine. These fibromata do not contain vessels. They are very frequently the seat of calcareous infiltration; the tissue then becomes yellow, opaque, and solid. A genuine petrifaction may, however, take place, when they are translucent and stony. The petrifaction may occur in superposed layers. Such are the formations which the old authors called osseous plates of the pleura, peritoneum, etc. The calcareous infiltration of these tumors always commences at their centre.

2D SPECIES: FASCICULATED FIBROMA.—To the naked eye, these tumors have a characteristic aspect. They consist of an agglomeration of a number of firm hard lobules. Upon section, the centre of each of these lobules forms a conical prominence, and the fibrous bundles which compose the cone are interwoven in a concentric manner. Several similar lobules are united together by a loose connective tissue, permeated by vessels which sometimes, but not always, penetrate the interior of the lobule. Under the microscope, the bundles of fibrous tissue which compose the lobules are seen to intercross in every conceivable direction, and to contain cells which form a network, as in young or adult connective tissue.

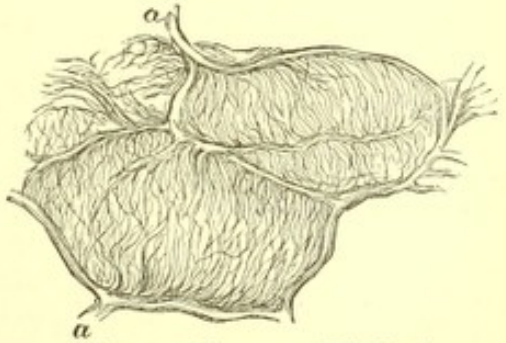
The varieties of fasciculated fibroma depend upon modifications of nutrition.

a. In some, the fundamental substance is infiltrated with serum, as in œdema; the tumor is then called *molluscoid fibroma* (Molluscum simplex). (Fig. 71.)

b. In other cases, a mucous metamorphosis of the fundamental substance and of the cells may cause a partial destruction of the tumor by the formation, in points, of cysts filled with detritus—*Mucoid fibroma*.

c. Except in those fibromata which have a syphilitic origin, fatty degeneration is rare. Syphilitic fibromata

Fig. 71.



Fibroma molluscum. (*Virchow.*)

soften at the centre, and through this degeneration, united with the mucoid, may disappear. We do not classify these tumors with gummata, which have a definite histological character.

d. Calcareous infiltration is so frequent in these tumors that few fibromata escape it entirely, after they have existed for a long time. It begins at the centre of the lobule, that is, at the point most distant from the vessels.

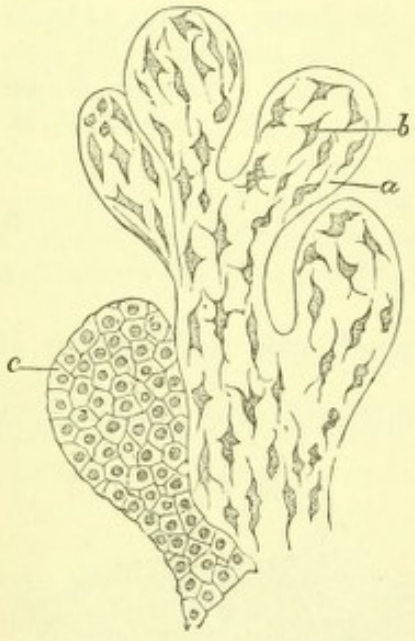
The fibrous tissue which exists to a greater or lesser extent in combination with lipoma, myxoma, carcinoma, etc., is only an accessory element in them, and should not therefore cause a classification among the fibromata of any growth in which the fibrous tissue holds only a subordinate position.

e. When fibromata have the form of a pedunculated polyp, they may from irritation inflame, ulcerate, and, like every suppurating wound, heal by granulation.

The DEVELOPMENT of fasciculated fibroma is not well understood, because generally they are removed only after they have completed their growth, when they are stationary and their process of development is dormant. Foerster states that there are islands of embryonal tissue in fibroma which are increasing. It may be supposed from this fact that each lobule may possess an independent centre of development.

The SEAT of fibromata is variable. They are found in the skin and in the subcutaneous cellular tissue. Upon mucous membranes they are observed less frequently than are myxomata. The retro-pharyngeal polypi form an exception to this rule. In the mammæ, they are seen under two forms: the one constitutes a single mass which presents the character of a fasciculated fibroma (fibrous bodies of the mamma, Cruveilhier); the other is diffuse, and is accompanied by a proliferation of the epithelium of the culs-de-sac and ducts of the gland. The canals enlarge and become transformed into genuine lacunar cysts, into which vascularized fibrous vegetations, covered with epithelium, may project. (*c*, Fig. 72.)

Fig. 72.



Papillary fibroma of the breast. Fibrous vegetations projecting into the galactophorous canals which have become cystic; they are covered by their epithelium at *c*, and are denuded of it at *a*; *b*, connective tissue corpuscles. × 300.

Fibromata are frequent upon the periosteum. A point in their differential diagnosis from sarcoma of the periosteum, which Virchow insists upon, is that the former do not penetrate into the bone, but are limited to its enveloping membrane.

The ANATOMICAL DIAGNOSIS of fibroma is easy; sarcoma and myxoma, in their cystic varieties, are the only tumors with which certain mucous fibromata could be confounded; but an examination of the parts external to the cyst will furnish the data for the solution of the problem.

PROGNOSIS.—These tumors are *benign* and generally single. As a rule, they do not return after their complete ablation. Retro-pharyngeal fibroma may form an exception to this law. Molluscoid fibromata have a certain malignity, by reason of their extension or their considerable size. The fibromata, as a class, are more innocent than the myxomata.

3D CLASS.—**Lipoma.**

SYNONYMS.—Cruveilhier has proposed the word *adipoma*. When the consistence of the tumor was firm and hard, it was formerly called a *steatoma*. Cruveilhier named the latter *adipo-fibroma*.

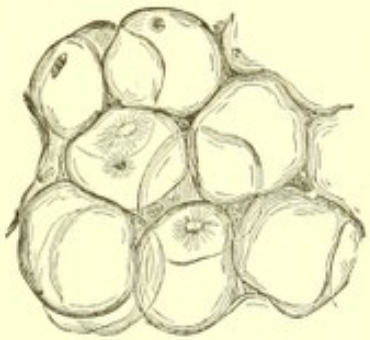
DEFINITION.—The definition of lipoma is based upon the cellulo-adipose tissue which constitutes it.

We do not recognize as a lipoma the masses of adipose tissue which replace an atrophied organ, nor do we think of lipoma when considering the presence of a large quantity of fat in the omentum or other parts in persons with an exaggerated corpulency. The name should be limited to abnormal circumscribed masses of adipose tissue having, to a certain extent, a vitality independent of the rest of the organism. This independent vitality is demonstrated by the fact that a person carrying one of these tumors may become emaciated without seeing his tumor diminish in volume.

DESCRIPTION OF LIPOMA.—In the physiological state, the adipose vessels are collected together in limited masses or lobules. These lobules are also met with in lipoma. They contain very large adipose cells, which are surrounded by an enveloping membrane; the nucleus of these transformed connective-tissue cells is very distinct. Both the lobules and the cells are much larger than in the normal state.

The naked-eye aspect of lipoma perfectly resembles that of the subcutaneous adipose tissue. Its peculiar structure gives it a softness and false fluctuation which is characteristic.

Fig. 73.



Lipoma. Some of the cells contain crystallized fatty acids. × 200.

The *size* of lipomata is variable; sometimes the tumors are of colossal dimensions.

In *form*, these growths are lobulated and have either diffuse or very sharply limited borders. They often form polypoid elevations, and may sometimes have a pedicle. They may be single or multiple.

Concerning their *location*, lipomata are frequently observed in the areolar tissue of the skin. They have been seen in the mucous membrane. Upon serous membranes, adipose polypi may exist in the normal state; such are the epiploic appendages of the large intestine and the fringes of articular synovial membranes. These may be the starting point of lipoma.

Lipomata may be found in muscular tissue. Here the muscular fasciculi remain normal, which is not so of any other new formations seated in muscular tissue. Lipomata of bones are rare.

In the mammary glands, the new tissue is disposed around the galac-

tophorous canals and the acini, while the organ preserves its form. It may acquire a volume and weight so enormous that it is imposible for the patient to walk.

Species and Varieties of Lipoma.

1st species: Pure lipomata are composed of nothing else than adipose tissue, with a very small amount of connective tissue surrounding the lobules; the latter are large, and give a distinct sense of a characteristic false fluctuation.

2d species: Myxomatous lipomata.—The myxomatous tissue is found in the lobules between the adipose vesicles.

3d species: Fibbous lipomata.—In them the interlobular connective tissue is very abundant (adipo-fibroma of Cruveilhier, and steatoma of old authors). By the naked eye, it might be confounded with fibroma and carcinoma.

4th species: Erectile lipomata.—The vessels may be very numerous and distended.

Nutritive alterations in *lipoma* which are worthy of study are:—

a. Fatty degeneration: the adipose vesicles rupture and become reduced to fine granules; the tissue has then a gray opaque appearance. *b. Gangrene* is possible in lipoma, and is most frequently seen in morbid masses arising from the peritoneum or synovial membrane. *c. Calcareous infiltration* may occur. *d.* The lipoma may inflame, in which case embryonal tissue is formed, the fat of the adipose vesicles is partially absorbed, whilst the tumor becomes harder.

Development of Lipoma.—Since it is in the plasmatic cells (connective-tissue corpuscles), whether they are newly-formed or pre-existent, that the fat first appears, they may be considered to be the starting-point of the morbid growth.

Prognosis of lipoma.—These tumors are grave only on account of the volume which they may attain, the inflammatory accidents which they may determine, and by reason of their location.

4th Class.—**Carcinoma.**

This class comprehends tumors which by their aspect and gravity appear to be separated from the other forms of tumors, the type of which is in the connective tissue. But nevertheless, they properly belong with connective-tissue growths, because of their origin, their mode of development, and their constitution.

Synonyms.—The word *carcinoma* corresponds to the terms alveolar, scirrhous, encephaloid cancer, etc., but the synonym is far from being absolute.

Definition.—The word carcinoma, employed at first in Germany in the same vague sense as cancer, has of late received a more precise definition, based upon histological structure. Nevertheless, it has not yet been sufficiently defined, for to-day many of the German pathological anatomists do not consider carcinoma and epithelioma as absolutely distinct.

We would define carcinoma in the following terms:—

Carcinoma is a tumor composed of a fibrous stroma limiting alveoli, which latter by communications with one another form a cavernous system; these alveoli are filled with free cells, which are separated from each other only by a fluid more or less abundant.

General Description of Carcinoma.—Let us study each of these two parts—the stroma and the contents of the alveoli. The cells contained in the alveoli in the midst of an intercellular fluid substance constitute, with the latter, the milky juice of cancer. This milky juice is easily squeezed from the cavernous tissue, or is readily obtained by scraping. When one examines this fluid under the microscope, there is always observed a considerable number of cells which present an inconceivable variety of form and dimension. Some round and uninucleated are small, measuring only .009 or .010 mm.; others, equally spherical, are more voluminous, reaching a diameter of .020 to .040 mm., and even more. Often they are polygonal, with obtuse or very sharp angles; such are the cells with sharp caudal extremities. Nothing can be more varied than these forms. Certain of these cells appear flat when they present their surface, and thin when seen in profile. They may be lengthened into the form of a spindle at their extremities, like the cells of fasciculated sarcoma. A polymorphous analogue, although less pronounced, may be met with in sarcoma, as we have seen.

These cells inclose one or more nuclei, sometimes as many as 15 or 20 in a single cell. The nuclei are large, oval or spherical, and contain one or more nucleoli, usually voluminous.

Fig. 74.



Cells from a scirrhus of the mamma. ×350. (*Green.*)

Fig. 75.



Cells from a cancer: showing cell-contents, nuclei, and nucleoli; the nuclei dividing. (*Rindfleisch*).

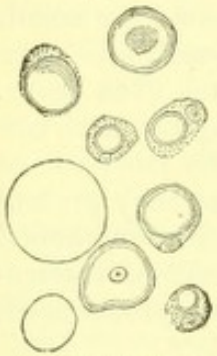
When they are very large, the nucleoli appear as vesicles. The nuclei often have a double contour. These forms of nuclei and nucleoli are often met with in the cells of sarcoma and even sometimes in simple inflammatory growths.

The cells of carcinoma are polygonal by reciprocal pressure when they are contained in a cavity with only a very small amount of intercellular fluid substance. The anatomical reason of this form of the cells

is the same as that which determines the pavement form of the cells of mucous membranes. From this analogy of forms some authors have concluded an analogy of nature, and have employed the term epithelial or epithelioid for the designation of the cells of carcinoma. These cells do not appear to have a proper membrane, and they are not closely united, which features sharply separate them from cells of epithelium.

Besides the foregoing variations of form, which are more or less due to pressure, the cells of carcinoma experience divers other aberrations. They are subject, like other cells, to all the changes of nutrition, such as vacuolation, vesiculation, mucoid degeneration, fatty degeneration, etc. These nutritive alterations give rise to varieties (see fig. 76).

Fig. 76.



Colloid cells, from a colloid cancer. (*Rindfleisch.*)

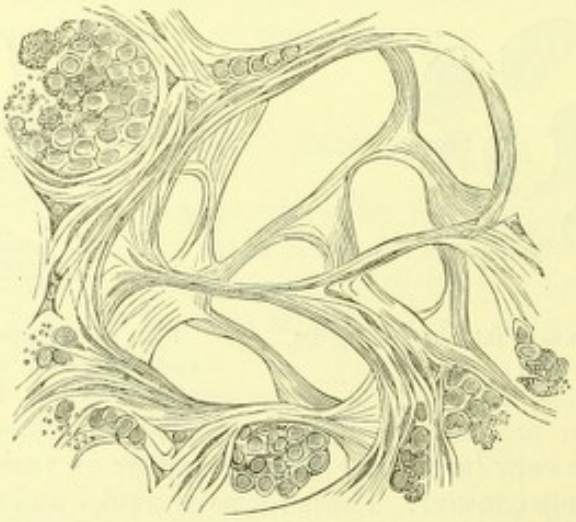
The *stroma*, the second essential constituent part of carcinoma, is obtained in fragments by scraping, or by making a thin section and afterwards brushing away the contents of the alveoli.

It consists of fibrous trabeculæ united together and forming a continuous whole. Each trabecula represents one or more fasciculi of connective tissue containing plasmatic cells. The latter become distinct when, by the addition of acetic acid, the fibrils have swollen and become transparent and homogeneous (see fig. 77).

It is especially at the nodal points or points of union of trabeculæ that the plasmatic cells are seen to contain one or more ovoid nuclei. In these fibrous trabeculæ arteries, capillaries, and veins form a very regular network.

Do carcinomata possess lymphatics? Schrœder van der Kolk has injected them, and Rindfleisch thinks that they form channels around the

Fig. 77.



Pencilled stroma of carcinoma, showing alveoli. The masses of cells remain in some. ×300. (*Rindfleisch.*)

bloodvessels, analogous to the perivascular lymph sheaths of the nerve centres. We shall soon return to the consideration of this point.

When a very thin section of a carcinoma is examined, it may be imagined that the alveoli are perfectly closed cavities, but when the section is thicker, it is very readily seen that we have to do with a cavernous tissue, the cavities of which communicate with one another.

DEVELOPMENT OF CARCINOMA.—The development of carcinoma brings us to its nature. Let us see what transpires in the development of carcinoma in the midst of bony tissue.

We observe at first just what takes place in the inflammatory process. The phenomena of rarefying or condensing osteitis constitute the *first phase* or period of hesitation of development of carcinoma in bone. Soon, however, the embryonal marrow becomes transformed into fibrous tissue; *second phase* or *fibrous phase*.

It is from this newly-formed fibrous tissue that carcinoma is developed by a peculiar method. This tissue possesses a fundamental fibrillar substance containing plasmatic or lymph spaces, within which the cells enter into proliferation and give birth to 3, 4, or 5 small cells. The lymph spaces grow in size and constitute irregular alveoli with canalicular projections which anastomose with those of neighboring spaces. These spaces after further enlargement become rounded, and, at the same time, the cells multiply and grow in their interior. Thus the cavernous tissue of carcinoma is formed.

Fig. 78.



Development of carcinoma in the mamma. *a*. Lymph spaces which enlarge by the multiplication of their cells; at *c*, they have preserved their angular form; at *d*, they have become spherical and form there the alveoli of carcinoma. × 150.

In the mammary gland an analogous development is observed. The trabeculæ of connective tissue which enter into the composition of the gland and which from thence radiate into the neighboring tissue, become more charged with juice than in the normal state, thicken and soften. Upon a thin section, it is discovered that the lymph spaces are in process

of enlargement, and that they end, by the proliferation of the cells which they contain, in the formation of carcinomatous alveoli.

This dilatation of the lymph spaces takes place without degeneration of the fundamental substance which, on the contrary, becomes more dense under the pressure which the contents of the alveoli exercise upon it. This pressure, exerted regularly in all directions from the centre of the alveolus, is the cause of the spherical or rounded form of the alveoli. (Fig. 78.)

In carcinoma of the mamma the adipose tissue is preserved; the tumor grows at the expense of the connective-tissue trabeculæ which separate the lobules of adipose vesicles, while the latter for a long time remain intact in the midst of the morbid mass. These islands of fat, angular and disseminated irregularly over the section of a tumor, have enabled us many a time to form, by the naked eye examination, an opinion which has always been verified by the microscope.

At the same time that these phenomena are transpiring in the fibrous trabeculæ, the epithelium of some of the canals and acini proliferates, on account of an adjacent irritation. The acini become distended with cells, and hypertrophied to such an extent that one might be inclined to believe in a direct relation between the proliferation of the cells of the epithelium and the development of carcinoma.

It has even been claimed that a carcinoma is a new gland destined to eliminate noxious elements from the organism, just as the kidney eliminates urea. The falsity of this conception is demonstrated by the fact that, instead of a thorough ablation of the morbid mass producing an intoxication, it is the only remedy which offers even a small degree of safety to the patient.

It is upon the existence of this new epithelial tissue in the acini and galactophorous canals of mammæ which are the seat of carcinoma, that is founded what analogy may exist between the latter and the glandular system. The force of this analogy is destroyed by the process of development which we have related. In epithelioma, on the contrary, we never see epithelial tissue developed in the interior of lymph spaces, but in embryonal tissue in the neighborhood of pre-existent epithelial tissue. What characterizes carcinoma is its development in the lymph spaces of the connective tissue, and the mammary gland does not escape this rule.

[At the present time most pathologists, and especially the German, are inclined to consider carcinoma as of glandular or epithelial origin rather than as developing from the cells of the connective tissue. In support of the former view, Rindfleisch says, "the majority of carcinomata proceed primarily either from the epithelial clad surface of the body, from the skin and mucous membrane, or from secreting glands. They depend upon an abnormal growth of the epithelial tissue." Billroth, in his work on "Surgical Pathology," "maintains a strict boundary between epithelial and connective-tissue cells," and says, "true carcinoma have a formation similar to that of true epithelial glands (not the lymphatic glands), and whose cells are mostly actual derivatives from true epithelium." This writer even goes so far as to say that "it is impossible for an epithelial cancer to occur primarily in a bone or lymphatic gland." Waldeyer defines carcinoma as an "atypical epithelial neoplasm." Birch-Hirsch-

feld also accepts this definition of Waldeyer for the histogenesis of scirrhus; but describes as endothelial cancer a tumor developed from the endothelial cells existing in tissues, and therefore of connective tissue origin. S. Samuel, Cohnheim, Klebs, and Lücke, all consider carcinomata to have their origin only from epithelial cells, and not from the connective-tissue cells. Rudnew, of St. Petersburg, in his work on general and special pathology, expresses himself as believing in the epithelial origin only of carcinoma. Perhaps all of these diverse opinions present a part of the truth concerning the nature and origin of carcinoma. But these are problems which should not, in the present state of our knowledge, be dogmatically decided. It remains for future investigators to determine the relative influences of proliferation of the connective-tissue corpuscles, of the endothelial cell, of the epithelial cell, whether glandular or investing, of the wandering white corpuscles, and of the infective power of certain elements, upon the genesis and the extension of carcinoma.]

The *increase of the tumor* is either by the growth of its own mass or by invasion of neighboring tissue. One finds a proof of the growth of carcinoma by proliferation of its own tissue, when upon sections of hardened pieces, one recognizes in the trabeculæ of the fibrous stroma, lymphatic spaces, which are distended with cells, and which are in process of conversion into carcinomatous alveoli.

Fig. 79.



Carcinoma of mammary gland—the ground substance of the section stained with nitrate of silver. *a*. Alveoli of the carcinoma filled with cells. *b*. Lymph spaces shown in the fibrous tissue after treatment by nitrate of silver. *c*. Lymphatics showing silver staining of the endothelium.

Growth by invasion of neighboring tissue is *continuous* or *discontinuous*. What is meant by these phrases has already been explained *à propos* of sarcoma. Both of these modes are common in carcinoma.

The *generalization* or the secondary production of tumors in dis-

tant parts is always, in carcinoma, preceded by a hypertrophy with induration of the lymph glands into which the lymphatics from the tumor empty.

Why is carcinoma the pathological tissue which most easily and most constantly determines lesions of the lymph glands? It is because *the alveoli of carcinoma communicate with the lymphatic vessels of the tumor and of the neighboring tissue.*

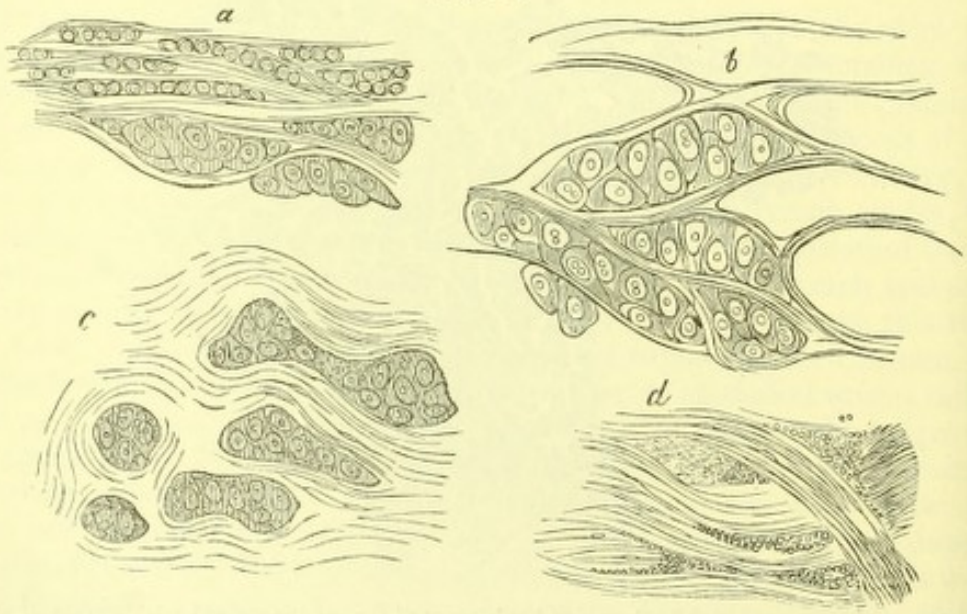
This truth is demonstrated by the study of preparations made by the impregnation of nitrate of silver. (Fig. 79.) This is a fact of the greatest importance, and which justifies the analogy claimed by us between carcinoma and connective tissue.

In carcinoma the fibrous tissue presents a hyperplastic aberration of certain of its elements.

The lymph glands in carcinoma generally, though not always, exhibit the structure of the primary tumor; but they may undergo simply a fibrous transformation. It is in this fibrous tissue that the alveoli will form if the original growth is reproduced. This fact, which is often very evident, has escaped the authors who have preceded us. It has for us great significance, for it adds to the support of our view of the nature of carcinoma.

Species and Varieties of Carcinoma.—These species are based neither upon the size nor upon the form of the cells; the latter, in effect, are usually small in a young carcinoma, and, on the contrary, voluminous

Fig. 80.



Scirrhous carcinoma. Carcinoma simplex mammæ. *a*. Development of nests of cancer cells. *b*. Fully formed carcinoma tissue. *c*. Commencing cicatrization, and at the same time a representation of the relation of stroma and cells in scirrhus. *d*. Cancer cicatrix. ×300. (*Rindfleisch.*)

in a carcinoma in full development; their round or polyhedric form is solely connected with the greater on lesser quantity of intercellular fluid. It is upon the amount and the condition of the stroma that the species of this class of tumors depend.

1st Species: Fibrous Carcinoma (Scirrhus).—When the trabeculæ of the stroma are thick in proportion to the size of the alveoli, and are resistant, we have to do with a hard or scirrhous carcinoma. The fibrillar aspect of the trabeculæ is not marked; this tissue condenses, becomes homogeneous and refracting. Sometimes a fatty degeneration of the cells in the alveoli is seen; the cells may break down, the fatty granules set free in the intercellular fluid are then borne away by the lymphatics; the fibrous tissue may then contract so that the alveoli which contain only a very small amount of fluid and some fatty granules become almost effaced—the condition of *atrophic scirrhus*. This atrophy is seen in some points, especially in the central portions of the growth, which then yield no juice, while the periphery of the tumor shows alveoli containing both cells and juice. The lymph glands are very quickly involved in this form of tumor. By secondary metastasis the growth constantly but slowly invades most of the organs and tissues, whilst the primary morbid mass may increase only very slowly or not at all, or may even undergo atrophy.

2d Species: Encephaloid or Medullary Carcinoma.—In this form of carcinoma the fibrous trabeculæ are narrow in proportion to the diameter of the alveoli. The fibrous tissue is not very resistant, consequently hemorrhages readily occur. Upon section the surface of the tumor is soft and diversely colored—mottled grayish-white or pink, and red, yellow, or brown.

The primary tumors grow much more rapidly in this form than in scirrhus, but then metastasis is less extensive.

We may distinguish several varieties of encephaloid carcinoma:—

The *pultaceous form*, in which the tissue is soft and the alveoli are so voluminous that they can be distinguished by the naked eye. By pressure the growth exudes a very thick and abundant juice. The *erectile hæmatode* is often associated with the preceding form: in it, the bloodvessels, which are very numerous, become dilated into diverticula or aneurismal sacs, visible to the naked eye as little red points; they project into the alveoli, and may rupture, and give origin to blood extravasations therein.

Fig. 81.

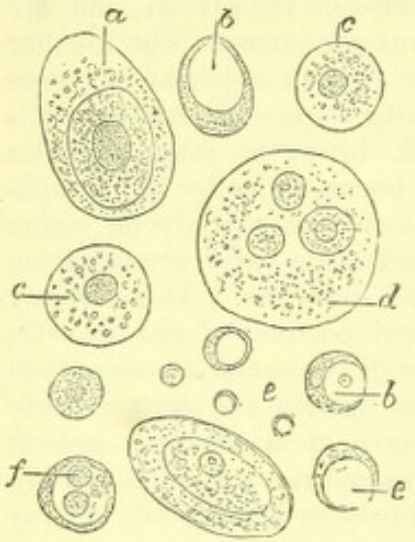


Encephaloid cancer, from a secondary cancer of the liver, showing the large size of the alveoli and the thinness of their walls. In the latter small cells are visible. The large epithelial cells are commencing to undergo fatty metamorphosis. × 200. (*Green.*)

The softness of an encephaloid carcinoma may be entirely due to the presence of only an extremely small amount of fibrous tissue, the alveoli themselves being small, but separated from each other by thin trabeculæ. Changes in the nutrition of the elements of carcinoma give rise to the three following forms:—

3d Species: Lipomatous Carcinoma.—The cells in the alveoli become filled with fat drops and resemble adipose cells of connective tissue, but

Fig. 82.

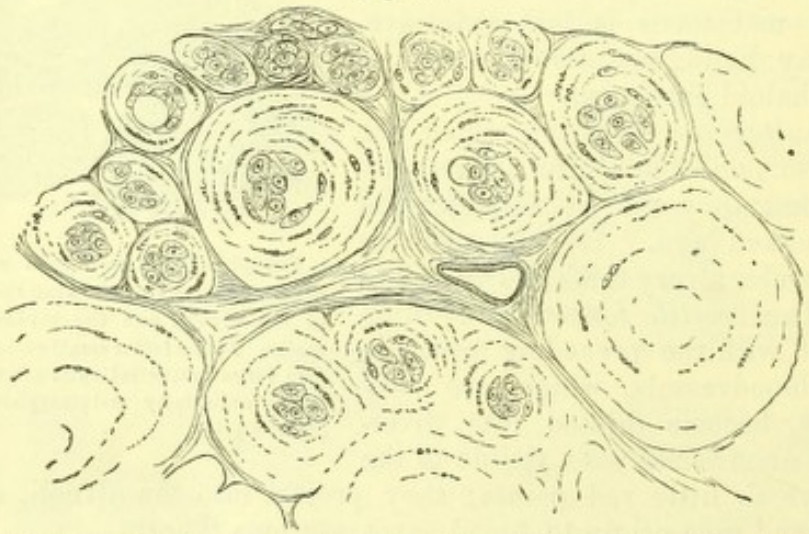


Cells of colloid carcinoma. *a*. A large cell containing another cell within it. *d*. Mother cell. *c*. Cells infiltrated with colloid matter. *b*. Cell filled with a colloid drop. *e*. Cells reduced to a disk in processs of destruction. ×350.

there are no bands of connective tissue which hold them together. These tumors so greatly resemble lipomata that they may be readily mistaken for the latter if they are not carefully studied. In these cases the cells are not destroyed. We have seen an example of metastasis of this species of carcinoma where all the secondary tumors presented the same characters.

4TH SPECIES: COLLOID CARCINOMA.— The metamorphosis of the cells of this species of carcinoma gives to it a characteristic gelatiniform aspect which is reproduced in the secondary formations. Colloid cancer has also been called *alveolar*, which is an objectionable word, because all carcinomata are alveolar. The alveoli of colloid carcinoma do not essentially differ from those of the other species; their trabeculæ are more easily seen only because the alveoli are filled with colloid matter, which is more or less transparent. (Figs. 76, 82, 83.) The cells become loaded with drops of colloid matter, become spherical, vesicular, and finally destroyed. Those which remain are sometimes colossal; there are then only a few cells

Fig. 83.



Colloid cancer; showing the large alveoli, within which is contained the gelatinous colloid material. ×300. (*Rindfleisch.*)

in each alveolus, in the midst of a fluid also colloid. The alveoli themselves are distended by this fluid, and have a regularly spherical form. As is the case with all colloid degenerations, here also there is united with it some fatty degeneration of the cells. The stroma of the tumor occasionally may be so little modified that the fibres of the connective tissue are very distinct; at other times the trabeculæ are œdematous, and their fibrils

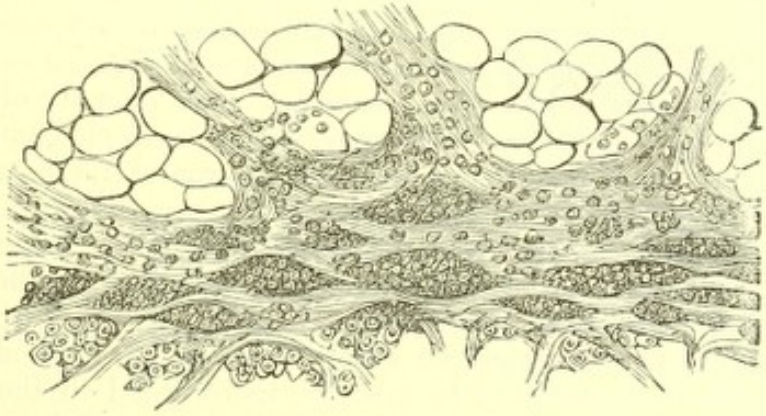
are separated by a small amount of fluid. They also may have undergone colloid metamorphosis, and have been destroyed or very much thinned. One then finds an anfractuous cavity, festooned at its periphery, and showing very fine intercrossing fibrils, the remains of thin trabeculæ forming arcs of regular circles (see fig. 83); a number of such anfractuous cavities, with some more perfect alveoli are collected together into a lobule bordered, however, by bands of fibrous tissue. It is this disposition which causes the naked eye appearance of alveoli, and which has suggested the name "alveolar carcinoma." The foregoing alterations are sometimes accompanied by dilatation of the vessels which may rupture and give rise to extravasations of blood.

5TH SPECIES: MELANO-CARCINOMA.—It is more rare than melano-sarcoma. The cells contained in the alveoli are in contact with each other, and present in their interior melanotic granules. The trabeculæ may also be infiltrated by the same granules, which are then deposited around the plasmatic cells which they contain.

Independently of the foregoing characteristics, which are reproduced in the secondary formations, many carcinomatous tumors may present modifications of nutrition which serve to establish varieties in each of the preceding species. These are:—

a. Fatty Degeneration.—All carcinomata, especially at their centre, present traces of fatty degeneration. The parts thus altered are yellow, more or less dry, and opaque. The degeneration may also affect the plasmatic cells of the stroma and the capillary walls. Consecutive to such a destruction of portions of the growth there results a retraction of the tumor. In the secondary deposits in the serous membranes, as in the liver, this atrophy is characterized by shrinking of the central part of the tumor, and umbilication of the surface. In the skin, and particularly in the mammæ, the atrophy shows itself by a depression in the form of a hard and callous cicatrix.

Fig. 84.



Cellular infiltration of the fatty tissues around a carcinomatous lymphatic gland. (*Billroth.*)

b. Caseous Metamorphosis.—In all tumors of rapid progress, especially in carcinoma, obliteration of the vessels may occur, when there often results a caseous degeneration. In the portions of the mass de-

prived of blood, ulceration may take place when the tumor is superficial, or an infarction result when it is deep seated. These infarctions also become caseous.

c. Calcareous infiltration is very rare in carcinoma; nevertheless, in the vicinity of bones the stroma may experience this change; this is what has been wrongly called ossifying carcinoma.

d. Inflammation and ulceration of carcinoma may follow traumatism or may occur in the ordinary growth of the tumor.

In these cases we observe in the neighborhood of an ulceration an intense proliferation of the cellular elements contained in the alveoli, the new elements presenting all the characters of embryonal cells. The alveoli disappear by becoming lost in a mass of embryonal tissue, in the midst of which are still found a few of the fibrous trabeculæ of the cancer stroma. This inflamed tumor, especially at the surface, is extremely vascular. A similar embryonal transformation is never observed in the cells of epithelioma, as we shall see.

e. Villous Carcinoma.—Whatever may be the species or variety of carcinoma, when it affects a cutaneous or mucous surface, we see granulations arise soon after ulceration. These villous buds have a much greater length than in a simple ulceration; they are numerous, and pressed closely together. It is these which have given to the tumor the name of villous carcinoma. The vessels which the villi contain may have small aneurismal dilatations, and may be the point of departure of hemorrhages more or less considerable and repeated.

Anatomical Diagnosis of Carcinoma.—It is very difficult by the naked eye. Carcinoma has, in effect, been confounded with all the malignant tumors, and even with infarctions until recourse has been had to microscopic analysis.

The presence of the so-called cancer-juice is not a sufficient characteristic, as we have already seen. And we shall see that a similar fluid is found in soft epithelioma, and in lymphatic tumors; this is so also of infarctions and sometimes of tissues attacked by a diffuse suppuration.

The cells of carcinoma have of themselves nothing characteristic. It is necessary to discover the presence of an alveolar stroma, and of clumps of cells contained therein. It is not from the study of scrapings, or of the juice of carcinoma, but only by the microscopic examination of thin sections of the tumor that we can be assured of the peculiar structure which we recognize as carcinoma. The special alveolar arrangement of the stroma of carcinoma, will always differentiate it from sarcoma, in which we may perhaps meet with fibrous trabeculæ parallel with the vessels, but seldom regular alveoli.

An atrophic scirrhus might be taken for a fibroma if we did not recognize the alveoli, which may be more or less effaced in the atrophied portions, but which are unmistakable at the periphery of the tumor.

The differential diagnosis from epithelioma will be spoken of when considering the latter.

Prognosis of Carcinoma.—The termination of carcinoma is always fatal; but the duration of the disease and its malignancy vary according

to the species. Thus the pultaceous or encephaloid form most rapidly acquires a considerable volume by invasion of the neighboring tissues. Scirrhus, especially the atrophic variety, is remarkable for the slight tendency of the primary tumor to extend, for the slowness of its progress, and especially for the certainty of its generalization, which is extensive in proportion as the disease is older.

It is difficult to decide whether the secondary metastasis is more closely connected with the particular variety of the tumor or with its long duration.

Seat.—Carcinomata may develop primarily in all the organs, but they are most frequently seated in the glands and in the viscera which are lined with mucous membrane, particularly the stomach, the uterus, the mamma, etc.

Here ends the study of a class of tumors characterized by a hypertrophic aberration of the cellular elements formed in the lymph spaces of the connective tissue, the type of which is in the connective tissue. We now propose to examine a series of tumors in which the same elements atrophy. Such are syphilitic growths, tubercular formations, and glanders. These three species of tumors have this in common, viz., that each of them is connected with a general constitutional disease.

5th Class.—Gumma.

In an anatomical point of view, the most characteristic lesions of syphilis are gummata. Every syphilitic product is not a gumma; most of the lesions of syphilis present no anatomical difference from those caused by simple inflammation. The lesions determined in connective tissue by hard chancre, do not essentially differ anatomically from those which inflammation produces in the same tissue. The cells resemble those of granulation tissue: they are embryonal, round, or fusiform; some correspond to pus corpuscles. They are situated in the midst of a fundamental substance, amorphous or fibrillar and resistant, to which the chancre owes its induration. If there be anything which may distinguish the tissue of chancre from ordinary inflammatory tissue, we think that it will be found in this fundamental substance.

When indurated chancre heals, the embryonal tissue which forms its base, tends to form adult connective tissue. All the products of the first period of constitutional syphilis, and all the malformations of the second period, consist of inflammatory tissue which possesses the property of reforming the old tissue, and which may leave no trace behind. This is no more true of lesions in the skin than it is of lesions of the same stage in the deep parts, for example, in the parenchymatous organs, the periosteum, and bone. Therefore the division of syphilis into primary, secondary, and tertiary periods, where the word secondary is applied to cutaneous syphilides, and the word tertiary designates lesions of the bones and the parenchymata, does not appear to us to be correct.

It would be nearer the truth, from the anatomical point of view, if we

should term *secondary* the purely inflammatory lesions of syphilis, and *tertiary* the later lesions which manifest themselves under the form of *tumors*.

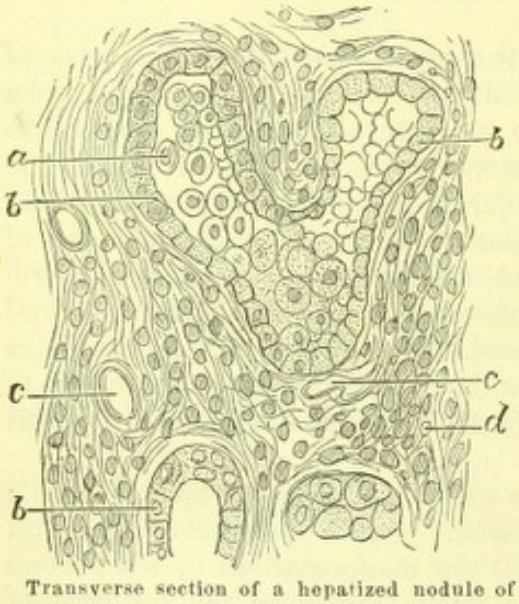
For a good understanding of the pathological phenomena of syphilis, it will be necessary to study what occurs in each tissue and each organ. In the bones we observe, contemporary with the secondary accidents, the rheumatoid pains of Ricord; they are not due to permanent lesions. Later we see manifested chronic inflammations at the surface of the bones (periostitis and resulting periostoses), or more deeply, osteitis, which may at first be rarefying, but which subsequently ends in the condensation of the osseous tissue—the obliteration of the Haversian canals, the latter occurrence often determining necrosis. At a later epoch veritable gummata may form.

In the liver, at first we have interstitial hepatitis, either general or circumscribed, but always characterized by a new formation of fibrous tissue. Later genuine gummata appear.

In the testicle we also have to do with interstitial fibrous products, afterwards with gummata.

In the lungs an interstitial syphilitic pneumonia may be diffuse or circumscribed. This lesion of the lung has received different names. Lorain and Robin called it epithelioma of the lung; it is the white hepatization of Virchow, which other authors regard as gumma. It is seen in new-born children, and up to the age of ten or twelve years. To a certain degree its characters approach the structure of the lung of the embryo. In syphilitic pneumonia the inter-lobular connective tissue enters into proliferation and presents a large quantity of embryonal cells; the alveolar walls are thick while the narrowed alveoli are lined, and even filled by epithelial cells, which are of the pavement form in contact with the walls, round in the centre of the alveoli. As the process progresses the epithelial cells become fatty degenerated, and subsequently broken down and absorbed, while the embryonal interalveolar tissue rapidly organizes into fibrous tissue. Thus results a small fibrous tumor. In this tissue a gumma may ultimately develop. (Fig. 85.)

Fig. 85.



Transverse section of a hepatized nodule of syphilitic interstitial pneumonia from a new-born child. *d*. Proliferating connective tissue of the lung. *b*. pavement cells arranged around the alveoli. *a*. Free spherical cells in the alveoli. *c*. Vessels. × 300.

Syphilitic fibromata, such as have already been mentioned in the liver, testicle, and lung, may show themselves in the skin and other organs. Ordinarily they exactly resemble fibromata, and may undergo similar degenerations. There is nothing in their structure which could characterize them as true gummata.

Authors are not in accord as to the position which syphilitic gummata should occupy among tumors.

Description of Gumma.—Gummata are tumors of variable size, which are so diffusely joined with the neighboring tissues that they possess no sharp boundary which can be recognized, and for this reason they cannot be enucleated. Nevertheless, they form an elevation upon the surface of organs where they are developed. Seen by the naked eye, upon section they appear to be constituted by a pinkish-gray, more or less vascular tissue, without juice. This absence of juice, joined to the firmness of their tissue, at once separates them from granulation tissue. Examining scrapings we find cells of various forms and sizes: *a*. embryonic cells; *b*. fusiform or irregular cells; *c*. smaller atrophic cells, measuring .005 or .006 mm, almost entirely filled by their nucleus, packed close together in a granular fundamental substance. But the elements thus obtained by scraping are not sufficient for the recognition of gumma, unless we also take into account the characters of the rest of the tissue, and the process of development.

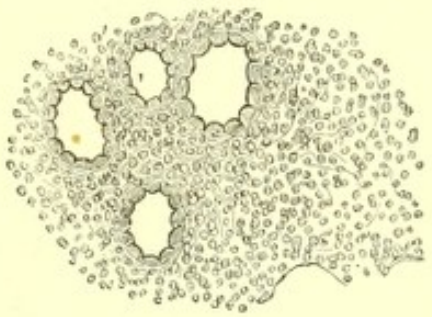
Under the microscope, a thin section from a gumma in process of evolution, presents a series of nodules, each possessing its own centre of formation. (Fig. 86.) These nodules are more or less distinct, and are

Fig. 86.



Gummatous growth from liver. *a*. Central portions of growth, consisting of granular débris. *b*. Peripheral granulation tissue. *r*. Blood-vessel. × 100.

Fig. 87.



The peripheral portion of a gummatous growth in the kidney, showing the small-celled granulation tissue in the intertubular tissue. × 200.

recognized by the fact that the cellular elements of their central portion are small, and have fallen into a molecular detritus, whilst those of the periphery are larger, round, or fusiform, and are confounded with the neighboring embryonal tissue.

The nodules themselves are very irregular in their form and their dimensions, averaging from $\frac{1}{15}$ to $\frac{1}{6}$ millimetre in diameter.

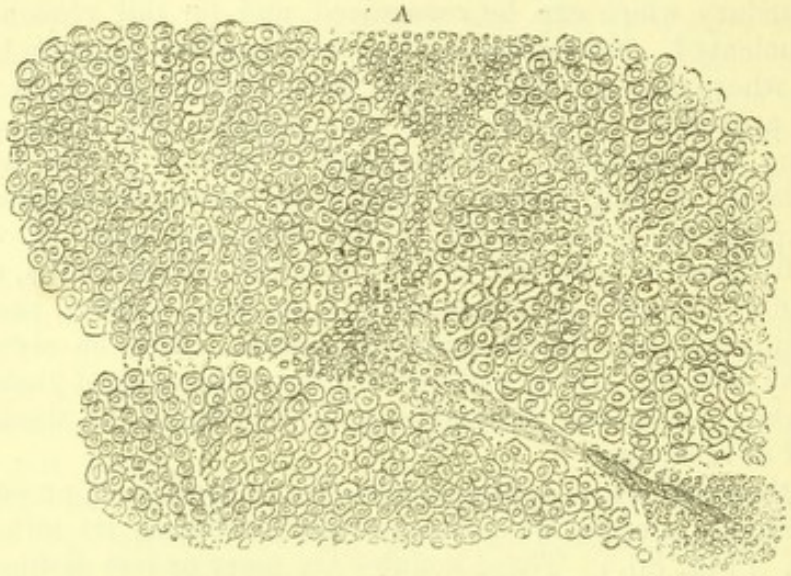
The bloodvessels penetrate to the periphery of each nodule, and may ramify there. They are permeable and contain blood even when the centre of the nodule is in a state of atrophic degeneration. Gummata are very vascular while they are developing. The internodular embryonal or fibrous tissue always is rich in vessels.

Gummata in process of evolution are rarely found upon the post-mortem

table in the adult, but they are frequently seen at the autopsies of newborn children.

The development of gumma is of great interest. We recognize two

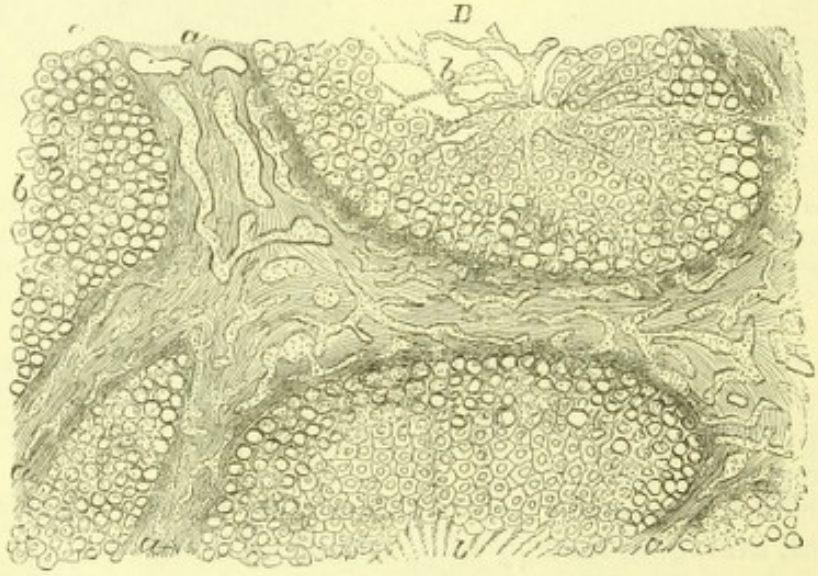
Fig. 88.



Indurating inflammation of the liver, first stage, *a*. Lumen of interlobular vessels in whose environs there is a small-celled infiltration. *b*. Lumina of intralobular vessels. × 300. (*Rindfleisch.*)

periods: The *first phase* consists in the proliferation of connective tissue or of an analogous tissue—for example, the medullary substance of bone.

Fig. 89.



Indurating inflammation of liver, second stage. *a*. Broad bands of a fibrous connective tissue, which is very rich in vessels without distinct walls, and is bounded towards *b* by an interrupted layer of young connective tissue. *b*. Groups of acini of the liver with their periphery infiltrated with fat. × 200. (*Rindfleisch.*)

In the liver, in the first place a multiplication of the elements of the interstitial connective tissue takes place; but this interstitial hepatitis is

very different to that which one finds in ordinary cirrhosis (as seen in figs. 88 and 89). In simple cirrhosis there is a proliferation of the interlobular connective tissue in such a manner that the lobules are separated from each other by wide bands of new connective tissue. There is a consecutive atrophy of the hepatic lobules.

In syphilitic interstitial hepatitis, the proliferation of the cells of the connective tissue takes place not only between the hepatic islands, but also in their interior, along the capillaries up to their entrance into the central vein. It naturally results that the trabeculæ of hepatic cells are everywhere surrounded by cells of new formation disposed in rows. This condition is seen as well in the new-born child as in the fœtus and adult.

When gummata are about to be developed in the liver, this formation of embryonal tissue takes place either throughout the organ or in limited points which are to become the seat of the tumor. The new tissue, which accumulates in masses, becomes riddled with numerous vessels.

Then commences the *second phase* of development of gummata. The cells multiply, diminish in size, are compressed against each other, and there are thus produced, in places, little nodules or irregular islands, in which the central cells are atrophied and granular, while the peripheral cells are more voluminous and present the character, of embryonal cells.

The fundamental substance is vaguely fibrillar, and resembles connective tissue.

In bone, a proliferation of the cells of the marrow occurs, and there results an embryonal tissue which fills the osseous canals. The osseous trabeculæ become thinned and absorbed, thus giving rise to large medullary spaces in which the gummatous nodules form, by the same manner of growth as in the liver.

Gummata are developed in an analogous manner in the skin, in the subcutaneous adipose tissue, and elsewhere.

Their ulterior alterations have not yet been well studied. In gumma, mucous metamorphosis is never seen; but, on the contrary, a peculiar caseous state, characterized by its consistence and duration. This consistence suffices for the differentiation by the naked eye of gummata, which are always hard, even when caseous, from infarctions and tubercles, which frequently soften when they have reached the caseous condition.

Gummata of the liver which have existed for ten or fifteen years, often exhibit singular characters. In the midst of the liver which may have preserved, around the gumma, its physiological condition, we find angular masses of a whitish or yellowish-white tissue, which are very dense and hard, which creak under the knife, and which are surrounded by fibrous tissue. At these places cicatricial depressions exist.

These masses may exist at the surface or in the depth of the organ; their extent may be such that the liver is divided into two parts by the new tissue which occupies its centre. This yellowish-white lardaceous tissue, studied in extremely thin sections, shows the characters of gummatous nodules which have undergone degeneration.

Between and around these angular masses exist fusiform or stellate groups of fatty granules, regularly disposed in concentric circles, and separated by a fundamental fibrous substance. One might, at first sight

believe that these groups of fatty granules correspond entirely to the plasmatic cells; but studying them more closely we see that many belong to spaces, more or less lengthy and sometimes wide, which represent the disposition of the lymph canals in the fibrous tissue; and we are right in concluding that the spaces filled by these groups of fatty granules are lymph vessels stuffed with the fat resulting from the decomposition of the morbid mass. The tissue between and around these angular lardaceous masses is vascular, while the entirely altered nodules themselves have no vessels.

Is this peripheral fibrous tissue of a formation contemporaneous with that of the nodules, or is it developed subsequently? The latter case is the more probable. However this may be, it is by means of the lymph vessels that the products of decomposition of the nodules are absorbed when, after yielding to proper treatment or to the processes of nature, the gumma diminishes. We have proof of this resorption in the circumstance of cicatricial retraction of gummatous products. And we have a positive proof of the absorption and disappearance of gummata in the skin and subcutaneous tissue, a disappearance which may or may not be followed by cicatrices, and which is easy to observe any day at the clinic.

SEAT OF GUMMA.—After the skin and the subcutaneous cellular tissue, the organs which are most frequently the seat of gummata are first the liver, then the kidneys—where the phenomena are identical with those in the liver—the testicles, and the bones.

The ANATOMICAL DIAGNOSIS of gummata is easy: they cannot be confounded with fibromata when carefully examined; their differential diagnosis from tubercle we will speak of *à propos* of the latter.

The PROGNOSIS of gummata is grave, because they destroy the tissue where they are developed, and finally convert it into cicatricial tissue. It is therefore readily comprehended how, in the different organs where they are developed, they disturb or suppress the functions. Their gravity, however, is very different from that of carcinoma, for they do not give place to secondary formations; and they may be arrested in their course or even be caused to disappear under proper treatment.

6TH CLASS.—Tuberculosis.[1]

The question of tubercle, bristling with contradictory opinions, is still obscure, but light commences to dawn upon it. Formerly, every caseous mass was called tubercle. [Laennec's thesis concerning the gray granulation and its change into yellow tubercle spread a welcome light over the nature of the entire process. The resemblance of the lesions in different organs was explained by the axiom that there was only one phthisis —a phthisis tuberculosa. Laennec's views soon spread widely; but opposition to them, never entirely silenced, has been more vigorous every

[1] The subject matter within the brackets has mainly been abstracted almost verbatim from Rindfleisch, Article Tuberculosis, Ziemssen's Cyclopædia of Medicine, from Woodward, Medical and Surgical History of the War of the Rebellion, second Medical Volume, and from Wagner, Manual of General Pathology.

year since 1844. The objection constantly urged against Laennec's doctrine was that most, if not all, the cheesy masses found in phthisical lungs are simple products of inflammation.

Virchow founded a new doctrine, that no process was to be called tubercular unless gray miliary granules were found. Cheesy masses could be formed from thickened pus, and other cellular formations, as well as from miliary tubercles. He almost entirely removed pulmonary phthisis from the domain of tuberculosis, and considered it to be altogether a cheesy broncho-pneumonia.

Thus the chain that had been formed of the tuberculous phthisis of different organs by Laennec and his followers was broken, and the most important link—pulmonary phthisis—was altogether taken away.

Niemeyer was the first clinical teacher who boldly adopted the new doctrine.

The experimental pathologist now took up the question. Villemin revived the old opinion of the infective character of tuberculosis.

Long before, Buhl had promulgated the idea that miliary tuberculosis was a "resorption disease."

Virchow had seen that in almost all cases of acute disseminated miliary tuberculosis, cheesy masses could be found somewhere in the body, usually a cheesy lymph gland.

In the experimental inoculations, therefore, it was interesting to note that in some cases the miliary tubercles were found in greatest number around a cheesy focus, as if the latter were the point of inoculation and resorption.

In this way, the miliary tubercle lost somewhat its character as a primary lesion, and seemed rather to be a result of resorption and dependent upon certain anterior conditions.

Waldenberg demonstrated that "in certain animals" the manner and matter of the inoculation are of no consequence. Next, Cohnheim and Fränkel proved that "in certain animals" it was not necessary to inoculate at all, and that the formation of a focus of suppurative inflammation in a rabbit or guinea-pig was sufficient to render the animal tuberculous.

It became evident that the species of animals employed for experiment is a matter of importance. In rabbits and guinea-pigs, any focus of purulent inflammation is very apt to pass into the cheesy condition.

It seems very natural, therefore, to suppose that the predisposition of these animals for tuberculosis is a consequence of their disposition to cheesy inflammation, and that such animals become inoculated from their own inflammatory products.

Thus far reached the experiments on animals. Their principal object was to demonstrate the infectious nature of tuberculosis, and the existence of a tuberculous virus, which, like syphilis, could be transmitted from one person to another.

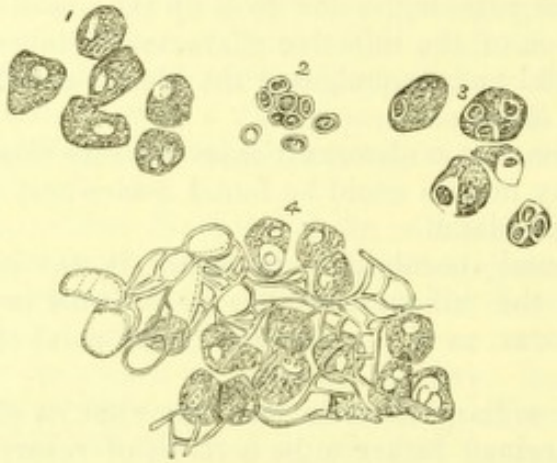
A very remarkable and significant fact is the great similarity between the predisposition of "certain animals" for tuberculosis, and the almost exclusive occurrence of tuberculosis in a special group of persons, the scrofulous. It is a characteristic of the constitutional disease called "scrofula," that all the inflammatory processes run a peculiar course. There is a well-marked tendency to protraction; the infiltration disappears

very gradually or it remains stationary and undergoes regressive metamorphoses of a cheesy character.

Virchow first called attention to the predominant cellular character of the scrofulous exudation, and its hyperplastic nature and to the low vitality of the cells which compose it.

Rindfleisch added that fresh scrofulous exudations contain relatively *large* cells with glistening protoplasm, and a nucleus in the act of segmentation, or containing a double nucleus. He received the impression that the migrating white blood corpuscles in scrofulous persons have a tendency to grow larger on their way through the connective tissue. They swell up by the imbibition of albuminous substances, and by this very swelling die and slowly degenerate.

Fig 90.



Elements of miliary tubercle, obtained by teasing. 1. Large tubercle cells. 2. Small tubercle cells. 3. Endogenous cell formations. 4. Fine meshed network from the interior of miliary tubercle, the cells partly removed by pencilling. (*Rindfleisch.*)

The consequences of this peculiar anomaly of vegetation are felt in all the inflammations of scrofulous persons. In scrofulous catarrh attention has long been called to the abundance of cells and the thick, quickly-drying character of the secretions. In this form of catarrh the exudation corpuscles lie so thickly together that they form a layer extending to the epithelium, and there is an infiltration with round cells extending deeply into the submucous tissue.

Many of these cells gradually wander to the free surface and are cast off, others pass into the radicles of the lymphatic vessels, while still others undergo a granulo-fatty degeneration. Their detritus is partly mingled with the lymph which flows from the inflamed tract into the neighboring lymphatic glands, and partly forms an element in the secretion, in which fine granules, possessed of molecular movement, are constantly found.

It seems that the formation and transportation of the tubercular poison is effected by the formation and transportation of this detritus.

In scrofulous inflammation there is a remarkable tendency to permanent infiltration of the affected tissue. In simple inflammation the infiltration is a temporary condition which terminates in suppuration, in organization, or in resolution. In scrofulous inflammation the only termination is a

cellular infiltration of connective tissues, which converts them into a hard, dense, grayish, semi-translucent mass, which constitutes the acme of the process. In such a mass the bloodvessels become occluded, and then necrotic processes ensue. There is no evidence that this scrofulous infiltration is capable of any other than degenerative changes. This degeneration begins as a cheesy transformation, first of the centre, then of the entire infiltration. After the cheesy degeneration, calcification or softening may follow.

The final degeneration of the scrofulous infiltration is effected by a chemical metamorphosis, which converts it into fat globules, albuminous granules, and a quantity of soluble substances which cannot be seen. All these substances must necessarily be absorbed.

Now, when we consider that scrofulous persons are especially predisposed to tuberculosis; that tuberculosis hardly ever occurs except in scrofulous persons; that tuberculous phthisis is only a combination of scrofulous inflammation and tubercles; and that in the scrofulous an inflammation brings with it the risk of tuberculosis, we can hardly fail to see that in certain men, as in certain animals, inflammation runs a peculiar course. The cheesy inflammations and suppurations of numerous membranes elaborate a poison which, when absorbed, produces tubercles. This constitutes the real relationship between scrofula and tuberculosis. The tubercular poison, in most cases, is thus manufactured by the patient himself, and it has not yet been demonstrated that this poison can be transmitted to perfectly healthy persons, so that the disease can hardly be considered as purely infectious.

There is first scrofula, then a cachexia from the absorption of scrofulous products. The intensity of this cachexia is only partially revealed by the irruption of miliary tubercles.

A scrofulous child has a protracted arthritis, from which the joint becomes the seat of a softening caseous mass. The detritus in contact with the deceased synovial membrane is absorbed. There results from this absorption first a local then a general tuberculosis.

In another scrofulous child, a catarrhal inflammation of the small intestine is excited, the adenoid tissue of the mucous membrane becomes infil trated with cells, which subsequently break down and are absorbed by the lymphatics. Then there are produced miliary tubercles along the course of the lymph vessels up to the mesenteric glands—*local tuberculosis*, or the virus may pass beyond and infect the system, when *general tuberculosis* is established.

Rindfleisch and Schüppel believe that scrofulous glands are always tuberculous.

The lymph glands in tuberculosis, as in the case of malignant tumors, are the situations in which the new growth is developed in the clearest and best defined manner.

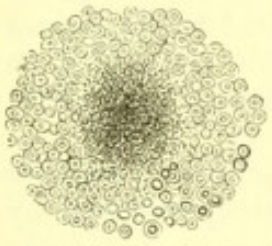
In tuberculosis, as with malignant tumors, the swelling and obstruction of the lymphatics may cause the disease to remain for a time localized in the glands. We know that for many years a scrofulous gland may remain as the only trace of youthful scrofula. It is eminently proper in such cases to extirpate such a gland in order to prevent the gradual infection of the whole body with tubercles.]

The Anatomy of Tubercles.—Miliary tubercles of the size of a millet seed are infrequent. Those of the size of a poppy seed are more common. Even the smallest nodules visible to the naked eye are made up of still smaller nodules—submiliary tubercles. The latter measure from $\frac{1}{5}$ to $\frac{1}{7}$ of a millimetre in diameter, so that from forty to fifty of them must be agglomerated to make a nodule as large as a poppy seed. There are no definite limits to the size which may be attained by the agglomeration of submiliary tubercles. Nodules as large as a pea or even a walnut are not uncommon.

Miliary tubercles or gray granules are hard, and form a relief; transparent when recent, they soon become opaque and yellow at the centre. They are most frequently surrounded by a reddish vascularized zone. They may be discrete or confluent When confluent they form yellowish masses, which are impossible to be differentiated by the naked eye from caseous inflammatory foci.

Under the microscope we often meet with cells as large as in carcinoma, and containing a great number of nuclei; there are often also fusiform and embryonal cells, but the elements which predominate are very small cells, measuring from .004 to .009 mm., the nuclei of which are surrounded by an extremely small amount of protoplasm. The latter are embryonal cells undergoing atrophy. The reciprocal arrangement of these cells is very important to study. In each submiliary granule can be distinguished a peripheral proliferating zone, in which exist multinuclear cells (giant cells) and fibro-plastic or spindle-form elements—a zone sometimes much more extensive than one would suppose at first view; and a central portion (fig. 91) where the elements become closely crowded, and atrophied in proportion as the centre is approached, and finish by falling into a granular detritus. All these elements secrete around them a granular or fibrillar fundamental substance, which agglutinates and holds them very firmly united together. By reason of atrophy and molecular destruction of the elements, the centre of the small nodule becomes opaque and friable.

Fig. 91.



One of the gray nodules from the lung in a case of acute tuberculosis, which is becoming opaque and soft in the centre. (*Diagrammatic.*) (*Green.*)

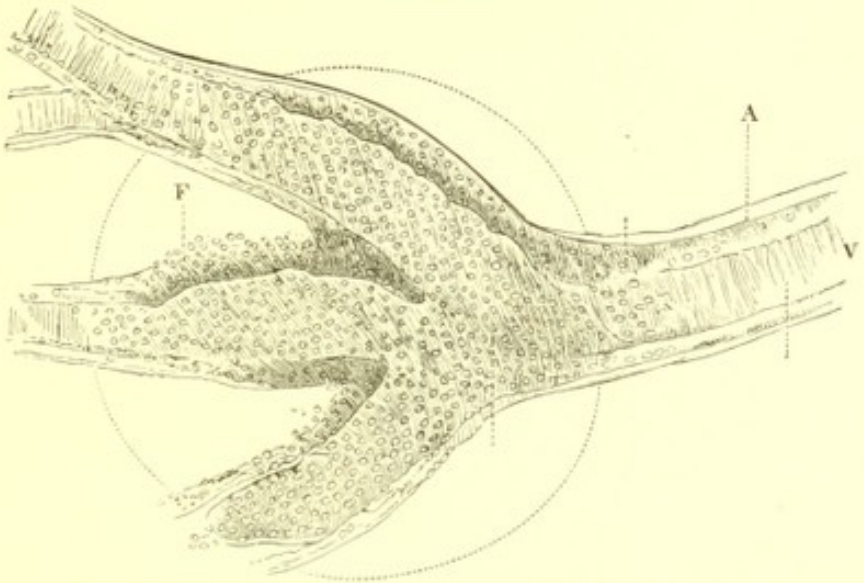
The vessels of the centre of the nodule are never permeable. This bloodlessness is the cause of the translucency of the tubercle. An examination of these vessels shows that their obliteration is effected slowly.

The obliterated vessels betray themselves by their contour; their lumen is filled by a coagulum of granular fibrin. In the midst, and especially at the border, of the granular contents of the vessels are found white blood corpuscles (*b*, fig. 94), elements which are distinguished from the adjacent elements belonging to the tuberculous granule by their larger size and by their regularly circular disposition within the vessel walls.

[Besides the cellular, granulation-like tubercles, such as are met with in inoculated guinea-pigs, there is a fibroid tubercle which is most frequently found in syphilitics, and a lymphadenoid tubercle, which occurs in the scrofulous. It appears then that the individual constitution not

only exerts an influence on the predisposition to inoculation, but also on the form of the tubercle thus produced. According to some writers, a

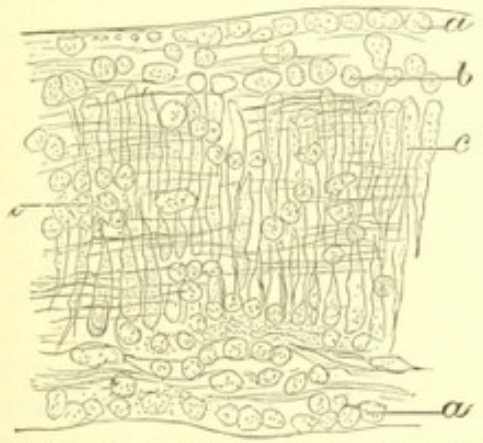
Fig. 92.



Miliary tubercle in the pia mater. The dotted line indicates the original size of the tubercular nodule. A. The lymphatic sheath. V. The bloodvessel. F. Proliferation of elements within the sheath. × 100.

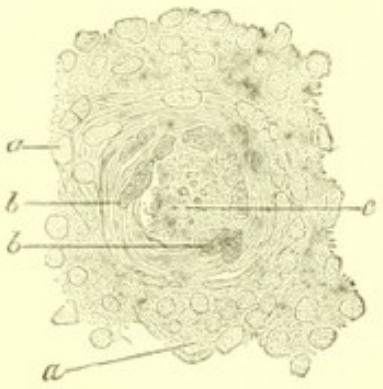
tubercle-granule consists of reticulated tissue, inclosing in its meshes certain cellular elements. It has, on this account, been termed a cyto-

Fig. 93.



Longitudinal view of an arteriole of the pia mater at the commencement of the proliferation of the elements of the tunica adventitia and of the perivascular lymph sheath in the neighborhood of a tubercle. *a*. Elements of lymph sheath in proliferation. *b*. Cells belonging to tunica adventitia. *c*. Layer of annular muscular fibres of the middle coat. × 400.

Fig. 94.

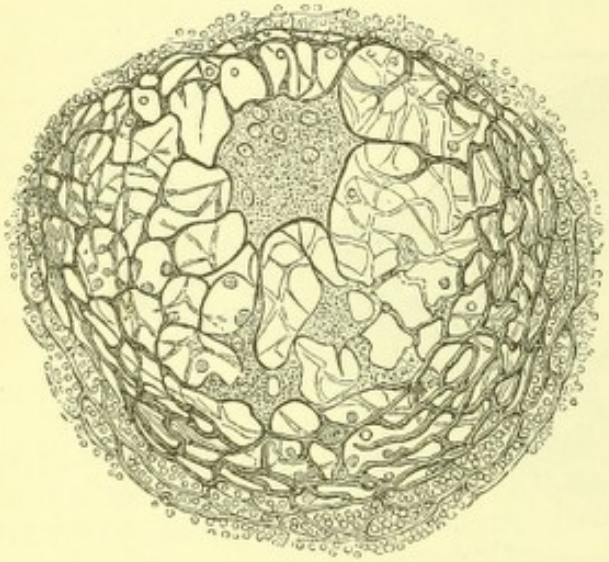


Transverse section of a vessel filled with granular fibrin. *a*. Tubercular tissue. *b*. white blood corpuscles. There is here a tubercle involving the vessel. × 400.

genic growth. In the words of Wagner, the reticulum is generally similar to that which is found in normal reticular connective tissue, except that the fibres of the network are somewhat broader. At the periphery of

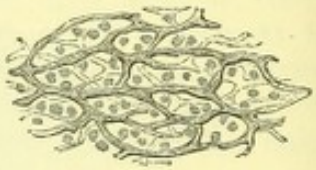
the nodule, the fibres are usually broader and denser and their course is nearly circular, so as to form a kind of girdle around the whole tubercle.

Fig. 95.



Multinucleated and branched cells (giant-cells) from a firm gray miliary tubercle of the lung in a case of acute tuberculosis. Wide meshes are seen in the immediate vicinity of the giant-cells inclosing a few lymphoid elements. The branched processes are directly continuous with the adenoid reticulum of the tubercle. ×200. (*Green.*)

Fig. 96.



A portion of a gray miliary tubercle of the lung, showing the adenoid-like structure. × 200. (*Green.*)

(See fig. 95.) This reticulum is void of bloodvessels, and in the youngest tubercles it is very scanty and soft. The reticulum incloses cellular elements. Besides small round cells, very similar to leucocytes, and more minute angular bodies, there are also seen—usually in the centre, rarely in the periphery of the nodule—one or more so-called *polynuclear giant cells*. (Fig. 97.) Moreover, cells are constantly found of an intermediate size; they are endothelioid in character. Authors are divided concerning the significance and the constancy of the presence of so-called giant cells in tubercular growths, some considering them as a constant and essential characteristic of tubercle, others denying the existence of true giant cells in these formations, while still others fail to recognize in their presence or their constitution a peculiarity of tubercle. It has been already mentioned that these so-called giant cells are not unfrequently found in many other formations.

Fig. 97.

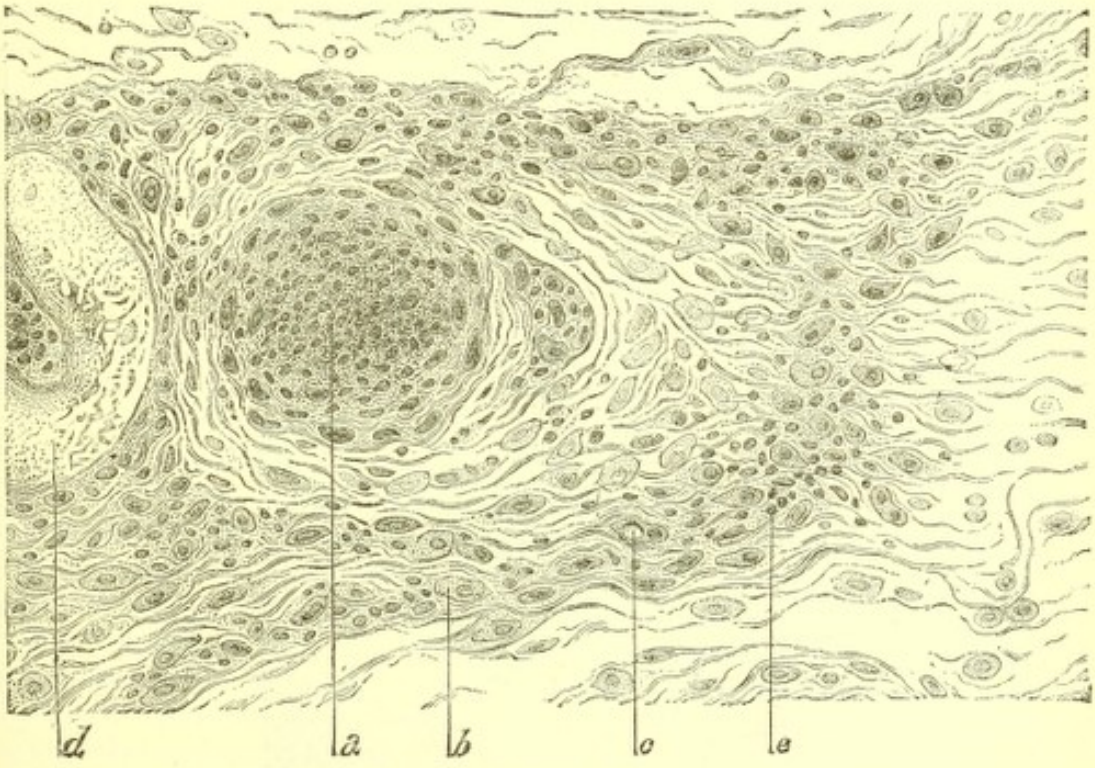


A multinucleated cell, from the lung in a case of chronic phthisis, showing a large number of nuclei with bright nucleoli. ×400. (*Green.*)

According to Rindfleisch, the size of the tubercle cells in scrofulous tubercle is unusual, they are twice or three times as large as a white blood corpuscle. At the same time they are more highly refractive, their nuclei are sharply defined and often shining. The nuclei may be segmented, but do not go on to the formation of cells; they simply produce multinuclear cells, sometimes giant cells. In this way is produced a peculiar large celled germinal tissue (see fig. 90), which Rindfleisch regards as a specific product of scrofulous tuberculosis. He considers tissue to be the acme of the process, which is not always reached. He thinks that this large celled tissue usually forms the middle portion of the submiliary nodules, while at their periphery there prevails a small celled inflammatory growth, which gradually becomes continuous with the normal connective tissue.

In his study of tuberculosis of the intestines, Woodward[1] gives a so

Fig. 98.



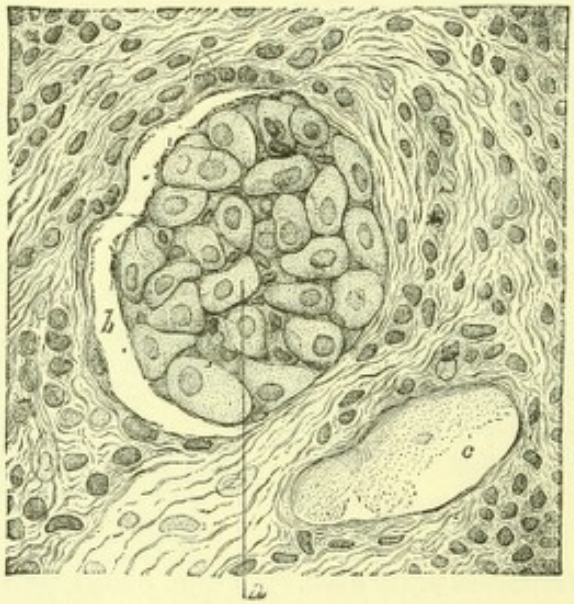
Small tubercle in the submucosa of the ileum. × 370. *a*. Central figure (lymphatic) cut across; it is stuffed with granular fibrin, in which lymphoid elements, and on the periphery, endothelial cells, are imbedded; indications of a limiting wall, and of a small branch are also seen. In the space around the central figure, are numerous granular nucleated endothelial cells, like those indicated at *b*. In one of these cells, *c*, a vacuole has formed. There are also numerous lymphoid cells; a group of four is indicated at *e*. A small vein, *d*, passes through the margin of the tubercle. Traces of a fibrillated connective-tissue matrix are seen everywhere outside the central figure, between the elements. (From a photo-micrograph, by Surgeon J. J. Woodward, U. S. Army. Copied from the second medical volume of the Medical and Surgical History of the War of the Rebellion.)

clear, and, as we think, generally accurate description of the minute anatomy of tubercle, that we have inserted it here almost verbatim.

[1] Medical and Surgical History of the War of the Rebellion, part second, medical volume, J. J. Woodward, Surgeon U. S. Army, p. 593.

According to him, the smallest, presumably the youngest, tubercle granulations in the submucous connective tissue are from $\frac{1}{500}$ to $\frac{1}{250}$ of an inch in diameter, or even larger. The sections of these are generally rounded or oval in form, and bounded by a distinctly recognizable external wall, like that of a small vein or lymphatic vessel cut across (see fig. 98). The space within this boundary is usually filled with a granular or indistinctly fibrillated material, resembling coagulated fibrin, entangling in its substance a number of cells; some resembling endothelial elements, and these usually lay on the periphery; others, and these the most numerous, ordinary lymphoid cells. Outside of the limiting wall of the central figure the granulation is made up of two kinds of cells: large, oval, nucleated cells, corresponding in size and form to the swollen endothelial elements seen in chronic inflammations of the submucous connective tissue of the intestine; and a swarm of small round cells resembling ordinary lymphoid elements. The relative number of these two kinds of cells varies very greatly. The small round cells occur sometimes in moderate numbers, chiefly on the periphery of the granulation; sometimes they infiltrate all parts of it, and are so numerous as to obscure the large oval cells, which, however, with a good

Fig. 99.



Transverse section through the lumen of a diseased lymphatic vessel in the submucosa of the ilium affected with tubercu ar ulcers. × 480. The lumen of the vessel is filled with a mass of large endothelial cells (*a*), between which a few lymphoid elements have crept. In preparing the specimen this mass has shrunk away from the wall of the vessel, leaving a space, *b*. In the vicinity of this stuffed lymphatic the section passed through a venous radicle, *c*. The surrounding connective tissue is infiltrated with lymphoid elements, and presents also a few large endothelial cells. (From a photomicrograph, by Surgeon J. J. Woodward, U. S. Army. Copied from the second medical volume of the Medical and Surgical History of the War of the Rebellion.)

immersion objective, can generally still be recognized between them. All these elements lay in the meshes of a fibrillated reticulum, continuous with the surrounding connective tissue. Woodward is inclined to interpret the significance of such a figure as above described as a section of a

lymphatic vessel, agreeing, in this, with Virchow, rather than with Cornil and Ranvier, who regard it as a bloodvessel.

For him, a large fibrin clot, completely filling the vessel and entangling cellular elements in its interior, forms the round or oval figure seen in the centre of the young tubercle granulations. It is easy to understand that some of these figures, if shrunken by the potent influence of chromic acid, would bear a striking resemblance to the description of giant cells (fig. 99). He, therefore, regards the so-called giant cells, in intestinal and peritoneal tubercles, as figures resulting from the action of chromic acid on sections of lymphatic vessels stuffed with coagulated fibrin and cells; and thinks that the large endothelioid elements of the primary tubercle granulation outside of the central figure, are formed by enlargement of the endothelial elements of the lymph spaces in the connective tissue. The cheesy metamorphosis of the tubercle granule appears to commence in the contents of the central lymphatic, but it speedily invades the adjacent exterior elements, and then all trace of a wall is lost, and the central portion of the tubercle appears simply occupied by a granular mass, in which shrivelled nuclei are imbedded. He believes that the development of a minute tubercle starts by the formation of a fibrin clot obstructing a small lymphatic vessel, and that the lymphoid elements grouped around the vessel at the point of obstruction, are probably a swarm of migrated white blood corpuscles, while the large endothelioid cells are produced by the gradual enlargement of the fixed corpuscles of the area of connective tissue involved.]

Varieties of Tubercle.—Tubercle granules are discrete, or by their union they form distinct masses of the size of a pea, a hazel-nut or walnut. *Discrete* tubercle granules are surrounded by a zone of proliferation in which vessels exist; this red zone makes the granulation itself very prominent, for the latter it is anæmic, semitransparent, or opaque.

Confluent granules are united together, often in great numbers, within a common enveloping mass of embryonal tissue. Each of the nodules presents at the centre an atrophy of its elements, similar to that which occurs in gummata. In each granule the vessels are early obliterated, while subsequently the vessels of the surrounding embryonal tissue are also closed. After that, the tubercle granules, being no longer separated by a vascular zone, are lost in a common anæmic mass, in which it is impossible by the naked eye to recognize the individual nodules. Very soon the whole mass becomes uniformly opaque, and may soften at the centre or throughout. These caseous nodules, when they are located in the lungs, are often reported, even by experienced observers, as caseous pneumonia. The lungs are not the only organs in which confluent tubercle may be met with.

Nutritive Modifications of Tubercle.—Tubercles appear not to be capable of an absorption similar to that of syphilitic gummata. The cicatrices which succeed them always result from a mortification and an eliminating ulceration. We often find, however, at the apex of the lungs caseous foci filled with a substance almost solid and calcareous, isolated in the midst of an indurated tissue. But it is impossible to determine the

origin of such foci, which may be remains of infarctions, of abscess, or of dilatations of bronchi separated from the rest of the air-passages, as well as cicatrized tuberculous cavities.

Caseous degeneration is constant in every old tubercle. It has been attributed to obliteration of the vessels; but we find also a degeneration of the same kind in gummata, the vessels of which remain permeable. The caseous state of tubercle instead of being accompanied by induration, as in gumma, ends in the softening of the tubercular mass, and its conversion into a focus filled with detritus and free elements which may discharge into a mucous canal, and be replaced by an ulcer or a cavern. If the tubercular mass remain inclosed in a deep parenchyma, it may undergo desiccation and *calcification*.

Development of Tubercle.—Tubercle is always developed in the midst of an embryonal tissue in such a manner that the tubercle granule is constantly surrounded by a zone of proliferation. It arises from the connective tissue. Thus, in the liver, the granules developed in the interlobular tissue are always preceded by an interstitial hepatitis. The development of tubercle granules in the bones is preceded by an osteitis, that is to say, by the formation of embryonal tissue in the medullary cavities.

Cannot tubercle originate from epithelial cells as well as from the connective-tissue elements? We ourselves have observed the epithelial cells contained in the alveoli of the thyroid body proliferate and take part in the constitution of a tuberculous nodule.

In the lung, the tubercle granule commonly springs from the interlobular, peribronchial, and inter-alveolar fibrous tissue. But we also meet with tubercles which occupy the interior of several alveoli, the elastic septa of which are still preserved. In such a case the embryonal tissue projects from the alveolar walls into the interior of the alveoli, and it is possible that the lining epithelium takes part in the formation of the new embryonal tissue.

[According to Rindfleisch and nearly every other writer, it is from the fixed cells of the vascular connective-tissue system that the miliary tubercle originates—the endothelium of the bloodvessels and of the lymphatics, the endothelium of the serous membranes, and the fixed connective-tissue corpuscles. Many of the more recent authors regard the formation of a giant cell as always the first step. On the other hand, as we have already seen, numerous investigators not only fail to recognize a special significance in this cell, but some even go so far as to deny the presence of true giant cells. Rindfleisch thinks that a giant cell is nothing more than an enlarged endothelial or connective-tissue cell, with an increased number of nuclei; and he has found them constantly and has often used them as "sign-posts." In the smaller tubercles he has usually found them at the centre, in the larger at the periphery of the granules. He states that no special reliance can be placed on them, for they occur in non-tubercular new formations. He regards the greater omentum as the most favorable tissue for investigation. Here he recognizes the smallest tubercle as a nodular swelling of a single non-vascular connective-tissue trabecula, and says that this swelling is due

entirely to a growth of the fixed connective-tissue cells, and of the endothelial cells upon the trabecula. He also admits that the endothelium of the lymph and blood capillaries and larger vessels proliferate and may supply the cells for the formation of a tubercle granulation, and that the walls of the capillaries in the neighborhood of the tubercles are in a state of proliferation, resulting in a partial obliteration of their lumen. He believes that when a tubercle has passed the first stage of its development, it itself becomes an irritant of the connective tissue in which it is situated; and that from this time on, therefore, the products of ordinary inflammation become mixed with the specific tubercular products.]

With respect to the intimate nature of the tubercle granules, different opinions have been advanced. Foerster ranges them among tumors constituted by lymphatic cells. Rindfleisch describes a reticulated tissue in tubercle; but we cannot recognize in this anything else than an artificial hardening of the intercellular substance. No such tissue can be seen in the fresh state. Virchow also considers tubercle as a lymphatic product, while, for him, gummata are analogous to granulation tissue.

We are unable to admit such a radical distinction between tubercle and gumma, but consider both as a kind of fibroma in which the cell elements arranged in nodules atrophy at the centre of the latter. There is no recognizable anatomical difference, if account be not taken of the state of the obliterated vessels in tubercle.

[Notwithstanding the great conflict of opinions, not only concerning the minute anatomy of the submiliary tubercle granules, but also regarding the anatomical history of the general disorder comprehended by the term tuberculosis, the following propositions may be considered as moderately well established:—

First, that the disease is of an infectious nature.

Second, that the infecting matter may be produced within the organism.

Third, that it has a close association with the caseous degeneration of inflammatory products, and the subsequent liquefaction of these caseous products.

Fourth, that certain animals as well as certain men (the scrofulous) are peculiarly prone to the caseous degeneration of inflammatory foci, and to self-infection through the absorption of a specific tubercular virus which appears to be vitalized, if not, indeed, generated, by the liquefaction of such caseous masses.

Fifth, that the formation, caseation, and subsequent partial liquefaction of inflammatory foci appears to constitute what may be regarded as the first active or *primary stage* in the production of tuberculosis. There still seems to be much doubt concerning the real inoculability of tuberculosis from one individual to another. It is very probable that it is only certain *predisposed* individuals (the scrofulous) who, under ordinary circumstances, are capable of being inoculated. Even in them, while tuberculosis has undoubtedly been excited after an attempted inoculation with caseous or tubercular matter from another individual, yet, in similar animals, the simple establishment of a caseous inflammatory focus following the introduction, under the skin, etc., of innocuous foreign bodies, seems to be an equally efficient method of producing the disease. The law of heredity appears to be most potent in occasioning this predisposi-

tion or so-called scrofulous state. Nevertheless, conditions of hygiene, of climate, and of regimen are powerful in counteracting or aggravating the inherited tendency, and, in the absence of the latter, they may occasionally be sufficient to originate a scrofulous diathesis.

Sixth, that usually the virus produces an irritation (specific?) of some of the cellular elements with which it comes in contact during its course through the lymph passages to the neighboring lymphatic glands—an irritation which results in the swelling and proliferation of the endothelial elements, a choking of the passage, an arrest of the lymph, its coagulation, and the formation of a bloodless nodule presenting the characters, already described, of the submiliary tubercle granule. The infecting virus may be arrested by the obstruction of the local lymph paths, and be prevented, either for a time or effectually, from entering the general circulation and causing an outbreak of the disease in distant parts. This is the *second phase* in the process, and has been termed *local tuberculosis*.

Seventh, that when the virus reaches the general circulation—either by passing beyond the lymph glands or by directly entering the neighboring bloodvessels, as is frequently the case when the liver becomes infected from foci in the intestines, and occasions an eruption of miliary tubercles in other and more or less remote localities—the poisoning has become general, and there is *general tuberculosis*.

Eighth, that, once formed, tubercles themselves, by their caseous degeneration and liquefaction, may form foci for secondary infection.

Not only has the transmissibility of tuberculosis by inoculation been supported by many investigators, but some recent experimenters are of the opinion that the disease can be communicated by the food. Viseur has seen tuberculosis produced in the cat after feeding the animal upon tuberculous material. O. Ballinger experimented upon herbivorous and carnivorous animals, and found that, by feeding with tuberculous matter, the herbivora become infected. He failed to find the same result with the few carnivora which he fed. Gerlach found that tuberculosis can be produced in animals by the use of the milk of tuberculous cows; and Klebs believed that the general tuberculosis thus produced usually begins with an intestinal catarrh, which leads next to tubercular affections of the mesenteric glands, and subsequently of other organs. Without expressing belief in the possibility of infection by feeding, Woodward remarks that so plausibly has the affirmative view been urged, The German Society for the Preservation of the Public Health, in June, 1875, adopted are solution declaring it to be their opinion, "that the results of the inoculating and feeding-experiments with the flesh and milk of animals affected with tubercle justify the assumption of a danger of infection to man, and therefore merit the greatest consideration by the sanitary police."]

[SEAT OF TUBERCLE.—According to Wagner, tubercle shows a varying frequency, in individual organs, according to the age of the attacked. In *children* it occurs most often in the lymph glands, in the lungs, in the brain, the spleen, the liver, in the intestinal mucous membrane, in serous membranes, and in bones. In *adults* it is found as a *primary* affection

by far most frequently in the lungs; more rarely in the lymph glands, urinary organs, genitals, and intestinal canal. *Secondarily*, it occurs in almost all organs, chiefly in the lymph vessels and glands corresponding to the seat of the primary lesion. Tubercle has never been seen in cartilage, in the external muscles, or in the great vessels. It has been very rarely met with in the pharynx, tonsils, œsophagus, vagina, ovaries, heart, tongue, salivary glands, thyroid gland, and skin. Not infrequently, tubercle is ultimately developed in many new formations, especially in the false membranes formed upon serous membranes.

Writers have variously placed the location of tubercle in the walls of the small bloodvessels, in their lumina, in their adventitious sheaths, in corresponding positions in the lymphatic vessels, upon the serous surfaces, and in the lymph spaces of the connective-tissue frame work of the organism.]

ANATOMICAL DIAGNOSIS OF TUBERCLES.—The recognition of the isolated tubercle granule, when it is sufficiently large, is very easy by the naked eye; but when the tubercles are confluent, and have undergone caseous degeneration throughout the entire mass, it is impossible to make a diagnosis in this manner. It is sometimes very difficult to distinguish by the unaided eye, confluent tubercle granules from gummata, when the latter are in process of formation. Upon microscopic examinations of thin sections made after hardening in alcohol or chromic acid, etc., it will be seen that in tubercles the vessels are entirely obliterated, or are occluded by a granular mass, whilst, on the contrary, in gummata they are empty, or contain red blood disks. When gummata are old, they form firm caseous, lardaceous, masses, in which the vessels are obliterated; they are sharply limited, and are imbedded in a thick, firmly adherent, fibrous tissue, which presents the characters already indicated (see page 109 *et seq.*). On the contrary, the caseous masses resulting from confluent tubercles do not have the same solidity; they break down into a grumous pulp, and are separated from the surrounding tissue, which simply presents the characters of inflammatory tissue.

PROGNOSIS OF TUBERCLES.—The grave prognosis of tuberculosis is so well known that it is scarcely necessary to enter upon it at all. The tendency of tubercles is to degeneration. We may ask if the tubercles can be healed, and if they always act like certain malignant tumors in determining, at a distant point, the formation of nodules similar to themselves.

Clinical analysis, and the results of autopsies, show that small isolated tubercles may simply undergo a caseous degeneration and remain almost indefinitely in the midst of indurated masses resulting from an interstitial pneumonia. [We know that generally tuberculosis in man is related to scrofula. Concerning the nature of scrofula we are still very ignorant. One fundamental characteristic of the disease seems to be a misproportion between the volume of the blood and the weight of the body. There is a deficiency of blood-supply. Dependent upon this condition exists an abnormality of the entire vegetation, which is especially evident in the course of any inflammatory processes which may arise. Hereditary scrofula usually manifests itself at two periods of life: in early youth, before the seventh year, and again after puberty, between

the ages of twenty and thirty years. The other years of life are not by any means exempt from the disease, but it is important to remember that between the ages of ten and fifteen years there is a period of comparative immunity. It is during that period that we may hope by care and treatment to obliterate the traces of previous scrofulous lesions and to prepare against future ones.

Upon what this periodicity depends it is hard to say. Its cause may probably with reason be sought for in the disproportion, during the development of the individual, between the volume of blood and the weight of the body.

As one of the essential features of the progress of the tubercular processes is in the anæmia which characterizes it, so one of the first steps toward recovery is an increased blood supply. The best treatment for scrofula is to increase the volume of the blood, and the best treatment for scrofulous or tuberculous infiltration is to produce and sustain for a time a moderate local hyperæmia.]

7TH CLASS.—Glanders.

In glanders, as in syphilis and tuberculosis, we observe two orders of lesions: the one purely inflammatory, the other constituting specific nodules. The inflammatory lesions in this affection are essentially suppurative.

The new formations in glanders have a great similarity to those of tuberculosis. Of spontaneous origin in the horse, glanders is observed in man only after contagion from the former.

The anatomical descriptions which have been given of glanders are wanting in the histological details which would enable us to give a complete histological account of it.

In man, as in the horse, the disease may commence by a primary tumor and ulcer, which are soon followed by lymphangitis, accompanied by abscess and acute or chronic suppuration, and the discharge of a serous pus.

The nodules of glanders, in the horse, are formed of small cells in the midst of a substance vaguely fibrillar; the cellular elements atrophy at the centre of the nodules, and it is absolutely impossible to distinguish one of these nodules in the horse from a human tubercle. We do not, therefore, comprehend why Virchow has ranged tubercles among lymphatic formations, and glanders among tumors formed of granulation tissue. Death is the constant termination of acute glanders.

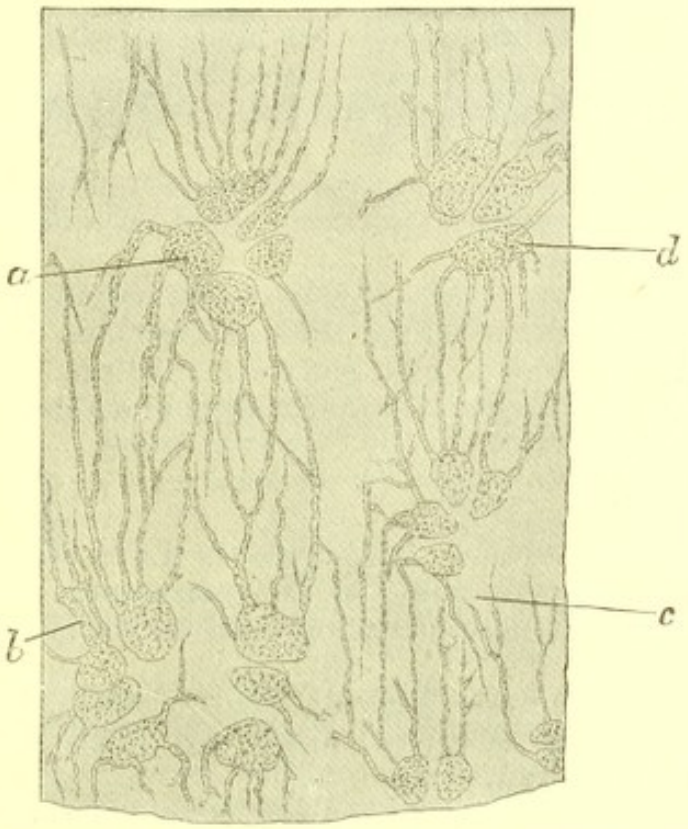
III.—TUMORS HAVING THEIR TYPE IN CARTILAGINOUS TISSUE.

Enchondroma.

DEFINITION.—The enchondromata being tumors which have for their types cartilaginous tissue, their definition is drawn from our knowledge of the latter. It is advisable to separate from enchondroma certain cartilaginous productions which spring solely from pre-existing cartilages, and to which the name *ecchondroses* has been given.

DESCRIPTION.—Enchondromata, properly called, never arise from pre-existing cartilaginous tissue. In them we meet with every conceivable form of cartilage; we find also another variety which has no existence in man in the physiological state, but which may be seen in the cephalic cartilage of cephalopods. In these animals, the cartilage cells instead of being inclosed in a capsule, present prolongations by which they anastomose with each other, resembling the plasmatic cells of the connective tissue. (See fig. 100.) Studying the development of this variety

Fig. 100.



Cartilage of a cephalopod: *a*, *d*. Body of cell. *b*. Anastomosing branches of the cells. *c*. Fundamental substance. ×400. (*Ranvier.*)

of cartilage, we learn that the capsules which primarily surround the cells become penetrated by anastomosing processes which they send to the neighboring cells. This readiness of the capsules to be thus traversed is remarkable. Later, the capsules become indistinct and disappear. These cartilages of the cephalopods have their exact analogies in certain enchondromata.

In the adult, cartilaginous tissue is void of bloodvessels; it is so also of most cartilaginous tumors. But it may happen that a cartilaginous mass becomes vascularized at its centre, whilst new layers of cartilage form at the surface. Generally, the points where the vessels penetrate soften; in this way the tumor becomes reduced to a cartilaginous shell inclosing a cavity filled with a vascularized medullary mass.

It is rare that an enchondroma consisting of a single lobe attains a considerable size. When they are of large size, they are formed of a number

of distinct cartilaginous masses, which are separated by connective tissue. Most frequently these masses are spherical, but sometimes they have irregular forms; their volume is variable; in the same tumor some have the size of the head of a pin, whilst others reach the dimensions of a pigeon's egg. It may also happen that in certain tumors the cartilaginous lobes have not the same structure; some being formed of hyaline cartilage, others of mucous cartilage; certain ones have the structure of fibro-cartilage; still others of cartilage with ramified cells. These different lobes are generally covered with a fibrous envelope, which acts as a perichondrium and in which the vessels run; beneath it, we find a layer of lenticular capsules flattened parallel with the surface; deeper, spherical capsules exist, and at the centre larger capsules, containing many generations of secondary capsules, are to be seen. It is in enchondroma that we find the largest cartilaginous capsules.

Varieties.—We meet with numerous varieties of enchondroma, some based upon the tissues which form them; others upon modifications in the nutrition of these tissues.

a. Unilobular hyaline enchondroma, covered with an enveloping fibrous capsule, containing at the surface lenticular capsules, and at the centre capsules similar to those of adult permanent cartilage.

b. Lobulated hyaline enchondroma, in which a number of lobules similar to the preceding are separated by connective tissue.

c. Certain forms of b, in which the lobules are separated by a vascular fibro-cartilage.

d. In some enchondromata, besides islands of well-developed cartilage, more or less considerable masses of embryonal tissue are found, mixed with the internodular fibrous tissue or with the embryonal cartilaginous tissue.

Should we, with Virchow, consider these tumors as chondro-sarcoma? We think not, for the embryonal tissue seen around the cartilaginous islands is simply the matrix whence the new cartilaginous tissue is formed, and represents the first phase of the development of cartilage.

e. The fibrous tissue which separates the cartilaginous lobules is sometimes predominant. Virchow makes these a distinct species, under the name of *chondro-fibroma*.

f. When enchondromata develop in glands, we always find the fibrous tissue, which separates the cartilaginous islands from the culs-de-sac and gland ducts, in a state of proliferation. We should not regard this as an *adeno-chondroma*, for the proliferation of the elements is only secondary. The same may be said of every tumor, of whatever nature, developed in a gland. Besides, when an enchondroma developed in a gland extends beyond the latter, the extended portion presents no such adenoid appearance.

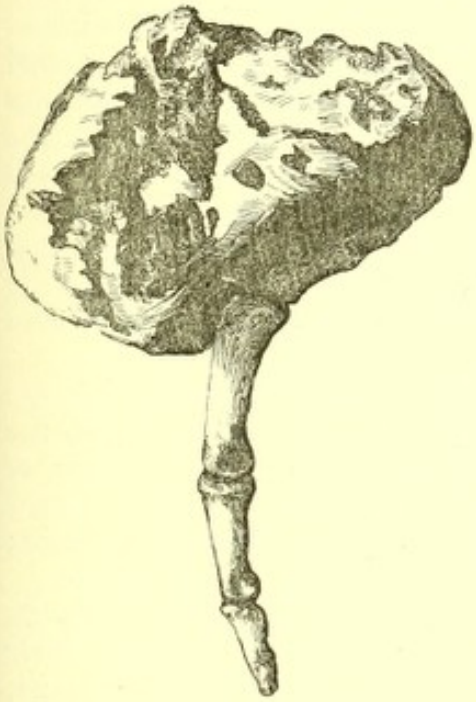
g. Certain enchondromata developed in bone may form an elevation at the surface of the latter, while invariably remaining covered by an osseous layer, which is sometimes extremely thin, often interrupted in places, but is always covered with periosteum.

h. The cartilaginous tissue of enchondroma may give rise to osseous tissue. The latter has usually only a transitory existence, as we shall see

à propos of development. They have been called *ossifying enchondromata.*

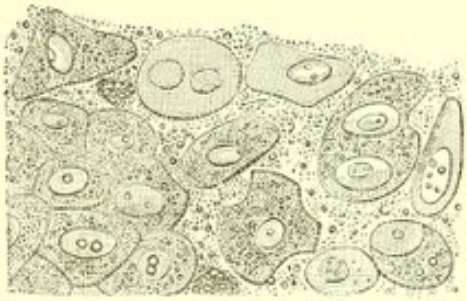
i. Some enchondromata are not formed in lobules, but in a diffuse mass, often presenting the characters of embryonal cartilage. This variety is chiefly met with in bones. *Diffuse enchondroma.* (See fig. 101.)

Fig. 101.



Enchondromatous tumor of metacarpus undergoing ossification. (*Gross.*)

Fig. 102.



Microscopic characters of enchondroma. High power. (*Gross.*)

j. There exist lobulated enchondromata the fundamental substance of which is mucous at the centre of some of the lobules. In these mucous points the capsules are preserved, but they float free in a surrounding fluid, as is observed normally at the centre of the intervertebral disks; often, also, the cellular elements are destroyed. In some cases the cartilaginous lobule may retain at the periphery a resistant layer and be transformed into a cyst. *Cysto-chondroma* of Virchow.

k. Certain enchondromata consist partly or entirely of cartilaginous tissue with ramified cells, as in cephalopods. *Enchondroma with ramified cells.* (Fig. 100.)

l. Often these different forms of enchondroma are variously combined. In reality, the majority of enchondromata are of *mixed* constitution.

Seat of Enchondroma.—Enchondromata, as we have said, never spring from cartilage. They may be located in all the organs, but they are developed more frequently in the bones, in the parotid gland, in the testicle, in the skin, in the subcutaneous cellular tissue, in the lungs, etc. In the glands, very complex forms are frequently met with, the different varieties of cartilaginous tissue being often combined. The epithelium of the culs-de-sac and ducts proliferates and finally undergoes divers retrograde metamorphoses. In the muscles, the connective tissue alone participates in the new formation. The fasciculi suffer fatty degeneration, atrophy and disappear, after having commenced with a multiplication of the nuclei of the sarcolemma.

Development and Ulterior Modifications of Enchondroma.—The development of enchondroma never takes place directly at the expense of

an adult tissue, but invariably after the transition of the latter into embryonal tissue. When enchondroma springs from bone, we first observe phenomena similar to those of osteitis. The embryonal cells thus formed soon become separated from each other by the interposition of a transparent substance. The adjacent osseous trabeculæ present notches into which newly-formed embryonal elements penetrate. In the oldest parts of this embryonal tissue the cells are widely separated by a fundamental transparent cartilaginous substance, in such a manner as to form a little island of cartilage at the centre of an enlarged medullary cavity. Around this little mass of cartilage the embryonal cells proliferate while the process of conversion of bone into medulla advances; at the same time, the bone trabeculæ are absorbed and neighboring medullary cavities are opened into each other, so that a large cavity is formed at the centre of which a cartilaginous nodule is found. The latter increases in size by the gradual inclusion of the embryonal cells which surround it. Later, the adjoining embryonal tissue is transformed into fibrous tissue, and thus is constituted a veritable perichondrium.

Analogous phenomena are produced when the enchondroma springs from connective tissue. Islands of embryonal cells are found; at the expense of these the growth of cartilage follows its ordinary type of development. In certain cases, when the formative movement is very slow, the fundamental fibrous substance of the connective tissue persists; thus fibro-cartilage is formed.

After cartilaginous islands become surrounded by a perichondrium, their increase is effected by a multiplication of cartilage cells in their interior. The elements of these islands being habitually very large, every phase of this multiplication can be very easily followed in them.

From their very beginning, enchondromata may exhibit nutritive modifications. Thus, when their increase is rapid, their cells may become infiltrated by a hyaline substance not well determined, yet named amyloid by Virchow, because they take an orange-yellow color in a very feeble solution of iodine.

The cells of enchondroma contain fat when the tumor is stationary. It frequently happens in points where interstitial growth is very marked that the cells may be simply infiltrated with amyloid matter, while in other places this substance is replaced by fat drops. Fatty degeneration is sometimes observed in the cartilage cells of enchondroma, when complete destruction of these elements is the result. It determines an arrest of development in the points affected.

When calcareous infiltration takes place, it almost never occurs at the periphery of the nodules, but always at their centre. It may present two different conditions, according as it accompanies a formative movement analogous to ossification, or as it is distinguished, on the contrary, by a calcification which invades, at the same time, all the secondary capsules. The latter does not differ from the calcareous infiltration to which we have previously alluded.

In the first case, there occurs an evolution comparable to that which takes place in ossification. The chief difference is that in enchondroma the embryonal marrow may: (*a*) remain in the embryonal state; (*b*) give origin to fibrous tissue; (*c*) become transformed into adipose tissue,

such as the marrow of a long bone; (*d*) in some rare cases, give rise to osseous trabeculæ, which have only a temporary existence, and which sometimes disappear again in order to give place to marrow.

Prognosis.—The method of development of the tumor enters into the prognosis of an enchondroma. If the morbid mass is sharply limited or surrounded by dense fibrous tissue, constituting a real perichondrium, and if it develops solely at the expense of its own elements, its gravity is slight. But if, around the tumor, one meets with tracts of embryonal tissue or of developing cartilage, the gravity is much greater. In the latter case, the tumor may return after extirpation, and it may even be generalized.

Osteoid Tumors.—Under the name of osteoid tumors, osteoid chondromata, J. Müller has described tumors formed of tissue analogous to that of bone, but possessing really not all the characters of the latter.

In studying the development of bone in rachitis, Virchow, after analyzing the particular tissue designated by Rufz and J. Guérin under the name of spongoid, called it osteoid tissue, and considered it as osseous tissue in process of physiological formation. We are obliged to anticipate here some of the history of rachitis, which we will describe later in detail, in order to explain the constitution of osteoid tissue. In rachitic bones we often find under the periosteum a tissue analogous to bone, in which the ossiform trabeculæ, instead of containing bone corpuscles and parallel lamellæ, show angular corpuscles in the midst of a substance which is homogeneous, or which has distinct calcareous granules scattered through it. Instead of being separated by medullary tissue, these trabeculæ are situated in the midst of a fibrous tissue which is permeated by vessels, and the lymph spaces and canals of this tissue freely communicate with the angular corpuscles of the osteoid trabeculæ.

From the preceding, an osteoid tumor seems to be constituted by trabeculæ of variable dimensions and form, composed of a refracting homogeneous or vaguely fibrillar substance, often infiltrated with calcareous granules, and containing angular corpuscles; these trabeculæ are separated by fibrous tissue, in which course the vessels.

This osteoid tissue, however, does not solely compose the mass of tumors of this name. They are almost always dotted with islands of cartilage, and infiltrated in places with calcareous salts. The cartilaginous areas develop in the intertrabecular fibrous tissue, and in this case alone should the name *osteoid enchondroma* be applied to them.

Calcareous infiltration in some part of these tumors is almost the rule. Isolated calcareous granules are deposited in the fundamental substance of the trabeculæ; nevertheless, the corpuscles surrounded by this deposit do not become bone corpuscles; whether there be only calcareous infiltration or complete petrifaction, these corpuscles show only few and imperfect processes. The fundamental substance never becomes lamellated.

These osteoid tumors may form a single mass, or they may be lobulated; but they never present the lobulated arrangement so markedly as in ordinary enchondroma. They may attain a considerable volume. They are very malignant, and are frequently reproduced in a great number of organs.

A naked eye examination can furnish no signs characteristic of these tumors; their aspect is, in effect, very like that of sarcoma, fibroma, or enchondroma. The anatomical diagnosis of this species of tumor must be made by the microscope.

IV.—TUMORS FORMED OF OSSEOUS TISSUE.

Osteoma.

The osteomata are tumors in which are reproduced the different varieties of osseous tissue.

We will divide them, according to the nature of their tissue, into three species:—

1*st*. *Eburnated osteoma*.—Virchow found, at the internal surface of the cranium, osteomata composed of concentric lamellæ parallel to the surface of the tumor. In the lamellæ, bone corpuscles were seen whose canaliculi were almost all directed toward the periphery, as in the dental cement. No vessels could be distinguished.

2*d*. *Compact osteoma*.—These tumors are formed of osseous tissue similar to that of the diaphysis of long bones. The osseous substance is disposed in lamellæ concentric to the vascular canals. They differ from the diaphyses of long bones in this, that the Haversian canals instead of being parallel have a more irregular course.

3*d*. *Spongy osteoma*.—These osteomata may consist of spongy or areolar tissue. The medulla forms the greater part of the tumor, and has various characters; it may be embryonal, gelatiniform, fibrous, or adipose.

Seat and Development.—According to their place of development, we distinguish two large groups of osteomata. The first comprises those which are attached to bones; the second those which arise at a distance from them.

The first may form at the periphery of the bone—*exostosis;* or in its medullary cavity—*enostosis*.

Exostoses.—At the surface of bones, the exostoses present Haversian canals which have a direction generally perpendicular to that of the Haversian canals of the old bones. The periosteum is lifted up by the tumor, so that there is a perfect continuity between the bone and the exostosis.

It is easy to explain the perpendicular course of the Haversian canals. In exostoses, when the subperiosteal tissue is transformed into bone, it is the periosteal vessels which determine the direction of the Haversian canals and the disposition of the lamellæ. These vessels are, as we know, perpendicular to the surface of the bone.

Exostoses may be divided into *epiphyseal* and *parenchymatous*.

The *epiphyseal* exostoses may be met with in all the bones. On the vault of the cranium, they are generally due to syphilis. Upon section, the new and the old bone are seen to be perfectly distinct, a fact which heretofore has escaped pathological anatomists.

Thus, under the exostosis, we very readily distinguish the old lamellæ in layers parallel to the surface of the old bone. Upon the long bones, these exostoses have the same disposition as upon the cranium.

The development of these exostoses takes place under the periosteum from a proliferation of its medullary layer. The bony trabeculæ generally form in the usual way, but in some rare cases the exostosis is covered with a continuous layer of cartilage, from which the bony tissue then develops.

Parenchymatous exostoses are those which arise in the depth of the bone, and in the following manner: There is a ramifying osteitis resulting in the conversion of an area of bone into inflammatory medullary tissue, which latter becomes the point of departure of an exuberant osseous formation.

In this case, also, the old tissue can be easily distinguished from the new, for here, too, the Haversian canals have a general direction perpendicular to that of the canals of the old bone.

Exostoses are formed at all ages. Sometimes they form upon the epiphyses while the person is still growing; they are then often multiple and symmetrical.

Exostoses are formed habitually of compact tissue, and encroach more or less upon the central canal of the bone. They consist of simple nodules, or the formation may be diffuse.

Not all of the osseous formations which arise at a distance from bone are tumors; nevertheless, we describe them here in order not to omit them entirely. They may arise in divers tissues of the organism. Certain cartilages frequently undergo osseous metamorphosis, solely from the progress of age, as the cartilages of the larynx, the trachea, the bronchi, and the ribs. In the thyroid cartilage, we observe this ossification in the aged and in the patients who have suffered from laryngitis, particularly tubercular laryngitis. In the latter it is an irritative process consecutive to inflammation of the mucous membrane. At the end of the ossifying process, which is identical with physiological ossification, the cartilages are more friable than in the normal state. Similar phenomena are observed in the trachea.

In the costal cartilages ossification is slower, and it is impeded by mucous metamorphosis. Cysts filled with mucous matter and the débris of cells incapable of organization often form.

In cases of chronic rheumatism osteomata often spring from the diarthrodial cartilages and synovial fringes. Similar tumors may form upon tendons by beginning at their point of attachment to the bone, and extending, in the form of long needles or stalactites, within the tendons and often into the attached muscles.

In the connective tissue of the arachnoid or of the pia mater, little plates often exist, composed either of connective tissue, incrusted with calcareous salts, or of true bony tissue.

The choroid coat of the eye may be transformed into a bony shell consisting of bone corpuscles and of osseous lamellæ.

Rokitansky has spoken of the frequent presence of osteomata in the biceps of the infantry and in the adductors of the thighs of the cavalry of the Austrian army.

Genuine bony plates have been found in the pericardium, and even in the muscular tissue of the heart. But most of such formations are fibrous tissue incrusted with calcareous salts. We cannot agree with Virchow that bony plates form in vessels affected with chronic endarteritis.

In the skin, osseous shells sometimes develop around the glands.

At the indurated summit of tuberculous lungs osseous productions often are present in the form of needles and radiating masses, which have been described by different authors. Their origin has been attributed to the bronchial cartilages.

We have been able to satisfy ourselves that their development takes place at the expense of the new connective tissue of interstitial pneumonia. Osseous trabeculæ in process of formation are surrounded by an embryonal tissue, from which their development proceeds in the ordinary manner.

Besides the osteomata of the arachnoid and pia mater, the central nervous system may be the seat of tumors of the same nature developed in the nerve substance of the brain.

Odontoma.—*Odontomata* are tumors formed of dental tissue.

Under this name have been described:—

1st. Exostoses caused by inflammation of the alveolo-dental periosteum. The cement of the teeth, a genuine osseous tissue, is in immediate relation with the periosteum of the alveolus. Under the influence of periosteal inflammation new layers of cement are added to the old.

2d. New formations of enamel and of ivory may occur either upon the neck of the tooth or upon the cement. These tumors resemble little drops of wax.

3d. A special tumor of the maxilla, consisting of one or more normal or deformed teeth, sometimes grouped together in a congenital malformation.

It is necessary to add to this group of odontoma, tumors in which teeth implanted upon osseous plates are met with in dermoid cysts, etc.

Odontomata are not usually voluminous tumors, nor are they grave.

V.—TUMORS FORMED OF MUSCULAR TISSUE.

Myoma.

The structure of myoma has its type in the muscular tissue of the economy.

At present we distinguish two kinds of myoma.

1st. Tumors containing striated muscle fibres. *Myoma strio-cellulare* (*rhabdo-myoma* of Zenker).

2d. Tumors formed of smooth fibres. *Leio-myoma* of Zenker. *Myoma* with unstriated cells.

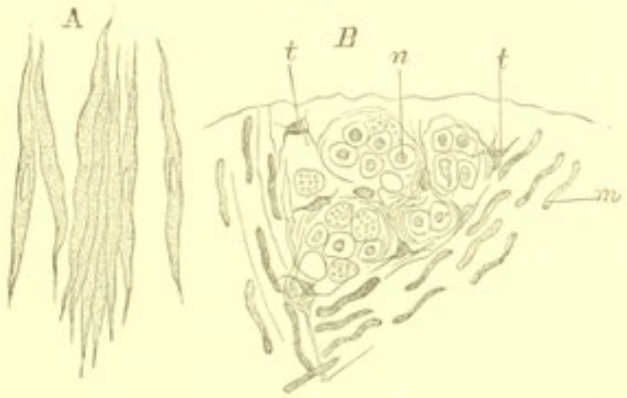
1st. Myoma Strio-cellulare.—These tumors are rare and are congenital. In dermoid cysts of the third variety of Lebert striated muscle fibres are often found; these are complex tumors, not myomata. In other tumors which develop in the fœtus, and which we shall soon describe, striated muscular fibres are frequent but the morbid growth is too com-

plex to be called a myoma, and its characteristics of development and of structure assign it to a separate place.

2D. LEIO-MYOMA, or MYOMA WITH SMOOTH FIBRES.—These tumors may present themselves under the form of an irregular, diffuse mass, with ill-defined borders, or may show a very distinct lobular form. They have a fleshy or fibrous aspect. The muscle cells offer the same characters as in the physiological state, and may be grouped into fasciculi or membranes, or may be isolated in the midst of connective tissue. The fasciculi are separated by connective tissue in which run the bloodvessels; the latter never penetrate the muscular fasciculi themselves.

When the muscular elements are isolated, they are recognized by their spindle form, and their rod-shaped nucleus in the centre of the cell. Leio-myoma may be formed of fasciculi which may all run in the same direction, or which may interlace. The section may take them transversely, obliquely, or longitudinally. In cross section the cells appear with a more or less circular outline, with the nucleus appearing as a little round spot in the centre. But obliquely, the cells may present a more or less oval section. In longitudinal section only do the muscular elements present the familiar spindle form, with a central rod-shaped nucleus.

Fig. 103.



Muscular cells from a leio-myoma. *A*. Cells separated by the action of nitric acid, 20 per cent. *B*. A hardened section colored with carmine and treated with acetic acid. *m*. Longitudinally cut, *n*, transversely cut nuclei. *t*. Connective-tissue cells.

A very interesting property of myomata is their contractility. Upon this property greatly depends the varying consistency which they possess at the moment when they are examined. This phenomenon is particularly noticeable in the myomata which are commonly called fibroid bodies of the uterus.

The VARIETIES met with in myomata are:—

1st. *Non-lobulated myomata*, formed of a homogeneous fleshy mass. They are soft, possess voluminous muscular cells.

2d. *Lobulated Myomata*.—They sometimes have large gaping vessels, like the uterine sinuses and the hepatic veins. In certain very rare cases the dilatation of the vessels is such that the term *erectile* has been applied.

3d. *Calcareous infiltration* is frequent in these tumors. It commences at the centre of the lobule; sometimes the infiltration is only into the cement substance; at other times, complete petrefaction of this substance and of the muscular elements occurs at the centre of the lobules or

throughout their entire mass. This transformation is particularly frequent in the uterine myomata which project upon the peritoneal surface.

4th. *Fatty infiltration* of the cells is sometimes associated with calcareous infiltration.

5th. *Mucous metamorphosis* is frequently associated with dilatation of the vessels in myomata. It insures the destruction of a certain number of elements and the formation of cavities or mucous cysts.

DEVELOPMENT OF MYOMA.—Sometimes in the fibrous tissue of the tumor and along the muscular bundles islands of embryonal tissue are seen; the contractile cells may develop in the same manner as in the embryo from a direct transformation of the embryonal cells. Some authors have thought that the pre-existing muscle cells may multiply by division.

True myomata are always SEATED in the muscular tissue of organic life. They are met with most frequently in the uterus, where they may appear as an interstitial mass, lobulated and encysted in the midst of the uterine tissue, or as polyps projecting upon the surface of the peritoneum, or into the uterine cavity. Their structure in these cases consists either of young muscular tissue, or of a muscular tissue invaded by recently-formed connective tissue, so abundant and predominating that the growth might almost be considered a fibroma, if, in naming tumors, we did not subordinate the commonest tissue to that which gives the tumor its special characters. The muscular tissue is of new formation in these tumors.

In old men the prostate is often the seat of a new formation of smooth muscular fibres, either diffuse or circumscribed in the form of tumors. There also exist myomata of the scrotum.

The digestive tract presents formations of the same nature, in the shape of polypi. The latter myomata, like those of the uterus, are at first interstitial, but after a variable time they become pedunculated, and project at one time into the visceral cavity, at another time into the peritoneal cavity.

The anatomical DIAGNOSIS of these tumors is impossible without the aid of the microscope. With this instrument their recognition is generally easy. In doubtful cases, recourse should be had to dissociation of the muscle cells with needles, after the use of nitric acid. An important point to be observed, when studying the tissue in sections, is the shape and relative position of the nuclei.

The PROGNOSIS of myomata is not grave unless by their seat and their volume they determine lesions of the neighboring tissues, or offer obstacles to the proper function of important organs. Thus a myoma of the uterus may compress the bladder or the rectum, and occasion congestions and hemorrhages of the mucous membrane, and other accidents. The pedunculated myomata of the intestine may give rise to symptoms of strangulation.

VI.—TUMORS FORMED OF NERVE TISSUE.

Neuroma.

Neuromata are tumors constituted by a tissue of new formation, of which the type is found in nerve tissue.

In the normal state, nerve tissue presents two different varieties: 1st, medullary substance, found in the gray centres of the encephalon and spinal marrow, consisting of nerve cells and neuroglia; 2d, fasciculated nerve tissue, the type of which is met with in the peripheral nerves.

These two forms of nerve tissue enable us to distinguish two kinds of neuromata: 1st. Medullary or ganglionic; 2d. Fasciculated neuroma.

1ST. MEDULLARY NEUROMA.—Medullary or ganglionic neuromata are very rare and of small importance clinically. Virchow has described them in the brain and spinal marrow as slightly projecting tumors. They must not be confounded with herniæ of the marrow. These tumors, of the color of the gray nerve substance, contain nerve cells, neuroglia, and vessels.

They may form in the corpora striata and upon the surface of the ventricles. Sangalli has described, in congenital encephalocele, tumors formed of gray substance. In some dermoid cysts we also find masses of gray nerve substance containing nerve cells and neuroglia.

2D. FASCICULATED NEUROMA.—At the commencement of this century, Odier (of Geneva), under the name of neuroma, included all tumors seated along the course of nerves. These were most frequently myxomata, as we have already learned. The word neuroma is still often applied by surgeons to every tumor, whatsoever may be its nature, which may happen to be seated along the course of a nerve. In the terminology employed to-day by pathologists, this word should be exclusively used to designate tumors constituted by nerve elements.

The fasciculated neuromata are then simply tumors constituted by nerve tubules of new formation.

The name of *painful neuroma* has been given to certain little subcutaneous tumors, simply on account of the great pain which they cause. Dupuytren called them painful fibromata. They probably contain nerves which are compressed by the new connective tissue.

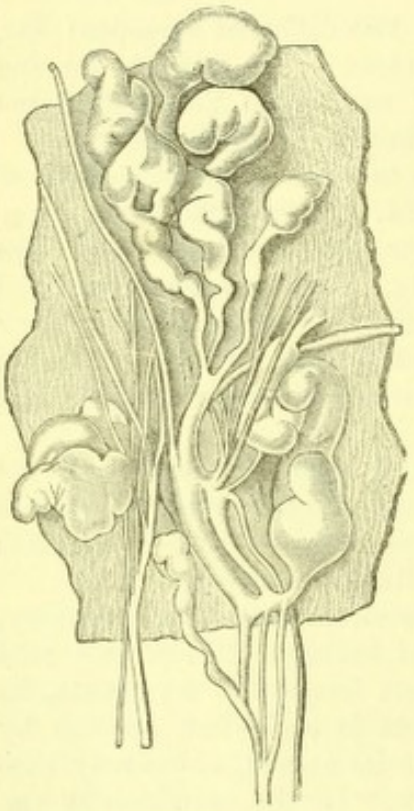
Verneuil has described, under the name of *plexiform cylindrical neuroma*, an interesting affection of the nervous system, characterized by an abundant production of fibrous tissue between the tubes of one or more nerve-bundles, so that the nerves have augmented considerably in size while preserving their cylindrical form. This affection is not accompanied by a new formation of nervous elements, and it should not be called a neuroma.

Genuine fasciculated neuromata are very rare. They are always seated upon the track of a nerve, and are in every case formed of tissue similar to that of the nerve. They are generally small and formed of a single lobe. Upon a cut surface, their tissue appears fibrous; it is dry, and, when the débris obtained by scraping is examined under the microscope, drops of myelin may be observed. By dissociation, one succeeds in isolating some nerve tubes. A magnified view of stained sections shows

nerve tubes in great numbers, diversely interlaced and separated from each other by connective tissue more or less rich in cell elements.

According to whether they contain nerves of double contour or fibres of Remak, Virchow divides them into two distinct species, designating the first as *myelinic neuroma*, the second as *amyelinic neuroma*.

Fig. 104.



True plexiform neuroma. (*Bruns.*)

The SEAT of these neuromata is extremely variable. One of the most interesting varieties is seen often at the cut extremities of nerves in amputation. The end of the nerve becomes, in these cases, the point of departure for the growth of a little pyriform tumor, which might be considered at first sight as a new formation of fibrous tissue. Valentin and Lebert have found in them a large quantity of nerve tubes with double contour. In dissecting these tumors, a bundle of nerve tubes is seen to penetrate a little swelling. Within the latter the nerve tubes interlace and form sinuosities and loops; it is difficult to determine if these tubes are continuous with those of the cut nerve. The very dense fibrous tissue which separates them makes dissociation and isolation of the tubes troublesome, and the winding course of the latter makes it difficult to follow them in the section for any considerable distance. We shall soon see, while studying the phenomena of cicatrization of nerves, that the embryonal tissue of the cicatrix has the tendency to produce nerve tubes.

Instead of being single, there may be numerous neuromata along the whole course of a nerve and its divisions, along a plexus, or along all the nerves of a considerable part of the body. Tumors of the optic nerve, which have been called neuromata, are, according to Virchow, mostly myxomata.

The ANATOMICAL DIAGNOSIS of neuroma, difficult in the amyelinic variety, is simple when they possess double contoured fibres.

In order that a tumor should merit the name of neuroma, it is not sufficient that they contain nerve tubes; it is necessary that the number of the nerve cells or tubes is such as to indicate a new formation of nerve elements.

PROGNOSIS.—Neuromata are usually grave only by reason of their seat, by the pain which they occasion, and sometimes by their multiplicity. These tumors are never capable of secondary reproduction in the different tissues of the economy.

EX LIBR. BIBL. COLL. REG. CHIR. EDIN.

VII.—TUMORS FORMED OF BLOODVESSELS.

Angioma.

Angiomata are tumors the type of whose structure is seen in the vascular system.

They have been designated as erectile tumors by Dupuytren, as angioses or ecchymoma by Alibert. To merit the name of tumor, it is necessary that the vessels which compose them shall be of new formation. A simple dilatation of old vessels should not be considered as an angioma; aneurism should not be classed among them; varices, or dilatation with hypertrophy of the veinous walls, should also be distinguished from them, and the same may be said of arterial varices, described by Virchow with the angiomata under the name of *angioma racemosum*.

We distinguish two species of angiomata:—

1st. *Simple angioma*, in which the newly-formed vessels which constitute the tumor are similar to normal arteries, veins, and capillaries.

2d. *Cavernous angioma*, in which the blood circulates in a lacunar system analogous to the cavernous system of erectile organs.

1ST. SIMPLE ANGIOMATA (congenital nævi, telangectases) show themselves under the form of polypi, or of flat, slightly elevated tumors, at one time effaced, at another swollen. They are red or violet, and are usually located upon the face, around the orbit, or upon the neck. They essentially consist of capillaries of new formation presenting regular ampullar or varicose-like dilatations. These vessels are very tortuous and generally have a corkscrew appearance. In a section of the tumor, the walls of these vessels are observed to be very rich in nuclei and to have a thickness of one- or two-hundredths of a millimetre, while still preserving the simple structure of capillaries. The vessels are imbedded in a fibrous or cellulo-adipose stroma. These tumors are congenital and are very common. They may disappear in the first months of life.

2D. CAVERNOUS ANGIOMATA (Nævi cavernosi, erectile tumors) are constituted by an erectile tissue, the cavities of which are filled with blood. The blood circulates very actively in these caverni. Their vessels form a direct communication between the arteries and veins, thus taking the place of the capillary system.

We study in angiomata—

1st. *The trabeculæ* which circumscribe the caverni. They are formed of dense fibrous tissue, in which plasmatic elements are to be distinguished after staining the section examined. The trabeculæ may also contain smooth muscle cells, or, when the tumor originates in muscular tissue, they may even exhibit striated muscle fibres. The trabeculæ may also contain fat vesicles, and they may sometimes possess vessels which have the relation of vasa vasorum. In one case, Esmarch was able to trace nerve filaments in them.

2d. *The cells* which pave these cavities are similar to the endothelium of veins.

3d. *The blood* contained in the cavernous spaces is similar to that in the rest of the vascular system.

After an incision of an angioma which has been removed, the blood

escapes and there remains a spongy tissue, slightly contracted. If, on the contrary, the blood is coagulated en masse, as when the tumor is placed entire in alcohol, a magnificent natural injection of the caverni is secured.

All these tumors are not erectile.

In the active DEVELOPMENT of angioma embryonal tissue and normal capillaries are first produced; subsequently, these vessels become dilated. Soon the dilated capillaries come in contact with each other; wide communications are established, and there results a capillary system with large cavernous dilatations. This method of formation has been demonstrated by Virchow in cavernous angiomata of the liver.

Cavernous angioma may undergo divers *nutritive alterations*. The walls of the vessels may become the seat of calcareous concretions, similar to those seen in the choroid plexus and in angiolithic sarcoma. Cysts filled with a serous fluid have been observed in angiomata. This modification is explained by the isolation of a vascular bud, and the subsequent coagulation and metamorphosis of the blood which it contained.

Can these tumors be converted into carcinomata or sarcomata? J. Müller thinks that he has seen malign cavernous angiomata with a tendency to extend, and which have even been followed by metastases. Certainly sarcomata and carcinomata with dilated vessels act in this manner. Many pulsatile tumors which have been diagnosed as erectile tumors, aneurism of the bone, etc., are really nothing else than sarcomata or carcinomata with very widely dilated vessels.

The tumor may be *diffuse*, that is, not separated from adjoining tissues by a sharp limit; or it may be *circumscribed* or even surrounded by a genuine capsule.

According to their SEAT, angiomata may be divided into internal and external.

External angiomata are located in the tissue of the derm or in the cellulo-adipose subcutaneous tissue. When they spring from the adipose tissue, Virchow calls them *lipogenous*, and *phlebogenous* when they arise from the vasa vasorum of the veins. They may extend into the intermuscular cellular tissue, and even into the bone itself.

Internal angiomata have been observed in the liver, the kidneys, and the spleen. The angiomata of the liver are the most common. Their size varies from that of a hazel-nut up to half the size of the liver. Notwithstanding that they project upon the surface of the liver, they generally do not augment its volume, for they are developed at the expense of the hepatic substance. When they are surrounded by a capsule, the latter is pierced by vascular openings. Around them the hepatic substance is normal, but is separated from the tumor by a zone of connective tissue in a state of proliferation. It is in this proliferating tissue, when the tumor is increasing, that the work of development proceeds. Ruptures of angiomata of the liver may occasion a peritonitis. Angiomata may retract after spontaneous coagulation, and give rise to cicatrices.

Schuh has published an imperfect observation of an angioma of the lung.

Their anatomical DIAGNOSIS is easy. We should be careful to exclude an erectile carcinoma or sarcoma. Around an angioma and in the inte-

rior we find only the normal tissues of the part invaded. It will sometimes be difficult to differentiate an angioma from a leio-myoma with dilated vessels; but here also the existence of a very great number of muscle cells will remove doubt.

PROGNOSIS.—Angiomata have no gravity other than that which may result from their seat and extent.

VIII.—TUMORS THE TYPE OF WHICH EXISTS IN THE LYMPHATIC SYSTEM.

Lymphangioma. Lymphadenoma.

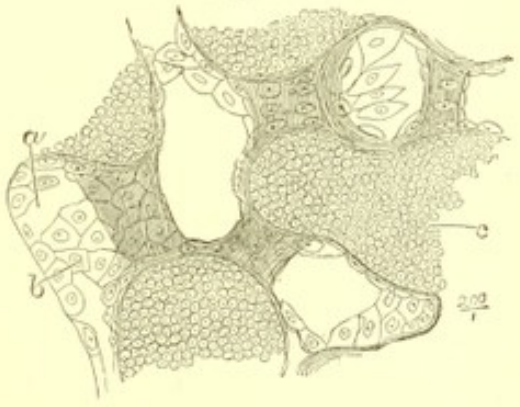
There are two kinds: 1st. *Lymphangiomata*, tumors constituted by a new formation of lymph vessels; 2. *Lymphadenomata*, tumors which result from a new formation of adenoid tissue, similar to that of the lymph glands.

1ST. LYMPHANGIOMATA.—These tumors, constituted by newly-formed lymph vessels, are frequently confounded with simple dilatations of the pre-existing vessels; perhaps the existence of lymphangioma, in the strict meaning of this definition, may be somewhat doubtful. Some authors have observed such tumors developed in subjects inhabiting countries where elephantiasis Arabum is frequent, but there is nothing to show that in them we have not a simple dilatation of pre-existing vessels.

The *adeno-lymphocele* of Nélaton, etc., in which the dilatations extend as far as lymph glands, should be classed with lymphangioma.

Lymphangiomata are soft, fluctuating, compressible tumors, which may or may not be adherent to the skin. They are constituted by networks of lymphatics, which communicate with each other as the bloodvessels in cavernous tissue, and which may even open externally and allow lymph to escape. The histology of these tumors has not been fully studied. Th. Anger demonstrated that the dilated lymphatics show a hypertrophy of their wall, caused by an increased number of smooth muscular fibres. He was unable to see the endothelium of these dilated vessels.

Fig. 105.



Dilated lymph vessels in a case of elephantiasis of the skin of the penis. *a*. Lymph vessel. *b*. Flat endothelium of the vessel. *c*. Embryonic connective tissue of the tumor.

Virchow is inclined to associate congenital hypertrophy of the tongue and of the lips with lymphangioma. In these hypertrophies we find dilated lymph vessels containing a fluid analogous to lymph, and located in the midst of a dense fibrous tissue. (Fig. 105.) In the connective tissue which forms the mass of the swelling of elephantiasis Arabum, we meet with irregular lacunæ filled with a fluid similar to lymph. The development of this elephantiasis is preceded by a series of "angioleucites," and the formation of the lacunæ is dependent upon the latter.

Certain pale and compressed congenital tumors of the skin, considered as lymphatic nævi, should be classed among lymphangiomata.

2d. Lymphadenoma.—Lymphadenomata consist of lymphadenoid tissue. After Virchow and Bennett, in 1845, discovered leucocythæmia, the attention of observers was drawn to peculiar formations in the liver and some other organs. In the liver the hepatic cells and lobules were separated by new round elements located in the connective tissue. These cells were regarded as white blood corpuscles, which had sprung from the connective tissue by proliferation, and the formations were looked upon as a point of supply for new white blood corpuscles. In the kidneys, spleen, and lymphatic glands, analogous productions were interpreted in the same manner.

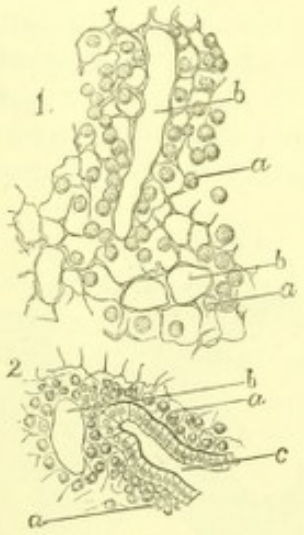
As early as 1801, Hodgkin had studied a fatal disease characterized by a progressive hypertrophy of the spleen and lymphatic glands.

Later, Bonfils discovered that the lymph glands and the spleen could become hypertrophied while the blood contained no more white globules than in the normal state; in these cases also the previously indicated new formations were found in the liver, kidneys, etc. Trousseau named this disease *adænia*.

For us, leucocythæmia and adænia constitute two varieties of the same morbid process: the essential lesions of the different organs are the same in all cases; they are lymphadenomata, or tumors which reproduce the adenoid tissue of His.

The definition of lymphadenoma is based upon that of the tissue of lymph glands, and in the reticular connective tissue of the intestinal tract. (Fig. 106.)

Fig. 106.



1. Reticulated tissue from a lymphoid follicle of the vermiform appendix of the rabbit, with the system of meshes, and remains of the lymph cells *a*. Most of the latter have been removed artificially. *b*. Lymph vessel. 2. Longitudinal section of a Lieberkühn's gland, showing the surrounding recticular tissue, in the meshes of which are seen the lymph cells *a*. *b*. Lumen of a vessel. *c*. Lumen of the gland. (*Frey.*)

We should apply the name *lymphadenoma* only to tumors constituted by an adenoid tissue of new formation, and not to other alterations which accompany leucocythæmia, and which will be noticed in the following description.

Description.—Lymphadenomata are tumors of extremely variable size, from that of a millet seed up to that of the head of a fœtus. They almost always have ill-defined limits. In the lymphatic glands they resemble a simple hypertrophy of these organs, but when several adjoining glands are involved, they are confounded in a common mass. They have a decidedly encephaloid aspect: they are soft, gray, with red points which correspond to dilatations of vessels and ecchymoses: they sometimes present opaque, cheesy portions. These tumors yield a very abundant milky juice, exactly like that of carcinoma.

This juice consists of a fluid in which floats small round cells, having a mean dia-

meter of .010 mm., and containing a single nucleus; larger cells measuring .020 mm., containing several nuclei; a few of the cells are still more voluminous and loaded with nuclei.

In the reddish-brown or yellow points of the tumors these cells contain blood pigment of different tints. There are also to be seen in the juice flat cells with oval nuclei from the vessel walls, besides, red disks and free nuclei of different size, the latter resulting from the rupture of the cells which contained them. By examining the scrapings or the juice alone, these tumors cannot be distinguished from sarcomata and encephaloid carcinomata.

For their recognition, it is necessary to study thin sections which have been pencilled. The reticulated stroma which forms the real basis of these tumors is then very evident, and is seen to be in connection with the capillaries. (See fig. 107.) In the case of adænia the bloodvessels are filled with globules which do not color by carmine. In leucocythæmia, on the contrary, the dilated capillaries are filled with white corpuscles, which are readily stained by carmine. Capillaries full of white blood-corpuscles are also met with in all the organs, so that by this characteristic alone we can diagnose after death the leucocythæmic condition.

Seat.—Lymphadenoma of the lymph glands determines a considerable increase in the size of the follicles, which are compressed and modified in form. The connective tissue of the medullary part seems to have disappeared, in order to make room for the hypertrophied cortex. Upon the cut surface open spaces are seen, which correspond to the lymphatic sinuses enveloping the follicle. Everywhere the enlarged glands present this same structure; they are entirely composed of the modified cortical substance.

The thymus gland, even at the age when it has undergone almost complete atrophy, may in leucocythæmia or adænia reassume its original form, and become the seat of adenoid tissue.

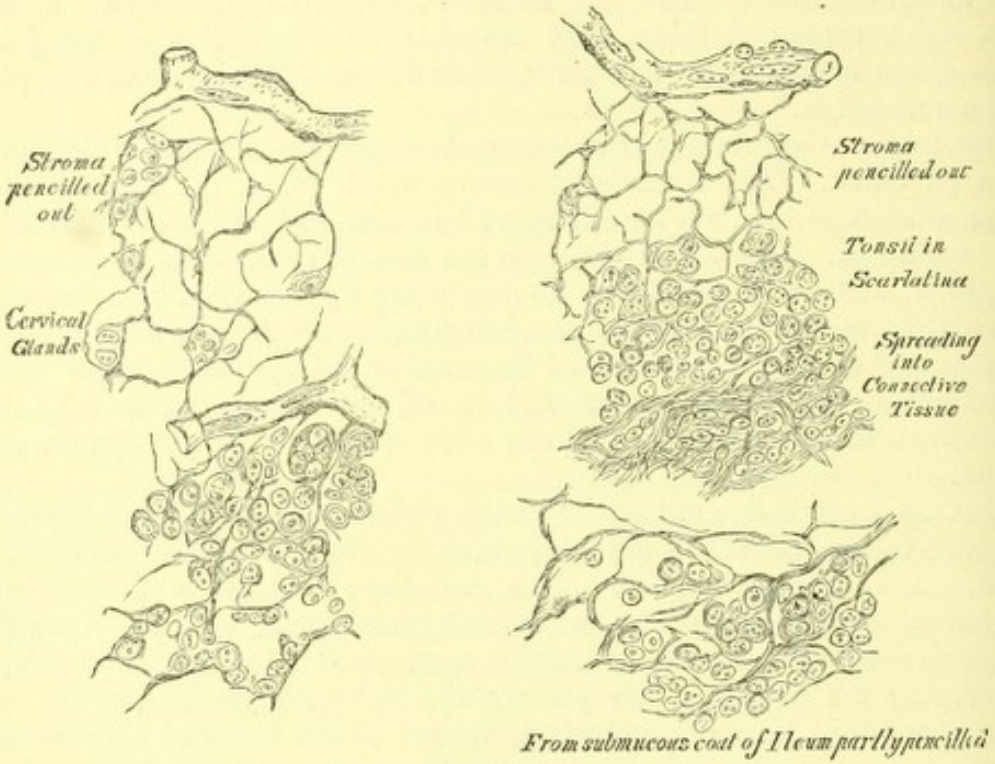
The spleen may suffer an alteration similar to that of the lymph glands. The lesion is in the Malpighian bodies, which correspond to the follicles of the lymph glands.

The liver presents many distinct alterations. The one which is peculiar to leucocythæmia consists in a diffuse apoplexy of white blood corpuscles. The whitish islands, which in the liver have been regarded as caused by a hyperplasia of the connective tissue, result in this case from an accumulation of white blood corpuscles; the hepatic capillaries allow the escape of a large quantity of white corpuscles, which spread themselves between the hepatic cells in a limited or diffuse manner. The liver cells undergo fatty degeneration, and may be thus destroyed. We have, then, not a formation of adenoid tissue, but a real apoplexy of the white corpuscles of the blood. Besides these small products, there are in the liver genuine new formations of reticulated adenoid tissue. Perhaps the extravasated white corpuscles above mentioned may be the starting point of this new tissue. In adænia it is almost certain that this is not so, and that there the origin of the lymphadenomata of the liver must be attributed to a hyperplasia of the connective tissue.

In adænia, we have constantly met with a notable hypertrophy of the

liver, connected with a congestive dilatation of the vessels. The kidneys present two kinds of lesions, which are in every respect similar to those of the liver. In the mucous membrane of the stomach and intestines lymphadenomata are frequent. Their nature may be suggested to the naked

Fig. 107.



Microscopic anatomy of lymphadenoma. (*Bryant.*)

eye, to which they appear as embossed, gray tumors, uniformly colored or spotted with ecchymoses, soft, and ulcerated at their centre. In their neighborhood the mucous membrane is thickened. Under the microscope, and in perpendicular section, these tumors show the tubular glands with granular contents. Between the latter and below them is a reticulated tissue of new formation, characterized by large meshes, thickened trabeculæ, and a few nucleated nodes. The glands often entirely disappear, leaving only adenoid tissue.

The tumors of the stomach are often extensive and 3 to 4 centimetres in thickness. These large lymphadenomata may be mistaken for other kinds of tumors; their softness, their ulceration, their juice, may easily cause them to be confounded with encephaloid carcinomata, or with epitheliomata with cylindrical cells, if use is not made of the microscope.

Lymphadenomata of the large and small intestines generally present a very great similarity to those of the stomach. But we also find in the intestine small acuminated tumors resembling very much the hypertrophied follicles of typhoid fever. When these are slightly ulcerated at their centre, they show a depressed area. One might think that there is simply a hypertrophy of a solitary follicle, but this is not so. In these little tumors the glands of Lieberkühn are surrounded by a reticulated tissue of new formation.

The lungs may be the seat of lymphadenomata; so also may the bones. Lymphadenoma is common in the divers organs which we have just passed in review, but it may be met with in other parts of the organism.

The DEVELOPMENT of these tumors can be well studied only in organs where adenoid tissue does not naturally exist, in the liver, in the kidneys, in the bones, for example.

The first phase of their development consists in the production of a mass of embryonal tissue at the expense of the interstitial connective tissue of the organs, of the marrow of the bones, and perhaps of the white blood corpuscles which have escaped from the vessels.

In a second phase, some of the embryonal cells put forth numerous prolongations which come in contact with each other, unite, and form a complete network. The trabeculæ of this network are at first thick and soft; little by little they condense and assume the character of a reticulated stroma. Those embryonal cells which do not undergo these changes remain imprisoned in the stroma and form lymph corpuscles.

Lymphadenomata are subject to diverse MODIFICATIONS of their tissue.

Diffuse hemorrhages are frequently observed. They may be limited to the tumors, or they may sometimes occur in tissues and organs where the new growth is not found. The latter is the case particularly in leucocythæmia.

Infarctions are common in leucocythæmia. It is not known whether they exist in adænia. They are characterized by whitish, opaque, caseous islands, in which we still see the structure of adenoid tissue, but the latter has suffered atrophic modifications, affecting at one time the stroma, at another the lymphoid cells. The vessels are then transformed into granulo-fatty tracts, opaque to transmitted light.

The DIAGNOSIS of lymphadenoma can be made only upon pencilled sections, when the truly characteristic reticulated stroma is revealed.

We will not dwell upon the PROGNOSIS, since it is always in subjects who have succumbed to the generally rapid progress of the disease that we find these formations.

IX.—TUMORS HAVING THEIR TYPE IN EPITHELIAL TISSUE.

In the skin we have a structure showing the variations which the epithelial cells can experience under varying physical conditions. We do not think that the distinction created by His between endothelium and epithelium can be accepted as absolute; and the opinion of Thiersch that all epithelia spring from an epithelium seems to us contradicted by what takes place in the formation of the epithelial cells which cover granulations and fistulæ. It is very probable in this case that the epithelia are derived from embryonal tissue.

The history of cancroids demonstrates very positively the formation of epithelial cells in parts which are void of them in the normal state; for example, in the medullary tissue of bone, in the lymphatic glands and in muscles.

In tumors, epithelial tissue may assume different characters which give rise to as many distinct classes.

1*st Class.*—New epithelial tissue having an arrangement into islands or masses, which do not take the shape of definite organs. These are *epitheliomata*, properly speaking.

2*d Class.*—Epithelial tissue covering papillæ; such are *papillomata.*

3*d Class.*—Epithelium arranged as in glands; such are *adenomata.*

4*th Class.*—Epithelium presenting a cystic cavity; these are *cysts.*

1st Class.—Epithelioma.

Definition and Classification of Epithelioma.—Epitheliomata are also designated under the name of *cancroid*, *epithelial cancer*, or *epithelial carcinoma*, by German authors. The *polyadenoma* and *heteradænic* tumors of several French writers are nothing else than certain varieties of epithelioma.

The cells of epithelioma are disposed in *stratified* layers—Pavement-celled epithelioma; or they are *cylindrical* and generally form only a single layer—Cylindrical-celled epithelioma.

Pavement-celled Epitheliomata present several species:—

1st. *Lobulated epithelioma*, in which there is an epidermic evolution.

2d. The epidermic evolution is no longer decided and the cells of the lobule having suffered desiccation have become corneous. *Epithelioma with concentric cell-nests.*

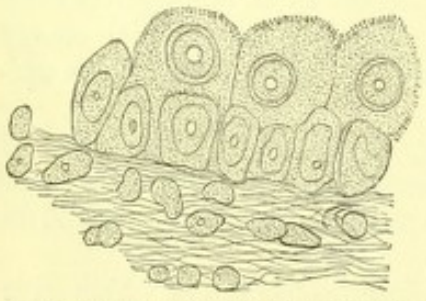
3d. The fibrous tissue which forms the stroma of the tumor is channelled by cavities in the form of tubes filled with pavement cells, which show no epidermic evolution. *Tubulated epithelioma.*

Cylindrical-celled epithelioma present only one species.

1st Species.—Lobulated Pavement-celled Epithelioma.

It is this species which has served as a type for the classical description of cancroid. It is usually seen on the skin and the mucous membranes covered with pavement epithelium. It presents to the naked eye a granular aspect; a cut surface shows a gray or pink tissue, upon which opaque or translucent points and fibrous tracts appear very distinctly. The consistence of the tumor is unequal, very friable in certain points, more dense in others. Usually its tissue may be broken very easily, which led Cruveilhier to give it the name of *fragile cancer*. By scraping these epitheliomata with the edge of a scalpel, a grumous opaque substance is obtained, which does not mix with water. Cancer juice, as we have seen, is readily miscible with water which it renders uniformly turbid. In the scrapings we find cells of varied forms: some resembling the epithelial plates of the mouth; others possessing one or several prolongations; they appear fusiform when seen in profile, and flat when seen in surface; sometimes spherical cells distended by a colloid vesicle,

Fig. 108.



Spinous epithelial cells of a cancroid epithelioma.

which contracts by the addition of acetic acid, are observed; rarely, we obtain in this way dentate cells like those of the rete mucosum. (Fig. 108.)

Very often in the grumous fluid thus obtained we find globes composed of epidermic cells disposed in concentric layers, like the leaves of an onion (*c*, *b*, fig. 109); these are the cell-nests, the pearly bodies, the epidermic

Fig. 109.



Elements from a lobulated pavement-celled epithelioma. *a*. Isolated cells with a multiplication of their nuclei. Figure to the right shows an epithelial peg with pearly bodies (cell-nests). *c*. Crushed pearly body. × 400.

spheres. The centre of these spheres in some cases contains colloid cells. They may also possess cells which contain a considerable number of nuclei. (Fig. 109, *a*.)

Thus, we see that by examining the scrapings from a cut surface of such tumors, some indications are furnished suggestive of the nature of the tissue. But, for a complete understanding of the morbid growth, it is necessary to study thin sections which have been cut from the tumor in various directions. If the section be made perpendicular to the surface, lobules formed of epithelium and connected together by bands of epithelium are seen. In sections parallel with the surface, only transverse cuts of isolated lobules are visible.

The lobules are formed of epithelium similar to that of the epidermis. At their periphery, the epithelium is composed of cylindrical cells implanted perpendicularly to the wall of the lobule. As we advance from the periphery towards the centre of the lobule, an epidermic evolution

similar to that of the skin, is observed; that is to say, we find first a layer of cylindrical cells, layers of dentate cells, then flat corneous cells, which becoming dry form an epidermic globe at the centre of the lobule. The mode of formation of these cell-nests is thus easily understood.

The lobules are separated from one another by a stroma, generally consisting of connective tissue, which serves to sustain the arteries, capillaries, and veins; these vessels never penetrate into the epithelial masses.

Lobulated pavement epitheliomata present varieties according to the histological alterations of the stroma. The stroma may be composed of—

a. Embryonal tissue with numerous vessels;

b. Mucous connective tissue;

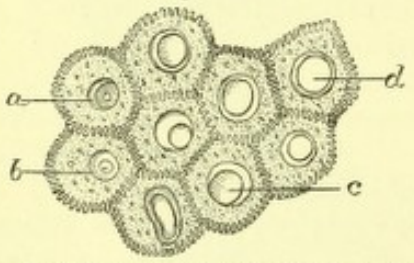
c. Adult or fasciculated connective tissue;

d. All these varieties of tissue combined.

Alterations in nutrition of the cells of epithelioma permit of the recognition of two varieties: *colloid* and *corneous*.

They are analogous to what we observe in the epiderm, where the epidermal cells, instead of drying, become colloid when there is an irritation of the skin. At the commencement of the alteration the dentate cells, from an increased nutritive supply, show a vesicular state of their nucleoli. The nucleus itself becomes distended by the transformed nucleolus. This modification is observed in the cells of lobulated epithelioma. Soon the cells themselves become vesicular and filled with colloid matter; they may then open into each other and form an areolar system, of which the trabeculæ are formed by flat epidermic cells. These elementary lesions, which are seen in vesicles and pustules of the skin, also sometimes appear in epithelioma. In the latter, the most common modifications consist in a colloid drop which replaces the nucleus, or the colloid matter may be formed around the nucleus in the protoplasm of the cell, and crowd the nucleus to the periphery. (Fig. 110.)

Fig. 110.



Epithelial cells, from the rete mucosum, during slight irritation. Dentate cells of the epidermis, the nuclei of which have become vesicular by a dilation of the nucleolus: *a*, normal nucleus and nucleolus; *b*, dilated nucleolus; *c*, *d*, a more advanced stage of the same alteration.

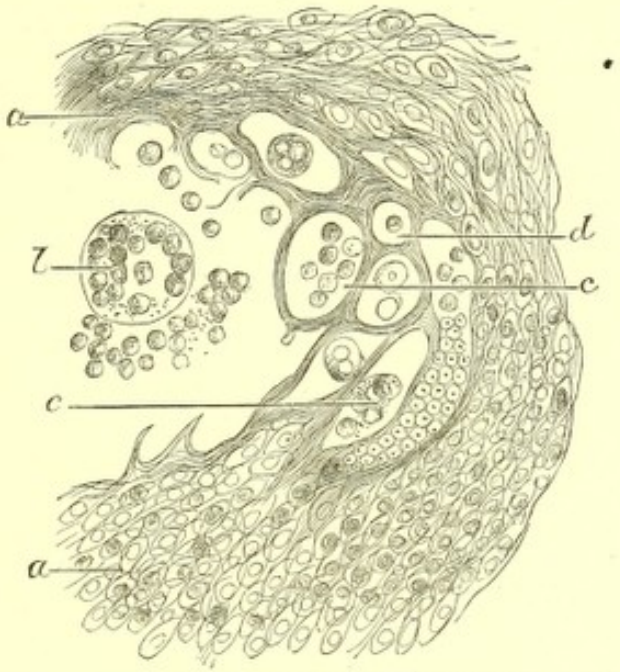
Both the colloid and corneous transformation of the cells of epithelioma may be present in the same tumor, which is rare, or one may exist singly, when we have colloid or corneous epithelioma.

Lobulated epitheliomata are subject to *ulceration*. This ulceration is caused by disintegration of the epithelial cells, or by gangrene following obliteration of the vessels.

In the first case, the cells constituting the lobules easily become detached from each other by softening of their cement substance, and form a grumous mass which can be squeezed from the tumor by lateral pressure upon it. The proliferation of the connective tissue at the surface of epitheliomata may be intense enough to give rise to granulations. We have then a papillary surface covered with epithelium, as in the adjoining figure. (Fig. 111.) A partial or a total gangrene of the tumor is brought about when the epithelial lobules increasing in size press upon

and obliterate the neighboring vessels. This is seen very frequently in tumors of the neck of the uterus.

Fig. 111.



Vertical cut of the rete mucosum at the location of a variolous pustule. *d*, *c*. Cavities caused by the vesicular state of the cells, and, at the same time, filled with pus corpuscles. *a*, *a*. Epithelial cells. *b*. Mother cells containing pus corpuscles. × 200.

Development.—Lobulated epithelioma has its origin in the epithelium of the skin and mucous membranes, or in neighboring embryonal tissue of new formation.

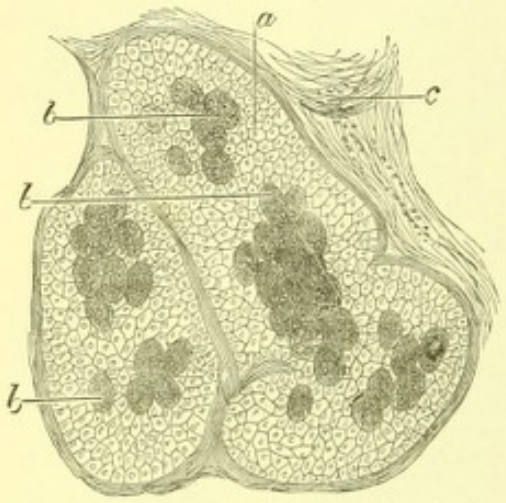
Rindfleisch entertains the opinion that the new epithelial tissue may also be developed by the apposition and metamorphosis of young and small cells in the connective tissue at the border of the epithelium. We admit the correctness of this opinion in many cases, and think that the fact is to be explained by a sort of *action de presence*, or epithelial infection. We recognize in this an occurrence analogous to that which is seen in embryonal tissue when, irrespective of its origin, it is transformed into bone in the neighborhood of bone, into muscle and nerve when it is in continuity with these tissues.

Lobulated epithelioma is usually developed by an extension of the rete mucosum at the bottom of the interpapillary projections. The epithelium penetrates the derm by a growth of new cells, formed very probably from adjoining embryonal cells. In fact, the tissue which is in connection with the newly-formed epthelial pegs is always an embryonal tissue. These epithelial offshoots bury themselves in the derm while presenting constrictions from point to point in such a manner as to afford a lobulated aspect. Epithelial shoots may also often arise from the lateral portions of old pegs. The epithelial masses may originate in the hair follicles. The epithelia of the sheath multiply, the hair soon falls out, the limiting membrane of the follicle disappears, the surrounding dermo-pap-

illary tissue is penetrated by epithelial buds, and the process is then the same as in the preceding case.

In the sebaceous glands, which normally present only one or two peripheral layers of pavement epithelium, while the centre of the acinus is filled with fat cells, we see at the beginning of epithelioma the peripheral pavement cells increase in number, and the limiting membrane of the gland disappear. In this way the sebaceous glands are transformed into lobules of epithelioma. (Fig. 112.) The phenomena which take place in the sudoriparous glands are more interesting. In the development of epithelioma from them, we observe at first an accumulation of epithelium in their interior; their central lumen is filled by the new formation, the whole sudoriparous tube is distended, and the limiting membrane soon disappears. These cylinders of epithelium invade the surrounding embryonal tissue by sending out epithelial buds; they anastomose and form a network. They consist of small pavement epithelium, and, by ulterior modifications in form, they become lobulated. Finally, the lobules may become isolated. [The growth of an epithelioma of the skin, according to the investigations of Koester, takes place through a proliferation of the endothelial lining of the lymphatics of the part.]

Fig. 112.



Proliferation of the epithelial cells of sebaceous glands in a case of epithelioma. *a*. Epithelial cells in process of multipication. *b*. Sebaceous cells filled with fat. *c*. Adjoining connective tissue. × 150.

Whatever may be its beginning, lobulated epithelioma may continue to increase in size by the growth of its own mass. Many histologists think that an epithelioma continues to grow without cessation. Where the progress of the tumor is very rapid, the neighboring parts show, in the papillæ, in the hair follicles, and in the glands, the same pathological phenomena as have been mentioned respecting the genesis of the tumor.

The muscles present at first the same modifications as those which characterize inflammation. The fasciculi are rarely intact; they usually show the results of compression and other interferences with their nutrition. They almost always present a fatty infiltration or a vitreous metamorphosis. The epithelioma spreads through the embryonal mass which has taken the place of the fasciculi, and which has sometimes extended among them a very great distance.

Osseous tissue presents analogous lesions. As in inflammation, we have the formation of embryonal marrow and the destruction of the osseous lamellæ. It is in the midst of this embryonal tissue that the epithelial formation takes place, and it is from this new tissue that the epithelial nodules grow.

Epithelioma may be generalized by the production of secondary nodules at a distance from the primary growth, in the nearest lymph glands,

at the angle of the jaw, in epithelioma of the lip, or in the internal viscera, as the lungs, the liver, the kidneys, etc. It should be stated, however, that secondary formations in the viscera are very rare, and their histological development has not yet been well studied.

Prognosis of Lobulated Epithelioma.—The gravity of lobulated epitheliomata varies greatly according to the structure of the tumor and its seat.

The most grave are those which possess a stroma entirely embryonal, and those in which at the periphery of the tumor the connective tissue presents the same embryonal condition. Such an appearance signifies that the epithelial mass is rapidly extending.

The parts of the body where the development of an epithelioma is most rapid are those which are most abundantly supplied with lymph vessels, those where the blood circulation is most active and which are most exposed to irritations. The lips, the tongue, the eyelids, the neck of the uterus, etc., often exhibit epitheliomata whose progress is as rapid and as promptly fatal as is that of the most malignant carcinomata. And yet their structure is identical with that of epitheliomata of the nose and of the cheek, which remain quiescent for ten, fifteen, and twenty years without inducing grave accidents or increasing in size. Epitheliomata of slow progress sometimes show a cicatrix at their centre while the tumor is spreading at the borders. After having remained stationary for a long time, they may suddenly commence a more rapid march. This fact shows that the malignancy of a tumor is not so closely related to its histological structure as to its seat and its mode of development.

2d Species.—Epithelioma with Concentric Cell-nests.

These tumors have a certain similarity to lobulated epitheliomata. They are lobulated and often encysted. Their cut surface is dry, opaque, whitish, slightly shining, like cholesterin.

There may be a few crystals of cholesterin in these tumors, as there are sometimes in the softened points of lobulated epitheliomata; but their shining aspect is usually due to desiccated epidermic lamellæ.

By scraping, we obtain small pearly grains, visible to the naked eye, having a regularly round outline, or such as would be presented by several lobules united by enveloping concentric layers. Under the microscope, these little granules very much resemble the spherules of the choroid plexus and of angiolithic sarcoma; but they contain no calcareous salts. When they are colored by carmine, one sees, in their exterior layer, united epidermic cells showing atrophic nuclei stained red. Besides these epidermic pearls, isolated cells of corneous epithelium may be observed. In some cases, spangles of cholesterine are also visible.

In thin sections a tissue characterized by lobules which resemble those of lobulated epithelioma is observed. But when these lobules are attentively examined, it is seen that the epidermic evolution is stationary. Instead of there being, at the periphery of the lobules, layers of cylindrical and stratified pavement epithelium, we observe only a single layer of flat cells, the nuclei of which are atrophied; the whole mass is seen to be

transformed into corneous cells. These pearls are sometimes completely separated from each other, sometimes united by very fine pedicles, which are also formed of corneous cells. Between the lobules thus constituted exists a dense connective tissue containing no vessels. (Foerster.) These tumors are so rare that we have seen only three examples.

Development.—Since they have acquired their full development and have been for a long time stationary at the time of their ablation, their histological development is not known. But their similarity of location and structure to lobulated epithelioma warrants a conjecture of a similar genesis.

Prognosis.—These tumors are very benign, but the reason of their benignancy is not understood.

3d Species.—Tubulated Epithelioma.

Tubulated epitheliomata have received different names. Billroth has described, under the name of *cylindroma*, tumors which appear to be related to them. Robin has classified lobulated and tubulated epithelioma and carcinoma, as well as many other kinds of tumors, under the *heteradœnic tumors*. Broca has named them *polyadenoma*.

The epitheliomata springing from the sudoriparous glands and well described by Verneuil, enter, in part, into this species.

Definition.—Tubulated epitheliomata may be defined as tumors composed of plugs or cylinders composed of pavement epithelium undergoing no epidermic evolution, anastomosing with one another and imbedded in a stroma, which consists of embryonal, mucous, or fibrous tissue.

The first stage of development of lobulated epitheliomata from sudoriparous glands gives exactly the same picture which tubulated epitheliomata present in their state of complete development. But it should not be inferred from this that tubulated epitheliomata are cancroids which have commenced in the sweat-glands and have been arrested in the first stage of development. They may appear in organs which have no sudoriparous glands, as in the uterus, even in parts which have no glands at all, as in the lymphatic glands.

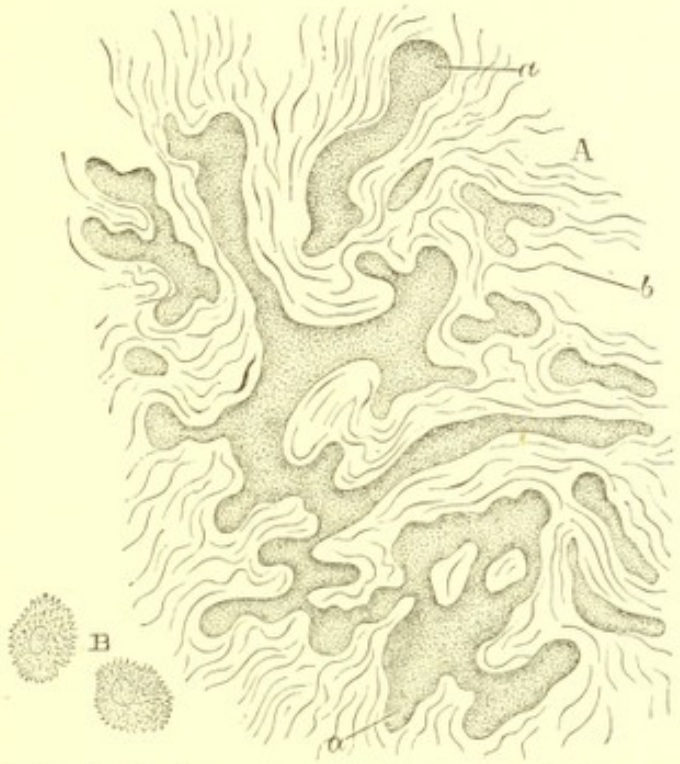
Description.—These tumors are regularly spherical, or ovoid. Upon a cut surface, they show a tissue resembling a gland or a sarcoma, but the naked eye is insufficient for a diagnosis. They yield no juice by pressure. By examining scrapings, we may acquire some idea of their structure. Segments of cylinders composed of pavement epithelium are thus obtained. These cylinders sometimes are branched; their bodies are regular and generally parallel; their extremities are limited by irregular sinuous edges, the result of breaking. The cells which constitute them are small, of equal size, and limited not by a sharp, but by a dentate border in such manner that with a slight enlargement and a poor objective, their boundaries cannot be easily distinguished. (Fig. 113, B.) In the scrapings, besides these cells, we also find fusiform cells, free nuclei, and the cells or perhaps the fasciculi of connective tissue.

But the various elements furnished by scraping are not characteristic of this species of epithelioma, for, at the commencement of the development of a carcinoma in a gland we may encounter in the scrapings frag-

ments of epithelium presenting the form of solid cylinders, which perhaps belong to an irritated gland of the region invaded.

Upon thin sections we see anastomosing cylinders of pavement epithelium, imbedded in a stroma of variable constitution. Because of the

Fig. 113.



A. Section of a tubulated epithelioma. *a*. Solid cylinders formed of pavement epithelium. *b*. Stroma channelled by tubes which lodge the cylinders. ×20. B. Epithelial cells from this same tumor, isolated and showing the dentations or spines by means of which they are united together by dovetailing. ×400.

spinous surface of the epithelia, the borders of the cells are not very distinct, unless the section is extremely thin. The stroma is usually fibrous and very dense; but sometimes it is mucous. In this mucous tissue, surrounded on every side by epithelial plugs, the plasmatic cells (connective tissue corpuscles) are sometimes degenerated and destroyed; a little cavity is then formed and filled with mucous fluid. It might be imagined that these cystic cavities come from a degeneration of the epithelium, while, on the contrary, they result from an alteration of the stroma. Rindfleisch has given to similar tumors the name of *cystic epitheliomata*.

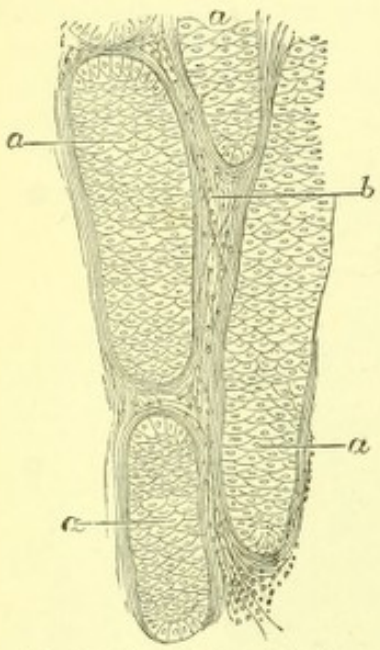
The pavement cells may undergo *colloid* degeneration.

These tumors may also show in certain points an epithelial evolution, there may be more voluminous lobules, with corneous cells at their centre, a disposition which establishes a relation between them and the previously described tubulated epithelioma.

Seat and Development.—When tubulated epitheliomata are seated in the skin, their development is from the sudoriferous glands. This origin was observed a long time ago by Verneuil. Because of their

development in the deep layers of the skin, these tumors ulcerate more slowly than the preceding species. Among the numerous tumors of the mammæ formerly described under the name of carcinoma, some correspond exactly to the description of tubulated epitheloma.

Fig. 114.



Section of a tubular epithelioma. *a*. Oblique sections of cylinders of epithelial cells. *b*. Fibrous stroma.

Many of these tumors after having attained a certain degree of development remain stationary. Sometimes they continue to increase in size. In the latter case the epithelial cylinders terminate in culs-de-sac in the midst of an embryonal tissue. Their extension is effected by an epithelial metamorphosis and apposition of the cells in the adjoining connective tissue.

Prognosis.—The gravity of these tumors is less than that of lobulated epitheliomata, but they often return after removal. The lymph glands are sometimes invaded by secondary formations of identical structure. When they are located at the neck of the uterus, their prognosis is as grave as that of other forms of carcinomatous or epithelial tumors in this region.

With tubulated epitheliomata we would class certain very rare tumors described by Robin, Foerster, etc., which present a very peculiar arrangement. They are constituted by epithelial plugs imbedded in the midst of fibrous tissue, and showing at their centre refracting oviform bodies connected together by prolongations. In the interior of these bodies stellate figures are sometimes seen. Foerster called these tumors epitheliomata; Robin classified them with his heteradænic tumors. Ordonez regarded the large oviform bodies as sporangia, sometimes containing spores similar to those of mushrooms.

4th Species.—Cylindrical-celled Epithelioma.

Discovered by Bidder, this particular kind of epithelioma has been described by Foerster, by Virchow, and we ourselves have analyzed and published a large number of cases. These tumors were formerly entirely confounded with epitheloid and colloid carcinoma.

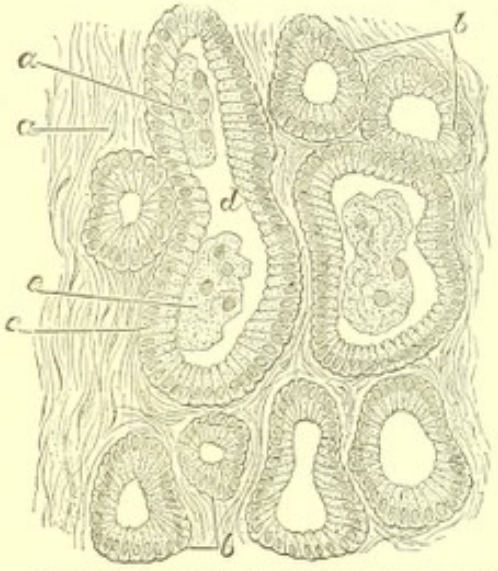
They are characterized by irregular or tubular cavities paved with one or more layers of cylindrical cells, and separated by a stroma which may be fibrous, embryonal, or mucous. Their cylindrical cells are similar to those which cover certain mucous or glandular cavities, and are always implanted perpendicularly to the wall. (Fig. 115.)

The aspect these tumors present to the naked eye is variable. They may appear as round masses or, in the intestine and stomach, as nummular prominences of varying number and diameter; they are in the latter case usually ulcerated at their centre. When, as is often the case, they are reproduced in the liver and other organs, they have altogether the

same naked eye appearance as encephaloid carcinomata. Generally they are very rich in a milky juice, and soft, but this softness and juice are probably in great part due to cadaveric alteration. Post-mortem softening being less rapid in winter than in summer, the quantity of juice varies accordingly.

The fluid obtained by scraping is decidedly grumous. The elements contained in the juice are cylindrical cells. They often have a double contoured border at their free extremity, and some present at this end a vesicular dilatation. They are usually elongated, but some may be polygonal and more or less irregular. They possess one or more ovoid nuclei, containing one or more brilliant nucleoli. Often in the juice several cylindrical cells are found united at the sides, and showing their double contoured free border, an object in itself sufficiently characteristic to justify one in affirming the presence of a cylindrical epithelium.

Fig. 115.



Cylindrical celled epithelioma from the large intestine. × 170. *a*. Fibrous stroma. *b*. Small cystic cavities lined with cylindrical epithelium. *c*. Cystic cavity constituted by the union of two adjoining cavities. At *d* there is a constriction, a trace of the original intermediate septum. In the interior of some cavities is an amorphous mass containing cells.

The histological nature of the tumor must be learned by examination of thin sections. In the latter one will see tubular or irregular cavities paved with cylindrical epithelium. These tubes and spaces, which sometimes are sinuous and present papillæ at their surface, appear to have no connection with the neighboring glands. The latter may, however, become hypertrophied, and form a very distinct layer upon the surface of the tumor. The cells are directly planted upon the stroma, without the interposition of any basement membrane. The free surface of the tumor is often the seat of papillæ, which are also covered by cylindrical epithelium.

If the tumor has completed its development, the stroma is generally fibrous. But it is often embryonal, and in certain cases it is entirely mucous, as in myxoma. The stroma always carries vessels, which are abundant and, if the stroma is embryonal, analogous to those of sarcoma. Usually small in amount, the stroma may, on the contrary, predominate and constitute the bulk of the tumor. The vessels may sometimes undergo dilatations which are frequent in the mucous form.

A very important and very common variety is characterized by a colloid transformation of the epithelial cells. The latter become transparent vesicles, and fall into the lumen of the cavity. Cylindrical cells are then observed to limit a cavity filled with colloid matter and the débris of cells. At other times the cells which line the wall are themselves completely degenerated, when the cavity no longer possesses the character

of an epithelioma with cylindrical cells. Fatty degeneration of the cells is habitually associated with the colloid metamorphosis.

These epitheliomata almost invariably ulcerate when they are seated upon the mucous cavities, especially in the stomach where the digestive and corroding action of the gastric juice is active. At the surface of tumors located in the stomach, we often find coagula of black blood in the vessels; this coagulation is due to the action of the gastric juice.

DEVELOPMENT.—It is probable that these epitheliomata are developed from the glands by a process analogous to that which has been studied in pavement epithelioma, but up to the present all the phases have not been thoroughly followed.

SEAT.—Cylindrical celled epitheliomata, with the exception of those of the ovary, have never been observed as a primary growth anywhere but upon mucous membranes covered with similar epithelium in the normal state.

In the ovaries we have seen non-cystic tumors resembling carcinoma to the naked eye, which were in reality epitheliomata with cylindrical cells.

Certain polyps of the nasal fossæ correspond in minute structure to this kind of epithelioma.

Secondary formations identical in structure with the primary tumors are met with, especially in the liver. There have been published observations of secondary nodules in the lungs and bones. As they are usually located in the internal organs, it is generally impossible to differentiate them, during life, from the various forms of carcinoma whose fatal progress and malignancy they, moreover, simulate.

DIAGNOSIS.—Their anatomical diagnosis is usually very easy. They should be carefully differentiated from medullary carcinoma when they are soft, and from colloid carcinoma when they have undergone the same degeneration. In those secondary formations in the liver which have rapidly progressed, the centre of the tumor is softened, the epithelial cells are dissociated and loaded with fatty granules; they have lost their characteristic form, and they entirely fill the alveoli. The forceps breaks them easily, and reveals an alveolar stroma similar to that of carcinoma. This similarity is such that, if one is not guided by the younger peripheral portions, it will be impossible to make a diagnosis. In order to distinguish a colloid epithelioma with cylindrical cells from a colloid carcinoma, it is necessary to study with the greatest care the recent portions which have not yet assumed the colloid aspect. We will speak of the differential diagnosis between these tumors and adenomata and papillomata, *à propos* of the latter.

Cylindroma.

[Rindfleisch gives the following account of this peculiar and rare form of tumor. Henle called the morbid growth a siphonoma, Billroth a cylindroma, Meckel a tubular cartilaginous tumor, Friedreich a tubular sarcoma, Foerster and the most recent examiners regarded it as a mucous cancroid. Notwithstanding the widely divergent opinions concerning the

nature of the tumor, it is probable that the different authors have reference to the same kind of new formation. The development uniformly in the face, especially in the cavity of the orbit and its surroundings, seems to warrant this assumption, while the differences of opinion concerning the minute structure of the growth may be explained by the circumstance that former investigators occupied themselves, by preference, with the most peculiar rather than with the most essential characteristics of the neoplasm.

The most peculiar products are certain *hyaline masses*, which may be isolated by teasing. Their peculiar outline is striking. Besides perfect spheres, cylinders are met with as also are club-shaped and cactus-like figures. There is often an appearance as if these hyaline bodies branched in various directions from a common point of union. Regarding the nature and development of these bodies, the opinion of Billroth that they should be regarded as perivascular mucous tissue-sheaths or their fragments, was the most widely entertained until Koester, after carefully studying the structure and growth of the whole tumor, advanced the hypothesis that the hyaline spheres and cylinders are the product of a secondary hyaline metamorphosis, which the cell trabeculæ of a cancroid of the lymph vessels undergo. According to the latter author, we have in all these cases to deal with a cancer-like proliferation of the cells in the lymphatic network of the part affected. The endothelia of the lymph vessels multiply by division and plug up these vessels. Hyaline degeneration begins first in the axes of these cellular cylinders. The hyaline matter thus formed may collect together into spherical or cylindrical masses. This hyaline degeneration beginning in the axis of the vessels may end in a total destruction of the endothelial covering (the peripheral layers of cells), when a relatively large hyaline cylinder appears imbedded in the connective-tissue stroma.

The condition of the bloodvessels in the axes of the hyaline cylinders which Rindfleisch saw most distinctly in a cylindroma of the brain, is explained by Koester by the well-known ensheathing of the bloodvessels within lymph sinuses.

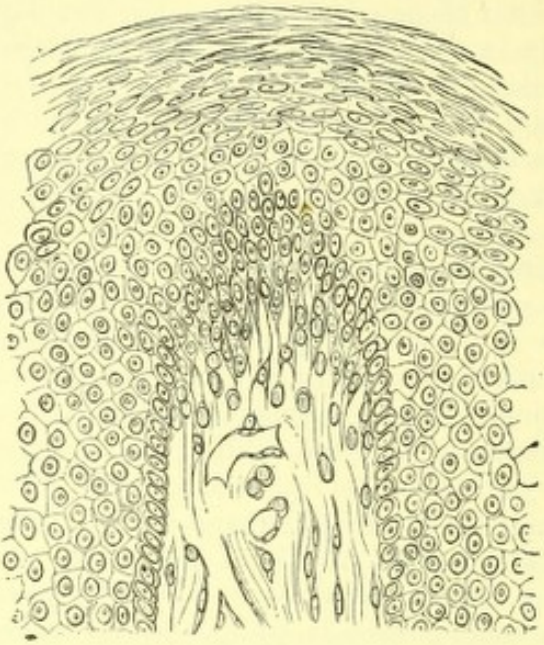
Cylindroma is a tumor which readily recurs, rarely exhibits metastases, and should therefore be classed near the cancers.]

2D CLASS.—Papilloma.

These tumors are not considered by all pathologists as worthy of constituting a separate group. For us, the definition of papilloma should correspond with that of the papillæ themselves. It is known that the papillæ are constituted by connective tissue serving as a support to vessels which terminate there in a network of capillaries or in a single capillary loop, and that they are paved by an epithelial covering. These normal excrescences upon the skin and certain mucous membranes, are, in some cases, covered by stratified and corneous layers of permanent epithelium—in others, are paved by a mucous epithelium.

These two normal forms afford us types of two *species* of papillomata —*corneous papilloma* and *mucous papilloma*.

Fig. 116.



Papilloma: showing a single enlarged papilla, covered by laminated epithelium. (*Rindfleisch.*)

For a tumor to be called a papilloma it is necessary that the papillæ shall be formed of connective tissue, and that the epithelial layers which cover them shall be disposed as upon normal papillæ; moreover, that the tissue which constitutes the base of the papillæ shall not form a portion of one of the special tumors previously described. Care must be taken not to confound papillomata with sarcomata, fibromata, carcinomata, epitheliomata, etc., which present at their surface papillary prominences, and which consequently should simply receive the qualification *papillary*.

1ST SPECIES: CORNEOUS PAPILLOMATA.—They constitute a numerous variety of tumors. Most authors include horns, warts, and corns.

Corns seated upon the toes are caused by repeated pressure or irritations. They commence by a hypertrophy of the papillæ; the corneous layers of the epiderm soon exert pressure upon these papillæ so as to depress and bury them like a nail in the dermis. The latter atrophies, the adipose tissue disappears at the point of pressure, and sometimes even there is formed at this point a mucous bursa in the subcutaneous cellular tissue.

In *warts*, the papillæ hypertrophy, vegetate, and give place to secondary papillæ; the covering, composed of cells identical with those of the epidermis, envelops the whole papillary mass in a common, smooth layer; or a certain number of the papillæ are separated by an epidermal covering common to each group. The connective tissue, which is permeated by bloodvessels, is less abundant as we proceed from the base of the tumor to the superficial secondary papillæ.

Horns may be considered as warts, of which the epidermal cells are intimately united in the same manner as in the nails. They are observed upon different regions of the skin, but especially upon the face; they are also encountered in dermoid cysts. The corneous epidermic cells are not desquamated, but they are preserved in many superimposed

layers. There thus result hard, more or less long appendages, formed of imbricated layers of corneous epithelium.

Certain congenital *nævi* also constitute *corneous papillomata*. They are formed of papillæ simple or compound. These congenital tumors are sometimes very deeply pigmented.

2D SPECIES: MUCOUS PAPILLOMA.—In these papillomata the papillæ are simple or compound. Villous papillomata, in which the papillæ resemble by their length and tenuity intestinal villi, are not infrequently met with.

These tumors are usually simply composed of papillæ; but tumors often exist where the papillæ are combined with cysts or with hypertrophies or new formations of glands. At present we are only concerned with true papillomata, but shall soon be occupied with tumors complicated by adenoma and papillary cysts.

The papillæ present for study two parts—the papillary body and the epithelial covering. The papillary body has the form of buds, more or less voluminous, giving origin to a greater or lesser number of secondary and tertiary papillæ. Its variable form is dependent upon a new formation of vascular loops. It consists of connective tissue in which run the vessels which terminate in loops at the extremity of the papillæ. The quantity of connective tissue is sometimes so slight that the epithelial covering seems in some cases to rest directly upon the vessels. In papillomata of recent and rapid development, for example, in certain cauliflower fungi of the genital organs, the body of the papillæ is formed of embryonal connective tissue.

The vessels of papilloma are arteries, capillaries, and veins, which possess their usual structure. The capillaries are often dilated regularly or into ampullæ, and their rupture sometimes gives place to hemorrhages which escape outward, or remain imprisoned in the papillary body and become transformed into pigment. The vessels of the papillæ may present buds and undergo calcareous degeneration.

The villous papillæ are generally simple, and they may attain a considerable length, especially when they are laterally compressed against each other.

The epithelial covering of the papillæ is different according as it is formed of pavement or cylindrical cells. In the first case, a great number of layers of cells undergo an evolution identical with that of the Malpighian layer of the skin or of the buccal mucous membrane. These cells are dovetailed into each other, and the superficial layers are flattened. Papillomata often possess a covering of pavement cells, while the mucous membrane whence they spring is covered with cylindrical epithelium. These pavement cells are frequently vesicular and in a state of colloid degeneration. When the papilla is invested with cylindrical epithelium, there is only a single layer.

DEVELOPMENT.—Mucous papillomata generally spring from the villi or papillæ of the mucous membrane, but they may form where there are no papillæ—for example, in the ventricles of the larynx. The minute phenomena of these hypertrophies and new formations have not yet been followed very closely, but the analogy of their structure with that of inflammatory granulations supports the supposition that their mode of formation is similar.

Moreover, inflammation may be the cause of the development of papilloma, as is often the case around callous ulcers, etc. We cannot, however, very closely assimilate papillomata with granulations, for the latter tend to heal by organization, while papillomata tend to persist indefinitely as tumors.

SEAT.—We find papillomata seated upon nearly all parts of the cutaneous and mucous surface. In the larynx they are generally combined with adenoma.

Often upon the external genital organs, so-called cauliflower papillomata develop. They may be very small or may reach a considerable size. We are obliged to extirpate them, and yet it often happens that the irritation attendant upon the operation causes them to return—an occurrence common to many forms of tumors.

Papillomata are observed upon the serous surfaces, and especially upon articular membranes. We have seen papillary new formations arising from the walls of the ventricles of the brain.

DIAGNOSIS.—The diagnosis of papilloma, very easy in certain typical cases, is generally very difficult, and must be based upon a very careful examination.

For the recognition of a papilloma we must find at the base of the papillæ neither alveoli, nor gland ducts, nor islands of epithelium. The cells situated between the papillæ must not be taken for lobules of epithelioma; this distinction is easy to make, for the latter penetrate deeply into the dermis or submucous tissue, whilst the most profound of the interpapillary cells of papilloma are upon the same level as in the normal papillæ. Diagnosis is easy only when examining good preparations.

PROGNOSIS.—The prognosis, generally very benign, can become grave only by reason of the location of the tumor in parts where it may interfere with vital functions.

Can papilloma become transformed into epithelioma? We do not consider it impossible, but, up to the present, we know of no observation which proves it.

3D CLASS.—**Adenoma.**

These tumors correspond exactly with the glandular hypertrophies described by Lebert. They have been confounded with many other tumors, under the names adenoid, polyadenoid, heteradenoid tumors, etc. For us, adenomata are tumors which offer the same structure as glands.

Normal glands are divided into racemose and tubular. We also have two species of adenoma: 1*st. Acinous adenoma;* 2*d. Tubular adenoma*, containing cylindrical epithelium.

1ST SPECIES: ACINOUS ADENOMATA.—In the mamma, Cruveilhier recognized them as *fibrous bodies of the breast.* Velpeau, before their structure was understood, named them fibrous tumors, afterwards *adenoid tumors;* Lebert, *hypertrophies of the mammæ;* Broca classified all these spical tumors of the preceding authors among adenomata.

We have very often examined tumors of the breast which have been

diagnosed as adenoid by Velpeau, and we have found them to be fibromata, sarcomata, myxomata, or true adenomata, the latter very infrequently.

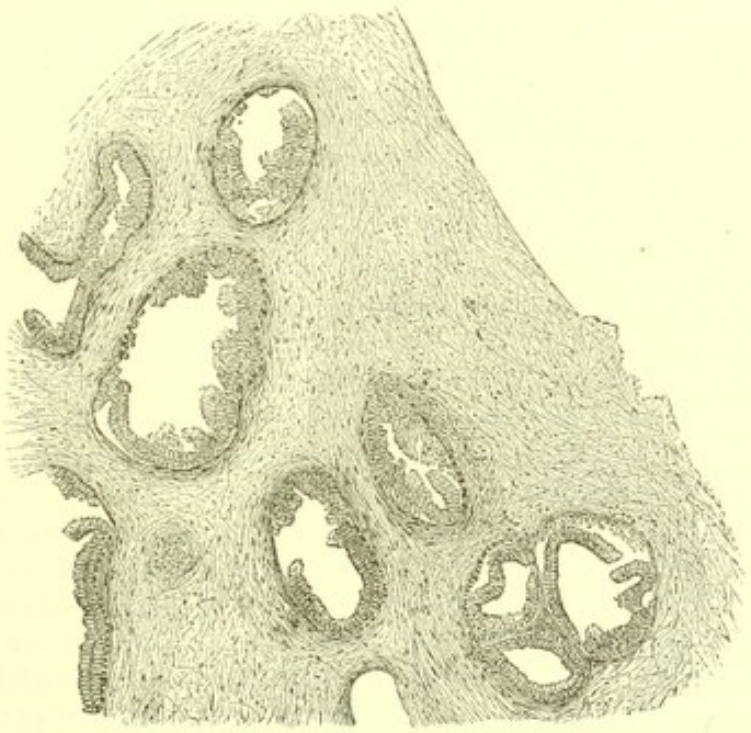
Fig. 117.



Adenoma of the mamma. ×300. (*Rindfleisch.*)

Adenomata of the breast are small and are usually blended with the mass of the mamma, whilst tumors which are sharply circumscribed and

Fig. 118.



Adeno-fibroma of mamma. Showing new growth of gland structure and of connective tissue. ×100; reduced ½. (*Green.*)

isolated are generally fibromata, myxomata, or sarcomata. Their size varies from that of a hazel-nut to that of a walnut. They do not inclose cysts, the presence of the latter, so far from characterizing adenoma, eliminates them entirely.

They are composed of acini disposed near together, separated only by a small quantity of fibrous tissue; the acini are limited by a very distinct membrane, which is lined by a very regular pavement epithelium.

The growth of these tumors is very slow, and they are never generalized. The possibility of their transformation into carcinoma has been mooted. But without observations the question cannot be positively answered.

Other acinous glands may be the SEAT of acinous adenoma. Lebert reported such tumors of the parotid gland, as well as an analogous hypertrophy of the lachrymal gland.

The arches of the palate and the pharynx may be the seat of tumors caused by a considerable hypertrophy of the acinous glands of the regions either circumscribed and salient under the form of tumors, or diffuse as a uniform thickening of the mucous membrane. The sole difference between such tumors and the normal parts is that the glands here are hypertrophied.

In the DIAGNOSIS of acinous adenoma, they should be separated from all new products which, by developing in the neighborhood of glands, determine a proliferation of the epithelium of their acini.

In the tumors which we have described up to the present, we have seen that every new formation affecting the stroma of a gland is, at a certain moment, accompanied by a multiplication of the epithelium of the culs-de-sac and of the excretory ducts, followed by a dilatation of these cavities and by various ulterior modifications of their contents. For example, every enchondroma of the parotid determines a proliferation of the glandular epithelium, and yet no one thinks of ranging these tumors with adenoma.

If the glands hypertrophy at the commencement and during the period of formation of tumors, they also undergo varied modifications, such as fatty or colloid degeneration of the epithelium, alterations which end sometimes in cysts or in hypertrophy of the acini.

Moreover, when a growth containing very many hypertrophied glandular acini, a sarcoma of the breast for instance, returns after removal, the new tumor no longer contains glands—an evident proof that there has been no adenoma, and that the hypertrophy of the glands in the primary tumor was accessory. If the primary tumor had been an adenoma, it would have returned with its primitive structure.

It is by a full knowledge of the structure of other growths with which they may be confounded, and by an attentive examination of each piece that we shall succeed in recognizing true adenomata. The latter are to be diagnosed by the condition of the interacinous tissue and the nature and disposition of the new acini which are entirely like those of the affected gland. We should add, moreover, that no tumor is more rare than this species of true adenoma.

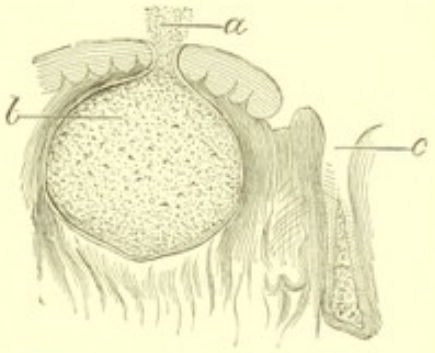
2D SPECIES: TUBULAR ADENOMATA WITH CYLINDRICAL CELLS.—They are very common in the mucous membranes which possess tubular glands. The tumor is soft, generally slightly translucid and somewhat vascular. Its surface has the same color as the mucous membrane. Upon section, it yields no milky juice, but rather a mucous fluid, in which the micro-

scope reveals cylindrical cells, isolated or united in bands, or round or cylindrical cells presenting a transparent globule at their base.

Thin sections from hardened pieces present different aspects according as the gland tubes are seen longitudinally or transversely. In the longitudinal sections, the gland tubes often show lateral buds or genuine bifurcations, terminating at the one end in the mucous membrane, where they open; at the other, in culs-de-sac situated at different depths. These tubes are generally so closely packed against one another that there seems to be no fibrous stroma. The epithelium which lines the tubes is very distinctly cylindrical; the cells are two or three times as long as in the normal state; it is especially at the level of the dilatation of the glands that one observes the colloid drops which we have mentioned. The tubes cut transversely appear as circles, with a central lumen and a border of very regular cylindrical cells.

Dilatation of the tubes constitutes the first phase of the formation of the cysts filled with colloid substance, which are common in this species of tumors. A nearly physiological type of these cysts exists in the "eggs of Naboth," resulting from modifications of the tubular glands in the mucous membrane of the uterus. (Fig. 119.)

Fig. 119.



Egg of Naboth of the vaginal mucous membrane of the cervix uteri. *b*. Spherical dilation of a gland, the orifice opening at *a*. *c*. Tubular gland. ×20.

We not unfrequently find hypertrophies of the gastro-intestinal mucous glands. In the stomach, the hypertrophied glands may become transformed into cysts of retention similar to the eggs of Naboth. The mucous membrane may be speckled irregularly or in limited spots by vesicles more or less large, which occupy the place of a tubular gland, or one of its portions. The hypertrophied glands and the cystic vesicles form a litttle tumor which often is pedunculated, thus constituting a polyp. In the uterus, these mucous polypi may at length project into the vagina, even as far as the vulvæ. In the uterus, as in the stomach, these hypertrophies of glands often unite with papillary new formations to form compound tumors, villous at their surface, cystic and glandular in the rest of their mass.

Analogous tumors grow in the rectum and large intestine. The stroma of the tumor is fibrous in the fully developed portions; it is embryonal in the points where the gland is budding. If such a tumor of the rectum protrudes from the anus, the investing cylindrical cells become transformed into squamous epithelia, which may even become corneous at the surface. In the projecting parts in contact with the air, the glandular depressions are filled by stratified pavement cells; the interglandular projections then represent papillæ, so that one sees a layer of tubular glands become transformed into a layer of papillæ covered by a squamous epithelium.

In the uterus, besides the vesicular transformation of the glands which we have indicated, we observe globular productions principally

characterized by a hypertrophy of the glands of the neck. These tumors are small, and inclosed in the cavity of the neck, or they pass through the os into the vagina. These growths, described under the name of mucous or utero-vesicular polypi (Huguier), either present the appearance of a red mass, soft, speckled with transparent vesicles whose size varies from the size of a millet seed to that of a grape seed, or they show the form of flattened granulations. The last form show at their surfaces prominences and depressions, which recall the arbor vitæ. In their structure they present a striking analogy with the mucous membrane of the cervix, only all the elements have become much hypertrophied.

The stroma of these tumors is habitually formed of a fibrous tissue impregnated with juice, and permeated by numerous dilated bloodvessels. It occasionally contains smooth muscular elements. In this case Virchow thinks that the tumor should be ranged among the myomata.

These uterine polypi, which are covered with cylindrical epithelium in the cervix, present in the vagina a pavement epithelium; when they project at the exterior, a rare occurrence, the epithelial covering is corneous. But these mutations in the form of the superficial epithelium does not extend to the cells which line the ducts of the tubular glands, nor even to the depressions, analogous to the crypts and folds of the arbor vitæ, which these polyps sometimes show.

Among nasal polypi there are those which are so like the cystic adenoma of the uterus, that it is impossible to distinguish differences in structure. Cases are also occasionally encountered in which the glands, lined with cylindrical epithelium and dilated into cysts, establish a perfect similitude with the previously described uterine tumors.

Nasal polypi, however, are most commonly constituted by mucous tissue, when they belong among the myxomata.

DIAGNOSIS.—The only tumors with which these adenomata with cylindrical cells may be confounded are cylindrical-celled epitheliomata. In the great majority of cases the diagnosis is very easy: the regularity of the glands, their opening upon the mucous surface, the presence of cysts regularly limited, establish the diagnosis with certainty. Epitheliomata with cylindrical cells never present small regular cysts; besides, they show aberrations in the form of the tubes and their cells, which separate them from the normal type. Moreover, they invade the profound tissues, while adenomata, always superficial, have the tendency to assume the form of polypi.

While the PROGNOSIS of epithelioma with cylindrical cells is very grave, that of adenoma is very benign. Adenomata are never generalized, but they return after they have been incompletely removed. [According to some authors adenomata are occasionally subject to metastases.]

4TH CLASS.—Cysts.

For us cysts are glandular aberrations which, up to a certain point, have their structural analogies in glands composed of closed vesicles, as the ovary and the thyroid body of the adult.

Cysts consist of a connective tissue membrane, an epithelial lining, and

contents which are fluid, colloid, or sebaceous. They should be carefully distinguished from mucous degenerations accompanied by the formation of cavities at the centres of the divers tumors which we have already studied; in these cases, really, we find neither a proper membrane nor an epithelial lining.

The process of the formation of a cyst is not so simple as may be imagined. By tying the duct of a gland, far from obtaining a cystic dilatation, we may determine its atrophy.

The structure, the mode of development, and the varieties of cysts are so different in their different species that it is impossible to give a general description of them. Hence we pass at once to their varieties of nature and of seat.

We would divide them at first according to the nature of their contents, into two groups:—

1st. *Sebaceous cysts.*

2d. *Mucous, serous, and colloid cysts.*

1ST. SEBACEOUS CYSTS.—*Sebaceous cysts* are *simple* or *dermoid*. The first consists in an accumulation of epidermal cells or of the product of secretion in a hair follicle or in a glandular cul-de-sac.

In the sebaceous cysts we find:—

a. Those little whitish grains projecting upon the skin of the face, especially at the external canthus of the eyelids, which have been called *millet grains* (milium palpebrare). They contain an accumulation of the epidermis which forms in the hair follicles.

The orifice of the hair follicle is obstructed and invisible; by incising the little granule we cause the escape of an epidermic spherule. These little grains are true cysts of retention. They are extremely common, in some persons advanced in years they are confluent upon the eyelids, and they form there an uninterrupted whitish layer, like plaster.

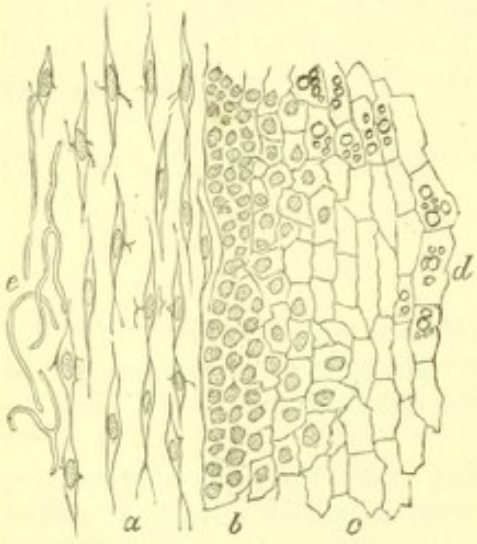
b. *Comedones*, little elevations formed by the retention of sebum in the hair follicles: the orifice is pervious to such a degree that by pressure the contents can be squeezed out. In this sebaceous material we often find *Demodex folliculorum*. Sometimes an accumulation of sebum occasions an inflammation of the follicle: pus globules are then mixed with the epithelial cells and oil drops, which form the sebum. It is thus that a pustule of acne forms.

c. *Wens*, so frequent among hairy persons, also consist of an accumulation of masses of epidermis and sebum in the hair follicles. They attain a much greater size than the preceding; even as great as that of a hazel-nut or a pigeon's egg, and they are habitually flattened and lenticular.

According as their contents are fluid or solid, they are called *melicerous* or *steatomatous wens*. The melicerous substance is a fluid-like honey, constituted by a great quantity of free fat and isolated epidermal cells. The more solid contents of steatomatous wens contain the same elements, but there are more epidermal cells and less free fat. In them the fat undergoes the same transformations; no longer subjected to nutritive changes it gives rise to crystals of stearic acid, margarin, and cholesterin, which are constantly met with in greater or lesser quantity. Often

upon the surface of a wen is seen a dark depressed point, which is the orifice of a hair follicle. The cyst is located in the subcutaneous tissue. The derm which covers it is thinned at the surface; its papillæ are flattened, or they have even disappeared, while the surface is consequently smooth, and the sebaceous glands are also atrophied. Concerning the structure of the cyst itself, there is presented for consideration first its fibrous wall, which is formed by connective tissue with flattened cells (fig. 120, *a*), and parallel layers of a fundamental substance—a tissue identical with that of the inner tunic of arteries and that of fibroma—with flat cells (see p. 92). This disposition is caused by the pressure exerted upon the walls by the incessant accumulation of elements contained in the cyst. In this membrane there are no elastic fibres, but the latter exist in the neighboring tissue. Fatty, atheromatous, and calcareous degenerations are very common in this connective tissue wall, which completes the previously mentioned analogy of this membrane with the internal tunic of the arteries and with the corresponding species of fibroma.

Fig. 120.



A vertical section of the wall of the sebaceous cyst. *a*. Fibrous wall of cyst composed of flat connective tissue cells. *e*. Elastic fibres. *b*. Epithelial cells. *c*. Corneous cells. *d*. Sebaceous cells. × 300.

At the internal face of this membrane exists a stratified pavement epithelium, which experiences an evolution similar to that which is observed in sebaceous glands. The cells in contact with the wall possess large nuclei surrounded by a small quantity of protoplasm (*b*, fig. 120); and it is probable that it is here that the new cells incessantly form. In certain cases the fatty evolution is very slow, and the layer of corneous cells, in which the nucleus has completely disappeared, is thick, and often detaches itself from the wall of the cyst, and forms a shell consisting of whitish, slightly translucent, almost cartilaginiform tissue; it is at the interior of this shell that the melicerous or steatomatous contents are found.

d. Dermoid cysts, which, like the preceding, contain a steatomatous matter, are developed outside of glands, and are characterized by a wall having a structure analogous to that of the skin. With Lebert, we may recognize the three following varieties:—

1st. The first variety of dermoid cysts is that which very strongly resembles wens; the sole difference relates to their seat. These cysts develop in regions where sebaceous glands have naturally no existence, and they never present orifices.

2d. In a second variety, the cystic membrane, together with papillæ analogous to those of the derm, possesses sebaceous glands and hair follicles. These hair follicles give origin to real hair. In the interior of these cysts we find matted hair in the midst of sebaceous matter. The

papillæ of the cyst wall may give rise to warts, condyloma, and horns. The latter developing from the deepest portion of the cyst wall, and increasing in size, may form a projection beyond of the cyst wall in such a manner that we have to do with a horn surrounded at its base by a calyx formed by the cyst.

3d. The third variety of dermoid cyst of Lebert is more complicated. Many different tissues—and even organs, for example, teeth—appear in the wall of the cyst, whose contents are the same as in the other varieties, viz., sebum, etc. The teeth are found in a dental follicle surrounded by fibrous tissue, or they are implanted upon bone of varied structure. Their disposition is very irregular; their development, according to Kohlrausch, does not differ from physiological growth. These teeth—canine, molars, and incisors—have the characters of the first and second dentition. There may be one or more teeth; in certain cases, their number is such that Reil and Autenrieth once counted as many as 300. This observation is ruinous to the hypothesis of many authors, that one of these cysts indicates a fœtal inclusion at this spot. For, if there had been a fœtal inclusion, it is incomprehensible why the teeth would be so numerous. Instead of a bony plate serving as an insertion for the teeth, sometimes only an osseous border representing an alveolus is encountered.

Teeth and osseous tissue in the form of plates are the commonest occurrences in the wall of these cysts; but there may be also long bones, cartilage irregularly disposed, masses of striated muscle, and even medullary nerves. We have seen cysts of this kind where this nerve tissue, characterized by small double-contoured nerves and nerve cells, was contained in a fibrous pouch adjoining osseous portions. Nothing is more irregular than the disposition and relative quantity of these diverse tissues. In places, the wall of these cysts presents plaques which have the same structure as the skin, possessing papillæ, sebaceous and sudoriparous glands, hair follicles, and hair; at other points the wall is thin, smooth, fibrous—analogous to that of cysts of the first variety. The volume of these tumors is variable between that of an egg and that of an adult heart. Their mode of development is not understood. It is only known that they are congenital. The most frequent seat of dermoid cysts is the ovary and the testicle, but they may be met with also in all the other organs.

2d. Serous, Mucous, and Colloid Cysts.—The second group of cysts is characterized by their contents, which are serous, mucus, and colloid.

They may develop: *a*, in natural serous cavities—for example, tendinous or periarticular bursæ; *b*, in glandular cavities; *c*, they may arise anywhere.

a. Serous cavities may be considered as spaces in the midst of the connective tissue which surrounds organs; they are lined with endothelium, which may desquamate, be destroyed, and reformed again. We should not be surprised, therefore, to see regular or trabeculated accidental cavities, lined throughout by endothelium, develop at any point in loose connective tissue.

Physiologically, the membrane of serous cavities secretes a serous fluid which is taken up again by the vessels with great facility. This

facility of resorption is demonstrated by the rapid disappearance of injected fluids. But, if the serous membrane is inflamed, the resorption of an injected fluid is impossible (Rindfleisch), and the irritation of the serous membrane determines an abundant secretion. Even a slight irritation is sufficient then to transform a serous bursa into a cystic cavity. Such a transformation of a subcutaneous serous bursa is known as a *hygroma*, and may be called a tumor because of its tendency to persist indefinitely.

The cystic membrane of a hygroma is generally thick, and formed of a dense connective tissue of cartilaginous appearance. According to Virchow, it should always be lined by a pavement epithelium. The fluid contents are transparent or slightly clouded by detached cells; they sometimes contain concretions very irregular in form (rice grains), consisting of concentric layers without a special histological structure and of which the origin is diversely understood. Velpeau considers them as fibrin; Virchow thinks that they arise by a budding from the cyst wall. The *sheaths of tendons* may present the greatest similarity of structure with subcutaneous serous bursæ. They possess, according to Gosselin, little depressions of the surface, like the finger of a glove, which penetrate into the surrounding connective tissue. An obliteration of the neck of these depressions may give rise to little cysts. The name of *ganglions* has been given to them, and they are observed especially at the wrist and the back of the foot.

Hydroceles of the tunica vaginalis and hydropsies of the articular serous membrane may be classed with the preceding cysts; they appear to have an analogous origin.

These occurrences serve really as intermediate links between the products of chronic inflammation and tumors.

b. Cysts developed from glands are very numerous. The *thyroid body* is almost a physiological location for them (see *Thyroid Body*).

The *Graafian follicles of the ovary* are often filled, even in new-born children, and before menstruation, by a large quantity of fluid; this constitutes hydropsy of the follicles. It is probable that a large number of ovarian cysts have such an origin (Foerster).

The *mucous glands of the lips* become transformed into little transparent cysts of retention. The buccal mucous membrane may be lifted up by voluminous cysts resulting from the distension of the ducts of Wharton and Rivinus; the latter swellings are designated under the name of *ranula*.

In the *stomach*, the *intestine*, and the *trachea* little mucous cysts, either isolated or agglomerated, often result from distension of the tubular or acinous glands.

The *liver* sometimes contains cysts inclosing bile or coloring matter, or simply a serous fluid, from distension of the biliary ducts.

The *kidney* is very frequently the seat of variously produced cysts: congenital cysts, sometimes very voluminous and very numerous, due to atresia of the papillæ, according to Virchow, who has found urates in the fluid of these cysts as we ourselves have also found it in cysts of the same kind; serous cysts, observed in the adult, some following Bright's disease, others due to interstitial nephritis, and sometimes containing a

serous fluid, at other times a colloid concretion. They are developed by distension of the uriniferous tubes or of the capsules of the glomeruli.

The *testicle* often shows similar formations outside of the gland, arising from the hydatids of Morgagni, or from distension of the seminiferous tubes. Their fluid frequently contains spermatozoa.

Some cystic formations of the *uterus* are almost normal, as the bodies which have been called *eggs of Naboth*. In the *mammæ*, cysts sometimes exist which, according to Virchow, are developed from the galactophorous ducts. They are filled by a caseous detritus analogous to milk, and are sometimes so distended that, before opening them, one would imagine that he had to do with a solid tumor. Similar products may also show themselves in various tumors of this gland.

c. Cysts no longer resulting, like the preceding, from the distension of pre-existing cavities, may arise under the following circumstances:—

1st. In the subcutaneous tissue at one time cysts possess a thin membrane and contain a serous fluid; at another they have a much thicker wall, and are then irregular, anfractuous, and paved by a cylindrical ciliated epithelium.

2d. Multilocular cysts may appear in muscles, tendons, bones, the brain, etc.

3d. In the ovaries, where they are very frequent, these cysts constitute a variety designated under the name of proliferous cysts. It is not certain, however, that at their origin these cysts arise from a Graafian follicle. What has lead Foerster and some other authors to consider them as formed of many cysts, is that their wall at a given moment itself forms new cysts. No one that we know of has ever studied the initial formation of these cysts. It is possible that they may be developed from the connective tissue of the stroma of the ovary, just as secondary cysts seem to arise from the connective tissue of the walls of primary cysts.

These proliferous cysts are most frequently encountered in the ovary, but sometimes also in the great omentum. They are all multilocular and have characters which distinguish them from all of the preceding varieties. They possess thick walls, which are independent or common to several cystic cavities; their inner membrane resembles a mucous membrane and presents at its surface papillæ or villosities disposed in tufts or budding masses; finally, in the walls of these cysts we find secondary cysts.

The tissue which separates and unites the different cysts is most frequently a young and very vascular connective tissue, entirely embryonal in some places. In some cases, we have found mucous tissue therein. The papillæ or villi vegetating upon the inner surface of the cysts are simple or compound; their arrangement is often extremely complicated, their body consists of embryonal connective tissue; their vessels are numerous and often dilated into ampullæ, sometimes they rupture and give rise to ecchymoses. The latter peculiarity explains why the fluid contents of the cysts are often more or less colored by the coloring matter of the blood or even by extravasated blood itself. The papillæ and the inner surface of cysts are covered by epithelial cells, sometimes small and cubical, but most frequently cylindrical, and the latter may be

ciliated. In the different layers of the walls of the cysts, particularly in the papillary layer, little cysts are often seen from the size of a pin-head up to that of a hazel-nut, exactly similar to the preceding.

The contents of these cysts is a serous or colloid fluid, whose color is extremely variable; sometimes colorless, it is often red or dark brown. It contains cells regular or deformed, in a state of colloid or fatty degeneration; free fatty granules; sometimes crystals of cholesterin, in such considerable quantity that they may be seen in the fluid by the naked eye.

In the colored fluid are encountered red blood disks, variously altered, granules, and crystals of hæmatoidin.

The DEVELOPMENT of secondary cysts has been studied by Foerster and Wilson Fox, who have reached different conclusions. Foerster observed in the wall of primary cysts islands of embryonal cells, the most internal of which undergo colloid degeneration and are destroyed, while the peripheral remain and constitute the epithelial covering of the cystic cavity. For Wilson Fox, the secondary cysts always form between the papillæ, the villi joining together by their free extremities form at their base cystic cavities lined by the same epithelium. Such is the mode of development that can be easily observed. We do not wish to deny the mode of development indicated by Foerster, but we have not been able to follow it completely. We have seen round islands of embryonal tissue in the wall of cysts, but we have not been able to recognize the transformation of these islands into veritable cysts.

These tumors are very analogous in structure and nature to adenomata and papillomata. In fact, if one examines a good preparation of the wall of one of these cysts, not knowing where it came from, one could hesitate between a proliferous cyst, an adenoma—such as those of the cervix uteri or of the nasal fossæ—a papilloma, and even an epithelioma with cylindrical cells. They also present great similarity in structure to sarcomata developed in glands. But when one examines the whole tumor, doubt is no longer possible; it is readily seen to be a tumor described by all authors under the name of proliferous cyst, a tumor which may attain such an enormous development as to induce death, but which is never generalized as are sarcomata and carcinomata. We shall also find genuine cysts in the following group of tumors.

X.—MIXED TUMORS.

In the fœtus or at birth, sometimes voluminous tumors are found, constituted by an embryonal tissue which has undergone such an evolution that nearly all the tissues find their representation.

We have observed two tumors of this kind located in the peritoneum. In the midst of an embryonal tissue containing vessels with embryonal walls, these tumors present: 1st. Striate muscle fibres in the process of development; 2d. Embryonal cartilage; 3d. Bone developing from cartilage, the two covered respectively by a periosteum and a perichondrium; 4th. Cysts possessing a membrane well defined and covered by a layer of pavement epithelium or of cylindrical ciliated cells; 5th. Long chan-

nels filled with cylindrical epithelium or with lobules of pavement epithelium. These tumors could not be regarded as fœtal inclusions, since there was no form recalling a fœtus. The name *teratoma*, as proposed by Virchow, does not appear to us to suit them, for they have no determined form recalling a superadded being. They have, on the contrary, the form of an enormous embryonal bud, which enjoys the property possessed by embryonal tissue of this age of forming all the organic tissues.

These diverse tissues, muscular, bony, etc., present a degree of development much less advanced than that of the normal tissues of the subject bearing the tumor.

As the new-born children soon die, it is not known what might be the ulterior course of these productions. These complex embryonal tumors might rigorously be considered as sarcomata developed in the embryo; but the multiplicity of the normal tissues which are met with in them, especially the presence of epithelial, cartilaginous, and muscular masses, separates them from sarcomata such as we have previously described.

CLASSIFICATION AND CONDENSED DESCRIPTION OF TUMORS.

ARRANGED ON VIRCHOW'S HISTOGENETIC BASIS, FROM THE LECTURES OF PROF. JAMES TYSON, UNIV. PENNA., ETC.

BY H. F. FORMAD, B.M., M.D.[1]

I. Tumors composed of connective tissue substances, and which proceed from the connective tissue group (Histoid Tumors).

II. Tumors composed of muscular tissue, and which proceed from it.

III. Tumors composed of nerve tissue.

IV. Tumors, the essential constituents of which proceed from epithelium.

V. Cystic tumors, composed of a closed sac, with more or less fluid contents.

VI. Mixed tumors, due to combination of the different forms of tumors.

VII. Granulation or infectious tumors, which ætiologically and histologically stand very near the inflammatory new formations.

I. TUMORS COMPOSED OF CONNECTIVE TISSUE SUBSTANCES, AND WHICH PROCEED FROM THE CONNECTIVE TISSUE GROUP (Histoid Tumors).

TYPICALLY CONSTRUCTED TUMORS.

FIBROMA.

Physiological Type.—Connective Tissue. Areolar and fibrillar.

General Macroscopic Characters.—a. Soft Fibroma: white, reddish, or yellowish in color; soft; often papillæ on surface; sometimes multiple; occasionally polypous form.

b. Hard Fibroma: white; sometimes pale reddish and glistening; exceedingly hard and dry; creaking under the knife when cut.

Both show even to the naked eye concentric fibrillation; usually have a limiting capsule; reach often enormous size; usually round in shape; often lobulated. Growth slow. Sometimes they are very vascular. Cavernous fibroids (see Retrograde Changes).

Microscopic Characters.—a. Soft Fibroma: Prototype in (loose) areolar connective tissue.

b. Hard Fibroma: Prototype in fibrillar connective tissue.

Both are made up of the elements of cicatricial tissue; connective tissue

[1] The excellence, judicial arrangement, and fulness of the following classification have led us, with the consent of the author, to substitute it, with but very little change, for the classification of tumors presented by Cornil and Ranvier.

fibres and their nuclei; latter more distinct by acetic acid. The fibres are arranged in bundles, and extend in every direction, without any definite arrangement, often concentrically around the bloodvessels. They contain usually but few vessels, and these sometimes have no defined walls.

Seat.—Cutis, submucous, and subserous tissues, fasciæ, interstitial tissue of organs, intermuscular connective tissue, periosteum; in uterus often intermingled with myoma.

Age.—Middle and advanced.

Nature.—Benign.

Combinations.—Myxoma, lipoma, sarcoma, chondroma, myoma (in uterus), angioma.

Retrograde Changes.—Fatty, mucoid, cavernous, calcareous, ossification (rarely), pigmentation.

Remarks.—Soft fibroma when diffuse somewhat resembles in structure elephantiasis arabum. Inflammation is sometimes observed in fibromata.

MYXOMA.

Physiological Type.—Mucous Tissue. Found normally in the subcutaneous connective tissue of the fœtus, in the umbilical cord, and in the adult in the vitreous humor of the eye.

General Macroscopic Characters.—Round, lobulated, usually circumscribed within a capsule. Consistence: soft, viscid, gelatiniform, fluctuating. Cut surface of pale reddish or grayish color; showing intersections by partitions of fibrous tissue. Yields a tenacious, translucent liquid. Growth pretty rapid; size various, sometimes enormous.

Microscopic Characters.—Roundish, spindle-shaped, and stellate cells united by their prolongations, imbedded in a homogeneous, translucent slimy matrix, in which, after addition of acetic acid, appears a fibrillar or granular precipitation of *mucin*. Bands of fibrous tissue containing few bloodvessels are occasionally seen, and give a somewhat alveolar appearance; red blood-corpuscles from the cut vessels and amœboid cells are also present.

Seat.—Adipose tissue, chorion (uterine hydatids from placenta), thigh, back, cheek, labia, scrotum, axilla, nose, marrow of bone, mamma, sheaths of nerves (multiple form), brain and membranes, parotid gland.

Age.—In new-born and adults.

Nature.—Considered by some benign. Recur *in loco* very frequently; and the lipomatous variety especially often infectious (S. W. Gross).

Combinations.—Lipoma, sarcoma, enchondroma, fibroma.

Retrograde Changes.—Fatty, fibrous telangiectatic.

Remarks.—Various tumors may contain myxomatous patches, circumscribed or diffuse, but the term myxoma is limited to tumors where the described appearance predominates, or appears to be the primary alteration.

GLIOMA. (Syn. Neuroglioma, Glio-sarcoma).

Physiological Type.—Neuroglia.

General Macroscopic Characters.—It usually occupies the place of a portion of the attached nerve tissue, which retains its normal shape, only

perhaps enlarged, never *lobulated*. It is softer and more glistening, but has the same color and appearance as brain substance: sometimes multiple upon nerves. Growth slow, reaches occasionally large size. Never involves the membranes of brain.

Microscopic Characters.—Roundish, spindle-shape, and rarely stellate cells in a granular matrix seem entirely to replace the nerve tissue. Sometimes gives the impression of a genuine hypertrophy of the nerve elements; or may appear as a circumscribed sclerosis (scleroma) but more frequently diffuse; corpora amylacea are sometimes seen. If there be dilated bloodvessels and extravasations of blood, Virchow calls it a hemorrhagic glioma. Resembles sarcoma.

Seat.—Brain, spinal cord, nerves of special senses (opticus, retina), suprarenal capsule, sacrum.

Age.—Occurs at all ages; more frequently in childhood.

Nature.—Semi-malignant; unfavorable for the patient through pressure, and tendency to extend by continuity.

Combinations.—Myxoma, sarcoma, fibroma, hemorrhagic cysts.

Retrograde Changes.—Fatty (yellow softening), cystic, caseous (green), calcification, ossification (Wagner).

Remarks.—Recently, Klebs and Cohnheim regard the glioma as a new growth of true nerve tissue, classifying it with the neuromata. Most authors consider it a variety of sarcoma.

LIPOMA.

Physiological Type.—Adipose Tissue.

General Macroscopic Characters.—Round, lobulated, soft, sometimes fluctuating, usually encapsulated. On section, the usual appearance of adipose tissue. May reach enormous size; may be multiple. Growth slow in beginning, but later, rapid. Have on surface sometimes purulent, bad-smelling ulcers and granulation tissue, from external irritation.

Microscopic Characters.—Cells and lobules both larger than in normal adipose tissue, otherwise identical. Bloodvessels in the fibrous septa. If stroma predominates: *Lipoma fibrosum.*

Seat.—Subcutaneous and submucous tissues, back, neck, stomach, intestines. More rare in intermuscular connective tissue, peritoneum, membranes of brain, cortex of kidney, liver, lung.

Age.—Adult.

Nature.—Benign.

Combinations.—Myxoma, Sarcoma, cysts.

Retrograde Changes.—Not common. Calcification of the fibrous framework and septa may occur; also mucoid and fibroid degeneration.

Remarks.—Lipoma is the most common tumor. Sometimes hereditary and symmetrical on two sides of the body. Occurs more frequently in emaciated than in fat persons (Birch-Hirschfeld). In starvation the entire normal fat in a person may disappear, but never in a lipomatous growth (Virchow).

CHONDROMA (Syn. Enchondroma).

Physiological Type.—Cartilaginous Tissue.

General Macroscopic Characters.—Usually roundish, lobulated, very firm and hard, except the mucoid variety, which resembles the myxomata. On section, milk-white, hard elastic resistance. Usually opaque or yellow spots are seen, which are due to calcification. If connective tissue is in excess, it has to the naked eye the character of fibroma. The tumor consists sometimes of individual lobules bound together by fibrous tissue into one mass. Growth often rapid at puberty; reach sometimes enormous size; often multiple.

Osteoid chondromata, as pear-shaped and fusiform swellings, may reach enormous size.

Microscopic Characters.—Histologically four kinds, corresponding to the four kinds of normal cartilage: 1, hyaline; 2, fibrous; 3, reticular; 4, mucoid; the latter variety is rare. The cells are round, oval, spindle-shaped, or stellate-fantastic; according to variety, numerous or few, in proportion to the homogeneous or fibrillated matrix. Very few blood-vessels in the bands of fibrous tissue which often intersect the matrix, giving it an alveolated appearance; none in the interior of the hyaline lobules. The most common is the reticulated variety, reminding of the alveolar structure of some carcinomata. All forms may be found in one specimen. Hyaline cartilage is usually in islands surrounded by the fibrous or reticulated varieties.

Variety: Osteoid chondroma. Highly refracting, dense, homogeneous matrix, and lacunæ with short processes. The cells smaller and without capsule. Becomes true bone after impregnation with lime salts.

Seat.—Three-fourths or four-fifths occur in osseous system, usually within the marrow; one-fourth in connective tissues (fibrillar variety). Favorite seats: tubular bones, lower jaw, scapula; less frequently, parotid, testicle, mamma, ovary, bronchial cartilages.

Seat of osteoid chondroma, between bone and periosteum of long bones.

Age.—Any age, sometimes congenital; usually early life.

Nature.—Benign, but not always.

Metastasis sometimes occurs, especially in lung.

Combinations.—Sarcoma, myxoma, osteoma (sometimes with a bony capsule).

Sarcoma.

Retrograde Changes.—Calcification, ossification, mucoid, fatty, cystic (degeneration easy because of scarcity of bloodvessels).

Osteoid chondroma is converted only into bone.

Remarks.—Birch-Hirschfeld and others consider the stellate cells in the enchondromata not as cells, but as little cavities or spaces. The same has been asserted of those in the cornea. According to Cohnheim, enchondromata never grow from pure cartilaginous tissue. Their development proceeds in bones from encysted particles of cartilage which have not ossified (Virchow).

Billroth classifies osteoid chondromata among the sarcomata.

Osteoma.

Physiological Type.—Bone.

General Macroscopic Characters.—The first two varieties are harder

and smoother than the enchondromata. The third and fourth varieties have such consistence as their names indicate. Exostosis, a homologous; osteophyte, a heterologous bony growth. May be multiple. Growth slow; may reach size of child's head.

Microscopic Characters.—Structure corresponds either to compact or cancellated normal bone tissue.

Varieties: 1. Osteoma eburnatum (rare), ivory-like and without bloodvessels; 2. O. durum; 3. O. spongiosum; and 4. O. medullosum.

Seat.—Bones (periosteum), marrow, fibrous tissue of soft parts (rare).

Age.—Early life. Congenital?

Nature.—Benign.

Combination.—Sarcoma.

Remarks.—Osteomata are *non-inflammatory* tumors which consist mainly of bone tissue.

LYMPHOMA, LYMPHADENOMA.

Physiological Type.—Cytogeneous Tissue. (Lymphatic glands and marrow of bone.)

General Macroscopic Character.—*a.* Soft Lymphoma: soft, brain-like consistence. On section, grayish-white in color. Yield juice. Several hypertrophied glands may unite and form a tumor of considerable size. Growth rapid.

b. Hard Lymphoma: consistence harder; smaller in size, and slower in development.

Microscopic Characters.—Type of normal lymphatic gland-structure. Two varieties:—

a. Soft Lymphoma: the cellular elements (lymph-cells) are increased in size and number, whilst the connective tissue of the follicles appears only as a delicate reticulum containing the thickened bloodvessels. Infiltration of surrounding structures is sometimes noticed.

b. Hard Lymphoma: cellular elements diminished and compressed by an overgrowth of reticulated connective tissue.

Seat.—Mediastinum, cervical glands. More seldom axillary and inguinal glands.

Age.—Early life, before thirty years.

Nature.—The soft variety quite malignant; the hard, comparatively benign.

Remarks.—Here is understood an idiopathic hyperplasia of non-inflammatory origin.

ANGIOMA. (Teleangiectasis.) Cavernous Tumor.

Physiological Type.—Bloodvessel Tissue.

General Macroscopic Characters.—*a.* Angioma simplex: bright red, slightly elevated spots; small lobulated. May become a prominent Nævus (a true cavernous tumor).

b. Angioma cavernosa: dark red, hard, sometimes encapsuled. Moderate size. Growth slow.

Microscopic Characters.—*a.* Angioma simplex or plexiforme, a true hypertrophy of capillaries without increase in number. The capillaries

are widened and lengthened, and sometimes thickened; held together by small amount of connective tissue.

b. Angioma cavernosa has, as its prototype, the structure of the corpus cavernosum penis; reticulated meshwork of fibrous tissue lined by endothelium and filled with blood or limy concretions.

[Cornil and Ranvier do not regard a simple dilatation of pre-existing vessels as a true angioma.]

Seat.—*a*. Angioma simplex: external integument; more seldom mucous membranes. *b*. Angioma cavernosa: adipose tissue around bloodvessels, liver.

Age.—*a*. A. simplex: often congenital, early life. *b*. A. cavernosa: old persons.

Nature.—Benign.

Combinations.—Sarcoma, Lipoma, Fibroma.

Retrograde Changes.—Mucoid.

LYMPHANGIOMA.

Physiological Type.—Lymphatic Vessels.

General Macroscopic Characters.—Produces vesicular elevations of the epithelium of the skin.

Represents: Congenital Macroglossia (large tongue); Congenital Hypertrophies of cheeks, lips, and eyelids.

Microscopic Characters.—A dilatation of pre-existing lymphatic vessels and lymph spaces, similar to dilatation of varicose veins (only here lymph instead of blood in the channels). Partitioned structure lined with endothelium, and containing lymph-like fluid. *Cavernous Lymphangioma* (Billroth) has the type of erectile tissue.

Seat.—Adipose tissue around bloodvessels, liver. In elephantiasis arabum.

Age.—Young persons. Always congenital.

Nature.—Benign.

Remarks.—Thought by some to be a cause of chyluria when involving lymphatics of kidney (chylous urine). Here belong also, according to Klebs and Lücke, many cystic hygromas of the neck.

SARCOMA.

Physiological Type.—Embryonic Tissue, the elements of which never become mature.

According to Rindfleisch, the prototypes of sarcoma are the different stages of inflammatory tissue.

Billroth considers as prototype not exclusively the embryonic state of connective tissue, but also that of nerves and muscles.

General Macroscopic Characters.—The different varieties of Sarcoma have, in their general character, many peculiarities in common. Most of them grow rapidly, and sometimes attain enormous size. They are all very vascular; may become erectile (Cornil and Ranvier) and pulsating tumors. They are usually round, encapsuled tumors, though they frequently infiltrate surrounding structures. Sometimes they present a fungoid growth, and in rare cases a polypous form. The color depends upon the vascularity, hemorrhages, and pigmentation. On scraping, the

cut surface usually yields a clear juice containing few cells. This is the case if the tumor is removed during life; if post-mortem, the juice will be milky (Cornil and Ranvier).

A.—a. Round-celled Sarcoma.—A yellowish or reddish, homogeneous, elastic, soft, usually encapsuled mass, resembling the roe of fishes. On scraping, the cut surface yields juice, perfectly clear, and containing a few cells.

b. Lymphadenoid round-celled Sarcoma.—Soft consistence, very vascular. On section, reddish, resembling flesh, often hemorrhages seen. Reaches large size. The large-celled variety is more brain-like, and is rare. These tumors were formerly classed with medullary cancers.

Lipomatous and myxomatous Sarcomata give an appearance corresponding to the degree of the combination; they may coexist and reach colossal size.

c. Round-celled Alveolar Sarcoma.—A rare form of tumor. Highly vascular, and frequently pulsates.

B.—a. Small spindle-celled Sarcoma.—More or less firm in consistence. On section, presents a fasciculated appearance. Often fungus-like projections. Size may be large. Met with more frequently than any other Sarcoma.

b. Large spindle-celled Sarcoma.—Consistence softer than the foregoing; attain larger size; often encapsuled.

Osteoid Sarcoma.—Pyriform and fusiform tumors, which may reach large size; consistence dense.

C.—Myeloid Sarcoma.—Moderately firm in consistence, sometimes exceedingly vascular, giving rise to distinct pulsation. They frequently have a bony capsule, which represents new-formed bone from the periosteum; or the capsule is membranous or osteo-membranous.

D.—Melanotic Sarcoma.—Firm in consistence, size moderate, generally multiple.

Psammoma.—Occurs in small, hard nodules.

Microscopic Characters.—The Sarcomata are tumors consisting of a tissue which, throughout its growth, retains the embryonic type. If stroma at all exist, it is formed, as are also the walls of the bloodvessels, of the same sarcomatous tissues. There are three principal forms of cells: 1st, round, resembling those of granulation tissue; 2d, spindle-shaped, resembling those of young cicatricial tissue, or young, smooth muscular cells; and 3d, myeloid cells (giant cells), made of a nucleated protoplasm, analogous to the giant cells (Myéloplaxes) met with in the marrow of bones. In size the cells vary considerably in the different varieties. The intercellular substance exists usually only in a minimum quantity; it is either fluid and homogeneous or may be gelatinoid, or it presents a network of adenoid tissue, sometimes apparently fibrillated. The *bloodvessels* are numerous, and present simple channels running in every direction, having *no distinct walls;* this is peculiar to the Sarcomata. Sometimes two or more forms of cells are met with in one tumor, but usually one form predominates, which determines the variety.

A. Round-celled Sarcoma (Sarcoma globo-cellulare). Varieties:

a. Granulation-like Sarcoma (S. globo-cellulare simplex). Resembles tissue of granulation. The cells small, round; nucleus very large, com

pared with the small amount of the protoplasm of the cell. The cell-body is very translucent and sometimes invisible, the intercellular substance sparse and transparent.

b. Lymphadenoid round-celled Sarcoma (S. lymphadenoides molle): cells imbedded loosely in a delicate intercellular, translucent network, suggesting the reticulum of adenoid tissue of lymph follicles (also structure of "proud flesh" [caro luxurians]). Besides the cells, the reticulum contains fluid, which accounts for softness of these tumors. The reticulum can be demonstrated by brushing out the cells. Bloodvessels abundant.

Subvarieties: *Large-celled, round-celled Sarcoma* (S. globo-magni cellulare). Characterized by approximation of cells to epithelioid type, reaching the size of large cartilage cells, and by an intercellular reticulated network, with proportional meshes.

Sarcoma lipomatodes is derived from this variety: part of the cell becomes infiltrated with fat; large and small fat cells are intermingled, the fat cells are not uniform as in Lipoma. Also *Sarcoma myxomatodes:* matrix having undergone mucoid degeneration.

c. Alveolar round-celled Sarcoma (Sarcoma medularis or Carcinomatodes). Small masses of round cells are most intimately surrounded and connected with an alveolated stroma, made up of spindle-shaped sarcomatous cells or of delicate fibrous tissue (S. W. Gross). The most intimate union between the cells and the reticulum is an important diagnostic point of difference from the Cancers (Billroth). The cells are larger than pus corpuscles, have round or ovoid vesicular nuclei and lustrous nucleoli; being irregular in shape, they approach very much the epithelial type. Rindfleisch considers it a cancerous degeneration of sarcoma.

B. Spindle-celled Sarcoma (S. fuso-cellulare). Varieties:

a. Small spindle-celled Sarcoma (S. fuso-cellulare durum) ("Recurrent fibroid," of Paget, "Fibro-plastic tumors," of Lebert, Fasciculated sarcoma). The cells fusiform in shape with oval nuclei, arrange themselves, with very little intercellular substance, into bundles which pass in every direction. Resemble spindle cells of recent scars and sometimes those of young Leio-myoma.

b. Large spindle-celled Sarcoma (S. fuso-giganto cellulare). Differs from the foregoing in the large size of cells. These may reach $\frac{1}{800}$ inch in width, and when magnified 200 times may reach three times diameter of field of microscope. The cells have large oval nuclei, with one or more lustrous nucleoli. Usually the cells are granular, and occasionally they are stellate. Rindfleisch recognizes three varities: radiated, foliated, and trabecular.

Subvariety: *Osteoid sarcoma*, distinguished by calcification or ossification of the matrix, and conversion of the cells into bone corpuscles.

C. Myeloid Sarcoma (Giant-celled Sarcoma) is characterized by large cells, often up to $\frac{1}{100}$ of an inch in diameter, consisting of a mass of protoplasm containing numerous (thirty or more) round or oval nuclei. These cells may occur in any variety of Sarcoma (Billroth), but usually are confined to the Spindle-cell Sarcoma of bones, to which the name of *Osteo-sarcoma* is often applied. It is known as *Epulis*, when springing from the periosteum of the upper or lower jaw.

D. Melanotic Sarcoma or Melanoma (Sarcoma pigmentatum). Any one of the varieties of sarcoma may be pigmented (Billroth), but most frequently the alveolar and spindle-shaped Sarcomata are thus colored. The pigment, either black or brown, is usually contained in the cells; rarely in the intercellular substance.

The term *Psammoma* is applied to Sarcomata containing concentrically formed masses of lime.

Seat.—The most common seats of the sarcomata in general are: skin, subcutaneous tissue, intermuscular connective tissue of mediastinum, eye, periosteum, marrow of bones, sheaths of nerves and vessels. Secondary growths: lung, liver, heart.

A.—Round-celled Sarcoma.

a. Small round-celled Sarcoma.—Periosteum and medulla of bones, sheaths of nerve-centres; occasionally skin, mucous and serous membranes and glands.

b. Lymphadenoid round-celled Sarcoma.—Subcutaneous, subfacial, and intermuscular connective tissue, most frequently of thigh; lymphatic glands; periosteum and medulla of bones.

Sarcoma Lipomatodes.—Loose connective tissue of the extremities, subperitoneal connective tissue.

c. Alveolar round-celled Sarcoma.—Marrow of bones, eye, subcutaneous tissue, skin, intermuscular connective tissue.

B.—Spindle-celled Sarcoma.

a. Small spindle-celled Sarcoma.—Fibrous membranes, sheaths of vessels and nerves, subcutaneous and submucous connective tissue, periosteum, marrow of bones, breast.

b. Large spindle-celled Sarcoma.—Fasciæ and fibrous membranes, periosteum, marrow of bones. More rarely in interstitial tissue of glandular organs.

Osteoid Sarcoma.—Grow from the periosteum and more rarely in soft parts.

C.—Myeloid Sarcoma.—Nearly always connected with bone, originating in the marrow.

D.—Melanotic Sarcoma.—Choroid of eye and skin.

Psammoma.—Meninges, choroid plexus, on the spinal cord, and on nerve-trunks.

Age.—Before the 35th year, on the average.

Nature.—Recurrence *in loco* is almost constant. Metastasis is also very frequent.

All varieties of sarcoma are malignant. The round-celled or medullary and the small spindle-celled sarcomata, especially those which have undergone myxomatous degenerations, are the most malignant of all tumors. The giant-celled variety is the least infectious of the sarcomata; while of the varieties, due to changes in the cells or intercellular substance, or in both, the melanotic, osteoid, lymphadenoid, and alveolar are eminently malignant (S. W. Gross).

Combinations.—The round-celled with Lipoma, Myxoma, Fibroma, Chondroma, Glioma, Osteoma, Lymphoma, Angioma, Cysts; the spindle-celled with Fibroma.

Retrograde Changes.—Fatty, myoxamatous, telangiectatic and hemorrhage, calcification, ossification, cystic, pigmentary. The sarcomata may become inflamed and may suppurate.

Remarks.—Billroth, Klebs, Birch-Hirschfeld, Cohnheim, Cornil, and Ranvier all positively oppose the view of Rindfleisch, that sarcomatous cells can become developed into true fibrous tissue. Connective tissue, if met with in these tumors, is regarded as the remains of the pre-existing normal structure.

The cells are generally spindle-shaped in sarcomata of hard consistence when compressed from all sides; they are flat if compressed in one direction (Cornil and Ranvier). Flat cells in profile may appear spindle-shaped and even like fibrils.

Differential Diagnosis of Sarcoma from Carcinoma.

Sarcoma.	Cancer.
Metastasis through bloodvessels, and as a rule does not affect the lymphatic glands.	Metastasis through lymphatics; usually affects lymphatic glands.
Originates primarily in deeper structures.	Originates primarily, always superficially (Samuel).
Is seldom hereditary.	Is hereditary.
Average before the thirty-fifth year.	After the thirty-fifth year (only in kidney and prostate met with even in children).
Primarily encapsuled; later, however, capsule frequently penetrated, and the cells infiltrate surrounding structures.	Never encapsuled. The cells primarily infiltrate and penetrate freely the connective tissue lymph-spaces, not bound by any limiting membrane (contrary to Adenoma).
Hardly ever contains fat.	Nearly always contains fat.

Acetic acid and caustic potash dissolve sarcomatous and embryonic cells; but do not act on muscular cells. Diagnostic point for leio-myoma (Rudnew).

Centrally growing sarcomata are less malignant; those of peripheric growth are more malignant; the softer and the more rapid in growth, the more malignant; most malignant are the melanomata. Rarely is cachexia observed as early as in cancers, though it may present itself late in the disease, especially after recurrences. Lücke considers the sarcomata more malignant than the cancers. Sarcomata occur usually in healthy, well-nourished persons (Billroth).

In early life sarcomata occasionally grow so rapidly that they have been mistaken for acute abscesses (Lücke).

II. Tumors composed of muscular tissue.

Myoma:

Rhabdo-myoma.

Physiological Type.—Striated Muscle.

General Macroscopic Characters.—The pure tumor is exceedingly rare in man. Is sometimes found in combination with other tumors.

Microscopic Characters.—Young striated muscle in this variety has been observed to consist of striated and spindle-shaped cells and fibres.

Seat.—Exclusively in the genito-urinary tract (Cohnheim).

Age.—Congenital?

Nature.—Benign. Metastasis observed in the pigmented variety.

Combinations.—Sarcoma, melanotic sarcoma, carcinoma.

Retrograde Changes.—Pigmentation.

Remarks.—Occurs more frequently in animals (Kolesnikoff).

Leio-myoma.

Physiological Type.—Smooth Muscle.

General Macroscopic Characters.—Very much resembling fibroma; firm and round, usually a limiting capsule. On section, grayish-white or pale red; concentric and radiating markings. Size from that of fist to pregnant uterus. Growth slow, sometimes multiple.

Microscopic Characters.—Include smooth muscular elements and connective tissue in varying proportions. Muscular cells either in bundles or separated.

Seat.—Uterus, walls of œsophagus, stomach, intestines, prostate.

Age.—Advanced.

Nature.—Benign.

Combinations.—Fibroma.

Retrograde Changes.—Calcification, mucoid, cavernous.

Remarks.—Originates only from pre-existing muscular tissue.

III. Tumors composed of nerve tissue.

True Neuroma.

Physiological Type.—Nerve Tissue.

General Macroscopic Characters.—Fibrillar neuroma. Small, hard swellings, white in color; sometimes nodulated. On spinal nerves often multiple.

Ganglionic neuroma. Has been met with once or twice.

Microscopic Characters.—Hard and soft variety, according to amount of fibrous tissue.

1. Fibrillar neuromata, subdivided into:

a. Composed of medullated nerve fibrils (myelinic neuroma).

b. Composed of non-medullated nerve fibrils (amyelinic neuroma).

2. Ganglionic neuromata, composed of ganglionic cells. In both the connective tissue stroma often predominates over the nerve elements.

Seat.—Fibrillar neuroma. Frequently on cut nerve-ends in amputation stumps.

Ganglionic neuroma. Dermoid cysts, brain and spinal cord.

Age.—Adult.

Nature.—Benign, cause great pain.

Combinations.—Glioma, myxoma.

Retrograde Changes.—Mucoid.

Remarks.—Produce often severe pain.

Besides the neuromata, the glandular cancers are often peculiarly painful; but, generally, any tumor may produce pain if pressing upon a part rich in sensory nerves.

IV. Tumors, the essential constituents of which proceed from true epithelium.

Clavus (Corns). Connu Cutaneum (Horns). Onychoma. Ichthyosis. Also some Corneous Warts.

Physiological Type.—Surface Epithelium.

General Macroscopic Characters.—Reach considerable size; vary in color.

Microscopic Characters.—Corns. They are all simple epithelial hypertrophies.

Horns. Consist histologically of epithelium alone.

Onychoma. Hypertrophic new formation of nail-tissue.

Ichthyosis. Hypertrophy of epidermis resembling scales of fish.

Seat.—At any part of body.

Age.—Often congenital.

Nature.—Benign.

Remarks.—Cohnheim regards as the sole cause of corns the local hyperæmia occurring during the time when pressure (the shoe) upon the seat of the corn is removed.

Papilloma.

General Macroscopic Characters.—If single, produce simple conical elevations. If dendritic, produce a fungous, often vascular mass (cauliflower-like growths). If many developed together, may form a tumor of considerable size.

Hard Papilloma.—Represents the dendritic warts, the pointed condylomata. Venereal warts.

Soft Papilloma.—The dendritic growths in mucous membranes.

Microscopic Characters.—Its physiological prototype is the papilla of the skin and the intestinal villus. We find the same conical projections repeatedly branching, made up of a basis of vascular connective tissue, and covered by epithelium. Sometimes the stroma and more rarely the epithelium predominates. The epithelium, being columnar or squamous, corresponds to the kind normally present in the part. There are two varieties:

Hard Papilloma.

Soft Papilloma (more vascular).

Seat.—Skin, penis, fingers, anus, labia, bladder, rectum, uterus, milk ducts, stomach, vagina.

Nature.—Benign.

Combinations.—Sarcoma, epithelioma, carcinoma.

Retrograde Changes.—Ulceration, hemorrhage.

Remarks.—These growths are purely superficial, but sometimes, when ulcerating, they penetrate the integument, proliferating into the cutis, thus becoming epitheliomata.

GLANDULAR HYPERTROPHIES.

Physiological Type.—Glandular Epithelium (of the different glandular organs).

General Macroscopic Characters.—Represented by mammary gland during lactation. Hypertrophies of one kidney or of one of the liver lobes. Deviations: Hypertrophy of mucous glands in catarrh of stomach, intestines, and respiratory passages; sweat and sebaceous glands.

Microscopic Characters.—Physiological type and arrangement is fully preserved while both the stroma and the epithelial elements hypertrophied; local hyperplasias. Connective tissue of follicular sacs thickened.

ADENOMA.

Physiological Type.—Glandular epithelium of the different glandular organs.

General Macroscopic Characters.—Lobulated, sharply circumscribed by a thin capsule; nodules replace portions of the gland structure they involve. On section, white; their racemose structure is sometimes visible to the naked eye. Hard, elastic; those originating from glands of mucous membranes are usually soft, and attain frequently polypous and cystic forms.

Microscopic Characters.—Columnar or squamous epithelium, resting on a basement membrane, forms tubes, imbedded in a more or less vascular stroma, like normal structure of the mamma and similar glands; but arrangement less regular, the epithelium proliferated and filling the lumen of the tubules.

Seat.—Axilla, mamma, liver, sebaceous and sweat glands, thyroid gland, rectum, nose, uterus, ovary, testicle, parotid (polypous forms).

Age.—At puberty.

Nature.—Benign.

Combinations.—Sarcoma, fibroma, carcinoma.

Retrograde Changes.—Fatty, colloid, mucoid, cystic.

Remarks.—Always develop from pre-existing gland-structures.

Atypically Constructed Tumors. Epithelioma, Carcinoma.

SQUAMOUS EPITHELIOMA. (Syn. Cancroid, Epidermal Cancer.) Varieties: Lobular Epithelioma, Tubular Epithelioma, Pearly Epithelioma.

Physiological Type.—Surface Epithelium. *a.* Squamous.

General Macroscopic Characters.—Present different appearance, according to locality. They are fungoid, if proceeding from a cauliflower growth; otherwise present flattened indurated elevations, covered with dried, odorless secretions, sometimes depressed in the centre. Frequently have the appearance of an ulcer, with indurated edges. On section, present a grayish-white, firm, inelastic, sometimes friable, dry mass. On squeezing, a turbid liquid, and in many cases a very characteristic curdy material, worm-like in shape, resembling "comedones," can be expressed. The pearly bodies in exceptional cases can be seen with the naked eye.

Microscopic Characters.—Squamous epithelial cells (forming usually the larger mass), arranged into simple or branched cylinders or cones of various length, which penetrate a vascular connective-tissue stroma (the original cutis or fibrous basis of the mucous membrane). In the cylinders the epithelium arranges itself often concentrically (onion-like) into peculiar nests, the so-called pearly bodies. Older layers of epithelium, when compressed and dry, have, like the pearly nodules, often a horny yellowish appearance. The cells in general are large, have one or two constantly large nuclei, and large shining nucleoli. Serrated epithelial cells have been observed.

Seat.—Skin and mucous membranes, lower lip, tongue, prepuce, scrotum, labia, eyelids, cheek, uterus, bladder.

Age.—Advanced.

Nature.—Malignant, but not always. Metastasis rare.

Retrograde Changes.—Fatty, atheromatous abscesses, calcareous, osseous.

Cylindrical Epithelioma.

Physiological Type.—Surface epithelium. *b.* Columnar.

General Macroscopic Characters.—Fungoid or flattened elevations of the surface, often with a depression in the centre. Consistence soft, sometimes gelatinous; light colored. May form extensive growths.

Microscopic Characters.—Columnar epithelium (analogous to the normal) and a vascular connective-tissue stroma arranged into organized papillæ, which grow in every direction, mostly inwardly.

Seat.—Only mucous surfaces, larynx, uterus, bladder, stomach, rectum, liver (from gall-ducts).

Age.—Advanced.

Nature.—Metastasis has been observed.

Combinations.—Colloid cancer.

Retrograde Changes.—Colloid, fatty.

Remarks.—All glandular cancers best considered modifications or degenerations of a single type (Tyson).

Birch-Hirschfeld considers the glandular cancers as of no more defined alveolar structure than the epitheliomata. Indeed, all the epithelial elements in the other cancers are formed into variously branching cones, which penetrate and separate the stroma in a similar way as in epithelioma, only more profusely and irregularly. Transverse sections of these cones give the alveolated appearance, which can be obtained in epithelioma by making sections horizontal to the surface of the tumor.

Hard Carcinoma. (Syn. Scirrhus, Simple Carcinoma, Connective-Tissue Cancer, Chronic Cancer.)

Physiological Type.—Glandular Epithelium.

General Macroscopic Characters.—More or less firm and hard (according to age and development and peculiarities of locality); sometimes depressed in the centre. On section, grayish-white, glistening surface, intersected with fibrous bands. Central portion hardest, towards the periphery softer. On scraping, yields a milky juice, rich in cells.

Microscopic Characters.—Both Scirrhus and Encephaloid consist of epithelioid cells, within a vascular alveolated connective-tissue stroma. The cells are irregularly packed in the variously sized alveoli without any intercellular substance. The cells are usually of considerable size, vary much in shape, and have prominent nuclei and nucleoli. There is seldom a line of demarcation between the cancerous growth and the surrounding normal structure; the latter is gradually infiltrated by epithelial cells. (Hence the malignancy of these tumors.)

In scirrhus the stroma predominates over the epithelial elements. The trabeculæ of the stroma are usually made of broad bands of vascular fibrous tissue, forming comparatively small, often narrow alveoli, in which the epithelial cells are closely packed. The proportion of the stroma and the epithelium differs at different portions of the tumor. In typical development there can be recognized four zones: 1st, the peripheral—developing zone; 2d, fully developed epithelial nests; 3d, partial retrogressive metamorphosis; and 4th, the oldest central part—cicatrization, atrophy.

Seat.—Mamma, pylorus, œsophagus, rectum, liver, glands.

Age.—Advanced.

Nature.—Malignant. Metastasis.

Retrograde Changes.—Fatty, fibroid, caseation.

Remarks.—Encephaloid cancers are invariably of epithelial origin, *i. e.*, glandular carcinoma. A certain large number of the scirrhus belongs, unquestionably, to this class, but a few have their origin from the tissues of the middle blastodermic layer (endothelia). Cornil and Ranvier believe carcinoma to originate from the connective tissue corpuscles.

Soft Carcinoma. (Syn. Encephaloid, Medullary Cancer, Soft Cancer, Acute Cancer.)

Physiological Type.—Glandular epithelium.

General Macroscopic Characters.—More or less lobulated; soft, brain-like consistence. On section, presents a white, pulpy, often bad-smelling mass; frequently extravasations of blood; central portion frequently fatty degenerated. Cicatrization never occurs. Milky juice is discharged, or can be easily expressed. May reach considerable size.

Microscopic Characters.—Here the epithelial elements predominate over the stroma. The trabeculæ of the latter are thin and delicate; they are very vascular, form large oval alveoli, loosely filled with epithelial cells.

There are all intermediate stages between encephaloid and scirrhus.

Seat.—Salivary glands, mamma, testicle, ovary, prostate, thyroid, nose, liver, kidney.

Age.—Advanced.

Nature.—Most malignant. Metastasis.

Retrograde Changes.—Fatty, colloid, cystic, mucoid, pigmentation.

Remarks.—Samuel describes an *acute miliary carcinosis*, accompanied by high fever, etc., perfectly analogous to acute miliary tuberculosis.

TELEANGIECTATIC CARCINOMA. (Variety of Encephaloid.) One form of Fungus Hæmatodes.

General Macroscopic Characters.—Consistence soft, color dark red; frequently parenchymatous hemorrhages, and pigmented spots. May reach large size. Cysts.

Microscopic Characters.—In this variety of cancer, the vascular development predominates. Sometimes the stroma is entirely made up of vascular ramifications, forming in some places diverticula.

Seat.—Stomach, intestines, rectum, mamma, ovary.

Age.—Advanced.

Nature.—Malignant.

Retrograde Changes.—Cystic.

COLLOID CANCER. (Syn. Gelatinous Cancer.)

General Macroscopic Characters.—Presents a soft, gelatinous, lobulated, yellowish, bad-smelling mass, intersected with bands of fibrous tissue. Surface frequently covered with hydatid-like vesicles.

Microscopic Characters.—A cancer (often scirrhus) having undergone colloid degeneration; has a very limited vascular supply. In the large alveoli, distended by the colloid matter, are seen a few remains of epithelial cells. The colloid cancer cannot be considered a special variety of cancer.

Age.—Advanced.

Nature.—Malignant by extension in continuity. No metastasis.

Retrograde Changes.—Cystic.

ENDOTHELIOMA(?). (Syn. Endothelial Cancer.)

Physiological Type.—Endothelium.

General Macroscopic Characters.—Similar to the glandular cancers; differs from them only by originating from the endothelium of lymphatic vessels and lymph spaces. Rare.

Microscopic Characters.—Nests of closely-packed proliferated endothelial cells are inclosed in alveoli made up of a vascular connective tissue stroma. The histological character of the cells and stroma is very similar to that of true cancers.

Seat.—Skin, membranes of brain, pleura, perineum, lymph glands.

Nature.—Malignant.

Retrograde Changes.—Mucoid, fatty.

Remarks.—Some consider the endothelial cancer as a variety of sarcoma, others as a true carcinoma. Samuel considers it identical with the alveolar sarcoma.

CYLINDROMA.

Physiological Type.—Uncertain.

General Macroscopic Characters.—Resembles myxoma. Found sometimes in other tumors. The hyaline masses are, perhaps, perivascular sheaths having undergone mucoid degeneration. Köster regards it as the product of secondary mucoid metamorphosis of a cancroid of the lymph vessels. Growth slow; size moderate; rare.

Microscopic Characters.—Presents peculiar cylindrical, spherical, or club-shaped hyaline masses, containing stellate or fusiform cells, and having in their centre one or more capillary bloodvessels, usually of large size. Between and around these hyaline formations, which usually are imbedded in a connective tissue stroma, are situated sometimes lymphoid and rarer epithelioid cells.

Seat.—Orbit and neighborhood of jaws in the adventitia and bloodvessels. Mixed tumors in the parotid, dura mater, peritoneum.

Nature.—Slightly malignant.

Remarks.—Waldeyer calls the cylindroma a plexiform angio-sarcoma. Rindfleisch suggests the name cancroid (cancer-like). It never affects lymph glands.

V. Cystic Tumors, made up of a closed sac, with more or less fluid contents (including also the Dermoid cysts (Virchow's Teratoms)).

I. *Cysts formed by the accumulation of substances within the cavities of pre-existing structures.*

A. Retention Cysts.—Cysts resulting from the retention of normal secretions. These include—

α. *Sebaceous Cysts.*—These are formed by the retention of secretions in the sebaceous glands. Such are comedones and atheromatous tumors.

β. *Mucous Cysts.*—These are formed by the retention of secretions in the glands of mucous membranes.

γ. *Cysts from the retention of secretions in other parts*, including—Ranula, from occlusion of the salivary ducts; Encysted Hydrocele, from occlusion of the tubuli testis; Cysts in the mammary gland, from obstruction of the lacteal ducts; Simple and some compound cysts of the ovary, from dilatation of the Graafian follicles; Simple cysts of the liver and kidneys.

B. Exudation Cysts.—Cysts resulting from excessive secretion in cavities unprovided with an excretory duct. These include Bursæ, Ganglia, Hydrocele, and many cysts in the broad ligament.

C. Extravasation Cysts.—Cysts resulting from extravasation into closed cavities. These include Hæmatocele, and some other forms of sanguineous cysts.

II. *Cysts of independent origin.*

A. Cysts from Softening of Tissues.—These are especially common in new formations, as in enchondroma, lipoma, sarcoma, etc.

B. Cysts from Expansion and Fusion of Spaces in Connective Tissue.—These include—

α. *Bursæ*, originating from irritation and exudation into the tissues.

β. *Serous cysts in the neck* (often congenital).

γ. *Many compound ovarian cysts.*

C. Cysts formed around Foreign Bodies, Extravasated Blood, and Parasites.

D. Congenital Cysts.—These include many Dermoid cysts. They appear often to be the remains of blighted ova. They contain fatty matters, hair, teeth, bones, etc.

VI. Mixed Tumors, due to combination of the different typical and atypical forms of tumors.

VII. Granulation or Infectious Tumors, which ætiologically and histologically stand very near to the inflammatory new formations: Tubercle, Glanders, Syphiloma, Lupus, Lepra; Lymphoma, of some infectious diseases, as typhoid fever, scarlatina, etc.

APPENDIX TO TUMORS.

After the definition which we have given of tumors, we should range among them neither accumulations of pigment under the form of circumscribed masses, nor hydatid cysts. We will briefly describe them in this appendix to tumors.

Simple Melanic Masses circumscribed in the form of Tumors.

Synonyms.—These simple melanic masses have been very frequently confounded with melanotic sarcoma and carcinoma under the name of melanosis or melanoma. We do not use the term simple melanosis to characterize these masses, because the radical of the word does not represent a tissue.

Definition.—The melanic masses which we here have in view are distinct from melanotic sarcoma and carcinoma in this that the melanic granules do not accumulate in the cells of new formation as in the latter tumors, but they infiltrate the pre-existing normal elements. Melanic pigment granules accumulate in the cells of normal tissue and destroy them, and if the accumulation continues, the tissue itself is destroyed and replaced by a nodule or a tumor softened at its centre.

We give the name of melanic masses to those accumulations of pigment occurring at the same time in great number at different points of the organism. They are distinguished from pigmentary infiltrations of the skin, *nævi materni*, and from the pigmentation which is sometimes met with around vessels in the nerve centres, by the fact that they destroy the tissues and are generalized in all the organs like the most malignant tumors.

Description.—Contrary to the habitually slow progress of simple melanosis so common in the horse, productions of this nature in man become generalized with very great rapidity, and cause the death of the patient. The progress of the malady is such that one is often embarrassed to know if a primary mass has determined a secondary infection of the

organism, or if the numerous masses which are observed proceed from the influence of the same general cause.

These melanic masses have variable dimensions. They are sharply bordered, and their periphery presents no intermediate zones of lessening color.

When they reach the size of an almond their consistence is usually soft at the centre, whilst at the periphery they still preserve the firmness of the tissue wherein they are developed. The largest contain at their centre a grumous fluid, in which the microscope reveals nothing else than melanic granules. For the microscopic examination of the peripheral parts which are yet firm, sections must be made after hardening. We find the elements of the original tissue infiltrated with melanic granules, without any indication of a cellular new formation.

In the subcutaneous cellular tissue the plasmatic (connective tissue) cells are infiltrated with pigment.

In the peritoneum the melanic granules are deposited in the plasmatic corpuscles exactly as in the skin. In those trabeculæ of the great omentum which contain no vessels, similar pigmentation of the cells is seen.

In the kidney the deposit of pigment takes place now in patches, again in little black granules. Sections of this organ examined under the microscope show the location of pigment in the cellulo-vascular tissue and in the glomeruli; the epithelium of the tubuli remains intact for a long time.

We have also seen the mamma present patches visible to the naked eye. The pigment was formed not in the connective tissue, but in the ducts and in the acini of the gland, in the protoplasm of the epithelial cells around the nucleus.

This pigment has been found deposited even in the muscles of the heart.

From these facts it is certain that the formation of pigment takes place at the same time in the cells of the connective tissue, in the cells of the epithelium, and even in muscular fasciculi, and that the pigment does not come directly from the coloring matter of the blood. It is not a simple penetration of the pigment, but is the result of an action of the cell.

This morbid product can only be confounded with melanotic sarcoma and carcinoma. From the naked-eye examination one may suspect a simple melanosis, if we do not find between the black and the healthy parts a zone presenting tints of intermediate coloration. Such a gradation of pigmentation is almost never absent in melanotic sarcoma and carcinoma.

But, to arrive at a precise histological diagnosis, it does not suffice to scrape the tumor or to examine the elements obtained by dissociation; as we have already said, it is necessary to make thin sections.

Generalization of the melanic masses is very rapid, and death follows in a few months.

Hydatid Cysts.

We describe these in the general part of this manual because they may be met with in all the organs and tissues. The other human parasites which have special seats will be mentioned *à propos* of the tissues and organs wherein they are found.

Definition.—Hydatid cysts, which owe their name to the aqueous fluid which they contain, are essentially constituted by vesicular worms which represent a phase of the development of tænia.

In man two varieties of hydatids are found—cysticerci and echinococci.

Cysticerci are always single in their cyst, while echinococci are contained in the primary cyst in considerable number. They proceed from various species of tænia, but most frequently *cysticercus cellulosæ* (Rudolphi) appertain to *tænia solium*.

Tænia solium, as seen in the small intestine of man, is a ribboned worm, whitish, and several yards long; it is composed of joints, the smallest of which are near the head, while the largest are found at the opposite extremity.

Fig. 121.



1. Head and neck of the *tænia solium*. *a*. Proboscis. *b*. Circle hooklets. *c, c*. Suckers. 2. An isolated hooklet. *a*. Free portion.

The head is about the size of the head of a pin (fig. 121). Upon it, besides four suckers, a little tubercle or proboscis is to be seen, whose base is surrounded by 24–48 hooks disposed in two rows.

The joints begin immediately behind the head, and increase in size progressively down to the extremity of the animal. The rings, which may acquire a breadth of 12 mm., are flat, and each is an individual hermaphrodite. The orifices of the male and female genital organs are united in a slight prominence at the lateral border of each joint. These organs are composed of sinuous ducts which represent the uterus and ovaries—the latter filled with ovi. The male apparatus consists of a falciform penis and a seminiferous duct. The fecundated egg in the mature joints contains an embryo which already possesses six hooklets. The last joints become detached. They are filled with fecundated eggs, and are eaten by animals; the eggs having arrived in the intestine loose their enveloping membrane, the embryo is liberated and traverses the intestinal membrane in order to pass into different parts of the organism where it becomes *cysticercus cellulosæ*.

Cysticerci cellulosæ, very rarely observed in man, appear in the muscles, in the pia mater, the brain, under the conjunctiva, in the chambers of the eye, in the retina, in the pleura, the peritoneum, etc. They are generally encysted. The cyst is formed by a membrane of connective tissue supplied by bloodvessels. This membrane is wanting when the cysticercus is situated in a cavity. When the membrane is incised the cysticercus presents itself as a round, transparent vesicle, from 8 to 20 mm. in diameter, filled with an aqueous fluid. At its surface is a little depression. By pressure upon the vesicle the body, the neck, and the

head of the animal are made to protrude from its caudal vesicle. The head is exactly the same as that of the tænia; the neck and the body of the animal present folds without distinct rings; there are no genital organs.

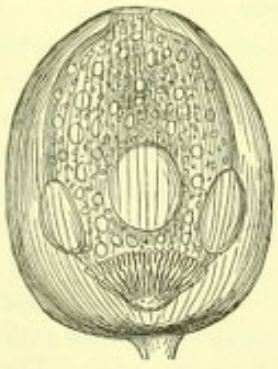
For the complete development of a tænia it is necessary that the cysticercus pass into the intestinal tube of another animal. The *tænia solium* of man is most frequently derived from the cysticercus contained in pork. Cysticerci cellulosæ are not the only species met with in man. Cysticercus from *tænia acanthotrias*, from *tænia serrata*, etc., have also been occasionally observed. While the preceding cysticerci are rare in man, the echinococci are, on the contrary, more common. The latter have the same relation to *tænia echinococcus* as the cysticercus cellulosa has to the *tænia solium*.

The tænia echinococcus, of which the existence is doubtful in man, lives in the intestine of the dog. It differs from the *tænia solium* particularly by the small number of its rings; the third or fourth from the head already possess ova, and become detached.

The ova of this tænia having reached the intestine of man lose their enveloping membrane, and their embryos migrate to the serous cavities and the parenchymas. They are the point of departure of cysts which arrived at their full development, are constituted by an adventitious membrane of fibrous tissue belonging to the organ affected, and by one or several vesicles either free or some contained within others.

These transparent, trembling vesicles, giving to the hand the peculiar sensation known as the hydatid crepitus, are spherical and of very variable size, from that of a hazel-nut to that of an adult head. They contain a transparent aqueous fluid coagulating neither by heat nor by acids. The membrane of the cyst is gelatiniform and transparent, and is formed of thin superposed leaflets, which can be separated from each other by dissection, and which roll up like elastic membranes. Under the microscope these leaflets appear to be constituted by lamellæ still more fine,

Fig. 122.



Invaginated echinococcus, detached from the mother hydatid.

Fig. 123.



Echinococci. (*Gross*)

amorphous, and separated from each other by beautifully distinct parallel lines. The most internal is named the germinal membrane, and it bears upon its free surface the echinococci, which appear to the naked eye as little whitish grains. A certain number of them are detached and float

in the fluid. In one of these large vesicles we often find smaller vesicles of identical structure.

Echinococci (see figs. 122, 123) are formed of a caudal vesicle adherent to the germinal membrane, in the midst of which one finds the body and head of the animal invaginated as in cysticerci. The diameter of echinococci varies between one- and two-tenths of a millimetre. Their head has a proboscis, a double row of hooks, and four suckers. The body of the animal contains calcareous disks.

Hydatid vesicles do not always contain echinococci, the germinal membrane being absent, or the animals having ceased to live. In the latter case one finds free hooklets in the hydatid fluid. This variety of sterile hydatid cysts has been especially designated under the name of acephalocysts. Sometimes the vesicles present a very thick wall, formed of a considerable number of superposed lamellæ, and their central cavity is very small.

Latterly has been described (Friedreich, Virchow, Ott, etc.) a variety called *multilocular hydatid tumor*, characterized by the presence of a great number of very small miliary cysts disposed in a fibrous stroma. These tumors are extremely rare in France. Each of these cysts contains one or more hydatid vesicles enclosing echinococci or a few hooks, and always showing the membrane peculiar to hydatids. These tumors at first sight very much resemble colloid carcinoma, with which they have been often confounded ; but the microscope removes all doubt.

When hydatid cysts have completed their development and still remain in the organism, their different constituent parts suffer considerable modifications. The fluid is absorbed, the echinococci shrink and decompose; the hydatid membranes contract, rupture, and break up into leaflets which float in a fluid rich in the salts of lime ; in cysts of the liver the membranes are rendered yellowish or reddish by the presence of the coloring matter of the bile and of the blood. The adventitious membrane becomes thicker, retracts, and undergoes fatty and calcareous infiltration. In one case of cyst of the liver, we observed a genuine formation of a few islands of osseous tissue containing bony trabeculæ, medullary tissue, and vessels.

PART II.

DISEASES OF ORGANS AND OF TISSUES.

CHAPTER I.

LESIONS OF BONES.

The lesions of bones are important, not only because they are numerous and varied, but especially because their easy determination, their exact development, and their appreciable evolution may guide pathologists in their investigations of other tissues, and suggest to them general considerations concerning pathological histology. Therefore, we have been led to commence in the osseous system the study of the alterations of the various tissues of the organism.

A study of the development of osseous tissue is necessary for the understanding of most of the pathological changes which occur in bone. Bone is not the result of a direct transformation of connective tissue or cartilage, the cellular elements of which first proliferate in order to form the embryonic marrow of bone; some of the embryonic cells thus formed subsequently become bone cells.

Among the embryonic cells of the medullary substance of bone, those which are not converted into bone cells undergo changes which separate them from their primitive type. Some appear to have a limiting membrane developed around them, others become adipose cells, a number assist in the formation of a true connective tissue, as may be seen surrounding vessels of considerable calibre and between the adipose cells of the medullary spaces or canals of the long bones; finally, some of these cells do not divide, while their nuclei multiply, thus forming the so-called giant cells (myéloplaxes).

Almost all of the pathological changes which take place in bones have their starting-point from the cells of the embryonic marrow, or from the cells which have undergone the modifications above mentioned. The bones of young persons, and those of the adult which contain embryonal marrow, as the sternum and bodies of the spinal vertebræ, are particularly liable to nutritive or formative pathological alterations. Moreover, different parts of a bone are not equally subject to disease; the youngest portion, the superficial or sub-periosteal, and that which forms the extremity, especially during the growth of the bone, are localities most frequently attacked.

Sect. I.—Congestion and Hemorrhage of Bone.

Congestion of bone is manifested to the naked eye by a red coloration of the marrow. In order to distinguish it, it is necessary to know the normal color of the marrow in different bones and at different periods of life. In the sternum and bodies of the spinal vertebræ, the marrow is red; where we have bone in process of formation, a similar color is seen. In young persons the epiphysis in the proximity of the ossifying cartilage presents a true physiological congestion, while in the older portions of the bone the marrow is fatty and resembles, in color, and translucency, adipose tissue. As age advances, the marrow in the bodies of the spinal vertebræ and in the sternum loses its red color and becomes lighter. The red color of the marrow is not always due to a congestion, and to determine the cause a histological examination is necessary. It is seen that the bone containing fresh red marrow shows not only the capillaries dilated by the accumulation of red corpuscles, but more frequently the congestion is accompanied with an abundant increase of the medullary cells, and a variable absorption of the fat; there is even at times diffuse hemorrhage, when the red corpuscles are found mingled with the medullary cells. The red corpuscles which have escaped from the vessels slowly undergo changes, which cause them to have their coloring matter set free, and to infiltrate the non-colored elements. It is in these cases that the young cells of the marrow contain granules of hæmatoidin.

The red color of the marrow in bone may be due to congestion, to hemorrhage, and to the staining of the medullary elements by the coloring material of the blood. The red color of the marrow may be due to a new formation of vessels, but in this case it is not a simple congestion. Simple or complicated congestion of the medullary substance is met with under numerous conditions—osteitis, caries, various tumors, rachitis, osteo-malacia, etc. It occurs with great readiness, owing to the vessels of the marrow not being supported by a resisting tissue. It is seen even in simple physiological changes, as above shown; it is present during ossification, and it accompanies the formation of new vessels which often permit the red corpuscles to escape into the medullary parenchyma.

Hemorrhages are frequent in the spongy tissue of bone and under the periosteum, on account of the vessels in these localities not being well supported. With traumatic injuries, such as contusions, wounds, and fractures, should be placed those lesions where there is a change in the walls of the capillaries, as seen in inflammations, and in other active new formations. The wall of the capillaries, formed at this time of embryonic cells, has become so soft that the red corpuscles easily escape and are found in the medullary parenchyma. In a third category of cases, osseous apoplexy is connected with one of those general diseases in which hemorrhages are easily occasioned: cachexia, purpura, leucocythæmia, etc. Almost always, when hemorrhagic foci have been found in the different viscera, there are similar foci to be seen in the epiphyses and under the periosteum.

Sect. II.—Osteitis.

Simple irritation of a bone, as denudation, injury, the presence of a foreign body, etc., causes it to undergo several changes, which constitute a pathological condition designated osteitis. The irritation causes an increased activity of the cellular elements of the bone, and the lesions which follow are simply a consequence. These lesions do not essentially differ from those which are produced in other tissues by similar causes, such as we have studied under general inflammation.

If a bone of an animal is denuded and the wound kept open, in a few days there is seen upon the denuded surface an enlargement of the Haversian canals through absorption of the osseous substance, while at the periphery of the denuded portion, beneath the periosteum, there is found a layer of newly-formed bone, a demonstration that an irritation causes at the same time both absorption and growth of osseous tissue. In order to understand why the same cause produces simultaneously a different effect, it becomes necessary to study the histological phenomena of osteitis.

The first change observed in a bone upon which artificial irritation has been employed, is the formation of embryonic cells in the medullary spaces, in the Haversian canals, and under the periosteum. These cells resemble those which fill the primary medullary spaces during the development of bone from cartilage, or those which are found under the periosteum while the bone increases in thickness. Irritation of a bone results, then, in its return to an embryonal condition, and herein we find an application of the general law which governs irritation of any tissue.

There are two changes which follow the formation of embryonic tissue in the medullary spaces and under the periosteum: *A. The enlargement of the canals* or medullary spaces by absorption of the osseous tissue which limits them; *B. The formation of new osseous trabeculæ.*

A.—The enlargement of the Haversian canals may be easily seen. The osseous lamellæ are found eroded in such a manner as to form notches (Howship's lacunæ) filled with embryonic cells. (Fig. 124.) The bone corpuscles at the edges of the notches open, permitting the contained cells to escape and join the cells already occupying the medullary spaces. Gradually the osseous lamellæ disappear, and adjoining Haversian canals unite to form irregular spaces in which the embryonic marrow proliferates. Several hypotheses have been advanced to explain the cause of the absorption of osseous tissue, but as yet it remains in great obscurity.

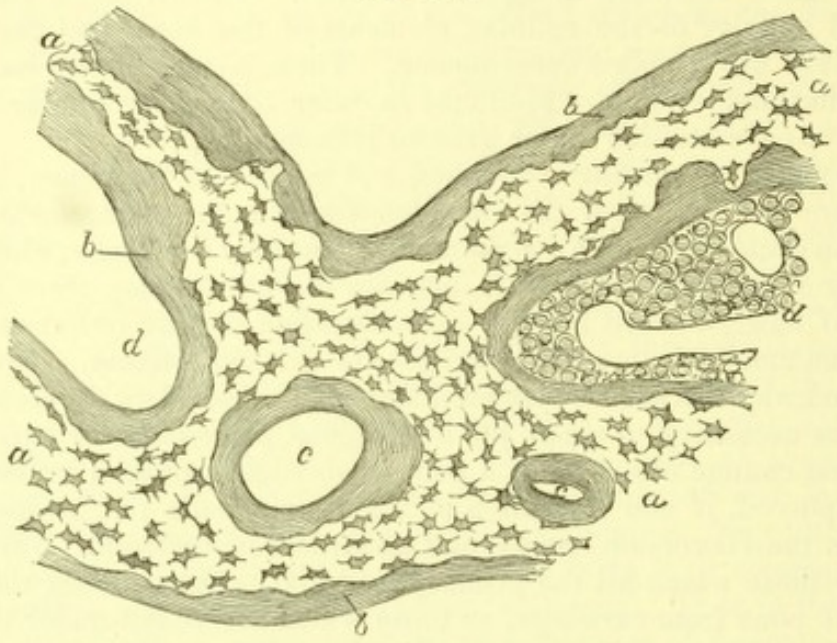
Billroth having noticed that the serous pus coming from an osseous abscess contained lactic and phosphoric acid, was led to think that the solution of bone was effected by these agents. The fact, however, that the action of pus upon fragments of dead bone which form sequestræ in cases of necrosis, is very slight, is sufficient to overthrow this conjecture.

Rindfleisch supposes that the absorption of bone is preceded by a mucous change. In some preparations we have noticed along the side of the osseous tracks undergoing absorption, areas of a substance brighter

than the neighboring osseous tissue, which, however, are nothing more than oblique cuts of those portions of the bone in process of absorption.

Virchow thinks that the bone corpuscles enlarge, change, and cause a solution of an area of the osseous substance corresponding to the carti-

Fig. 124.



Softening of bone. Spicula of bone from the spongy substance of an osteo-malacic rib. *a*. Normal osseous tissue. *b*. Decalcified osseous tissue. *c*. Haversian canal. *d*. Medullary spaces. The space to the right is filled with red medullary tissue, in which the lumina of the capillaries are open. × 300. (*Rindfleisch.*)

laginous capsule from which the bone corpuscle and its territory are formed, and bases upon this interpretation his theory of cellular territory. At the present time such an explanation cannot be admitted, since we know that bone corpuscles do not proceed directly from cartilaginous capsules.

O. Weber and Volkmann consider the absorption of osseous tissue to depend upon a fatty degeneration of the bone corpuscles. They have confounded caries with rarefying osteitis. Later it will be shown, that true caries is the only disease in which there is a fatty degeneration of the bone corpuscles, and in which the diseased part dies without being again absorbed.

The bone corpuscles which are found at the boundary of the inflamed part, are frequently observed unbroken; the cell within being slightly increased in size. Rarely do we observe any signs of proliferation; never in these cases do the corpuscles contain granular fat. From these statements it is very difficult to understand exactly in what manner absorption of bone takes place during osteitis. It is, however, probable that, in accordance with the opinion of Virchow, the bone cells play an important roll in the process, since in those conditions where this cell has lost its active vitality (caries and necrosis), the solution of bone does not occur, notwithstanding the bone may be in contact with elements similar to those which, in ordinary osteitis, fill the enlarged medullary spaces.

B.—The formation of new osseous trabeculæ takes place at the expense of the embryonal cells, which were developed during the first stage of the inflammation. Irritation first prepares the materials for ossification, but these materials are not utilized for the development of new osseous trabeculæ until the irritation has lost its first intensity. Thus, it is not at the points where the inflammation is intense, that new osseous tissue is formed, but in those parts only which adjoin the inflammatory focus.

The sub-periosteal marrow possesses in the highest degree the property of forming bone. The rapidity with which osseous tissue is formed beneath the periosteum, under the influence of irritation, is truly astonishing. The manner of its development does not differ from that observed in physiological ossification. The trabeculæ spring from the old bone and traverse the embryonic tissue; along the sides of these trabeculæ are seen numerous cells, which become angular; some are partly imbedded in the young osseous substance, which is forming around them. It is not necessary that the periosteum should cover the bone, in order to have a new formation of osseous tissue upon its surface; but the preservation of the periosteum, and especially the vessels of the under surface of the periosteum, which enter the Haversian canals, assist greatly in the formative action. The external surface of bone is not the only part in which we have a new formation of osseous tissue during inflammation. When the inflammation has been alleviated, the anfractuous cavities which have been excavated in the bone are very soon filled by layers of new osseous tissue, which are developed in a similar manner as upon the external surface of the bone. Even the medullary canal, if the irritation attacks the central medulla, may also become the seat of new osseous formations.

The relation between rarefaction of osseous tissue and its formation, or between rarefying osteitis and formative osteitis has been clearly indicated by the foregoing. In inflammatory rarefaction of bone, the materials for rebuilding are already prepared, and they are employed by the organism at the moment the irritation lowers its intensity. While, on the contrary, if the intensity of the irritation continues, the surface of the bone is covered with granulation tissue and pus.

These granulations are formed directly from the marrow contained in the enlarged medullary canals, and they show, as has been observed by Troja, that at this time the osseous tissue included between several canals has been absorbed. This absorption continues until the whole of the denuded surface is covered by a granular and very vascular soft layer.

A general description of osteitis having been given, we may proceed to the study of the several varieties, neither making special chapters for acute and chronic osteitis, distinctions more interesting clinically than in a pathological point of view, nor considering separately periostitis and osteo-myelitis; periostitis being in fact simply a superficial osteitis. Histologically every osteitis is in reality an osteo-myelitis.

We will describe separately *simple osteitis*, *rarefying osteitis*, *formative osteitis*, and *diffused phlegmonous osteitis*. Caseous osteitis being always connected with caries, tuberculosis, and gummata of bone, requires no special description.

1. Simple Osteitis.—In consequence of contusions, injuries, fractures, wounds, etc., when not followed by necrosis, we have occurring the phenomena as previously described. The best example is seen in the extremity of the stump of a bone eight or ten days after amputation. In this case the marrow under the periosteum, in the Haversian canals, and in a portion of the medullary canal, becomes embryonic; the periosteum is congested, slightly tumefied, and infiltrated; it is easily detached from the bone, from which it is separated by a layer of round or angular cells resembling those of the embryonic marrow. The Haversian canals are enlarged and filled with similar elements; these canals anastomose one with the other, forming an anfractuous lacunar system. The Haversian canals, which open upon the cut surface of the bone, are visible to the naked eye as red points, or openings from which project small fleshy granulations. We see at the same time new osseous trabeculæ form beneath the periosteum from the embryonic marrow developed under the influence of the irritative process.

These osseous formations never commence at the point where the irritation is most active, that is to say, upon the cut surface of the bone and in the midst of suppuration, but some distance above. When the stump is conical, and the bone projecting, the lateral portions which form part of the wound do not then present any traces of ossification, while a little higher up a new formation of bone is seen.

The sub-periosteal osseous formations, coincident with the absorption of the old bone, should not be considered as indicative of an osteogenetic property of the periosteum; they in reality spring from the embryonal elements which have their origin beneath the periosteum and in the Haversian canals, under the influence of irritation.

During the cicatrization of the wound newly formed osseous tissue is also produced, both in the enlarged Haversian canals and in the medullary canal. When recovery is completed, the medullary canal is obliterated by an osseous plug, and the extremity of the bone consists of a round mass of compact osseous tissue covered by a new periosteum.

A simple osteitis terminating in recovery, is at the beginning a rarefying but subsequently becomes a condensing osteitis. Therefore we have no more reason to term the inflammation of a bone of a stump undergoing suppuration *rarefying*, than to give to this same osteitis the name of *condensing* when the stump is cicatrized.

2. Rarefying Osteitis.—Inflammation of bone in which the absorption of the osseous substance is a prominent feature, and in which the enlargement of the Haversian canals continues until the complete disappearance of the bone, is named rarefying osteitis. This variety of osteitis is peculiar in the absence of any attempt at new ossification: the new embryonic tissue generally protrudes externally, is covered with large fleshy granulations, and discharges pus.

Rarefying osteitis, as above described, is a disease not frequently met with. It occurs in the short bones of the upper and lower extremities, either as a result of injuries, or following a continued irritation, as a perforating ulcer of the foot. In the latter disease especially several

phalanges may completely disappear without any necrosis, yet necrosis is generally met with during the course of a perforating ulcer.

The diseased bone is found at the bottom of a suppurating sinus, the walls of which are covered with fleshy granulations. These large red or gray granulations, rich in secretions, are connected with the surface of the bone by inflammatory tissue, which is continued into the enlarged osseous canals. This inflammatory tissue is characterized by granulation tissue, described on page 70, and resembles very much some of the bone sarcomata, but in this variety of osteitis a suppuration is established at the beginning of the disease, and is continued until its termination. Again, this osteitis differs from the sarcomata in the possibility of a spontaneous recovery. The inflammatory tissue which serves as a basis for the fleshy granulations, developed in the body of the bone, at times entirely surrounds pieces of bone, so forming living sequestræ, which possess vessels coming from the embryonal marrow, and are consequently capable of

Fig. 125.



Rarefying osteitis. Canaliculization of the osseous tissue. × 500. (*Volkmann.*)

being absorbed. It is necessary to guard against confounding these living sequestræ with the dead sequestræ found in necrosis, in which there is an absence of vessels. The absorption of osseous tissue in rarefying osteitis, occurs in a similar manner as in ordinary osteitis;

the process only being more intense and continued; extending from the suppurating focus until both extremities of the bone are reached. When the epiphysis of the bone is absorbed, there is produced a suppurative arthritis. There remains no trace of the bone or cartilage, except perhaps a thin, opaque, friable lamella, formed by a calcified layer of the diarthrodial cartilage, which may be readily recognized with the microscope.

3. Formative Osteitis.—Every osteitis which terminates in recovery determines a new formation of osseous tissue. This new formation is sometimes effected before the cessation of the osteitis. In a number of cases the ossification ends before exceeding the limits of the old bone; when it should not be considered a formative osteitis. In other cases, the new formation is exuberant, exceeds the limits of the old bone or causes it to become more dense; the disease is now designated as hyperostosis, exostosis, enostosis, and condensing osteitis, all being included in formative osteitis. Every osseous formation must not be considered as the result of an osteitis (see Osteoma, p. 132). The long duration and slight intensity of the inflammation of the bone are the usual causes of formative osteitis. Therefore, it occurs especially in deep and chronic abscesses of bone, in necrosis, in syphilitic osteitis, etc., these diseases, as we know, being characterized by their slowness.

New osseous formations may be developed upon the surface of the bone under the *periosteum*, in the *body of the bone*, or in the *medullary cavity*.

a. Upon the surface of the bone we meet with that variety of formative osteitis, in which the inflammation has been of long duration and of slight intensity. The irregular osseous masses are named *osteophytes*. The trabeculæ and vessels of these superadded parts always have a direction different from those of the old bone, so that they are readily distinguished one from the other. In making a transverse section of a long bone covered with osteophytes, the Haversian canals in the old portions of the bone are cut transversely, while those in the new are mostly cut longitudinally. The direction of the Haversian canals follows that of the vessels; for the osteo-periosteal or granulation vessels come from the Haversian canals at the surface of the bone, and it is around these vessels that the new osseous lamellæ are formed, as in the physiological ossification from elements of the embryonal tissue. The new bone with its Haversian canals thus formed is ingrafted with its vessels perpendicular to the surface of the old bone.

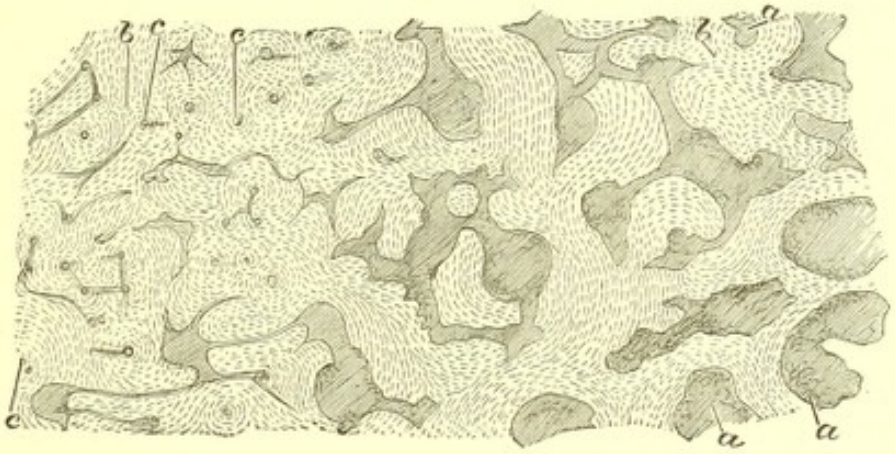
In the formation of osteophytes which are occasioned by inflammation, cartilage is never found.

b. Formative osteitis occurring in the body of bone causes it to become dense (condensing osteitis, sclerosis of bone, eburnation). This change is habitually preceded by an inflammatory rarefaction, traces of which are readily found with the microscope.

If the embryonal elements contained in the cavities enlarged by the inflammation do not undergo extreme irritation, they assist in the formation of new osseous layers, which cover the old eroded trabeculæ; so

that the characteristic boundary of rarefying osteitis is recognized in a very distinct manner in bones which have undergone repeated attacks of eburnation. When the irritative action continues for several years in the same bone, as, for example, in cases of necrosis or deep abscesses, there occurs from time to time inflammatory outgrowths. These bones generally attain considerable size, double or triple the normal state. At this time their structure presents a very great irregularity. The systems of lamellæ are arranged in an unusual manner.

Fig. 126.



Syphilitic sclerosis of the frontal bone. *a*. Medullary spaces of the diploë. *c*. The same spaces much narrowed. *b*. Bony substance. × 20.

Eburnation of osseous tissue causes not only a narrowing of the Haversian canals, but in some cases complete obliteration of some. (See fig. 126.) A necrosis then supervenes, on account of the arrest of the capillary circulation in the bone.

c. Formative osteitis in the medullary canal of bone is seldom observed. However, examples of the ossification of the medullary substance of bone in consequence of osteitis have been reported by Troja, Ténon, Broca, Ollier, etc. We have ourselves communicated to the Society of Biology a case in which bone was formed in the interior of the medullary canal of a necrosed bone.

Finally, in amputations resulting in recovery, the medullary canal is always closed by a compact osseous plug, the length of which varies.

4. Diffused Suppurative Osteitis.—This variety has received the names of *osteo-myelitis* (Chassaignac), of *phlegmonous periostitis* (Giraldès), of *epiphyseal osteitis*, etc. We believe this disease to consist essentially in a diffused suppurative inflammation, which may be located in any part of the bone, under the periosteum, in the superficial layers, in the substance of the bone, or in the central medullary substance. As it attacks young persons especially, and as the phenomena of growth of the bone takes place under the periosteum and at the epiphyses, the physiological activity of these parts favors a more intense inflammation than in the other portions of the bone.

The primary and predominant symptom of the disease consists in the rapid formation of pus. If an incision is made under the periosteum, about twenty-four or forty-eight hours after the beginning of the malady, a purulent centre is usually opened (Louvet). It is in these cases of rapid and extensive suppuration that we find the bone necrosed in its whole extent, detached from its epiphyses and periosteum, and floating in a vast abscess. A purulent infiltration of the spongy tissue of the extremities and of the medullary tissue is now found; from such a quantity of pus accumulating between the osseous walls of the Haversian canals and the vessels, the latter are compressed and arrest completely the circulation of the blood, causing a necrosis. It is essentially a suppurative inflammation, and the pus is the only inflammatory new formation. Rarefaction of the osseous substance is never observed in these cases. The necrosed bone has the appearance as if it had been macerated in water. So intense or extensive a suppurative inflammation of bone seldom occurs. It may be limited to the neighborhood of an epiphysis; an abscess forms upon the surface of the bone, which, when opened, occasions a series of anatomical changes in the diseased bone, varying according to the case. In the less serious, the inflammation being superficial is followed by the same lesions which occur in simple denudation of the bone, namely, rarefaction of the osseous tissue succeeded by formative osteitis.

In another class of cases, the suppurative inflammation having invaded the medullary canal, openings by which the deep abscess empties itself are produced very slowly and by a process yet unknown, openings either in the middle of the diaphysis, or in the proximity of the epiphysis. In these cases the irritation is intense at the centre of the bone, while at the periphery it is very slight, but it continues upon the surface as long as the inflammatory action at the centre lasts. As a consequence, there are formed under the periosteum new osseous layers, which, being placed one over the other, cause a considerable increase in the diameter of the bone. This peripheral formative osteitis is produced according to the process previously described. A partial necrosis is a very frequent result of suppurative osteitis, when the latter is limited.

Sect. III.—Necrosis.

With the majority of authors, we give the name necrosis to mortification of bone which occurs in consequence of an *injury* or an *osteitis*. Necrosis is occasioned by arrest of circulation, most frequently owing to compression of the vessels in the Haversian canals by pus or by osseous new formations. The mortified bone in process of elimination is named a sequestrum.

French surgeons separate the sequestræ of necrosis from those of caries. When speaking of caries, it will be seen that this distinction is legitimate, not only from the naked eye characters, but also by the process of formation as revealed by the microscope. At present we will consider necrosis proper.

The fragments of bone in a compound comminuted fracture are named splinters. Those which are removed by the surgeon or eliminated by

suppuration do not merit consideration here. Necrosis of the stump after amputation occurs when the inflammation of the end of the bone is intense, or when the bone projects considerably. *À priori*, it is difficult to understand why a thin layer of the cut bone is not always necrosed. After the bone has been sawn, hemorrhage is arrested only in consequence of the coagulation of the blood in the small vessels of the bone close to where they have been divided. The bone cells situated here are deprived of their ordinary means of nutrition, and if they continue to live until the circulation is re-established, they must have other ways of obtaining nutrition, or during a certain length of time they exist without it. The blood plasma which is found in the wound may be a source of nutrition for these cells. In a conical stump, where the bone is in contact with the dressings or external air, mortification of a small portion of the bone very frequently occurs.

The condition of a denuded bone in a wound resembles exactly a cut bone. When necrosis follows an injury, a suppurative osteitis, or a formative osteitis in which the Haversian canals are obliterated (see p. 203), the phenomena of separation and elimination of sequestræ are the following:—

The piece of mortifying bone acts as an irritating foreign body, occasioning around it a rarefying osteitis, and there are seen developed granulations which inclose it. The Haversian canals in the neighborhood are enlarged by the proliferation of the marrow and the absorption of the osseous lamellæ. This absorption continues destroying the living trabeculæ and also those in which the vessels are obliterated, until the canals communicate one with the other. The disappearance of the trabeculæ entirely isolates the sequestrum in the midst of a granulating marrow. The result of this process is that the sequestrum is bounded by a sinuous surface, the prominences of which correspond to the vascular distribution where the circulation has ceased.

The process of elimination differs according to the situation of the sequestrum. If at the periphery of the bone under the periosteum or at the end of a cut bone, it is very soon separated and surrounded by pus; upon the surface of a large wound, as an amputation or denudation of the bone, the mortified part is eliminated without difficulty. If there is no wound communicating externally, a deep abscess is formed, which, when opened, either spontaneously or with the knife, the sequestrum completely detached, is discharged with the pus. But, when the entire bone or the diaphysis is transformed into a sequestrum, the subperiosteal marrow proliferates, becomes embryonic, and occasions the formation of new osseous tissue under the periosteum. The new osseous layers gradually grow thicker until the old necrosed bone is inclosed in a new bone, from which it is separated by a layer of granulations. The sequestrum is now said to be invaginated.

The invaginated sequestrum is never in contact with the enveloping bone. The latter is covered with a layer of granulations which constantly forms pus. When the pus is not readily discharged by fistular openings, it accumulates, desiccates, and undergoes caseous transformation.

Some writers admit that this necrosed bone may be absorbed and gradually disappear by the action of the pus. They base their opinion upon the inequalities and depressions seen upon the surface of the sequestrum. We cannot consent to this manner of view; for, if they had examined with care several sequestræ which had macerated for a long time in pus, they certainly would have found upon them some smooth surfaces. A microscopic examination of a section from these surfaces shows the peripheral lamellæ of the bone. We have found them upon several sequestræ which had macerated thirty years in pus. So that the solvent power of pus for bone is very slight, if it exists at all.

Sequestræ and the bone from which they come present different characters according to the course and cause of the necrosis. In acute suppurative osteitis the sequestrum shows the normal structure of the bone, or the lesions of rarefying osteitis. In a slow form of osteitis, as occurs in syphilis, in phosphorus match-makers, etc., the necrosed bone shows special lesions. In syphilitic necrosis, so common in the bones of the cranium, the sequestrum resembles a fragment of normal bone both externally and internally. At times it presents here and there a loss of substance, giving it the appearance as if there was a rarefaction of the bone. But, if a section is made through the middle of the sequestrum, it will be found that the diploë has been changed into a compact tissue. An invagination like that which occurs in long bones is absent in flat ones; there is in the latter a new osseous formation which takes place at the edges, and incases the sequestrum as a watch-glass. Formative osteitis in syphilis is generally of considerable extent. The diploë of the cranial bones becomes more compact, and upon their external surface small hyperostoses are met with.

A microscopical examination of these sequestræ shows the medullary cavities of the diploë replaced by very narrow canals; and, in good preparations, it is seen that this transformation has taken place in consequence of the formation of osseous tissue, which, being deposited layer by layer in the interior of the canals, has narrowed them. The new osseous layers may be so arranged that the lumen of the canal does not correspond to the centre of the original canal. This process continuing, the canal may be completely obliterated, so that at the centre of the concentric layers, instead of a canal, there is found one or more bone corpuscles. (Fig. 126.)

Necrosis of the maxillary bones occurring in persons employed in manufacturing phosphorus matches furnishes sequestræ which are dense, eburnated, and frequently present upon their surface spongy osteophytes which may be easily detached. In those parts of the sequestrum which belong to the old bone there are found the lesions of condensing osteitis. The density of the osseous tissue and the formation of osteophytes indicate very evidently that the necrosis has been preceded and produced by a formative osteitis of long duration.

Sect. IV.—Caries.

The disease of the osseous system designated as caries is very indefinitely defined by pathologists.

Among surgeons, every suppuration of the osseous tissue, accompanied with great friability of this tissue, is caries. In order to diagnose this disease they introduce, through the fistular opening, a probe, which breaks down the bone, producing a crackling sound, or giving to the hand an equivalent sensation. Pathologists themselves do not agree upon the anatomical characters of this disease. The Germans employ the word caries to designate every rarefaction of bone. Virchow believes the changes which take place in the bone after amputation, the loss of substance in the cranial bones caused by syphilitic gummata, to belong to caries. Billroth considers "the term caries as absolutely synonymous with chronic osteitis with solution of the bone." He describes several varieties according to location, whether internal or external, according to the aspect of the diseased parts, if vascular (caries fungosa), if quite anæmic (atonic, torpid, and caseous caries), also a necrotic caries.

The various lesions described by different authors under caries are consecutive to an initial lesion, which consist in *the destructive fatty degeneration of the cells contained in the bone corpuscles.*

Personal investigations have led us to recognize two distinct stages in caries:—

In the first, *the bone cells undergo fatty degeneration without any previous inflammatory action.*

In the second, the cellular elements of the osseous trabeculæ having died, they constitute so many *small foreign bodies, which occasion around them a suppurative inflammation.*

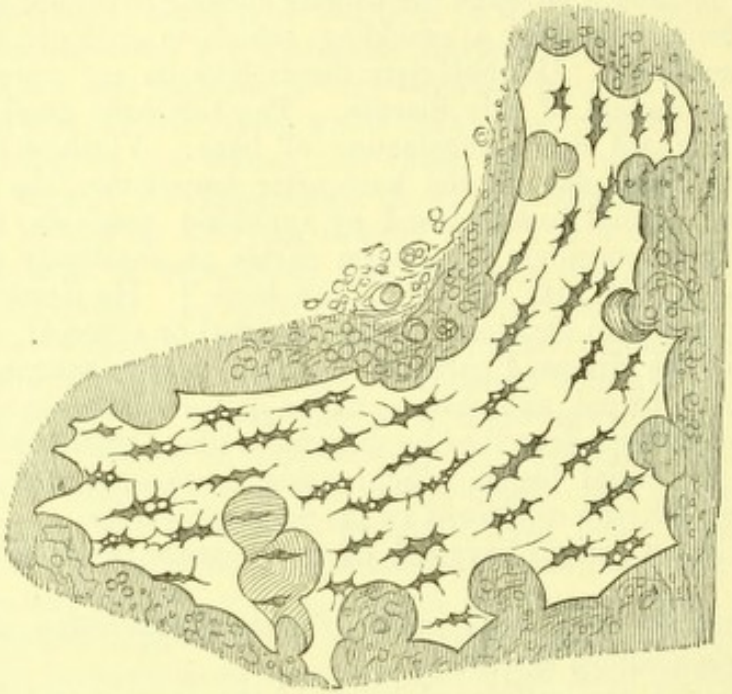
This second stage—in which the osteitis presents special characters in consequence of the cause which has produced it—is the only one which has been described by writers.

Caries generally occurs in the proximity of the articulations; it is always accompanied or preceded by a chronic affection of the joint—*white swelling.* The epiphyses of an articulation attacked with a recent white swelling are formed of very thin trabeculæ surrounded by an adipose marrow. By a stream of water we are able to wash away the fat tissue and isolate the delicate osseous reticulum, which, by microscopical examination, is seen not to have undergone any loss of substance, such as the eroding or notching occurring in osteitis. Their thinness at this time can only be explained by a regular absorption of their surface, or by an arrest of development—a satisfactory hypothesis, if it occurs in a subject whose bones are growing. It is in these trabeculæ that are found the bone corpuscles metamorphosed into granular fat with atrophy of their nuclei. This fatty degeneration of bone cells is found only in caries.

The characteristic alteration of the first stage is continued into the second. New lesions now occur, which are appreciable to the naked eye, and correspond to the anatomical description of caries as given by the old surgeons. These changes are of an inflammatory nature; their

production seems to be connected with the presence of numerous dead trabeculæ irregularly scattered through the osseous tissue, and caused by fatty degeneration. The medullary substance becomes very vascular; the adipose cells disappear, and are replaced by embryonic cells; suppuration is established; those bone cells, not completely destroyed by the

Fig. 127.



Caries fungosa. A fragment of bone with Howship's lacunæ and bone corpuscles containing fat. × 300. (*Rindfleisch.*)

fatty degeneration, become active, and the osseous substance which surrounds them is liquefied; the necrosed osseous trabeculæ become free, and are surrounded by granulation tissue formed by the embryonic marrow. Entering into the constitution of the granulations are numerous and dilated capillaries, which when occurring in fistular tracks or articulating cavities may attain considerable size. Rupture of these dilated blood-vessels may occur, causing interstitial or external hemorrhages. These large granulations form what are known as fungi.

Similar granulations, but smaller and connected together, exist in the enlarged areolar spaces of the epiphyses; sometimes inclosed in this tissue are found osseous trabeculæ, the cells of which are infiltrated by fat. In some cases these small islands of osseous tissue are necrosed; the granulations surrounding them penetrating even to the centre of the trabeculæ of which they are formed.

The characters of the sequestræ of caries are entirely different from those occasioned by a simple osteitis, for they are composed of trabeculæ undergoing fatty change, thin, but not notched; while the sequestræ of osteitis always present the characters of rarefaction or of inflammatory sclerosis, and never contain fat granules in their corpuscles. If fistular openings are established, small trabeculæ and larger fragments are carried by

suppuration to the exterior. When anfractuous cavities exist lined by granulation tissue, which gradually undergoes fibrous organization, there is formed a kind of cyst containing inspissated or caseous pus, frequently mistaken for an old tubercle. In old and suppurating white swellings there are at times observed islands, several centimetres in extent, formed of a badly organized fibrous tissue which is analogous to that which is seen around old fistular openings leading to a diseased bone.

In caries, the embryonic marrow or granulative tissue may undergo caseous transformation in portions of the mass. This change is probably owing to vascular obstruction, and has frequently been considered to be of a tuberculous nature.

Inflammation supervening in a bone attacked with fatty degeneration has a reparative effect; when, by the process which has been indicated, it has succeeded in eliminating all the necrosed fragments, and it becomes less intense, regeneration of the tissue begins. But previous to this, there are exuberant formations in the neighboring parts of the inflammatory centre, under the periosteum, especially around the fistular tracks. The new subperiosteal layers, sometimes thickened, are formed of thin lamellæ slightly separated from each other. The carious processes being very irregular, some parts are eliminated by the long-continued suppurative inflammation, while at the same time, other parts show only slight inflammatory lesions. In the first, eburnation is frequently seen, while in the other, rarefaction still exists. This eburnation may even lead to true necrosis.

In a bone affected with caries the course of the lesions described is not identical in different portions of the bone. Only during the first stage does the entire epiphysis present the same appearance in all its parts. During the second stage, the osseous tissue varies in the consistence and color which is considered, with good reason, to be characteristic of caries. Some parts are yellow, translucent, slightly vascular, with fine osseous trabeculæ (first stage); other parts are vascular and light red in color; sometimes whitish and opaque (carious change, torpid or caseous caries of Billroth); here and there spongy sequestræ are imperfectly detached, and surrounded by bleeding fungi (necrotic caries of Billroth); elsewhere are islands of eburnated osseous substance; finally, upon the surface of the bone newly-formed osseous layers exist, varying in extent and thickness.

From this description of caries, based upon accurate observations, it cannot be considered a simple osteitis, and if inflammation plays an important part in this disease, it certainly does not perform the principal one. The primary fatty degeneration of the bone cells, although often not marked, is nevertheless the true cause of all these disturbances.

Sect. V.—Formation of Callus.

The word callus is employed to indicate not only the cicatrix which is formed between the fragments of a fractured bone, but also the neoplasm which precedes it.

The anatomical phenomena of the formation of callus are complex and

serve as a connecting link between the inflammatory neoplasms and those which constitute tumors.

Fractures may be divided into three classes: A. Those which communicate with the external air (compound fractures); B. Those not complicated with wounds (simple fractures); C. Those which supervene in consequence of a lesion of the bone, which renders it friable (cancer, rachitis, etc.).

A.—Fractures complicated with wounds (compound fractures) are the most simple in a histological point of view, those in which bone is most rapidly produced. The changes occurring are identically the same as in osteitis; at all the irritated points of the surface of the solution of continuity, the marrow becomes embryonic and undergoes changes similar to those of a simple osteitis. Under the periosteum the new embryonic marrow soon forms osseous trabeculæ; five or six days after the accident they may be found. The Haversian canals opened by the fracture are enlarged through the absorption of the osseous substance limiting them; the vessels and marrow which they contain contribute to the formation of the granulative tissue. The marrow in the central medullary cavity undergoes the same modifications, although more slowly. Thus, over the whole surface of solution of continuity there are formed granulations which enlarge and by uniting together constitute an embryonic or inflammatory tissue, in the midst of which osseous trabeculæ are developed, as in the physiological method of ossification. The needle-like points of the old bone seem always to act as a base for the new osseous formation. Growing in every direction, uniting one with the other and with the opposite fragments, they limit the spaces filled with the embryonic marrow. These spaces are gradually narrowed by the addition of new osseous layers, and consolidation is brought about by a firm adhesion between the two fragments of bone.

In experiments made upon small mammiferæ, it frequently occurs that the suppurative inflammation is limited to the part which is in connection with the external wound, while the deeper part of the fracture, not in contact with the air, sometimes presents cartilaginous masses. It will be seen that this formation of cartilage occurs in fractures not complicated by wounds. Suppuration not confined to the surface of the ossifying parts, is similar to that which is seen in suppuration caused by a sequestrum. The formation of callus in this case does not essentially differ from the formation of bone as observed in necrosis.

B.—Fractures not complicated with wounds (simple fractures), both in man and animals, give rise to a cartilaginous callus, which later becomes ossified. Until the time of the excellent work by Cruveilhier, the formation of callus was interpreted differently by different writers. Their theories may be classified into three groups: 1st, that of Duhamel, who derived the callus from the periosteum; 2d, that of Heller, in which an osseous fluid was exuded between the fragments; 3d, that of Troja, according to whom the ends of the fractured bone put forth granulation tissue, which is afterwards ossified. According to the last theory, cicatrization of the bone is effected through the granulation tissue.

By experiments, the results of which were observed by the naked eye, Cruveilhier demonstrated that callus "is formed by the ossification of all the soft parts which surround the fragments." In his description he added that it is the connective tissue which contributes to the formation of the callus, whether it be in the muscle or periosteum.

The only objection to this doctrine is that it is not general enough, for the marrow contained in the medullary cavity and in the Haversian canals may furnish the elements of consolidation.

The first phenomenon occurring in consequence of a fracture is a hemorrhage, which undergoes all the changes of an ecchymosis. The extravasation is generally of such extent as to gradually manifest itself under the skin.

Soon changes due to irritation are produced in the subperiosteal marrow and in that contained in the Haversian canals. This irritation reaching the periosteum and neighboring connective tissue, occasions the formation of numerous cellular elements, so that in five or six days after the fracture all these tissues, swollen and rich in cells, assist in the formation of a peculiar mass, of firm consistence, but not yet cartilaginous. Under the periosteum and between the two fragments, appears a thin pulpy layer which, when examined with the microscope, is found to consist of cells, varying in shape, like those of the embryonic marrow; in the midst of these cells red blood corpuscles and blood pigment are seen. The mass of peripheral embryonic callus is entirely separated from the bone by this pulpy layer. The peripheral mass is bounded internally by the smooth pearly surface of the periosteum. When the surface of the bone is completely stripped of the preceding pulpy layer, the Haversian canals appear in the form of red points or lines, like those seen in the beginning of osteitis.

At a later period, about the eighth day, the cellular elements of the peripheral callus in the course of formation are increased to such an extent that the fasciculi of the connective tissue and the elastic fibres have almost entirely disappeared, while the bloodvessels especially at the margin of the callus have become greatly enlarged. It is at this time that the cells of the peripheral callus are found to be imbedded by a cartilaginous substance, while the cells of the peripheral marrow remain always free. At the period when the peripheral callus is cartilaginous, the bone itself is entirely free of cartilage.

From the tenth to the fifteenth day, calcareous infiltration takes place; it is seen in disseminated spots in the proximity of the bone. This infiltration, however, is preceded by a proliferation, which is similar to that occurring in the physiological ossification of a short bone. There are seen large cartilaginous capsules filled with secondary capsules which open one into the other; afterwards the calcareous incrustation of the cartilaginous substance which separates them takes place in such a manner as to form areolar spaces which communicate with the periosteal marrow, the vessels of the old bone sending out prolongations into them. Osseous trabeculæ are soon developed, the base of which is always implanted upon the old bone.

In most of the cases that we have studied, the first formation of true bone does not take place about the ends of the fragments, but near

the superior or inferior margins of the callus. While bone is found at the margin of the callus, the formation of cartilaginous tissue is extended between the two fragments.

From the fifteenth to the twentieth day, the callus offers a firm resistance, but although the mass is solid throughout, it necessarily has not become true osseous tissue in every part. The peripheral portions, infiltrated with calcareous salts, are not reached by the ossification; it is very probable that they are absorbed without undergoing this change, while the latter is completed in the proximity of the bone between the two fragments. Here the new osseous tissue developed from the intermediate cartilage gradually becomes dense, forming a solid disk, which divides the medullary canal into two parts. At a much later period and by a process imperfectly understood, the osseous disk is perforated in order to re-establish the primitive medullary canal. When this slow process is effected, the peripheral callus has disappeared, so that in some cases it is with difficulty an old fracture can be recognized. Therefore, Dupuytren was right in naming peripheral callus provisional.

We said that all the adjacent soft parts contribute to the formation of callus. Muscle is no exception to the rule, as has been pointed out by Cruveilhier, yet the fasciculi of the muscles take no part; the interfascicular connective tissue alone is the active element. The primary fasciculi undergo fatty metamorphosis, atrophy, and gradually disappear.

Thus two methods for the formation of callus are observed, depending upon the nature of the fracture, whether it is simple, or accompanied with an external wound (compound). In the latter, ossification takes place directly from the embryonic or granulation tissue, while in the former bone is formed from cartilaginous tissue, as occurs in physiological ossification. In the present state of science it is impossible to explain this difference. The presence of bone acting upon inflamed tissue cannot be the cause, since it is the same in both cases; neither can it be a different degree of irritation, for in formative osteitis, whether acute or chronic, the formation of cartilage is not observed. When in a small mammifera the bone is scraped so as to open the medullary canal, the loss of substance is supplied by an osseous tissue of new formation, which is not preceded by cartilage, even when the wound has united by the first intention.

Sect. VI.—Tumors of the Bones.

All the varieties of tumors previously described are met with in the bones; but those occurring most frequently are the sarcomata. In studying the seat of tumors of the bones, an important distinction should be made according to whether the tumor is primary or secondary. In the first case, it is generally the bones exposed to external injuries which are most frequently affected, as the tibia, frontal, maxillary; while the bones most frequently attacked by secondary formations are the spinal vertebræ, sternum, and ribs, that is, those in which red marrow is found. Soft primary tumors, of rapid progress, which are developed in a bone, invade it gradually by destroying the osseous tissues as

they grow. The process of absorption of the osseous tissue does not essentially differ from that occurring in destructive osteitis. Embryonic tissue is developed in the medullary cavities, and causes the solution of the osseous lamellæ; the cells contained in the corpuscles become free, and are added to the mass of embryonic tissue. The morbid tissue of the tumor does not touch the osseous trabeculæ, but is separated from them by a layer of embryonic tissue, from which the tumor is developed. In some cases the morbid process is extended as far as the extremities of the bone; but there, as in osteitis, it is arrested at the calcified cartilaginous layer; seldom is this barrier crossed. Nevertheless, there is generally found at this time a chronic arthritis.

Metastatic formations are much more common than is usually supposed; autopsies must be made very thoroughly in order to discover them.

The PROGNOSIS of tumors of the bones depends upon the nature of each, and we have nothing to add to what we have said *à propos* of tumors in general, except to say, that the medullary system being continued through the entire bone, the tumors are, therefore, very easily diffused, and an operation limited simply to removing the apparent tumor, leaving intact the neighboring osseous tissue, is generally followed by a return of the growth.

VARIETIES OF TUMORS OF THE BONES.—*Encephaloid or round-celled sarcoma* (see p. 79) occurs frequently in the bones, attains considerable size, and is of rapid growth. It is frequently erectile in its nature, and then gives rise to symptoms, which clinically resemble aneurisms of the bones. It sometimes happens that dilatation of the capillaries may be so extensive that they open into one another and form a large sac. In the interior of those sacs there are found thin, soft, and floating shreds, the structure of which resembles that of the morbid tissue which exists at the margins of the sac. From a naked-eye examination carelessly made, these sacs are liable to be considered as aneurisms. Mucoid metamorphosis is also seen is these tumors (see p. 86).

Fascicular or spindle-celled sarcomata of the bones are more common than the preceding variety. The fascicular character of the tumor is more or less complete, and gives them a variable consistence. It is at times difficult to distinguish between encephaloid sarcoma and fascicular sarcoma, especially in cases, not uncommon, where both varieties of tissue are found in the same tumor. The soft fascicular sarcomata are found most often in the body of the bones, while the hard have a preference for the periosteum. We constantly see, in the fascicular sarcomata of bones, large multinuclear cells (giant cells), which here acquire their largest dimensions; but the presence of these cells alone, does not suffice for the recognition of a variety of tumor, neither does it indicate the benignity of the growth. These cells are met with in every variety of bone sarcomata.

Encephaloid and fascicular sarcomata are very often invaded by calcareous infiltration, which does not change the gravity of the tumor. The infiltration is generally in the form of nodules or friable trabeculæ,

in which are found cells from the morbid mass, inclosed in small cavities without prolongations.

Bones affected with sarcoma are very easily fractured at the seat of the tumor. From the sarcomatous tissue there are then developed small islands of cartilage, which do not unite to form a firm callus; but their presence seems to indicate that the fracture acts upon the morbid tissue in the same manner as a simple fracture upon the neighboring connective tissue.

Myeloid sarcomata are quite rare. Their tissue resembles the embryonal marrow of bones, and presents similar histological characters. It is composed chiefly of round cells, distinct and larger than in the normal state. The multinuclear cells (giant cells) are not very numerous. In this variety of tumors, the walls of the bloodvessels are not embryonic, but appear normal.

Ossifying sarcomata are a very common variety: they form almost all the epules, the subungual, and most of tumors known in France by the name of *tumeurs à myéloplaxes*. However, all the tumors which surgeons designate by this last name do not correspond to the ossifying sarcomata, for fascicular sarcomata may contain numerous multinuclear cells (myéloplaxes), and they should not be confounded with the former, for they are relatively non-malignant, while the fascicular sarcomata are decidedly malignant. There are found in the bones other varieties of sarcomata, the *lipomatous* and the *melanotic*, the last as metastatic productions.

Myxomatous tumors of bones are met with in the form of round masses, distinctly limited. They are generally developed under the periosteum, and cause an absorption of the bone upon which they lie. We have never seen them infiltrate the osseous tissue. They should not be confounded with a nutritive lesion of the marrow of bones, which is seen in cachexies of long duration, and is characterized by a gelatinous appearance, due to the absorption of the fat from the adipose cells, which is replaced by serum. This lesion is analogous to that which occurs in the subcutaneous cellular tissue in the same cases.

We have seen an example of a *lipoma* of bone. The tumor was developed in the substance of the tibia, and quite large. The lobules of adipose tissue, instead of being limited by fibrous bands, were separated by trabeculæ of osseous tissue.

Every variety of *carcinoma* has been met with in bones. Well-authenticated primary carcinoma of bone has been seen, but secondary or metastatic is much more frequent. Hard carcinoma of the breast of long duration, is almost always accompanied by secondary growths in the vertebral column. The carcinoma is seldom large; most frequently, the osseous tissue is substituted by the morbid tissue, for example, the body of a vertebra may be almost entirely formed of carcinomatous tissue, without its shape being notably changed. There may even be considerable atrophy of the bones without either ulceration or wearing away. When carcinoma develops in one or more vertebral bodies, a loss of substance occurring, there is caused a convexity of the column, as seen in Pott's disease. The development of the morbid product in the body of long bones or in their extremities, gives rise to

spontaneous fractures. There is then seen a bloody effusion, but never have we been able to discover the least attempt at ossification. The irritation caused by the fracture occasions a transformation of the neighboring tissue into carcinomatous tissue. For the development of carcinoma in bone see page 99.

Tubercles of bones are met with in the spongy tissue of long and short bones, but their favorite seat is the bodies of the spinal vertebræ, the sternum, and the ribs.

In the adult, the medullary substance of the sternum, ribs, and bodies of the vertebræ, is red, inclining to a violet, and very slightly translucent; it consists of the ordinary cells of the marrow, a few adipose cells regularly distributed, and bloodvessels, around which there exists a thin layer of ordinary connective tissue. A tuberculous granulation, situated in such a tissue, has such decided characters that it is impossible to mistake it. It forms a circular spot of one or two millimetres, frequently a little irregular in its contour, quite anæmic, and slightly translucent. The centre is often opaque, while at its circumference the marrow is deep red. The tuberculous nodule cannot be felt with the finger, owing to the presence of osseous trabeculæ.

Tubercles of bones are of two kinds: *disseminated tuberculous granulations* and *confluent tuberculous granulations*.

Disseminated Tuberculous Granulations.—A microscopic examination of a tuberculous granulation, removed with the aid of a needle, and placed under the microscope without being covered with a thin glass, appears, under a power of 150 diameters, to be formed of medullary cells only. But this is not true, the tubercle is only enveloped by the cells of the marrow; for, if the granulation is pencilled, it is not disintegrated; and if now examined, after slight pressure by a thin glass cover, it is seen to consist of very small nucleated cells in a granular or very slightly fibrillated substance. If the granulation is caseous at the centre, it is there opaque.

This method of examination, however, is very unsatisfactory; in order to study the tissue of the granulation, and obtain good results, thin sections should be made from the diseased bone. A granulation included in the section presents the following characters: at its periphery, the marrow contains no adipose cells—the bloodvessels are dilated, and have no connective tissue around them; this zone of irritation frequently extends some distance into the spongy tissue, where the osseous trabeculæ are eroded as in osteitis. Not only around the granulations are the phenomena of irritation to be seen, but at distant points, from which it is rational to suppose that the irritation has preceded the appearance of the granulations. In a word, osteitis precedes tubercles in bones. The tissue of the granulation is composed of small refracting cellular elements, which diminish in size gradually from the periphery to the centre. These elements are imbedded in a resisting granular substance.

Confluent Tuberculous Granulations.—It is very probable that many of the changes described by Nélaton under tuberculous infiltration belong to confluent tuberculous granulations, but his description may serve also for caries with caseous change of fat, for eburnated sequestræ, or for some syphilitic gummata. Without the aid of the microscope it is frequently

impossible to recognize a lesion as tubercular. The granulation is the only characteristic product of tuberculosis, and this cannot be distinguished with the unaided eye when the disease is confluent. A large number of tuberculous granulations forming at once in the same medullary cavity never become so large as the disseminated granulations; they very rapidly undergo the cheesy metamorphosis, and cause a similar transformation of the interposed medullary substance. Again, the development and structure of the tuberculous granulation are always the same, whether disseminated or confluent.

Tuberculous granulations when developed in bone occasion an obliteration of the vessels. Therefore, if several granulations are included in the same medullary cavity, occupying different positions, it is evident that perhaps all the vascular branches of this cavity will have their circulation arrested. The spongy tissue, not containing granulations, but surrounded by the tubercles, is also strikingly anæmic. The parts of bone where the circulation has been arrested undergo caseous transformation, for the same reason that infarcti become cheesy.

Frequently the areolæ, which have become caseous by obliteration of the vessels, are different from those which have undergone the same modification by a breaking down of the tuberculous granules. In the first, the adipose cells are not destroyed, or their place is marked by groups of stearic acid crystals; in the second, the adipose cells have disappeared, leaving no trace, from the fact that osteitis has preceded the tubercles.

The caseous metamorphosis of the marrow claims consideration. Before undergoing fatty degeneration it becomes at first translucent, the medullary cells appear to shrink and unite together—this stage is of short duration, and is seen in a very limited area, and it is soon followed by the caseous metamorphosis. It is not possible to determine where this change first occurs, whether in the marrow or in the tubercle.

The osseous trabeculæ included in the caseous mass have seldom undergone either condensation or rarefaction. External to the tuberculous formation, it is not customary to meet with any considerable alteration of the osseous tissue, except rarefaction.

The bone corpuscles do not participate in the caseous change of the marrow, their nuclei become irregular, but around the latter there are no fatty granules. This may be learned by coloring with aniline red, which distinguishes the caseous transformation consequent upon confluent tubercles, from that which accompanies caries. In caries the bone corpuscles break down by a fatty degeneration, while the portions of bone invaded by tuberculosis not receiving blood are necrosed, and elimination takes place at the time the eruption is completed in a part. The elimination very probably is produced, as in a simple necrosis, by means of a rarefying osteitis, which occasions the absorption of the osseous trabeculæ, and even the development of a granulation tissue. In this manner is formed a cavity in which is found a sequestrum surrounded by pus.

At the present time, when there is found in a bone a cavity lined with granulation tissue or a smooth membrane filled with pus or cheesy material, it can be logically considered of tuberculous origin only when there exist in the surrounding tissue tuberculous granulations appreciable to

the unaided eye or with the microscope. A sequestrum of spongy tissue surrounded by pus or infiltrated with caseous matter should be attributed to confluent tubercles only if disseminated or confluent granules are present in the surrounding bone. Indeed, simple osteitis, caries, and gummata may occasion modifications of the osseous tissue, to the unaided eye, similar to confluent tubercles at their time of evolution or elimination.

Gummata of bones are found in the same localities as tubercles. It should, however, be remembered that the bones of the cranium never contain tuberculous granulations, while they are a favorite seat for gummata. Anatomical observations of gummata of bones are rare; although clinically very frequent, patients seldom die of syphilis. Two forms occur: in one they are limited, resembling in appearance and consistence a hard sarcoma; in the other they infiltrate, as it were, the osseous tissue, and it is to this latter variety the name of gummatous osteomyelitis is given.

Circumscribed gummata of the bones of the cranium develop first under the pericranium or beneath the dura mater, and sometimes even simultaneously at both of these points; growing in the form of a cone into the osseous tissue, in which they occasion a progressive rarefaction. They undergo albuminoid degeneration, and, if we accept the description of Virchow, are slowly absorbed (probably under the influence of appropriate treatment). In their place there is formed a stellate cicatrix of osseous tissue derived from the fibrous tissue. Although it is seen from the description even of Virchow that these cicatrices correspond to old gummata, yet this author designates them by the name of *dry syphilitic caries*. It is very evident, from the description given of caries, that there is nothing in common between this lesion and that due to syphilis. This singular loss of substance, truly characteristic of syphilis, is limited by a sclerosed osseous tissue, and at times by flat osteophytes which surround the central depression.

Diffused gummata of bones are particularly common in the subcutaneous parts of the osseous system and palatine arches. Their formation takes place under the periosteum and in the corresponding osseous tissue at the same time; at first in the form of a soft, slightly gelatinous, red tissue, soon becoming firmer and opaque. Upon section of the bone at this stage a whitish surface is seen, of cheesy appearance, similar to confluent tubercles of bone. But a very evident difference may already be recognized: under the periosteum there exists a pulpy layer, also whitish, over a space corresponding to the bone lesion.

A microscopic examination shows the osseous trabeculæ, as in rarefying osteitis and the enlarged medullary spaces, to contain gummatous nodules (see p. 200). In these nodules the bloodvessels have remained permeable, differing in this respect from tubercles. At the margin of the gumma are seen all the characteristics of simple osteitis.

What ultimately becomes of these diffused gummata of bones? An answer to this question by a complete series of anatomical data would be desirable; but, in their absence, the clinical and anatomical observations may be referred to. It is well demonstrated that gummata, for example of the tibia and sternum, may entirely disappear under the

influence of anti-syphilitic treatment, or leave in their place hyperostoses analogous to those which accompany circumscribed gummata of the cranial bones. Again, syphilitic necrosis is seen in which the sequestræ, instead of being eburnated, are excavated with numerous cavities filled with a caseous detritus at the time of examination, and which probably previously contained gummatous tissue. Virchow believes that every syphilitic necrosis has a like origin; but, from what has been said concerning necrosis, it is very certain that the death of bone results frequently from a condensing osteitis or sclerosis, continued until the obliteration of the vascular canals is accomplished.

Chondromata are developed more frequently in the osseous tissue than in any of the other tissues. They should be named *perichondromata* when seated under the periosteum, and *enchondromata* when developed in the substance of the bone. They may be diffused or lobulated; the latter form is the most common.

Every variety described at page 128 may be met with in bone, for example hyaline chondromata, lobulated chondromata containing fibrous trabeculæ or fibro-cartilaginous, ossifying chondromata, mucous chondromata, with ramifying cells, etc.

These different tumors are developed as described at page 129. In regard to their prognosis, see page 131.

Osteomata or tumors of osseous tissue, are named exostoses, hyperostoses, or osteophytes, according to the shape of the new formation upon the surface of the bone (see p. 132). The name enostoses has been given to the osseous formations developed in the medullary canal.

In leucocythæmia, *lymphatic tumors*, or lymphadenomata, have been found in bone. In a case published by us in 1867, the tumor was quite large, consisting of a whitish tissue which, when scraped, exuded a lactescent fluid, containing cells analogous to the white blood corpuscles. In some localities the tumor had undergone caseous transformation. A microscopic examination of thin sections showed the reticulated stroma of adenoid tissue. To the unaided eye, the tumor resembles a carcinoma.

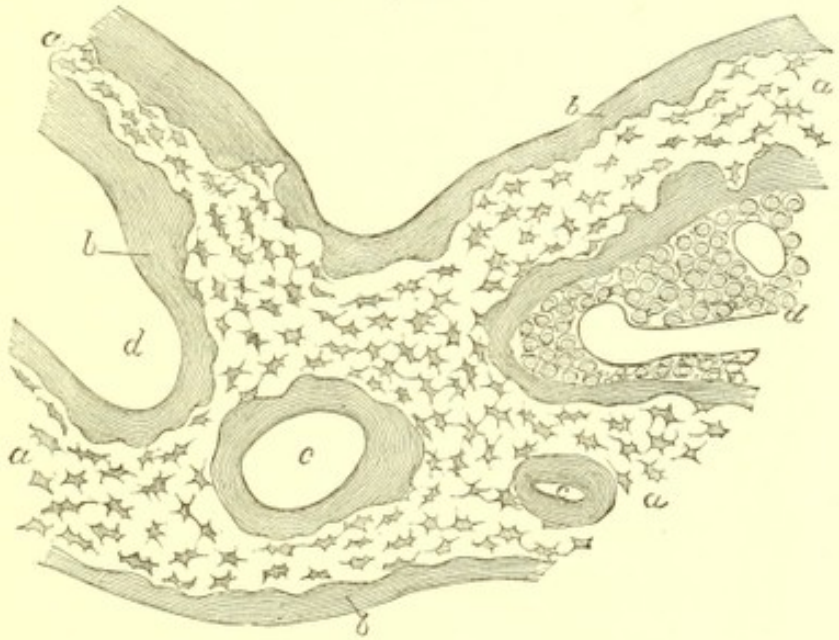
Epitheliomata of bones.—It is uncertain if there is ever a primary epithelioma in bone, but its extension from neighboring tissues is not uncommon. An epithelioma of the lips may extend to the bones of the jaw, of the palate to the palatine epiphysis; an epithelioma of the extremities may also extend in depth and reach the underlying bones. The development of the morbid mass is by epithelial pegs, which penetrate and develop in an embryonic tissue formed at the expense of the osseous tissue, as in osteitis. (See p. 197.) Tubular epitheliomata are met with in bones, being not uncommon in the superior maxillary, and they are then consecutive to tumors of the soft palate or maxillary sinuses. A case of cylindrical epithelioma has been reported by Gawriloff; this is not surprising when it is remembered that these epitheliomata behave as carcinomata in their generalization.

Cysts are sometimes met with in bones, presenting the usual characters of such formations.

Sect. VII.—Osteomalacia.

True osteomalacia is a disease which most frequently occurs in women after one or more labors; it is characterized particularly by a nutritive lesion of the bones, which results in the absorption of the calcareous salts of the osseous substance and the solution of the osseous trabeculæ. At the same time, important changes occur in the marrow. During the first stage, the bones retain their size and present no rarefaction, yet they may be cut with a knife. At this time the middle of the osseous trabeculæ still contains calcareous salts, while their edges are deprived entirely of them. According to Rindfleisch, it is this last portion alone

Fig. 128.



Softening of bone. Spicula of bone from the spongy substance of an osteomalacic rib. *a*. Normal osseous tissue. *b*. Decalcified osseous tissue. *c*. Haversian canal. *d*. Medullary spaces. The space to the right is filled with red medullary tissue, in which the lumina of the capillaries are open. × 300. (*Rindfleisch.*)

that is capable of being colored by carmine. The vessels of the marrow are congested with blood; the adipose cells less numerous than normal; in their place are found round or irregular, sometimes fusiform or flattened cells. Soon there occurs in the marrow diffused hemorrhage in the form of ecchymotic spots. These hemorrhages may also take place beneath the periosteum.

In the second stage, the bones become greatly deformed, they either bend upon themselves or fracture, and it is at this time that such extraordinary deformities are seen. In this second period, not only are the osseous trabeculæ decalcified in their entire thickness, but they are also even in great part absorbed. The enlarged medullary cavities are filled by an embryonic marrow having the appearance of the splenic pulp. The coloring matter of the blood is constantly found in the medullary cells in the form of yellow, red, or brown pigment. This pigmentation arises from the bloody extravasations above mentioned.

Fractures during the course of this disease are not generally united; nevertheless, authors have reported cases in which there has been formation of callus; but it is only when the disease is in process of recovery.

We have not yet been able to give any satisfactory explanation of the decalcification or absorption of the osseous tissue. The formation of an acid capable of dissolving the lime salts has been suspected, but the acid is not known. Weber has found free acid in the urine of persons suffering with this disease. Rindfleisch believes that the calcareous salts are dissolved by the action of an excess of carbonic acid. The venous congestion of the marrow that occurs during the first stage occasions a stasis. The blood, charged with carbonic acid, is in contact with the osseous trabeculæ and causes a solution of the calcareous salts. This, however, is only an ingenious theory.

Senile osteoporosis, also described as *senile osteomalacia*, is a rarefaction of the osseous tissue by an enlargement of the medullary spaces. In this disease the friability of the bones is owing simply to their rarefaction; there is not a softening of the bones by decalcification as in true osteomalacia. Accompanying the rarefaction there are important modifications of the marrow, presenting some analogy to those occurring in true osteomalacia. There is also, to a greater or less extent, disappearance of the adipose cells, and a formation of cells similar to those of embryonal marrow. Newly-formed young connective tissue is at times found in the medullary spaces.

The bones most frequently attacked with this disease are the ribs and vertebræ. The vertebral column becomes curved, the ribs are fractured by the slightest effort, and, what is very singular, they are afterwards firmly united by the formation of a cartilaginous callus, which afterwards is ossified.

Fatty osteoporosis is a rarefaction of the osseous tissue which is seen especially in the epiphyses of long bones or in short bones. It is characterized by an abundant formation of adipose cells in the medullary spaces and in the Haversian canals The osseous trabeculæ of the spongy tissue at first become very thin, and finally disappear. The bone is reduced to a parchment-like shell, pierced by numerous vascular openings. This disease is met with in chronic affections of the articulations with immovable joints.

Sect. VIII.—Rachitis.

Rachitis is a disease of the osseous tissue occurring only during the development of the bone. Characterized histologically by disturbances of nutrition and of development of the tissues which contribute to ossification; these tissues are the epiphyseal cartilage, the periosteum, and the marrow. It is a very common affection, especially in large cities, and principally among the poor.

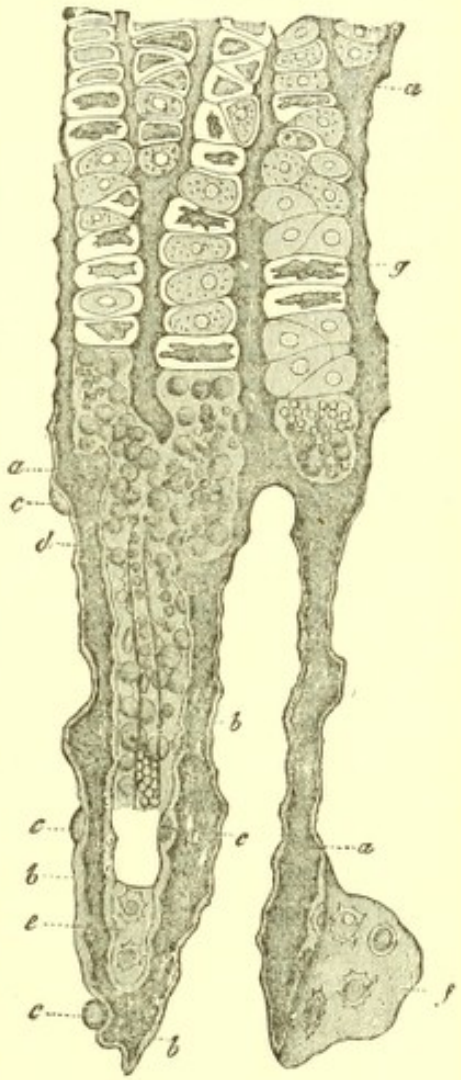
During the first stage of this disease there is no deformity; in order to ascertain how frequently it occurs, the bones of every dead child should be examined.

Three periods of this disease are recognized: first, one in which the

bones are not deformed; second, one in which deformities exist; and finally, a third, in which the diseased bones are consolidated.

If the histological lesions only are considered, there is not any very marked difference between the first and second periods. The same process continues, extends further into the bone, and determines modifications, appreciable upon the living subject.

Fig. 129.



Vertical section from edge of ossifying portion of the diaphysis of a metatarsus, from a fœtal calf. *a*. Ground substance of the cartilage; *b*, of bone. *c*. Newly-formed bone cells in profile, more or less imbedded in intercellular substance. *d*. Medullary canal in process of formation, with vessels and medullary cells. *e*, *f*. Bone cells on their broad aspect. *g*. Cartilage capsules arranged in rows, partly with shrunken cell-bodies. (*Müller.*)

Normal ossification of cartilage occurs with great regularity. (See p. 28.) The cells of embryonic cartilage swell, while the capsule surrounding them becomes spherical; the cells afterwards divide and are inclosed within secondary capsules in such a manner that each primary capsule contains from four to ten secondary capsules. The primary enlarged capsules are elongated by mutual pressure, so as to converge towards the point of ossification. The layer in which these changes takes place is bounded by two parallel lines, one to one and a half millimetres apart; this layer is apparent to the unaided eye by its translucency and bluish color, and is found between the formed osseous and cartilaginous tissues. This layer has been badly named by Broca *chondroid*, which would indicate that it consists of a tissue only having the appearance of cartilage, while it is in reality formed of proliferating cartilage.

When rachitis begins, there are seen in this layer modifications which are continued during the duration of the affection. With the unaided eye it is seen to be increased in thickness to the extent of several centimetres; instead of being regular, it is upon both sides very irregular. Sometimes very long prolongations extend into the bone, frequently so thin that they are separated and form small islands. The layer is also furrowed by medullary canals, containing dilated bloodvessels.

A microscopic examination of this layer shows a striking analogy to that presented by the physiological proliferating layer of cartilage. In the diseased layer, however, the primary capsules are much more distended and contain a greater number of secondary capsules which are larger than in the normal. Beneath this layer and continuous with it, there exists a red vascular and spongy tissue resembling a bone that has been

partially softened by an acid. In order to understand the significance of this layer, it is necessary to recall in a few words the tissue existing here in a physiological condition.

In the physiological state, beneath the proliferating cartilage, is found a thin layer, formed of areolar tissue, the trabeculæ of which are composed of the fundamental substance of cartilage infiltrated with calcareous salts; the alveoli containing embryonal marrow and vessels. Beneath this the true osseous tissue is formed. To this layer is given the name of ossiform, bone-forming.

In rachitis we do not think with Broca, that it is a simple increase of thin layers of bone, but there is formed upon its surface a peculiar tissue, to which Guérin gave the name of *spongoid*. This tissue, which often extends from the margin of the cartilage to the diaphysis, frequently invading both, is red, formed of alveoli of very irregular dimensions; it appears to contain much blood, its consistence is that of a fine sponge, or better, that of the osseous tissue of the epiphysis, which has been incompletely softened by an acid. The boundary between this spongoid tissue and the cartilage is very distinct. At times small islands of hyaline cartilage are found in its interior. On the side of the old bone, it is often impossible to indicate exactly where it ceases.

At the periosteal surface, the spongoid layer, especially at the margin of the diaphysis, is mingled with a tissue formed of osseous lamellæ, separated from each other by a soft tissue, of which we will presently speak.

A microscopic examination of fresh sections of the trabeculæ of the spongoid tissue shows angular corpuscles arranged irregularly in a granular non-laminated substance. These corpuscles, larger than bone corpuscles, do not present any anastomosing canaliculi at their margins. To understand the importance of the tissue which form these trabeculæ, their formation from hyaline cartilage must be traced. There is then seen starting from this cartilage a calcareous infiltration of the segmented fundamental substance which separates the large corpuscles; this calcareous infiltration extends to the secondary capsule (which never is the case in physiological ossification); it results in the whole cartilaginous tissue being invaded by calcareous granules, which remain distinct, that is, separated by cartilaginous tissue which preserves its flexibility. The secondary capsules are not dissolved—an essential difference from physiological ossification. At the same time that this calcareous incrustation occurs, the vascular canals of the cartilage are enlarged by the dissolving the calcified tissue which surrounds them, uniting with each other and opening into the medullary spaces of the old bone. By their union they form a cavernous system to be later studied.

The spongoid tissue is, therefore, formed of trabeculæ representing portions of cartilaginous tissue infiltrated with calcareous salts. These trabeculæ, when young, permit the cartilage with its capsules to be distinguished—the margins of the latter, however, are difficult to recognize, owing to the calcareous incrustation. In older trabeculæ, the capsules are entirely hidden, but in order to make them visible, it suffices to dissolve the calcareous salts with hydrochloric or chromic acid. It may happen that these reagents do not reveal the presence of cartilaginous

capsules, but disclose only angular corpuscles arranged in a fundamental substance which seems homogeneous after the solution of the calcareous salts. Never in these trabeculæ can be recognized osseous lamellæ, or a laminated appearance resembling that seen in osseous trabeculæ treated by acids. The spaces which these trabeculæ of the spongoid tissue bound continue to enlarge if the process persists, which is the opposite to normal ossification, where the medullary spaces are narrowed by new osseous layers. The marrow contained in these spaces is at first soft, red, and by microscopic examination is seen to be composed of round or angular cells, some of which are pigmented, and to contain numerous blood corpuscles. But in the older medullary spaces, the contents are more consistent, the cells become stellate, and separated by a slightly fibrillated fundamental substance.

This attempt at fibrous organization of the marrow, takes place not only in the medullary cavities formed during the evolution of rachitis, but in the old marrow contained in the spongy tissue, in the Haversian canals, in the central canal and in the sub-periosteal marrow.

In the medullary canal, the peripheral layers of the marrow are those which are the most modified. While the central portions of the marrow are red and fluid, composed of embryonic marrow, the peripheral portions are organized into a kind of young connective tissue, which has the appearance of a medullary membrane. It is possible that it was this condition which led the old anatomists to admit the existence of a medullary membrane.

The layer of marrow beneath the periosteum, which has been mentioned several times, is changed at the commencement of the disease into a soft connective tissue ; later it becomes more solid, adheres to the under surface of the periosteum and to the bone, so that its separation from the bone is much more difficult than is customary in young persons. This connective-tissue layer, truly sub-periosteal, at times acquires a considerable thickness. It undergoes a very interesting modification, the nature of which is not determined, consisting in the appearance of waving refracting trabeculæ, anastomosing one with the other, which come from a transformation of intercellular substance of the young connective tissue. These trabeculæ are the analogues of Sharpey's fibres, which are seen in the ossification of the secondary bones of the cranium ; they differ from them however by containing cells in their interior. The tissue which forms these trabeculæ is considered by Virchow as representing the first phase of ossification, and is named by him osteoid. Sections of this tissue made perpendicular to the axis of the bone, colored by carmine and treated with acetic acid, show stellate bodies, with an anastomosing appearance, throughout the whole thickness of the preparation, both in the refracting trabeculæ and in those parts which look like ordinary connective tissue. In the refracting trabeculæ the stellate bodies seem larger and have a more distinct contour.

When rachitis of a bone is very much advanced, there is found beneath the osteoid tissue thin lamellæ forming complete cylinders around the bone, and separated from each ether by a soft and vascular connective tissue. These lamellæ which are formed of true osseous tissue, are spongy, and the cavities which they contain are filled with young con-

nective tissue. This singular form of tissue is a result of a fibrous transformation of the old marrow, with partial absorption of the previously formed bone.

As the disease progresses the marrow in the Haversian canals undergoes fibrous transformation in the whole thickness of the compact part of the diaphysis, at the same time the osseous trabeculæ are absorbed, and the bone cells become free. A bone which has undergone such changes loses its resisting power, may become curved by the weight of the body, or suffer incomplete or complete fracture.

In a fracture, the callus is entirely composed of osteoid tissue, analogous to that which is formed under the periosteum. The callus of osteoid tissue is generally very large. It is not necessary to insist upon the importance of this accidental new formation, resembling exactly that which is formed under the periosteum in the natural course of this disease. We have seen old callus in rachitis, but produced when the disease was progressing, and the union was effected by true osteoid tissue, and not formed from osseous tissue.

It is not yet known what changes are produced in bones affected with rachitis when the recovery supervenes through osseous consolidation. Some believe the recovery occurs by a simple deposit of calcareous salts; but this hypothesis is not supported by any histological evidence, and is not in harmony with the phenomena of physiological ossification.

CHAPTER II.

LESIONS OF CARTILAGE.

Cartilaginous tissue is a living tissue capable of undergoing a series of primary alterations. In the adult, in the normal state, it never contains vessels. Nevertheless, it is susceptible of experiencing lesions of irritation (see p. 55), besides lesions of nutrition which affect the cells or the intercellular substance.

Lesions of nutrition which affect the cells of the cartilage are:—

a. Fatty degeneration, which should not be confounded with the fatty infiltration constantly met with in the cartilages of adults.

This fatty degeneration causes the death of the cellular elements of the cartilage, so that in a cartilage where it is present, there is seen, instead of the capsule and cell, small collections of fatty granules. The intermediate fundamental substance is softened, often cracked. This alteration is primary; it does not belong to inflammation, which in cartilage is characterized by an opposite phenomenon, the disappearance of the fat contained in the cells.

b. Infiltration of urates, which begins in the cells of the cartilage, has been already mentioned, page 52, and will be fully explained under gout.

Lesions of nutrition which affect the fundamental substance are:—

c. Mucoid degeneration occurs physiologically in the costal cartilages (see p. 44), and may occasionally occur in other cartilages; it is usually accompanied by a segmentation of the fundamental substance.

d. Calcareous infiltration, which is the reverse of infiltration of urates, begins always in the capsules of the cartilage, and extends into the fundamental substance, never invading the cells.

e. Infiltration of urates into the fundamental substance; it consists in the formation of crystalline needles of urate of soda.

Lesions from irritation of the cartilage are explained by the modifications which occur at the same time in the cells, in the capsules, and in the cartilaginous substance. In most cases, as the cells within the capsules are divided, they generate around them new cartilaginous capsules; but it also happens at times that the cells which result from the division of the old cells have lost the property of forming new capsules, and then they remain in the state of embryonic cells. This last phenomenon is seen in cases where the irritation is very intense, or when it is associated with calcareous infiltration. The embryonic cells which result from this proliferation remain as such, or they become the point of origin of an osseous or fibrous new formation.

These lesions are essentially similar to those occurring in cartilage in the proximity of points of ossification.

The phenomena resulting from this process vary a little, according to

the cartilages affected. In the diarthrodial articulations the cartilages are free at the articular surface, and are not there covered by a perichondrium; there is then seen upon this surface a series of alterations, which will be described under acute and chronic arthritis.

When the cartilages are covered by a fibrous membrane, as the cartilages of the larynx, the costal cartilages, and the intervertebral disks, the cells of the cartilage multiply, and are surrounded always by secondary capsules, giving rise to the formation of new masses of cartilage. It then almost constantly happens that the irritation terminates in a true ossification. This is noticed particularly in the thyroid cartilage of young persons suffering for several years with phthisis; the ossification is here caused by a process similar to that of physiological ossification.

A slight continuous irritation of cartilage always terminates in osseous new formations. The facility with which the ossification of proliferating cartilage occurs explains why, in fractures of the costal cartilages, the callus is frequently entirely osseous. It has been previously stated that, in fractures of the costal cartilages, the irritation supervening at the ends of the fragments occasions inflammatory changes. The fundamental substance is infiltrated by calcareous salts; the primary capsules are greatly enlarged and communicate with one another; the cells become free in the interior of these cavities; the formation of marrow and of bone takes place in a physiological manner. The formation of osseous tissue in fractures of cartilage is truly a singular occurrence, for, subperichondrial resections, made by M. Peyraud, always gave him cartilaginous regenerations. Suppuration of the wound which extends into the resection does not prevent the regeneration of the cartilage which takes place from the preserved perichondrium, the regeneration contributing to form the wall of the abscess. Therefore suppuration does not prevent the new formation of cartilaginous tissue any more than it does the formation of osseous callus in a compound fracture.

There are tumors developed from pre-existing cartilage which are composed of cartilaginous tissue. By their slow development and their unimportance they are entirely separated from chondromata proper. These cartilaginous formations are named ecchondroses, and are found most frequently in arthritis, under which they will be described.

CHAPTER III.

PATHOLOGICAL ANATOMY OF THE ARTICULATIONS.

Sect. I.—Normal Histology of the Articulations.

Previous to beginning the anatomical study of articular affections it is expedient to give, in a concise manner, the structure of the most important parts which enter into the composition of joints in a normal state. The cavities of the diarthrodial articulations are limited by the surfaces of the cartilages and the synovial membrane. The elements of the diarthrodial cartilages have an unvaried arrangement. When a transverse section of these cartilages is made, there is seen a number of superimposed layers in regular order. At the free surface the capsules are flat and lenticular; beneath these the capsules are round, containing only one cell like the preceding; deeper the capsules are lengthened perpendicularly to the surface, and contain two, three, or a greater number of secondary capsules placed one behind the other. The enlarged primary capsules form linear series which are continued into the deepest layers, where there is an infiltration of calcareous salts, uniting the hyaline cartilage with the osseous tissue. All the cells contained in the capsules at the surface and in the middle layer inclose granules and even drops of fat. The calcified layer is bounded on the cartilage side by a sinuous line; on the bone side are hollows and prominences, in which fit papillary prolongations from the extremity of the bone. In the centre of each of these osseous papillæ there exists a medullary and vascular cavity in communication with the medullary and vascular tissue of the spongy substance of the bone. If, therefore, the plasma of the vessels goes to the hyaline cartilage, it must pass through the osseous layer and the layer of calcified cartilage. Yet these last layers do not contain canals, and do not appear permeable; so that the nutritive material reaches the cartilage in some other way. Very probably the nutriment comes from the fluid which bathes the articular surfaces, and which is exuded from the vessels of the synovial membrane.

The synovial membrane presents for consideration a plane surface and a villous surface. The plane surface is composed of layers of fibrous tissue intermingled with numerous elastic fibres, in continuity with the periarticular connective tissue, and lined with a single layer of flat epithelial cells, resembling those on the large serous membranes. The villous surfaces named synovial fringes, are especially seen at the points where the membrane forms folds in order to pass from one surface to another. Their base is constituted by two supporting layers of the synovial membrane, resembling the peritoneum where it forms the mesentery. Between these two layers there are found loose connective tissue, groups of adipose cells, and numerous bloodvessels. All of these, on account

of their thinness and transparency, may be examined by cutting the synovial fringe from its base. If the vessels are a little congested, the large size of the arteries and veins is noticeable. The capillaries form a very dense plexus at the free extremity of the synovial fringes.

From these extremities proceed bodies of various shapes; some are filiform prolongations made up of an axis of connective tissue, and covered by two, three, or more layers of epithelial cells. The latter are provided with prolongations which join them together, and contain nuclei, the membrane of which presents a double contour. This epithelium resembles very closely that seen upon the choroid plexus. At times the prolongations have the shape of a club, covered with a similar layer of epithelium; their axis formed of connective tissue frequently contains cartilage capsules. Vessels are never found in the prolongations. At their base, which is generally wide and continuous with the synovial fringe, there are seen one or more vascular branches.

The physiological function of the synovial fringes is very important. The cells which cover the prolongations are the true organs for secreting the synovial fluid, and the large and numerous vessels found in the fringes carry the material for this secretion.

The synovial membrane does not cover the surface of the diarthrodial cartilages at the points where the cartilages slide upon one another.

The synovial fluid is a very complex liquid containing albumen, mucin in large proportion, and a small quantity of fat, which, under the microscope, appears as granules and small drops. Epithelial cells and cells resembling white blood corpuscles are also found.

The varieties of arthritis are *acute arthritis*, *chronic arthritis*, *scrofulous arthritis* or white swelling, and *gouty arthritis*.

Sect. II.—Acute Arthritis.

A.—Simple Acute Arthritis and Rheumatic Arthritis.—Traumatic arthritis in man very probably presents the same lesions histologically as rheumatic arthritis. The anatomical lesions of the latter do not differ from traumatic arthritis artificially provoked in the higher animals.

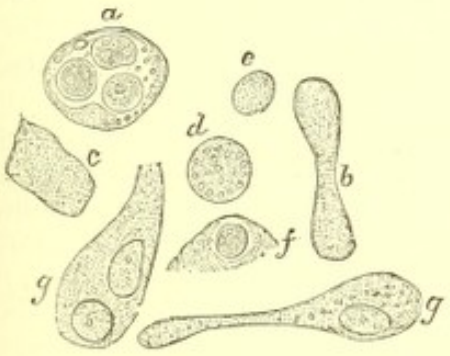
When an inflamed articulation is opened, there flows from it a viscid ropy fluid, the amount and appearance of which vary according to the degree and duration of the inflammation. In some cases, this fluid resembles the normal synovial fluid, but is more abundant; like synovia, it coagulates by the addition of acetic acid; it contains a large number of cellular elements, some of which resemble pus cells, others much larger, are round, and contain one or more vesicular nuclei. In the protoplasm of these cells fatty granules are generally seen, which sometimes are very abundant, and the cell then has the appearance of a granular body (corpuscle of Gluge). The synovia is more or less cloudy, depending upon the number of cellular elements and the degree of their fatty change.

There are usually seen in the liquid mucous flakes similar to sputa. These flakes are transparent or slightly opaque, and present all the inter-

mediate degrees between mucous and purulent sputa. At times these flakes have a greater consistence, and when examined with the microscope are found to contain the cellular elements above mentioned, separated from each other by granules or fibrils bathed in the synovia. The puriform appearance of the flakes depends upon the number of cells they contain. In some cases of acute rheumatism, where the inflammation has attacked several articulations, or only a single one, the articular cavity is filled with a creamy pus analogous to that of an acute abscess.

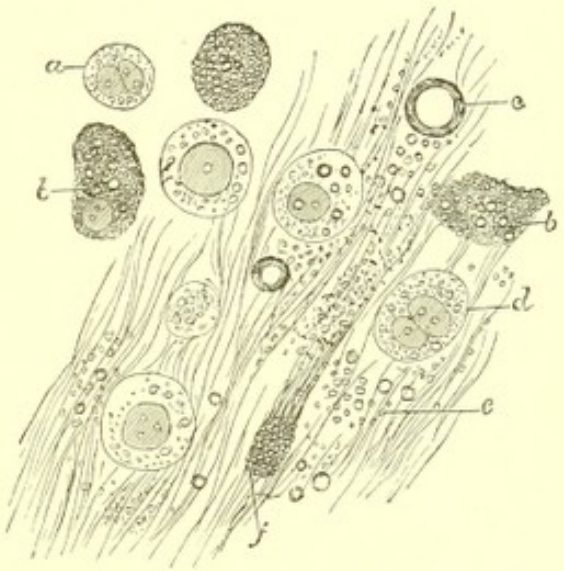
The synovial membrane is injected, the capillaries are dilated into ampullar or spindle-forms. The cells of the synovial fringes present very evident signs of multiplication, their nuclei become vesicular and show one or more bright nucleoli. The nuclei are seen in the process of dividing, and some cells possess as many as ten or twelve separate nuclei.

Fig. 130.



Cells contained in the exuded fluid from the articulation at the knee of a dog, the articular cavity having been opened four days previously in order to cause a suppurative inflammation. *a*. Mother-cells. *b*. Hour-glass cells. *c*. Cells which do not show the nucleus without the addition of water. *e*, *d*. Pus corpuscles. *g*. Cells containing two nuclei. High power.

Fig. 131.



Mucous and fibrinous flakes of the synovial fluid in acute articular rheumatism. *d*. Large cell. *f*, *b*. Granular bodies (corpuscles of Gluge) resulting from the fatty degeneration of cells. *e*. Drops of free fat. *a*. Corpuscle resembling pus or lymph. *c*. Fibrinous reticulum, entangling cells, fatty granules, and fat drops. High power.

In a case of acute articular rheumatism examined twenty-four hours after death, the epithelial cells of the synovial fringes were much more transparent, their nuclei were seen without the aid of any reagent, and surrounding them were some fat granules or small drops of mucin. The shape of these cells in man is always spherical; they may attain a large size; their nuclei are vesicular, their nucleoli round and refracting, giving them the shape and dimensions previously ascribed to the cells of cancer.

Generally, in this form of arthritis, the connective and adipose tissues are not notably changed; but, if the inflammation has continued a long time, the lesions of inflamed connective tissue are then seen.

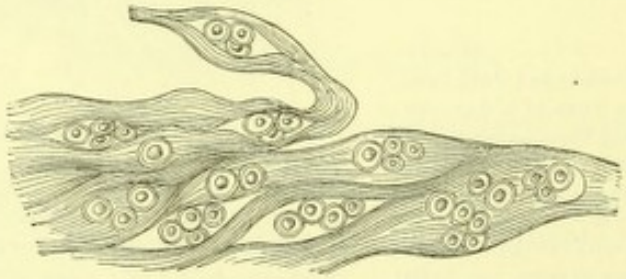
The synovial membrane is not the only part of the articulation which

may be affected in acute arthritis; even in slight attacks, a modification of the diarthrodial cartilage is constantly seen. For this reason, we object to the names of synovitis and arthromeningitis, given by Volkmann. We do not think that in acute inflammations of the joints the synovial membrane is the only part affected.

The lesions always present in the cartilage consist of a nutritive irritation and a proliferation of the cartilage cells, which is very readily appreciated, since the arrangement of the cellular elements and capsules in diarthrodial cartilages is very regular.

As seen in transverse sections, the superficial lenticular capsules which inclose the cellular elements, not very distinct in the normal state (see p. 227), are the first to be influenced by the inflammatory irritation. The protoplasm of these cells swells, the nuclei increase in size and become vesicular. A very distinct nucleolus appears; the capsules, which were flat, become spherical. (Fig. 132.) By the application of picric acid upon fresh pieces, all these changes are rendered very manifest, as is also the division of the nucleus which involves the segmentation of the protoplasm. The capsule may at one time contain several cells, but soon each cell is inclosed in a secondary capsule, so that the lenticular capsules of the surface which, in the physiological state, never contain more than a single cellular mass, envelop now two or a greater number of secondary capsules. Most writers who have remarked this phenomenon (Redfern, V. Weber, etc.) in chronic arthritis only, have taken the secondary capsules for the cells. This mistake may be avoided if a solution of iodine is added, which colors the protoplasm of the cells brown and gives a lighter color to the secondary capsules.

Fig. 132.



Acute articular rheumatism. Condyloid surface of the femur. Oblique splitting up of the cartilage. A shred of the cartilage turned back, containing a primary capsule, in which are seen several secondary capsules. × 200.

This increase of the superficial cellular elements generally does not include the whole extent of the investing cartilage, but is seen in disseminated spots. The same irregular distribution of the lesion is met with in the deeper layers, which may be affected in cases where the arthritis is intense or of long duration. When these layers are implicated, the cartilage presents changes appreciable without the help of the microscope, consisting of swellings which to the finger are not so firm as normal cartilage, and when cut with a knife do not offer much resistance. Frequently there are seen upon these prominences clefts, or villi pressed against each other, or even shreds free at one of their extremities and adhering to the cartilage by the other, several millimetres or even a

centimetre long. In some rare cases of acute mono-articular arthritis, ulceration of the cartilage has been seen, not similar to that occurring in white swelling or chronic arthritis, but a true loss of substance as a result of a rapid breaking down of the cartilage matrix.

A microscopic examination of a vertical section from the tumefied part of the cartilage demonstrates a new formation to have invaded the deep layers and even the calcified layers of the cartilage. The new-formed cells and the formation of secondary capsules do not differ from those described in the superficial layers. Since the primary capsules of the middle layers are arranged in a linear manner and pressed against one another, they are elongated and form rows perpendicular to the surface of the cartilage, while the lenticular capsules of the surface are filled with secondary capsules, forming lines which have a direction parallel to the surface.

The proliferation of the cells is always accompanied by a segmentation of the fundamental substance between the primary capsules, causing striæ parallel to the long axis of the primary capsules (see fig. 132). So that in the deep layers this segment lineation is perpendicular to the surface, while in the superficial layers it is parallel.

In an advanced stage of the disease the striæ give rise to clefts, which divide the cartilage, as if an incision had been made with a knife. These incisions are parallel to the surface in the superficial layers, and perpendicular in the deep layers. This change in the cartilage may be confounded with the villous state of chronic rheumatism, from which it notably differs, as will be later seen.

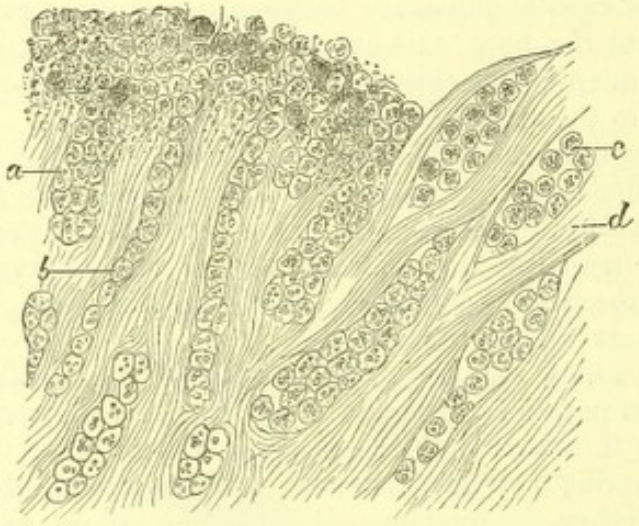
These clefts which end the segmentation of the cartilage may separate it in shreds parallel or oblique to the surface, and may therefore be larger than the thickness of the cartilage. Very frequently these shreds inclose proliferating cellular elements. When a true ulceration of the cartilage supervenes, the fundamental substance softens, undergoes a kind of liquefaction, and the proliferated cells become free.

From this description it is seen that in acute arthritis the diarthrodial cartilages are affected as well as the synovial membrane; lesions are produced in the cartilage at the same time as in the synovial membrane. Yet the hyperæmia and exudation, which have their origin in the vessels of the synovial membrane, play an important role in the inflammatory lesions of the cartilage. It has been shown that the superficial cells of the cartilage are the first affected. This may be attributed to the circumstance that they are in direct connection with the exuded liquids, from which they draw their nutritive material. It has been seen that the nutritive material of cartilage is not derived from the vessels of the bone, since the calcified layer of the cartilage prevents it. The cellular elements of cartilage have in arthritis an individual activity; for, although all may be equally surrounded by the liquid, yet all do not equally participate in the proliferation. This is very important, because at the present time there are some pathological anatomists, who are inclined to deny any creative activity to the cellular elements in inflammation.

B.—Purulent Arthritis.—By purulent arthritis is understood, not suppurative arthritis, such as met with in acute rheumatism, in traumatic arthritis, or in suppurating white swellings, but only those rapid and

abundant formations of pus, suppurations which are not in proportion to the other inflammatory phenomena. This form of arthritis is seen in purulent infection, in puerperal fever, in malignant smallpox, glanders, etc. The synovial membrane and fringes are more or less injected; sometimes to the unaided eye the alterations in the cartilage cannot be distinguished. The prominent lesion consists in a very large quantity of pus, such as met with in an abscess. In these cases it is very evident that we cannot explain the formation of the pus cells by a simple proliferation of the epithelium. The process indicated by Cohnheim may account for it, although it is difficult to conceive how such a great number of pus cells can come from the blood, since in purulent arthritis several articulations are affected at the same time, and inflammations of the same nature are present in other organs.

Fig. 133.



Arthritis from purulent infection. *c*. Primary capsule filled with free cells. *d*. Fibrillated matrix. *a*. Primary capsule opened upon the surface. *b*. Similar capsule as the preceding, in which the free cells are arranged in a row. The upper left edge shows a purulent layer upon the surface of the cartilage.

In a few cases of purulent arthritis, lesions more or less advanced of the diarthrodial cartilage are found. In one case of purulent infection, the cartilaginous covering had almost entirely disappeared, and only a small part of the surface of one of the condyles of the femur was covered by cartilage. The rest of the articulating surface belonging to the bone was simply covered by the calcified layer.

A microscopical examination of a vertical section of the remaining piece of cartilage, plainly showed the process of the disappearance of the cartilage, and a direct transformation of its cellular elements into pus corpuscles. The primary capsules were elongated, filled with free cells, the secondary capsules being dissolved, and forming long rows, perpendicular or oblique, to the articular surface.

The most superficial rows opened upon the surface into a purulent mass, which consisted of elements not differing from those contained in the elongated rows. These cellular elements had the diameter of pus cells, were spheroid or angular, and inclosed fat granules, some had even become

granular corpuscles. It was very evident that all the pus cells, filling the articular cavity, were not derived from the cartilages, but that a great number of them had their origin from it, is not less certain.

Sect. III.—Chronic Arthritis.

A.—Hydrarthrosis.—Authors who have studied articular diseases have not agreed upon the place hydrarthrosis should occupy in the nosological list; some, as Blandin, Bonnet, Billroth, Volkmann, place it among the inflammations; others, as Dupuytren, Nélaton, among dropsies. This difference of opinion seems to be owing to the circumstance that various articular affections are known by the name of hydrarthrosis. In reading over the reports of the autopsies, among others those of Dupuytren, Blandin, Brodie, and Bonnet, it is found that there are in the diseased joints lesions which belong to acute or chronic rheumatism, such as congestion, thickening of the synovial membrane, hypertrophy of the fringes, and even ulceration of the cartilage; in other cases, on the contrary, there does not exist any lesion appreciable to the unaided eye—the synovial membrane is smooth (Dupuytren).

Opportunities to study the lesions in hydrarthrosis seldom occur; persons suffering from the disease die only from some other intercurrent affection, and at the present time, we know of no histological examination except of the liquid obtained by puncture. There are found in this liquid epithelial cells, clear or containing fatty granules (Volkmann), but these elements are met with in normal synovial fluid, and their presence does not furnish anything positive of the nature of the disease.

B.—Chronic Arthritis by Continuity of the Inflammation.—This form of arthritis is very common. The articular cartilaginous covering is very notably affected, while the synovial membrane does not present any appreciable lesion. The disease supervenes in the articulations corresponding to the two extremities of a bone attacked with inflammation, or a rapidly growing tumor (sarcoma, carcinoma, etc.). When an articulation is invaded by a suppurative inflammation, as seen in the second period of white swellings, and when the corresponding bones are affected, then the neighboring articulations present the lesions to be described.

The articulating cavity does not contain more than the normal amount of fluid. The synovial membrane is generally slightly hyperæmic; its fringes, however, may present a very marked congestion.

The cartilages, and especially those which correspond to the diseased bone, are more or less deeply eroded, the surface is bare or covered by a connective tissue of new formation. The shape of these erosions is usually very irregular, their size varies, they are located chiefly at the periphery of the cartilage, thus reaching the margin of the synovial membrane; but solitary or confluent erosions are frequently seen in the centre of the cartilaginous surface. The loss of cartilage at the periphery is often replaced by a vascular connective tissue, which is con-

tinuous with the synovial membrane; but when it takes place in the centre of the cartilage, it remains bare, or is filled by a soft mass.

An examination of these erosions, made from perpendicular sections of the cartilage, shows that the loss of substance is due to a solution of the cartilage in consequence of the cellular proliferation. This appears to be a slow process, affecting layer after layer, so that the capsules in the proximity of the ulceration, exhibit only phenomena of proliferation analogous to those described in acute arthritis.

The margins of the parts where there has been a loss of substance are festooned; each cavity of a festoon corresponds to an opened primary capsule, the cells of which have become free, and have floated off in the synovial fluid, or remain and form a collection of embryonic cells, which fills up the cavity caused by a breaking down of the cartilage. These cells may give origin to an embryonic connective tissue, especially when the erosions are in connection with the connective tissue of the synovial membrane; the vessels of the synovial membrane enter into the middle of the embryonic tissue, and afford an excellent opportunity for the study of the development of new vessels.

Seldom in this form of arthritis is the inflammation so active as to give rise to suppuration. This latter occurs, however, in cases of intense suppurative osteitis, when the bone is absorbed and replaced by granulation tissue; the cartilage also disappears, only the layers of the calcified portion remaining. This condition is seen in diffused phlegmonous osteitis, in deep paronychia, and in some cases of destructive osteitis of the phalanges which accompanies perforating ulcers of the foot.

C.—Chronic Rheumatic Arthritis.—Also called arthritis deformans, formative, or proliferating, nodular rheumatism, *morbus coxæ sinilis*. Although the names nodular rheumatism, dry arthritis, and *morbus coxæ senilis* are given to distinct clinical affections; yet the anatomical lesions and evolutions are the same in these different maladies. They are essentially characterized by a villous state of the cartilages, by a hypertrophy of the synovial fringes and by ecchondroses or osteophytes in the circumference of the cartilaginous covering; these serious lesions are not accompanied by any notable effusions into the articular cavities.

The lesions of chronic rheumatism differ according to the articulations affected, and according to the stage of the disease.

In the phalangeal articulations, for example, the changes consist in the progressive disappearance of the centre of the cartilage by the villous transformation, which will be described later; afterwards small cartilaginous nodules (ecchondroses) are developed at the margin of the cartilaginous covering. These give to the digital articulations a peculiar appearance, which has caused the disease to be named nodular rheumatism. At a more advanced stage of the disease, the central parts of the cartilage have disappeared, and the ecchondroses have become ossified. In these cases the articulating surfaces formed by an eburnated osseous layer, have lost their original form, and present furrows or grooves, which may be determined by articular movements.

In the large articulations, as the knee, there is seen the same disappearance of the cartilage in its central portions, the same formation of

marginal ecchondroses. But the synovial fringes and inter-articular ligaments undergo considerable modifications. The fringes are hypertrophied; their villi enlarge and form secondary villi, which have received the name of dendritic vegetations of the synovial membrane. These new formations are accompanied by great vascular development.

The synovial villi generally become cartilaginous, and form spherical or oval masses of varying size, reaching sometimes that of a hazel-nut, connected by a pedicle at times very thin. The pedicle may be broken, and the mass set free, thus forming an articular foreign body. In some cases the cartilaginous formations are infiltrated with calcareous salts, or they present to the unaided eye all the characters of a vascular bone. There is also seen in the articulations a considerable hypertrophy of the inter-articular ligaments which assume the characters of cartilaginous tissue.

The ecchondroses, which are developed around the articulation, later undergo osseous transformation, and so form compact or spongy osteophytes, sometimes colossal in size, and very varied in shape. The most remarkable examples of these osteophytes are seen in the articulations of the hip, in the disease designated *morbus coxæ senilis*, a form of dry arthritis. The tendinous insertions, which border on the articulations, may become a starting point for the formation of osteophytes, and in these cases the diseased articulations present the most singular deformities.

Whatever may be the articulation affected, and in every form of the disease, the histological process is the same.

It consists essentially in a proliferation of the old cartilage, and in a new formation of cartilage in the fibrous parts, therefore the name defining it best is *proliferating* arthritis.

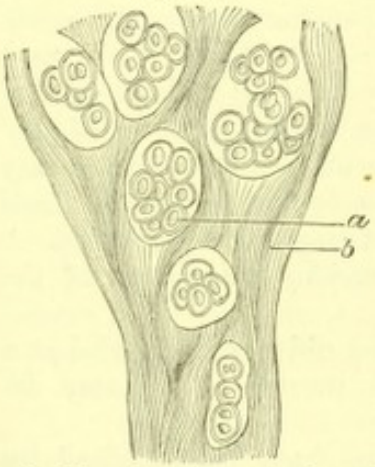
The histological lesions in chronic rheumatism have been studied by Redfern, O. Weber, Volkmann, etc. These authors have distinctly seen what takes place at the centre of the cartilage in passing into the villous state; but they have not understood the change in the cartilage at its periphery resulting in the formation of ecchondroses. Throughout the whole extent of the cartilage there is seen in perpendicular sections a multiplication of the cells of the cartilage, with the formation of capsules around each. The enlarged primary capsules contain a large number of secondary capsules. Very often these secondary capsules form groups enveloped in a common capsule. In other cases, the primary capsule is filled with small round capsules, which are not held together. Former writers have taken these round capsules for true cells. This error may be avoided by the employment of a solution of iodine, which colors the protoplasm of the cells brown, and leaves the secondary capsules uncolored or slightly tinged.

The primary capsules on the surface become globular and much distended, finally rupture and open into the articular cavity. The capsules of the second row and those located deeper can enlarge only perpendicularly to the surface of the cartilage. As they are arranged in a linear manner, they open one into the other and form parallel rows. These different alterations are similar to those seen in cartilage in proximity to a point of ossification (see p. 28).

Upon the surface, the enlarged primary capsules gradually pour their

contents into the articular cavity, and the rows, deprived of their secondary capsules, contain only synovial fluid or cellular débris. The fundamental substance of the cartilage, included between the spaces left empty by the falling out of their elements, remains for a long time in the form of long or short villi, floating at the surface of the cartilage. These filaments, generally very thin, are constituted simply of the fundamental substance of the cartilage, or they contain a few cartilage capsules. These last are found especially at the free extremity of the villi which are club-shaped. The filaments vary in length, appearing sometimes a millimetre long. They are perpendicular to the surface of the joint or slightly oblique ; one or more swellings may be seen in which exist primary capsules containing secondary capsules. (Fig. 134.) As the disease advances, the cartilaginous filaments, deprived of their cells and submitted to the articular friction, gradually disappear as far as the calcified layer of the cartilage. This in turn is worn off, and the underlying bone wears away by the articular movements, and undergoes *eburnation*. This is observed particularly in chronic arthritis occurring in locomotor ataxia.

Fig. 134.



Nodular rheumatism. Surface of the cartilage. *a*. Mother capsules filled with secondary capsules about to open into the articulation. *b*. Splitting up of the matrix. × 200.

In the majority of cases it is difficult to know how the eburnation of the superficial layers of the bone occurs. Yet we have observed some facts which may explain this process. While the superficial capsules of the cartilage are filled with new cellular elements, those situated deeper, found in connection with the calcified layer, undergo analogous changes. In enlarging they extend toward the bone, and cause the absorption of the calcified layer. The osseous trabeculæ, which separate them from the medullary cavities, are in their turn absorbed by a process similar to that seen in osteitis, and finally the enlarged capsules open into the medullary spaces of the bone. The cells contained in capsules are emptied into these spaces, as the superficial capsules are emptied into the articular cavity. As a consequence, the medullary spaces which border on the investing cartilage are filled with newly-formed cells developed in the cartilage—cells presenting all the characters of embryonic marrow. (Fig. 135.)

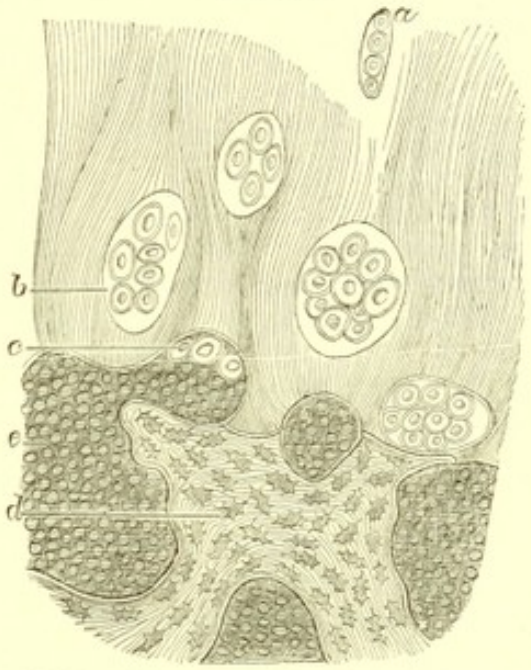
The subchondral osseous layer which contains the embryonic marrow is thin, and, to the unaided eye, appears as a red border. This layer is transformed into the eburnated lamella by successive metamorphoses of the embryonic cells into bone cells, by a process of ossification similar to that occurring in the physiological state. It is probable that the metamorphosis of the subchondral compact osseous lamella does not always take place by the process mentioned. It is possible for the inflammation to extend in a direct manner into the spongy tissue, and occasion an inflammatory eburnation.

In the other portions of the epiphysis the marrow is highly fatty, the trabeculæ of the bone are thin, being easily broken with the finger,

which may penetrate deeply into the spongy tissue. These thin trabeculæ, under the microscope, are very regular, showing the osseous corpuscles containing cells but no fatty granules.

Ecchondroses are not characteristic of chronic rheumatism. They are sometimes met with in other forms of arthritis which have a slow course, due to scrofula or gout. Every notable proliferation of cartilage, when it attacks the margin of the investing cartilage, causes the formation of nodes. The central portion of the cartilage at this time always disappears by a villous transformation. Therefore we have the same disease determining upon the same articular surface, a disappearance of a great part of the investing cartilage, and at the same time an exuberant production of cartilage. These two lesions, however, are caused by the same histological process. The difference which exists between them comes from the circumstance that the margin of the articular cartilage is covered by the synovial membrane, and that the proliferated elements collect beneath this membrane instead of being discharged into the articular cavity. A vertical section of one of the ecchondroses shows successively, first a fibrous tissue membrane, then fibro-cartilaginous tissue, and finally proliferating hyaline cartilage. The fibrous membrane, which is in some cases distinctly vascular, varies in thickness, and is directly continuous with the synovial membrane and periosteum. Beneath is seen a fibro-cartilaginous layer which unites it to the hyaline cartilage. This latter incloses large capsules with secondary capsules, forming by their union a complicated system.

Fig. 135.



Nodular rheumatism. Deep layer of the cartilage. *a*. Normal capsule. *b*. Mother capsule containing secondary capsules. *c*. Opening into the medullary spaces. *d*. Osseous tissue of new formation. *e*. Embryonic marrow. × 200.

This tissue has a very close analogy to the cartilaginous layers which precede ossification in the short bones. The ecchondroses, however, become ossified in time, the ossification always beginning at their base, and from the old bone. The process is similar to physiological ossification (see p. 28). The osseous tissue invades the ecchondrosis, which finally disappears, in order to give place to a spongy or eburnated osteophyte. In chronic rheumatism, the osteophyte is usually eburnated only upon the surface, while in the deeper layers it is spongy and contains a medullary tissue which is fatty, as in the other portions of the head of the bone. The boundary between the old and new bone in osteophytes is always very distinct; these osteophytes belong to the epiphyseal exostoses.

The synovial fringes become vascular; the adipose tissue that they contain disappears, and is replaced by embryonic cells, which accumulating

give rise to the secondary deridritic vegetations. Some of the embryonic cells contained in the vegetations form cartilaginous tissue, the peripheral cells form a layer continuous with the fibrous tissue. The cartilaginous nodules so produced may be small in size, but very numerous; those located at the base of the synovial fringes constitute by their union thick plates, which extend a varying distance upon the synovial membrane; others, situated in the villi of the fringes, are fastened to the synovial membrane by a pedicle varying in length and thickness.

These nodules of cartilage may undergo calcareous infiltration, or even a true ossification. This latter is always accompanied by considerable vascularity; we have met with cartilaginous nodules fastened to the synovial membrane by a very thin pedicle, and which have undergone very complete ossification, but then bloodvessels were included in the pedicle. Frequently these suspended bodies, whether cartilaginous, calcified, or osseous, are detached, and become articular foreign bodies.

Notwithstanding that this articular disease is accompanied by an exuberant formation of cartilaginous tissue at first and osseous afterwards, it never occasions osseous ankylosis, differing in this from other forms of chronic arthritis, which, however, do not result in osseous formations of such large dimensions.

The immobility of articulations in chronic rheumatism often depends upon the osteophytes, or in very rare cases upon a fibro-cartilaginous transformation of the synovial membrane, and even upon a fibrous union of the two articular surfaces bared of their cartilage.

D.—Scrofulous Arthritis, or White Swelling.—Up to the present surgeons have described white swelling without defining it either clinically or anatomically. Their descriptions include several forms of articular disease. Clinically they designate under the name of white swelling all chronic articular affections having a tendency to suppurate, or which are suppurating.

The swelling and the pallor of the integuments also enter into the clinical definition that has been given by them, although they recognize, that in certain stages of white swelling, the skin and subcutaneous tissue may be the seat of an inflammation accompanied by redness.

In this disease they have pointed out all the possible alterations of the synovial membrane, of the cartilages, and of the bones. Bonnet is the only author who has endeavored to find in white swelling a constant anatomical character in the existence of fungous granulations of the synovial membrane and bones. But these granulations do not exist in all the stages of white swelling, and they do not differ from large granulations developed elsewhere.

In the clinical course of this affection there are generally two periods; the first long, characterized by uneasiness or slight pain; the second indicated by the consequences of suppurative inflammation.

The anatomical lesions of white swelling differ in the two stages of the disease. In the first stage, they consist in a fatty degeneration of the cells of the cartilage, and very often of the bone cells of the epiphysis. In the second, the parts which have died from the fatty degeneration occasion around them an eliminative inflammation (arthritis, rarefying

osteitis, suppuration, granulations of the synovial membrane and of the bone, caries, abscess of bone, hyperostosis, sclerosis of the bone, necrosis, chronic phlegmon and circumscribed abscess).

The anatomical definition of white swelling is based upon the initial lesion, viz., upon the initial fatty degeneration of the cellular elements of the cartilage and bone. The other lesions belong to inflammation.

First Stage.—White swelling is seldom seen in the first stage; however we have had the opportunity of examining two cases during suppurative inflammation, and were able to recognize traces of the primary lesions in the cartilages and bones. The synovial membrane appeared altered; yet the synovial fluid was not more abundant than in the normal state. In one case there was found upon the surface, as well as upon the cartilage, a concrete mucous exudation, grayish and gelatinous, which upon section showed a very handsome network, in the meshes of which was found a liquid substance destitute of cellular elements. The exudation was adherent to the surface of the cartilage.

The cartilages had preserved their polished surfaces; they were slightly opaque, and had lost a little of their elasticity. Vertical sections examined under the microscope show all the layers successively described on page 227. The cells contain fine fatty granules, and some are completely destroyed by fatty degeneration. This change begins in the superficial layers and gradually extends to the deeper parts, at times affecting the whole thickness of the investing cartilage. Generally the changes are not equally distributed over the whole of the cartilage, not differing in this from other cartilaginous lesions; one part of the investing cartilage may be completely transformed, while another is modified only upon the surface, or even does not present any alteration.

Fig. 136.



Section of cartilage during the first stage of white swelling; complete fatty degeneration of the cartilage cells. High power.

The fatty degeneration terminates by the complete destruction of the cells contained in the capsules, wherein are found only fatty granules, the nucleus of the cell having disappeared. At the same time, the fundamental substance of the cartilage is softened, and does not resist the movements and pressure of the articulation. After this process, the capsules containing only fatty granules, are deformed and irregular in shape, as shown in fig. 136.

Frequently these lesions extend into the second stage, and even when the cartilage has undergone fatty degeneration throughout its entire thickness, it may persist without experiencing any other modification.

The epiphysis presents the lesions of the first stage of caries. There is a great thinness of the osseous trabeculæ, the cells of which have mostly disappeared, and undergone fatty degeneration, while the marrow is yellow, slightly vascular, and fatty. The periosteum and soft parts surrounding the articulations appear entirely healthy.

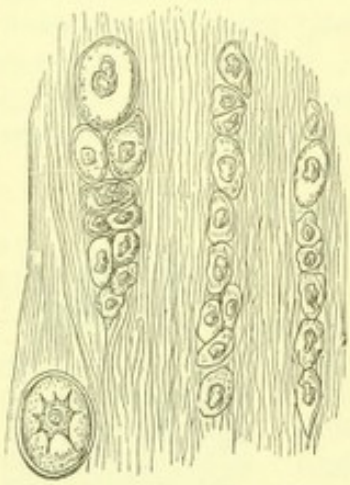
Second Stage.—The lesions of the second stage vary according to the intensity of the inflammation succeeding the mortification of the cartilage

and bone. The synovial membrane becomes vascular and thickened; its adipose tissue disappears in order to give place to an embryonic tissue, which forms granulations and produces pus which is discharged into the articular cavity.

When the disease is more advanced, after the destruction of the cartilage, the extremities of the bone are seen, also covered by granulation tissue which is confounded with that of the synovial membrane. If an external opening exists its fistular track is also lined with these granulations. In white swelling the granulations are specially named fungating or fungus. These very often rest upon a semi-transparent, friable, very vascular layer of tissue, which may become lardaceous in consistency when the suppuration ceases. Subsequently this tissue has a tendency to complete organization. Sometimes these fungous granulations undergo a caseous metamorphosis. The structure of the granulations varies according to the degree of their evolution (see Caries, p. 207.)

The changes which supervene in the cartilage are not always the same; where the investing cartilage has undergone fatty degeneration of its cells throughout its entire thickness, it acts as a foreign body. It is softened, so that, by the articular movements which still continue, it is detached in large or small layers, which either attached at the border or perfectly free, float in the articular cavity. The granulations developed in the epiphyses may uplift and also detach the cartilage.

Fig. 137.



White swelling; second stage, or inflammatory period; mother capsules forming rows filled with secondary capsules; the matrix is fibrillated. × 200.

When the investing cartilage has been only partially involved, the deeper layers, which generally escape, present in their elements lesions which produce localized thickenings, ulcerations of its villous surface, new formations of fibrous tissue, and even ecchondroses. All these lesions are due to proliferation of the cells of the cartilage, which during this evolution of an irritative nature, do not present fatty granules.

The superficial layer of cartilage having become inert through the destruction of its cells, the capsules of the deep layer filled with secondary capsules, and arranged in long rows, cannot open upon the surface of the joint. At the same time that this proliferation is taking place, the fundamental substance becomes transparent, and is segmentated parallel to the axis of the rows. It is this process that causes the increase in thickness of the investing cartilage, which in places may reach seven millimetres. These hypertrophies are generally limited, and, besides exuberant cartilaginous portions, which form regular islands, there is seen granulation tissue or fibrous tissue in the process of organization, or again ulcerated cartilaginous surfaces. These surfaces present villous filaments, the shape and development of which are the same as in chronic rheumatism.

In some white swellings which develop slowly in the second stage, there are seen marginal ecchondroses, less perfect and more irregular than

in chronic rheumatism. Their origin and structure are, however, the same in both diseases. They are developed beneath the thickened fibrous tissue, which has taken the place of the synovial membrane.

When the cartilage has been raised en masse by the granulation tissue of the bone, or when it has been destroyed by the villous degeneration, it disappears, and is replaced by granulation or embryonic fibrous tissue.

In the first case, the articulation is transformed into a true abscess, lined by a pyogenic membrane, which, when the pus is discharged externally, is covered with vegetations.

Instead of the articular cavity, there exists a continuous layer of embryonic tissue, which unites and separates the two osseous surfaces of the articulation. In this young tissue osseous trabeculæ develop, and cause a complete consolidation of the two bones. This is a favorable method of termination for the disease, yet osseous ankylosis may exist without cessation of the suppuration.

The lesions of the epiphyses in white swellings consist of caries, and all the consequences that this disease induces. It is doubtful if true caries is ever developed far from an articulation (Volkmann), and it is frequently accompanied by the articular changes of white swelling. To what has been said of caries, it should be added that the granulations often form prominences in the articular cavity, after the partial or complete disappearance of the cartilage. The caseous sequestræ or the small sequestræ of caries may also be discharged into the articular cavity.

In the soft parts adjoining the articulation, in the connective tissue, in the sheaths of the tendons, and in the tendons themselves, there are seen all the lesions of chronic inflammation. It is especially around the fistular openings that these new inflammatory formations are manifest; there is no essential difference between these different lesions, and those which occur around a necrotic bone. However, at the beginning of the second stage, there is seen a puffiness of the connective tissue, which somewhat resembles œdema. This œdema will be studied under connective tissue.

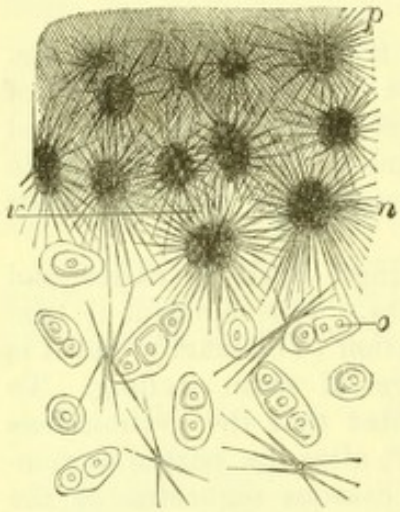
E. Gouty Arthritis.—Gouty affections of the articulations, like scrofulous arthritis, are divided into two stages. In the first there is seen a simple nutritive lesion of the cartilage, of the synovial membrane, and of the surrounding fibrous tissue, which in the second stage excites a true inflammation.

First Stage.—The lesions of this stage consist in an infiltration of urate of soda, generally in the form of needle-like crystals, into the cartilage, the synovial membrane, neighboring fibrous tissue of the articulation, and even into the periosteum and areolæ of the spongy tissue of the epiphyses.

In the cartilage, at first the urate of soda is deposited in the superficial portion, never upon the surface, as an examination with the unaided eye would seem to show. When the articular surface is examined, it appears like a chalky and polished layer, usually glistening although very opaque; at times scarcely perceptible ridges are distinguishable, and are very irregularly arranged.

A perpendicular section of the cartilage shows that the deposit only occurs in the most superficial parts; examined with the microscope, very often the urate of soda is found to have accumulated in such large quantities that nothing but an opaque and granular border can be distinguished. Where it joins the deeper parts, the needle-shaped crystals are seen radiating from a centre, which is generally a cartilage cell. These needle-shaped crystals, which are from five to six millimetres long, are either rectilinear or curved. When the deposit of urates is considerable, and all the needle-like crystals radiate from a centre, the mass resembles very much a thorn-apple.

Fig. 138.



Vertical section of an articular cartilage infiltrated by urate of soda, from a gouty patient. *p*. Articular surface of the cartilages. *v*, *n*. Amorphous and crystallized urate of soda. *o*. Capsules and cartilage cells. ×200.

To ascertain if the dark border upon the surface of the cartilage is not simply a deposit formed upon the surface, acetic acid or potassa is employed. The salts are gradually dissolved, and it is seen that they are deposited in the cartilage. The reagent acts upon each group of crystals from the periphery to the centre, so that the fundamental substance of the cartilage may be completely deprived of its urates, while that in the cells remains. When acetic acid is used, at the same time that the urate of soda disappears, there is seen the formation of lozenge or hexagonal, transparent, and colorless crystals of uric acid.

To the unaided eye, upon the connective tissue of the synovial membrane, are seen small white opaque spots, caused by a deposit of urate of soda in the interior of the membrane; although very superficial in appearance, these deposits are very intimately connected to the fibrous tissue, and cannot be removed by scraping.

The synovial fringes, ligaments, periosteum, sheaths of the tendons, peri-articular connective tissue, sheaths of the nerves, external sheaths of the vessels, and the skin itself may be be invaded by analogous deposits.

These deposits appear to be between the fibres of the connective tissue, so formed that the white and opaque mass cannot be isolated. In their centre, besides granules and crystals of urates, are found fibres of connective tissue.

When the peri-articular deposits of urates attain such a size as to be observed during life, they are called a *tophus* (*chalk-stone*). Very often in the centre of these chalk-stones there is found a white pulp, which being removed leaves a cavity, the wall of which varies in thickness, being composed of connective tissue infiltrated with urates. The soft chalky mass contained in the centre, when diluted with water, shows very beautiful needle-shaped crystals of urate of soda.

In a *second stage* of the disease, considered only histologically, the cartilages through the irritation occasioned by the presence of the urate of

soda, undergo changes which should be considered of an inflammatory nature.

This irritation of the cartilages is recognized, with the unaided eye, by a peculiar appearance of the deep cartilaginous layer, not infiltrated with urates, and by ecchondroses. Beneath the superficial layer, incrusted with urates, the cartilage is more transparent than customary, and presents a bluish color, when studied by a perpendicular section. This layer varies in depth, at times being thicker than the normal investing cartilage, again it may be scarcely seen. Sometimes the entire investing cartilage may be infiltrated with urates or have completely disappeared.

By a microscopic examination there is seen in the bluish layer a proliferation of cells with enlargement of the primary capsules, which form rows between which the fundamental substance has become transparent and segmented. These phenomena of irritation, which are much less marked than in chronic rheumatism or in scrofulous arthritis, never lead to villous degeneration, because the superficial infiltrated layer becomes inert, and does not permit the enlarged capsules to open into the articular cavity. Therefore there is at times a true accumulation of new cartilaginous elements, and consequently a hypertrophy of the cartilage.

The disappearance of the cartilage is caused by the progressive wearing away of the surface of the cartilage infiltrated with urates; there is a loss of elasticity; it does not resist the action of friction. The opposed surfaces are worn away by the articular movements. This may be demonstrated in preparations after the action of a solution of potassa, when we see at the surface of the cartilage the round or elongated capsules perpendicular to the surface—a very clear indication that the superficial layer formed of flattened capsules has completely disappeared. This wearing away of the cartilage, however, only occurs in the very movable articulations, while in those less movable it is not seen even in chronic cases of gout.

When the cartilages have disappeared there remains in their place chalky matter, which separates the end of the bones, or, as we have seen in one case, there is a true osseous ankylosis. In place of the articular cavity, the areolæ of spongy tissue, which contained urate of soda, were seen to have enlarged, so that the interarticular line was only represented by a white mark. A longitudinal cut of the bones showed this singular arrangement very distinctly. The ankylosis evidently resulted from an osteitis limited to the extremities of the bones.

These are not the only conditions in which the medullary tissue of bones may be infiltrated with deposits of urates. They have been found in the extremities of bones, the investing cartilage of which has been preserved.

Formative irritation of cartilage may, in gouty arthritis, as in other forms of arthritis, cause the formation of ecchondroses. Generally these ecchondroses are smaller than those in chronic rheumatism, and the periarticular nodules in gout are chiefly due to chalk-stones, yet they may be considered partly as ecchondroses.

Gouty arthritis is never suppurative, but sometimes very chronic

eliminating suppurative inflammations are seen in the neighborhood of subcutaneous chalk-stones. The pus cells are then associated with granules and crystals of urates.

The two stages that have been given to the histological lesions of gout are not so distinct as the preceding description would lead one to suppose. The deposits of urates may occur in proliferating cartilages; for the primary capsules containing a large number of secondary capsules indicate very positively a formative irritation, and the large spherical capsules have an analogous signification, and may contain crystals of urate of soda. From the clinical symptoms it is very probable that the deposit continues during the whole course of the disease, and that the attacks of gout have some connection with the inflammatory extensions alongside of the joints. It is known, from the observations of Garrod, that there is no excess of urates in the blood during the attacks; and it is proven, at least in birds in whom the ureters have been ligated, that infiltrations of urates are not dependent upon an excess of urates in the blood.

Sect. IV.—Tumors of the Articulations.

Primary tumors of the structures which constitute the articulations are extremely rare, if we except the ecchondroses which are produced in consequence of an arthritis.

Ecchondroses originating in the intervertebral disks, however, do not seem to be connected with inflammation; their cause is not known. They are found at the autopsies of subjects generally advanced in age, and usually several are present. The intervertebral disk is adherent to the body of the vertebra in the same manner as the diarthrodial cartilages. Upon each osseous surface there is seen successively a layer of calcified cartilage, then a layer of homogeneous or segmented hyaline cartilage, which limits a cavity filled with a mucous mass. The vertebral ecchondroses are developed from the hyaline cartilage. They appear in the form of two masses held together and separated by a layer of fibro-cartilage, which indicates the inter-articular line. In subjects advanced in age these ecchondroses are frequently ossified, and the osteophytes often are separated into two parts by a longitudinal plane in which fibro-cartilaginous tissue still exists. It may also happen that the fibro-cartilaginous layer has undergone ossification, and then the two vertebral bodies are consolidated.

J. Müller has pointed out in the articulations a form of *lipoma* which he calls *dendritic*, characterized by a number of lobules separated from each other in the articular cavity, yet united like a bunch of grapes. Physiologically, the synovial fringes contain adipose tissue; the dendritic lipoma may simply be an exaggeration of this. The affection is very rare; we have never met with it.

Tubercles of the Synovial Membrane.—There is another neoplasm of the synovial membrane which seems to be more common, although it has not often been described. It consists of miliary tuberculous granulations

of the synovial membrane. Virchow simply mentions it. Köster has collected a few cases, but has not yet published them. The preparations he showed us in Würtzburg, and a case of the same nature that we have since seen, will serve us for a description of tubercles of the synovial membrane.

The articular cavity contains pus; the synovial membrane is thickened and changed into a pulpy layer resembling a pyogenic membrane, in which are seen semitransparent or opaque granulations. By cutting through the membrane these granulations are seen throughout its entire thickness. These tuberculous granulations are found disseminated or confluent, translucent or caseous, possessing all the characters pointed out on page 112; between these granulations embryonic tissue exists, traversed by dilated vessels. The adipose tissue has disappeared.

The cartilage, to the unaided eye, appears normal, or it has lost its elasticity, and its surface is not smooth. In the case that we examined, the lesions of acute arthritis were found; the most superficial portion of the cartilage was softened and segmented; the most superficial capsules seemed to have disappeared, and there was a proliferation of the deeper capsules.

The spongy tissue of the epiphysis was not rarefied, differing from what is seen in white swelling, and the bone cells of the trabeculæ did not contain fatty granules.

It is certain that, up to the present time, the arthritis which accompanies this tuberculous new formation and its results have been confounded with scrofulous arthritis; yet these two affections seem to us very distinct. The symptomatology of tuberculous arthritis is entirely unknown.

Tumors having their Origin in the Neighboring Parts and Penetrating into the Articular Cavity.—Tumors of the bones, and especially sarcomata which are the most common of all, seldom penetrate into the articular cavity. The calcified layer of the cartilage does not so readily absorb as does the bone when irritated by a neoplasm; sometimes, however, this layer yields, and then the morbid mass grows into the articular cavity. This penetration has been preceded by all the phenomena which have been previously described under chronic arthritis by continuity.

In some persons, and particularly in children, there is seen a loss of substance of the articular surface, cut out as if by a punch, establishing a communication between the joint, and a cavity of varying size excavated in the tissue of the epiphysis. The osseous tissue which limits this cavity is rarefied, filled with granulation tissue infiltrated by pus, or is condensed. The surface of this cavity is lined by granulation tissue or by a caseous layer. In the interior of the cavity there is found pus or caseous matter more or less concrete. The articulation contains pus, and all the changes of suppurative arthritis are seen. All surgeons, Nélaton especially, have considered this lesion to be tuberculous in its nature.

The histological examinations that we have been able to make upon this subject have not permitted us to form a definite opinion, for we know, at the present time, that caseous degeneration is not necessarily

specific. In the osseous tissue which surrounds the openings we have only found modifications belonging to osteitis.

The margins of the perforations in the cartilage show a proliferation of the cartilage cells as in other cases of chondritis.

It is necessary, therefore, before coming to a positive conclusion, to wait for new cases where the changes are more recent, or cases in which, by the side of the old alterations, we may find points presenting the characters of tubercles of bone, as has been seen in Pott's disease.

CHAPTER IV.

CHANGES OF THE CONNECTIVE TISSUE AND SEROUS CAVITIES.

Sect. I.—Normal Histology of the Connective Tissue and Serous Cavities.

By injecting with a hypodermic syringe serum of the blood into the subcutaneous cellular tissue of an adult mammifera, a portion of the tissue will be distended in the form of a spherical ball; the size of this mass depends upon the quantity of the liquid injected; once produced, by further injection it may be enlarged to a considerable size. This fact alone demonstrates that there are not in the connective tissue spaces analogous to those which Bichat designated by the name of cells. The connective tissue consists of innumerable filaments of great flexibility. When fluid is injected with some pressure it causes them to be compressed, they are then closely applied one to the other at the border of the ball, where they finally surround a sort of cyst. This kind of limiting membrane of the spherical ball is formed of fibres which slide one upon the other, so that if we inject more fluid the cyst is enlarged, but always has a spherical form. A few filaments traverse the injected substance in different directions, so that it is inclosed in meshes, and upon section the mass presents a gelatinous appearance.

A microscopic examination of the infiltrated portion of the œdematous ball, removed with scissors, shows the presence of filaments which are fasciculi of connective tissue and elastic fibres. The fasciculi of connective tissue are longitudinally striated; they seem to be formed by a collection of fibrils, and are therefore named fasciculi. They appear wavy or zigzag; their diameter varies greatly, and carmine colors them red. After the action of carmine, if examined in water or glycerine to which acetic or formic acid has been added, they swell, lose their color and fibrillar appearance. The swelling is not equal at all points, and there are seen constrictions in the form of rings or spirals, which seem to be caused by a kind of fibre, stained red. Henle has named these fibres annular or spiral fibres, and considers them to be elastic in nature.

Elastic fibres are found along with the fasciculi, and are characterized by their refraction, their perfect cylindrical shape, their anastomoses, and their resistance to the action of acetic acid.

Between the fasciculi there are found two kinds of cells: one, placed along the fasciculi of the connective tissue, are large, flat like the endothelial cells of the serous membranes, and contain a nucleus, also very flat, in which one or more nucleoli are seen. The other cells are found free, and have all the characters of white blood corpuscles or lymph cells. In normal connective tissue all the fasciculi touch and slide easily one upon the other.

From the preceding description it is clear that the cellular tissue may be considered as a vast cavity traversed by fasciculi which are continued into the skin, aponeuroses, periosteum, etc.—these fasciculi sliding upon one another, as the opposite surfaces of a serous cavity. Between the fasciculi there is found in the physiological state a fluid in which are suspended lymph cells, and the fluid itself appears to be the same as that of the lymph.

In the serous cavities there is also found a fluid containing the same elements. By physiological experiments has been recognized a direct communication of these minute serous cavities with the lymphatic vessels.

In the frog, the small lymph spaces of the subcutaneous cellular tissue are replaced by vast sacs, named serous or lymphatic sacs, traversed by fibrous bands with muscles and nerves. By injecting into the lymphatic sacs of the frog, fine particles of coloring material, they are found to be taken up by the lymph corpuscles and carried into the blood (Cohnheim and Recklinghausen). In the serous cavities of mammiferæ similar phenomena have been observed by Recklinghausen, who has studied the subject very attentively. When milk, red blood cells, or particles of colored substances are placed in the peritoneal cavity beneath the diaphragm, they pass through the endothelial layer by means of small orifices (stomata) between the cells, and enter into the superficial lymphatics. Fine particles of colored substances injected into the subcutaneous cellular tissue of man and mammifera soon reach and accumulate in the corresponding lymphatic glands, but when they are injected into the bloodvessels they do not pass into these glands (Langerhan's). These different physiological facts demonstrate very positively the relations between connective tissue lymph spaces and serous cavities.

A physiological or accidental subcutaneous mucous bursa results from the fasciculi of the connective tissue being separated and pushed aside at a certain point, where they are closely pressed together and form a resisting membrane. Generally mucous bursæ are traversed by connective tissue fasciculi arranged as a membrane. The internal surface of the cavity is lined by an endothelium which forms a complete or incomplete covering, the cells of which do not differ from those found upon the fasciculi of the connective tissue. The sheaths of the tendons are analogous to serous cavities, they are lined by a single layer of flat endothelial cells. The external layer of connective tissue fibres blends with the surrounding connective tissue.

The large serous cavities (the pleura, pericardium, peritoneum, and arachnoid), although very complicated in their anatomical structure, are all of the same histological type, and very simple; a layer of dense connective tissue lined by a single layer of flat endothelial cells. The size and shape of these cells are very variable. The connective tissue which constitutes the wall of serous cavities contains very numerous lymphatic vessels, the most superficial being immediately beneath the endothelium (Recklinghausen, Ludwig and Schweigger Seidel.)

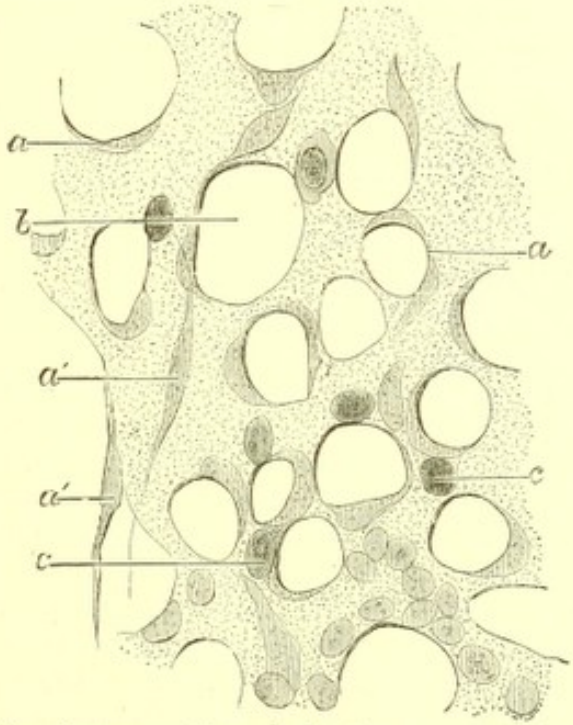
Sect. II.—Congestion and Hemorrhage of the Connective Tissue.

Simple congestion of the connective tissue is frequently seen during life without leaving any trace after death. Yet when it occurs in connection

with inflammation or hemorrhage, the vessels of the connective tissue in the cadaver are often found filled with blood. By removing a piece of the congested tissue, and examining it with the microscope, the capillaries are seen filled with red blood corpuscles, which twenty-four hours after death appear crenated. The capillaries, especially in inflammation, are seen regularly dilated or moniliform. There may be œdema with the congestion.

The effusion of blood into the connective tissue is very common; it occurs in contusions, wounds, general diseases which are accompanied by hemorrhages, etc. The blood escaping from the vessels runs between the fasciculi of the connective tissue and separates them. A microscopic examination of a section in which this lesion has occurred, shows the fasciculi of the connective tissue cut longitudinally or transversely, separated from each other; the spaces filled with blood, resembling very much a cavernous angioma.

Fig. 139.



Transverse section of the subcutaneous tissue of a dog in a wound dusted with vermilion. *a*. Connective tissue cells arranged to form half circles around the fasciculi, *b*, of the connective tissue which have become transparent from the action of glycerine. *a'*. Connective tissue cells seen longitudinally. *c*. Lymph corpuscles infiltrated with vermilion, situated in the inter-fascicular spaces, which are enlarged and filled with a granular exudation. The connective tissue cells here seen are slightly swollen; they also contain granules of vermilion

Later, within ten days, the extravasated blood has undergone considerable change; the fibrin which coagulates around the blood corpuscles and supports them experiences a molecular metamorphosis. The red corpuscles are destroyed, and the products of their decomposition are found—granular hæmatoidin or at least an analogous red matter, yellow or brown granules derived from the hæmoglobin, albuminoid granules coming probably from the paroglobin, and finally fat granules.

At the same time that these metamorphoses are taking place in the blood,

there occur in the infiltrated connective tissue changes of an irritative nature, which terminate by eliminating all the products of decomposition. White blood cells, containing colored granules which they have absorbed, are very numerous. They afterwards return to the blood or lymphatic circulation, and carry with them the contained granules. The flat or fixed cells of the connective tissue are swollen and contain foreign granules. It is to these two histological phenomena that must be attributed the complete disappearance of ecchymoses, and also the persistent pigmentation of some cicatrices.

The different colors of an ecchymosis, visible to the unaided eye, are due to the hæmoglobin; at first soluble, the latter is gradually changed into colored granules named hæmatoidin or melanin. These granules act towards the surrounding living elements like fine colored particles injected into the connective tissue. They cause an irritation which determines the appearance of numerous white blood cells, which finally absorb and carry away the solid granules.

The irritation produced by the colored granules which come from the blood, varies in intensity. Sometimes it passes away unperceived, again there is suppuration and an abscess.

Sect. III.—Œdema.

Histologically œdema is essentially characterized by an effusion of albuminous fluid, which takes place between the fibres of the connective tissue and separates them from one another.

When œdematous loose connective tissue is incised, instead of a dense felt-like tissue, there is seen a gelatinous, transparent, trembling mass, in the midst of which are found small collections of adipose tissue, thin white markings and red trabeculæ which correspond to the vessels. This appearance results from the retention of fluid between the fibres of the connective tissue, as water is retained when imbibed by a piece of cotton. If a fragment of œdematous connective tissue is examined without stretching, the fasciculi of the connective tissue and elastic fibres contract, and expel the fluid, and the tissue returns to the normal state. That this is due to the contraction of the fibres, may be proven by placing the fragment in fluid, when it is found that the tissue does not again become filled with the liquid. This property of the connective tissue fibres is retained for a long time notwithstanding their distension, and explains the easy and continual discharge of fluid from punctures made through the skin of dropsical patients. The fluid which flows from the punctures is transparent and albuminous; it neither coagulates spontaneously, nor after the addition of red blood corpuscles, which indicates that it does not contain fibrinogenic substance, and therefore it may be separated from inflammatory fluid. There are always found in an œdematous fluid a few white blood cells.

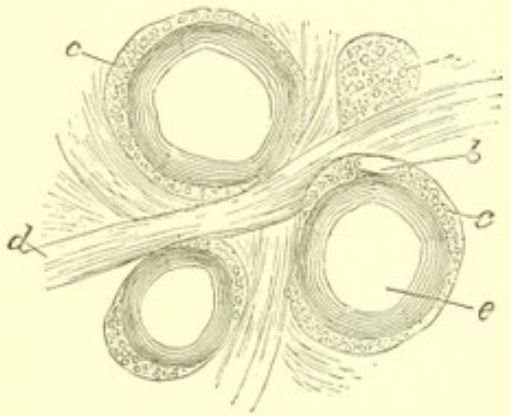
A histological examination of this infiltrated tissue shows the fasciculi of the connective tissue separated from one another. In the spaces formed by this separation, there is found a fluid which contains white blood corpuscles or lymph cells, more numerous than in the physiological

condition. The cells applied along the fasciculi, the fixed cells of the tissue, are more or less swollen, contain a very distinct nucleus and refracting granules. In the composition of these granules there is fat; but it is not perfectly formed, since chromic, acetic, and picric acids have not the same reaction upon them as is obtained upon pure fat granules. These reagents diminish their diameters and increase their refraction. It is probable that these granules seen in the cells of connective tissue are a combination of fatty principles with an albuminoid substance, and that a separation is produced by the acids.

Sometimes in the cells of œdematous connective tissue, there are seen colored granules, bright yellow, very small and often angular, formed possibly from the coloring substance of the red corpuscles of the blood. This pigmentation of the connective tissue fibres and the elastic fibres does not undergo any appreciable change.

The bloodvessels which traverse the œdematous parts are filled with red corpuscles, the proportion of white blood cells is increased. In some cases the red corpuscles are so numerous and so compressed one against the other, that they cannot be distinguished, the vessel appearing as if injected by a homogeneous mass. The vessels are very readily recognized, and they are separated by the fluid as are the fasciculi of the connective tissue.

Fig. 140.



Adipose cells of the subcutaneous connective tissue of a dog. Artificial œdema, produced by ligature of inferior cava and section of the sciatic. *a* Lymph corpuscle infiltrated with fatty granules. *c*. Globule of fat. *b*. Nucleus of the cell. *e* Protoplasm infiltrated with fatty granules. ×400.

The adipose cells, in œdema, generally undergo a change. When œdema is artificially produced in the dog, there is seen a fatty degeneration of the protoplasm situated between the membrane of the vesicle and the central drop of fat. So that the adipose cell, instead of being formed of a single refracting mass, has surrounding the central drop of fat a circle of granules.

In the cachectic œdemas the fat contained in the cells has undergone partial absorption. This occurs, for example, in phthisis. There is also sometimes seen a breaking up of the fat of the adipose tissue into delicate little drops. This change of the fat is due to the presence of an albuminous fluid within the adipose cell, and is analogous to an artificial emulsion of fat with albumen. The nuclei of the adipose cells are always very distinct.

Formerly it was believed that œdema was the result of a stasis of the blood. The physiological theory of Lower was accepted by all pathologists. He said that when the veins are obliterated, the blood cannot pass from the arteries into the veins, its serous portion passes through the walls of the vessels, as through a filter. However, Hodgson did not see œdema result in man if a vein was ligated. The theory of Lower was abandoned when Bouillaud showed that in most local dropsies there is

an obliteration of the corresponding veins. Yet clinically it is seen that there are dropsies without obliteration of the veins, and again a vein may be obliterated without dropsy occurring. In animals the simple ligation of a vein does not produce dropsy, since the collateral circulation is always sufficient to prevent the pressure of the blood from exceeding the limit of resistance of the walls of the vessels. But if upon an animal in which a vein has been ligated, the vaso-motor nerves are divided, the arteries being dilated, a greater amount of blood passes into them, and the pressure becomes sufficient to cause the transudation of serum.

This exaggerated pressure is the true cause of dropsy; if the pressure is sufficient, œdema is produced, independent of obliteration of the veins. Every œdema, except perhaps cachectic œdema, may be referred to the same cause.

The obliteration of the veins may be regarded as one of the causes of dropsy, since it increases the blood pressure in the corresponding capillaries; this obliteration produces œdema in cases where there is at the same time an atomic state of the vascular system.

In œdemas which are very rapidly developed, the large cells of the connective tissue are infiltrated with a greater amount of fatty granules than are the cells in an œdema which has slowly formed, as in disease of the heart.

Sect. IV.—Inflammation of Connective Tissue.

When the subcutaneous connective tissue has been divided by a cutting instrument, an inflammation is produced which terminates in recovery, and constitutes the process necessary for the recovery.

An open wound of the connective tissue, after a few hours, has its surface covered with a thin grayish opalescent layer, plastic lymph of J. Hunter. J. Hunter, his followers, and the French surgeons, up to the present time, have maintained that this plastic lymph is derived from the vessels by exudation, is susceptible of organization, and of the formation of the different tissues met with in cicatrices. There are found in this gray layer filaments of fibrin, white corpuscles or pus cells, and red blood corpuscles. Beneath this superficial layer the fasciculi of the connective tissue and the blood capillaries are separated from each other by the same opalescent substance, so as to constitute a kind of membrane, continuous and extremely thin. From this description it is seen that at the moment when this so-called lymph becomes solid, it contains cellular elements. At the present time these facts might be explained by the white blood corpuscles passing out of the vessels, and the coagulation of the fibrinogenic substance (Cohnheim). Yet this explanation is not sufficient, for it is very possible that the lymph contained in the lymphatic vessels, and in the meshes of the connective tissue, plays some part in these phenomena. It has been mentioned, that the white or lymph corpuscles are found free between the fasciculi of the connective tissue. Again, the conditions for the formation of fibrin are far from being perfectly understood. It is only known that the plasma of the blood abstracted from the vessels, coming in contact with the paraglobulin (Kühne), and other substances contained in the histological elements, takes the

form of fibrin. What is difficult to understand is, why the blood plasma, lymph, and serum of the pericardium, which contain the fibrinogenic substance, never give origin to fibrin in the living organism, although these fluids are in contact with elements containing the fibrino-plastic substance.

The phenomena of superficial exudation, which at first are slight, soon become exaggerated and suppurative in character. The connective tissue sustains great modifications; loses several millimetres of thickness, also its fascicular appearance, becoming pulpy, translucent, and has the nature of embryonic tissue.

There are still found from the second to the third day after a simple wound, fasciculi of the connective tissue in this embryonic layer. They are smaller, less distinctly fibrillar; they do not appear enveloped by a special layer which limits them, and which causes them to swell irregularly when acted upon by acetic acid. They are separated by round or angular cells, consisting of a mass of protoplasm containing a nucleus. In most cases there are not found, in this layer of embryonic tissue, any large flat cells of the connective tissue.

The infiltration of connective tissue by a notable quantity of round elements, generally extends as far as two millimetres to one centimetre from the solution of continuity; but this infiltration can only be recognized with the microscope. In this peripheral zone there is very manifestly seen a swelling of the flat cells of the connective tissue, a division of their nuclei, and a consequent proliferation of these cells.

From this description it is seen that the abundant production of new cellular elements, between the constituent parts of the connective tissue, may come from two sources; the passing out of the white blood corpuscles and the multiplication of the cells of the connective tissue: but science has not yet been able to determine the influence of each of these processes in the phenomena of the reparation of wounds.

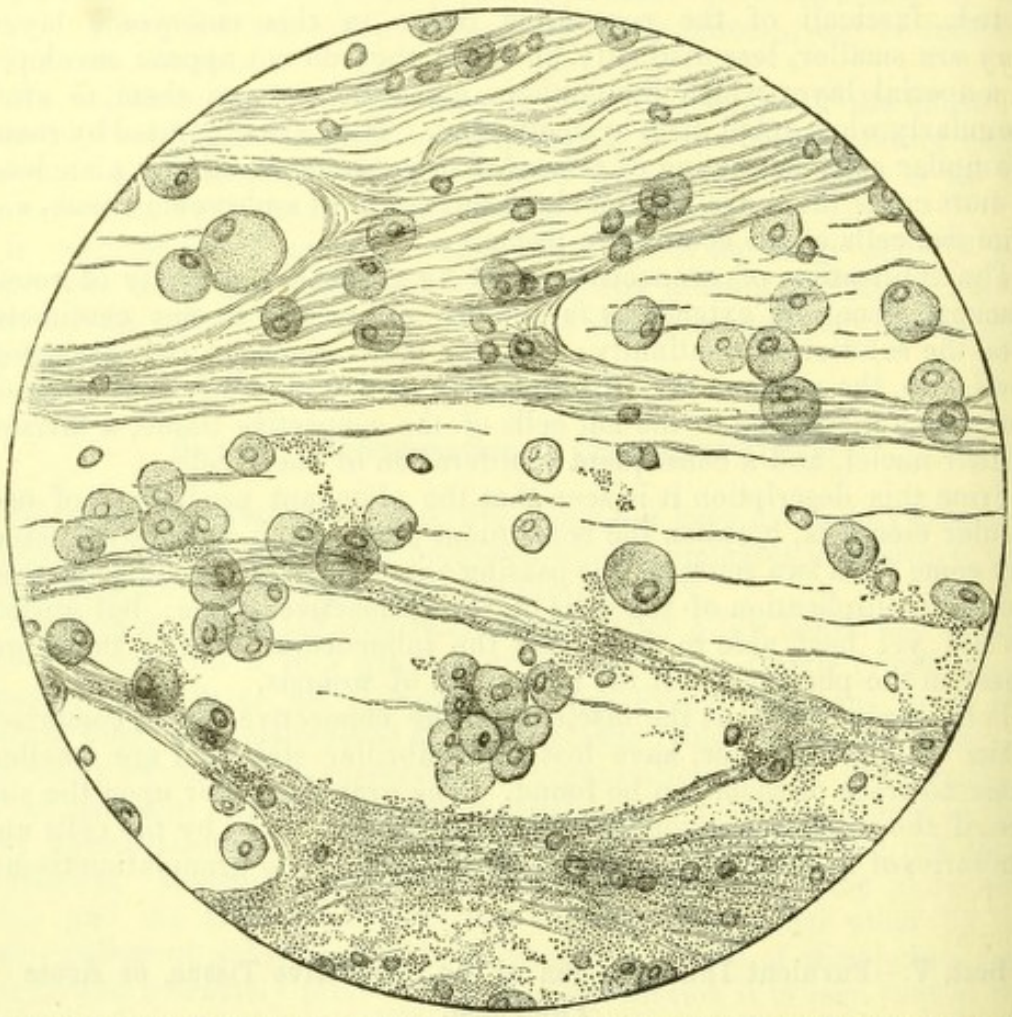
It has been seen that the fasciculi of the connective tissue, comprised in the embryonic layer, have lost their fibrillar state and are smaller. Later no trace of them can be found. The granular layer upon the surface of the wound, or pyogenic membrane, formed only by the cells and capillaries of the embryonic membrane, gives origin to granulation tissue.

Sect. V.—Purulent Inflammation of the Connective Tissue, or Acute Phlegmon.

The name purulent inflammation, or acute phlegmon, is chosen, since in rare cases where the disease terminates by resolution, there is nevertheless a great number of pus cells in the meshes of the connective tissue. The evolution of acute phlegmon is very rapid; redness, increase of temperature, swelling, œdema, and the sharp pain, are all simultaneously manifested. The histological changes occurring in the connective tissue during the first stage, can seldom be studied in man. Phlegmon artificially produced upon animals, is probably identical with that occurring in man, and may be satisfactorily examined. In order to excite an acute phlegmon in a dog, it is only necessary to inject a solution of nitrate of

silver into the connective tissue. After ten or twelve hours there is œdematous and painful swelling of the region. The connective tissue has become gelatinous, the vessels are dilated and filled with blood, at first there appears to be no difference between this tissue and that of œdema. But the fluid does not flow so readily as in œdema, and there is a notaable difference between the two lesions. Among the fasciculi of the connective tissue separated from each other, there are seen, as in œdema, numerous white corpuscles or pus cells, but there also exists a fibrinous reticulum, which is never seen in simple œdema. Moreover,

Fig. 141.



Portion of a perpendicular section through the submucous connective tissue of the ilium, in a case of acute dysentery showing the appearance of connective tissue in an early stage of suppurative inflammation. × 480. The lymph spaces are dilated, and lying free in these and adhering to their walls are numerous rounded nucleated cells (altered endothelium), and also a number of smaller granular bodies (lymphoid elements). The granules in the lower portion are micrococcus groups. From a photo-micrograph, by Surgeon J. J. Woodward, U. S. Army. Copied from the second medical volume of the Medical and Surgical History of the War of the Rebellion.

there occurs a true acute inflammatory œdema, which very probably is connected with the same cause as œdema, from the circumstance that there results a paralysis of the vessels, and greater pressure of the blood on the vascular system. The blood capillaries are dilated and filled with blood, causing an increase of temperature of the part. At this stage the

fasciculi of the connective tissue do not present any appreciable changes. The large flat cells swell, become spherical, some contain two nuclei; their protoplasm is very granular, and even granules of fat may be distinguished.

The first stage of phlegmon is characterized by the formation of numerous pus cells and a fibrinous exudation. The pus cells increase in number and the fibrin becomes more abundant; this material extends between the fibres and consolidates them; the inflammatory tumor becomes firm, giving a sensation of resistance to the fingers. There is no fluid present which may be displaced as in œdema, and it is to the presence of fibrin filling the meshes of the connective tissue that the limiting of the phlegmon should be attributed, in cases where the course has been slow.

In man, this first stage is followed either by *resolution*, *induration*, or *suppuration*. When resolution is produced, it is probable that the escaped white corpuscles are taken up by the lymphatics, either in their normal state or after having undergone a molecular separation, and that the fibrin and extravasated red blood cells experience the same change.

Induration without suppuration has a very close analogy to the induration which succeeds the opening of an abscess; the histological changes are probably the same in both cases. There is a production between the fasciculi of the connective tissue of new cellular elements, while around them there exists a new fundamental substance, transparent and of soft consistence. Later, the cellular elements present a fatty degeneration, and the new tissue is absorbed.

In every phlegmon pus cells are formed in the meshes of the connective tissue. When their production is very abundant, the connective tissue fasciculi are separated or undergo inflammatory softening and absorption, thus forming a purulent collection or an abscess. The phlegmon is now said to have suppurated.

The pus of a circumscribed phlegmon is creamy, homogeneous, and does not contain fasciculi of connective tissue. Examined with the microscope, the purulent fluid presents: 1st, round cells exactly resembling white blood corpuscles containing only one nucleus; 2d, cells of the same diameter possessing several small nuclei; 3d, similar cells with fatty granules varying in amount; 4th, large cells inclosing fat granules, the granular corpuscles of Gluge; 5th, red blood corpuscles perfect or broken.

The sac which incloses the pus is anfractuous and lined by a layer similar to that which is formed the second day upon the surface of a wound. Here the fasciculi of the softened connective tissue are united together by a layer of coagulated fibrin, in which are seen pus cells.

When the abscess is opened by the surgeon, the pus escapes, the walls of the empty sac coming together are united, and there results an induration which persists for a few days. Generally, the bottom and sides of the abscess granulate and form pus, when the phenomena are those of a simple wound.

In diffused phlegmon, the inflammatory changes are so intense that the layers of connective tissue have not time to undergo inflammatory absorption. They die and act upon the neighboring parts as foreign bodies. Properly speaking, a diffused phlegmon is a true necrosis of the connective tissue, and is very similar to a suppurative osteo-myelitis.

When the purulent centres are opened, there are found mingled with the

pus macerated shreds of connective tissue, and from the bottom of the abscess float gray filamentous masses.

If the patient dies during this stage, an incision made through the phlegmon shows the whole of the connective tissue of the part to be infiltrated with serum, blood, and a varying amount of pus. In the midst of the infiltrated region there are seen whitish, opaque, filamentous masses, free or adherent, formed of mortified connective tissue, the whole exhaling an odor of gangrene.

A histological examination of this gangrenous connective tissue offers for study a fibrillar mass, in which it is difficult to distinctly recognize the fasciculi. In the midst of the separated fibrils there are seen albuminoid granules, yellow or black pigment, fat granules, and fat drops, these last coming probably from the adipose tissue. The shreds of connective tissue which are detached and float in the pus present a similar structure. The effect produced by maceration in the pus is the dissolving of the uniting substance of the fibrils (*Kitt-substanz* of the Germans).

Sect. VI.—Chronic Phlegmon.

The name chronic phlegmon is given to inflammations of the connective tissue of long duration, characterized by a lardaceous induration usually accompanied by suppuration. It is not a primary disease of the connective tissue; it accompanies chronic affections of the bone or of the vascular system.

Sometimes the thickening of the connective tissue is considerable and simulates a tumor; but the tumefaction is never clearly circumscribed, it blends with the neighboring healthy parts, so that it is difficult to assign any definite limits to the lesion. Upon the surface of the skin there may be seen either ulcers, fistular openings, or papillary hypertrophies.

Upon making an incision into the morbid mass, the tissue presents a lardaceous appearance, and a serous or opaque fluid flows from it. Carefully examining the surface of the section, distinct fibrous portions are recognized, which correspond to the tendons or aponeuroses; parts translucent and infiltrated with fluid, as in œdema; irregular, opaque, and purulent spots; dilated congested vessels, and hemorrhagic points.

In order to study with the microscope this complex tissue, it is necessary to employ several methods. The elements obtained by teasing a fresh piece are pus cells, granular corpuscles, and cells larger than those of pus, of varied shape, round, fusiform, flat, irregular, similar to those seen in a sarcoma. Besides these cellular elements, there are seen fat granules, drops of fat, and fibres of connective tissue.

In thin sections after hardening the tissues, there are found fasciculi of connective tissue running in different directions and separated by collections of cells. Some resembling white blood corpuscles, others larger and fusiform, representing the fixed cells of the connective tissue. In these sections the bloodvessels present embryonic walls, and are surrounded by an irregular mass of pus cells. At times small spots of atrophied adipose cells, with a multiplication of their nuclei, are found; they are generally separated from one another by collections of embryonic or

pus cells. Finally, at some points of the preparation, cells analogous to those of a sarcoma predominate and form collections varying in size.

It is seen from this description that there is no fundamental difference between the structure of this morbid mass and that of some sarcomata; it would be impossible to distinguish preparations of these two tissues selected from those which closely resemble each other. But if a complete and comparative analysis of different portions of these neoplasms is made, differential characters are soon found. A sarcoma, for example, at least when not inflamed, does not contain purulent spots as does a chronic phlegmon; again, in a chronic phlegmon, the constituent elements of the tissue persist a much longer time than in a diffused sarcomatous tumor.

Since a chronic phlegmon is occasioned by a cause which may generally be determined, such as a white swelling, a diseased bone, etc., while the cause of the development of a sarcoma is unknown, it is almost always easy to make the diagnosis by considering all the information furnished both clinically and pathologically.

Another very important differential character is given to us by therapeutical surgery. When the anatomical cause of chronic phlegmon is removed, there is recovery. When in a surgical operation, an amputation for example, there is comprised in the flap some of the indurated tissue of a chronic phlegmon, the resulting cicatrix is regular, while if sarcomatous parts are left the tumor again grows with renewed activity.

Sect. VII.—Tumors of the Connective Tissue.

All tumors without any exception may be developed in the connective tissue, but it does not follow that the cells of the connective tissue are the only source of these neoplasms, as Virchow has maintained. It has been previously shown that almost all the neoplasms constituting tumors, at their beginning consist of an embryonic mass, which is the origin of the new tissue. The method of formation of embryonic tissue from connective tissue is the same in a simple inflammation and in the beginning of a tumor. The cells which form it are probably the white blood corpuscles escaped from the vessels, and the cells of the connective tissue multiplied by division.

The most frequent tumors of the loose connective tissue are those which have their analogues in the varieties of this tissue.

The epitheliomata which are developed in the connective tissue always have their origin in the inter-papillary epithelium, or in the embryonic tissue in contact with pre-existing epithelial masses. All other tumors, the osteomata, chondromata, etc., may also have their origin in the loose connective tissue.

Serous cysts of the connective tissue are always lined with endothelial cells similar to those of the serous membranes, and of the connective tissue. Their wall is formed by the fibres of the connective tissue placed one upon the other; between the fibres there are found flat cells arranged parallel to the surface of the membrane. The development of these cysts has not been studied, but it is very probable that it is the same as that of serous bursæ.

There have been seen in subcutaneous connective tissue hydatids with echinococci. The mother vesicule is then surrounded by a complete connective tissue membrane containing numerous vessels.

Sect. VIII.—Hemorrhages of the Serous Membranes.

The alterations of the serous membranes are here studied, on account of their analogy with those of connective tissue.

Hemorrhages of the serous membranes are common, such as meningeal hemorrhages, peri-uterine hæmatoceles, and hæmatoceles of the tunica vaginalis. The effused blood coagulates, undergoes the metamorphoses observed in all blood extravasation, and occasions an inflammation of the serous membrane. This inflammation is generally slow, and does not cause suppuration. It produces exudations and new formations in the form of false membranes upon the surface, or bands and adhesions between the two surfaces of the serous membrane. The retrograde changes of the effused blood consist in the disappearance of the red cells, the elimination of the hæmoglobin, the formation of hæmatin granules or crystals of hæmotoidin, the breaking up of fibrin, etc.

In traumatic hemorrhages of the serous membranes, notably in the hemorrhages of the peritoneum following a wound of the abdomen, the hæmatin which comes from the decomposition of the red blood cells is so abundant that, upon opening the abdomen, it appears as if soot had been spread upon the great omentum and intestines. Upon the great omentum the black matter is seen in the form of very deep brown opaque granules, spherical or angular in shape. They are located in the white blood corpuscles which form collections between the fibres of the reticulum, in the endothelial cells lining the fibres, and in small groups of cells that surround the adipose tissue, which they partly conceal. Upon the intestines the peritoneal endothelium is also infiltrated with black granules, and has the appearance of the epithelium upon the choroid coat of the eye.

The absorption of the hæmatin granules from these locations is effected probably as in the connective tissue, by the lymphatic vessels, through the intermediation of the white corpuscles.

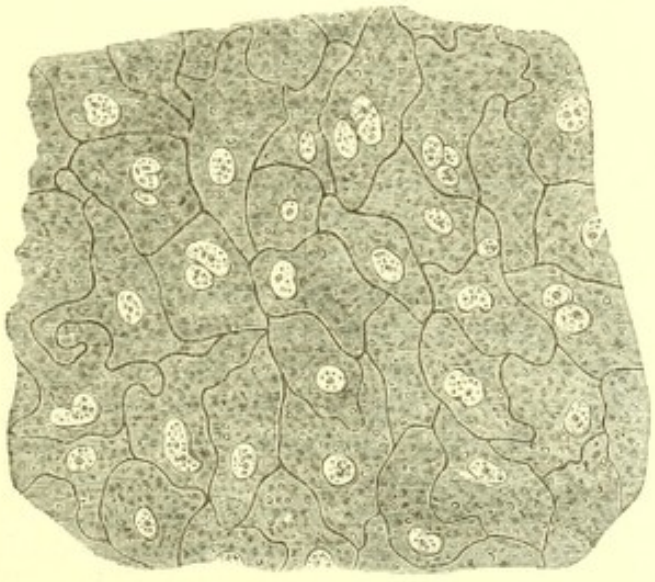
The phenomena observed in the peritoneal cavity of a rat in which defibrinated blood has been injected, are the following: spherical swelling and proliferation of the endothelial cells of the serous membrane; the penetration of broken or entire red blood cells into the interior of these cells, some of which are detached and float free in the cavity; afterwards the formation of pus cells and a fibrinous exudation. The red blood cells undergo changes, first studied by Rindfleisch, similar to those seen in blood when heated to 45° C. They are decomposed into spherical, refracting, colored granules, easily recognized, and their different stages of disintegration may be seen.

Sect. IX.—Inflammation of Serous Membranes.

The essential changes met with in all inflammations of the serous membranes are exudations and multiplication of the endothelial cells. The exudations of inflamed serous membranes always contain fibrin. This is not unexpected, since the fluid of serous cavities in the physiological state contains a considerable quantity of fibrinogenic substance. In the acute inflammations of serous membranes, the fluid in the cavity becomes more abundant and still contains a larger amount of fibrinogenic substance.

The fluid obtained by puncturing the chest during an inflammation of the pleura, is at first clear and fluid, but if exposed to the air in a few hours it becomes a gelatinous mass. This change was first observed by Virchow, who concluded that the fibrin does not exist already formed in the exudation, but that the latter only contains a substance susceptible of becoming fibrin under the influence of the action of the air. Therefore he named this substance fibrinogenic. Yet it is certain that the action of the air is not the only cause that determines the coagulation of fibrin in this fluid. The addition of red blood cells or even the serum of the blood after it has coagulated, will immediately occasion the appearance of fibrin in the exudation. These are very important facts, since they explain the process of the formation of fibrin deposited upon the surface of the inflamed serous membrane in the form of laminæ, while the distended cavity contains a clear fluid. Yet the central fluid may present some fibrinous flakes, or may coagulate to a greater or less extent throughout.

Fig. 142.

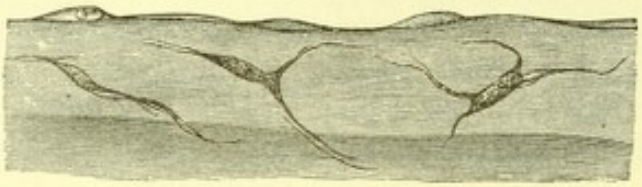


Normal endothelium of visceral pericardium of a toad, silver treated and high power. (*Chapman.*)

If the fluid exudated is abundant and clear it is termed serous, although there always exists upon the surface of the membrane a layer of fibrin varying in thickness. In this serous fluid there are found suspended many pus cells and red blood disks. When concrete fibrinous layers exist upon the surface of inflamed serous membranes, and the exudation

does not contain either blood or pus cells appreciable to the unaided eye, the exudation is termed fibrinous; when the exudation contains blood, it is named hemorrhagic; and purulent, when it contains a large amount of pus.

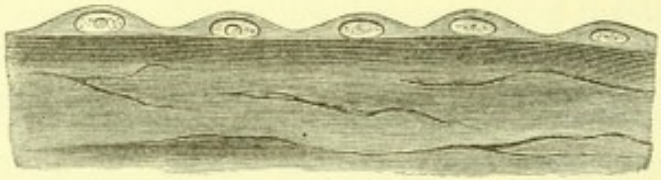
Fig. 143.



Profile view of normal endothelium of pericardium of a toad, treated with gold; the endothelium showing at the upper edge. The stellate cells below are connective tissue corpuscles. High power. (*Chapman*).

The *fibrinous exudation* formed upon the surface of serous membranes varies in its arrangement and microscopic appearance. When recent the surface is seen to be reticulated, having very small meshes with slight depressions, at first thin, but soon thickened by the deposit of new layers.

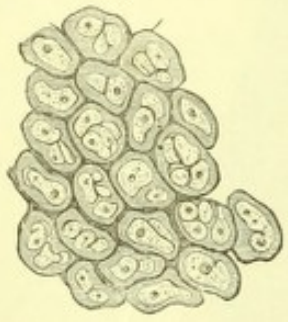
Fig. 144.



Profile view of endothelia of pericardium of toad twenty-four hours inflamed. Gold stained. High power. (*Chapman.*)

It is yellowish-gray, semi-transparent, gelatinous, soft, and friable. It can be detached with the nail in the form of shreds, which when broken have a clear fracture. In the pericardium the fibrinous exudation has a special arrangement, its surface has been compared to a cat's tongue; it is villous, covered with granulations or shreds; this arrangement is produced by the agitation of the fluid caused by the movements of the heart. When the exudations are chronic they become smooth, opaque, and are formed of layers placed one upon the other, which may be separated by dissection.

Fig. 145.



Transformed endothelia of parietal pericardium of frog, two days inflamed. Gold treated. High power. (*Chapman.*)

In order to study microscopically the structure of the fibrinous exudation, and the changes in the subjacent serous membrane, several methods should be employed. The most simple consists in removing shreds of the exudation, and examining them after spreading upon a glass slide. When very thin there is seen with low power a very beautiful reticulated arrangement; from a central thick point trabeculæ of fibrin radiate, increasing and dividing towards the periphery. When the exudation is thick or chronic, this reticulated arrangement cannot be distinguished. By tearing with needles there are found cells varying much in shape and size. Some resemble white blood corpuscles,

generally containing large, oval, very distinct nuclei, with one or more bright, large nucleoli, similar to the nuclei formerly considered characteristic of carcinoma. Other cells which contain nuclei are flat, resembling endothelial cells of the serous membranes, others possess long prolongations and numerous nuclei, are flat, resembling multinuclear cells of bone marrow (myéloplaxes, giant cells). Langhans has pointed out these last cells around tuberculous granulations of serous membranes; but we have found them in all the fibrinous inflammations of serous membranes.

Fig. 146.



Transformed endothelia of visceral pericardium of toad, six days inflamed. Gold treated. The cells are irregularly stellate. High power. (*Chapman.*)

To study the situation of these cells in the exudation, the relation of the exudation with the subjacent membrane, and the changes in the latter, vertical sections are to be made after hardening. They show upon the surface of the serous membrane a layer of amorphous or granular fibrin, limited by a very distinct although sinuous contour. Beneath are seen successive layers of cells previously described, and fibrin arranged differently according to the case. Usually the fibrin forms a network, the flattened meshes of which limit elongated alveoli containing the cells.

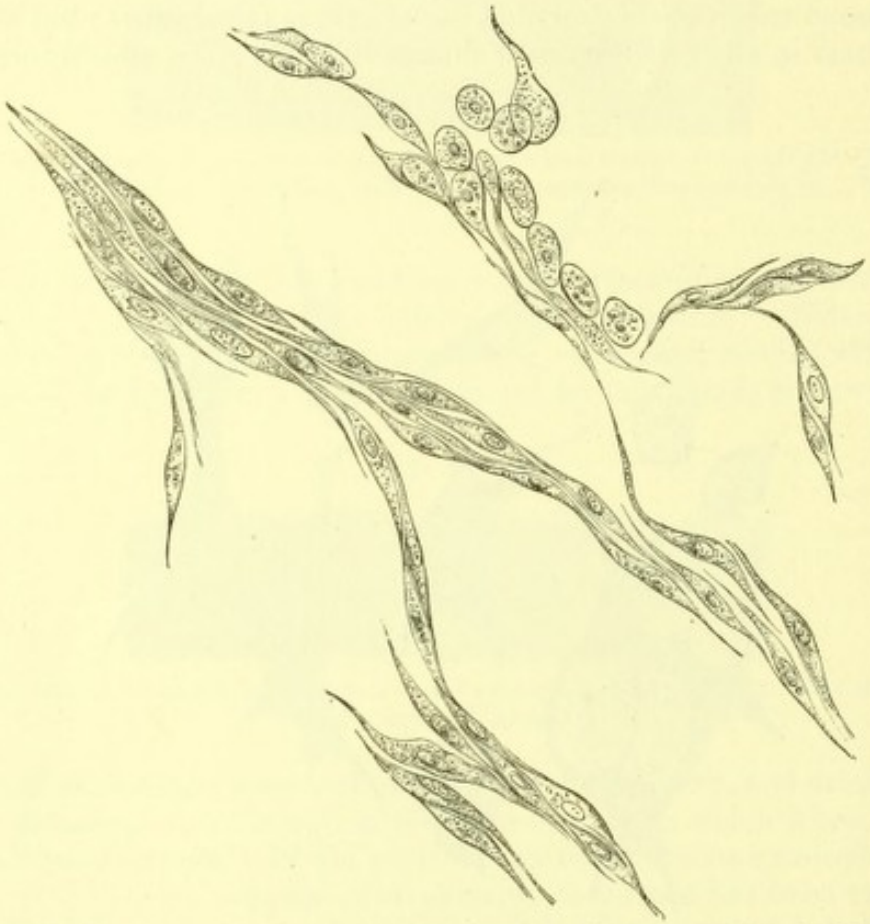
The limit of the serous membrane is always very distinct, the exudation is simply applied to its surface, and is separated from it, at intervals, by collections of endothelial cells, forming several layers, and resembling the cells found in the alveoli of the exudation. It is very probable that all the cells come from the proliferated and detached endothelial cells of the swollen serous membrane.

At present we can logically infer that the endothelial cells, modified by inflammation, act as the fibrino-plastic substance, and determine the

formation of fibrin from the fibrinogenic substance of the primary fluid exudation.

The superficial elastic layer of the serous membrane is in most cases unchanged. Between the fasciculi of the subjacent connective tissue

Fig. 147.



Transformed endothelial cells of parietal pericardium of toad, six days inflamed. The cells are spindle-form and arranged in rows to form more or less compact false membranes. Gold treated. High power. (*Chapman.*)

there are seen numerous cells, normal in character, similar to white blood corpuscles or lymph cells. Besides these, distinctly limited circular elliptical or cylindrical spots are observed, which are only the transverse or longitudinal sections of the lymphatic vessels of the serous membrane filled with lymph cells. Ernest Wagner recently, in studying fibrinous pleuritis, pointed out the filling of the lymphatic vessels with fibrin, and concluded that this obstruction of the vessels interfered with the absorption of the exudation; he also mentioned the existence upon the surface of serous membranes of large cells with many nuclei, which are found also in chronic inflammations (Rokitansky). We have ourselves observed the lymphatics filled with fibrin, and again, in pericarditis and fibrinous peritonitis we have proven the existence of modified epithelial cells in the mass of the exudation, and the dilatation of the lymphatics by an accumulation of lymphoid cells.

Hemorrhagic inflammations of serous membranes are characterized by the presence of a varying amount of blood added to the fluid or fibrinous

exudation. Between simple fibrinous inflammations and true hemorrhagic inflammations there are distinguished many intermediate forms. In the most simple the fibrinous exudation is studded with ecchymotic spots, especially very distinct upon the under surface of the exudation, at the moment of separating it. At other times the fibrinous membrane is red throughout its entire extent, and the serous surface of the exudation is at the same time colored by the blood. These hemorrhagic inflammations are very frequently connected with the formation of new vessels which develop upon the surface of the serous membrane, and penetrate as flattened granulations into the under portion of the exudation. The newly formed vessels have an embryonic wall, and are surrounded by an embryonic tissue; they form branches which radiate from a central vessel. Thus in hemorrhagic meningitis (pachymeningitis), there are at times found upon the internal surface of the dura mater, small nummular red patches, which upon very careful examination present fine vascular tufts and small ecchymoses. These small patches, rudiments of new membranes, if extensive, as is frequently the case, may be readily detached. A vertical section of the dura mater through one of these points shows the continuity of the dural vessels with those of the new membrane.

In hemorrhagic inflammations of other serous membranes, sometimes there is observed, as pointed out by Rindfleisch, in the middle of the exudation, the new formation of vessels, the friable embryonic walls of which easily torn give rise to hemorrhages. But in cases where the exudation is infiltrated with blood, although vessels are recognized in the exudation and false membrane, it is difficult to determine if the hemorrhage proceeds from the new or old vessels. When the process is chronic, the false membrane is composed of embryonic tissue and vessels, with layers of interposed fibrin of considerable thickness and is bathed in a bloody exudation.

The blood effused into the exudation undergoes the usual changes terminating in the formation of granular or crystalline hæmatoidin. When hemorrhagic inflammations result in suppuration the fluid within the serous cavity contains pus, which examined closely with the unaided eye presents red granules consisting of large crystals of hæmatoidin isolated or in groups.

Hemorrhagic inflammations of serous membranes occur particularly in alcohol drinkers, and in the inflammations connected with tuberculosis and cancer.

Purulent inflammations of the serous membranes are primary or secondary to a fibrinous or hemorrhagic inflammation. Thus, in some fibrinous pleurites, where a primary paracentesis thoracis gives a serofibrinous fluid, a second puncture made several days after the first will give pus. Primary purulent inflammations, however, are much more common; they occur in puerperal fever, purulent infection, glanders, rheumatism, etc. Generally in this affection the organs covered by a serous membrane contain metastatic abscesses or some lesion of the blood or lymphatic vessels, which will be considered under the vascular system. When the course of the purulent inflammation is very rapid, the serous cavity is filled with a recently formed pus, and there is no solid exudation upon its surface. The vessels are dilated, their walls

embryonic, and the connective tissue of the serous membrane is infiltrated with pus cells. It is almost beyond doubt that the pus cells come from the blood and that the endothelium of the serous membrane takes but little part in their production. In man, the change of the endothelia cannot be followed; at the time of the examination, they are either not found or are seen in the form of shreds composed of granular fatty cells. Usually yellowish flakes varying in size and shape are found, forming a fibrinous network, the meshes of which are filled with pus cells generally fatty and granular.

If the course of the purulent inflammation is less rapid, a fibrinous exudation is seen upon the surface of the serous membrane, the structure of which is exactly similar to that of the preceding flakes. The number of pus cells is here so great that they completely conceal the fibrinous network. The lymphatics and bloodvessels of the serous membrane present at this time the same changes as in fibrinous inflammation.

If the purulent inflammation occurs after a simple fibrinous inflammation, at the autopsy there are found very thick false membranes infiltrated with pus, vascular granulations similar to those described under hemorrhagic inflammations. Almost always red blood-disks or pigmented matter derived from them are present.

The pus formed in serous cavities very rapidly undergoes nutritive changes: the cells are filled with fatty granules, and when the fluid has been partly absorbed, they become caseous. This caseous pus forms yellow opaque masses having the consistence of putty; formerly it was considered to be tuberculous. When the pus remains in a fluid state in the serous cavity, its cellular elements are destroyed, at least in great part. There are formed, as in the caseous centres, crystals of the fatty acids and cholesterin; at times pigmented granules and hæmatoidin crystals are present.

Solid fibrino-purulent exudations undergo the same changes as pus cells; they become caseous, shreds are detached from their surfaces and float in the serous cavity. The shreds and exudations, yet adherent, are composed of a granular substance produced by the molecular separation of the fibrin and of collections of fat granules, of crystals of fatty acids, of cholesterin, and of blood pigment.

The serous membrane at this time is considerably thickened and vascular, or it resembles cartilage. It consists of parallel lamellæ of connective tissue, between which are found flat cells; this indurated tissue is in every way similar to fibromata with parallel lamellæ and flat cells. This new tissue is very liable to calcareous infiltration, which forms hard bone-like plates, varying in regularity and extent. We have never seen bone corpuscles in these bone-like plates.

A thickening of the pleura is especially seen around masses of caseous pus. Sometimes the change is limited to a single portion of the serous membrane, thus forming a cyst with thick walls containing caseous matter, around which there exists, in a few cases, a gelatinous transparent material studded with opaque spots. These chronic encysted pleurisies have an analogous arrangement to old hydatid cysts. The gelatinous material that they contain is nothing more than fibrin.

Hyperplastic or adhesive inflammations of serous membranes are characterized by a growth of embryonic tissue traversed by bloodvessels, which is definitely organized and gives rise to thickenings or adhesions. Adhesions occur in the form of bands, or they cause a complete fusion of the two opposite sides of the serous membrane, frequently occasioning the obliteration of the serous cavity.

The adhesive inflammations occur after inflammations which present the adhesive character from the beginning, or they follow fibrinous or purulent inflammations; but very often it is impossible in old adhesions to determine their origin. It is probable that many of them are of congenital origin, and may be connected with malformations.

In a few autopsies there are found upon the surface of serous membranes and especially the pleura, soft vascular growths, composed of embryonic tissue and vessels, the walls of which consist entirely of cells; some, according to Rindfleisch, present considerable length. These growths as they develop meet with similar formations from the opposite surface, are united, become fibrous, and so form bands, very variable in form and extent. Their surface is now covered with flat endothelial cells similar to those upon the rest of the serous cavity. (Fig. 148.) When the adhesion is complete, there is found between the two serous surfaces a homogeneous layer of fibrous tissue which blends them into a single membrane.

Fig. 148.



Endothelium covering the fibrous bridles which unite opposite surfaces of the pleura after inflammation. Silver treated. ×300.

Thickening of a serous membrane, or hyperplastic inflammation appears to have the same origin, but as the new formation is limited to a single surface, the growth does not terminate in adhesion. If it is very slight, it is termed a milky spot, on account of the whitish appearance, due to a fibrous tissue composed of superimposed and parallel laminæ. If the new formation is thicker, it constitutes the cartilage-like plates previously described. In the milky and chondroid plates the bloodvessels are very few or entirely wanting. At times the chondroid plates become infiltrated with calcareous salts, and then form solid "carapaces," which are met with in the pericardium, pleura, peritoneum, tunica vaginalis, etc.

Sect. X.—Tumors of the Serous Membranes.

Primary tumors of the serous membranes seldom occur, while secondary tumors, through extension or generalization, are frequent.

Primary tumors of serous membranes are those of which the type is found in connective tissue: fibromata, lipomata, myxomata, sarcomata, carcinomata, and tubercles.

The most frequent *fibroma* of serous membranes is the laminated fibroma, or corneous fibroma. (See p. 92.)

At certain parts of several of the serous cavities there are seen villous appendices formed of adipose tissue and vessels covered by the serous

membrane, like the finger of a glove. Such are the epiploic appendices of the intestines, the folds of adipose tissue of the peritoneum, the villi of the pleura, and the synovial fringes. These cellulo-adipose appendices are subject to hypertrophies and constitute the *dendritic lipomata*, the evolution of which is slow. In these same appendices mucous or fibrous tissue may form, constituting pedunculated *myxomatous* or *fibromatous* tumors.

Miliary *tuberculous eruptions* of serous membranes are common. They are primary or are associated with a generalization of miliary tuberculosis, or are developed in the proximity of tuberculous foci of organs covered with a serous membrane. The granulations are prominent, lenticular, whitish, translucent, non-vascular, sometimes opaque at their centre. The smallest are scarcely visible to the unaided eye; if they are numerous, they join at their borders and form areas varying in size, with serrated edges and uneven surfaces. The neighboring serous membrane is congested and ecchymotic spots are seen very often upon the peritoneum, either red, violet, slate-color, or black. They are generally upon the visceral layer of the serous membrane, but are also found upon the parietal layer.

Tuberculous granulations of serous membranes are very superficial, appearing at times as if placed upon the serous membrane. They may also be situated in the membrane, and in different layers of it, when it acquires considerable thickness, and presents the structure of interstitial inflammation. In the peritoneum, and especially in the great omentum, sometimes the layers are united together, and the destroyed trabeculæ replaced by a solid mass one to two centimetres thick, formed of tuberculous granulations, imbedded in a soft and vascular tissue. To the unaided eye this new formation may be taken for a cancer.

The evolution of tuberculosis occasions in some membranes different varieties of inflammations, fibrinous, hemorrhagic, purulent, or formative. Frequently, when the tuberculous eruption is recent, the entire surface of the serous membrane is covered with a thin and transparent fibrinous layer. This is easily detached from the membrane, and often the tuberculous granulations are separated with it. The surface of the serous membrane, at the points where the granulations have been, does not appear to have undergone any loss of substance, when the false membrane is removed. In other cases the fibrinous exudation being very abundant, the tuberculous granulations are not at once observed, so also when the exuded fluid is hemorrhagic or purulent they are concealed, and after removing the exudation, the surface of the serous membrane should be washed, when the granulations become apparent.

Chronic tuberculous inflammations almost always cause soft vascular granulations, varying in extent, covered by an exudation, and in the tissue of which tuberculous granulations are developed. This granulation tissue may undergo caseous degeneration. In these cases the connective tissue of the serous membrane is thickened, soft, changed into embryonic tissue in which exist numerous tuberculous granulations.

In tuberculosis of serous membranes there are also formed upon the opposite surfaces of the membrane, bands or filamentous adhesions, which may be invaded by tuberculous granulations.

Tuberculous granulations of serous membranes, at their beginning, are formed of small cellular elements crowded one against the other, which are gradually continuous with the cells situated upon the surface of the membrane or in its deeper layer. These superficial cells are similar to those previously described in fibrinous exudations. They are round or flat, some reach several millimetres in size, and are filled with nuclei (giant cells).

When the tuberculous eruption is abundant, the connective tissue of the serous membrane is changed; between its fasciculi there are found embryonic cells in varying numbers. The bloodvessels are dilated, and the lymphatic vessels filled with lymph corpuscles.

The exudation which accompanies tuberculous granulations, presents the characters that have been studied under inflammation proper.

The thickenings and granulations developed upon the surface of serous membranes infiltrated with tuberculous granulations, are composed of embryonic tissue containing capillaries whose walls are formed of swollen cells. When there is a development of tubercles in these granulations, the vessels corresponding to the tubercles present the modifications which have been explained at page 116.

The development of tuberculous granulations upon the surface of serous membranes, at the beginning of their evolution, is not always from the connective tissue of these membranes, for there are found, beneath the tubercles, cells which appear to be derived from the endothelial layer, and again the lamina of connective and elastic tissue of the serous membrane has not suffered any loss of substance. Do the cellular elements of the granulation come from the endothelium of the serous membrane, from the white blood corpuscles, or from both of these sources? At present it is impossible to decide. Yet Rindfleisch maintained, at a time when the emigration of the white blood corpuscles was unknown, and also very recently, that the proliferated endothelial cells were the point of origin of tubercle. It is very probable that these cells take part in the formation of superficial granulations, but it has not been demonstrated that they alone are the origin of them. When the tuberculous granulations are developed in the depth of the connective tissue of serous membranes, or in the granulation tissue, they spring from embryonic tissue, which may be derived either from the proliferated flat cells of the connective tissue or from white blood corpuscles.

Primary *carcinoma* of serous membranes is very rare, but secondary carcinoma, by extension or generalization, is very frequent. Of all the primary carcinomata which have been observed, the most common is colloid carcinoma of the peritoneum, either upon the peritoneal surface of the liver, stomach, or in the great omentum. It presents the form of gelatinous plates with vascular markings and of ecchymotic points. It is developed from the connective tissue of the serous membrane or the subserous connective tissue. In the great omentum the reticulum is transformed into a flat mass, having none of the structure of the omentum, but only that of colloid carcinoma.

The other varieties of carcinomata have their origin in the organs covered by serous membranes; while increasing they form round masses which cause inflammation in the serous membranes, the exudation of which is almost always hemorrhagic.

When there exists a carcinomatous mass formed upon a serous membrane, there are generally developed around it smaller, separate, nummular secondary masses, having an umbilicated central depression. This depression is occasioned by a granulo-fatty degeneration in the centre, and by an active development at the periphery of the nodule. The lymphatic vessels which pass from the morbid masses frequently form upon the serous membrane hard, knotty, whitish cords, separated or arranged in a reticulum, while small granulations are developed near them. The tissue of the serous membrane around these degenerated lymphatics and granulations is always very vascular. The bloodvessels are dilated and have embryonic walls.

Cylindrical-celled epithelioma may extend to the serous membranes, but it is very rare. Frequently an epithelioma of this nature developed in the intestines, stomach, or biliary passages, causes secondary formations of considerable size in the liver, without the serous membrane being involved.

Sarcomata, *squamous epitheliomata*, and *chondromata*, are very seldom met with, and are secondary formations in serous membranes; the *osteoid tumors* are propagated more frequently to serous membranes.

CHAPTER V.

CHANGES OF THE MUSCULAR TISSUE.

Sect. I.—Normal Histology of Muscular Tissue.

We have divided muscles into three distinct kinds: 1st. Rapid and voluntary contracting muscles; 2d. Cardiac muscles, in which the contraction is rapid and involuntary; 3d. Slow and involuntary contracting muscles.

Voluntary muscles essentially consist of striated muscular fasciculi described on page 31. The fasciculi are arranged parallel one to the other, bound together by extremely thin fibres of connective tissue so as to constitute distinct groups known as secondary fasciculi. These secondary fasciculi are not surrounded by an amorphous continuous membrane similar to the sarcolemma, which surrounds the primary fasciculus.

Between the secondary fasciculi are placed the arteries and veins. The capillaries penetrate the secondary fasciculi and are distributed between the primary fasciculi, forming elongated rectangular meshes which envelop in their network the primary fasciculi. These capillaries are always situated external to the sarcolemma. The entire muscle is ensheathed by an aponeurosis formed of close connective-tissue lamellæ, which can be separated, as shown by injecting a fluid into the muscle beneath the aponeurosis; the fluid will pass through the aponeurosis to the external surface of the muscle. A fluid may, therefore, penetrate throughout the whole extent of a muscle between the primary fasciculi, the connective-tissue fibres and vessels. Consequently, a muscle possesses a vast interstitial lacunar system belonging to the connective tissue, and which is in communication with the lymphatic system. All muscles have tendons of insertion. It was believed for a long time that the primary fasciculi of the muscle were directly continuous with the fibres of the tendon. Kölliker, however, had seen that when the muscular fasciculi came obliquely upon a tendinous surface they were not continuous with the tendinous fibres: but he persisted in believing that in cases where the tendinous fibres have the same direction as the muscular fasciculi they were continuous. Weismann, in studying the muscular insertions by chemical methods, found that a solution of potash demonstrated the union of the muscular fasciculi with the tendon by means of an organic cement or uniting substance, which under the action of this reagent is softened and afterwards completely dissolved.

Sect. II.—Nutritive Lesions of Muscles.

The lesions of the primary fasciculi of muscles consist in changes of nutrition of the muscular tissue, or in a division of the nuclei of the sarcolemma and of the protoplasm which surrounds them. It frequently occurs that the lesions of nutrition are accompanied by a division of the nuclei of the sarcolemma; yet these two phenomena are not always associated; there may be multiplication of the nuclei of the sarcolemma without any nutritive change in the muscular fasciculi, or, vice versa, very advanced modifications may occur in the contractile substance, without any alteration of the nuclei.

Atrophy of Muscular Fasciculi.—Atrophy of muscular fasciculi may coincide with general atrophy of the muscle, or with the preservation and even increase of the size of the whole muscle, when there is an increase in thickness of the connective and adipose tissue. The various tumors of muscles always cause an atrophy of the muscular fasciculi.

The muscular fasciculi of the entire body are atrophied in emaciation. All the fasciculi of a muscle may be affected at the same time, as in infantile paralysis, or only a few are attacked by the atrophy, as occurs in low febrile diseases. It is not certain that in the physiological state the muscular fasciculi of man are not renewed, since in the adult very considerable differences in the diameter of the fasciculi of a muscle exist. Some are scarcely the one-hundredth of a millimetre, while others measure three, seven hundredths of a millimetre, and even more. In the aged, this difference is more marked, and there are constantly found in their muscles fasciculi containing fatty granules, and others also undergoing atrophy.

The atrophy is simple, or is caused by some of the nutritive changes which will be later studied. Usually these changes at the beginning occasion an increase in the size of the fasciculi, the atrophy occurring subsequently. The atrophied muscular fasciculi are very variable in size and shape. Any fasciculus in the adult not exceeding the four-hundredth of a millimetre may be considered atrophied. When the fasciculi have an average diameter of one-hundredth of a millimetre, the atrophy is considerable. Finally, the sarcous substance may have completely disappeared, at least in some of the fasciculi; the latter are represented only by rectilinear filaments formed by the sarcolemma, empty and shrunken. In an extensive and uniform atrophy of muscles the striation of the muscular substance may be manifestly preserved in fasciculi measuring only the three-thousandth of a millimetre. These fasciculi possess nuclei, and opposite each of the latter the fibre presents a slight swelling. This variety may be seen in progressive muscular atrophy, in infantile muscular paralysis during its second stage, and in all atrophies which depend upon the nervous system.

In some cases of club-foot and infantile paralysis, the connective tissue at times has so increased that it more than compensates for the atrophy of the muscular fasciculi, so that the muscle truly atrophied, in its essential elements, is considerably larger than in the normal state. This

increase in size is especially shown, when adipose tissue is formed in great abundance between the atrophied muscular fibres.

In tumors of the muscles the development of the neoplasm occurs in irregular masses; the muscular fasciculi have undergone atrophy in a part of their course, while in the remainder of their extent, they may have preserved their primary size. It thus happens that the muscular fasciculi are divided into irregular segments the extremities of which are rounded or tapering. Generally in their preserved portion the muscular fibres present numerous nuclei, disseminated in a granular substance which replaces the striæ and which resembles cells with many nuclei.

Hypertrophy of Muscles.—Histological study of the hypertrophies is very difficult. When a muscle increases in size through physiological or pathological exercise, it is difficult to determine if this hypertrophy be due to a new formation of muscular fasciculi, or to an enlargement of the old fasciculi. The difficulty is due to the fact that the fasciculi vary very much in size in the same muscle in the normal state.

In cases where the hypertrophy of a muscle is owing to the formation of new muscular elements, the phenomena of new formation can be very well seen. It was in such cases that Bardeleben studied the origin of new muscular fasciculi from cells of the connective tissue, in a hypertrophy of the intercostal muscles occasioned by a prolonged dyspnœa. A new formation of muscular fasciculi constantly occurs in adults suffering with an acute disease; some of the fasciculi are destroyed by nutritive changes. The physiological restoration of muscles, after febrile emaciation, is due, not only to an increase in size of the shrunken, yet unaltered fasciculi, but also to a formation of new muscular fasciculi which are developed between the old. These phenomena have been studied by Zenker in several febrile diseases (typhoid fever, scarlatina, etc.). (See B, fig. 151.)

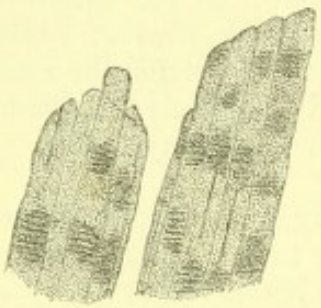
The same year Cölberg demonstrated an analogous regeneration of muscle following trichinosis. It is always from the cells situated outside of the fasciculi, that are developed the new-formed muscular fibres. The nuclei of these cells are multiplied, their protaplasm is increased, forming blunt or tapering prolongations; this nucleated mass is very similar to the large giant cells of bone marrow. Neighboring cells unite at their extremities; the substance which forms them is transversely striated, and takes all the characters of striated muscular substance.

Increase in the size of a muscle is not always due to an increase in size of the fasciculi, or to their new formation; it may result from the production of connective tissue, of adipose tissue, or even to an abnormal development of blood or lymphatic capillaries. Hypertrophic paralysis of muscles has been previously mentioned; congenital hypertrophy of the tongue is principally due to a considerable thickening of the connective tissue of the organ and a dilation of the lymphatics.

Cloudy Swelling of the Muscular Fasciculi.—This is very often the first phase of fatty degeneration. In this alteration the muscular fasciculus is more opaque than normal, its substance contains numerous fine granules, the striation is not distinct or it has completely disappeared.

By the action of acetic acid the fine granules in the fasciculus disappear; the fibre becomes transparent, and the striation is less distinct than in a normal fasciculus treated by the same reagent. Sometimes the acetic acid in causing the fine granules to disappear, makes visible other transparent and refracting granules, of a fatty nature and varying in number. The sarcolemma is as transparent as customary; the inclosed nuclei are normal, or present signs of proliferation. Whenever this granular condition of muscles is accompanied with a proliferation of the nuclei of the sarcolemma, parenchymatous inflammation is present. This lesion may be observed in inflammations of muscles, as in suppurative intra-muscular phlegmon; but it is also recognized in cases where the inflammatory nature is doubtful, as in all the acute general low diseases (typhoid fever, eruptive fevers, purulent infection, etc.). In grave fevers this cloudy swelling is frequently accompanied with fatty or vitreous transformation. (Fig. 151.) Unusual care should be exercised in the preparation of muscle in order to study the histological changes of this transformation.

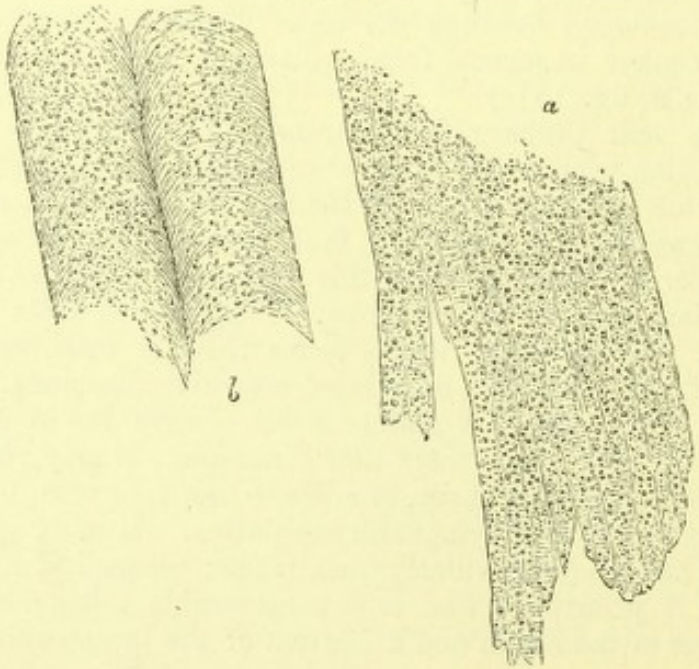
Fig. 149.



Muscular tissue of the heart, from a case of severe typhoid fever. Showing the cloudy swelling of the fibres and the loss of their striation. × 400. (*Green.*)

Fatty Degeneration of Muscles.—In children and adults there are always found some muscular fasciculi, which contain extremely fine fatty

Fig. 150.



Acute fatty degeneration of heart and other muscles. *a*. Heart. *b*. Rectus abdominis. The whole of the heart-tissue was affected, and also the muscles in other parts of the body. × 400. (*Green.*)

granules, visible after the action of acetic acid. These granules are very few, and a careful examination is necessary to discover them. But in

old age the number of granulo-fatty fasciculi is more considerable, and the fasciculi containing the fatty granules are larger, so that it is not necessary to employ acetic acid to distinguish them.

There always exists in muscles a certain amount of fatty material in a state of soluble combination, the base of which is probably an albuminoid substance; it is not then visible with the microscope. Separated fat only is seen in the form of an insoluble product; microscopic examination does not then reveal the amount of fatty material contained in the muscle, but only that which is seen in a neutral state. A chemical analysis of a muscle in an average state of fatty degeneration, therefore, does not furnish more fat than comes from a physiological muscle (Rindfleisch).

Yet the presence of a large number of fatty granules in a muscular fasciculus, always indicates important nutritive trouble, since the fat in this state cannot be utilized for the work of the muscles as can the fat in combination; it, therefore, interferes with the function of this tissue.

Muscular fasciculi, which have undergone a fatty degeneration, are more friable than normal, and require more care in preparing them for microscopic examination. The fatty granules of the degenerated muscular fasciculi present a certain regularity in their arrangement, being placed in longitudinal series in the primary fasciculi. They render prominent by their presence the longitudinal striation, while the transverse striation is very much less distinct, and may have even disappeared. To distinguish these changes it requires a power of at least 250 diameters.

The sàrcolemma retains its transparency. The nuclei are very distinct, and the protoplasm surrounding them is granular and fatty. The degeneration begins in the protoplasm immediately around the nuclei. It is very probable that the fasciculi which have undergone fatty degeneration may again return to their physiological state, if our conclusions are based upon what occurs in frogs, in whom during winter a great many of the fasciculi are fatty, which in summer return to their normal condition. In man, however, frequently the fasciculi which have experienced this change are destroyed by a process the different phases of which cannot be well followed. The fatty granules become more and more abundant, the fasciculus becomes opaque, the striation cannot be distinguished, and at the end of the process the sarcolemma sheath is filled by a fatty granular mass which gradually disappears, leaving only the shrunken sarcolemma. It is chiefly in tumors of muscles, and in callus when it invades the muscular substance, that these modifications may be investigated in detail in the human being.

In infantile paralysis and progressive muscular atrophy, the muscular fasciculi may in part or completely disappear from the effect of fatty degeneration. Fatty degeneration is also met with in fevers, in purulent infection; it is very decided in metastatic inflammations of muscles, while in white infarcti consecutive to arterial obliteration by an embolus, we have found the muscular fasciculi free from fatty degeneration. In myositis or in the neighborhood of wounds, at times some of the fibres are seen in a state of fatty degeneration, but only in the midst of the embryonic tissue; in the surrounding parts, although there may be a notable formation of new cells between the muscular fibres, the fasciculi are not degenerated.

In poisoning by phosphorus, arsenic, etc., fatty degeneration of the muscles is very evident.

Pigmentary Degeneration.—There are found physiologically in the cardiac muscle, but only pathologically in other muscles, round or angular granules, brown in color, situated under the sarcolemma, or in the substance of the muscle fibre. These granules probably come from a transformation of the coloring material of the muscle, analogous to that of the blood, and which may be designated as muscular hæmoglobin.

This transformation of muscular hæmoglobin into pigment happens when the muscle dies in the living organism (the heart being of course excepted), for example, in infarcti, in metastatic abscesses. A fœtus, which has remained in the uterine cavity some weeks after its death, also contains pigmentary granules in its muscles.

Vitreous Degeneration.—We have described this alteration on page 45, and gave it the name of *vitreous degeneration*, which seems to us preferable to *waxy* given by Zenker, who first discovered this lesion. This change of the muscles should not be confounded with a modification of the muscular fibre produced by the method of preparation. The vitreous metamorphosis consists in a transformation of the muscular substance; the latter loses its striation and becomes hyaline and transparent as glass. In the first stage the muscular fasciculi are increased in size, they retain their cylindrical regularity, the nuclei of the sarcolemma are more distinct than in the normal state, the sarcolemma itself does not appear to have undergone any change. The nuclei of the fibres and the protoplasm which surrounds them entirely escape the vitreous change; they appear upon the homogeneous fasciculus as a distinct granular mass. Carmine colors the vitreous substance quite intensely. Acetic acid swells, without dissolving it. This substance is very much more brittle than muscular substance, and if the preparation is not made with great care numerous and irregular fractures are caused. When a small cylinder becomes separated by fracture, it is isolated from the neighboring fragments, and the folded sarcolemma upon its surface seems to be shrunken.

The sarcolemma by compressing the broken extremities of the fragments, gives them the form of a cylinder swollen in the centre, resembling a small cask. When the preparation has been made with great care, the vitreous muscular substance retains its cylindrical form.

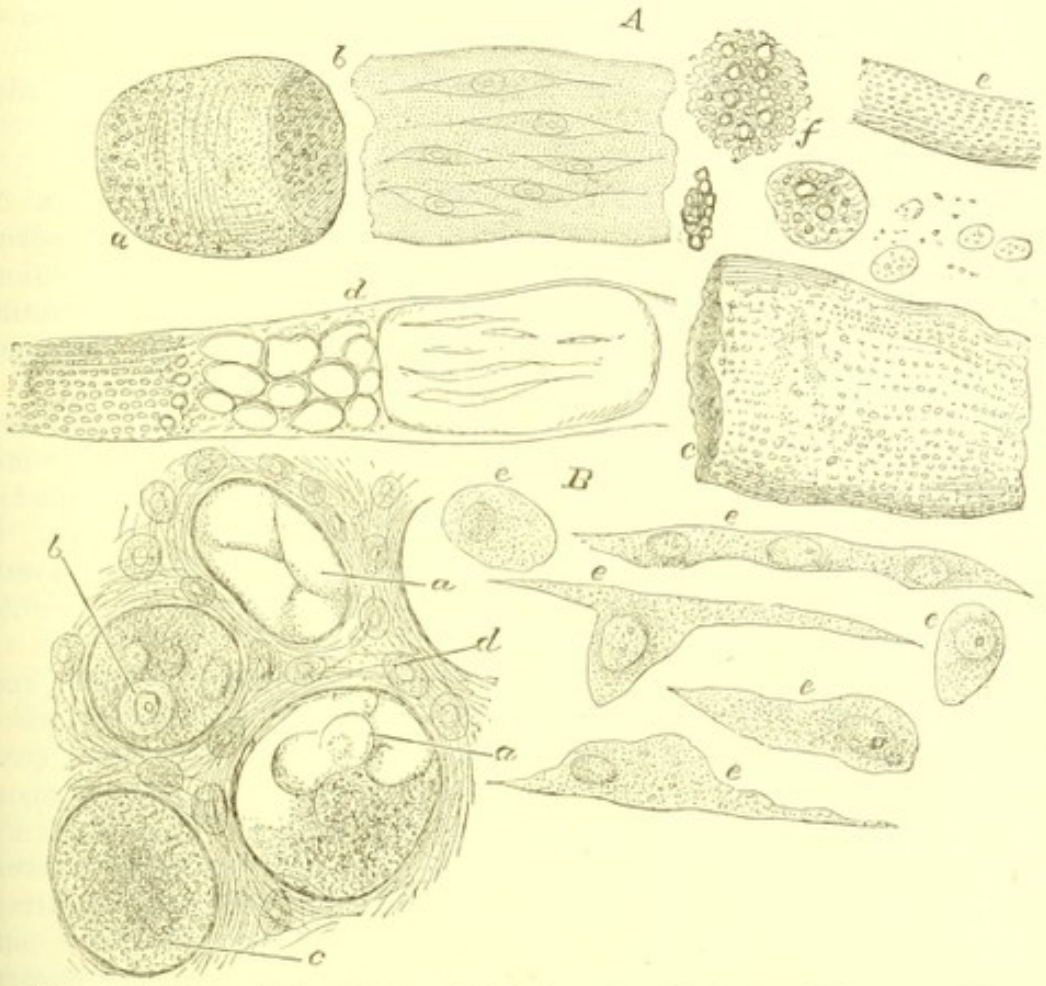
The number of fasciculi affected by the degeneration is always limited. All the muscular fasciculi of a muscle are never found metamorphosed; therefore an examination should include a group of fasciculi, rather than an isolated primary fasciculus. There are seen homogeneous and transparent fasciculi presenting at their edges a characteristic appearance due to the refraction of their substance; others are normal or fatty degenerated. By the side of the vitreous muscular fibres, which have lost their physiological properties, there are found others intact and able to contract.

The changes which we shall now discuss are most marked in chronic vitreous metamorphoses, such as found in the proximity of tumors, or better in the chronic phlegmon which surrounds the osseous fistular open-

ings following caries, necrosis, or white swelling. We are not warranted in affirming that the peculiar appearance of these fasciculi is due to the method of preparation. The vitreous substance, under the influence of the movements of the muscular fibres which remain healthy, has experienced a true breaking up into fragments, and is separated into blocks, which in their arrangement sometimes resemble the stones in a wall.

At the termination of the process, the fragments become gradually smaller and form granules, each one of which still possesses the optical

Fig. 151.



A The principal elements found in the wall of a hæmorrhagic infarction of the rectus abdominus muscle, in a case of variola, twelfth day of eruption. × 300. *a*, *b*, *c*, *d*, Granulo-vitreous fragments of muscle fibres. *e*. Atrophied granular muscle fibre. *f*. Granular corpuscles and leucocytes, more or less altered.

B. Alteration of muscles in a caseous focus in the neighborhood of a hemorrhage into the rectus abdominus in a case of phthisis. Section transverse to the muscular fibres. *a*. Fibres whose striated contents are transformed in part or in toto into vitreous substance. *b*. Fibre containing muscular cells in process of development. *c*. Normal fibres. *d*. Cellular elements, larger and more abundant than normal, contained in the inter-fascicular connective tissue. × 300. *e*. The latter elements (*d*) × 600, not different from similar elements belonging to the muscle fibres themselves.

In this connection, see also Fig. 31.

characters of the vitreous substance. At this time absorption begins, the sarcolemma folds upon itself, its nuclei become larger and more numerous, many of them presenting the signs of multiplication by division. This proliferation of the nuclei of the sarcolemma seems to be a phenomenon consecutive to the degeneration.

In the grave fevers, when a certain number of the muscular fasciculi have been destroyed by this alteration, there occurs a new formation of muscular fibres, and a complete regeneration of the muscle. The cells of the connective tissue adjacent to the diseased fasciculi are enlarged, their nuclei multiply without division of the cells, they afterwards become elongated in the direction of the fasciculi, and before they have lost the character of cells in order to become primary fasciculi, they present a very manifest striation. This development does not essentially differ from the physiological development of striated muscle. Muscles attacked by this lesion are brittle and are frequently ruptured. The changes occurring in consequence of rupture will be better studied under hemorrhages of muscle.

The *cause* of this degeneration is local or general. In the former case it is localized at the seat of the affection which occasions it, as a tumor of a muscle, an abscess, or a chronic phlegmon. When the disease supervenes during a fever, it is most frequently seen to attack the anterior muscles of the thigh and abdomen; yet it may occur in any locality. To the unaided eye, it is very difficult or even impossible to recognize this lesion. Zenker has pointed out a special color analogous to fish flesh; but this color may be seen in muscles which do not present the degeneration, so that a histological examination is necessary to determine it.

Hemorrhages of Muscles.—Simple congestion of a muscle is manifested by distinct signs upon the cadaver only in the neighborhood of inflammatory foci, of hemorrhages and of infarcti.

By the old French and Germans authors, hemorrhages of muscles were designated hemorrhagic infarcti. This term by no means implies the idea of a primary arterial obliteration.

Hemorrhages in the muscles may be caused by contusions, wounds, rupture of muscles, or they may depend upon a general hemorrhagic affection, such as purpura, scurvy, hemorrhagic fevers, leucocythæmia, etc.

If the hemorrhage is recent, it forms in the muscle a dark-red mass, very different from the light-red color of the muscle. This mass, the extent and shape of which is very variable, may be limited or diffused. As the blood coagulates, the muscle at this point becomes more consistent and loses its elasticity. The muscular fasciculi contained in the part have not undergone any alterations, or perhaps they have become granular.

In order to study the relative relations of the blood and the muscle fibres and vessels, thin transverse sections are to be made and colored with carmine. It is then seen that the muscular fasciculi are separated by collections of red blood disks. In these collections and between the fasciculi the blood capillaries and vessels of larger calibre are dilated and filled with red blood disks. The blood coagulates in the vessels, as well as in the interfascicular spaces, in consequence of arrest of the circulation.

When hemorrhage follows a rupture of a muscle, the blood coagulates; the torn fasciculi of the muscle project into this coagulum, and the blood to a greater or less extent penetrates between them. The muscular fasciculi now present various alterations depending more or less upon the cause of the rupture; sometimes they are in a state of vitreous

degeneration, or fatty metamorphosis; the muscular fasciculi at the point where they are ruptured, have always undergone complete fatty degeneration. This is frequently seen in the recti muscles of the abdomen during typhoid fever. In rupture of the muscles, all the bloodvessels included in the rupture contain a clot, in which if the lesion is recent the red blood cells are well preserved, or granular if the lesion is old.

The blood thus effused into the muscle seems to be absorbed with great facility. The muscular movements certainly have considerable influence upon the intra-muscular lymphatic circulation, and, consequently, upon the transportation of materials which are derived from the changes occurring in the extravasated blood; but as yet neither upon animals or man has the method of this absorption been determined. It is known, however, that the effect of severe contusions, which are always accompanied with considerable intra-muscular hemorrhages, may disappear in a few days without leaving any trace. The changes occurring in the blood do not differ from those described under hemorrhages of the connective tissue. The extravasated blood experiences the usual metamorphoses; at first it coagulates, then decomposes; the fibrin undergoes molecular changes, it becomes soluble, or broken up into very fine granules which are taken up by the circulation.

The production of muscular hemorrhages varies according to their cause. When they are the result of direct injury, such as muscular rupture, fracture of bones, contusions, the torn vessels permit the blood to escape until by its coagulation it occludes the ruptured vessels. Hemorrhages may also be due to obliteration and thrombosis of the veins, when the arterial pressure transmitted to the capillaries is sufficient to cause their rupture. But the obliteration of arteries, either by thrombosis or embolism, cannot cause intra-muscular hemorrhage, any more than can ligation of an artery.

The phenomena of muscular hemorrhages in general diseases, such as purpura and the hemorrhagic fevers, are not yet known.

Embolic Infarction of Muscles.—True embolic infarcti of muscles have been seldom seen. We understand by this term the alteration consecutive to the obliteration of a muscular arteriole and its branches. This lesion differs from hemorrhagic infarcti by the absence of effused blood. Metastatic abscesses, such as have been described under inflammations, should not be confounded with embolic infarcti of muscles. We have only met with two examples of this lesion, occurring in consequence of emboli from endocarditis and endarteritis. In these cases, in the muscular substance, were found whitish, slightly opaque, cone-shaped masses, which were in very distinct contrast to the red and translucent muscle. Microscopic examination of these parts showed that the muscular fasciculi had very plainly preserved their striation; they contained no fatty granules, but inclosed only a few pigment granules derived from the muscular hæmoglobin. This pigmentary change is similar to that occurring in a fœtus dying before its expulsion. The changes in the bloodvessels will be studied under infarction in connection with the vascular system.

Multiplication of the Cellular Elements of the Sarcolemma.—This is present, as already shown, in vitreous metamorphosis and even in granular transformation, but it also occurs sometimes as a separate lesion. In the inflammation of a muscle following a wound, in the proximity of tumors, for example an epithelioma of the lip or tongue, in some forms of paralysis, and in animals after the division of a nerve, this lesion is seen. When a nerve is divided in an animal, fifteen days or three weeks after the operation, the only lesion found of the muscles is an increase of the nuclei of the sarcolemma; they become larger, divide, and form elongated groups (Vulpain). In these groups the nuclei are arranged in series in a granular protoplasm. This is the usual method of proliferation of the nuclei of the sarcolemma; the nuclei remain in a common mass of protoplasm. Only in exceptional cases do we see the protoplasm isolated in distinct masses around each nucleus, as in the last stage of the vitreous change. In epithelioma the multiplication of the cellular elements of the sarcolemma is often very marked; while at the same time there is more or less atrophy of the fasciculi, so that the nuclei and their surrounding protoplasm are very distinct. Because of the resemblance of these elements to epithelial cells, some writers believe that they contribute to the formation of the cells of the epithelioma, but we have never seen anything which could justify this conjecture. It has not been positively determined that the proliferation of the cellular elements of the sarcolemma take part in the formation of pus cells.

Inflammation of Muscles or Myositis.—The most simple and most easily studied inflammation of muscles is that following wounds. If a muscle is divided in a wound, there are seen upon the cut surface all the phenomena of the formation of granulation tissue. The new formation takes place in the midst of the inter-fascicular connective tissue; it is effected by the production of embryonic tissue and the growth of vessels. The embryonic cells are found not only upon the surface of the wound but also between the primary fasciculi, at a depth varying according to the intensity of the inflammation and the stage of the process. In contused wounds, as also in gunshot wounds, the extension of the embryonic tissue into the muscle reaches several centimetres when the wound is suppurating. Upon an examination of a transverse section of an injured muscle twelve days after the accident, there is seen first a layer formed of embryonic tissue, in which dilated capillaries with embryonic walls form loops. Beneath this layer, the thickness of which varies from one to five millimetres, there is found a second where the embryonic tissue encloses atrophied primary fasciculi, which, instead of all having the same direction, as in a normal muscle, are very irregularly arranged; their size varies from .01 to .03 of a millimetre; only their longitudinal striation can be distinguished, they appear to be constituted of fibrils separated by an exudation. The nuclei of the sarcolemma multiplied to excess, form groups or series one upon the surface, the other in the centre of the fasciculus; the sarcolemma seems to have completely disappeared. Around these fibrils, which are the remains of the fasciculi, the embryonic tissue shows the beginning of organization, and presents a reticulum,

the fibres of which, at many points, are mingled with the muscular fibrils, so that the line dividing one from the other is not very distinct.

Passing to the deeper layers of this tissue, the interfascicular connective tissue contains fewer cells, and the atrophy of the muscular fasciculi is not so marked. The fasciculi show only an increase in the number of the nuclei of the sarcolemma, which, in a transverse cut of the muscle, forms a beautiful circle around each fasciculus. There are also found in several points of the interfascicular connective tissue, free spherical cells containing brown granules of hæmatin. This shows that there have been hemorrhages into the deep layers; their resolution takes place according to the process explained under hemorrhages of the connective tissue.

The changes that have been described as occurring in a simple case are seen, with slight variations, in all inflammations of muscles. Final recovery takes place by the organization of the embryonic tissue at the surface and its disappearance between the fasciculi. Yet this simple and natural course may be complicated by accidents—hemorrhage or suppuration.

Suppuration of Muscles.—Suppuration of muscles may be either diffused or limited. Limited suppurating foci may be met with in the proximity of wounds, or they may be connected with purulent infection, etc.

Metastatic abscesses from purulent infection differ entirely from white embolic infarcti. Their size varies from a hemp seed to that of the fist. The pus contains the débris of connective tissue and disintegrated muscular fasciculi. The purulent focus is surrounded by a greenish brown zone, in which the inter-fascicular connective tissue is found infiltrated with pus cells and red blood corpuscles, and in which the muscular fasciculi contain fatty and pigmentary granules.

In diffused inflammations, which are very often seen in the divided muscles of amputations in purulent infection, or in inflammation of the psoas muscle, the purulent infiltrations occasion fatty degeneration of the primary fasciculi, and finally their death.

Chronic Inflammation of Muscles.—This follows as a secondary change around articulations suffering with white swelling or chronic rheumatic arthritis. The lesion is also met with in the proximity of purulent fistular openings from carious or necrosed bone. The alterations of the interfascicular connective tissue consist in an hypertrophy due to an exuberant production of cells and an exudation; the cut surface of the muscles, instead of presenting, to the unaided eye, the characteristic fascicular appearance, when cut transversely resembles marble, fibrous tissue when divided longitudinally; the muscle has lost its natural color, it is whitish or light red, its consistence is increased and its elasticity is partly lost.

The changes in the muscular fasciculi vary: some retain their striation, and the nuclei of the sarcolemma are more numerous than normal; others have undergone cloudy swelling or fatty degeneration; finally, in a few cases, most of the muscular fasciculi present the lesions of vitreous degeneration.

Most writers still class with chronic inflammation, the fibrous nodules and osseous formations which are produced by the repeated contusions and frictions connected with many occupations. Rokitansky first described the osseous formations in the biceps of soldiers who exercise with the musket according to the German method, and in the adductors of horsemen who remain a long time in the saddle.

Rupture of Muscles.—Ruptures caused by contused wounds are not here considered, only those ruptures connected with muscular contractions. If the muscle is healthy, in order to produce a rupture it requires considerable effort; but if it is diseased the accident may readily occur. In low typhoid fever for example, where the muscles are degenerated, the recti muscles of the abdomen may be ruptured by the effort of the patient to sit up in bed. It is especially this rupture that has been anatomically studied, for most of the other ruptures are followed by recovery of the the patients.

Rupture of the recti muscles of the abdomen in typhoid fever most frequently occurs without the physician being aware of it, and it is only at the autopsy that the lesion is discovered. It is then seen that the rupture is very irregular, the space between the two fragments is occupied by a clot of blood, generally dark red-brown, with opaque whitish striations. Where the muscle is cut longitudinally, there are found at the point of rupture and for an extent of one or more centimetres, a brown coloration and stiffness. The blood clot is formed of red blood corpuscles contained in a fibrinous reticulum, and it undergoes the different modifications seen in interstitial hemorrhage.

The muscular fibres, at the point of division, present a very advanced fatty degeneration, or vitreous metamorphosis. Between the muscular fasciculi, the connective tissue is infiltrated with coagulated blood and the bloodvessels are also filled. If the muscular fasciculi near the rupture are compared with those of the same muscle situated further off, it will be seen, that in the latter very few of the fasciculi are in a state of fatty degeneration, although many of them may have undergone the vitreous metamorphosis. While, near the rupture all the fasciculi contain a great quantity of fatty granules, and the striation has disappeared. It is then very probable that the fatty degeneration, at least for most of the fasciculi, is consecutive to the rupture.

Sect. III.—Tumors of Muscles.

Sarcomata.—Primary sarcomata of muscles we have never seen, but tumors of this nature developed by continuity are very frequent. The most common of all is the fascicular (spindle celled) sarcoma. There are also seen round celled or encephaloid sarcoma, lipomatous sarcoma, mucous sarcoma, erectile sarcoma, and melanotic sarcoma. It is unnecessary to give a description of these different tumors, which, when developed in muscles, present the structure already described in the chapter upon tumors in general. The development of the morbid mass is always by the formation of embryonic tissue in the interfascicular connective tissue; this embryonal tissue compresses the primary fasciculi of the muscle, causes an

atrophy simple or accompanied by a fatty degeneration. The latter form of atrophy is especially met with where the development of sarcomatous tissue is very rapid. It is also seen in exuberant callus which invades the muscles and which during a certain period of its development presents the structure of a sarcoma.

Fibromata.—Simple fibromata of muscles are usually the result of a mechanical irritation. These tumors once developed cease to grow, and cause very little functional trouble of the muscle.

Myxomata and *Lipomata* are met with in muscles as simple or combined tumors, the latter named lipomatous myxomata. They are found most frequently in the muscles of the tongue, lips, and buccal walls, but are liable to occur in the other muscles of the body.

Gummata of muscles, although they seldom occur, are very well known clinically, but have not yet been studied histologically; they have been found in the cardiac muscle.

Carcinomata.—Carcinoma of muscles is secondary by extension or by metastasis; it is developed in the interfascicular connective tissue with the usual characteristics of the evolution of carcinoma, while the primary fasciculi undergo simple atrophy with multiplication of the nuclei of the sarcolemma, or the atrophy is associated with fatty degeneration. Encephaloid and scirrhous carcinomata are most frequently met with, but the other varieties are found. The extensions of a scirrhus of the mammary glands to the pectoral or intercostal muscles, and of an encephaloid of the uterus to the psoas and iliac muscles, are to be particularly remembered.

Epitheliomata.—Epithelioma of the orbicularis oris muscle occurs almost constantly in an epithelioma of the skin and mucous membrane of the lips. It is here that the study of the development and growth of an epithelioma into the muscle is most frequently made. Before the epithelial pegs have penetrated among the primary muscular fasciculi, there is formed in the interfascicular connective tissue a growth of embryonic tissue which separates them from one another. A few of the fasciculi may remain in bundles, but they are always few in number. There are always seen in them a hypertrophy and an increase of the nuclei of the sarcolemma, while the sarcous substance is generally atrophied but retains its characteristic striation. It is in the embryonic tissue developed between the fasciculi that the epithelial pegs advance deeply into the muscle. The muscles of the tongue are attacked in a similar manner in epithelioma of this organ; these tumors belong to the lobular epitheliomata. A tubular epithelioma developed primarily in the antrum or nasal fossæ may also spread to the muscles of the face either in a diffused or circumscribed form. Epitheliomata by extension or metastasis may invade other muscles of the economy, notably the heart.

Enchondromata may invade the intermuscular connective tissue, as occurs in some cases of enchondromata of the parotid gland and of the hand.

Osteomata of muscles caused by mechanical irritants have been considered on page 133. In the proximity of articulations affected with very old chronic inflammations there is at times seen an ossification of the tendons which extends to the muscles, forming nodules or spiculæ situated in the middle of the muscular mass.

Angiomata of muscles, either simple or cavernous, are not very rare; they should not be confounded with varices.

Sect. IV.—Parasites of the Muscles.

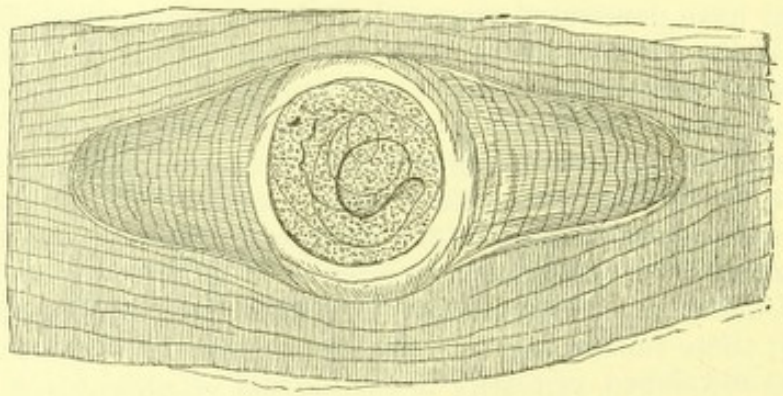
There are found in the muscles of man only three kinds of parasites, the cysticerci, the echinococci, and the trichinæ.

In man the cysticercus in muscles is rare, especially in France. The parasite does not give rise to any symptoms during life, and it is only accidentally discovered at the autopsy. We have had an opportunity of examining the muscles from one case. The cysticerci were within whitish cysts as large as a small pea, situated between the muscular fasciculi, and surrounded by a fibrous membrane. The cysticerci were infiltrated with calcareous granules, but we were able to find their heads, suckers, and hooklets.

Very few observations of hydatid cysts of muscles have been so thoroughly made as to leave no doubt of their nature. Histological examination of the parasite has been made only in a small number of cases; the wall of the cyst, showed that they were formed by the echinococci.

Trichinæ (*Trichinæ spiralis*), discovered by Owen in the muscles (and by Leidy in pork), are recognized as small worms coiled up and contained in cysts. The cyst is situated in the interior of a muscular fasciculus, or in the interfascicular connective tissue; it is oval or lemon-shaped. These cysts are scarcely visible to the unaided eye as small white points. They

Fig. 152.



Trichina spiralis coiled up and encysted in a muscular fasciculus.

have two envelopes, one formed by the sarcolemma or connective tissue, the other belongs to the animal. In one cyst there exist one, two, or three of the animals, coiled upon themselves. The worms are characterized by a transverse striation, a mouth, anus, and digestive tube. Calcareous infiltration is met with when they are old and obscures the cyst. The trichina itself becomes brittle the neighboring muscular fasciculi undergo granular metamorphosis. The irritation resulting from the presence of the cyst causes a vascular new formation at its circumference.

In the muscles, the trichinæ are sexless; but being swallowed by a

mammifera and reaching the digestive tube, they become free and sexual. The males are 1.5 millimetres long, the females 3 millimetres; their anterior extremity terminating in a mouth and containing the œsophagus, is elongated and pointed; their posterior extremity is blunt and rounded; the sexual organs are placed in the middle third of the body and are simple; the testicles are in the posterior third. Copulation takes place in the intestinal tube, and a few days after, the female produces a considerable number of young. The latter perforate the intestinal walls and wander throughout the whole economy; finally, they lodge in the striated muscles, with the exception of the heart. At the insertion of the tendons, the trichinæ are arrested in their migrations. They become encysted in the muscles and occasion nutritive changes in the fasciculi.

CHAPTER VI.

BLOOD.

The office of the blood in diseases of the vessels and heart is so important that it is impossible to understand the lesions of these organs without having studied the liquid which fills them.

The microscopic alterations of the blood will only be studied in this chapter.

Sect. I.—Normal Histology of the Blood.

The morphological elements of the blood in the normal state are red and white corpuscles; there are also found elementary granules which float in the serum, and when the blood coagulates, a reticulum of fibrin. Crystals are formed either spontaneously or artificially.

The red corpuscles of man are disks slightly depressed in their centre upon both surfaces; when seen in profile, they have the form of a biconcave lens; seen upon the surface, their centre is dark and the border bright, according to the position of the objective. When the objective is nearer than the point of distinct vision, the centre is dark; when it is beyond the point of distinct vision, it is bright. These details are given that the depressed centre may not be taken for a nucleus.

The higher the magnifying power employed in examining red corpuscles, the less they appear to be colored. Thus, with a power of 800 diameters, they have only a very slight yellow tint; in profile, they are more colored than when seen upon the surface. The red corpuscles are not of uniform diameter, yet they vary very little; their average diameter is .007 mm. Besides the disk-shaped corpuscles, there are often found spherical red corpuscles having only .005 mm.; their tint is darker, which is due simply to their shape.

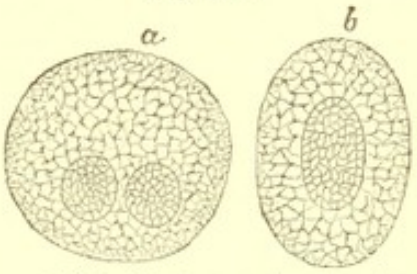
[There are besides the spherical red corpuscles of .005 mm. in diameter, especially in the blood of the venæ portæ, variable numbers of very minute spherical granules, whose constitution appears to be identical with that of the larger red corpuscles. The size of these small spherical bodies varies between a minute dot scarcely visible under a magnifying power of 300 diameters, and .005 mm. Some authors believe that they come from the breaking up and division of the red blood disks in the spleen; that during the passage of the splenic blood through the liver a part of the proper function of the latter is to complete their destruction; and that their presence in considerable numbers in the general circulation is an indication either of a disease of the spleen or of the liver, or perhaps of both these hæmopoietic organs.

Of late years several authors have testified to the existence in the

normal red blood corpuscles of a certain amount of contractile power, and one or two have even affirmed the presence of a genuine nucleus within the ordinary biconcave red blood disk of man.

It now seems to be established that instead of the red blood corpuscle being composed of a homogeneous, structureless mass, as was formerly taught, it is constituted by a delicate reticulum which pervades the entire mass of the corpuscle, and which holds in its minute meshes the homogeneous fluid which contains the coloring and other matters of these corpuscles. This reticulated structure is typically represented in fig. 153, *b*. Although the illustration is a reproduction of the reticulated appearance of a nucleated ellipsoid red blood corpuscle of a batrachian, yet, excepting the nucleus, the same condition has been frequently recognized in the blood of man.]

Fig. 153.



a, White blood corpuscles, showing an intra-cellular and an intra-nuclear reticulum. *b*, Elliptical colored blood corpuscles, showing similar reticula. High power. (*Klein.*)

At the margin of the drop of blood under the thin glass cover, where it has dried by contact with the air, the red corpuscles show notches, the extent and number of which vary and increase proportionally as the drying progresses. When this change is much advanced, the red corpuscle becomes spherical, appears crenated or covered with spines; it is in this form that the red blood corpuscle of the cadaver is often found. When the drying is complete, the red corpuscles form a cracked mass.

Water acts upon the red corpuscles by removing their coloring matter and causing them to become spherical; their diameter is reduced to .005 mm., and they become so transparent that the field under the microscope must be shaded, or they must be treated with iodine in order to render them visible.

The coloring material of the blood dissolved in the serum is named hæmoglobin; it is soluble in large quantities of water without being decomposed. The spectroscope detects it in very weak solutions; in concentrated solutions it crystallizes. Crystals of hæmoglobin are obtained by several methods, all having for their end the destruction of the corpuscles and the liberation of the hæmoglobin without the aid of water. The crystals are of a beautiful red color when looked at en masse; their form varies in different animals, in man it is that of rhomboidal plates.

By the action of acids or alkalies on hæmoglobin, there is formed a new substance named hæmatin, not crystallizable, but precipitated as darkish granules. This combines with hydrochloric acid, forming a crystallizable salt known as hæmin, but it is really hydrochlorate of hæmatin.

Hæmatin is of pathological importance, since it is formed from blood extravasated into the tissues. Its formation is slow. The varied colorations of ecchymoses, as has been shown, are due to the slow transformation of hæmoglobin and hæmatin. This change is much more rapid if the blood passes into the digestive tract, especially into the stomach, where, by the action of the gastric juice, the hæmoglobin becomes hæmatin with

great rapidity; this is the reason of the color of black or melanotic vomit, and the brown color of ecchymoses of the stomach.

When the blood remains among the tissues, there is found besides the hæmatin another substance, which has not been produced artificially and the composition of which is not known; it is named hæmatoidin. It occurs as granules or rhombic crystals of a beautiful orange-red, so intense that it remains brilliant under very high powers. It is particularly in encysted hemorrhages, notably those of the brain, that the most beautiful specimens of these crystals are met with.

The *white corpuscles* are seen as spherical bodies or have an irregular contour; they are granular, and under the microscope have a gray tint.

Prolongations of various shapes are sometimes seen at their borders. In the frog and other cold-blooded animals, these prolongations are very distinct at the moment the blood is drawn from the vessels and submitted to examination, but become more and more prominent as the observation is continued; they change their shape, form secondary prolongations, and again return to their original form, thus presenting the amœboid movements. The white corpuscles possess the property of seizing the bodies which are near them and causing them to penetrate into their interior (Recklinghausen). This phenomenon can be directly observed under the microscope by mixing with a drop of frog's blood a small amount of granular carmine or vermilion. The absorption of solid particles may also be studied in the organism by injecting into the vascular system of a frog or a warm-blooded animal fine particles suspended in a fluid, and examining the blood of the animals a few minutes after the injection. The white corpuscles are then seen to have in their interior grains of the injected substance. The red corpuscles never contain any of the injected particles. The power that the white corpuscles have of absorbing solid particles when removed from the organism, shows that they still live, although the conditions of their existence seem changed. These vital manifestations may be prolonged for a long time if the blood is protected in a suitable medium.

[Besides the above-mentioned white corpuscles found in the blood, there are occasionally seen other colorless elements. There are a certain number of larger, more granular, and less mobile colorless cells, met with. In the frog, especially during the spring, a few large ellipsoid, slightly granular uni- or bi-nucleated colorless cells are found. Elements very similar to the latter are found in the blood of the splenic veins of mammals in health, and in the general circulation in some pathological states.]

The white corpuscles are much less numerous than the red. In a healthy man there is one white to three or four hundred red. The numeration is difficult; therefore, to estimate the physiological as well as the pathological proportion, it is well to have some rapid method. By the action of water the white corpuscles become spherical, transparent, and in their interior appear one or more nuclei. If the action of water is prolonged the cell is dissolved, the nuclei only remaining.

Fibrin does not exist ready formed in the blood. The theory of Schmidt which prevails at the present time is accepted, although not yet perfectly demonstrated. This author admits that there is in the blood, besides albumen, two other albuminoid substances—fibrinogenic and

fibrinoplastic; and that a very minute quantity of the fibrinoplastic substance is sufficient to change into fibrin a large amount of the fibrinogenic substance. The fibrinoplastic substance is found in the red blood corpuscles, and the fibrinogenic exists in the plasma. These two substances have been extracted from the blood, but it is not known if by mixing them fibrin will be produced. It is positively known, however, that red blood corpuscles added to certain exuded fluids—that of pleuritis, for example—cause the formation of fibrin. Blood collected in a vessel in a few moments forms a mass or clot, which at first accurately represents the volume of blood drawn, without any change in its appearance. But in a few hours the clot is contracted, and surrounded by a lemon-colored or slightly red serum. When the formation of the clot is slow, as in inflammatory diseases, the red corpuscles, being denser than the other constituents of the blood, fall to the bottom of the vessel, and the superficial part of the coagulum is colorless. The colorless portion of the clot presents reticulated striæ and whitish spots.

Microscopic examination of the clot demonstrates that the coagulation is due to the formation of cylindrical fibres and granular laminæ anastomosing one with the other, constituting a network, in the meshes of which are red blood corpuscles and serum. The diminution in the size of the clot is owing to the contraction of the fibrinous reticulum, which retains the red globules, but permits the escape of the fluid portions. In order to recognize the fibrinous reticulum, which is concealed by the red blood corpuscles, the clot should be hardened in alcohol, and thin sections made, which, after macerating in water, should be pencilled. The water dissolves the red corpuscles without acting upon the fibrin; the latter is seen as an irregular anastomosing reticulum.

In the colorless portions of slowly formed clots the fibrinous reticulum is more distinct and regular. The small whitish spots found in the colorless portion immediately above the layer formed by the red corpuscles consist of collections of white globules contained in a fibrinous reticulum.

Sect. II.—Pathological Histology of the Blood.

The alterations of the blood in disease are numerous; they are almost all recognized by chemical analysis, but a few are distinguished by the microscope; the latter only will be here considered. They consist in variations in the number of the corpuscles, in the presence of bodies which do not exist in the blood in the normal state, and finally in the coagulation of the blood in the interior of the heart and vessels.

Changes in the number of Corpuscles.—The corpuscles of the blood may be diminished in comparison with the amount of serum, the red and white remaining in the same relation, constituting *hydræmia*. If this change is very decided it can be recognized by the unaided eye in a drop of blood placed upon a glass slide. Examined microscopically the small number of corpuscles contained in the blood is very evident; but the elements preserve their natural shape.

The name *leucocytosis* (Virchow) is given to a transient and slight increase in number of the white blood corpuscles. This state is met with

in acute and inflammatory diseases, pneumonia, phlegmon, erysipelas, smallpox, and the other eruptive diseases, etc. Instead of three or four white corpuscles in the field of the microscope, five, six, or twenty are seen.

Leucocythæmia (Bennet), or leukæmia (Virchow), is a disease characterized by a persistent and growing increase of the number of white blood corpuscles. Towards the end of the disease the white corpuscles are as numerous or even more numerous than the red; the blood is pale, without having the watery appearance seen in hydræmia. When a preparation is examined without the addition of water, the white corpuscles are seen as granular bodies varying in size from .007 mm. to .012 mm.; after the addition of water, these corpuscles swell, become more transparent, and in some a single spherical nucleus is distinguished, in others two or more nuclei are seen. Virchow has described two forms of leucocythæmia, one, in which white corpuscles containing several nuclei predominate; the other, in which uni-nucleated corpuscles are more numerous. He recognizes a leucocythæmia connected with hypertrophy of the spleen, and another with the lymphatic glands. This distinction cannot be maintained, for if the blood of a leucocythæmic patient is examined several days in succession, it is found that sometimes the corpuscles containing several nuclei predominate, and again those with a single nucleus are in excess. Besides, this distinction of Virchow which is founded upon the analogy of the white corpuscles with the cells of the spleen in one case, and with the cells of the lymphatic glands in the other, is not admissible at the present time on other grounds. It is known that the glands or new lymphoid organs contain, in leucocythæmia, elements larger than those of the splenic parenchyma. Again, in leucocythæmic patients, the changes of the spleen, of the lymphatic glands, and of other lymphoid organs most frequently occur at the same time. There are often formed, in patients suffering with this disease, new lymphoid organs (see Lymphadenomata, p. 141).

A few writers have described in leucocythæmia, besides the ordinary white corpuscle, red corpuscles containing a nucleus, and which they consider as intermediate elements between the white and red corpuscles. We have searched for these intermediate corpuscles in several leucocythæmic patients without ever finding them. Many of the white corpuscles, especially the largest, contain very small, amber-colored, spherical granules, grouped around the nuclei. This can be explained by the destruction of the red corpuscles, particles of which have been absorbed by the white corpuscles.

Melanæmia.—This name signifies the presence of particles of pigment in the blood; this change is seen when the spleen has experienced frequent attacks of congestion, especially in malarial poisoning. In the cases that we have observed, the pigmentary particles existing in the blood, were round or angular, deep black, varying in diameter from extreme smallness to .008 mm. or .009 mm.; they were all contained in the white corpuscles, or enveloped in a colorless granular zone, which very probably represents the protoplasm of a white corpuscle.

At the autopsy of persons dying during the presence of this lesion, most of the organs, especially the spleen and liver, are found of a grayish-slate color. Examining thin sections from these organs, pigmentary

granules are found in the white corpuscles contained in the vessels, in the cells of the vessels, in the cells of the peri-vascular connective tissue, and in the cells of the parenchyma. The splenic lymphatic glands are also pigmented.

Pathological pigments act in a manner similar to inert granular matter contained in the blood, vermilion for example. If vermilion, in minute particles suspended in water, is injected into the blood of an animal, the granules are taken up by the white corpuscles and carried by them into the different organs; they pass through the vascular walls, and are finally fixed in the elements which are the seat of pathological pigmentation. It is probably correct to consider that melanæmia consists of a pigmentary change of the blood in the spleen, and a carrying off of the pigment in the blood by the white corpuscles.

The pigmented corpuscles are generally larger than the non-pigmented, and are liable to accumulate in some of the bloodvessels, and obstruct the circulation. This does not cause true embolism, as maintained by Frerichs and Virchow, but a phenomenon analogous to that of stasis of the white corpuscles in leucocythæmia (see p. 143).

[*Parasites.*—According to the investigations of many histologists there exist in the blood of persons affected with some diseases (the infectious in particular) various forms of minute organisms which are thought by some to be the germs of contagion, or in some way to be more or less directly the cause of disease. These are micrococci, bacteria, filaria, etc.]

CHAPTER VII.

THE HEART.

THE anatomical changes of the three constituent parts of the heart, will be successively described; the pericardium, the myocardium, and the endocardium.

Sect. I.—Pericardium.

HEMORRHAGES.—Hemorrhages of the pericardium are of two kinds: 1st. Ecchymoses of the membrane; 2d. Hemorrhages into the cavity of the pericardium.

Ecchymoses are more frequent upon the visceral than upon the parietal layer. When recent, they are seen as lenticular spots of a uniform red tint; sometimes they are confluent, forming spots varying in extent, with sinuous margins. These ecchymoses are not accompanied by any inflammatory phenomena. They occur in asphyxia, leucocythæmia, scurvy, etc., or they complicate inflammatory lesions of the pericardium, when their description belongs to hemorrhagic pericarditis.

Hemorrhages into the pericardial sac are consecutive to inflammation or to a rupture of the heart or a large vessel covered by the visceral layer, for example, the rupture of an aneurism of the ascending portion of the aorta.

DROPSY OF THE PERICARDIUM—HYDRO-PERICARDIUM.—The quantity of fluid found in the pericardium twenty-four hours after death, always exceeds thirty grammes. When the fluid is very much more abundant, as is seen especially in cases of general dropsy, there is said to be dropsy of the pericardium. In the fluid there exist epithelial cells, separate or in shreds, which usually contain fatty granules. Very frequently during summer there are also seen, in the pericardial fluid, articulated and motionless bacteria of unusual size.

Gases are sometimes found in the pericardium of subjects which have commenced to undergo putrefaction, but it should not necessarily be concluded that these gases have existed during life. The existence of a special pneumotosis should therefore be rejected.

INFLAMMATION OF THE PERICARDIUM. PERICARDITIS.—Fibrinous inflammation of the pericardium differs from fibrinous inflammation of other serous membranes only by the appearance to the unaided eye of the solid exudation. Generally it covers the whole surface of the pericardium, but may be limited, especially at the base of the heart where the aorta and large vessels have their origin. The exudation is found

upon both visceral and parietal surfaces of the pericardium in a layer which always presents upon its surface papillary prominences. These prominences are not true papillæ, as the connective tissue and vessels of the serous membrane do not form any part of their structure; this is demonstrated by detaching the false membrane, which is perfectly smooth at its union with the pericardium. The false membranous solid exudation consists only of fibrin, cells from the endothelium and pus corpuscles. The papillary prolongations of the free surface are flattened or elongated and much varied in shape. They are seen even when the layer of fibrin is extremely thin. Their formation is due to the movements of the heart in the pericardium at the time the fibrin coagulates. Fibrinous pericarditis occurs in acute articular rheumatism, pneumonia, scarlatina, smallpox, Bright's disease, etc.

Hemorrhagic pericarditis is met with in tuberculosis, cancer of the lung, and in cachectic disease; it differs from the preceding lesion, only by the presence of a greater number of red blood cells or the products of their decomposition (hæmatin, hæmatoidin) in the fluid and solid portions of the exudation. In this disease the demarcation of the serous membrane and exudation is not so distinct as in simple pericarditis; the dilated vessels, with embryonic walls, of the serous membrane penetrate into the fibrinous exudation as loops; they are seen surrounded by embryonic cells, and from them hemorrhages escape into the exudation as ecchymoses.

In *tuberculous* pericarditis hemorrhages are more frequent. The tuberculous granulations may be in the pericardium, or in the vascular part of the exudation. When the pericardium and exudation are infiltrated with numerous tubercles, caseous transformation of the exudation may occur; the altered exudat may then be partly separated, and form irregular gray or ochre-colored masses, free in the cavity of the pericardium. By microscopic examination there are found fatty granules, granules of hæmatin, or crystals of hæmatoidin, if the disease is chronic, there are also calcareous granules.

Purulent pericarditis does not occur so often as the preceding affections; it is characterized by the presence of a large quantity of pus, which causes the fluid to have a creamy appearance, and the false membrane is rendered opaque. The purulent exudation may undergo a caseous and calcareous change as with the hemorrhagic exudation.

Adhesions of the pericardium following inflammations are not very common, especially if compared with those of the pleura. Incomplete adhesions are effected by laminæ or filaments of vascular connective tissue, generally situated at the base of the heart between the visceral and parietal layer opposite the aorta and vessels; they are also seen at the apex of the heart.

Complete adhesion of the pericardium obliterating the cavity may result from a recognized pericarditis, or it may be found at the autopsy without having given any symptom of its formation during life.

The prominent patches formed of laminated connective tissue, which are seen upon the visceral layer, may be considered as lesions consecutive to pericarditis. As has been explained on page 93, this tissue, in the pericardium as in other organs, may undergo calcareous infiltration, thus

forming calcareous plates which vary in extent and sometimes send prolongations into the cardiac muscle. Usually the calcareous plate is not denuded in the cavity of the pericardium, but is covered by a thin layer of fibrous tissue.

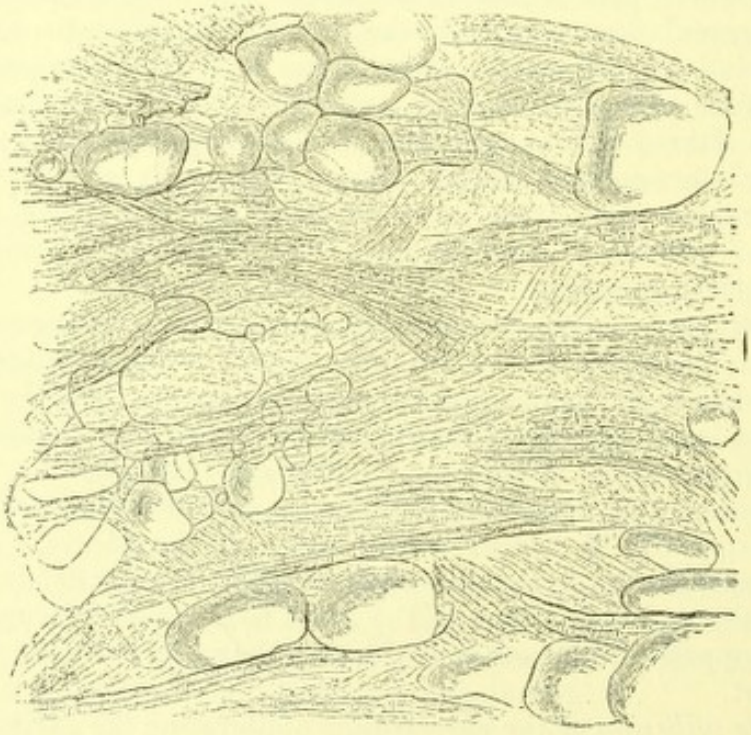
Milky patches have been considered by most writers as having an inflammatory origin: they are smooth, opaque, and of pearly aspect, generally forming a slight elevation upon the surface of the membrane; their seat is particularly upon the anterior surface of the ventricle, they are very variable in size and possess irregular sinuous margins; they are very frequent (45 in 150 autopsies, Bizot) and consist of laminated connective tissue with elastic fibres.

Primary *carcinoma* of the pericardium is very rare. The secondary form is however quite frequent. It grows into the cavity of the pericardium, causing a pericarditis, generally hemorrhagic.

Sect. II.—Myocardium.

Atrophy.—Atrophy of the heart occurs in general atrophy of the muscles of the economy, in cachectic diseases of long duration, in phthisis, at the termination of typhoid fever, etc. The form of the heart is not

Fig. 154.



Fatty infiltration of heart. A section from the more external portion of the left ventricle of the heart, showing the growth of fat between the muscular fibres. The fibres are in some places atrophied and commencing to undergo fatty metamorphosis. × 200. (*Green.*)

changed when the atrophy is general. The coronary arteries, which do not take part in the atrophy, are tortuous and prominent; at some parts of their course the visceral pericardium is seen as a membrane connect-

ing the vessels to the heart. The atrophy may be so great as to cause wrinkling of the pericardium. Some authors believe that they have seen in atrophy a diminution of the size of the muscular fibres. But this is very difficult to appreciate on account of the great variation of their diameters.

Atrophy of the heart may exist with an abundant formation of adipose tissue beneath the visceral pericardium, so that notwithstanding the cardiac muscle is atrophied, the heart at first sight presents its normal size; but if the organ is cut into, the adipose tissue under the pericardium is found to be considerably thickened. Irregular prolongations of this tissue extend between the fasciculi of the cardiac muscle. This lesion resembles fatty infiltration of voluntary muscle. (Fig. 154.)

Hypertrophy.—Hypertrophy is connected with exaggerated work of the heart in diseases of the orifices or vessels; the object of the work is to overcome an obstacle to the course of the blood. Therefore, most often only a single ventricle is affected, for example the left ventricle in changes of the aortic orifice. Hypertrophy of the left ventricle in atrophy of the kidney has been referred by Traube to an analogous cause. This coincidence of hypertrophy of the left heart, and of atrophy of the kidney is an incontestable fact, but in the explanation given by Traube, it is difficult to understand how the inconvenience to the circulation in so few vessels can cause such an enormous increase of work in the heart.

Hypertrophy is general or partial. The shape of the heart is not notably changed in general hypertrophy. In hypertrophy of the right ventricle, the apex of the heart is not so pointed as normal, it is enlarged; it is formed by the extremity of both ventricles which are upon the same level. In hypertrophy of the left ventricle, the apex is formed by the left only. In hypertrophies of the heart there is always seen a thickening of the endocardium. The muscular fibres of the hypertrophied parts either do not present lesions of nutrition, or they have undergone fatty pigmentary degeneration.

It is not yet known if the hypertrophy is due entirely to an increase in the size of the muscular fibres of the heart, or to a new formation of these fibres. In hypertrophy of the heart the phenomena of development of new muscular fibres have never been observed, so that the first hypothesis is the more probable.

Fatty Degeneration.—The heart is more frequently the seat of fatty degeneration than any other muscle of the organism. When all the muscles of the body are submitted to the same influences capable of producing fatty degeneration, the heart alone may be attacked. In a fœtus dying in the uterus and retained for more than a week, the voluntary muscles are not in a state of fatty degeneration but the fibres of the heart are; there are, however, important changes produced in the voluntary muscles—the coloring matter is separated in the form of black granules, which are located beneath the sarcolemma or in the substance of the primary fasciculus.

Fatty degeneration may occur in a hypertrophied or atrophied heart. It is seen in poisoning by phosphorus and arsenic, in grave diseases, such

as typhoid fever, smallpox, leucocythæmia, etc., in endocarditis and pericarditis. The degeneration may involve the whole of the myocardium or only a part. To the unaided eye, the changed portions appear gray or yellow, and by their opacity are distinguished from the healthy parts, which are slightly translucent and of a more decided red tint. But it is not possible always to recognize fatty degeneration without the aid of the microscope. (Fig. 155.)

Fig. 155.



Fatty degeneration of muscular fibres of heart. *a*. Earlier stage. *b*. More advanced. ×400. (*Green.*)

The muscular fasciculi present very varied degrees of fatty degeneration. At times there are found only fine granules scattered over all the fasciculi, but not masking the striation completely; again, the fatty degeneration may be so far advanced that the fasciculi of the heart resemble cylinders which are formed entirely of fatty granules.

Pigmentary Degeneration.—In the normal state, with the adult and old persons, the muscular fasciculi of the heart at times present around the nucleus, spherical yellow or brown granules, the nature of which is still undetermined. Their color has caused them to be regarded as formed of a pigmentary substance derived from hæmoglobin.

In chronic diseases resulting in emaciation, and in senile weakness, the atrophied heart presents a brown color, and its muscular fasciculi contain a greater quantity of these granules than in the normal condition; the presence of these granules accounts for the brown color. (Fig. 156.)

Fig. 156.



Pigmentary degeneration of the heart. Showing the granules of pigment and the atrophy of the fibres. The latter have in some parts undergone slight fatty metamorphosis. ×400. (*Green.*)

In melanosis, there is found a pigmentary infiltration of the heart which differs from the preceding by the black color of the granules, by their seat in the connective tissue and in the muscular tissue at the same time, and by the localization of the degeneration in small circumscribed points or spots.

Congestion, Hemorrhage, and Inflammation of the Myocardium.—*Congestion* of the myocardium may exist during life, but it has not been positively demonstrated after death. *Hemorrhages*, on the contrary, leave evident traces and they are certainly preceded by congestion. The hemorrhages are generally seen as small ecchymotic spots, usually seated upon the internal or external surface of the heart. *Ecchymoses* occur most frequently in all diseases which terminate by asphyxia (diseases of the lungs and heart, in poisoning by phosphorus, arsenic, etc., in leucocythæmia, in purulent infection, and puerperal fever). The blood escaping between the muscular fibres of the heart soon coagulates, so that the small hemorrhagic mass forms a hard, red or brown nodule, of greater consistence than the neighboring parts; the muscular fasciculi included in this mass have experienced fatty degeneration.

There are sometimes accidentally found at autopsies blackish spots in

the myocardium, which very probably come from old hemorrhages, since in these points the interfascicular connective tissue contains cells infiltrated with pigmentary granules, and the neighboring muscular fasciculi are also pigmented.

Large hemorrhages of the heart occur in ruptures of the myocardium either primary or consecutive to fatty degeneration or to aneurisms. A rupture due to fatty degeneration is single or multiple and always occurs from within outwards; it is irregular, and if death is not instantaneous, the blood infiltrates the muscular tissue in a diffused manner. If the rupture does not extend as far as the pericardium an aneurism is formed; but most frequently the rupture breaks through the pericardium and fills the sac with partly coagulated black blood. The fatty degeneration is always more decided in the proximity of the hemorrhagic focus.

Aneurisms of the heart are found especially in the interventricular septum and at the apex of the left ventricle. The aneurisms of the septum and base of the heart are generally the result of the extension of a valvular aneurism, the origin and structure of which will be later studied. Those of the apex of the heart, which occur most frequently, are probably consecutive to a fatty degeneration or an inflammation combined with endocarditis and myocarditis; but all the changes of an aneurism occurring in this locality cannot be followed, as in the aorta, and it is only through reasoning by analogy that the method of their formation can be understood.

At the apex of the heart, the aneurism is seen as a sac varying very much in size, from a hazel-nut to that of the heart itself. When the size of the sac is very small, it is included, as it were, in the walls of the organ, and can only be recognized by opening the heart and examining its internal surface.

The communication between the ventricle and the cavity of the aneurism is by a funnel-shaped aperture, or by an orifice in the form of a ring. The wall of the aneurism is firm and rigid, so that the aneurismal sac is not emptied at the time of the ventricular systole. Yet the stasis of the blood is not sufficient to form laminated clots, as takes place in aneurisms of the aorta. At the autopsy, there are very often found in the sac, recent fibrinous clots. Where the aneurismal sac is anfractuous, there are seen dense fibrinous clots adherent to the wall.

The internal surface of the sac is usually smooth; sometimes it is irregular and anfractuous.

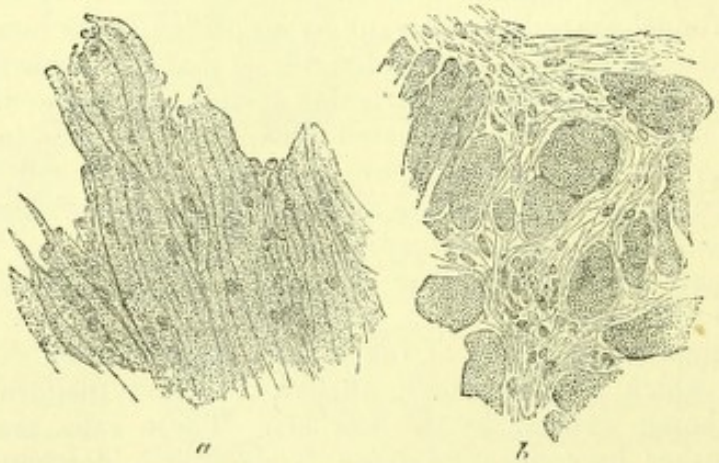
A histological examination of the wall of the aneurism shows layers of flat cells, which seen in profile appear thin and fusiform, owing to their centre being swollen by the nucleus. These cells are separated from one another by connective-tissue fasciculi and bloodvessels. The entire wall of the aneurism may consist of this tissue, but frequently only the internal surface of the sac is of this structure, and there are found in the external part muscular fibres of the heart grouped in small fasciculi or isolated among the layers of flat cells. By examining a fresh piece of the aneurismal sac, it is possible by dissection to obtain the flat cells. They accurately resemble the cells of perfectly formed connective tissue. Isolated and floating in a fluid, they present surfaces and borders and folds which indicate that they are flat cells of extreme thinness.

Their contour is sinuous and sometimes shows prolongations, which are flat like the body of the cell. The form of these cells and their arrangement in layers parallel to the internal surface of the aneurism, are due to the pressure exerted by the blood perpendicularly to the wall. The same cells and tissue are found in aneurisms of the arteries. The aneurisms produced by an extension of valvular aneurisms are generally diffused, or the sac is very anfractuous and occupied with irregularly arranged clots. These aneurisms, located most frequently in the interventricular septum, cause its destruction and a communication of the two ventricles. The tissues are torn or separated in such a manner that the shreds are forced into the right ventricle, by the blood passing from the left ventricle into the right, the pressure being stronger in the former. The muscular fibres at the margins of these aneurisms, which are generally acute in their course, are torn and are fatty degenerated.

Inflammation of the myocardium is not believed by us to be peculiarly characterized by a fatty degeneration of the muscular fibres of the heart, for this degeneration may exist in a number of affections of the heart or of general diseases which have nothing in common with inflammation. On the other hand, fatty degeneration of the muscular fibres is not seen in cases of well-marked myocarditis characterized by a growth of the connective tissue of the myocardium.

The muscular fibres become fatty in myocarditis only when they are compressed by exudations and pus cells; for example, in abscess of the heart. The fatty degeneration does not differ then from that seen in cardiac hemorrhages. This inclines us to deny the parenchymatous myocarditis of Virchow, which is characterized by a fatty degeneration of the muscles of the heart.

Fig. 157.



a *b*

Acute myocarditis. From a case of acute rheumatism. *a*. A thin section of the left ventricle made in the direction of the muscular fibres, showing the granular and swollen condition of the fibres, and the prominence of their nuclei. *b*. A transverse section, showing the cellular infiltration of the intermuscular tissue. × 200. (*Green*.)

Myocarditis occurs as an extension of endocarditis or pericarditis, or as a manifestation of purulent infection, when it is characterized by intramuscular abscesses.

[*Fibroid Induration of the Heart.*[1]—This comparatively rare condition is probably in most cases a result of myocarditis. The change is characterized by the development of a fibrillated tissue between the muscular elements. The process commences in the intermuscular septa around the bloodvessels. (Fig. 158.) These become infiltrated with cells, which tend to become developed into a fibrillated structure. The growth of new tissue gradually extends between the bundles of muscular fibres, so that ultimately each fibre may be surrounded by a tract of dense fibroid tissue. (Fig. 159.) The muscular fibres themselves, owing

Fig. 158.



Fibroid induration of the heart. A thin section from the wall of the left ventricle showing the small-celled growth in the intermuscular septa around the bloodvessels *a*, *a*, vessels. ×200. (*Green.*)

Fig. 159.



Fibroid induration of the heart. A section from the left ventricle of the same heart as fig. 158, showing a more advanced stage. The fibroid tissue surrounds the individual muscular fibres, which are undergoing fatty degeneration. ×200. (*Green.*)

to the resulting interference with their nutritive supply, atrophy, undergo fatty degeneration, and are gradually replaced by the fibroid growth. Very frequently the cellular nature of the growth is not seen, the new tissue being simply fibroid.

This fibroid induration of the heart appears in most cases to be induced by inflammatory processes commencing in the peri- or endocardium. When secondary to pericarditis the change is usually most advanced in the more external portions of the cardiac walls, and it commonly affects both the right and left ventricles. When, on the other hand, an endocarditis is the precursor of the indurative process, the change is more marked in the internal muscular layers, and inasmuch as inflammatory processes in the endocardium occur almost exclusively in the left cardiac cavities, the left ventricle is principally involved. In other cases the fibroid growth appears to be the result of syphilis.

This lesion is by no means uniformly distributed through the cardiac muscle. It should be regarded as the result of a chronic inflammatory process, which might be termed chronic myocarditis. It interferes materially with the movements of the organ; it therefore is one of the most grave of cardiac diseases.]

Abscesses of the heart occur but seldom; they vary much in size, from a pin-head to a hazel-nut. The pus is found between the muscular fibres of the heart, or is enveloped in a zone of embryonic tissue. In

[1] Abstracted from Green.

the former, the muscular substance in the proximity of the abscess is of a slate color; the pus forming the abscess contains débris of muscular fasciculi, if the suppurative inflammation is recent. In the slate-colored zone surrounding the small non-cysted abscesses are found fatty and pigmentary granules in the muscular fasciculi which are separated by blood corpuscles, pus cells, and brown granules.

There are sometimes found in the substance of the heart caseous encysted masses, which Foerster considers as the result of an old metamorphosed abscess. There are a few records of anfractuous cavities excavated in the cardiac muscle and opening into the left ventricle; these have been considered as abscesses, which have opened and discharged their contents into the circulation; such cases should be interpreted as aneurisms following endocarditis.

Tumors of the Myocardium.—Gummata have been described in the heart (Ricord, Virchow) as also secondary nodules of carcinoma and epithelioma (Paget, Lionville). Recklinghausen has published a case of striated myoma in the heart of a new-born child. Thirty cases of hydatid cysts of the heart, due always to echinococci, have been reported. These cysts may form a prominence in one of the cavities of the heart, may rupture, or even become free without rupturing.

Sect. III.—Endocarditis.

Normal Histology.—The endocardium lining the whole internal surface of the heart presents for consideration three layers: 1st, the endothelium forming a single layer of flat cells; 2d, a layer formed by flattened cells separated by a laminated fundamental substance; 3d, a layer formed by elastic tissue and fasciculi of connective tissue.

1st. The first of these layers disappears twenty-four hours after death.

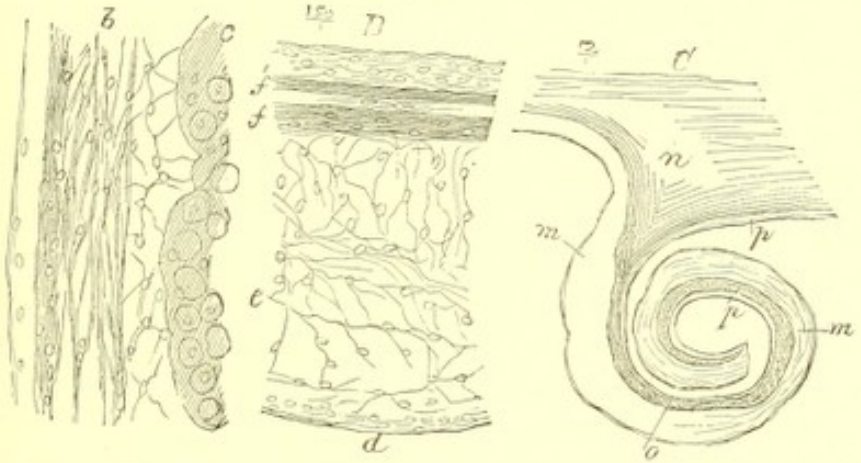
2d. The layer of flattened cells is very thin upon the ventricles and both surfaces of the arterial and auriculo-ventricular valves; it is thicker upon the auricles, and more so upon the left than the right. The flattened cells are thin, and generally possess prolongations which vary in number; they contain a lenticular nucleus, a little swollen at the centre; they are arranged parallel one to the other, and are flattened in a direction parallel to the internal surface of the endocardium.

The laminated fundamental substance which separates the cells is not reduced to fibrils by macerating in baryta-water, as is the case with ordinary connective tissue; it seems but slightly fibrillated and almost hyaline. This layer, like the endothelial layer, is continued without interruption upon the superior and inferior surfaces of the valves.

3d. The connective and elastic tissue layer of the endocardium varies the most, according to the different regions of the heart, and so considerably that, for example in the apex of the left auricle, where it is most developed, it is about ten times thicker than upon the ventricles. This layer is directly continuous with the layer of flattened cells on the one side, and with the connective tissue surrounding the muscular fasciculi on the other. Figure 160 represents at the left, a section of the

ventricular endocardium, showing the flattened cells, *a*; the fibro-elastic layer, *b*; and the connective tissue which serves as a means of union to the muscular fibres, *c*. It consists of cells and elastic fibres; the latter are very fine, and are arranged in layers parallel to the surface in the endocardium of the auricles; they are very close together and very numerous. It is these fibres which give the opaque, grayish-yellow color to the surface of the left auricle in the normal condition. In the layer which these fibres form in the ventricular endocardium they are not so close as in the auricles.

Fig. 160.



The figure to the left represents a section of the ventricular endocardium: at the extreme left is the inner layer, with flattened cells; *b*, fibro-elastic layer; *c*, transverse section of muscle fibres. × 150.

B. Section of an aortic valve: *d*, layer of flat cells of the upper face of the valve; on the opposite side, the same layer of the lower or ventricular face of the valve: *e*, *e*, fibro-elastic layer of the portion of the valve divided from the aorta: *f*, *f'*, fibro-elastic layer of the ventricular portion of the valve. × 150.

C represents a section of the whole of a valve and its insertion at the fibrous ring of the aorta: *n*, base of this ring; *m*, fibro-elastic portion derived from the aorta; *p*, fibro-elastic portion derived from the ventricular endocardium; *o*, elastic fibres. × 12.

The fibro-elastic tissue of the valves is arranged in the following manner: Upon the auriculo-ventricular valves, the fibro-elastic layer of the auricles is continued somewhat thinner upon the superior surface of the valve. The fibro-elastic layer of the ventricular endocardium is continued upon their inferior surface; it is very much thinner than the preceding; and it is from it, at the free border of the valve, that the tendons proceed, enlarging to their origin from the papillary muscles. The two elastic layers at the centre of the valve are separated from each other by a very thin layer of connective tissue. In a transverse section of the valve we distinguish, at its periphery upon the superior and inferior surfaces, the layer of endothelium and flattened cells; then the two layers, superior and inferior, of fibro-elastic tissue, the superior being thickest; and, lastly, at the centre a thin lamina of connective tissue. It is always the superior or auricular surface of the auriculo-ventricular valve which is first and to the greatest extent altered in valvular endocarditis.

The arterial valves are formed by the ventricular endocardium upon one side and the internal membrane of the artery upon the other (fig. 160, *B* and *C*). Beneath the endothelium exists the layer of flattened cells (*B*,

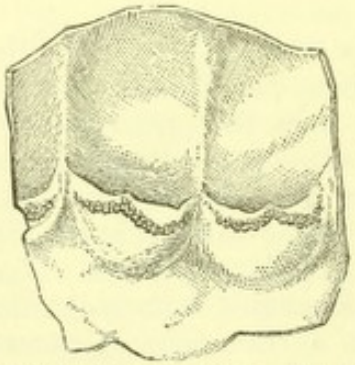
d, d'), which is everywhere continuous, and is reflected at the free border of the valves; this layer is thicker upon the ventricular surface, d', than upon the arterial surface, d. The fibro-elastic tissue of both laminæ is very thick at the origin of the valve (C, n); it forms the support for the valve, but very unequally—according as we consider the part which comes from the fibro-elastic tissue of the ventricular endocardium or from the internal membrane of the artery; it constitutes four-fifths of the thickness of the valve. The fibro-elastic tissue is arranged so that, beneath the layer of flattened cells, there is found a very thin layer of connective tissue upon the inferior or ventricular surface, and a thick layer upon the superior or arterial surface of the valve (fig. 160, B, e); beneath these layers exist two layers of fibro-elastic tissue, separated by a thin lamina of connective tissue.

Valvular endocarditis is most frequently localized upon the internal surface, near the free border of the arterial valves, in the layer of flattened cells, which is here thicker than upon the external surface (B, d').

Endocarditis.—*Acute endocarditis* occurs in articular rheumatism, in puerperal fever, in the eruptive fevers, etc.

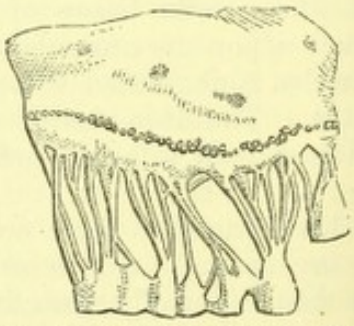
Of all the cavities of the heart the left ventricle is the one in which the lesion is most frequently met with, especially on the aortic and mitral valves, and, as will be seen, it is upon the auricular surface of the mitral and tricuspid valves, and ventricular surface of the aortic valves, that the lesion first appears. The older pathological anatomists accorded an exaggerated importance to redness; but, except when it presents itself as a vascular arborization, the redness indicates simply an imbibition. This redness is seen both upon the endocardium and the internal membrane of the vessels; it is due to the impregnation of the membrane by the coloring matter of the blood coming from the red corpuscles, which have been

Fig. 161.



Inflammation of aortic valves. The earlier stage of the process. Showing the situation of the inflammatory granulations. (*Green.*)

Fig. 162.



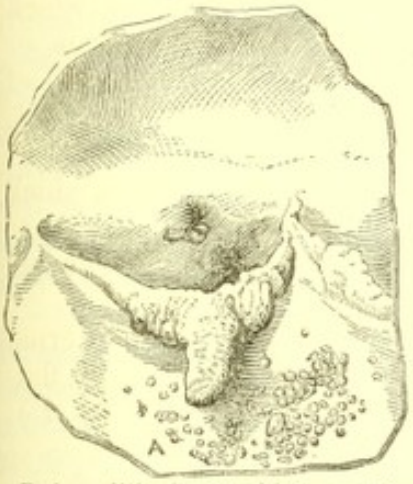
Inflammation of the mitral valve. The earlier stage of the process. Valve seen from the auricular surface. Showing the situation of the inflammatory granulations. (*Green.*)

destroyed either by an infectious disease or by a rapid decomposition of the cadaver. Endocarditis is essentially characterized by vegetations, erosions, and ulceration of the endocardium, sometimes causing perforations and lacerations of the valves.

Vegetations, which constitute the essential phenomenon of endocarditis,

are at times extremely small and numerous, so that the membrane, to a varying extent, has a roughened appearance. These small vegetations may be uniformly scattered over a large surface of the auricle and left ventricle. They are seen in this state at the beginning of endocarditis;

Fig. 163.



Endocarditis due to friction. The drawing represents a long vegetation on one of the segments of the aortic valve, which by rubbing on the endocardium below has produced numerous inflammatory granulations (A).

Fig. 164.



Acute endocarditis. A granulation from the mitral valve, showing a fibrinous coagulum upon the surface of the granulation. × 10. (*Rindfleisch.*)

but if the disease, no matter how mild, has continued, the vegetations are considerably larger, and may become as large as a pea. Their form varies very much; it is conical, nummular, or resembles a raspberry. Some of the groups of vegetations are very irregular, at times arranged on the borders of the aortic valves or on the border of the auricular surface of the mitral valve, near the insertion of the tendons, resembling very irregular wreaths; their seat is determined by the limit of the vascular network of the border of the valves. Upon the aortic valves, they are not seated upon the edge of the valves, but a little distance from the border. It is chiefly in an endocarditis of rapid course, as in puerperal fever, or very severe acute articular rheumatism, that this arrangement is observed. The largest vegetations are seated only upon the valves or upon the fibrous zone of the cardiac orifices.

If the course of the endocarditis is irregular and slow, the vegetations are very unequal in size. In chronic forms, the vegetations are not so prominent—they rest upon an indurated base, are harder, cartilaginous, and often opaque; while, in the acute forms, the recently formed vegetations are soft, friable, and semi-transparent. The translucency and friability of recent vegetations caused them for a long time to be considered as consisting only of fibrin; yet their attachment to the wall should have banished this hypothesis. When they are removed with the fingers, the surface of the membrane is not seen, but there is a tear, which very distinctly demonstrates that the vegetation is part of the membrane.

A microscopic examination shows this relation most satisfactorily. Sections from acute endocarditis exhibit vegetations formed entirely of embryonic cells separated by a very scanty amount of amorphous substance; this tissue is continued into the endocardium beneath, and forms a zone varying in extent around the vegetation. This zone of proliferation should be carefully studied, in order to understand the formation of vegetations on the endocardium. It is seen that it is not distinctly limited, but that there is a progressive multiplication of new cells, as one

advances from the periphery towards the centre. The new formation takes place in the layer of flattened cells, the flat cells also assisting, but it is by no means demonstrated that a few cellular elements do not come from another source, for example, the white blood corpuscles.

The vegetations are covered by a thin hyaline layer formed of fibrin.

In *chronic endocarditis* the vegetations have a different structure; the cellular elements, instead of being round, are elongated or flattened, separated by an intercellular fibrillar substance, always very abundant, which gives them their cartilaginous consistence. The indurated plates upon which they are implanted present an analogous structure; in a word, these vegetations and their base recall the structure of the internal layer of the endocardium. According to what is known of the cause of all inflammatory products, it may be affirmed, that all indurated and prominent plates have at first been soft vegetations which have ultimately undergone a fibrous organization.

In the tendons of the mitral valve there are seen the phenomena of acute and chronic endocarditis. In the former, the tendons soften, become friable, and may rupture. In chronic endocarditis hypertrophied chordæ tendineæ are frequently met with; they are diminished in length, rigid, of cartilaginous consistence, and smooth upon their surface.

The soft vegetations of endocarditis, instead of undergoing changes which render them fibrous, may, from the constant passing of the blood over their surface, be torn into fragments, and they then are seen as shreds. The cause of the friable nature of these new formations is owing to the great abundance of cellular elements produced by the very acute inflammatory process. It also at times occurs that the increased formation of cellular elements results in a fatty metamorphosis, on account of insufficient nutrition; so that all the growing tissue becomes a granular mass; there then remains an anfractuous ulcerated surface, formed of a tissue in which are found granular fatty cells, free fat granules, and blood pigment. The portions torn, softened, and separated by the circulating blood, are extremely small, and may be carried into the capillaries, or their size is such that they are arrested in the arterioles, producing septicæmia and embolism. This entire morbid process has received the name of ulcerous endocarditis, but it does not constitute a distinct variety from other acute forms of endocarditis.

Valvular Aneurisms.—The lesion described as valvular aneurism (Thurnam, Foerster, Pelvet), is a consequence of acute endocarditis affecting the valves. The multiplication of the cells, their embryonic state, the softening of the intercellular substance, and the disappearance of the elastic fibres, phenomena connected with endocarditis, cause the valve to lose its power of resistance, and it is not able to support the blood pressure. When, from the action of acute endocarditis, the softening rapidly extends to all the layers of the valve, the latter is at first distended, but is soon ruptured. When, however, the action of the inflammation is slower, the valve having lost part of its resisting power, slowly dilates without being ruptured.

Valvular aneurism has so far been observed only in the left heart, upon the aortic and mitral valves. In the aortic valves, the orifice of the aneurism is always upon the superior or arterial surfaces; in the

mitral valve, the opening of the orifice is always upon the inferior or ventricular surface. This arrangement is owing to the blood pressure, which is exerted when the valves are closed from below upwards in the ventricle at the moment of the ventricular systole, and from above downwards upon the aortic valves at the moment of the diastole of the ventricle.

Two forms of these aneurisms are met with: 1st. A valve softened by the inflammatory process, may be distended throughout, and remain in this condition when the inflammation ceases, the tissues again regaining their primary firmness; 2d. The endocarditis continuing in the acute state, one or more valves present upon a part of their surface soft aneurismal sacs, round or funnel shaped, or they show ragged tears. These lesions may exist at the same time upon two neighboring valves. An irregular tearing of a valve is very often seen, the shreds of which project from the ventricular side on the aortic mitral valve. These shreds are ragged, grayish, and covered by a thin layer of fibrin.

A histological examination of the shreds shows them to consist of nuclei and round cells in a mass of granular substance; there is neither connective fibrillar substance nor elastic fibres. This same tissue, however, is always seen in the walls of recent aneurismal sacs, whether they are intact or torn.

Spherical or funnel-shaped valvular aneurisms without any tear are rare. Frequently, if the sac has not been ruptured into a great number of pieces by the blood pressure, it is torn to a greater or less extent. We have seen, for example, a funnel-shaped aneurism of the aortic valve presenting a single perforation at its extremity.

Acute endocarditis, by the vegetations and thickening of the endocardium upon the orifices, is a cause of narrowing (stenosis), and by the rupture of the valvular aneurism, it may occasion insufficiency. These lesions, however, are more often produced by chronic endocarditis.

A series of lesions of the heart, occurring especially at the orifices, are connected with *chronic endocarditis;* some have for a cause acute endocarditis, which has passed into the chronic state; the others are developed slowly, and are seen in alcohol drinkers, old persons, in lead poisoning, etc.

Chronic endocarditis is essentially characterized by cartilage-like, translucent, or opaque thickenings. In many instances the indurations contain calcareous salts and become like bone. These lesions are especially seen in the fibrous zone of the orifices, and in the chordæ tendineæ, and valves; they are very analogous to the alterations occurring in endarteritis deformans, and it is probable that upon the endocardium as in the arteries, primary atheroma exerts some influence.

The lesions of the valves, in chronic endocarditis, have the form of globular or wart-like vegetations, seated generally upon the ventricular surface of the aortic valves and upon the auricular surface of the auriculo-ventricular valves. The chordæ tendineæ of the auriculo-ventricular valves are increased in size, indurated, and shortened; the fibrous zone limiting the orifices is hypertrophied and indurated. When the heart is dilated by blood pressure, the fibrous rings of the orifices frequently experience a similar dilatation; or they may present a notable narrowing.

The valves themselves may be three or four times thicker than normal. Their tissue has become rigid, their borders form irregular swellings, and they are also thickened at their insertion, where they are connected to the fibrous zone, which presents an analogous induration. As a result, the general form of the orifice is greatly modified. There may exist at the same time insufficiency and stenosis of the orifices, insufficiency from rigidity of the valves, stenosis from the new formations growing upon their borders; it is very rare to find stenosis without insufficiency.

Perpendicular sections of the indurated tissue show considerable changes from the arrangement of the normal endocardium. Instead of finding the successive layers which have been described and which are so characteristic for each part of the valves and orifices, there are seen only irregular layers of flat cells separated by a fibrous substance and irregularly distributed elastic fibres. Sometimes the cellular new formations which have caused the irregularity of structure become the starting point of a new organization tending to reproduce the primary tissue, but never perfectly succeed. The origin of these new formations is always the layer of flattened cells situated under the endothelium.

There are always found in this imperfect fibrous tissue small points of fatty degeneration. These points, uniting together, may form atheromatous foci filled with granular detritus; these atheromatous points may be stationary or they have a tendency to open upon the surface.

The formation of calcareous granules and plates is very often seen in the indurated tissues of chronic endocarditis.

It is very important to know if the indurated tissue, developed in the endocardium and valves, undergoes cicatricial contraction. The great narrowing of the mitral orifice, for example, can only be explained by a process of this nature, but it is impossible to follow the process from histological observation.

The Formation of Blood Clots in the Heart.—Frequently at the autopsy the left ventricle is found contracted and empty of blood, except it be a few filamentous clots between the columnæ carneæ of the mitral valve; it is only in cases where the person dies of syncope, that the ventricle arrested in diastole at the moment of death contains blood and clots.

The right ventricle is frequently distended, and filled with coagulated blood, chiefly owing to the agony generally being accompanied by asphyxia and hinderance to the pulmonary circulation, which prevents the right ventricle from emptying itself. The auricles, on account of the feebleness of the contractions, are always filled with blood during life and occasionally after death.

When the heart ceases to beat the blood contained in its cavities is slowly coagulated—much more slowly than if it is exposed in a vessel. This has been established by the experiments of Brücke, who remarked that blood from the cavities of a heart removed from the body of an animal coagulated only after several hours, a phenomenon which he attributes to the influence of the endothelium of the endocardium. It is now known that when blood coagulates slowly the red corpuscles, which are the heaviest part, settle to the dependent portion, while the superficial portion

destitute of corpuscles coagulates into a colorless fibrinous mass. The clot is then formed of two layers, one superficial, light in color, consisting of fibrin inclosing serum (buffy coat), the other deeper, colored red by the corpuscles. Coagulation takes place in this manner in the heart when there is a notable quantity of blood in its cavities, and the subject has remained in the same position some hours previous to the autopsy, upon the back for example, as is usual. All large clots of the heart are then colorless upon their superior portion, while they are cruoric upon their inferior surface.

These clots are considered by most physicians to be formed during the agony; on account of their decoloration, they have accorded to them a vital origin, and have named them active clots. What we have said in reference to the mode of formation of these clots is sufficient to demonstrate that this interpretation is erroneous, and it is useless longer to insist upon it.

Some clots merit the name of active clots, if by this word it is understood those which are formed during life; they are the fibrinous coagulations developed in thin layers upon the surface of the denuded endocardium in endocarditis, or upon vegetations of the orifices, or upon the torn valves. These clots are white or yellow; they contain no red blood corpuscles, only layers of granular fibrin and white corpuscles. According to the theory of A. Schmidt, which is generally accepted, their formation results from the condensation of the fibrinogenic substance of the blood in contact only with the inflamed wall. The slow coagulation for this reason does not include the red elements.

Other larger clots are formed by a slowing of the circulation of the blood, as occurs in asystole, especially that produced by an impediment to the pulmonary circulation, and in hypertrophies of the heart with dilatation.

These clots vary in size and form; they generally cover the columnæ carneæ, are adherent to the wall, and are uniformly yellow. If they are not very old, they may be separated into lamellæ by tearing, and their central part does not differ in consistence from the superficial layers. If they are older, their superficial part is more consistent, while their centre is soft, and forms a granular mass. When the changes of the blood have been great, as in hemorrhagic smallpox, puerperal fever, poisoning by phosphorus, etc., heart clots formed after death are soft, friable, and do not contain distinct layers, while in leucocythæmia the clots are but little colored, and there exists besides a fluid which sometimes has the appearance and consistence of pus, as Virchow has observed. This is due to the enormous quantity of white corpuscles contained in the fluid.

CHAPTER VIII.

LESIONS OF THE ARTERIES.

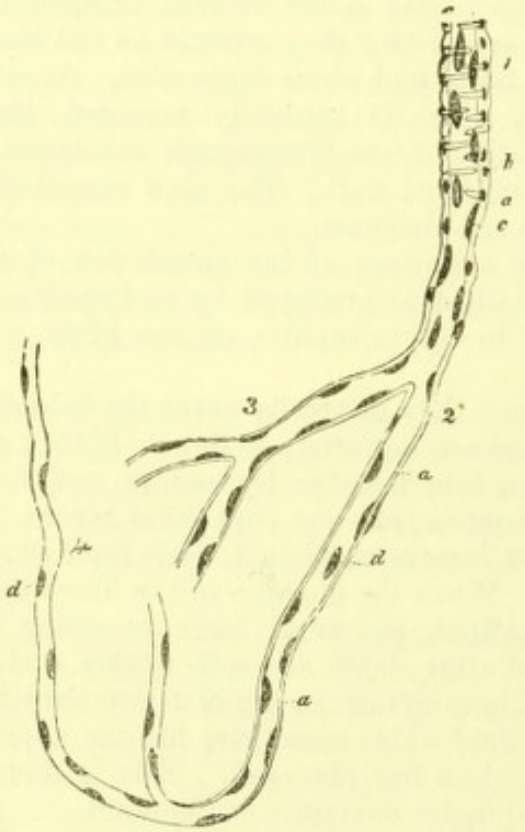
Sect. I.—Normal Histology of the Arteries.

THE arteries present for examination an internal, middle, and external coat.

The internal coat of large arteries consists of two parts: 1st, the endothelial layer; 2d, a thin layer lying upon the middle coat.

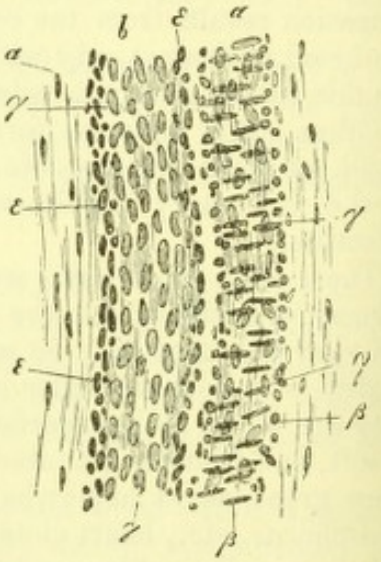
The *endothelial* layer may be demonstrated by means of nitrate of sil-

Fig. 165.



Finest vessels on the arterial side. 1. Smallest arteriole. 2. Transition vessel. 3. Coarser capillaries. *a*. Structureless membrane still with some nuclei, representation of the tunica adventitia. *b*. Nuclei of the muscular fibre cells. *c*. Nuclei within the small arteriole appertaining to an endothelium. *d*. Nuclei in the transition vessels. From human brain. × 300. (*Gray*).

Fig. 166.



a. An arteriole. *b*. A veinule from the mesentery of a child. (*Gray.*)

ver. The polygonal very flat endothelial cells are then limited by a line black with transmitted light; they all contain a flat nucleus, round or elongated.

The *sub-endothelial layer* is formed of flat cells irregularly stellate, containing flat nuclei, and of a fibrillar substance running longitudinally; it does not contain vessels. In the small arteries this layer is so thin that it is only recognized by the longitudinal striation, and by the presence of a single layer of flat cells separated from one another, and which can only be distinctly recognized after the action of nitrate of silver.

The *middle coat* of the large and medium size arteries consists of elastic laminæ and fibres forming by their anastomoses a continuous system in which are found smooth muscular fibres passing in a transverse direction.

Next to the internal coat, the middle coat is limited by a thicker elastic lamina and also more refracting than the others; in transverse sections it has a festooned appearance. The recognition of this lamina is very important in pathological investigations; we have named it the *internal elastic lamina of the middle coat*. [Most authors regard this elastic lamina as the external layer of the tunica intima, recognizing three layers of this coat.] In the external coat elastic fibres mingle with the fasciculi of the connective tissue in every direction, to form the framework of the tunica adventitia.

The external coat is traversed by arteries, capillaries, and veins (vasa vasorum) and, by lymphatics whose lumina appear as clefts when cut transversely. Small nerve trunks and isolated nerve fibres are also seen in this coat. The small arteries possess a middle coat formed by smooth muscular cells arranged transversely, constituting a continuous membrane. The tunica adventitia of these arteries consists of very fine fasciculi of connective tissue having a general longitudinal direction.

Sect. II.—Pathological Histology of the Arteries.

Arteritis.—The inflammation of arteries presents for consideration many varieties when examined from a pathological point of view. The inflammation may be considered in reference to its location in large, medium, or small arteries, and in the external, middle, or internal coats; atheromatous and calcareous tumefaction also enters into the history of arteritis; finally, spontaneous aneurisms and the obliteration of arteries by a clot followed by organization belong to arteritis.

1*st*. Acute Arteritis.—Acute endarteritis or acute inflammation of the internal coat of the aorta, has been seen by us several times as an isolated lesion. To the unaided eye, it is characterized by a swelling of the internal coat in the form of prominent patches more or less extended, with a contour somewhat regular and generally circular. The smaller ones are regularly round, and present a sharply raised surface; others, larger, more irregular in their contour, are evidently formed by the confluence of several small round patches, and exhibit prominences and depressions upon their surface. Their color is light red, transparent, or opalescent; their consistence is elastic and soft as jelly; they have been named gelatinous patches of the aorta; their surface is very seldom ulcerated. These patches are frequently accompanied by a somewhat analogous change in the neighboring internal coat, so that this membrane appears saturated with fluid

translucent, light red, or colorless. In some cases where the endarteritis was very intense, we have been impressed with the paleness of the internal coat, and, again, we have frequently met with an intense redness of the vessels and endocardium, due solely to imbibition, without any histological trace of endarteritis or endocarditis; it is sufficient, however, to allow an artery to macerate in water colored by blood, in order that its primarily pale surface may become red by imbibition.

There is frequently seen in endarteritis a roughened appearance of the internal surface of the artery, due to an irregular tumefaction of the internal coat, and not to a falling off of the endothelium, as has been supposed. As we have already mentioned, this endothelium is normally destroyed within twenty-four hours after death. This is no less true also of pathological conditions, both upon the smooth surfaces as well as upon those which are roughened.

A vertical section of these patches is seen to have a color and semi-translucency similar to that of the surface, and to the unaided eye their separation from the middle coat is distinctly recognized.

The elements constituting these patches can be separated without difficulty, by dissection with needles. Large shreds of the internal coat may also be stripped off; this coat is transparent or slightly striated, and is easily separated into thin laminæ, a demonstration that the cells of the coat are arranged in layers parallel to the surface of the vessel.

The elements forming the patches are round or irregularly spherical cells having an average diameter of .01 mm., and in which a nucleus is seen upon the addition of acetic acid. These elements have all the characters of embryonic cells. Large flattened cells with several prolongations containing at times two nuclei, are also observed; they exist normally in the internal coat. Examination of the tissue by dissociation shows round cells, which are not free nuclei, as has been believed.

On microscopic examination of thin sections, the patches appear as a thickening of the internal coat. With low magnifying power, the great thickness of these patches can be appreciated by comparison with the normal portion of the internal coat and with the middle coat; for they may be a hundred times thicker than the internal normal coat, and two or three times thicker than the middle coat. With a power of one hundred diameters, which permits the whole of the preparation to be seen, the cellular elements are found to be very numerous, arranged in lines parallel to the surface of the patch, and diminishing in numbers as the middle coat is approached, offering a very striking analogy to the phenomenon which takes place in inflamed diarthrodial cartilages, where the cells at the surface are also the first to proliferate.

This circumstance of the multiplication of the elements at the surface of the internal coat is peculiar to acute endarteritis, and separates it from endarteritis with a tendency to atheroma where the proliferation occurs, as we shall see, in the deepest layer of the internal coat. The same distinction may be made in endocarditis.

At the periphery of the patch, where it is continuous with the internal coat, the changes in this coat may be observed and the process of formation and growth followed. Even in the tumefied portions there is seen upon the surface of the internal coat a great number of round cellular

elements, while deeper the flattened cells with their lenticular nuclei are still found. Upon the surface of the patch the elements are very near together, and seem to touch. The nuclei are biscuit- or wallet-shaped—a precursor of the division which is to occur—and series of two to five nuclei in contact one with the other are seen. Towards the deep layers the ground substance is more abundant, and the groups of cellular elements are more separated from one another.

In acute endarteritis, where the new elements are found upon the surface of the internal membrane, in order to explain their formation, the theory of Cohnheim, according to which the white corpuscles emigrating out of the vessels constitute the products of inflammation, does not readily apply. A careful study of these elements distinctly demonstrates that they come from a division of the fixed cells of the tissue.

The gelatinous patches of the arteries at times present superficial and fungoid ulcerations, which are covered by a thin layer of adherent fibrin; this occurs more frequently in valvular endocarditis than in endarteritis. The semi-transparent, soft, fibrinous layer is often uniformly red in color, and striated, or it is so in patches. It cannot be determined without microscopic examination whether the structure is fibrin or the modified internal membrane. The parts composing the transparent layer, when studied by dissociation, are seen to be numerous round, small, nucleated cells; by their shape alone, it is not possible to determine whether these embryonic elements come from the proliferation of the cells of the internal membrane or from white corpuscles of the blood. But if sections are made, it is seen that they consist of fibrin inclosing cellular elements. It is very probable that the fibrinogenic substance of the blood is transformed into fibrin by the action of the fibrinoplastic substance of the inflamed parts, and that this fibrin incloses either the white blood corpuscles or the proliferated and free elements of the diseased surface.

In every case of acute endarteritis there exists a considerable thickening of the *external coat*, a *periarteritis*, corresponding to the whole extent of the diseased part. Its tissue becomes homogeneous, gelatinous, light red or amber color. Microscopic examination of sections shows considerable thickening and a new formation of cells between the fasciculi of the connective-tissue fibres.

The *middle coat* does not generally present any alterations in acute endarteritis. Between the most acute endarteritis and that which ultimately becomes a chronic endarteritis, every intermediate stage is found; all the phases of the lesion may be seen in the same section of an artery.

Acute *periarteritis* characterized by a purulent infiltration of the external coat, occurs in phlegmon. The inflammation is most frequently limited to this membrane, or it occasions only a slight lesion of the internal coat. In this case the middle coat, which is not modified, is sufficiently resisting so that there does not result any serious interference with the local circulation, and the artery performs its functions.

In arteries of medium size and smaller, spontaneous acute endarteritis seldom occurs; but in granulation tissue of wounds, arteritis is common, for example, in the fungoid tissue of paronychia, and in chronic ulcers. By making a section of these tissues, a small artery is seen as a red point

surrounded by a translucent and thick circular zone. If there is an attempt at dissecting out the artery, it will be found very difficult to follow, on account of the external coat being infiltrated with fluid and inflammatory elements, and blended with the neighboring connective tissue, forming with it a lardaceous mass. The dissection is also rendered difficult, because of the friability of the vessels, and the slightest traction is sufficient to cause a rupture. It is especially these arteries which are difficult to distinguish from the neighboring nerves, on account of their naked-eye resemblance to a solid cord.

Histological examination of the diseased vessel and its surrounding tissue shows vegetations of the internal coat, that is, of all the tisue inclosed between the internal surface of the vessel and the first elastic lamina of the middle coat. These growths consist of round or flattened cells separated from each other by a small amount of intercellular substance. Vessels coming from the tunica adventitia may penetrate into this tissue and form loops. This vascularization is seen very often when the middle coat is transformed into connective tissue. The external coat formed of fasciculi of connective tissue and elastic fibres is subject to phlegmonous lesions, that is, there is a formation of embryonic cells between its fibres and an absorption more or less complete of the elastic fibres.

The middle coat in this form of arteritis does not remain inactive; proliferating elongated cells of smooth muscle are seen, while the elastic fibres are broken down and absorbed. Finally, the different arterial coats are blended together in areas varying in extent.

Under the influence of inflammation the several tissues which constitute the arterial wall tend to assume a structure like that of the inflamed internal coat.

Where the growth of the internal coat is sufficient to hinder or arrest the circulation of the blood, there is a coagulation of it constituting one of the forms of arterial thrombosis.

2d. Chronic Arteritis, Fatty and Calcareous Degeneration and Atheroma—The lesions of chronic arteritis are analogous to the preceding, except that they are complicated by fatty degeneration, atheroma, and calcareous transformation. Atheroma and calcareous infiltration are always accompanied by arteritis; but this is not the case with fatty degeneration which may occur separately, and which we believe to be one of the causes of arteritis.

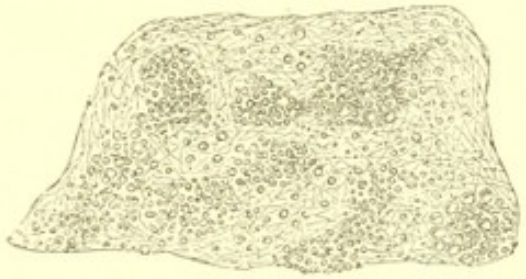
Primary fatty degeneration of arteries is seen chiefly in the aorta, immediately above the aortic valves, where in almost all adults there are found white, opaque, striated patches forming a scarcely perceptible elevation. These patches may be considered as the first stage of fatty degeneration which, with atheromatous and calcareous patches, in some aged persons extends over considerable space. The white or yellowish patches should be studied principally by longitudinal sections, or by detaching shreds of the internal coat. In these shreds are seen small collections of granules and small oil drops, frequently having the shape of the flat ramifying cells of the internal coat. (Fig. 167.)

In transverse sections it is found that the fatty degeneration is not limited to the internal coat. The neighboring layers of the middle coat are attacked with the same fatty degeneration.

In the internal coat the fat granules form flattened or fusiform layers in which remains of nuclei are sometimes distinguished; they are recognized by staining red with carmine, while the fat granules are not colored. Most of the spots do not contain nuclei, they having disappeared by atrophy.

In the middle coat, the fatty granules are arranged between the fibres and elastic laminæ, and when they are very abundant the muscular elements cannot be distinguished. At the margins of the fatty degenerated patches the muscular cells, which can be still recognized, are infiltrated with granules.

Fig. 167.



Fatty degeneration of the internal coat of the aorta. Minute yellowish white patches scattered over the lining membrane of the vessel. A very thin layer peeled off, showing the groups of fat molecules, and the distribution of fat in the intima. × 200. (*Green.*)

From these facts it may be concluded that this lesion occasions the atrophy of the cellular elements of the tissue invaded; there is a fatty necrobiosis in the full acceptation of the word.

Chronic Arteritis.—When a part of the arterial coats has undergone the change that we have described, the necrosed portions determine around them a slow irritation, producing in this manner a chronic endarteritis, but this is not the only cause of chronic endarteritis; it may appear from the first or follow an acute rheumatism, puerperal fever, alcoholic endarteritis, etc. The lesions of chronic endarteritis, whatever may be its origin, are always complicated by a fatty degeneration of the arterial coats; they terminate in the formation of atheromatous foci and calcareous plates. It is important to make as complete analysis as possible of all these phenomena in order to demonstrate that they follow a fatty degeneration which occasions arteritis or succeeds it.

In acute arteritis which is not very intense, the gelatinous patches themselves inclose ramified cells containing fatty granules. This fatty metamorphosis continues when the inflammation loses its first intensity; most all the cellular elements of the patch are generally filled with fat, and instead of being semi-translucent the patch becomes yellow and opaque. The fatty degeneration continuing, the groups of granules which at first had the form of the cells are fused together, and there results a small patch, visible only with the microscope; later it enlarges, and becomes evident to the unaided eye as a characteristic atheromatous focus.

This *atheromatous focus* is situated in the thickened internal coat; it is large, superficial, and its borders are irregular. When it remains intact it is separated from the current of blood by a thin, cartilage-like pellicle which is formed by the most superficial layers of the internal coat. The pellicle is tense yet movable; at its periphery there is frequently seen a swelling formed by a thickening of the internal coat in such a manner that the slightly depressed centre of the atheromatous focus has been compared to an umbilicated pustule of smallpox.

When an incision is made through the centre of the atheromatous patch,

the knife, after being arrested by the hardness of the internal layer, opens a focus from which escapes a thick whitish pulp; examined with the microscope it is found to consist of numerous cholesterin crystals, free fat granules, compound granular corpuscles, and crystals of fatty acids.

The atheromatous foci sometimes open, during life, into the artery in consequence of the thinness of its coats and under the influence of the mechanical force of the circulation; the opening may be either a small slit or have a stellate shape. The atheromatous pulp then passes out into the circulation, and the blood enters into the cavity. The contents and edges of the atheromatous focus are now colored yellow, brown, or black, from the transformation of the hæmoglobin.

Such ruptures of foci may be the beginning of aneurismal dilatations, which will be considered later. In sections passing vertically through the atheromatous focus and its borders, it is found that the bottom is formed by the innermost layers of the internal coat, which present the modifications of endarteritis with fatty degeneration. The most superficial layers of the middle coat show the modifications of primary fatty degeneration.

At the edges of the atheromatous point the swollen portions present microscopic atheromatous foci lodged in a refracting slightly fibrillar substance; further from the atheromatous focus there are found nuclei colored red by carmine, and surrounded by fatty granules. The fundamental substance is made up of a fibrillation very much like that seen in the centre of the costal cartilage; and again, the fibrillar mass limits small cavities which contain cellular elements recalling the cells of cartilage, except that they possess no capsule. It is a kind of chondroid, but not cartilaginous, transformation of the internal coat. If the atheromatous evolution occurs slowly, while the cells experience the fatty metamorphosis, the fibrillar fundamental substance is infiltrated with calcareous granules. These granules at first discrete, are later united together, so that they form imbriated, semi-transparent, friable, slightly elastic plates.

The calcareous plates are seldom completely exposed at the surface of the vessel; generally they are covered by a lamella of the fibrous tissue of the internal coat. These hard laminæ are at times extremely thin, and are destroyed by the movements of the circulation; or they are thickened at the edge, and the thin layer of tissue which covers them is ruptured, forming irregular slits through which the blood enters and occasions a deposit of black pigment.

Since the calcareous plates are transparent, friable, and but little elastic, by the unaided eye they are easily distinguished from osseous tissue, which is resistant, opaque, and quite elastic. Under the microscope the structure of osseous tissue is never seen; irregular masses with clefts and dark striæ are found in a very transparent substance, which does not present either the lamellar arrangement or vessels of bone. The clefts and striæ have no analogy with bone corpuscles.

There are frequently found in persons advanced in age all the preceding lesions united, and accompanied with the dilatation of the vessel; the

name *arteritis deformans*, has been given to this complex pathological condition.

When the aorta is removed and opened, its increase in size, the irregularity of its diameter, the inequalities of its surface, and the variety of the lesions that are discovered by careful examination, are very striking. The lesions are generally more decided and older at the origin of the aorta, than in the remainder of its length, and they are continued as far as its main divisions; it appears that the change had its origin in the first portion of the aorta and progressively invaded it. Above the aortic valves, usually indurated, there are found calcareous plates, separated by clefts or imbricated one upon the other, sometimes limited at their periphery by a swelling due to an endarteritis. These calcareous plates very often extend to the coronary arteries, to the innominate, to the carotids, and to the subclavian, invading them to a greater or less extent. The origin of these arteries from the aorta almost always presents a nearly perfect bone-like ring. The arch of the aorta is the portion the most dilated; it frequently has the form of an elongated funnel. In the thoracic aorta there are found calcareous plates, open atheromatous foci, atheromatous pustules, translucid or somewhat opaque cartilage-like plates. The shape and thickness of the cartilage-like plates vary. The excrescences which they cause are nummular or vegetating; they may be covered with layers of fibrin which project in the direction of the blood current.

When there exist upon the inner surface of the aorta thin, calcareous vitreous plates, formed in the rigid and hypertrophied internal coat, or extending over the atheromatous foci, they often break, forming very narrow slits into which the blood infiltrates. This blood undergoes the usual pigmentary metamorphoses, and occasions black or melanotic patches varying in size, giving the diseased part a peculiar appearance.

The preceding description is particularly appropriate to the aorta, but the same lesions are seen in the medium and small-sized arteries, where the calcareous transformation is found frequently in old persons, in the arteries of the membranes of the brain, in the coronary arteries, etc.; it occurs in the hypertrophied internal coat at first by a chronic endarteritis. This endarteritis is histologically characterized by a multiplication of the cells of the internal coat, and by the formation of a slightly fibrillar, resisting, intercellular substance, which soon gives to the membrane a cartilaginous consistence. This chondroid tissue may develop regularly in the internal tissue in such a manner as to diminish the calibre of the vessel, or its development is greater at some points than others, constituting prominent plates or projections into the lumen of the vessel. In consequence of this lesion, the blood is arrested or sufficiently retarded so that coagulation takes place.

These arterial coagula or thrombi cause gangrene in the extremities, softening in the brain, and fatty degeneration of the heart when they occupy one of the coronary arteries.

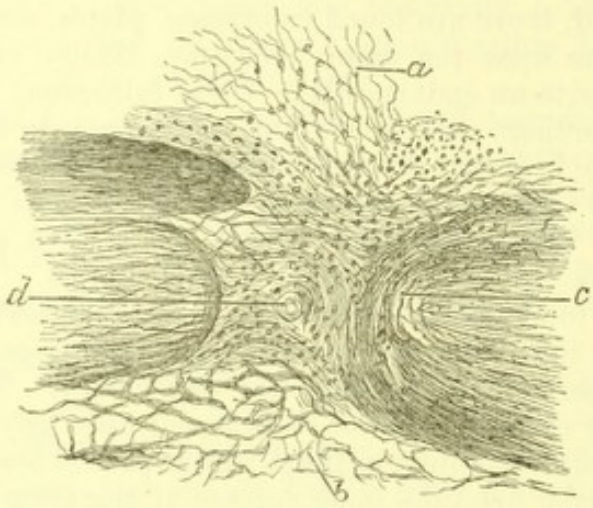
Every endarteritis of long duration is accompanied with a thickening of the external coat, with the production of numerous cells between the fasciculi of the connective tissue—a *chronic peri-arteritis*.

In the dilatations of the aorta accompanying arteritis deformans, there

is a constant disappearance of the middle coat at some points, when the hypertrophied internal coat is united to the external coat.

The portions of the destroyed middle coat are replaced by connective tissue from the proliferating external and internal coats. Figure 168, from a section of the aorta, shows an interruption of this nature of the middle coat; it is seen as a bridge of connective tissue placed between the internal and external coats.

Fig. 168.



Section of the aorta at a point where the middle layer is interrupted by embryonal connective tissue. *a*. Internal membrane. *b*. External membrane. *c*. Middle coat. *d*. Vessel in the midst of the embryonal tissue which unites the external and internal coats. × 100.

Vessels may penetrate the band of connective tissue, as shown in the drawing, which explains how the internal coat may become vascular. The destruction of the middle coat is the only cause of spontaneous aneurisms of the aorta.

In the disappearance of the middle coat, the destruction of the elastic fibres is preceded by a decomposition of its elements into small refracting granules. The external coat is so modified in its structure as to have the histological characters of the altered internal coat. It is formed of flat cells parallel to the axis of the vessel, and separated by a slightly fibrillar fundamental substance. This alteration may be attributed to the pressure exerted by the blood upon the irritated connective tissue of the external coat, when unprotected by the elastic and resisting elements of the middle coat. These very interesting phenomena are seen in the development of every spontaneous aneurism.

3d. Aneurisms.—Authors have divided aneurisms, according to the shape of the sac, into *cylindrical*, *fusiform*, *sacciform*, *crater-like*, or *cup-shaped*. They have also been classified, according to the structure of the wall of the sac, into *true aneurism*, formed by the dilation of the three coats of the artery; *mixed external aneurism*, formed by the external coat, the other two coats being torn; and *mixed internal aneurism*, in which the sac consists of only the internal coat, forming a hernia between the two torn or separated external coats. *False aneurisms* are those in which the sac is composed only of the neighbor-

ing tissues of the vessel, after the destruction of its walls; and, finally, *dissecting aneurisms* are those in which, the internal and middle coats being torn, the blood infiltrates between them and separates them to a greater or less extent.

Authors who have adopted this classification have relied upon anatomical principles, the majority of which are false, as we have demonstrated in a former work. Their error is owing to the fact that they considered the formation of aneurisms as the result of a simple mechanical action exerted upon a healthy artery.

Spontaneous aneurisms are always developed in arteries which have been for a long time the seat of inflammatory lesions

It has been seen that in the formation of the most simple aneurism—dilatation of the aorta in arteritis deformans—the internal and external coats are greatly changed and hypertrophied, while the middle coat has partially disappeared. Therefore this aneurism cannot be considered as a true aneurism, since the middle coat is at places absent; and it is not a mixed external or mixed internal aneurism, since both the external and internal coats are at the same time modified in their structure and are distended. It is the same with every other form of spontaneous aneurism, so that the anatomical classification of authors should be rejected.

All spontaneous aneurisms are believed by us to be the same histologically, that is, their sac is formed by the internal and external coats, modified by inflammation and dilated by the blood pressure, the middle coat having disappeared completely or in part.

Fusiform aneurisms are produced by a circumscribed dilatation of an artery, in which a limited portion is distended in a uniform manner. The arteritis has extended regularly over the entire surface of a portion of the vessel.

If the arteritis is located only upon one side of the artery, or there attains its greatest intensity, it destroys the middle coat, and the dilatation occurs solely at this point, forming a *sacciform* aneurism.

Finally, small aneurisms communicating with the artery by a sharp edge—the sac of which is regularly hemispherical in shape, most frequently situated at the origin of the aorta, and which appear to be formed by an opened and distended atheromatous focus—are named *cystogenic* or cup-shaped.

Dissecting aneurisms, described first by Laennec, owe their formation to a rapid dilatation during an endarteritis. Laennec supposed that, after the rupture of the internal and middle coats, the blood escaped between them, dissecting the external coat. But Peacock has demonstrated that the blood is diffused either between the hypertrophied internal coat and middle coat, or between the laminæ of the middle coat. Physiologically, the external coat is formed of fasciculi of connective tissue which slide one upon the other, and is incapable of retaining the blood under the arterial pressure. Several investigators, Ball and Duguet among others, have verified the views of this English author. Every circumscribed, sacciform, fusiform, or cup-shaped aneurism presents for consideration the membrane or wall which surrounds the sac, and the *stratified clots* which line the internal surface.

When an aneurismal sac is opened, there are found fluid blood, soft

cruoric clots of recent formation, and laminæ of elastic, grayish, or translucent fibrin, presenting grayish opaque striæ, and separated into lamellæ. The last of these laminæ can be detached from the internal surface of the sac.

Frequently it occurs, especially in the large aneurisms of the aorta, that in the most external laminæ, namely in those which are in contact with the walls of the aneurism, the fibrin has undergone a granular degeneration. These laminæ at first become opaque, afterwards break down into detritus; here anfractuous cavities filled with an atheromatous pulp are formed in the fibrin.

The arrangement of the stratified laminæ in the interior of the sac varies. In the most simple cases, particularly in cup-shaped aneurisms, the layers of fibrin form lamellæ placed one upon the other, the most external of which line only the bottom of the sac; those forming afterwards are larger, only the most internal reach the neck of the sac. These lamellæ consequently vary in extent, the smallest being the most external and the largest the most internal. This arrangement marks the progressive growth of the aneurism; the oldest deposits, that is, the most external, were formed when the sac was small; the successive layers are more and more extensive in proportion as the sac increases in size.

In the large aneurisms, the order of the stratified clots is not so simple; the changes are seen to be much more abrupt than in the preceding.

The laminæ of fibrin are much more resisting and thinner the more external they are. In thin sections, recently coagulated fibrils of fibrin are not found, but irregular laminæ, between which small collections of fatty granules and blood pigment are seen; it is these collections which form the opaque striæ. Lacunæ resembling canaliculi are also observed. In these clots, a true organization in the sense of a tissue is not seen: neither living cells nor vessels are observed; but after the action of carmine and acetic acid, bodies colored red are noticed, being the remains of white blood cells confined in the coagulated fibrin. In the atheromatous pulp, which is sometimes substituted for the laminæ in contact with the wall of the sac, there exist albuminous and fatty granules, crystals of cholesterin, and caseous white corpuscles.

In thin sections, the membrane of the aneurismal sac appears in some preparations formed by a single tissue, the structure of which is the same as that of the internal coat of arteries modified by inflammation. At some points, the middle coat is very thin, and the external coat has become like the internal; in other preparations, there are found only some irregular pieces of the middle coat, enveloped in the tissue of the aneurismal sac, which has taken the characters of the internal inflamed coat. When the different regions of the same aneurismal sac are studied carefully, the middle coat is found to have entirely disappeared around the middle of a fusiform aneurism and at the bottom of a sacciform aneurism; irregular shreds of this coat are met with as the non-dilated portion of the artery is approached, and in the neighborhood of the neck of the sac, the middle coat is thin but continuous, or is interrupted only by small foci of vascular connective tissue interposed between the external and internal coats. The new-formed tissue, which,

partially or entirely, constitutes the sac of aneurisms, consists of layers of flat cells separated by a slightly fibrillar substance; it undergoes the same alterations as the tissue of chronic endarteritis, namely, fatty degeneration, atheroma, and calcification. Old aneurismal sacs are at times formed by a solid, inextensible, calcareous shell.

From what has been previously said of chronic endarteritis, and of the structure of the aneurismal sacs, it is very easy to understand the development and growth of aneurisms. Of the different coats of the arteries the middle one only, by its elastic and contractile elements, is able effectually to resist the blood pressure. When, from the combined effects of endarteritis and periarteritis, the middle coat has disappeared in consequence of the fatty degeneration of its muscular fibres, and from the granular breaking down of its elastic fibres, the resistance of the vessel becomes insufficient and it is distended. This dilatation does not arrest the formation of morbid tissue; neither is the thickness of the walls of the sac in inverse relation to its extent. Sometimes the wall of the sac, at least in points, is much thicker than all the united coats of the primary vessel.

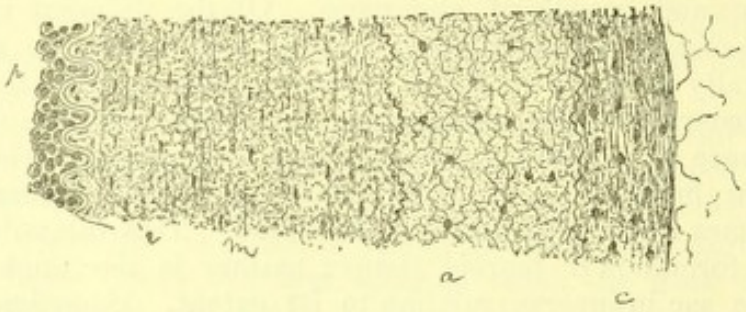
The wall of the aneurismal sac may, however, become thin and break. This rupture is followed by an escape of blood into the neighboring tissues. The lesion has been named a false consecutive aneurism.

One of the most interesting points in the anatomical history of aneurisms consists in the changes occurring in the surrounding parts by the extension of the sac. In aneurisms, especially of the arch of the aorta, where the bones cannot be pushed aside or separated, the latter undergo a very singular loss of substance, which the older anatomists explained by mechanical wearing away. When the aneurismal sac extends and comes in contact with the sternum, ribs, clavicle, or bodies of the vertebræ, excavations or a loss of substance limited by a red vascular surface result. Sections of these bones, to the unaided eye, show the characteristic lesions of osteitis: enlargement of the vascular or medullary spaces, and the formation of embryonic marrow, are recognized by microscopic examination. The osseous lamellæ are irregularly eroded; and the marrow formed of young cells does not contain adipose vesicles. It is, therefore, not a mechanical wasting away, but a vital process, through which the bone disappears. The mechanical action occasions an irritation, and it is this that causes the absorption of the bone.

The irritation excited by the pressure of the aneurismal sac causes the neighboring organs to unite to it, giving rise to inflammatory complications. Inflammation of the organ at the point of adhesion is added to that of the wall of the sac; softening of the tissue, and a perforation are produced. In this manner aneurisms of the ascending aorta may open into the pleura, pericardium, trachea, œsophagus, superior vena cava, pulmonary artery, right auricle, or ventricles. Adhesive inflammations of the neighboring organs at times may extend to more distant parts; thus, a phlegmon of the mediastinum, catarrhal and caseous pneumonia may occur in aneurism of the thoracic aorta, and phlegmon of the subcutaneous connective tissue arise in aneurisms of the extremities.

Arterio-venous aneurism consists essentially in the accidental and direct communication of an artery with a vein, characterized particularly by the dilatation of the vein and usually by the presence of an intermediate sac. To the unaided eye, the vein gradually takes the characters of an artery.

Fig. 169.



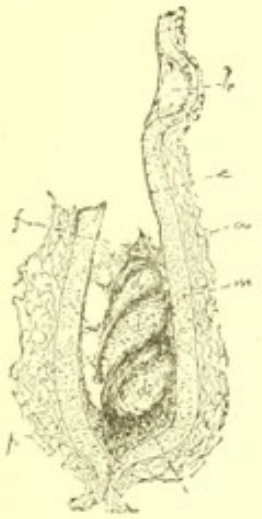
Portion of a transverse section of the femoral artery of a dog 24 hours after ligature. High power. Section passed just above the level of the bottom of the blood-clot which has fallen out while handling, and which has not been drawn. *a*. Adventitia; not much cell increase at this level. *m*. Media not perceptibly altered. *e*. Elastic folds of intima, unaltered. *p*. Thick layer of colorless cells closely adhering to each other and to the elastic layer of the intima. Teasing showed these cells to be in the main endothelioid in character. (*Shakespeare.*)

Arterial Obliterations.—The most simple obliterations of arteries are those produced in consequence of wounds, by a coagulation of the blood in the small arteries, or by the surgeon (ligature, torsion, acupressure, cauterization).

Obliteration of Arteries by the Ligature.—The phenomena following the ligature of an artery are very easily observed in animals. Twenty-four hours after tying the carotid or femoral artery of a dog, there is formed a clot in the central end as far as the first collateral branch. At this time the endothelium of the internal membrane presents important modifications: the cells are swollen and granular, containing a spherical nucleus and frequently several nuclei. The following days a thickening of the internal coat is seen, especially in the proximity of the ligature, that is, all that portion of the artery comprised between the clot and the first elastic lamina or internal elastic lamina. The latter, which in transverse cuts is seen as a clear, refracting, and festooned band, is a very important point, indicating the internal boundary of the middle coat. The thickening of the internal coat is formed almost entirely of cells entangled in a complex manner; they appear fusiform, but are in reality flattened cells. These cells exactly resemble endothelia, or cells of the connective tissue swollen by inflammation. They do not differ from the cells found in acute endarteritis. On the eighth day the internal coat puts forth low elevations, nipple-like in form, which are particularly well marked at the point of ligation, and are seen very distinctly in transverse sections; in longitudinal sections from the level of the upper point of the coagulum to the place of ligature, there is seen a gradual thickening of the internal coat. By the twelfth to the fifteenth day, the nipple-like elevations originating in the neighborhood of the ligature have increased in height on the cardiac side of the ligature, and penetrated into the blood

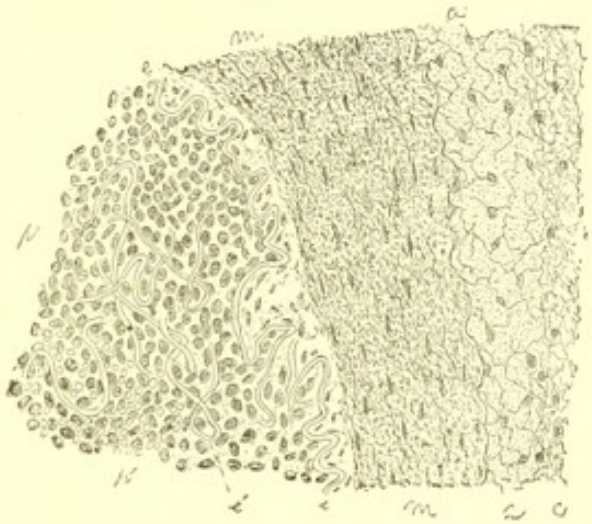
clot; in sections they appear as complete circles separated by the blood. These circles, representing transverse sections of the elevations, are

Fig. 170.



A longitudinal section of thrombus in the femoral artery of a dog, 48 hours after ligature. Low power. *a*. Adventitia. *m*. Media. *p*. Plastic clot. *e*. Intima. *d*. Blood clot, the three lower portions laminated. *f*. Apex of blood clot. *g*. Band of fibrin, uniting the blood clot to the vessel walls rather tightly on one side, loosely on the other. *b*. Small collateral branch. (*Shakespeare*.)

Fig. 171.



Portion of transverse section passing through the plastic portion of a clot in the femoral artery of a dog. Preparation 48 hours after ligature. High power. *e*. Cellular tissue, showing cell increase. *a*. Adventitia, also showing increase of cell elements, but not markedly. *m*. Media, in its inner layer there was considerable cell proliferation, not shown in the cut. *e*. Folds of elastic layer of intima still very distinct and highly refractive, yet showing a tinge of carmine which cannot be so distinctly seen in younger preparations. *é*. Elastic bands from the lacerated intima, not so highly refractive or so free from carmine staining as the preceding. *p*. The cellular elements of the plastic clot, which, when separated by needles, correspond in outline and character with swollen and proliferating endothelia. (*Shakespeare*.)

formed of cells separated by an intercellular substance, and contain very distinct capillary vessels filled with blood; the vessels run parallel to the axis of the elevation. In longitudinal sections it is found that, at the place of implantation of these elevations, the middle coat of the artery has disappeared, so that they appear to spring from the external coat; their vessels come from an extension of the *vasa vasorum*. The several elevations may unite one with the other, and there then remains no trace of the clot, or there is found between them clefts filled with decolored red blood corpuscles, granules, and a few white corpuscles. It is very probable that such preparations suggested to O. Weber the idea of the organization of the clot following the obliteration of arteries. This hypothesis, the fallacy of which we have demonstrated, cannot be maintained in the presence of the above simple experimental analysis. However, when we examine the figures given by O. Weber, and by those who adopt his views, it is seen that the so-called organized clot extends as far as the internal elastic lamina, so that the internal coat and its endothelium have completely disappeared or are confounded with the clot. But it has been seen that at no period of the arterial obliteration is there any fusion between the internal proliferated coat

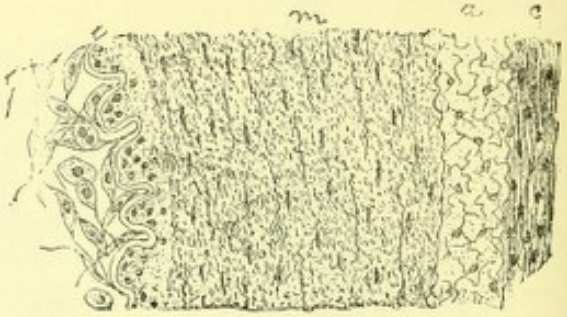
and the coagulated blood. Neither can we agree with Bubnoff, who has endeavored to demonstrate that the clots are truly organized, but by

Fig. 172.



Apex of the thrombus represented at *f*, in figure 170. × 200. *d*. Top of third laminated portion of the thrombus (*d*, fig. 170). *f*. Lower stratum of the homogeneous clot constituting the apex. *f'*. Middle stratum. *f''*. Upper stratum. The white corpuscles are seen evenly scattered among the red disks, and a few endothelial cells are intermingled with the other elements. (*Shakespeare.*)

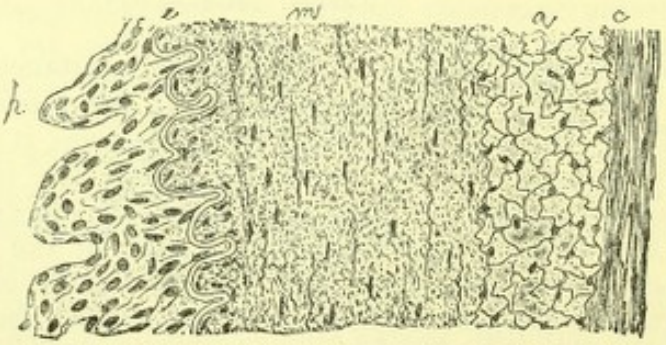
Fig. 173.



Highly magnified view of a portion of a transverse section of a thrombosed femoral artery of a dog, 94 hours after ligature. The section passed through the middle of the plastic clot. An attempt to loosen the thrombus from its attachment to the arterial wall had been successfully made, thus performing without the aid of needles a dissociation of the cells which were next the intima. *a*. Adventitia. *m*. Media. *e*. Elastic folds of intima perfectly defined, and showing as yet not much, if any, tendency toward breaking down. *p*. Oval- and lozenge-shape cells of the plastic portion of the thrombus—their outlines, processes, and nuclei being well seen. (*Shakespeare.*)

a process different from that advanced by O. Weber. He supposes that the white corpuscles, which appear in great numbers in the external coat

Fig. 174.



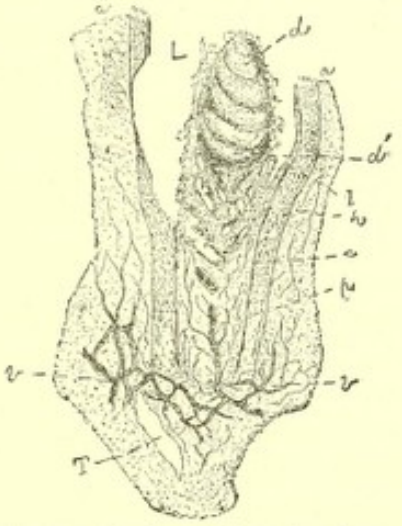
Portion of transverse section of the femoral artery of a dog, 8 days after ligature. High power. *a*. Adventitia. *m*. Media. *e*. Elastic layer of intima still sharply defined. *p*. Granulations springing from the mass of cells developed from the cellular elements of the intima; they consist of spindle cells, the direction of whose long axis in the main is parallel to that of the axis of the granulation. The surface of the granulation is covered with one or two layers of epithelioid cells; not the slightest sign of a capillary loop occupying the axils of the granulation, nor the least trace of a vessel to be seen anywhere in the inner layers of the media preparing to send a vascular loop through the elastic layer of the intima. The blood was supplied from the open artery above the thrombus. (*Shakespeare.*)

after ligation, pass through the middle and internal coats in order to enter into the blood clot and assist in its organization. The experiments of Bubnoff were made upon the veins with a double ligature; ver-

milion was spread upon the wound. After a few days, white corpuscles containing vermilion had passed through the walls of the vessel as far as the clot. This fact is unquestionable as regards a double ligature of the veins. We have repeated this experiment with success; but never in the single ligature of arteries and veins, when the bottom of the wound has been covered with vermilion, have we seen the corpuscles containing vermilion pass through the walls of the blood vessel. Durante again very carefully performed these experiments, and arrived at the same conclusion. He admits that, in the double ligature of veins, there is a necrosis of the coats of the vessels, and that the white corpuscles then pass through as they would penetrate an inert membrane, the elements of which are separated by the mortification. We fully accept his views.

We, therefore, believe that the definite obliteration of arteries in consequence of a ligature is due to a new formation, the origin of which is an arteritis, consecutive to the traumatic lesion. The blood clot disappears by a series of retrograde changes similar to those experienced by the blood when it has escaped into the tissues outside of the vessels.

Fig. 175.



Longitudinal section of femoral artery of a dog, 25 days after ligature. The blood or fibrinous clot (*d*) has been uplifted from its primitive position. Low power. *a*. Adventitia. *m*. Media. *e*. Elastic layer of intima at side of the artery where this layer appears unbroken and unchanged. *l*. Thickened cellular portion of intima on a level with blood clot. *v*. Varices in the cellular tissue at the end of the artery where the ligature was applied. *T*. Large vascular trunk which establishes the anastomosis of external vessels with those within the organized clot. *p*. Thoroughly vascularized plastic clot, now showing commencing cavernous transformation. The fibrinous or blood clot (*d*, *d'*) still shows a serpentine lamellation, and exhibits no sign of approaching organization. (*Shakespeare.*)

[The observations of one of us[1] confirm in many respects the foregoing views of the intimate nature of reparatory inflammation in arteries after ligature, yet in some important points they not only diverge from the statements of Cornil and Ranvier, but also are in conflict with the writings of nearly every other author. It has been thought best to briefly relate them here.

[1] Toner Lectures. Lecture VII. Reparatory Inflammation in Arteries after Ligature, Acupressure, and Torsion. By E. O. Shakespeare, A.M., M.D., of Philadelphia. Smithsonian Institution, Washington, D. C., 1878.

When a single ligature in the continuity of an artery of a dog is applied in the ordinary way, the following phenomena arise.

Soon after the blood included between the ligature and the first collateral branch above is placed aside from the circulation, a fibrinous coagulum begins to form at the bottom of the arterial cup. This coagulum is not homogeneous, as Rindfleisch, Billroth, and others have declared; neither does it at once fill the calibre of the occluded vessel up to the first collateral branch. The fibrinous clot is built up little by little from the bottom to the top by the superposition of successive portions (*d*, fig. 170). It may require hours and even days for the formation of the entire fibrinous clot, and its apex may never reach as high as the level of the first collateral branch. The general outline of this blood clot is that of a cone or a spindle blunted at the end near the ligature. The constitution of the separate portions of the blood clot, which have been deposited at intervals, is not homogeneous, but it presents unmistakable evidences of lamination of a peculiar kind. The separate portions appear to be composed by coils of a cylinder consisting of coagulated blood—the coils arranged very much like those of a rope or distilling pipe. This curious order of deposition of the successive portions of a blood clot was watched, during life, in a small arteriole of the tongue of a frog. By this observation it was learned that the serpentine stratification of the clot above alluded to was not an optical illusion, but a genuine fact. Some, not all, of the completed blood clots were capped by a stratum of homogeneous clot. In this stratum of homogeneous blood clot are to be seen, scattered among the red and white blood corpuscle, a variable number of swollen granular uni- and polynucleated endothelial cells (see fig. 172). Here we may remark that by a homogeneous clot is meant one in which the fibrinous reticulum incloses red and white blood corpuscles scattered evenly throughout the entire extent.

Rindfleisch states that the most convenient method of preparing a ligated artery for microscopic study, is by making thin sections transverse to the axis of the vessel. Our experience leads us to prefer, in the main, sections longitudinal to the axis of the artery, although in every case transverse sections should also be examined. It is perhaps from exclusive examinations of one or two cross sections which passed through the upper part of the blood clot, that Rindfleisch has formed his erroneous conclusions concerning the structure and the formation of the arterial thrombus after ligature. Otherwise it is difficult to understand how such an experienced microscopist could so completely fail to recognize the varied constitution of the arterial plug, which in fifty or sixty observations we found to be nearly constant. (Only in one or two instances was the clot homogeneous, and in these cases, even after the lapse of some days, there was not the slightest indication of a reparatory process at work.) Leaving for a moment this curiously constructed blood coagulum, which for the sake of distinction we term the *fibrinous clot*, let us turn our attention to other objects.

So soon as the ligature is tied and the liquor sanguinis in the ligated vessel is nearly in a state of stasis, the elements of the tunica intima begin to increase in number. The lining endothelium and the subjacent cellular elements very soon present the appearances of an acute endar-

teritis (*p*, fig. 169). Both the endothelia and the other cells of the inner coat rapidly multiply. This inflammatory condition is most marked in the neighborhood of the ligature and shows itself by a greatly increased thickness of the inner tunic (*p*, fig. 170) The evidences of this acute endarteritis gradually grow less and less marked as the first collateral branch is approached. The irritation seldom passes beyond this point. The butt or base of the *fibrinous clot* is more or less closely attached to the mass of colorless elements forming the swollen and inflamed tunica intima, by means of filaments of fibrin. Similar fibrinous filaments also usually attach the blood clot to the inflamed tunica intima at one side (see fig. 170); sometimes the fibrinous clot is firmly attached on all sides.

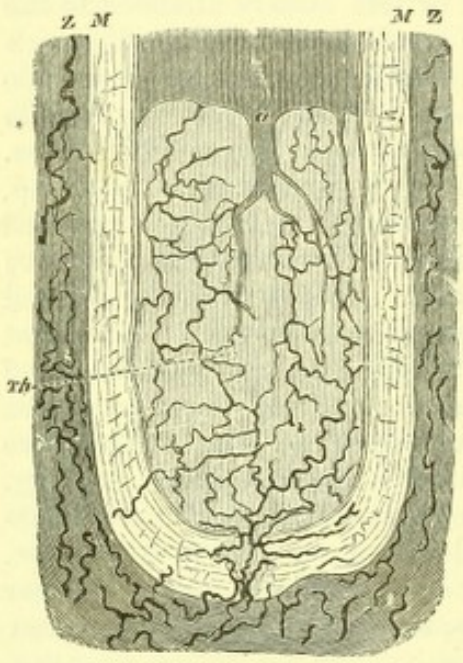
The swollen and inflamed tunica intima might be considered as a cup, within which the blood clot is placed, and to which the latter is attached at the bottom and sometimes also at the sides. The walls of this cup are thinnest at the top and thickest at the bottom. This cup we have termed the *plastic clot* (*p*, fig. 170). Dissociation with needles and subsequent staining with carmine show that the mass of the plastic clot is composed almost entirely of large, granular, uni- or multinucleated membraneless cells of various forms, mainly due to reciprocal pressure. They are usually flattened and more or less endothelial in appearance (see fig. 173). Among these large granular endothelioid elements are a considerable number of lymphoid cells and a few red blood corpuscles. These elements are held together more or less firmly by an intercellular substance, which is sometimes structureless, sometimes granular, and occasionally slightly fibrillar (fig 171).

In a few days the walls of this mass forming the plastic clot begin to bud and put forth granulations, which soon fill the spaces originally left between the blood clot and the walls of the cup in which it is lodged. A little later still, these granulations have increased to such an extent that they must have room. The space required for their growth is furnished at the expense of the blood clot. If the latter is only feebly attached at the sides, the lateral filaments of fibrin which form the attachments are torn loose, and the blood coagulum is uplifted bodily and pushed before the growing plastic formation.

In this case, but little alteration is seen in the fibrinous clot for a long time. Even at the end of twenty-five days there is no sign of organization. (See fig. 175.) If, on the other hand, the fibrinous clot be firmly bound to the walls of the vessel, the granulations from the tunica intima invade the cracks and crevices of the blood clot. The latter gradually softens and wears away through the pressure and absorbent power of the enlarging granulations, and after twenty or twenty-five days there is often no trace of its presence except some accumulations of pigment and fatty granules between and upon the granulations. These granulations have much the same structure as those upon the surface of ordinary granulation tissue. They are covered by a layer of endothelial cells, such as lines the surface of arteries. Their base is upon the elastic lamina of the tunica intima which, up to the twentieth or twenty-fifth day, is still perfectly distinct, forming a sharp boundary between the middle coat of the artery and the proliferation of the inner tunic. (*e*, Fig. 174.) There is usually no indication of its perforation by a capillary

loop from the vasa vasorum, as has been claimed by Cornil and Ranvier and other investigators. Neither is the axis of the granulation occupied by a capillary vessel. Granulations growing in opposite directions may meet and form a union. In this manner a cavernous tissue is formed, in the spaces of which, up to the eighth or tenth day, flows the arterial blood from the open lumen of the vessel above the thrombus. After the sixth or seventh day, varices of capillaries begin to form at the bottom of the plastic clot; they receive their blood from the cavernous spaces above mentioned. At the same time, capillary varices form in the embryonal tissue of the outer coats of the vessel in the neighborhood and at the location of the ligature; they receive their blood from the vasa vasorum. In a few more days, the two systems of capillary varices form a communication with one another by means of anastomosing loops which pass through the injured elastic layer of the intima at the point of ligation. Up to the time of the establishment of this anastomosis in the manner described, the capillary and cavernous circulation of the blood of the plastic clot is independent of the vasa vasorum. After this time, there exists a free anastomosis, almost exclusively at the bottom of the plastic clot, rarely, if ever, through its sides.

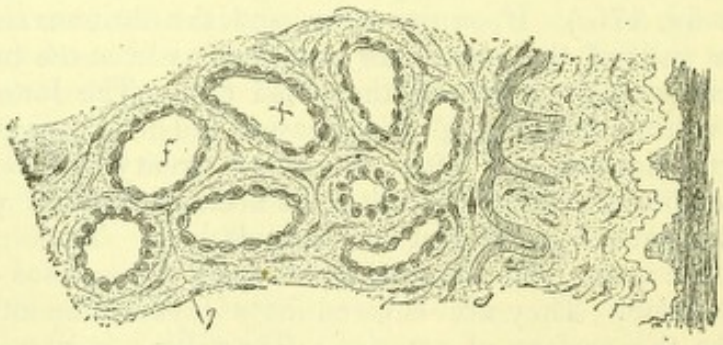
Fig. 176.



Longitudinal section of the ligatured end of the crural artery of a dog, fifty days after the application of the ligature. Showing the newly-formed vessels in the thrombus and their communications with the vasa vasorum. *Th.* Thrombus. *M.* Muscular coat. *Z.* External coat and vasa vasorum. × 20. (*O. Weber.*)

Fig. 176, after O. Weber, very well represents the blood circulation of the arterial stump some weeks after ligature. The tissue of the plastic clot, now progressively undergoes a

Fig. 177.



From the cross-section of an arterial thrombus of three months. *f.* Lumina of vessels in the thrombus. The tissue represented as filling the lumen of the artery is undergoing the cavernous metamorphosis of fibrous tissue. × 300. (*Rindfleisch.*)

change which has been termed cavernous metamorphosis (fig. 177), while the newly-formed granulation tissue experiences the cicatricial contrac-

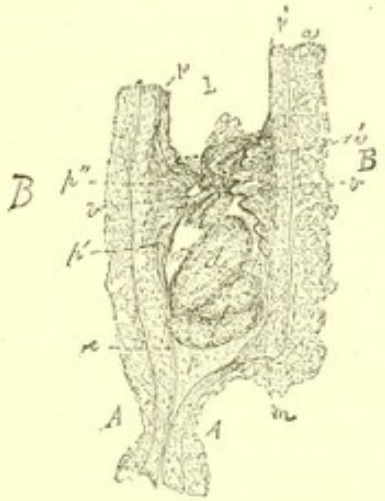
tion common to all such products. By means of this cicatricial metamorphosis the obliterated artery with its obstructing thrombus finally contracts into a small band of connective tissue, in which no trace of the former structure of the vessel can be discovered.

From these observations it appears that the *fibrinous clot* does not organize as has been almost universally believed of late years, but that it suffers no other change than that of destruction.

The injury of the artery is repaired by a cellular tissue (the *plastic clot*), which is furnished by a proliferation of the tunica intima, and the new elements of repair are, in great part, derived from the fixed cells of that coat, both the endothelia and the stellate and flat cells of the deeper layers. A similar process secures the obliteration of the vessel after acupressure and torsion.

Before ending this brief abstract of the brochure from which it is taken, attention is directed to fig. 178, which partly explains itself. This

Fig. 178.



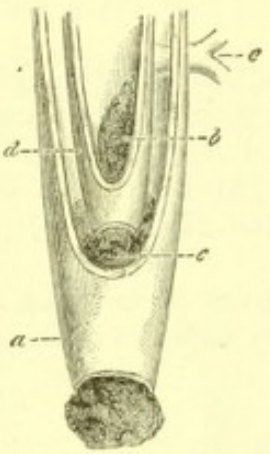
A thrombus, 10 days old, after modified ligation. Longitudinal cut. Low power. After ligature at *A*, the artery was seized and compressed at *B*, between the arms of a pair of forceps. *a*. Adventitia. *m*. Media. *c*. Cellular tissue. *p*. Cellular formation at bottom of clot, non-organized, and apparently not larger than such an accumulation usually is at five days; it consists mainly of cells similar to white blood corpuscles; only a few epithelioid cells are scattered through it, and no granulations springing from it penetrate the crevices of the laminated clot (*d*) immediately above. At *p'*, *p''* there is an ingrowth of the intima and inner layers of the media. At *L*, above the point of compression, a blood clot like that at *d*, rested, but handling caused its displacement. (*Shakespeare.*)

observation showed that the reparatory inflammation was most active, not at the point of ligation, but at the point of compression by the forceps. At this latter level, the tunica intima by the eighth day was so much proliferated and granulated as to occasion a complete obstruction of the lumen of the artery, while at the point of ligation the parts presented the appearance of a process of elimination of the thread, without any tendency to repair.]

Spontaneous Obliteration of Arteries.—When an artery of small calibre has been divided by a cutting instrument, there is first a jet of blood; if the bleeding is spontaneously arrested, the obliteration of the vessel follows, by the formation of a clot in the artery, as far as the first

collateral branch. The origin of this clot is in the contact of the blood with the connective tissue sheath of the artery at the point of division. The artery retracts within its sheath by virtue of its own elasticity. (See fig. 179.) Later, the coagulum acts as a foreign body, occasioning around it a vegetating endarteritis, forming thus a cicatrix by the same process as above described.

Fig. 179.



Natural hæmostasis. The divided ends (*d*) of the artery *retract* within the sheath (*a*), and by *contracting* diminish the calibre of the canal. Blood coagulates in the sheath (*a*) around the orifice of the divided vessel, and in the artery itself (*b*) up to the first large branch (*c*); and, lastly, *plastic lymph* is poured out from the divided coats of the vessel, and by its organization the permanent closure of the vessel takes place. (*Jones.*)

Obliteration of Arteries by Endarteritis and Thrombosis.—Endarteritis, consecutive to the obstruction of an artery and the coagulation of the blood, has been described; but acute or chronic endarteritis may be the cause of a coagulation of the blood. If at any part of a medium-sized or small artery—as the arteries at the base of the brain, or those of the extremities, etc.—the internal coat is the seat of elevations due to acute or chronic endarteritis, the vessel being almost completely closed by these vegetations, the blood coagulates on the cardiac side as far as the first collateral branch.

In chronic endarteritis with atheromatous and calcareous change, the cartilage-like vegetations are at times quite large, especially in the basilar and coronary arteries, causing almost entire arrest of the circulation in the vessel and the formation of a coagulum. There is no doubt that, in these cases, the coagulation of the blood has followed the obstruction of the artery.

In wounds, ulcers, and chronic phlegmons it is frequently seen, in sections made for microscopic examination, that the internal coat of the arteries has swollen so as to completely obstruct the calibre of the vessel. There may form in these elevations vascular networks, so that, at some points, the same appearances are presented which have been described in connection with the ligation of arteries.

In the small arteries there is another cause for the coagulation of the blood which is very important; it is the arrest of the circulation in the capillary vessels. When in consequence of an interstitial suppuration, of a catarrhal inflammation of the lung, or of an interstitial hemorrhage, the blood is arrested in the capillaries by the pressure of the morbid product and is coagulated, the coagulum extends backward into the arteriole to a point corresponding to where the circulation is effected by a collateral vessel. An arteritis occurs at the point of coagulation, and may be the origin of a rupture of the vessel and a hemorrhage, or the cause of a complete obliteration.

Obstruction of Arteries by Embolism.—In the arterial obliterations previously studied, the coagulation occurs at the point of obstruction; this phenomenon is named *thrombosis*. But when a clot formed at any

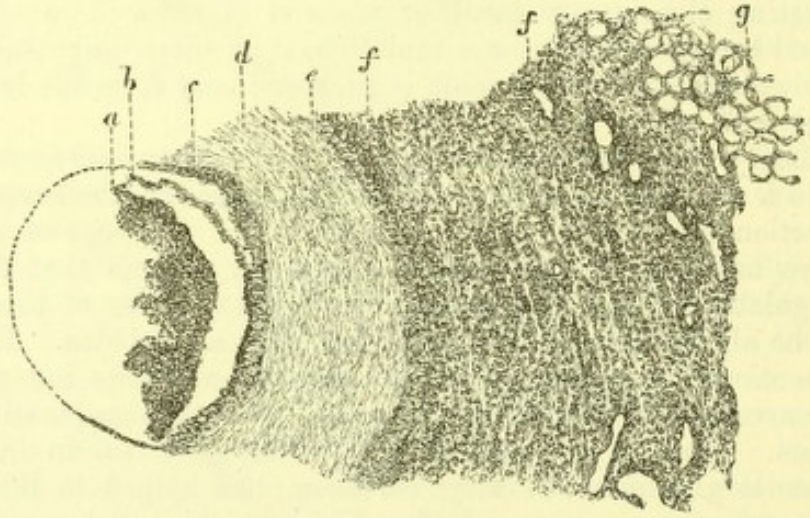
point of the circulatory system, especially in the veins, has been detached by the blood current and thrown into the arterial system, it is stopped in an artery too small to afford it a passage; this is termed *embolism*, and the migrating clot has received the name of *embolus*. For example, as a result of the coagulation of the blood in the femoral vein, it may happen that this venous clot (*thrombus*) shall become detached, pass into the iliac vein, the inferior vena cava, the right auricle and ventricle, and the pulmonary artery, where it may meet with a ramification too small to allow it to pass. It is then arrested, and finally becomes an *embolus*, and causes arterial obstruction by embolism. In this example it is easy to follow the most important phases of embolism, since during life there is the certainty of obstruction in the femoral vein, and great hindrance to the pulmonary circulation causing rapid death. At the autopsy, there is found in a branch of the pulmonary artery a clot which has certainly not been formed at this point, for it presents an outline entirely different in shape and diameter from that of the obstructed artery. The obstructing clot is whitish or yellowish in color, it may be folded upon itself, and have branches which do not correspond to the ramifications of the pulmonary artery. Frequently it is surrounded by a recently formed cruoric mass; but as this recent clot has much less consistence than the embolus, and as there is not a firm adhesion, it may be easily separated from the old clot, when it will be seen that the embolus has the form and calibre of the vein in which it was primarily contained. Such is the simplest and most easily verified case; but when the migrating clot is very small, or when it is reduced to very small pieces, and transported by the circulation, it is often impossible to find the embolus, the existence of which is supposed only from the lesions and the symptoms.

This theory of embolism has been employed without sufficient evidence to explain a series of anatomical changes, such as the abscesses of purulent infection and puerperal fever, in which the existence of migrating clots have not been demonstrated. It is not enough that the blood may coagulate and the circulation stop in the arteries of the focus, in order to be able to affirm that there has been an embolus. Indeed, as before mentioned, every interstitial hemorrhage, and some inflammations, cause an arrest of circulation in the capillaries and consequently arterial thrombosis. Virchow, by employing the word *infarctus* in order to designate certain lesions following embolism, has helped to throw great obscurity upon this question. Before Virchow, this word was applied to a series of indefinite changes, in particular to parenchymatous hemorrhages. Laennec called the foci of pulmonary apoplexy, hemorrhagic infarcti. Since then the doctrine of embolism has been generalized, and there has been a tendency in science to connect with embolism everything the older writers called infarctus. It is incontestable that a certain number of infarcti have an embolus for their origin, as in the kidney, spleen, liver, etc., when there are seen white, yellowish, anæmic foci, having the shape of a cone with the base turned towards the surface of the organ, and which represent the distribution of an arteriole. At first it would seem that this tissue differed very much from that of the organ affected, but by examining sections with the microscope, there are found all the constitu-

ent parts of the organ, the elements of which have undergone fatty degeneration, and the vessels are filled by a granular mass derived from the coagulated blood. It is only at the margin of the altered parts that inflammatory lesions are seen; they extend but a very short distance. These infarcti are associated with valvular endocarditis, both ulcerous and vegetating, or with valvular aneurisms, or with chronic endarteritis. Fragments of the inflamed vascular wall or fibrinous clots have been torn off and carried along the arteries. The loss of substance from the valves may be seen in some cases, but seldom is it possible to discover the infarctus in the migrated clot.

The obstruction of an artery by embolism is followed by various lesions, which may be demonstrated by experiment. If a single artery of small calibre is obstructed by an embolus, there may be no lesion visible to the unaided eye in the vascular territory of this artery; the circulation is re-established by anastomosis, and the embolus acts much like a simple ligature. By introducing into the jugular vein of an animal a single embolic fragment, as a small ball of sealing-wax, it passes into the lung, and there is not observed any pulmonary lesion appreciable to the unaided eye for several days after the experiment. But if fine powders, which may be again recognized (as starch or lycopodium) are injected, congestions, hemorrhages, and inflammation are met with in the lungs after a few days.

Fig. 180.



Transverse section of radial artery plugged by an embolus of septic origin some days before death. From a case of ulcerative endocarditis. Low power. *a*. Clot. *b*. Internal coat. *c*. Internal elastic or fenestrated membrane. *d*. Middle muscular coat. *e*. Outer elastic membrane. *f*. Adventitia crowded with abnormal nuclei and proportionately thickened. *f'*. Region of vasa vasorum. *g*. Fat. (*Bryant.*)

The sequelæ of embolism in the arteries of the extremities and all the other organs vary according to the size, number, and nature of the embolic fragments. Necrosis or mortification occurs when there are several embolic fragments distributed in the arterial system of a limb in such a manner that collateral circulation is impossible. In organs where the vascular territories are limited, a single embolic fragment may produce the same effect, as is often seen in the kidney, spleen, liver, and brain.

But in the extremities a single embolus does not cause gangrene any more than a ligature does.

If the embolus has irritating properties, like almost all solid foreign bodies, it causes in the part where it lodges a suppurative inflammation, which does not differ from that occasioned by the same foreign body if introduced into the cellular tissue, and a phlegmon is the result. The walls of the artery at the point where the embolus is situated are pressed upon; they suffer necrosis or purulent infiltration, and the inflammation of the neighboring connective tissue appears to be the result of an extension of the primary lesion. (Fig. 180.)

When the embolus is derived from the organism, for example, a small fibrinous clot coming from the heart, it obstructs the artery, and occasions a coagulation of the blood as far as the first collateral branch. The obliteration of the artery does not differ from that following the application of a ligature; it is effected by the process of endarteritis, while the collateral circulation re-establishes the course of the blood.

In embolism of the arteries of the kidney, liver, or brain, the initial secondary phenomenon is a limited swelling of the part supplied by the obliterated artery, and the tumefied part is bluish-red in color. The blood accumulates in this area, stagnates, and later coagulates. At this time the lesion is usually cone-shaped, and is called a red infarctus, which, consisting of the elements of the organ and coagulated blood, forms a lifeless mass. This blood experiences the changes which have been previously studied, viz., granular decomposition and the separation of the coloring substance in the form of pigment. The parenchymatous cellular elements undergo fatty degeneration; the infarctus now becomes yellowish-white; it still retains a firm consistence, and contracting a little is somewhat smaller than the red infarctus. This yellow infarctus consists of a mass within the organs so distinct, that it could be mistaken for a tumor if it were not cone-shaped, with the base turned towards the periphery of the organ. A microscopic examination of the morbid tissue reveals the texture of the organ; the vessels are found injected with a granular mass due to a transformation of the blood, and the parenchymatous cells of the organ are infiltrated with fatty granules.

At the margin of the white infarctus the vessels of the living part are dilated and filled with blood; the connective tissue is infiltrated with white corpuscles; frequently in this portion there are found interstitial hemorrhages varying in extent. The parenchymatous elements, the epithelial cells of the uriniferous tubules, or the hepatic cells for example, present multiple nuclei and at times fatty degeneration. In the kidney the tubules contain fibrinous casts, blood, and sometimes white corpuscles.

In the third stage the white infarctus is softened; the softening begins at the centre, as a result of molecular destruction of all the necrosed parts. This molecular detritus is then taken up by the lymphatics of the connective tissue which acts as a cyst wall around the dead part. This occurrence is very much like that described as taking place in caseous gummata. (See pp. 111, 112.)

Sometimes the softened infarctus is infiltrated with calcareous granules and desiccation takes place; there is formed either a dry atheromatous mass, or a true petrifaction.

Finally, all the necrosed portion may be absorbed; there remains instead a stellate cicatrix. The death of a part of an organ, without true gangrene, has been described by Virchow under the name of *necrobiosis*.

[The vascular engorgement of the embolic area was formerly supposed to be due to the increased stress which is thrown on the collateral vessels. The investigations of Cohnheim, however, show that it is really mainly owing to the impairment of the vitality of the walls of the bloodvessels, and the consequent exudation, emigration, and ultimate necrosis of the vascular walls. When the force of the blood-stream in the artery is annihilated by the impaction of the embolus there is a backward pressure and regurgitation from the veins into the capillaries, so that there is produced considerable venous engorgement of the last-named vessels. There is thus a substitution in the capillaries and small arteries of venous for arterial blood, and owing to this the vitality of these vessels becomes impaired, and hemorrhage results. The infarction consequently does not occur immediately after the impaction of the embolus, but only after the lapse of a certain time.

Fig. 181.

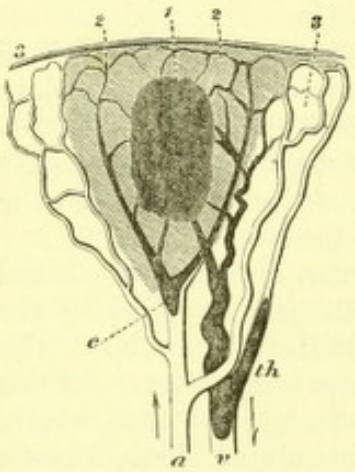


Diagram of a Hemorrhagic Infarct.—*a*. Artery obliterated by an embolus (*c*). *v*. Vein filled with a secondary thrombus (*th*). 1. Centre of infarct which is becoming disintegrated. 2. Area of extravasation. 3. Area of collateral hyperæmia. (*O. Weber.*)

The subsequent changes which take place in the infarct depend upon its size, upon the extent to which the circulation in it is interfered with, and upon the nature of the embolus which caused the infarction. If the infarct is small and the embolus possesses no infective properties, the coagulated blood may gradually become decolorized, and the mass undergo a gradual process of absorption. The infarct then changes from a dark red to a brown or yellow tint, its more external portions becoming organized into connective tissue, and the whole gradually contracts, until ultimately a cicatrix may be all that remains to indicate the change. If, however, the infarction is considerable, the molecular disintegration and softening may be so extensive as to convert the mass into a pulpy granular material. This may subsequently dry up and become encapsuled. In all these secondary changes which take place in the infarct, its most external portions are surrounded by a red zone of hyperæmic tissue. This is exceedingly characteristic.

If an embolus possesses irritating or infective properties, as when it is derived from a part where putrefactive inflammatory changes are going on, it sets up inflammatory processes both in the vessel within which it becomes impacted, and also in the surrounding tissues. These inflammatory changes frequently lead to the formation of abscesses, which are known as *embolic abscesses*. The formation of such abscesses may be associated with more or less infarction of the embolic area.

SYPHILITIC LESIONS OF THE ARTERIES.—Certain changes in the *cerebral* arteries have been recently described by Huebner as characteristic of syphilis. These changes have been brought prominently before English pathologists by Drs. Greenfield, Barlow, and others, and the investigations of the first named of these observers would tend to render it probable that similar changes occur in arteries in other situations.

In the cerebral arteries the changes produce opacity and marked thickening of the vessel, with considerable diminution in its calibre. It is this diminution of the lumen of the vessel which is especially characteristic.

When transverse sections of the vessels are examined microscopically, the principal change is seen to be situated in the *inner* coat. It is well shown in the accompanying drawings made from specimens of Dr. Barlow. (Fig. 182.) This coat is considerably thickened by a cellular

Fig. 182.



Syphilitic disease of cerebral arteries.

A. Segment of middle cerebral artery, transverse section—*i*, thickened inner coat; *e*, endothelium *f*, membrana fenestrata; *m*, muscular coat; *a*, adventitia. × 200, reduced ½.

B. Small artery of pia mater, transverse section. Showing thickened inner coat, diminished lumen of vessel, and considerable infiltration of adventitia. The cavity of the vessel is occupied by a clot (? thrombus). × 100, reduced ½.

growth. The growth, which is limited internally by the endothelium of the vessel (fig. 182, A, *e*), and externally by the membrana fenestra (fig. 182, A, *f*), closely resembles ordinary granulation tissue, consisting of numerous small round and spindle-shaped cells. This tissue appears gradually to undergo partial development into an imperfectly fibrillated structure.

In addition to this change in the intima, the outer coat is abnormally vascular and infiltrated with small cells (fig. 182, A, *a*), and this cellular infiltration usually also invades the muscular layer (fig. 182, A, *m*).

The result of these changes in the inner coat is to diminish very con-

siderably the lumen of the vessel (fig. 182, B); and the consequent interference with the circulation frequently leads to coagulation of the blood (thrombosis) and cerebral softening.

Dr. Greenfield's observations, as already stated, tend to show that similar arterial changes occur in other parts, and that they account for the degeneration of syphilitic gummata.][1]

Amyloid Metamorphosis of the Small Arteries.—The general characters of the amyloid transformation of the arterioles has been previously described at page 46, where we have insisted that the middle coat of the small arteries is peculiarly disposed to this degeneration. The amyloid substance is first infiltrated into the muscular elements of the vessel, these elements retain their form and relations, so that they are recognized when iodine is employed as a reagent alone, or in combination with sulphuric acid. Sometimes the organ treated with iodine shows its arterial network so distinctly and so perfectly colored that it appears as if injected.

In a very advanced stage of this metamorphosis the muscular cells are fused into a single mass, and the wall of the artery seems to be constituted by a homogeneous and thickened tube. The calibre of the vessel is lessened, and this may be to such an extent as to arrest the circulation of the blood.

The organs most frequently the seat of amyloid degeneration of arteries are the spleen, liver, kidney, mucous membrane of the intestines, and the lymphatic glands. This arterial lesion which is associated with a similar transformation of the parenchymatous cells of these organs, is a consequence of prolonged suppuration, of phthisis, of syphilis, etc.

Tumors of the Arteries.—Primary tumors of the arterial system consist of a new formation of arterial tissue as seen in dilatations and elongations of arteries in simple angiomata (see p. 139), and in a peculiar essentially arterial form of angioma—the arterial varices or varicose aneurism. In these tumors the arteries are dilated, elongated, tortuous, and thickened; they present numerous anastomoses and partial dilatations. They are most frequently located on the temporal and occipital arteries.

The arteries which are connected with some tumors, for example in the breast, thyroid body, etc., are extremely hypertrophied, and there often occurs a true new formation of arteries at the same time that the tumor grows. This new formation appears to take place by a transformation of the capillaries into arterioles and larger arteries by the formation of smooth muscular elements developed from the embryonic cells surrounding the vessel. However, this evolution is very difficult to follow, and there still remains great uncertainty upon the subject.

Tumors which grow rapidly around arteries of a certain calibre, occasion the phenomena of an arteritis; namely, a vegetation of the internal coat, a disappearance of the middle coat, and an embryonic state of the external coat. At times the artery may be obstructed by these vegeta-

[1] Abstracted from Green.

tions, or by hemorrhages which occur on account of the weakness of the walls of the vessel.

These lesions are observed especially in sarcomata and carcinomata of rapid development; the tissue of the tumor is seen to grow into the vessel after the middle coat has disappeared. When the circulation is impeded or interrupted by these lesions of the arteries, the parts supplied by them mortify; if the mortified portion is superficial, as is the case in tumors of the neck of the uterus, there is softening and ulceration. If the necrosed mass is deeply situated in an organ, it gives rise to a caseous focus.

Tuberculous granulations are very often developed in the tunica adventitia of arterioles. The result is the obstruction of the small artery and a coagulation of the blood in its interior.

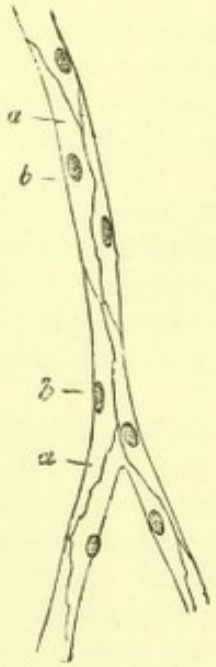
CHAPTER IX.

CAPILLARY VESSELS.

Sect. I.—Normal Histology.

Capillary vessels are essentially formed of flat cells united at their edges, and arranged so as to constitute canals anastomosing one with the other to form a network. They have nearly the same structure in all organs and tissues, but their size and the form of their network vary in each organ and tissue. The capillaries are surrounded with fasciculated or reticulated connective tissue, or they traverse spaces which do not contain connective tissue, which are simply lymphatic spaces. In fascicular connective tissue, the capillaries covered with flat cells are found situated in the spaces of the connective tissue along side of the fasciculi, without adhering to the latter, and the lymph of the connective tissue is seen in direct relation with the vascular wall, so that in reality a capillary of the connective tissue is located in a lymph space. This arrangement exists not only in the subcutaneous cellular tissue, but in the skin, muscles, nerves, and in the cellular tissue of organs. In the lymphoid organs (lymphatic glands, lymphatic follicles of the intestines, the tonsils, etc.), the capillaries are covered with a dense fibrillar layer, which comes from the fibrils of the connective tissue. The lymph contained in this tissue is separated from the blood by two layers, the cellular membrane of the capillaries and its investing reticulum.

Fig. 183.



Capillary from the mesentery of a guinea-pig, after treatment by nitrate of silver; *a*, cell; *b*, nuclei of the same. (*Frey.*)

In the glands the capillaries which are found in connection with the glandular acini, and which consequently are very important in the function of secretion, are situated in the lymphatic space which surrounds each acinus, and separates it from its neighbor. The same arrangement is seen in the lymph sinuses of lymphoid organs.

The capillaries of the nervous centres are also surrounded by a lymph sheath. When a capillary occupies a lymph space it is always covered by an endothelial layer, and is connected to the wall of the space by bands of connective tissue, varying in thickness.

From the constant existence of lymph spaces placed between the capillaries and the constituent elements of the tissues of organs, it is seen

that these elements are not in direct connection with the exuded plasma of the blood, but that the plasma escapes first into the lymph spaces, and is thence taken up by the elements bathed in the lymph. It must not be concluded however from this arrangement that the exuded fluids have no effect upon the functions of these elements. It has been seen that the modifications of the flat cells of connective tissue in œdema are considerably influenced by the serous exudation. In conclusion, it is not the blood which nourishes the elements, but the lymph derived from the blood.

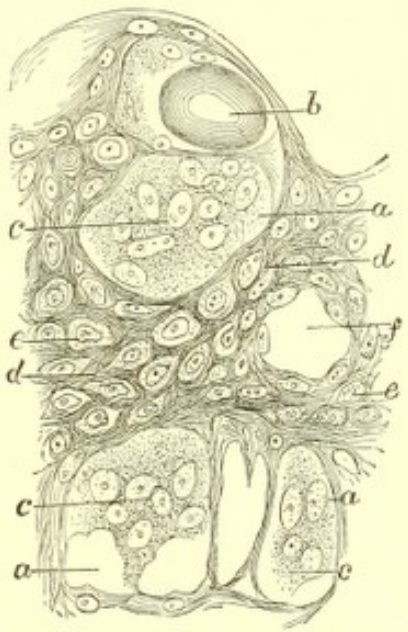
Sect. II.—Pathological Histology of Capillaries.

Inflammation of the Capillaries.—In the first part of this manual, although we did not entirely reject the results of the experiments of Cohnheim, of the passing out of the white corpuscles from the vessels, yet we reserved some doubts regarding them. From repeated experiments, we are convinced of the emigration of the white corpuscles (diapedesis). This diapedesis occurs not only in inflammation, but also in congestions, œdema, and in the physiological state. In inflammation, it is true, the phenomenon is exaggerated, like all the phenomena of nutrition. Inflammation is indeed nothing more than an exaggeration of the normal processes of nutrition, and inflammation has therefore been attributed to the irritation of tissues.

The inflammatory phenomena present in the capillaries consist in a modification of their walls, and in the formation of new capillary vessels, which always take their origin from the old.

There is first observed in the capillaries a swelling of the cells and their nuclei; the cells which were flat, homogeneous, and could not be distinguished, now appear granular, and when viewed in profile are fusiform and distinct one from the other. This arrangement is especially appreciable in transverse sections of the vessels in inflamed tissue. (See *f*, fig. 184.)

Fig. 184.



Adipose tissue from a deep wound in a dog, in progress of healing. *a*, Spaces left by the absorption of the fat vesicles *b*: they are found filled with newly-formed nuclei *c*, surrounded with granular protoplasm; *e*, embryonic cells; *f*, section of a vessel which has embryonic walls.

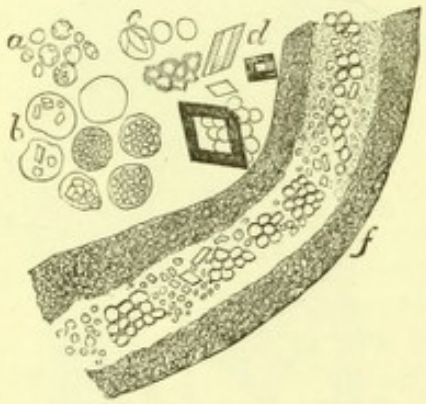
In the mesentery of the frog, which has been exposed to the air, it is much more difficult to see the swelling of the endothelia. The separation of the cellular elements of the capillary vessels permits of their dilatation, and favors the passing out of the white corpuscles, the red corpuscles and the fibrinogenic plasma. It is in inflammations of long duration, occurring upon free surfaces, that the dilatation of the capillary vessels is particularly marked, as in catarrhal inflammations of the mucous mem-

brane. In these cases the capillaries remain full of blood after death, and form the red arborescent spots, visible to the unaided eye, while the capillaries not diseased are always empty of blood on account of the contraction they experience, after death. This circumstance alone demonstrates that the vessels modified by inflammation have lost one of their most important properties, elasticity. The modification of the walls, joined with an increase in the blood pressure, frequently causes ruptures, which are very common in the brain. In softening and hemorrhage of this organ, there are often seen small red points or nodules which consist of a dilatation of the capillaries, sometimes with rupture and effusion of blood into the lymph sheath. This latter lesion has been named dissecting or miliary aneurism of the capillaries.

The return of the vascular walls to the embryonic state appears to be the starting point of the new formation of capillaries. It may be added, that the most usual mode of formation of numerous new capillaries consists in the production of cellular diverticula, which spring from an inflamed capillary and extend to a neighboring capillary, or form loops, the two extremities of which being attached to the wall of the same capillary. These cellular cords are afterwards hollowed out for the passage of the blood.

Nutritive Lesions of the Capillaries.—The most frequent lesion of nutrition consists in the fatty degeneration of the cells of the capillaries. It may occur in all organs, but is especially common in the kidney and nerve centres. It is always seen when nutrition is much lessened or arrested, and it accompanies fatty degeneration of the neighboring elements. Physiologically the capillaries of the brain of adults frequently contain a few scattered refracting granules. In cerebral softening, the capillaries are loaded with fatty granules, which at some points give to the capillary the form of a dark granular cylinder. The lymph sheath at this time contains blood and granules of hæmatoidin (fig. 185), which indicates that the degenerated capillary has been ruptured. At other times the lymph sheaths are dilated and contain granular bodies, in which almost always a nucleus may be found if the reparation is treated with picro-carminate of ammonia. These granular bodies are either lymph corpuscles loaded with fatty granules, or similarly altered endothelial cells of the lymph sheath.

Fig. 185.



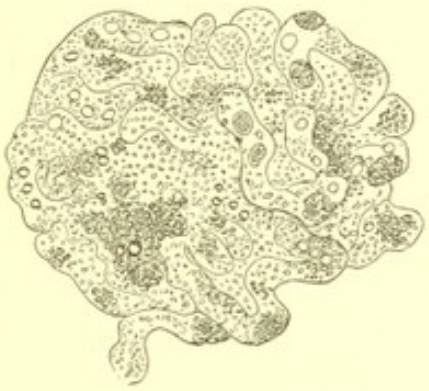
Crystals of hæmatoidin. *a*. Red disks, becoming granular and losing their color. *b*. Neuroglia cells, a few containing granular pigment and crystals. *d*. Crystals of hæmatoidin. *f*. Occluded capillary; its lumen is seen filled with red granular pigment and crystals. × 300.

Following experimental division of nerves, the capillaries of the periphery undergo fatty degeneration, and granular bodies are found in their neighborhood. In infarcti consecutive to obliteration of the arteries, in chronic inflammation with fatty degeneration, in Bright's disease of

the kidney (figs. 186, 187), and in portions of tumors which experience the same change, this fatty degeneration involves the cells of the capillaries.

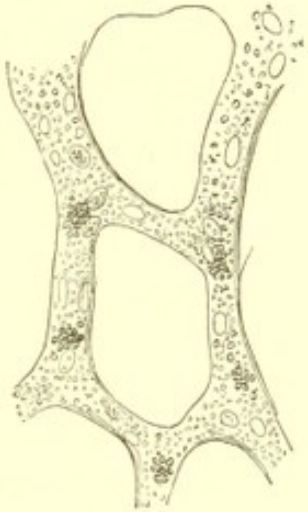
Calcareous infiltration is seldom seen in the capillaries. Nevertheless, it sometimes occurs either in the form of granules, or in plates, particularly in the angiolithic sarcomata (psammomata) of the dura mater.

Fig. 186.



Fatty degeneration of the capillaries of the Malpighian tufts in the kidney in a case of Bright's disease. × 250.

Fig. 187.



Fatty degeneration of intertubular capillaries. Case of Bright's disease of the kidney. × 250.

Another common lesion of the capillaries is *amyloid degeneration* of their cells, which changes these vessels into vitreous tubes. This metamorphosis is especially well marked in the capillaries of the Malpighian bodies of the kidney. Sometimes it is seen limited to these capillaries, while in the other organs the amyloid alteration begins most frequently in the arteries.

CHAPTER X.

VEINS.

Sect. I.—Normal Histology of the Veins.

The three coats which are generally admitted as belonging to veins, are not nearly so distinct as those of the arteries. Again, veins of the same calibre do not have the same structure in different regions of the body; the muscular and elastic elements present neither the same arrangement nor the same thickness.

The internal coat of veins is lined with flat polygonal endothelial cells, shorter than those of the arteries. The internal coat proper consists of flat cells separated by a fibrillar substance.

The middle coat begins internally by circular elastic fibres or laminæ. [It has already been stated for the arteries that this internal elastic lamina is regarded by most authors as the outermost layer of the tunica intima.] From this primary elastic layer arise elastic fibres, which form a network. In this elastic reticulum are found smooth muscular fibres and connective-tissue fasciculi. The line of demarcation between the middle and external coat is not clearly marked, but all that part of the vein which contains muscular fibres may be considered as the middle coat, and those veins which do not contain muscular fibres (sinuses of the dura mater, subclavian veins, veins of the retina) we should say posses no middle coat. The middle coat of veins of large and medium calibre demands a special description, at least for some of those veins which are most frequently the seat of anatomical alterations.

The elastic reticulum forms near the internal coat a close network, which becomes gradually looser as the external coat is approached, where the elastic fibres are blended with those of the latter. The muscular fibres in this coat have a longitudinal or transverse direction, according to the vessel under consideration. Thus the inferior vena cava, the portal vein and renal veins present internal circular fibres and external longitudinal fibres; the femoral and popliteal veins possess an internal longitudinal layer. In the saphena veins, the muscular coat is still more complicated; there is seen an internal longitudinal layer, then a series of transverse and longitudinal fibres placed one upon the other. The veins of the neck present only a few scattered muscular fibres situated in the elastic meshes immediately external to the internal coat.

The valves of the veins, in the normal condition, are extremely thin. They are formed by a duplication of the internal coat supported by a few elastic and connective-tissue fibres.

The *vasa vasorum* are found upon veins, especially where there is connective tissue, and they penetrate into the middle coat.

Sect. II.—Pathological Histology of Veins.

Inflammation of Veins; Phlebitis.—Spontaneous phlebitis is met with only in the veins of the uterus in consequence of pregnancy. Phlebitis frequently complicates inflammation of the surrounding connective tissue, or it is seen in consequence of wounds, of ligation of veins, or following a primary coagulation of the blood in their interior.

In injuries of the veins, the coagulation of the blood and the phlebitis occur at the same time, so that in these cases the phlebitis is at least in part dependent upon the thrombosis.

When a ligature is applied to a vein, an operation almost entirely abandoned in surgical practice, the blood coagulates in the peripheral end as far as the first collateral branch; there is also a clot formed in the central end. During the first few days there is observed only swelling and multiplication of the endothelial cells, but soon the entire internal coat thickens from the formation of new cells, and forms elevations especially well marked at the place of the ligature. Later the elevations become vascular, unite together and obliteration of the vein takes place as in arteries. The clot does not appear to be organized in the veins any more than in the arteries; it undergoes a granular change and gradually disappears.

The simplest wound of a vein is that occurring from the operation of bleeding at the bend of the arm, including the vein and skin; it heals by the first intention. As previously described, this mode of healing is not accomplished without inflammation playing an important role. A thin clot remains between the lips of the wound; the following day there is seen a redness and slight œdematous swelling of the skin; about the fourth day the scab which has formed upon the incision falls off, and the cicatrix is completed. The histology of these simple phenomena has not yet been studied, but it is probable that the union of the vein takes place as in connective tissue of the skin, by the interposition, between the lips of the wound, of an embryonic connective tissue and its organization into ordinary connective tissue. (See pp. 71, 252.)

When in consequence of a suppurating wound or of a phlegmon located near a vein, the connective tissue of the external coat of the vein participates in the inflammation, there are seen embryonic cells or pus corpuscles between the fasciculi of the connective tissue of this coat. The external, middle, and internal coats of the vein may ulcerate and be destroyed, by means of the same process which causes the formation of an abscess (softening and necrosis). This is observed particularly in a phlegmon of the axilla, of the groin, and of the posterior mediastinum; frequently the ulceration of the veins is accompanied with a coagulation of the blood in the interior of the vessel. The danger of a direct introduction of pus into the circulatory system is prevented by this coagulation of the blood. At times, however, the clot does not completely plug the vessel, and then septicæmia and pyæmia supervene; again the clot already formed may undergo further modifications, it may soften in the centre, and form on the cardiac side an anfractuous canal which connects the suppurative inflammatory focus with the vascular system. The loss

of substance, seen in such cases in the wall of the veins, varies in extent, and their external surface is then blended with the surrounding phlegmonous tissue; the vessel does not contract but remains open when cut. The external margin of the part where there is a loss of substance, is blended with the indurated or fungoid layer limiting the purulent focus. The internal surface of the vein shows the loss of substance to be limited by a more distinct margin, although the different coats are infiltrated with pus, and consequently thickened or partially necrosed. This infiltration of pus is seen under the microscope, in sections of the venous wall. The process in these cases being rapid, organized vegetations upon the internal coat of the veins are not found.

In wounds of the veins such as occur in amputations, all the blood between the point of division and the nearest valves flows out, and this portion of the vein remains empty. A clot forms above the valves as far as the first collateral branch. The empty extremity of the vein participates in the inflammation of the wound; there occurs adhesive periphlebitis and endophlebitis like that which follows a ligature, and obliteration of the vessel is the result.

From the preceding description it is seen that coagulation of the blood accompanies phlebitis; until a few years past it was believed that every coagulation of the blood in the veins was caused by the phlebitis. Virchow endeavored to show that primary phlebitis is extremely rare, and that when a coagulation is seen in a vein with phlebitis, the coagulation has most frequently preceded the inflammation. This theory, which seems to us too positive, has however been accepted by most German pathologists.

The causes of *venous thrombosis* are of two kinds: a slowing or arrest of the circulation, or changes of the internal coat of the veins.

After death, the blood which has collected in the venous system coagulates. It is important that the pathologist should be able to recognize these post-mortem clots in order not to confound them with those of thrombosis. They are met with especially in the large veins, in the vena cava, iliac and femoral. These post-mortem clots occupy only a small part of the calibre of the vessel, never filling them completely; they do not adhere to the wall, and after opening the vein and removing the coagulum, it is found that prolongations have entered the collateral branches. These clots are red-brown streaked with yellowish-white, or are in part fibrinous and cruoric; the whitish or pink portion is seen always in the superior layer, the red in the inferior dependent part according to the position of the cadaver. In the same vein these clots present great inequality of thickness, due to the presence of the valves and tortuosities of the vein. They have the consistence of fibrin and may be torn into laminæ, or they are curdled. The latter variety are seen especially in poisoning by phosphorus, arsenic, and in infectious diseases.

The arrest or impediment of the circulation which causes thrombosis during life is due to a weakness of the heart, or to a local interference of the capillary circulation belonging to the vein which becomes the seat of the thrombosis.

Such, for example, are all asystolic cardiac lesions causing the forma-

tion of clots in the right heart and large veins; the direct action exerted by ligatures, by tumors, by abscesses, by compression of the gravid uterus upon the iliac veins, etc. The retardation of the blood in varicose dilatations may also be a cause of thrombosis.

Thrombosis of the pulmonary veins in pneumonia is due to the pressure exerted upon the capillaries by the exudation which distends the alveoli. Thrombosis of the veins of the kidney and spleen, in caseous infarcti, etc., is from the arrest of the capillary circulation. It is the same in leucocythæmia; the capillary circulation being interfered with on account of the great number of white corpuscles, clots are readily formed in the veins.

When an artery is obstructed by an embolus, the blood is arrested in the capillaries; it does not circulate in the veins, but there coagulates. Such are the phenomena always seen in embolic infarcti of the liver, spleen, kidneys, and embolic gangrene of the extremities.

The venous thrombus fills completely the calibre of the vessels; it is adherent to the wall and terminates at the cardiac end in a point or groove. It is formed by a series of layers joined together, the most superficial of which are the most recent, and may be still cruoric, while the central and middle layers are gray or yellow. When the clot is old, there is frequently found in its centre an anfractuous cavity filled with a puriform, white or opaque detritus.

A microscopic examination of this detritus shows numerous white corpuscles which have experienced caseation; they are irregular, present in their interior fatty granules, and do not contain any apparent nuclei. Besides these corpuscles are found granules, which disappear by the addition of acetic acid, and free fatty granules. A section of the clot shows red blood corpuscles at the peripheral portion of the thrombus, which can be still recognized, separated by reticulated layers of fibrin, in which are seen white corpuscles. In the interior of the layers, the fibrin forms closer laminæ, between which are seen granular collections varying in size and shape, containing pigmentary masses.

There are always in the thrombi of veins numerous white corpuscles, a phenomenon which cannot be attributed either to a new formation or to a migration. It has been seen that always when there is a retardation of the circulation of the blood at any part of the vascular system, the white corpuscles are there accumulated. Since thrombosis is preceded by a retardation of the blood circulating in the vein which is the seat of the lesion, it is natural that the blood coagulating under this condition should contain a greater number of white corpuscles. These are free in the centre of the clot, which is the oldest part, because the fibrin there undergoes a granular change.

The disposition of the thrombus into concentric layers is due to the primary clot being formed by the blood coagulating in a body in the vein and undergoing a shrinking by the contraction of the fibrin. There thus is formed a space between the clot and the wall of the vein, which is soon filled with blood which circulates, although slowly. The coagulation of this last blood is followed by a new shrinking, and these phenomena are continued until the vein, completely distended, is applied so accurately upon the clot that the circulation is arrested. Until the clot

entirely fills the vein, it is frequently retained where it is formed by prolongations which it sends into the collateral veins; this peculiarity explains why the clot is not always detached and thrown into the circulation in order to form emboli. At this time there arises in the venous wall a series of inflammatory changes, the first of which consist in the swelling and proliferation of the endothelial cells. The internal coat soon participates in the inflammation; there are formed new cellular elements which produce elevations (endophlebitis); the external coat also contains new cellular elements between its fibres and is notably swollen (periphlebitis). Generally the middle coat is not modified; yet, in cases where the inflammation is very intense, a true suppuration of the coats of the vein may occur, and involve even the middle coat. Thrombosis may be the origin of an abscess of the external coats of a vein.

Suppuration is far from being the usual termination of thrombosis; sometimes the clot is partially or completely detached from the vein, and the circulation is re-established in the peripheral vein and carries the thrombus on to obstruct a branch of the pulmonary artery.

The most frequent termination of venous thrombi is the permanent obliteration of the vein; vegetations of the internal coat and absorption of the old clot consecutively supervene, and the vein is transformed into a fibrous cord.

Varices, Varicose Veins.—The term *varices* is applied to dilatations of the veins accompanied by persistent modifications of their wall. The word varices is not absolutely synonymous with phlebectases, for simple dilatation or phlebectasis may be seen, for example, around tumors, without there being any varices. When the tumor is removed, the simply dilated veins return again to their primary condition.

Varices are observed especially in the superficial veins of the inferior extremities. In order to see the arrangement of varicose veins, they should be dissected for their entire extent, when it is found that they are not only dilated, but elongated, and form numerous curves. The calibre of the vein is very irregular; fusiform or ampulla-like dilatations are seen. Their walls are not uniform in thickness, which can only be demonstrated by opening the vein. The valves are found to be insufficient, or reduced to loops, or flattened against the wall, or partly destroyed. There is frequently noticed at the position of the valves a considerable thickening, in the form of nodules. The internal surface of the vein presents longitudinal prominences and depressions, which appear as longitudinal folds. The wall of the vein is in places extremely thick, so that, in transverse sections, its calibre remains gaping like that of an artery.

Sometimes there are seen, in chronic varices, calcareous incrustations in the form of plates, nodules, or spheres with concentric layers. Examined in the fresh state, small calcareous plates are not visible; but, when the altered veins are dried, the calcified part becomes very evident by its opacity and the prominence which it forms while the normal parts contract and become transparent.

Calcareous infiltration is seen in the form of spheres or phlebolites in the varicose diverticula. An extensive calcareous induration several centi-

metres in length, is also sometimes observed, the vein being transformed into a calcareous tube with the ramifications also varicose.

When the varices are old and greatly developed, the dilated veins, doubling upon themselves, form cavernous tumors with large meshes, so that a section of the tumor opens a great number of cavities, filled with blood and communicating one with the other. The veins constituting this tumor cannot be isolated by dissection.

Around all old varices the subcutaneous cellular tissue has undergone chronic inflammatory modifications; it is infiltrated with fluid, very vascular, and of lardaceous consistence. This tissue may be the point of origin of callous ulcers and of osseous formations, sometimes extensive.

A histological examination of the walls of varicose veins shows, in a varying degree, an alteration which consists in a new formation of fibrous tissue in the internal part of the middle coat, separating the muscular fasciculi of this coat which are themselves hypertrophied.

The internal coat is not evidently hypertrophied, and usually does not present vegetations upon its surface, unless it is at the position of the valves, or when there is a thrombus. In section this coat appears as a band, which colors slightly by carmine, and possesses two or three rows of lenticular nuclei.

Beneath this layer there exists an elastic network, the meshes of which are formed by large fasciculi of connective tissue, generally having a longitudinal direction. It is these which cause the longitudinal ridges upon the internal surface of the vein, visible to the unaided eye. These fasciculi are covered with large connective-tissue cells.

Next to this internal layer of the middle coat, the thickness of which is always considerable, come fasciculi of muscular fibres, which, when cut transversely, appear under the microscope as a series of clear circles presenting in their centre the section of a cylindrical nucleus. The largest of the muscular fasciculi are elliptical. Those at the most external part of the middle coat almost always are circular in direction, and run at right angles with the longitudinal fasciculi. These fasciculi are separated one from the other by connective tissue, so that there is a continuity of connective tissue from the internal to the external coat. From such an arrangement of structure, it follows that the muscular elements may be easily separated one from the other, and that fluids can penetrate into or exude from the vessel, which explains the frequency of œdema and chronic inflammation in these cases.

Between the fasciculi of connective tissue there are frequently found granules, or collections of granules, of a beautiful yellow color. They are composed of blood pigment, and demonstrate that the red corpuscles of the blood have infiltrated this tissue. The thickness of the middle coat, changed in this manner, is two or three times greater than normal.

The dilatation is not confined to the principal vein, but extends to all its branches, and especially to the *vasa vasorum* of the venous walls. The latter are much dilated, sinuous, and their walls are thickened. In some cases where the dilatation is more decided, a vessel of considerable diameter is seen in the midst of the middle coat, and may often extend to its most internal part. Finally, the tortuous dilations of the *vasa*

vasorum, added to the dilatation of the principal vessel, form very complex cavernous tumefactions.

The calcareous plates of the veins are developed in the fibrous and internal portion of the middle coat. At the beginning they consist of granules, deposited in the fasciculi of the connective tissue or between them; these soon unite and form transparent plates with granular striæ.

In certain parts of their course, varicose veins are frequently spindle-shape or spherically dilated. Their wall is then very thin, and sections including the different layers, show a process analogous to that of aneurismal dilatations of the arteries. The muscular coat has partly or completely disappeared, and the internal and external coats blending together alone constitute the wall of the tumor. The walls of the dilatations may be so thin as to rupture, and give rise to hemorrhages.

The indurated connective tissue and the hypertrophied skin near the varices present to the microscope the histological changes of chronic inflammation and elephantiasis. Ulceration is due to the uniting together of small suppurating foci which open and form an ulcerating wound, with indurated borders and base similar to the subcutaneous cellular tissue attacked with chronic phlegmon.

The extent of these ulcers is sometimes considerable. In the midst of the surrounding lardaceous tissue small points of suppuration are found near the ulcers, the remaining part of the tissue being infiltrated with white corpuscles, which collect together to form the small abscesses.

The inflammation often attacks the surface of bones, causing the formation of new osseous tissue, in the shape of osteophytes, which at times are very large.

Tumors of Veins.—Except the angiomata, which are developed in their wall, and which have been described at pages 139, 140, primary tumors of veins do not occur.

Secondary tumors of veins occur frequently. Often when a vein is surrounded by a malignant tumor, carcinoma or sarcoma for example, its walls are converted into morbid tissue which sends vascular elevations into the calibre of the vessel. These elevations occasion an impediment to the circulation anda coagulation of the blood, when they are found enveloped within a clot. Portions of the elevations may be detached and form emboli. It is very probable that the generalization of certain sarcomata, especially encephaloid sarcoma, occurs by the transportation of fragments of this nature. The fragments of morbid tissue, carried away by the circulating current, are engrafted in the different organs, particularly in the lungs, and become the origin of secondary formations.

Thus from primary tumors developed in the general venous system, in the testicles, in the kidneys, in the extremities, metastasis takes place most frequently in the lungs, while in tumors of the stomach and intestines the portal vein and liver are the usual seat of the metastasis. The sarcomata appear to us to be generalized through the venous system, and the carcinomata through the lymphatic system.

CHAPTER XI.

LYMPHATIC VESSELS.

Sect. I.—Normal Histology.

The structure of lymphatic vessels is so like that of veins of the same calibre, that it is unnecessary to repeat the description. But while veins have their origin in the capillary network, the lymphatics have their source from the tissues, and do not directly communicate with the vascular system. The lymphatics empty into the subclavian veins, on the left side by the thoracic duct, on the right side by the right lymphatic duct.

One of the most interesting and most disputed questions is the origin of the lymphatic vessels in the tissues. When they were studied by means of mercury injections, it was believed that the reticulum thus injected was the only origin of the lymphatic system. But since fluids which are much more penetrating have been employed for injecting, it has been found that a great number of vessels, not injected by the mercury, are rendered visible by these fluids. It is only necessary to use a hypodermic syringe, introduced into the connective tissue, to demonstrate that the lymphatic vessels communicate directly with the lymph spaces of the connective-tissue system of the body. (See fig. 10.) It has been seen how the serous cavities are appendages of the lymphatic system, inasmuch as there exists a direct communication between these cavities. The lymphatic vessels of the serous cavities are situated very superficially under the endothelium, so that any pathological change of the serous membranes cannot occur without the corresponding lymphatics experiencing at the same time an alteration.

Lymphatic vessels forming a reticulum are always found around arteries; in many organs this reticulum is very extensive. The spaces of this network are in communication with a lymphatic sac, which partly surrounds the artery as an imperfect sheath. The lymphatic sacs are then equivalent to a peri-arterial reticulum. This arrangement of perivascular lymph sheaths was first observed by Ch. Robin, in the arteries of the brain.

Sect. II.—Pathological Histology of the Lymphatic Vessels.

Lymphangitis or *inflammation* of the lymphatic vessels has as yet been studied histologically only upon the surface of serous membranes, in the brain, and in the uterus. In pleuritis, pericarditis, and peritonitis, sections including the exudation and subjacent serous membrane,

very distinctly show lumena of lymphatic vessels cut in different directions. These vessels are dilated and contain a substance similar to that of the exudation upon the surface of the serous membrane, consisting of pus or fibrin enclosing pus corpuscles. The endothelium of the vessels is always swollen, desquamated, and proliferated; the wall of the vessel is infiltrated with new elements and even pus corpuscles.

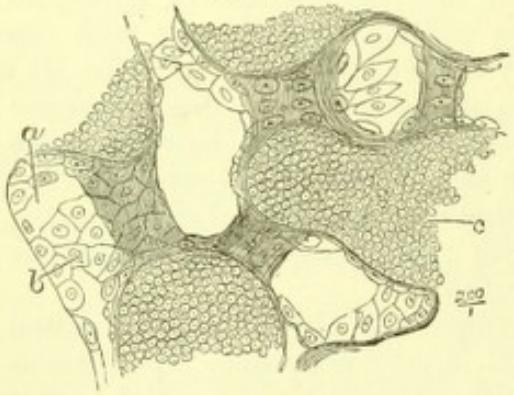
The lymphatic sheaths in the brain, representing the true lymphatic vessels of the organ, show in encephalitis, in cerebral softening and hemorrhages, a series of changes which may be easily studied. They consist in the production of granular pus corpuscles, and in a proliferation with desquamation of the endothelium. Generally, these lesions are accompanied with an escape of red corpuscles, which give rise to blood pigment and crystals of hæmatoidin.

In the chronic forms, particularly in chronic softening of the brain, the much distended lymphatic sheaths present an endothelium loaded with fatty granules, and contain numerous granular corpuscles and pus corpuscles. It is probable that the granules resulting from the breaking down of the focus of softening may be taken up by the lymphatics and gradually removed.

In puerperal metritis, the lymphatic vessels found in the horns of the uterus and in the broad ligament, are frequently seen dilated and filled with pus, and the coats of the lymphatics are infiltrated with pus corpuscles.

Dilatation of the Lymphatics (*Lymphangiectasis*).—In elephantiasis, in congenital enlargement of the tongue, the lymphatic vessels are dilated without any very considerable modification of their structure. Their endothelial cells are enlarged and readily recognized. The injection of the vessels is always easier than in the normal state (see p. 141).

Fig. 188.



Dilated lymph vessels in a case of elephantiasis of the skin of the penis. *a*. Lymph vessel. *b*. Flat endothelium of the vessel. *c*. Embryonic connective tissue of the tumor.

Lesions of the Lymphatic Vessels in Tumors.—Tuberculosis of the lymphatic vessels is very frequently seen upon the serous membranes (pleura, pericardium, peritoneum).

Upon the visceral peritoneum, opposite a tuberculous ulceration of the intestine, there are often found knotty, opaque, white cords, which radiate from the indurated base of the ulceration. These cords, which form elevations upon the peritoneal surface of the intestine, traverse the mesentery as far as the neighboring lymphatic glands. Upon their surface there are frequently found prominent tuberculous granulations; if a transverse section is made of them, a white or yellowish opaque substance flows out. The contents of these vessels consist of white blood corpuscles, of larger corpuscles filled with fatty granules and of free fat granules. By a microscopic examination there are found all the phases of development of tuberculous granulations. In the first stage the lymphatic

vessels are found filled with white blood corpuscles, and cells varying in shape coming from the endothelium of the vessels; the wall of the vessel and the neighboring connective tissue are infiltrated to a great extent with embryonic cells. In the second stage, the cells grouped in the wall of the lymphatics and in the connective tissue form with the existing cells of the vessels, a nodule having all the characteristics of a tuberculous granulation. These nodules situated along the course of the lymphatic vessels are located at more or less regular intervals. In many cases they are close together, or are confluent with neighboring granulations which have developed in the connective tissue, thus forming in places a collection of granulations.

When a carcinoma excites an irritation in the lymphatic vessels which come from the tumor, the latter form hard cords, gradually increasing in size, at times becoming as large as a crow's quill. For example, in a hard carcinoma of the mammary gland, where after repeated attacks of angioleucites they terminate by transforming the lymphatic vessels into hard cords, true scirrhus.

Fig. 189.



Carcinoma of mammary gland—the ground substance of the section stained with nitrate of silver. *a*. Alveoli of the carcinoma filled with cells. *b*. Lymph spaces shown in the fibrous tissue after treatment by nitrate of silver. *c*. Lymphatics showing silver staining of the endothelium.

In secondary carcinomata of the lungs and pleura there are at times seen upon the surface of this serous membrane nodulated and indurated lymphatic networks, gray or opaque in appearance. Upon the vessels so changed, there are sometimes found small secondary carcinomatous nodules, and a transverse cut of the vessels causes a milky fluid to exude. The same degeneration of the vessels may be seen in other serous membranes, notably in the peritoneum.

From the description which we have given of the evolution of the carcinomata, and the communication of the alveoli with the lymphatics, it is very probable that the cells of the alveoli penetrate into the lymphatic vessels and become the starting point of their transformation.

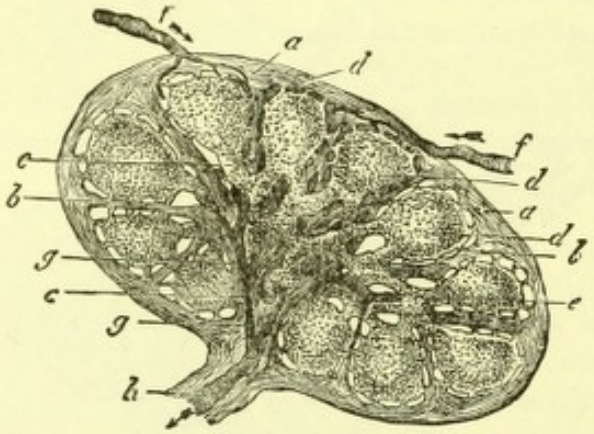
CHAPTER XII.

LYMPHATIC GLANDS.

Sect. I.—Normal Histology of the Lymph Glands.

LYMPHATIC glands are organs situated along the course of the lymphatic vessels. If their structure is judged according to the description of writers, it is very complicated, but in reality it is very simple. The glands are surrounded by a capsule of connective tissue, which does not constitute a close membrane, but is only a layer of connective tissue in which the fasciculi form a denser structure than in ordinary connective

Fig. 190.



Section of small lymphatic gland, half diagrammatically given, with the course of the lymph. *a*, the envelope; *b*, septa between the follicles or alveoli of the cortical part; *c*, system of septa of the medullary portion, down to the hilum; *d*, the follicles; *e*, lymph-tubes of the medullary mass; *f*, different lymphatic streams which surround the follicles, and flow through the interstices of the medullary portion; *g*, confluence of these, passing through the efferent vessel, *h*, at the hilum.

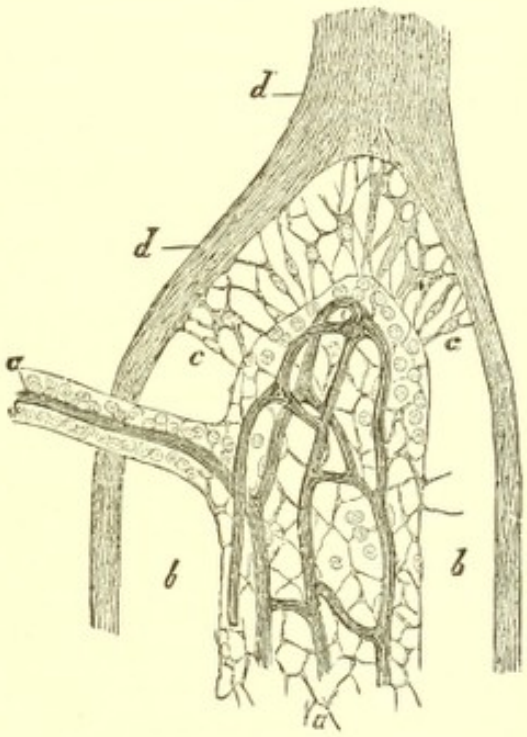
tissue. From the inner surface of the capsule connective-tissue septa penetrate the gland and divide it into follicles. In these septa, as well as among the connective-tissue fibres of the capsule, are frequently found a varying number of smooth muscle fibres. This capsule is traversed by bloodvessels, and by the lymphatic vessels which enter and those which pass out of the gland.

The afferent lymphatic vessels when they reach the gland penetrate it at different points upon the surface, and empty into a system of cavities. The efferent vessels form distinct canals in the hilus of the organ, where they pass out of the gland. This system of cavities which corresponds to the sinuses and lymphatic paths of His is permeated by the arteries and veins of the gland. From the wall of the bloodvessels proceed small

fasciculi of connective tissue, which divide and anastomose with neighboring fasciculi, forming a complete reticulum, which histologically does not differ essentially from the great omentum, except that the trabeculæ radiate in all directions, while in the great omentum the trabeculæ are placed in the same plain. A section of a gland, cutting an artery transversely, shows the vessel to be surrounded by a ring from the margin of which proceed, in a radiating manner, reticulated fasciculi of connective tissue. These fibres gradually become thinner the more distant they are from the artery.

The fibres of the reticulated connective tissue, which pass through the lymphatic cavity of the gland, never possess nuclei in their interior, or in their continuity, or at the point where they cross one another. These fibres are covered with flat endothelial cells similar to those seen upon the small trabeculæ of the great omentum. All the cavities are filled with lymph extremely rich in white corpuscles, so that the reticulum can only be seen after pencilling thin sections of the gland. If a lymphatic gland is injected with a solution of Prussian blue, by means of a puncture, the fluid fills all this lymphatic system, and passes out through the efferent vessels. If the organ is now divided, it is found that the colored fluid occupies only a part of the gland, which portion remains to be described, and corresponds to the follicles and follicular cords of His.

Fig. 191.



Portion of medullary substance of miniature gland of an ox. × 300. *a*. Medullary substance (follicle) with capillary network, fine reticulum of connective tissue, and a few lymph corpuscles. *b*. Superficial lymph path traversed by a reticulum (*c*) with numerous anastomosing prolongations. The lymph corpuscles have been brushed away. *d*. Trabeculæ composed almost exclusively of unstriped muscle fibres. (*Frey.*)

The follicles are very distinct in the glands of the mesentery during digestion, being slightly translucent, while the lymphatic paths previously described are filled with chyle, and form opaque zones. The follicles are round upon the free surface of the gland, while at the hilus they form one or more sinuous prolongations, which properly belong to them, although they have been given a distinct name, *follicular cords*. We designate all the follicles, as above described, by the name of *follicular system*, while for the passages through which the lymph travels we employ the name *cavernous lymphatic system*. The latter corresponds to the arteries and veins of the gland; the former, the follicular system, corresponds to the blood capillaries. The follicle differs in structure from the tissue which forms the cavernous system only by the greater thinness of the fibrils. The capillary network of the follicles consists

of large regular meshes. A transverse section of the capillaries shows them surrounded by a ring from which proceed fibrils, which anastomose and form a reticulum. There are neither nuclei nor cells in the fibrils, nor are they found in their continuity nor at the nodal points of the fibrils. This observation is different from that of other histologists. This conclusion has been arrived at by the employment of concentrated picric acid in order to harden the glands for making sections. After macerating in this reagent the reticulated connective tissue can be separated, so that their remains not a single cellular element, neither in the meshes of the stroma nor in the fibrils. If the pencilling has not been complete, there are seen upon the surface of the fibrils or at their points of junction, flat nuclei connected to the fibrils by a layer of protoplasm, the extent of which we do not yet know. In acute irritations of the lymphatic glands, the removal of all the cellular elements is much easier than in the normal state.

The boundary between the follicles and the cavernous lymphatic system is made quite distinct, either by interstitial injections of Prussian blue fluid, or by an incomplete pencilling. The meshes of the cavernous system being larger, and the cells less numerous than in the follicular system, the pencilling removes them first, but there is not seen between these two systems a true limiting membrane. It may, however, be experimentally demonstrated that there is a natural communication between the follicles and the cavernous system of the glands. By introducing vermilion, in fine powder suspended in water, into the connective tissue which surrounds the sciatic nerve of a rabbit, and killing the animal twenty-four hours after the operation, the lymphatic vessels which proceed from the region where the vermilion has been introduced are found filled with the red substance, as if they had been injected, and the lumbar glands also contain vermilion; the latter is especially seen in the cavernous system of the gland, so that the follicles appear upon the surface as white circles surrounded with red borders. In sections made after hardening the gland in picric acid, all the particles of vermilion are seen in the cells, which latter are of two kinds; lymphatic corpuscles, and endothelial cells which cover the fibrils. Some of the grains of vermilion are also found in a few of the lymph cells of the follicular system. In the physiological transportation of the chyle through the mesenteric glands during digestion, fatty granules are found not only in the spaces of the cavernous lymphatic system, but also in the cells of the follicular system, yet in a much smaller proportion. It is then very probable that the meshes of the reticulated tissue of the follicles are in communication with the reticulated meshes of the cavernous system. It may be inferred therefore, that a lymphatic gland is nothing more than a complicated lymphatic cavity or serous cavity situated along the course of the lymphatic vessels.

The afferent vessels enter into this cavity at different points, and the efferent vessels pass out after being collected together in the hilus, where they are placed alongside of the arteries and veins, which latter possess distinct walls, while the efferent lymphatics are simply canals excavated in the connective tissue and lined by an endothelium.

Sect. II.—Pathological Histology of Glands.

Pigmentation of Glands.—Frequently there is seen a black coloration of the peri-bronchial lymphatic glands in the adult and in old persons. A similar coloration may also be seen in other glands, when the regions from which their afferent vessels proceed have been the seat of infiltrations of blood or foreign granular matters. Thus, when colored powders have been introduced into the skin, as by tattooing, the corresponding lymphatic glands present colored particles in their interior. If the colored substances exist or are introduced into the blood instead of being deposited in the connective tissue, pigmentation of the glands does not take place, or it is very limited. It has been previously stated how rapidly colored particles penetrate into the lymphatic glands when deposited in the connective tissue. It has also been seen that when blood escapes from the vessels into the tissues, it undergoes a series of metamorphoses which terminate in the formation of colored granules; these are taken up by the lymphatic vessels and are arrested in the glands.

The colored particles found in glands are of two kinds: they come from the blood, or are foreign to the organism and are introduced into the glandular parenchyma through the lymphatic passages. The first are yellow, red, brown, or black, and are round or angular in shape; some writers (Rebsamen) have found crystals of hæmatoidin. The second, formed by opaque substances, appear always black or dark to transmitted light.

Glands infiltrated with pigment are slate-gray or dark-gray, marbled with white and black. In the latter case the pigmentation is seated especially in the cavernous lymphatic system, and the follicular system is less colored. When there are only a few dark striæ in the glands, they exclusively occupy the spaces of the cavernous system.

The glands affected with pigmentation are generally larger and more consistent than in the normal condition. The increase in size of a gland by pigmentation may be demonstrated by experiment upon animals; it is thus seen that the glands corresponding to the lymphatic vessels communicating with the pigmented region, are twice the size of the same glands on the opposite side of the body.

A few of the pigmentated glands are hard, and present a dry, glistening surface upon section; no juice exudes under pressure.

These latter glands have experienced, from the slow irritation caused by the presence of the pigmentary substance, a true fibrous transformation. By microscopic examination, it is found that the arteries are surrounded by a thickened fibrous zone, and that the interfascicular cells are infiltrated with pigment.

The reticulated fibres of the cavernous system are hypertrophied; their endothelial cells contain granules of pigment; the lymph cells also contain them. The follicular system is no longer distinct from the cavernous system, and everywhere the gland has the appearance as described. The reticulated tissue may have completely disappeared, and only the peri-vascular connective tissue infiltrated with pigment may

occupy the entire organ. But these are examples of complete transformation, which exist only in old persons or in the lesions of miners' phthisis.

The glands which are only slightly pigmentated, as the bronchial glands in a case of pneumonia for example, present very different characters. They are hypertrophied, and rich in a juice in which are found small spherical cells containing yellow, red, or brown pigment granules; in a more advanced alteration, all the pigmentary granules are absolutely black. In the juice there also exist large, ramifying, or angular cells containing several oval nuclei and grains of pigment.

In thin sections, the cavernous system is found to be the principal seat of the pigmentation, and, besides the pigmentated lymph cells, other smaller colorless cells are seen. There also exist colored granules in the endothelial cells of the reticulated fibres. These cells are slightly swollen and more readily detached.

Inflammation of the Lymph Glands; Acute Adenitis.—Inflamed lymph glands are at times considerably increased in size; they have a tendency to become spherical, or, if they come in contact with neighboring glands equally tumefied, they are flattened one against the other. The surrounding connective tissue is the seat of an inflammatory œdema with congestion of the bloodvessels, which frequently causes small ecchymoses. In intense adenitis, the œdematous connective tissue presents small purulent collections, or an abscess; thus the lymph gland may be surrounded by a layer of pus.

In the gland itself are found alterations which vary according to the stage of the inflammation. In the first period, there is congestive and inflammatory œdema, particularly well marked in the cavernous lymphatic system, so that the follicles and follicular cords are much more distinct than usual, on account of their forming whitish, opaque spots or lines upon a slightly translucent ground.

In a few cases, the hyperæmia and extravasations which accompany the inflammation occasion an increase in size, and a red or red-brown coloration of the whole parenchyma of the gland, resembling the tissue of the spleen. Such is the lesion generally seen in the bronchial glands in pneumonia, or intense capillary bronchitis.

At a more advanced period, the distinction between the two systems of the gland is not apparent, and, by scraping the cut surface, a very abundant juice is obtained, as in soft carcinoma. In a normal gland, twenty-four hours after death, it contains a slightly milky juice, analogous to that obtained from an encephaloid sarcoma. But, in the case of inflammation, the juice is much more abundant and more milky.

Under the microscope, this juice in inflammation presents numerous lymph cells and large endothelial cells, containing one or more nuclei. The latter cells are swollen, and resemble the multinucleated cells of the bone marrow (giant cells); yet they are not so numerous, and they contain fewer nuclei than those found in certain forms of a chronic nature, which will be studied later.

Inflammation of a lymph gland may continue until small purulent points are formed in its interior, or a single purulent focus is produced.

Hemorrhages may also occur, and the blood then infiltrates into the parenchyma of the inflamed gland.

The corpuscles which are found in the purulent foci do not notably differ from the lymph cells; they frequently contain fatty granules; large granular corpuscles are also seen. An examination of an inflamed gland, hardened in picric acid and pencilled, shows, in the first period of the inflammation (swelling and œdema), the changes in the cells which have been already described, especially the swelling and the multiplication of the nuclei of the endothelial cells. The fibres of the cavernous system are tumefied; instead of appearing formed by a homogeneous substance, they are seen to be constituted by a fibrillar and granular material. The fibres have reached five or six times their normal diameter.

In the follicular substance the fibres are less swollen and do not exhibit a fibrillar structure; they are simply strewn with granules.

When the inflamed lymph gland resembles the spleen in color, the capillaries of the follicular system are very much dilated and filled with red blood corpuscles, and between the lymph elements which fill the meshes of the stroma there are seen small collections of red corpuscles, or red corpuscles are disseminated between the lymph elements.

If the adenitis has gone on to suppuration, there are seen small collections of pus, irregular loss of substance, at the margins of which the process of destruction of the fibrils of the reticulated stroma may be followed. These fibrils are swollen, softened, and finally form a granular detritus, which is absorbed by the neighboring lymph cells.

Acute adenitis is seldom primary; it generally occurs in lymph glands whose lymphatic radicles have their origin in an inflammatory focus, or are in communication with an ulceration. It is very probable that the inflammation of the gland is then connected with a transportation of irritating substances, elaborated in the inflammatory focus or coming from the exterior. Pneumonia, bronchitis, soft chancre, ulcerations, especially of the intestines in typhoid fever, etc., may be cited as examples of inflammations which cause adenitis. Adenitis is also seen in infectious diseases (scarlatina, smallpox, etc.), diseases in which there are very probably virulent substances carried by the lymphatic passages.

Chronic Adenitis.—The changes following chronic inflammation of the lymph glands are simple fibrous induration, simple caseous or scrofulous degeneration, and finally calcareous infiltrations.

Fibrous induration of lymph glands occurs frequently in the bronchial and inguinal glands of persons advanced in age. Generally it is accompanied with a slight hypertrophy and pigmentation; it consists in an increased thickness of the perivascular connective tissue of the cavernous system; the reticulated trabeculæ of the cavernous spaces are double or triple in size, and at many points they appear fibrillated.

A varying amount of atrophy of the follicular parenchyma is observed; even its complete disappearance may occur. Usually there are found small irregular disseminated areas of this tissue, located especially at the periphery of the gland.

In *scrofulous* persons the engorgement of the lymph glands which occurs in consequence of catarrhal inflammations of the mucous membranes, or of cutaneous eruptions, terminates in a degeneration of the previously hypertrophied glands. In the first stage the lesion appears in the form of small wax-like points in the cortical substance and in the parenchyma. In the second stage, these points fuse together and form a whitish, opaque, grumous mass, the consistence and dryness of which vary according to the age of the lesion. When the alteration is of long standing, the hypertrophied gland becomes transformed into a dry, non-vascular chalky substance, readily broken down, and is enveloped by the capsule of the gland, which in this case forms a cystic membrane.

Fig. 192.



Chronic inflammation of a lymphatic gland. Showing the increase in the stroma, and the diminution in the number of the lymphoid cells. × 200. (*Green.*)

Calcareous transformation supervenes as a last stage of this lesion. Frequently in old persons, the glands are found to consist of a fibrous capsule containing a slightly lobulated calculus connected with the capsule by fibrous filaments which penetrate into its interior. The calculus is friable, or it may have sufficient consistence to rebound when thrown upon a hard surface. It is seldom, however, that the calcification is so complete; generally, the calcified glands inclose only one or more small masses, the size and shape of which vary much.

These different *degenerations* of lymph glands may be designated by waxy, caseous and chalky, or calcareous degeneration.

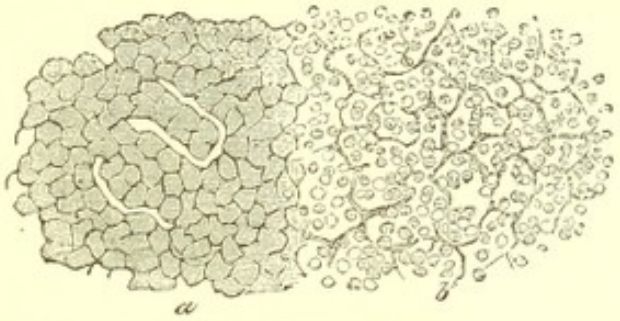
Pencilled sections of *waxy* degenerated glands show that it is impossible to separate the reticulated stroma from the degenerated spots, wherein all the elements are fused together into a semi-transparent mass in which the histological forms cannot be distinctly recognized. The waxy portions are colored by picrocarminate of ammonia.

When *caseous* degeneration supervenes, there frequently remain parts of the gland in which the waxy change is still seen, and in which all the intermediate stages may be observed. Caseous transformation consists in the fatty degeneration and molecular separation of the elements remaining between the waxy parts. Caseous alteration may also take place from the first, in consequence of a fatty degeneration. By pencilling a section of a caseous lymph gland, the stroma is found more or less perfect; the fibrils are thinner and less flexible than in the normal gland. The caseous, slightly angular blocks separated by pencilling are formed of fatty granules (caseous lymph corpuscles), granular corpuscles, and crystals of fatty matters.

In the *chalky* transformation, the reticulated stroma cannot be distinguished, and the mass effervesces upon the addition of hydrochloric acid. The calcareous areas of lymph glands do not possess the structure of bone. Examined in thin sections, they are transparent and present fissures and irregular striæ. They are partly soluble in hydrochloric acid, giving off carbonic acid gas.

Amyloid Degeneration of Lymph Glands.—This lesion is met with in connection with similar changes in the spleen, kidney, liver—that is, in cachexies with a suppuration of long duration. It occasions a uniform hypertrophy of the gland, which latter, upon section, presents over the entire surface, or in its cortical substance, small, semi-transparent, gray points. By the application of a solution of iodine,

Fig. 193.



Amyloid degeneration of the spleen—"sago spleen." A portion of one of the infiltrated Malpighian corpuscles *a*, with the adjacent normal splenic tissue *b*. Showing the increase in size and, in many parts, the coalescence of the cells, of which the corpuscle is composed. ×200. (*Green.*)

these points are colored a mahogany-red, and sometimes when sulphuric acid is added they become violet, blue, or green. The lymph corpuscles are transformed into small, homogeneous, angular, and transparent blocks. The capillary vessels and arteries undergo the amyloid change that has been previously described.

Colloid Transformation.—We have several times met with a transformation of the lymph glands, the cause of which we have not been able to determine. It consists in a colloid appearance of one or more glands similar to that of the thyroid body.

By microscopic examination, the degenerated parts are seen to be formed by a series of alveoli, varying in size, filled with a refracting substance similar to that found in the alveoli of the thyroid gland. The alveoli are separated by fibrous trabeculæ, and frequently present at their periphery rows of spherical cells, some of which are vesicular and contain colloid substance.

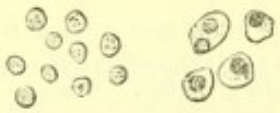
This change is without clinical importance, and is especially seen in old persons; it appears to be dependent upon an arrest of the function of the gland.

Tumors.—*Sarcoma* of the lymph glands, except one variety which has been named by Billroth *adeno-sarcoma*, is always a secondary pathological product. Its occurrence is not so frequent as carcinoma and epithelioma. It has been seen that carcinoma and epithelioma are propagated especially by the lymphatic passages, while sarcoma is generalized by the bloodvessel system. This is due to the circumstance that the alveoli of the carcinoma are connected with the lymphatic system, while on the other hand, the development of sarcoma occasions an embryonic transformation of the vessels, and at times a vegetation of the morbid tissue into their lumen.

When a sarcoma is formed in the neighborhood of lymph glands, the continuous development of the tumor may cause their involvement, when their capsules and glandular parenchyma may present a numerical increase in their cells and a resulting transformation into sarcomatous tissue.

Adeno-sarcoma, the position of which in the classification of tumors has not yet been definitely determined, and which may be a variety of carcinoma, is usually generalized through the lymphatic passages; it causes the successive alteration of a chain of lymph glands, a change characterized by a considerable hypertrophy of the invaded glands. It has an encephaloid appearance, and it contains a large quantity of juice, in which are seen large cells of various shapes, possessing enormous nuclei. Sections of these glands present fibrous trabeculæ, from which

Fig. 194.



Cells from a lymphatic growth in the liver. Those to the left are the ordinary lymph corpuscles which constituted the greater part of the growth. To the right are some of the larger elements. × 350. (*Green*).

Fig. 195.



Lymphoma. Section of a firm lymphoma of the mediastinum. Showing a very thickened reticulum, within the meshes of which the lymphoid cells are grouped. × 200. (*Green.*)

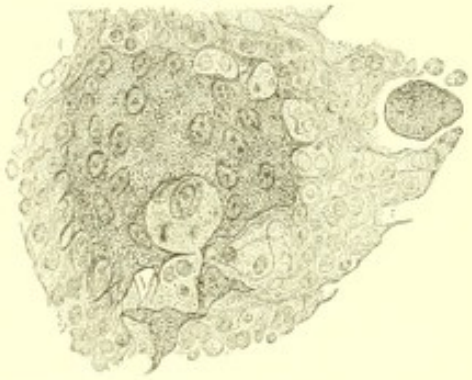
arise a fibrillar reticulum with large meshes, the fibres of which are lined with flat cells.

Carcinoma of the lymph glands is very common; carcinoma of the mammary gland is almost always associated with what is called an engorgement of the axillary glands. These engorged glands are either small, firm, and of a fibrous appearance, or they have exactly the aspect of the primary tumor, upon section. Fibrous induration of lymph glands always precedes the formation of the characteristic cancerous tissue, as described at page 102. The histological process of fibrous induration is very simple. All the fibrils of the reticulum, both in the cavernous and follicular systems of the gland, are hypertrophied in such a manner that the alveolar spaces gradually become smaller; a few entirely disappear, and the lymphatic passages of the gland are almost completely obliterated. A gland so altered is, for a certain time, a barrier to the propagation of cancer. A gland which has experienced this primary fibrous change, later presents all the characters of carcinoma, and becomes itself a new centre for the infection. When secondary carcinoma of lymphatic glands is rapidly developed, the lymph elements included between the fibrils of the reticulum take the form of the so-called cancer cells, while the fibrils gradually increase in thickness in order to form the stroma of the alveolar tissue, which characterizes carcinoma. (See p. 99.)

Tubercles of the lymph glands present the same characters as in

other organs. They are disseminated or confluent, and are developed in the follicular or cavernous systems along the vessels. To the unaided eye they appear in the form of granulations, gray, semi-transparent, or opaque at their centre, or as small spots in which are seen the primary granulations, with an opaque point occupying the centre of each. Granulations in a tuberculous gland cannot always be distinguished by the unaided eye. A histological study of the gland can alone determine the nature of the alteration.

Fig. 196.



Tuberculosis of a lymphatic gland. The earliest stage of the process. Showing the so-called giant-cell. ×200. (*Green.*)

From a pencilled section of a lymph gland affected with tubercle, it is impossible to disengage the stroma from the tubercle. The same sections colored with picrocarminate of ammonia, show in the peripheral layers of the tubercle, and sometimes at distant points, large flat cells, containing numerous nuclei. These cells, pointed out by Foerster, and afterwards by many other writers, have been considered as giant-cells. They are evidently irritated and swollen endothelial cells. In the most central portion of the tuberculous nodule the reticulated stroma has disappeared, the lymph cells have become gradually smaller; they are united together by a new intercellular substance, and form with it a caseous mass in which the elements cannot be distinctly recognized. In the centre of the granulation, at the point where the caseous degeneration has occurred, the cellular elements become free. A central loss of substance is thus occasioned. Therefore, we cannot understand how Rindfleisch has been able to maintain that the tuberculous granulation is formed of reticulated connective tissue, since the granulation developed in this tissue begins by transforming it. In the tuberculous granulation of these glands, vessels are found varying in size, according as they are located in the cavernous system or follicular tissue; these vessels are obstructed by a fibrinous coagulum or by white blood corpuscles.

When the granulations are confluent, all portions of the intermediary parenchyma of the gland undergo caseous transformation, and the entire organ may be affected and assume the character of a scrofulous gland. In many cases the differential diagnosis between a tuberculous gland and a scrofulous gland is impossible, either to the unaided eye or with the microscope. But, when the tuberculous evolution is rapid, other granulations may be developed alongside of the caseous mass, so that the tuberculous matter can be distinguished from a simple caseous degeneration.

Syphilis occasions inflammatory hypertrophies in their different forms, including caseous degeneration. Gummata of the lymph gland have not yet been studied.

Enchondromata of the lymph glands seldom occur; they may involve the glands by a progressive invasion or by continuity.

Every variety of *epithelioma* may be met with in the lymph glands; their development differs from that of carcinoma in that the first epithelial nodule usually begins in a part of the cavernous lymphatic system, sending its pegs in different directions, while the structure of the gland is yet preserved. These pegs are surrounded by embryonic tissue and always present the structure of those of the primary tumor.

CHAPTER XIII.

NERVE TISSUE.

Sect. I.—Normal Histology of the Nerves.

NERVES consist of nerve fibres without medullary substance or fibres of Remak, and nerve fibres with a double contour or medullated nerves. The latter are limited by an exterior structureless envelope of extreme thinness, known as the membrane of Schwann (neurilemma). This membrane does not form a continuous cylindrical sheath, as previously believed; it presents at regular distances constrictions in the form of rings. These annular constrictions are placed upon the large nerve fibres at

Fig. 197. Fig. 198. Fig. 199.

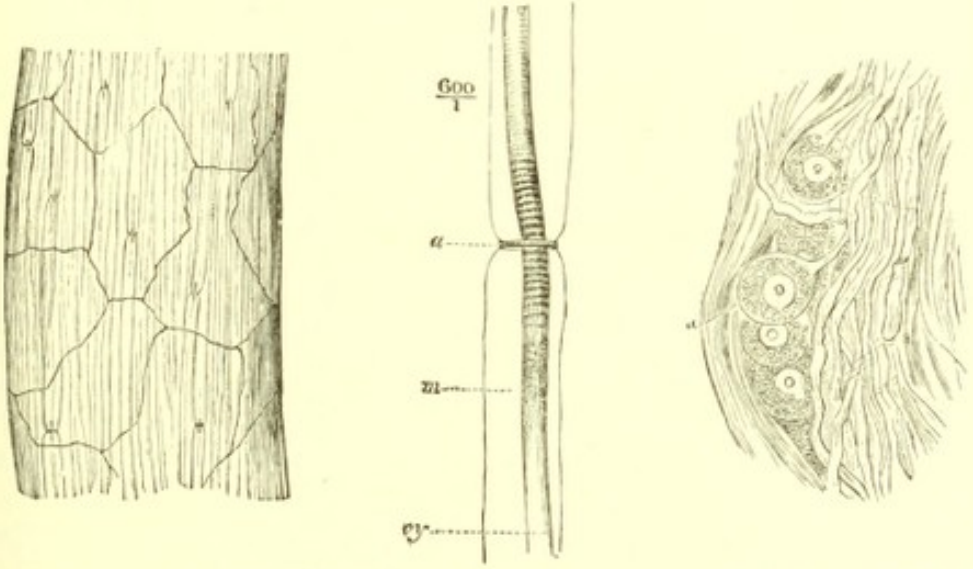


Fig. 197.—Nerve fasciculus of a mouse after impregnation with silver nitrate. Large flat endothelial cells are seen covering its surface. The explanation of the small cross is seen by reference to the next figure. (*Carpenter.*)

Fig. 198.—Nerve fibre from the sciatic nerve of a rabbit after action of nitrate of silver. *a*. Constricting ring. *m*. White substance of Schwann, rendered transparent by glycerin. *cy*. Axis cylinder which, just below the level of the back of the annular constriction, presents the striæ of Fromman. High power. (*Carpenter.*)

Fig. 199.—Microscopic nerve ganglion from heart of frog. High power. (*Carpenter.*)

distances varying from 1.3 mm. to 1.5 mm., and upon smaller fibres .8 mm. to 1 mm.; they limit segments, called *interannular segments*. At the centre of each of these segments, and upon the internal surface of the membrane of Schwann, there exists a flat oval nucleus, surrounded by a layer of protoplasm. Running through the entire length of the interannular segment is the axis cylinder, the essential element of the nerve

fibre. Between this axis cylinder and the membrane of Schwann, lined by its layer of protoplasm, is found the medullary sheath.

The neurilemma and medullary sheath are organs of protection for the axis cylinder, which alone appears to possess the function of conducting the nervous impressions. The nutritive interchanges occur at the annular constrictions. (Fig. 198.)

The nerve fibres are grouped into bundles in order to form a nerve. These bundles vary in diameter from .050 mm. to 2. mm.; they are surrounded by a laminated sheath similar to the aponeurosis of muscles. (Fig. 197.) The bloodvessels carrying the blood for the nourishment of the nerves, after forming a network in the peri-fascicular connective tissue, pass through the laminated sheath of the fasciculi and form a network in the interior of the fasciculi.

Sect. II.—Pathological Histology of Nerves.

Congestion, Hemorrhage, and Inflammation of Nerves.—Congestion of nerves frequently occurs, since it is seen in all nerves which form a part of an inflammatory focus, often extending beyond the focus. If the nerves involved in a wound are dissected with care, they are found slightly swollen, and upon their surface are seen red lines running longitudinally which indicate the congestion existing during life. The nerves in wounds, in cases of tetanus, have been principally examined, and, by some, it has been thought that their congestion was the cause of the convulsion. But this is certainly an error, since congestion may be observed in nerves in almost all wounds where there is a slightly intense inflammation.

In congestion of nerves, the hyperæmia can be recognized with great facility in the peri-fascicular vessels, as the nerves are distinct from the surrounding parts. Hyperæmia of the intra-fascicular vessels also exists, but it is not always easy to recognize with the unaided eye, for it is necessary to tear the laminated sheath in order to see the vessels filled with blood. To judge of the dilatation of the capillaries, transverse cuts of the nerve should be made.

In inflammations of the fingers, the nerves present a congested appearance, and it is very probable that intra-fascicular hyperæmia of the nerves is an important cause of the acute pain accompanying these lesions.

Congestion of nerves occasions an increase of the blood pressure and a serous exudation into the peri-fascicular connective tissue; frequently miliary hemorrhages are also produced.

Inflammation of nerves characterized by congestion and serous exudation frequently occurs; but suppurative inflammation is rare in the nerve bundles. The laminated sheath forms an almost insuperable barrier to the diffusion of pus into the interior of the fasciculi; thus, nerves included within a suppurating focus—the peri-fascicular tissue of which is the seat of hyperæmia, serous exudation, and even suppuration—frefrequently preserve their properties. If the nerves in a purulent focus are examined with the microscope, it is surprising to find the nerve

fibres normal. The resistance of the nerves to the diffusion of pus into their fasciculi is in part due to the laminated sheath, and in part to the numerous anastomoses of the vessels, either in the peri-fascicular connective tissue or in the intra-fascicular connective tissue, which insures the independence of the circulation.

Inflammations of long duration and neoplasms of continuous development affect the nerves to a greater extent. Such cellular new formations extend into the peri-fascicular connective tissue and between the laminæ of the laminated sheath of the nerve fasciculi, separating and compressing them; the nerve fibres undergo below this point a series of changes similar to those seen in the peripheral end of a divided nerve.

The nerves of paralyzed extremities in chronic hemiplegia, accompanied with rigidity, present a very manifest increase in size, which may become double that of the healthy nerve. In such cases, the nerve fibres have retained their normal structure, the hypertrophy is due only to a thickening of the connective tissue.

Lesions following the Division of Nerves.—By experiments upon animals, it is possible to follow the different phenomena which follow in consequence of the division of a nerve. The opportunities to study them in man are rare, although, in war, wounds of the nerves are common; but the wounded soon die, or recover and experience a series of symptoms similar to those which may be produced in animals submitted to experiment.

Some writers, Foerster among others, speak of the immediate union of nerves. Very probably their opinion is based upon mere clinical facts, such as the rapid re-establishment of the function of a nerve after division. Recently, Arloing and Tripier have explained this by a complementary nervous action exerted by the recurrent peripheral branches; they have supported their interpretation by direct experiments.

In animals, division or resection of a nerve is never followed by immediate union. Therefore, it may be doubted if it ever takes place in man.

When a nerve in an animal has been divided, the peripheral end undergoes a special degeneration, and after a variable time, not less than three months, there is a restoration of the nerve and its function. There is by this time a union of the two ends of the nerve, by a process which is not included in any of the methods admitted by surgeons. It is neither immediate nor secondary union, but a special histological evolution which has not yet been definitely determined.

Four days after division, in a mammifera, the peripheral end of the nerve has lost its neurility, and from this time the degeneration begins. When a nerve is destroyed by certain processes, its physiological properties may disappear immediately, and the degeneration also soon follows. Thus, by the action of water upon a portion of the sciatic nerve of a rabbit, causing its destruction, degeneration and loss of neurility may be occasioned in about forty-eight hours.

The degeneration of nerves consists essentially in a segmentation of the medullary substance, which continues until regeneration begins. This segmentation terminates in the formation of fine granules, which lose the characters of medullary substance and take those of neutral fat, such as

found in the organism. Reduced to fine fatty granules, the medullary substance gradually disappears, by an interesting process, several phases of which are not yet known. From eighteen to twenty-five days after the division, there still remain, in the nerve fibres, at certain points along their course, oblong masses, formed of cylinders of the medullary substance, a few myelin drops and fatty granules, while in other parts of the fibre there are only scattered fatty granules.

A portion of the medullary substance escapes from the nerve fibre by traversing the sheath of Schwann. The fatty granules become free among the nerve fibres, and form granular corpuscles similar to those met with in the peri-vascular lymphatic sheaths of the brain (corpuscles of Gluge), in simple softening or hemorrhage of this organ, and which are very probably lymph corpuscles loaded with fatty granules, and are again taken up by the lymphatic circulation.

The cells forming the walls of the intra-fascicular vessels also contain numerous fatty granules.

In about twelve to eighteen days, when the wound of the cellular tissue and integument is united by the first intention, the two ends of the divided nerve are joined by a slightly opaline line of cicatricial tissue, which proceeds from the peri-fascicular tissue of the superior end, to blend with the peri-fascicular tissue of the inferior end. The essential parts of the nerve are not yet connected, their path is only marked out.

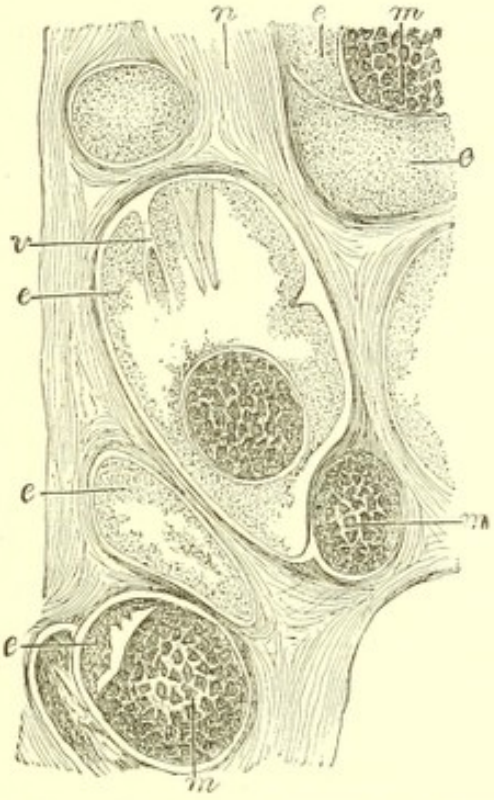
A microscopic examination of a transverse section of the peripheral end of a nerve, twenty-one to thirty days after the operation, presents most of the nerve fibres without axis cylinders; it is only in a few fibres, the diameters of which are considerable, that swollen and misplaced axis cylinders are found. Twenty-five days after division, the nerve fibres have therefore lost their essential element, the axis cylinder.

The proximate cause for the degeneration of nerve fibres in consequence of division, is yet unknown. Waller taught that the nutrition of nerves depends upon ganglionic cells, which through their connection with the nerves act as trophic centres; thus the nerves degenerate when they are separated from their centres. The motor roots of the spinal marrow have their trophic centres in the spinal marrow itself, while the posterior roots have their trophic centres in the spinal ganglions. Thus if both roots of a nerve are divided in the vertebral canal, the peripheral end of the anterior root and the spinal end of the posterior root alone experience granular degeneration. If a mixed nerve is divided as it passes out of the vertebral canal, degeneration occurs in all parts, which have been separated from the centre. When regeneration has occurred, that is, from the third to the fifth month after division, the peripheral end exhibits under the microscope slender nerve fibres containing normal medullary substance, alongside of degenerated nerve fibres which are not completely destroyed. Waller thinks that perfect new fibres are formed in the intrafascicular connective tissue spaces. Schiff, Vulpian, Remak, etc., believe that it is the previously degenerated fibres which again become regenerated and assume their former structure and function.

Tumors of the Nerves.—Besides medullary and non-medullary neuromata (see page 137), fibromata (see page 91) and myxomata (see page

89)—which were formerly named neuromata, and are still by the French surgeons so designated—are met with in nerves. This name was employed at a time when pathologists did not recognize the true nature of the tumor, but it should now be rejected.

Fig. 200.



Transverse section of the sciatic nerve in a case of cylindrical-celled epithelioma propagated to this nerve from the uterus. The inter-fascicular tissue *n* is penetrated by the neoplasms *e*, which are also developed in the lymph space surrounding the secondary bundles of nerves. The nerve fibres *m* are not involved. × 40.

Carcinoma and epithelioma are generally seen in nerves as the extension of a tumor primarily developed in a neighboring tissue. The perifascicular connective tissue is first invaded, the laminated sheath is separated by the new formation, the nerve fibres undergo fatty degeneration and disappear. Foerster has observed primary carcinomata of the nerves, which at the beginning were the size of a lentil, and in developing caused complete destruction of the nerve. (Fig. 200.)

CHAPTER XIV.

CENTRAL NERVOUS SYSTEM.

Sect. I.—Alterations of the Meninges.

The alterations of the cerebral and spinal meninges being analogous they will be described together, but those alterations peculiar to the pia mater and dura mater will be indicated separately. The arachnoid is only an appendage of these two membranes.

Congestion and Inflammation of the Meninges.—Very frequent in the pia mater, the congestion varies in extent, and may be active or passive. Active congestion, when intense, causes the desquamation of the endothelium which properly constitutes the arachnoid, and the exudation of fibrinogenic fluid with white blood-corpuscles.

In *cerebral rheumatism* the pia mater is congested throughout its entire extent, and presents patches or small spots, upon the surface of which the congestion is more intense, and may even go so far as the effusion of blood. The spots are vermilion-red in color, as if the blood contained in their vessels was highly oxidized. The laminæ of the arachnoid and the pia mater so changed show uniform or fusiform dilations of the blood-vessels, around which are frequently extravasated red blood corpuscles. The choroid plexus is found to be congested, as is also the *velum interpositum*.

The fluid contained in the large cavity of the arachnoid, in the ventricles, and in the subarachnoid spaces, is increased in quantity. In this fluid numerous cellular elements are found, large granular epithelial cells, white and red blood corpuscles, although it may not be notably turbid.

When cerebral rheumatism has existed for twenty-four hours or longer, the fluid contained in the arachnoid, ventricles, and sub-arachnoid spaces, is more abundant and is cloudy or even slightly puriform—appearances due to the great number of epithelial cells and white blood corpuscles which it now contains.

This condition is not peculiar to rheumatism, it may be met with in all cerebral congestions accompanied with delirium, as those caused by pneumonia, variola, typhoid fever, etc.

Primary cerebral meningitis is extremely rare; it may be caused by insolation. Inflammation extending over the whole surface of the nervous centres, or *cerebro-spinal* meningitis is generally epidemic and usually occurs in armies or hospitals.

The most frequent form of meningitis is that which follows tuberculosis of the meninges, or tumors of the meninges and of the brain. It is characterized by the presence of pus upon the surface of the pia mater, by

thickening and opacity of the connective tissue of this membrane, and by the accumulation of pus corpuscles around and along the vessels, where the connective tissue is most abundant.

The vessels appear to the unaided eye surrounded by an opaque zone. When studied with the microscope, lymph corpuscles are found located in the loose connective tissue surrounding them, these elements besides accumulate in the lymphatic sheath of the vessels, and envelop them as a capsule.

The sero-purulent fluid found upon the surface of the membrane is sometimes very thin, and accumulates in the anterior and posterior sub-arachnoid spaces, or it may be thick and mixed with fibrin.

When the meningitis is intense, and has lasted several days, the pus mixed with fibrin forms under the visceral arachnoid a continuous, opaque, yellow layer, thicker in the sulci. The vessels are partly imbedded in this false membrane, and are seen as red lines covered with a film. From a section it is found that this fibrinous layer may even reach five millimetres in thickness over the sulci. The false membrane can be removed, and the gray substance beneath is seen marked with red points. From each red point one of the vessels which penetrate into the nerve substance has been detached, and it is found to be surrounded by a purulent layer and at times with escaped blood.

In cerebro-spinal meningitis, a similar exudation is found around the spinal marrow and pons. The pus occupies the arachnoid cavity of the spinal marrow and the meshes of the spinal pia mater; but it does not penetrate beneath the fibrous part of this membrane. The gray substance of the spinal cord presents a pink color to the naked eye. Microscopic examination of thin sections does not show any modifications of the nerve elements, only a simple hyperæmia of the vessels of the pia mater, and a few pus corpuscles between the connective tissue fasciculi of this membrane. Sometimes suppuration is so rapid that the amount of pus is considerable, even when the symptoms of the disease have existed only a few hours.

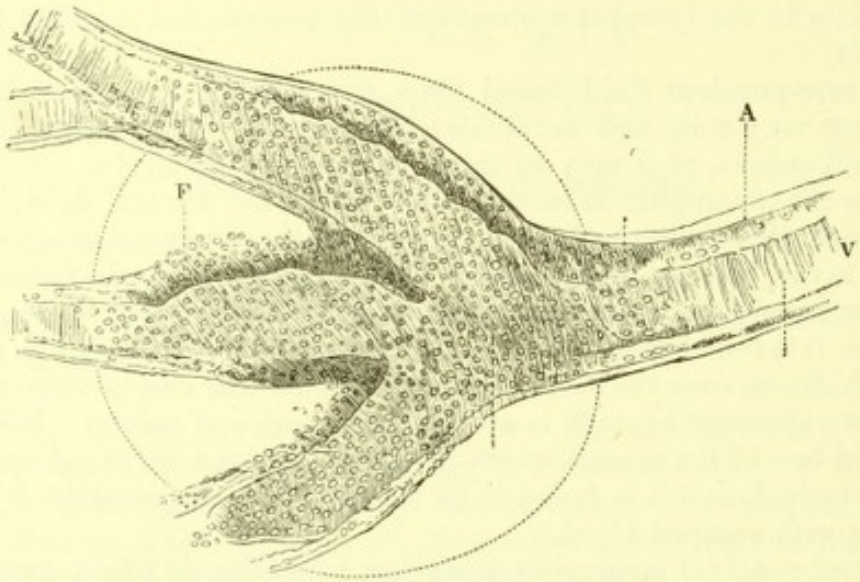
Tuberculous Meningitis.—This is analogous to that described under purulent exudation, but differs from it by the presence of tuberculous granulations, which are generally located along the course of the vessels in the pia mater.

Frequently, at an autopsy of meningitis, it is thought that the meningitis is acute and primary, because evidence of granulations are not at first found. It is not rare, in these cases by careful investigation, to recognize abundant, but small granulations, which have escaped a careless examination. In order to find them, the pia mater is removed at the points where the tubercles are usually developed, which are the fissures of Sylvius and the anterior peduncles of the cerebellum. A shred of the membrane should be washed in water to separate the adherent fragments of the cerebral pulp, when they are seen as small whitish granules. This examination is not sufficient, the pia mater should be spread out with care upon a glass slide, when with low magnifying power the granulations, which could not be recognized by the unaided eye, are now perceptible.

The study of a single granulation shows it to be formed of a collection

of young or embryonic cells, developed in the lymph sheath of the blood-vessels, and neighboring connective tissue. The larger granulations encroach upon the neighboring tissue, and completely fill up the lymph sheath (fig. 201). The vessel which is in the centre of the granulation

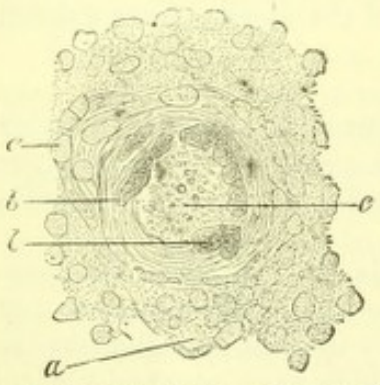
Fig. 201.



Miliary tubercle in the pia mater. The dotted lines indicate the original size of the tubercular nodule. A. The lymphatic sheath. V. The bloodvessels. F. Proliferation of elements within the sheath. × 100.

is obstructed by a fibrinous coagulum. Ordinarily these collections of cells are found at the bifurcation of a small vessel, where the lymph sheath offers a greater extent of surface. Finally, it is not unusual to notice upon the same vessel several granulations placed at intervals, giving to the vessel the appearance of a string of beads.

Fig. 202.



Transverse section of a vessel filled with granular fibrin. *a*. Tubercular tissue. *b*. White blood corpuscles. There is here a tubercle involving the vessel. × 400.

The neoplasm quite often has the form of a sheath, surrounding the vessel for some extent by a tissue composed of small elements pressed closely one against the other, situated in the pia mater and lymph sheath.

In a great many cases of tuberculous meningitis, the pia mater and arachnoid covering the spinal marrow are strewn with granulations.

Chronic Meningitis.—This form of meningitis frequently occurs, especially in *diffused meningo-encephalitis*, an anatomical lesion corresponding to the symptoms of general paralysis of the insane. It is characterized by a new formation of connective tissue, which occasions thickening of the pia mater. The walls of the bloodvessels undergo the same thickening. Those which are imbedded in the cerebral pulp adhere to this substance, so that it is torn when the pia mater is removed. To this alteration of the vessels is added a proliferation of the connective

tissue of the brain, a diffused interstitial encephalitis, and an atrophy with pigmentation of the cells of the cortical layer of the convolutions. In a few rare cases there exists a special degeneration of the walls of the bloodvessels. This lesion, described by Magnan under the name of colloid degeneration, appears to consist in a chronic endarteritis and periarteritis.

Meningitis of the dura mater is named *pachymeningitis*. It is always chronic.

Upon the internal surface of the inflamed dura mater there are formed small elevations or buds, possessing vascular loops, which are continuous with the pre-existing vessels of the membrane. Around the vessels and to some extent upon the surface of the membrane is developed a new formation of connective tissue, which constitutes a thin and very vascular false membrane. When the latter is recent and very thin, the bloodvessels have embryonic walls; they are fragile, frequently rupture, and allow the blood to escape into the tissue of the false membrane, giving it a deep-red color. This may be mistaken for a simple spot of blood, if in scraping the surface of the dura mater it is not detached as a fine pellicle. After having removed a portion of the membrane, it is carefully placed upon a glass slide and examined with the microscope, when there is seen a dense network of bloodvessels, between whose meshes exists a new connective tissue containing extravasated red blood corpuscles.

When the false membrane is older, there are found around the bloodvessels collections of red-brown blood pigment, and crystals of hæmatoidin. Frequently the membrane is formed of several parallel layers.

If, in consequence of ruptures of the vessels, a quantity of blood escapes between the layers of the false membrane, there is formed a blood cyst, named *hæmatoma of the dura mater*. This lesion for a long time was believed to be due to an effusion of blood upon the surface of the dura mater, surrounded by a layer of fibrin which became organized into a false membrane, encysting the blood.

Tumors of the Meninges.—Fibromata.—Pacchionian bodies may be described as fibromata. They may be developed in great numbers and form true tumors, capable of wearing away the bones of the cranium. These bodies are composed of laminated fibrous tissue, with flat cells, analogous to those forming the fibrous patches of the spleen, and arranged concentrically (fibroma with flat cells, see page 92). This structure is readily recognized, yet they are often mistaken for tuberculous granulations; they are frequently incrusted with calcareous salts.

Fig. 203.



Psammoma. (*Hamilton.*)

True fibromata adherent to the dura mater are met with, but they are rare.

Cysts.—There are frequently found in the choroid plexus small

serous cysts, which are developed from the vascular diverticula; similar formations are met with in the meshes of the pia mater, especially near or within the fourth ventricle.

Tubercles.—They ordinarily exist only in the pia mater, but they may be met with in the false membranes of the dura mater.

Sarcomata.—They frequently occur in the dura mater, and, like those of the brain, may be of two different varieties: glioma (neuroglia sarcoma) generally developed along the course of the cephalic nerves; and psammoma (angiolitic sarcoma.) (See pp. 83, 85).

Carcinomata and Epitheliomata.—These new formations are very rare in the meninges.

All tumors of the meninges may perforate the bones of the cranium.

Sect. II.—Alterations of the Cerebrum and Cerebellum.

Cerebral *anæmia* is characterized only by a paleness of the nervous substance, without any appreciable modification of the elements.

Cerebral Congestion.—Cerebral congestion which has continued for some time always leaves characteristic traces. There is a very decided injection of all the vessels; the convolutions are pinkish, increased in size, and closely pressed against the dura mater, which appears stretched; sometimes the convolutions are so flattened one against the other that the depressions separating them are almost effaced.

Upon the surface of the cerebellum reddish points or patches are at times met with. The surface of a section of the cerebral substance shows the cortical substance to be grayish-pink, and the white substance to be spotted all over with red points, which correspond to sections of the capillaries filled with blood. When these red points are numerous and very close together, the brain appears speckled.

Microscopic examination shows in places a pigmentation, collections of pigment granules, seen especially in the lymph sheath of the small vessels. The accumulation of red or yellow pigment is particularly abundant at the bifurcation of the vessels, where the sheath is separated from the vascular wall by a considerable space.

The nerve cells and elements of the neuroglia are not much altered. In the colored spots, the nerve cells do not seem to have undergone any change. Repeated congestions, which accompany diffused meningo-encephalitis, occasion a pigmentation of the nerve cells. The congested state of the brain may be caused by cerebral contusions.

Œdema of the Brain.—By œdema of the brain is implied an accumulation of fluid in the cavities of the ventricles and in the subarachnoid cavity, accompanied with anæmia and a softening of the fornix. The only histological lesion found corresponding to this condition is simply imbibition of serum by the cerebral substance.

The principal cause of œdema is pressure upon the veins of Galen. The softening of the fornix which coincides with an accumulation of serum in the ventricles, occurs, as a rule, in cases of tuberculous meningitis.

MELANÆMIA.—This name is given to a special general lesion, which is characterized by the accumulation of pigment granules in the capillaries of several organs, especially the brain and liver.

Numerous capillaries are frequently obstructed by these accumulations; at some points the small arteries are dilated in the form of aneurisms and are also filled with black pigment. This lesion often supervenes during low types of intermittent fevers in which there is considerable alteration of the spleen.

CEREBRAL HEMORRHAGE.—Cerebral hemorrhages are sometimes caused by changes in the blood, as occurs in grave fevers, in variola, in scurvy, leucocythæmia, etc.; sometimes they are due to changes in the heart and bloodvessels. Hypertrophy of the heart coincident with an atheromatous induration of the walls of the aorta, internal carotid, and branches from the arteries at the base of the brain, has been regarded as a very common cause of cerebral hemorrhage. In these conditions the flow of the blood, driven by the heart at each systole, is jerking or irregular, and is not transformed into a continuous current by the action of the elasticity of the arterial walls. The jerking impulse of the blood transmitted to the cerebral capillaries is very probably, in some instances, a cause of dilatation of the small vessels and of their rupture. But the most frequent lesion preceding hemorrhages, and which may be regarded as their proximate cause, consists in aneurismal dilatations of the small arteries and capillaries of the encephalon.

Two distinct forms of hemorrhage are met with in the brain: capillary hemorrhage, and that where the extravasated blood is collected into a mass, or so-called focus.

Capillary hemorrhage, or capillary apoplexy of Cruveilhier, is either located in the convolutions or in the central portions of the brain. The part of the brain where the lesion occurs is softened and strewn with red points, which at first sight resemble small drops of dark and coagulated blood. When the cerebral tissue around these red points is torn with needles, it is found that they correspond to vessels, which may be followed and isolated for some distance. Around the very dark red points the slightly softened cerebral tissue is colored red or pink.

One of these hemorrhagic points examined with the microscope shows at first only a collection of blood, but by careful washing, it is found to have in its centre a capillary vessel, the lymph sheath of which is distended and filled with blood. The red corpuscles have also escaped beyond the lymph sheath, among the nerve fibres which have been separated and broken. Each of these small hemorrhagic spots is therefore composed of a vessel and its lymph sheath distended with blood, and of an interstitial hemorrhage into the neighboring nerve tissue.

A fatty degeneration of the wall of the central capillary is frequently observed; the lymph sheath is considerably enlarged; but the rupture or fissure through which the blood passed out of the vessel is not usually found, nor is the opening of its sheath recognized through which infiltration of the elements of the nervous tissue occurred. The shape of the dilatation of the sheath varies; it may be cylindrical, fusiform, or spherical.

These different forms have been described as *dissecting aneurisms* of the capillaries.

The nerve fibres are torn and separated, but, when the capillary hemorrhage is recent, they have not undergone any degeneration except the breaking up of the medullary substance into small drops. Patients frequently die during the first period of the hemorrhage, but, when they survive this stage, there is found in the circumference of the vascular dilatation yellow or brown blood pigment, free or contained in the white blood corpuscles. These latter also contain fatty granules, derived from the medullary substance of the destroyed nerve fibres. The blood contained in the dilated vessels has become brown; blood pigment may also be seen in the interior of the vessels or in their lymph sheath.

The small points of capillary apoplexy are brown or slate-color, and, by microscopic examination, are especially characterized by pigmentary transformation of the coloring matter of the blood. Brown or black pigment granules, and even crystals of hæmatoidin, are found in the white blood corpuscles and in the lymph sheath of the vessels. In the sheath and in the peripheral nerve tissue, granular corpuscles are seen.

Round lacunæ as large as the head of a pin, or cylindrical spaces traversed by the altered bloodvessels, are also frequently observed in this lesion.

Hemorrhagic Foci.—A hemorrhagic focus may follow the rupture of a large artery, or be the result of the confluence of numerous points of capillary hemorrhage. The lymph sheath distended by blood may rupture; small foci thus formed fuse together, and intimately mingle with the cerebral substance. "Capillary hemorrhage may then precede a true hemorrhage; it is the first stage of a hemorrhage which later accumulates to form a focus" (Bouchard). Frequently there are found around hemorrhagic foci, even the largest, a number of small points or foci of capillary hemorrhages.

If the hemorrhage occur at the corpus striatum or thalamus opticus, the blood may break into one of the lateral ventricles.

A hemorrhage in the cortical layer of the brain near its surface, gradually spreading as the blood escapes, may force a passage through the cerebral substance and uplift the pia mater, or even break through this membrane and escape into the large cavity of the arachnoid.

The most common location of hemorrhages is the corpus striatum, thalamus opticus, and more rarely the white substance. They are also met with in the cerebellum and pons. Hemorrhages sometimes occur in several foci at different times, but are generally unilateral. When the quantity of blood is considerable, it breaks through into one or more of the ventricles.

Large extravasations occasion a tumefaction and softening of the cerebral mass, and a flattening of the convolutions of the hemisphere which is the seat of the lesion, to such a degree that the existence of the lesion may be suspected before making a section of the brain.

When the accident occurs only two or three days previous to death, the blood and clot are red, as also the walls of the focus. This is the most favorable time to study the condition of the vessels which surround the focus, and to investigate the direct cause of the hemorrhage. For this

the method of Charcot and Bouchard should be employed: the internal surface of the focus is carefully cleaned, the clot is removed, and the part so prepared is placed in water, which is renewed with care. After a few days of maceration, the cerebral substance is reduced to a detritus, which may be washed away by a small stream of water, leaving the vessels. These vessels are placed upon a glass slide and examined. Frequently there is found a ruptured aneurism, belonging not to a capillary, but to an arteriole, which explains the large amount of blood and size of the focus. Finally, there may be recognized, as Charcot and Bouchard have pointed out, a dilated, ruptured arteriole within a lymph sheath, also ruptured, and, in the interior of the arteriole, a fibrinous clot continuous with that of the focus—a most palpable proof of the cause of the hemorrhage.

The places of election for these aneurisms are, in the order of their frequency, the thalamus opticus, the corpus striatum, the cerebral convolutions, and the pia mater.

These small aneurisms, described as *miliary aneurisms* by Charcot and Bouchard, are, according to these authors, due to arterial sclerosis, particularly to periarteritis. They insist upon the point that hemorrhages are generally caused by miliary aneurisms and periarteritis, while, on the other hand, softening is most usually connected with endarteritis and atheroma. But it is to be remembered that the lesions of periarteritis and atheromatous endarteritis are very often united.

In every case of cerebral hemorrhage occurring in old persons, there are found, disseminated in the substance of the brain, miliary aneurisms, which in developing have excavated spaces in the white or gray substance.

A hemorrhagic focus, formed by the rupture of a large vessel, or by the union of several small foci, displaces the lacerated cerebral substance, the nerve fibres of which are broken. The wall of the focus is formed directly from the cerebral pulp; it is ragged and stained red by the blood.

If the patient does not die immediately after the accident, certain modifications take place in the hemorrhagic focus. The escaped blood undergoes the transformation that has previously been described: the fibrin coagulates, the fluid is gradually absorbed, and the coloring material of the blood passes into the state of red or yellow granules, which finally become brown, or form crystals of hæmatoidin. During this time, the wall of the focus becomes smooth; an abundant formation of new connective tissue springs from the elements of the neuroglia, and forms a true fibrous membrane, which is visible a month after the occurrence of the hemorrhage.

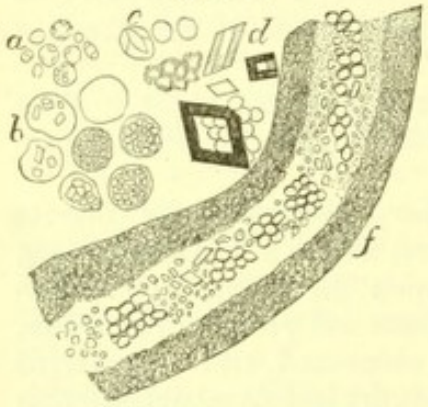
The isolated nervous elements undergo fatty degeneration, and the medullary substance is reduced to granules.

Secondarily there is produced an inflammation, which terminates in the formation of fibrous tissue in which are found fatty granules and granules of hæmatoidin. Thus the wall of a focus may have a considerable thickness, a structure which consists of connective tissue in the process of fibrous organization, and may inclose crystals of hæmatoidin, pigment,

and granular corpuscles. After four or five years, or longer, the focus contracts and forms a cicatrix, which sometimes does not show any trace of coloration, but most frequently presents numerous crystals of hæmatoidin. At times a cyst remains, filled with a lemon-colored fluid and limited by a fibrous membrane. These cysts are difficult to differentiate from similar cysts which are the result of softening, of which the method of formation will be later described.

In the majority of cases, the cerebral tissue surrounding the focus undergoes a series of modifications, which consist in the infiltration of the coloring matter of the blood between the nervous elements, and into the lymph sheaths. The latter now contain irregularly shaped red blood corpuscles, granules, and crystals of hæmatoidin. The granules and crystals are usually contained within the white corpuscles. It is to the existence of these granules infiltrating the cerebral substance or situated in the lymph sheath, that the nervous tissue in the proximity of the hemorrhagic focus owes its ochre color. This colored zone, varying in extent, is opaque, on account of the number of granular corpuscles it incloses and which are contained in the lymph sheaths. The granular corpuscles frequently contain pigment granules. These bodies are nothing more than lymph corpuscles loaded with the fatty granules, which come from the broken down nerve elements, and which enter the lymph passages.

Fig. 204.



Crystals of hæmatoidin. *a*. Red disks, becoming granular and losing their color. *b*. Neuroglia cells, a few containing granular pigment and crystals. *d*. Crystals of hæmatoidin. *f*. Occluded capillary; its lumen is seen filled with red granular pigment and crystals. × 300.

Cerebral Softening.—Cerebral softening may be the result of emboli, of an arterial thrombosis consecutive to atheroma, or of an obstruction to the arterial circulation caused by atheromatous or other lesions of the vessels, etc.

Embolic Softening.—Frequently, during the course of an attack of articular rheumatism accompanied with cardiac lesions, or in consequence of an atheromatous degeneration of the walls of the large vessels, there suddenly occurs hemiplegia. This accident is the result of an obstruction in one of the vessels of the brain by an embolus, the origin of which is to be found in the diseased heart or large vessels.

The left middle cerebral artery is more frequently obstructed than any other cerebral vessel.

The first phenomenon manifest in the parts which the vessel supplies is a stasis of the blood, followed by a more or less rapid fatty degeneration of the cells and nerve fibres. Notwithstanding the constancy of the histological lesions which characterize these successive changes, the altered part may present to the unaided eye very varied appearances.

In one variety, the elements simply undergo a slow fatty degeneration. The medullary sheath of the nerve fibres is segmented and transformed

into small fat drops. The nerve cells are altered and destroyed in a similar manner.

An analogous change occurs in the protoplasm of the neuroglia elements, which are transformed into true granular corpuscles. It has previously been shown that all granular corpuscles come from living cellular elements, especially white blood corpuscles, which absorb fatty granules. Therefore a nucleus is always found in these granular corpuscles, when treated with picro-carminate of ammonia.

Fig. 205.

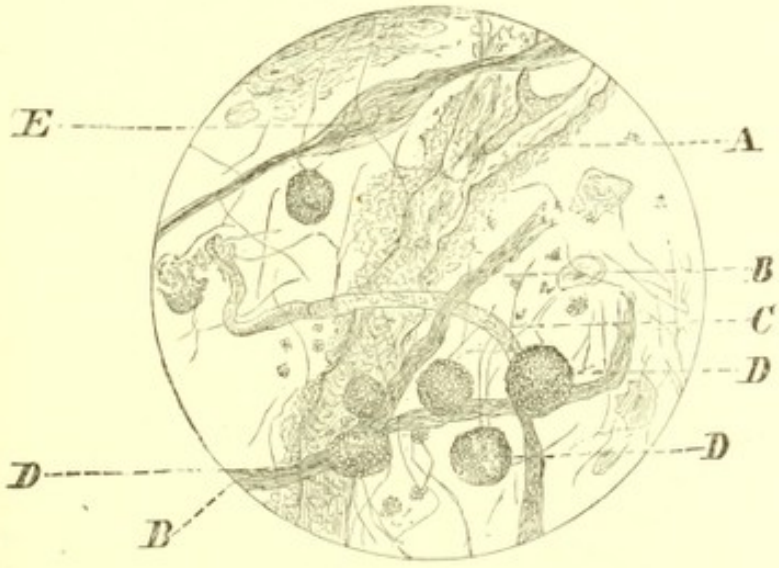


Chronic white softening of the brain; showing the granular corpuscles (corpuscles of Gluge), broken-down nerve fibres, and fat granules, of which the softened substance is composed. One or two nucleated cells (probably nerve-cells) are also visible. × 250. (*Green.*)

Finally, in the vessels filled with coagulated blood and fibrin, the blood pigment is precipitated, and the fibrin becomes granular. The vessels are now filled with fatty granules and pigment.

The repletion of the vessels fully explains why at the beginning of the process the diseased portion, when it is superficial, is tumefied and raised above the level of the surface of the brain. But so soon as the altered elements experience a true retrograde change, the infarctus becomes dry and slowly contracts. Frequently the fat is changed into margarin and stearic acid. These new substances are found as round bodies, which, from their opacity, resemble granular corpuscles; but examined with a high power, they are seen to be formed of numerous needle-shaped crystals united together.

Fig. 206.



Tissue change in softening of the central nerve substance. Diagrammatic. *A.* Vessel. *B. B. C.* Nerve tubes. *D.* Gluge's corpuscles (granular corpuscles). *E.* Swollen nerve tubes. Highly magnified. (*Hamilton.*)

The cerebral pulp, thus dried and collapsed, is yellowish white, opaque, and firm; but the solidity is only apparent, for, it is readily broken up

by a stream of water. This variety is especially met with in the infarcti, located in the cerebral substance near the surface of the brain.

The second variety of transformation of infarcti is characterized by a grumous softening of the centre of the diseased part, especially seen in the white substance of the brain. There occurs a true liquefaction of the centre of the infarctus, forming a cavity, with irregular walls, filled with a whitish fluid resembling chalk and water. From the internal surface of the cavity project numerous filaments, which float in its interior, and which are formed from the débris of the vessels that have resisted degeneration. If the wall of the softened focus is examined, there are found the detritus of the nervous elements and some granular corpuscles. The vessels themselves are covered with the same fatty granules; by shaking in water, their surface is freed from this granular débris, and the following peculiarities are observed. They are empty or filled with blood or a yellow granular mass. The lymph sheath surrounding them is dilated, generally in a very irregular manner. In the interior of the sheath are seen cells loaded with pigment and fatty granules (granular corpuscles), and the detached or partly adherent endothelial cells also contain a few fat granules.

The softened foci may cicatrize by a process similar to that described for the apoplectic foci.

A portion of the fluid is absorbed, the elements of the neuroglia which surround the focus undergo proliferation, and there is formed a limiting membrane varying in thickness, in which are seen many vessels. Finally, after one or two years there is found a true cyst, filled with a transparent serous fluid; the walls of which differ from those which are caused by apoplectic foci in not containing a notable amount of blood pigment.

The infarcti which involve only the surface of the convolutions, present analogous modifications, but less marked. Sometimes they become softened and are transformed into a soft, diffluent patch, presenting a peculiar yellow color, suggesting the presence of hæmatoidin, although no trace of it can be found.

A small stream of water is sufficient to completely break down these yellow patches. The size of a patch may be so large as to extend over the entire surface of a cerebral lobe. Sometimes they are dried and sunken, and appear hard. But the resistance is only apparent, for they may be disintegrated by a small stream of water. The cerebral convolutions stretched, flattened, and yellow, still retain a form which recalls their normal appearance.

Softening from Atheroma and Arterial Thrombosis.—It is generally the result of atheromatous disease of vessels, beginning usually in the arteries at the base of the brain. The endarteritis causes a narrowing of the calibre of the vessels, and the blood stasis which then results, occasions necrosis of the cells and nerve fibres. Sometimes the irregularities of the internal surface of the atheromatous arteries, also determine the formation of thrombi which obstruct the vessel. This takes place, for example, in consequence of an acute or chronic endarteritis of one of the arteries at the base of the brain, when prominent elevations or vegetations project into their lumen. These vegetations may separate from the wall of the vessels, and, carried along by the circula-

tion, become the cause of coagulation of the blood in the vessels they partly obstruct. The lesions of the cerebral substance in these cases are similar to those in an infarctus, only here the disease of the walls of the vessels is primary.

When the lesion is recent there is observed a superficial softening of a pink color, involving perhaps a group of convolutions; if the changes are more chronic *yellow*, *soft*, or *hard*, dry and sunken *patches* are present. In chronic softening of the convolutions, their form is preserved, although they are atrophied in the highest degree. The pia mater is œdematous over their surface, and fills up the loss of substance caused by the atrophy.

As in old embolic infarctions, softening from atheroma is often manifested in the central portion of the brain, by a focus filled with a serous fluid, or a fluid resembling chalk and water. The histological lesions are the same as in an infarctus.

ENCEPHALITIS.—Encephalitis, or inflammation of the brain, occurs in the form of diffused or circumscribed inflammatory neoplasms; the latter constituting abscesses of the brain.

The brain substance is sometimes red, when the change is described as *red inflammatory softening* by some authors; again it is yellow, due to the abundance of pus corpuscles, this is the white or *yellow softening* of authors. The histological process of inflammation of the brain, has been experimentally studied by Bouchard and Hayem. They produced the disease by the direct action of foreign bodies or chemical substances upon the cerebral tissue. They affirm that in inflammatory softening there exists a proliferation of the cellular elements of the neuroglia. It is, however, very probable that some of the new cellular elements are white blood corpuscles from the bloodvessels. The new elements are collected into masses, varying in size. Accumulations of new elements also are found in the lymph sheath, between its limiting membrane and the wall of the bloodvessels. These elements are nothing more than white blood corpuscles accumulated in the lymph system.

At the same time that the neuroglia participates in the inflammatory new formations, the nerve elements undergo fatty degeneration.

The inflammatory process studied by experiments, is similar to primary acute inflammation. This may terminate either in an abscess or softening of the cerebral substance. The color of the softening may be either yellow, whitish, or red, due to hemorrhages in the lymph sheaths, or to intense congestion of the capillaries.

Subacute inflammation of the brain may be idiopathic, and at the beginning occupy the centre of a hemisphere. It may also develop spontaneously in the fœtus and new-born children, a form described by Virchow as *diffused congenital encephalitis*.

In this lesion, according to Virchow, the cellular elements of the neuroglia, first proliferate and undergo fatty degeneration. The nervous elements also become granular. There results an abundant production of granular corpuscles, and a true softening, to which capillary hemorrhages give a pink or red color. But these statements do not seem conclusive, and the appearance may be simply due to the normal fœtal con-

dition of the brain. In the fœtus, as in old persons, the vessels of the brain present granular corpuscles upon their surface and in their adventitious sheath.

Encephalitis is observed upon the surface of the convolutions in tuberculous meningitis and in diffused meningo-encephalitis (general paralysis of the insane).

In *tubercles of the meninges*, the surface of the convolutions, especially at the base of the brain, shows considerable congestion with proliferation of the neuroglia, followed with softening. These facts are easily demonstrated, and the lesion should not be confounded with localized œdema of the base or fornix, which is due to pressure upon the veins of Galen.

Diffused meningo-encephalitis is characterized by several lesions, which united occasion a peculiar softening of the surface of the convolutions, readily seen with the unaided eye.

The pia mater and the vessels, which are imbedded in the gray substance, are thickened by the increase of their cellular elements. The membrane is separated from the brain with difficulty, carrying with it pieces of the gray substance, which adhere to the thickened walls of the vessels. These are frequently congested, and there is found in the lymph sheath surrounding them red or yellow pigment, the result of a destruction of the red blood corpuscles escaped into the sheath. Finally, the brain tissue presents the alterations previously described—multiplication of the elements of the neuroglia, degeneration of the nervous elements, and softening of the gray substance. These lesions are limited to the cortical layer or gray substance of the convolutions, which may be easily removed by scraping, when the white substance is seen distinct and firm beneath the softened gray substance. The white substance has even been considered more dense than normal, due to an increase in the neuroglia. The entire surface of the brain is implicated in the disease, and the ependyma ventriculorum is also altered and thickened.

Frequently there exist small transparent granulations, visible to the unaided eye, prominent upon the surface of the ependyma of the ventricles, particularly the fourth ventricle. These granulations consist of embryonic elements traversed by a few capillary vessels.

The nerve cells are atrophied, but the successive lesions, described by Meschede as occurring in them, consisting first in the granular state, then pigmentation, and finally atrophy, seem very doubtful. It cannot be said that they do not exist, but it is very difficult to define them, since the physiological state of these cells varies according to age, sex, etc., even in the same person.

Abscess of the Brain.—Abscess of the brain occurs in purulent infection, whatever may be its cause, and in traumatisms.

It may also supervene in consequence of osteitis and necrosis of the bones of the cranium, especially in tuberculous osteitis of the petrous portion of the temporal bone and syphilitic necrosis of the frontal bone. The abscess is connected with the purulent focus of the diseased bone, or it is developed near the focus without any direct communication with

it; the dura mater, for example, may remain intact between the abscess in the brain and the diseased bone.

Abscesses of the brain are generally small in size, and are formed by the same process as in other organs. They may be single or disseminated in great numbers throughout the cerebral substance. They are characterized by a yellow fluid, sometimes ropy and viscid, containing numerous cellular elements, and inclosed in a cavity with irregular walls. We have observed several abscesses of the brain in which the fluid was ropy, mucous, and contained granules of mucin not acted upon by acetic acid, and very similar to mucous saliva. The walls may thicken by the formation of connective tissue elements and become fibrous. They at times discharge externally, or open into one of the ventricles, or remain as purulent cysts. Abscesses, the size of a hen's egg, have been found after death, never having caused pain during life, or a trace of cephalalgia.

Chronic Encephalitis or Sclerosis.—Frequently primary in the brain, this lesion may also follow an analogous alteration which began in the spinal cord. Two distinct periods or stages may be admitted as characterizing its evolution.

In the first stage, the rapid multiplication of the elements of the neuroglia gives to the cerebral tissue a soft consistence, almost gelatinous, similar to that seen in tissues composed of embryonic elements.

The second stage is remarkable for the atrophy of the new elements, and the development around them of numerous fibrils, which are extremely fine and interlace in every direction. Thus, the cerebral tissue is hard, resisting, and if examined with high magnifying power the fibrils are seen to form a true network, in the midst of which are found atrophied nervous elements and small round or oval nucleated cells.

In the same brain both stages of the disease may be found.

Idiopathic sclerosis of the cerebrum and cerebellum is met with in idiots, cretins, and sometimes in epileptics; most frequently the lesion is then localized.

When the disease involves only one or two of the cerebral convolutions, they are at first found turgid, semi-transparent, soft and gelatinous to the touch; later they are small, not prominent, and so hard that the nail can barely indent them.

This sclerosis almost exclusively invades the convolutions. There is seen a lesion of the nerve cells in the convolutions, which we have several times noticed; it consists in a very evident removal of pigment from them. The cells are absolutely free from pigment, and transparent, a little atrophied although they preserve their angular shape. When the lesion is very chronic, and the tissue very hard, the nervous elements, both cells and fibres, are nearly all atrophied or have completely disappeared.

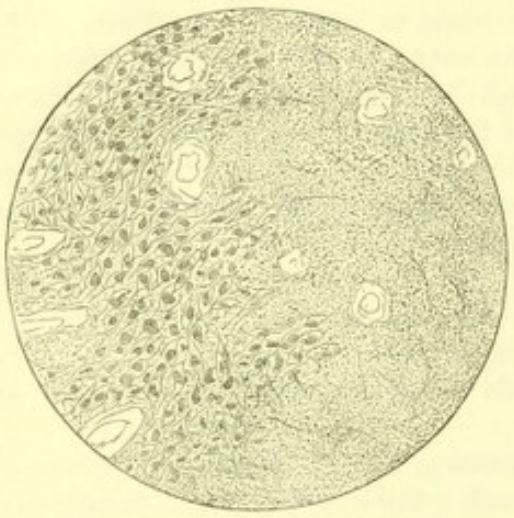
There almost always constantly exist, in sclerosis of the brain, upon the surface of the atrophied convolutions and in their substance, numerous disseminated corpora amylacea.

Finally, with sclerosis may be classed the lesions of the brain, occurring around cerebral tumors and particularly large tubercles. There occurs a new formation of embryonic tissue which atrophies and is replaced by fibrils, exactly as in the second stage of sclerosis. Chronic

encephalitis is seen as a concentric zone, frequently of considerable thickness, surrounding cerebral tumors.

Tumors of the Brain.—*Sarcomata.*—These occur in two distinct varieties, the same as in the meninges. The neuroglia sarcoma (glioma), and the angiolithic sarcoma (psammoma). (See pp. 83, 85.)

Fig. 207.



Sarcomata of brain. Figure shows the boundary between the nervous tissue and the sarcomatous growth, sarcomatous growth to the left. High power. (*Hamilton.*)

Fibromata.—Fibromata of the brain are rare. We have had the opportunity of studying one, which was located in the white substance of the right cerebral peduncle. It was extremely hard, and composed of fine waving fibrils, not changed by acetic acid, and small nucleated cells.

A *lipoma*, part of which was ossified, has been reported by Benjamin.

Carcinomata seldom occur in the brain; sarcomata have frequently been confounded with them.

We have observed a *papilloma* of considerable size situated upon the ependyma of the third ventricle, and projecting into the lateral ventricles through the foramen of Monro. This budding mass, engorged with a milky juice, surrounded by softened cerebral tissue, could have been mistaken for a carcinoma. It consisted of a cauliflower-like growth, formed of vessels more or less dilated, covered with pavement cells, which in desquamating gave to the fluid its milky appearance.

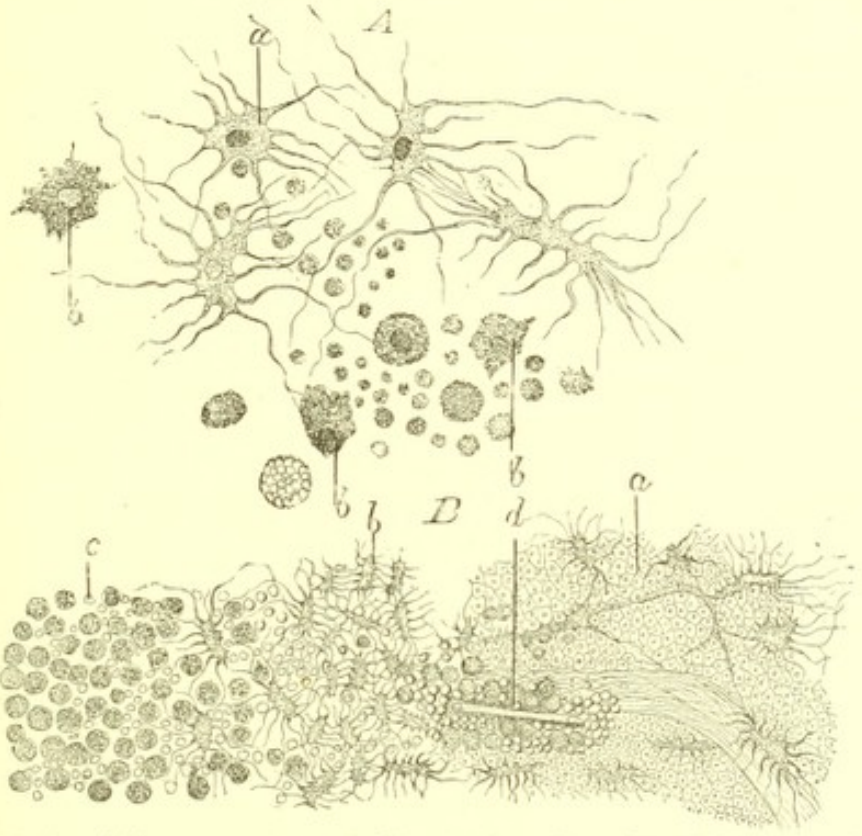
[*Syphilitic alterations* of the bloodvessels in the brain have already been mentioned (see p. 331). Charcot and Gombault describe a syphilitic lesion of the brain substance which essentially consists in the formation of disseminated or confluent small nodules, either upon the surface or in the depth of the nerve centres. These nodules usually present three zones, the histological characteristics of which will be understood by reference to fig. 208. The initial lesion seems to affect the connective tissue corpuscles of the neuroglia. They first hypertrophy, then either fatty degenerate and disappear, or, after the irritative hypertrophy has reached its acme, the progressive alterations common to irritated connective tissue elsewhere may supervene, viz., cicatricial contraction, etc. These authors are not positive whether there is an actual new formation of branched cells of the neuroglia, but they declare that such cells are present in greatly increased numbers.]

Tubercles.—In external appearance, tubercles of the brain resemble sarcomatous formations. Instead of being small, like tuberculous granulations of other organs, they may attain the size of a pea or even that of the fist.

Their external characters are generally marked. They are hard, compact, and so blended with the brain tissue that it is not possible to enu-

cleate them. By making a section through their centre including the surrounding tissue, it is seen that the centre is yellow and soft, and that their peripheral layer gray and semi-transparent is directly continuous with the cerebral tissue. The portion of brain which surrounds the

Fig. 208.



Syphilitic lesion of the nerve centres. *A*. Elements from *B*. *a*. Branched cells, much enlarged, belonging to the neuroglia. *b*. The same elements fatty degenerated. *B*. Portion of a thin section through a small syphilitic nodule in the cortex of the brain. *a*. External zone nearly normal, in which enlarged ramified cells are scattered among the nerve tubes. *b*. Middle zone, almost exclusively constituted by large branched corpuscles mixed with a few round cells. *d*. Bloodvessel, partly covered by a mass of granular cells. *c*. Central portion of nodule, consisting of round granular cells.

tubercle, presents all the stages of active neuroglia proliferation. Large cells with several nuclei, as well as changes of the vessels are met with. If a vessel running into a tubercle is carefully examined, its lymph sheath is found filled with numerous embryonic elements, united together by an intercellular substance, when it is yet in the midst of normal nervous elements. As soon as it penetrates the gray, semi-transparent zone of the tubercle, the sheath suddenly dilates, and the entire vessel appears three times its normal size. Reaching the central part of the tubercle, it is lost in a mass of granulo-fatty degeneration.

Throughout their whole course in the tuberculous mass, the vessels are obstructed by fibrin.

Tubercle of the brain may appear as a single tumor. Very often tuberculous granulations, disseminated or in groups are seen at their periphery.

An examination of cerebral tubercles with the microscope reveals the same characters, the same arrangement of structure, as found in tubercles

of other organs: small cells united by a granular substance, vessels obliterated by fibrin, granular degeneration of the elements in the central part of the tumor, etc.

Neuromata.—Medullary or ganglionic neuromata, that is, tumors consisting of nerve cells and neuroglia, have been seen upon the surface and in the substance of the brain. (See page 137.)

Cysts.—These often develop from the vessels of the choroid plexus; they are serous and transparent. It has already been seen that cysts may result from softening of a hemorrhagic focus, or of an area of infarction.

Sect. III.—Pathological Histology of the Spinal Cord.

Congestion.—Congestion of the spinal cord occurs during congestion and inflammation of the spinal meninges, in typhoid fever, in some cases of rheumatism, in febrile diseases, and in chronic lesions of the heart. It is characterized by distension of the vessels. Schröder van der Kolk has advanced the opinion that, in every case of epilepsy, the medulla oblongata is congested; but this has not been sufficiently established by observations.

Hemorrhage.—This lesion is very rare comparatively to that of the brain; however, it is sometimes met with, and is characterized by an extravasation of blood into the gray substance. The hemorrhage is usually seated in the gray centres of the cord, and it may extend some distance (15 centimetres, Liouville).

According to Charcot and Hayem, this lesion is always consecutive to myelitis.

Softening.—A softening which follows an arterial embolus or an atheroma of the vessels of the spinal cord seldom occurs; the lesion is limited to a region of the organ varying in extent.

The color, consistence, and structure of the softened portion vary exactly in the same manner as in the several forms of cerebral softening studied above, so that a minute description is not necessary. Sometimes the softened part is diffluent, whitish, and opaque, giving upon section a milky fluid; or it may be dry, yellow, shrunken, and atrophied; the hardness is only apparent, for a small stream of water causes a separation of the elements, which, mixing with the water, give to the latter a milky appearance. In both cases there are found, by microscopic examination, as in the brain, numerous granular corpuscles coming from the granular destruction of the medullary substance of the nerve fibres, as well as altered vessels the lymph sheath of which is filled with the same elements.

Softening of the spinal cord is very frequently seen in cases of compression by a tumor of the spinal meninges, by an osseous tumor or by chronic affections of the vertebræ, as in Pott's disease of the spine. It may also be caused by a disease of the brain, which has destroyed a large portion of a cerebral hemisphere.

Secondary Degeneration of the Spinal Cord.—Whenever a focus of softening or hemorrhage of any extent exists in the corpus striatum, in the thalamus opticus, or upon the surface of the convolutions, the white fasciculi which go from this part to the periphery undergo atrophy with fatty degeneration of the medullary substance.

The cerebral peduncle of the diseased side is gray and atrophied; the pyramid shows the same atrophy and change in color, so that the olivary body is more prominent upon this than upon the opposite side.

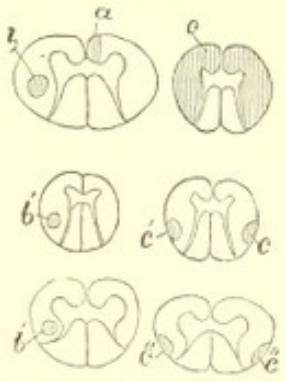
After the decussation in the pyramids, it is the side opposite to the cerebral lesion, and in the lateral columns of the spinal cord, that the changes of the nerve fibres are continued to a varying extent.

The softened portion of the lateral column is confined to its most posterior region. (See b, b', b'', fig. 209.)

It is in hemorrhages or softening of the corpus striatum, accompanied with destruction of the internal capsule, that these secondary descending lesions of the spinal cord are most marked.

When the secondary degeneration is considerable, it may be recognized, upon section of the fresh cord, by the unaided eye. In the areas above mentioned the white substance has become gray or yellow in color. But generally, in order to localize the seat of degeneration, it is necessary to harden the cord and examine it microscopically.

Fig. 209.



Secondary degenerations of the spinal cord. b, b', b'' were obtained from a case of an old lesion of the right hemisphere. The shaded portions indicate the location of the secondary degeneration. b. Location of the alteration in the left lateral column of the cervical region. b'. The same lesion in the dorsal region. b''. The same lesion in the lumbar enlargement. The three preparations c, c', c'', show sections of the spinal cord in the dorsal and lumbar region below a point where the marrow was completely destroyed by compression, the shaded parts represent the location and extent at the descending degeneration.

Preparations made from the fresh cord show, in these areas, numerous granular corpuscles possessing a nucleus, elements which are free or contained in the lymph sheaths, and an atrophy or almost complete disappearance of the nerve fibres. In cases where the disease could be traced back for a considerable time, the granular corpuscles were found to be less numerous, and there existed a greater number of neuroglia cells, or embryonic cells, than in the normal condition; there was, in a word, chronic inflammation of the spinal cord in these regions.

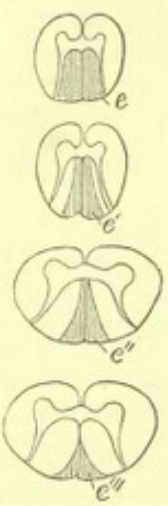
When the spinal cord is injured by the pressure of a tuberculous, carious, displaced or destroyed vertebra in Pott's disease, there generally follows a very complex process.

Suppuration and chronic inflammation of the tissues which surround the diseased vertebræ and spinal meninges are always present. Tuberculous granulations of the meninges are sometimes seen. These inflammations and irritations by contiguity of the spinal cord explain the fact of the great frequency of softening in Pott's disease of the spine, while in

the greatest displacements of the vertebral column caused by rachitis, the spinal cord remains intact because the spinal meninges are normal.

In Pott's disease of the spine, and in all tumors either of the vertebræ or the membranes of the spinal cord, which occasion an inflammation of the meninges and a softening of the cord, the latter is softened, whitish and opaque, or yellowish, for a space corresponding to the size of the tumor.

Fig. 210.



Ascending degeneration of the posterior columns of the spinal marrow in a case of compression of the cord at the lower portion of the dorsal region. *e*. Lesion of the posterior columns in the dorsal region above the point of compression. *e'*. Lesions above less extensive. *e''*, *e'''*. Lesion less and less extensive in proportion as the cervical region is traversed.

When the spinal cord is thus destroyed in a segment, the parts of the spinal cord situated above and below undergo changes which, according to the investigations of Türck, Bouchard, and ourselves, seem to be constant. They are as follows:—

The posterior columns show a secondary degeneration almost throughout their entire extent (see fig. 210) above the point of softening, while below only the lateral columns experience a change (see fig. 209, *c*, *c'*, and *c''*); the alteration consists in fatty degeneration of the nerve fibres, in their atrophy, and in the presence of numerous granular corpuscles.

The extent of the lesion in the posterior columns gradually tapers, as one ascends the cord, so that it terminates in a thin filament in the middle and posterior part of the posterior column. (Fig. 210, *c*, *c'*, *c''*, and *c'''*.)

The lesions in the anterior columns terminate also in the same manner as one descends the cord; their seat is nearly the same as that of degeneration consecutive to a destruction of a hemisphere, that is, the posterior part of the lateral columns.

A sarcoma which we saw in the nerves of a horse's tail, had compressed and degenerated the nerves at the point of the tumor; in this case the posterior columns of the cord had undergone a similar degeneration throughout its entire length. (Fig. 211.)

What is the cause of secondary degenerations ascending in the posterior columns and descending in the lateral columns? It is certainly connected to the circumstance that divided nerve fibres become granular in the part separated from their nutritive centre. The experiments of Waller have shown that if the motor nerves or anterior roots of spinal nerves are divided, their peripheral portions degenerate, while the central ends preserving their connection with the nerve cells of the anterior cornua of the spinal cord, remain normal. The same experimenter has shown that the lesion of nerves pursues an opposite direction when the posterior roots are divided; the part of the roots remaining in connection with the cells of the spinal ganglia is normal, while the sensitive root which penetrates the spinal cord becomes granular.

Thus, the changes which are seen in the nerve fibres of the spinal cord, in these cases, are explained by a separation from their trophic

cells. But there still remains much obscurity about this question, especially in relation to the course of the nerve fibres in the spinal column.

The results of physiological experiments made by Vulpian to elucidate this question do not agree with those given by pathologists. He did not succeed in producing ascending and descending lesions of the spinal cord in guinea-pigs or pigeons by the destruction of a segment of the spinal marrow.

In the disease which will be described as *sclérose en plaques*, in which the gray centres and white columns of the spinal cord are irregularly destroyed, secondary degenerations of the nerve fibres are never seen.

Vulpian concludes that the secondary degeneration is not solely due to the separation of the nerves from their cells, but he believes that the change is due to the persistence of the irritation.

Finally, when an examination of the spinal cord is made, from persons who have previously suffered amputation of the thigh, or from animals which have had the sciatic nerve divided, the secondary lesions of the spinal cord may occur not only in the posterior white columns, but also in the anterior columns and in the cells of the anterior cornua. (Vulpian.)

Fig. 211.



Secondary degeneration of the posterior columns of the spinal marrow in a case of compression of the nerves of a horse's tail. *d*. Lesions of the posterior column of the low part of the lumbar enlargement. *d'*. The same lesion at the upper part of the lumbar enlargement. *d''*. Lesion in the dorsal region. *d'''*. The same lesion in the cervical enlargement.

MYELITIS.—Under this name may be described a series of very different pathological states, in which there exists acute or chronic inflammation of the several elements of the spinal cord. By the term *myelitis* is understood not only true inflammations, characterized by the formation of new elements, embryonic cells, white blood corpuscles or pus corpuscles scattered between the elements of the cord, but also increase of the elements and thickening of the neuroglia, known as *sclerosis*. Certain atrophies of the nerve elements, which constitute the only lesions found at the autopsy, are likewise dependent upon inflammation.

Acute suppurative myelitis may occur in epidemic spinal meningitis, or in consequence of ulcerations of the sacrum which involve the spinal dura mater. The myelitis is then superficial and consecutive to the meningitis.

In some cases of gangrenous ulcerations in the insane, the puriform exudations, the inflamed membranes, and even the surface of the spinal cord, assume the characters and odor of gangrene. This lesion may extend as far as the medulla oblongata, pons, and inferior part of the brain.

Metastatic abscesses may occur in the spinal cord from purulent infection, as they do in all other organs.

Simple acute myelitis, non-suppurative, is at times diffused, involving a considerable extent of the axis of the gray substance of the spinal cord (central myelitis); sometimes it is localized. The histological lesions in

both varieties are the same as in encephalitis. The medullary substance is softened; its color is whitish, pink, yellowish, or chocolate, depending upon the congestion of the vessels, and numbers of red corpuscles escaped into the softened part. Points of ecchymoses and distended vessels may sometimes be seen with the unaided eye. By microscopic examination there are found granular nerve fibres, numerous white blood corpuscles, some normal others filled with blood pigment, fatty granules, and granular corpuscles. The same elements exist in the perivascular lymph sheaths.

This form of myelitis, when it is diffused and general, extends for some distance from the central mass of the spinal cord, and, according to Charcot and Hayem, it is in these cases that hemorrhages of the spinal cord occur. It is certain that in the cord as in the brain, softening may be the cause of hemorrhages, but it is difficult to decide which is the primary lesion, for primary hemorrhages also occasion a softening of the tissue and infiltration of the neighboring tissue with white blood corpuscles, pigment, and granular corpuscles. This variety of the disease is rapidly fatal. Localized myelitis may present further modifications, such as complete degeneration, separation, and atrophy of the parts where the lesion is located, in which case it exactly resembles limited chronic softening.

The lesions described as characteristic of myelitis, the importance and nature of which have not yet been determined, are:—

1st. Hypertrophy and varicose condition of the axis cylinder of the nerve fibres, observed by Frommann in sclerosis, afterwards verified by several authors; Charcot has seen this condition of the axis cylinders in recent acute myelitis.

2d. A colossal hypertrophy of the cells in the anterior cornua of the spinal cord, observed by Charcot in the same conditions, and appearing to be due to the same cause.

3d. Foci of granular degeneration, described by Lockhart Clarke, consisting in irregular masses, which seem to come from a coagulation of albuminous fluid containing granules. These masses are contained in irregular cavities excavated in the spinal cord. As these cavities are seen especially after hardening the cord in chromic acid, and as, on the other hand, the least traction is sufficient to tear the medullary fibres, it seems to us probable that they are produced artificially.

4th. The numerous and excellent works, which have recently been published in France by Charcot, Vulpian, and their pupils, Prévost, Joffroy, etc., demonstrate that there exists an atrophy of the cells and of the anterior cornua of the spinal cord, in infantile paralysis, in general spinal paralysis of the adult (Duchenne), and in progressive muscular atrophy. Charcot is inclined to believe that this atrophy is due to a primary myelitis, limited to certain groups of cells in the anterior cornua, which opinion has been adopted by Dujardin-Beaumetz. Laborde, Roger, and Damaschino, regard infantile paralysis as caused by a myelitis with proliferation of the cellular elements of the neuroglia. These very interesting observations do not, however, seem to us sufficient to establish in a positive and definite manner the pathological anatomy of the preceding diseases.

Interstitial Myelitis or Sclerosis.—In this variety of myelitis the cel-

lular elements of the neuroglia are increased, this tissue is thickened and the nerve fibres are secondarily atrophied. The lesion occurs frequently in the spinal cord, and is limited to certain regions, giving rise to special symptoms depending upon the location of the disease.

Thus *sclerosis of the posterior columns* is the anatomical lesion of progressive locomotor ataxia; *disseminated sclerosis* (sclérose en plaques) irregularly distributed corresponds to paraplegias, with contraction or relaxation of the limbs, and tremblings, etc. Sclerosis has been found localized in the lateral columns alone, *lateral sclerosis* (*sclérose rubanée*), and upon the surface of the spinal cord in consequence of a chronic meningitis (*sclérose annulaire*).

Fig. 212.



Posterior spinal sclerosis. (After Charcot.)

Sclerosis of the Posterior Columns.—The *gray degeneration* of the posterior columns seen in all cases of progressive locomotor ataxia, is characterized macroscopically by a gray color and a peculiar translucency of the posterior columns. The pia mater is almost always thickened, and very closely adherent to the diseased portions of the cord.

Two different stages may be distinguished in the course of this alteration.

At the beginning there exists an increase in the number of the neuroglia elements, and the diseased parts appear slightly tumefied; in the second stage there is atrophy of the cellular elements of the neuroglia, thickening of its fibrous tissue, and atrophy of the posterior columns.

A small portion of the semi-transparent gray substance of the diseased part prepared from a fresh cord, after teasing in water, presents in the first stage numerous embryonic elements possessing a round or an oval nucleus. These cellular elements are imbedded in an amorphous granular substance. The nerve fibres are preserved, as also are the nerve cells in the anterior and posterior cornua. The vessels in the diseased region have their lymph sheaths dilated, and filled with granular lymph corpuscles.

Thin transverse sections of the cord, studied microscopically, show the antero-lateral columns healthy, and the posterior columns altered. In the former, the nerve fibres are seen to be regularly separated from each other by their partitions of neuroglia and by the vessels. The neuroglia presents at intervals a few small cellular elements.

In the posterior columns, the nerve fibres vary in diameter, some are very small, although still retaining their axis cylinder and sheath of medullary substance; others are normal in size, or larger than in health, and their axis cylinder may be considerably hypertrophied. Between the nerve fibres, the neuroglia presents linear or round collections of small elements, the nuclei of which are alone visible.

Longitudinal sections of the spinal cord, where we are able to compare

the posterior columns with the anterior columns, show the same histological details.

In a more advanced stage of the disease, the posterior columns are fused together by the formation of new connective tissue in the pia mater, which, in the normal condition dips into this fissure, and separates them one from the other. This connective tissue acts as cicatricial tissue, and intimately unites the two columns which previously were only in contact with each other. From this fusion as well as from the considerable atrophy which all the nerve fibres undergo, there result a very notable atrophy and shrinking of the entire posterior columns, so that the posterior cornua of the gray substance are brought nearer together. (See fig. 212.)

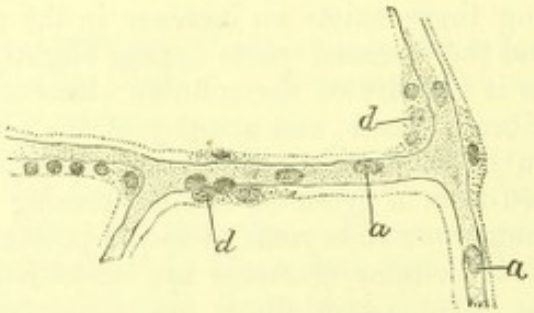
Fig. 213.



Sclerosis of Spinal Cord. A transverse section, showing much increase of the neuroglia between the cut ends of the nerve-fibres. × 200. (*Green.*)

Transverse sections show that the nerve fibres are separated by a tissue which with low power appears granular, but with higher power it is found composed of very fine interlacing fibrils, with a few oval atrophied nuclei at intervals. The nerve fibres are thin, but their axis cylinder always exists. By some authors it is maintained that the nerve elements have disappeared when the sclerosis has reached this stage; but

Fig. 214.



Appearance of capillary bloodvessels in an early stage of sclerosis. *a*. Neuclei of endothelia, which are not much altered. *d*. Increase and proliferation of the pervascular cells. High power.

they are always present, and may be demonstrated in sections colored with carmine; when the lesion is far advanced, the fibres may be reduced to their axis cylinder, the medullary sheath having entirely disappeared.

A peculiarity of these scleroses consists in a thickening of the walls of the capillaries and small vessels. This thickening is due to a proliferation of the elements which constitute their walls; they become rigid, and their calibre is diminished. At the same time, numerous corpora amylacia are observed in the neuroglia, alongside of the vessels and especially beneath the fibrous membrane of the pia mater.

The pia mater covering the posterior columns also participates in the chronic inflammation; it is thickened, and becomes closely adherent to the spinal cord.

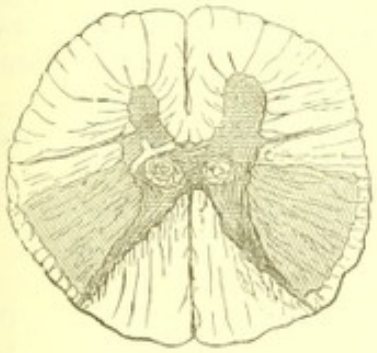
The posterior roots of the spinal nerves have become transparent, and so small, that, instead of being double the size of the anterior roots, as

they are in the normal condition, they are only half the size, or even less.

In locomotor ataxia, the lesion is not always limited to the posterior columns; it sometimes encroaches a little upon the contiguous cortical portion of the lateral columns.

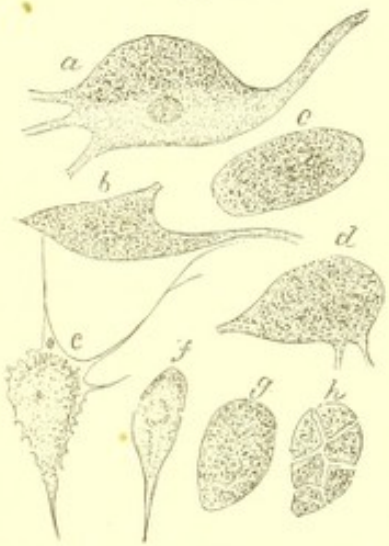
It is generally in the lumbar region that the lesion of the posterior columns is oldest and most advanced; the dorsal and cervical regions are usually less diseased. The tubercula quadragemina, the optic tracts, and the optic nerves themselves may be atrophied, grayish, and semi-transparent; at times, even the hypoglossal nerve may present the same lesions.

Fig. 215.



Antero lateral sclerosis. (*Charcot.*)

Fig. 216.



Isolated ganglion cells of the spinal cord, showing the various stages of degeneration. *a*. Normal nerve cell, with its prolongations and nucleus. *e*. A nerve cell still showing its branches, but the latter are atrophied, and the body of the cell is so filled with colored granules that the nucleus cannot be seen. *b, f, d*. Nerve cells still more altered. *c. g*. Nerve cells more altered; they have lost their prolongations. *h*. A nerve cell in the last stage of degeneration, the granular element is breaking up into small fragments. High power.

The symptoms of locomotor ataxia may be due to a lesion confined entirely to the posterior columns. In an observation made by Pierret, these columns were only altered in close proximity to the posterior cornua.

The cells of the spinal ganglia, and those of the gray centres of the spinal cord, appear absolutely normal in the majority of cases.

With respect to the white columns of the cord, *disseminated sclerosis* (sclérose en placques) and *lateral sclerosis* (sclérose rubanée) are histologically identical with the above-described lesion, the only difference being the parts involved. [In lateral sclerosis, in disseminated sclerosis, in progressive muscular atrophy, and in some other spinal lesions, the nerve cells of the gray cornua are either primarily or secondarily involved. Some of these nerve-cells undergo a cloudy swelling, which is succeeded by pigmentation, and granulo-fatty degeneration. The final result

may be a marked atrophy of these elements or they may break up into small fragments and totally disappear. (See fig. 216.)] The connective tissue surrounding the central canal, in the majority of cases of sclerosis, is in a state of proliferation, and the canal itself is filled and distended with epithelial cells.

In *tetanus*, Demme has described lesions similar to those of sclerosis, disseminated throughout the entire spinal cord. Michaud recognized analogous appearances—in particular, a hypertrophy of the neuroglia elements which are found in the gray commissure surrounding the central canal. Our examinations of analogous cases showed only a normal condition in this location.

TUMORS OF THE SPINAL CORD.—Tumors of the spinal cord very seldom occur, and, when met with, are generally located upon the meninges. They do not differ from tumors of the brain and cerebral meninges. Lancereaux has reported a *fibrous tumor*, developed in the central canal, occupying a part of its length. We, also, have seen a small fibroma developed in the pia mater of the spinal cord.

Glioma and psammoma may occur in the spinal meninges; tubercles also are met with in the same structures.

In the inferior part of the spinal canal, frequently in old persons, the arachnoid and pia mater present calcifying and ossifying patches.

PART III.

DISEASES OF ORGANS.

SECTION I.

RESPIRATORY APPARATUS.

CHAPTER I.

NORMAL HISTOLOGY.

The respiratory apparatus consists of a system of ramified passages, which terminate in the lungs, an arrangement something like the ducts of acinous glands. The different parts comprise the *larynx*, the *trachea*, the *bronchi*, and the *air vesicles*. The mouth and the pharynx appertain more particularly to the digestive apparatus, and their lesions will be considered under that head. The nasal fossæ, however, may be properly reckoned as a part of the respiratory apparatus.

Several portions of the *nasal fossæ* present a difference in structure. The anterior entrance bristles with hairs stiff enough to arrest small foreign bodies suspended in the air, and is covered with a stratified pavement epithelium. The nasal fossæ, properly named, are lined by the *Schneiderian membrane*.

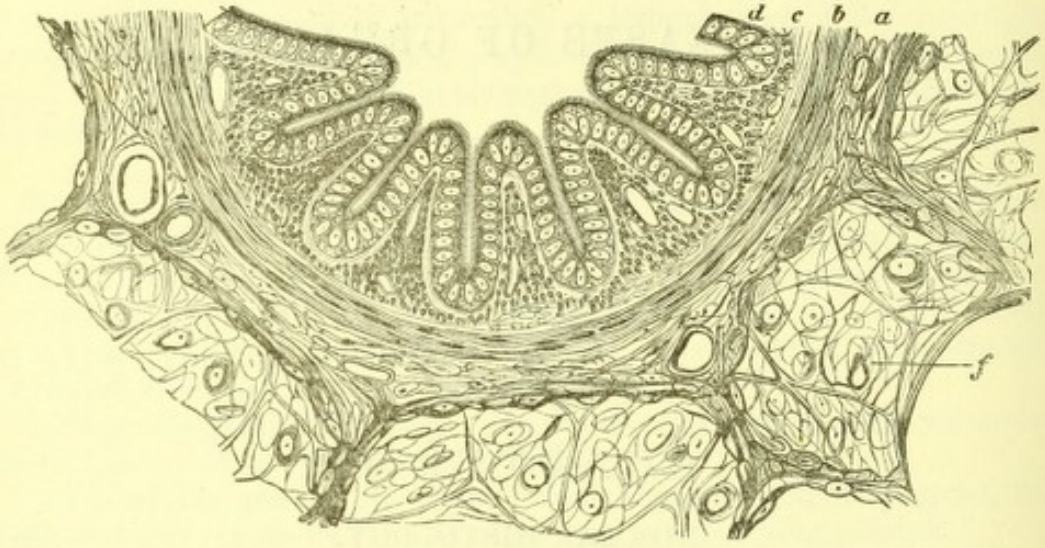
The *Schneiderian membrane* possesses over its entire surface a ciliated cylindrical epithelium, and, throughout the greater part of its extent, is thick and very vascular. Moreover mucous glands are imbedded in it, and empty upon its surface. The olfactory region is especially remarkable for the termination of the olfactory nerves. In this region the mucous membrane is thickest, and presents a yellowish tint. Its cells, cylindrical and implanted upon the connective tissue by a filiform ramifying extremity, do not always possess vibratile cilia. The mucous glands are replaced by tubular glands analogous to those of Lieberkühn, which contain cells infiltrated with yellow or brown pigment granules. The pale nerve filaments of the olfactory nerve terminate in a long, slim rod, situated among the cylindrical cells. Upon the course of these terminal nervous filaments, which are a little varicose, is often found an ovoid vesicular nucleus.

The *larynx*, the *trachea*, and the *bronchi* are composed of a mucous

membrane, which covers their internal surface, of a fibro-cartilaginous framework, of striated and unstriated muscles, of vessels and of nerves.

The *mucous membrane* upon the epiglottis and the inferior vocal cords is covered with a stratified pavement epithelium; upon the rest of the laryngeal cavity as well as upon the trachea and bronchi, it presents at

Fig. 217.



Part of a transverse section of a bronchial tube from the Pig, having a diameter of about 1-60th of an inch. × 240. *a*. External fibrous layer. *b*. Muscular layer. *c*. Internal fibrous layer. *d*. Epithelial layer. *f*. One of the surrounding alveoli.

its surface cylindrical cells with vibratile hairs; at the termination of the bronchioles in the pulmonary acini the epithelium becomes squamous.

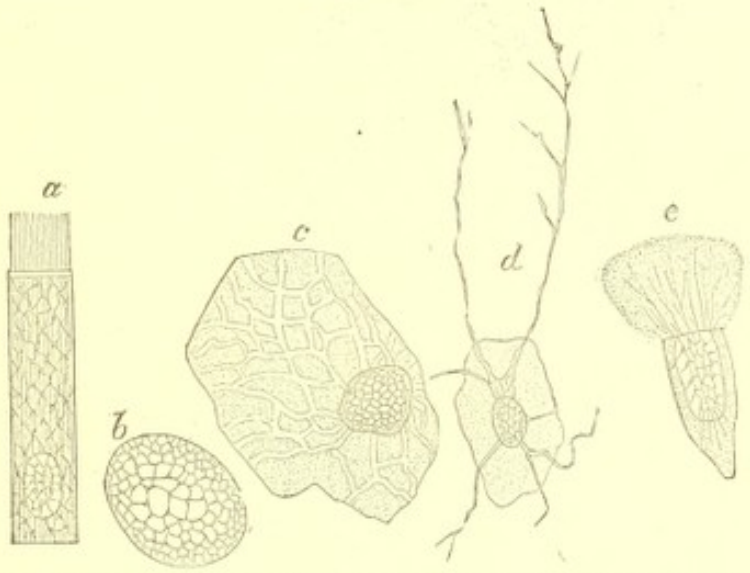
Beneath the epithelium the corium of the mucous membrane is composed of two layers; immediately below the epithelium in the larynx and trachea the first layer is mainly composed of elastic fibres, and it is limited internally by a thin homogeneous layer (.011 mm.) upon which are planted the cylindrical cells. At the salient part of the inferior vocal cord there are numerous papillæ which resemble those of the palmar aspect of fingers. They are covered by pavement epithelium. This superficial layer of the chorium consists everywhere of reticulated connective tissue, like that of the small intestine. This layer possesses a few closed follicles (30–50), exclusively located in the mucous membrane lining the ventricle and larynx.

The second layer is composed of fibrous tissue and elastic fibres, which lodge the acinous glands, and which connect the mucous membrane with the muscles and the cartilages.

The mucous glands of the larynx, trachea, and bronchi are very numerous and are racemose. The rounded acini of these glands contains pyramidal cells with the base applied to the basement membrane. The cell nucleus is at the base of the pyramid, and the protoplasm is clear and contains mucus. The ducts are paved with a cylindrical epithelium. The structure of the fibro-cartilaginous framework of the larynx is that of ordinary fibrous and cartilaginous tissue, except that the body of the epiglottis and the cartilages of Santorini and of Wrisberg consist

of reticulated cartilage. The fibres of the ground substance of the cartilages are continuous with the elastic fibres of the mucous membrane. The rings and plates of the trachea and bronchi are represented by ordinary hyaline cartilage. The ligaments which unite the cartilages are chiefly composed of elastic tissue.

Fig. 218.



Cells showing the reticulum of the protoplasm and nucleus. *a*. Columnar epithelial cell provided with cilia, the latter being prolongations of the intra-cellular network. *b*. Nucleus of a glandular epithelial cell from the stomach of a newt, showing the intra-nuclear network. *c*. Endothelial cell of the mesentery of a newt, containing in a hyaline ground substance a plexus of fine fibre bundles —intra-cellular network—in connection with the intra-nuclear network. *d*. Connective tissue corpuscle from mesentery of newt, showing very clearly the intra-cellular network of fibrils and the hyaline ground substance, the former extends into the branched processes, and is also connected with the more delicate intra-nuclear reticulum. *e*. Goblet cell from the stomach of a newt showing the intra-cellular network in connection with fibrils of the intra-nuclear network, the upper part of the cell is greatly swollen by mucus. (*Klein.*)

The muscles of the respiratory passages are striated in the larynx, unstriated in the trachea and bronchi. The distribution of the blood and lymph vessels in the different layers of the mucous membrane presents nothing unusual.

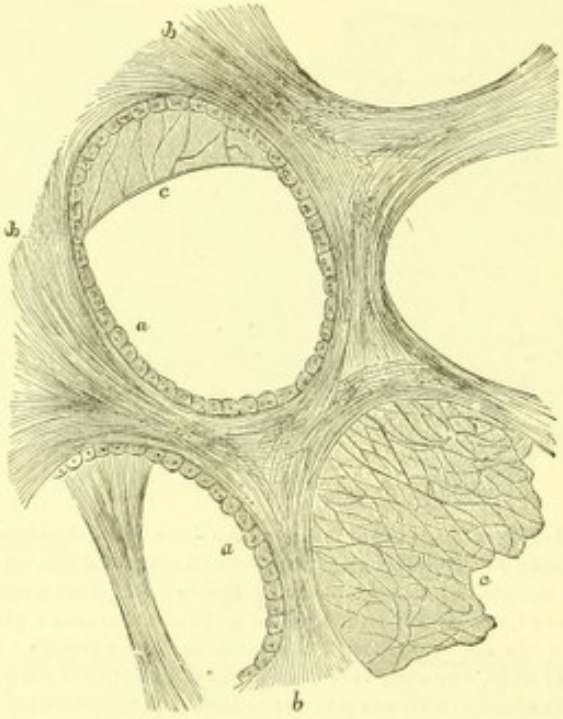
The inferior laryngeal nerve is composed of particularly large fibres, while in the superior laryngeal the nerve fibres are fine. Upon the terminal plexus of the latter, microscopic ganglia are to be found.

The *lungs* suspended in the thoracic cavity by the bronchi and trachea, are composed of lobes and lobules. The bronchioles terminate in the primitive lobules or infundibula. An infundibulum is constituted by a group of alveoli communicating with each other by a common cavity, in which the bronchiole terminates. The form of the infundibulum is conical; the air vesicles or alveoli which constitute it are round or polygonal; they may not only be grouped together in the infundibulum, but isolated air cells may occasionally appear upon the bronchiole itself.

Upon a thin section of an inflated and dried lung the alveoli present the form of round or oval cavities bounded by thin septa of connective tissue containing elastic fibres. This extremely dilatable fibrous frame-

work of the lung, which is continuous with the wall of the terminal bronchioles, serves as a support for blood and lymph networks, as well as for the nerves, and also affords a basement for the pulmonary epithelium which lines the alveoli. In the terminal bronchioles the epithelium is small, very regular, and of the pavement variety; upon the walls of the air vesicles a pavement epithelium may be demonstrated by staining a

Fig. 219.



Air-cells of human lung with interalveolar septa. *a*. Epithelium. *b*. Elastic trabeculæ. *c*. Membranous wall with fine elastic fibres. (Carpenter.)

section of fresh lung with nitrate of silver. These cells are thus shown very readily in the frog and small mammifera, but the same treatment does not work very successfully with man because of the extreme difficulty of securing an autopsy soon enough after death; in new-born infants, however, the epithelium is very easily seen. The cells uniformly cover the walls of the alveoli, and their nuclei are placed opposite the meshes of the vascular network.

The bloodvessels of the lungs are derived from two sources: from the bronchial arteries which are distributed to the bronchi, they are the nutrient vessels; and from the pulmonary artery whose ramifications are especially concerned in hæmatosis. The ramifications of the pulmonary artery form in the inter-alveolar septa a network with extremely fine meshes which are .004, .005 to .018 mm. in diameter, while the capillaries forming them are from .006 to .011 mm. wide. In the state of contraction or semi-inflation of the alveoli these vessels are tortuous, and they elevate the floor of the alveoli into ridges corresponding to their course.

The lymph vessels of the lungs are very numerous. The deep lymphatics arise from the walls of the bronchi, and of the bloodvessels, particularly the pulmonary arteries, and, according to Wiwodzoff and others, from the walls of the air vesicles also.

The pleura, the serous membrane of the thoracic cavity, presents two portions: the one, the visceral, covering the surface of the lung, is thin and consists of a layer of loose connective tissue invested upon the external surface with large flat pavement cells; the other, the parietal, is also lined upon its free surface with similar cells, and on the other side is continuous with the connective tissue framework of the intercostal muscles and the ribs. The parietal pleura is thick and consists of two layers of connective tissue, the one loose, situated immediately under the endothelium, the other distinctly fibrous and containing a large number of elastic fibres. This membrane possesses blood and lymph vessels, nerves, and according to some histologists a few smooth muscular fibres.

CHAPTER II.

PATHOLOGICAL HISTOLOGY OF THE RESPIRATORY APPARATUS.

Sect. I.—Nasal Fossæ.

Congestion; Hemorrhage.—Congestion of the nasal fossæ is the initial phenomenon of inflammation or hemorrhage. Hemorrhage or epistaxis is either primary, as that which is seen in young subjects, or secondary, such as in typhoid fever, scurvy, etc. We do not know the lesions of the vessels which explain the hemorrhages or indicate their proximate or remote cause.

Inflammation of the Mucous Membrane of the Nasal Fossæ; Coryza.—Acute coryza is a congestion accompanied by a serous exudation. The first drops of this exudation are transparent, yet they already contain lymph corpuscles. The immediate presence of these corpuscles in the serous discharge of coryza occasions the suspicion that they are white blood corpuscles escaped from the bloodvessels, rather than the product of multiplication of the epithelial cells. Nevertheless, we have here a very good opportunity for studying the metamorphosis of the epithelial elements. The cylindrical cells become globular and divide in such a manner that the parts have the diameter, the form, and the reactions of a pus corpuscle, yet possess vibratile cilia, a fact which very strongly suggests their origin. (*e*, *f*, *d*, fig. 220.) Such cells become detached and mingled in the exuded serum with the numerous lymph corpuscles which have escaped from the bloodvessels, or have formed in the deep layer of the mucous membrane. They give to the exuded fluid a mucous, cloudy, or puriform appearance, according to the number of cell elements held in suspension.

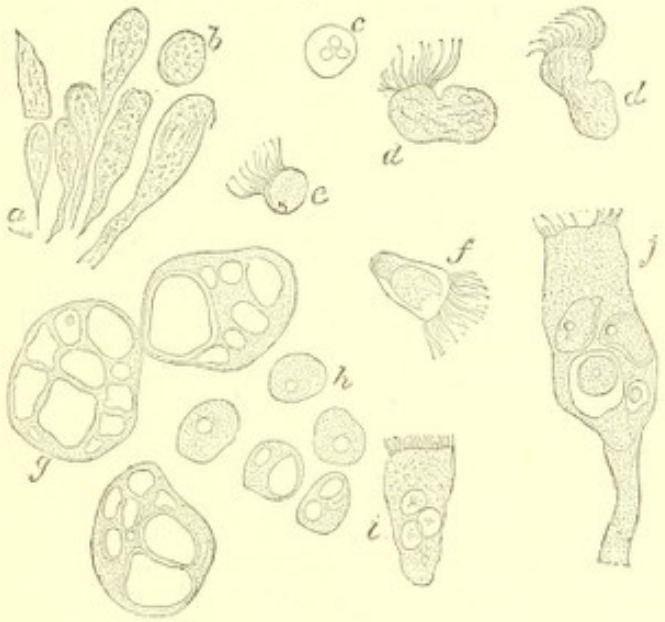
An acute coryza, of a secondary character, is observed in the exanthemata, especially in rubeola, in erysipelas of the face, in diphtheria, and glanders. Each of these diseases may manifest itself upon the mucous membrane of the nasal fossæ by the local character and the progress which characterize them upon the cutaneous surfaces.

The acute inflammation may be arrested, or it may become chronic. Chronic coryza and frequently recurring acute attacks determine a thickening of the submucous tissue, as well as of the connective tissue of the mucous membrane itself, which has been pointed out by authors as a possible origin of polypi of the nasal fossæ. It may also be accompanied by ulcerations and even by small abscesses in the submucous tissue. Rarely do the periosteum or the bones become involved.

Chronic coryza of a specific character, or *ozæna*, is seldom observed,

except in the scrofulous or the syphilitic. Profound lesions of the mucous membrane and of the submucous tissue, the ulcerating gummata, the necrosis of the bones which form the skeleton of the nose or of the roof

Fig. 220.



Mucous transformation of cells, from a catarrhal inflammation of the air passages. *a*. Degenerated cylindrical cells. *b*. Pus corpuscle; *c*, the same acted upon by acetic acid. *e*, *d*, *f*. Cells coming from the division of a cylindrical cell, showing cilia. *g*, *h*. Mucous degenerated cells from the nasal fossæ in coryza. *j*. Cylindrical cells, showing endogenous cells. ×450.

of the palate, give rise to perforations of the vault or of the arches of the palate, to the discharge of fragments of bone, and to sinking of the nose, etc.

Tumors of the Nasal Fossæ. *Mucous Polypi*.—Mucous polypi, generally found in the anterior portion of the nasal cavities, are single or multiple. Their pedicle is more or less thick, their form is determined by that of the cavity in which they are located, their size varies from that of a pea to that of a walnut. They are soft, of a trembling mucous appearance, and are easily torn.

They arise by a localized increase of the corium and submucous tissue of the mucous membrane, which latter covers their whole surface. When the latter is bosselated and irregular, the mucous membrane dips into the depressions.

Examining a thin section of these tumors, it is seen that their free surface is bordered with a stratified layer of ciliated cylindrical epithelium, and in some cases glands opening upon this free surface are to be observed. These glands may be considerably hypertrophied or they may have undergone cystic dilatation, etc. To this variety of tumor appertain those of the antrum, described by Giraldès. In certain mucous polypi of the nasal fossæ, on the contrary, we do not meet with glands. The mucous tissue which forms the mass of the tumor is very vascular. In a gelatinous or mucous ground substance are imbedded, besides the vessels, connective tissue cells, which may be round, fusiform, or stellate, often having pro-

cesses which may unite to form a cellular network, and in varying amount also bundles or fibres of connective tissue. A striking characteristic of these tumors is that the portion which may project beyond the nostril possesses a covering of stratified pavement epithelium.

Fibrous Polypi.—The fibrous polypi of the nasal fossæ arise from the periosteum, or they may have their origin even in the bones. They usually have their point of attachment in the posterior portion of the cavity. They send prolongations in every direction into all the cavities, either bending around obstacles or breaking through them, enlarging the nasal fossæ, thinning or destroying the bones, and penetrating by new ways or by natural openings (the spheno-palatine canals, for example), into the sinuses which surround the nasal fossæ, especially the zygomatic fossæ. They consist of fibrous tissue, and according to Muron, they possess a considerable number of capillary vessels with embryonal walls, liable to hemorrhage.

Among the polypi of the nasal fossæ there occur genuine *papillomata.* These are composed of numerous compound papillæ, compressed against each other, or perhaps united by a common epithelial covering. Their stroma is fibrous and vascular, and their thick epithelial investment consists of pavement cells.

The *sarcomata* may have the same seat and progress, and it is possible that many tumors described as fibrous polypi of the nasal fossæ may in reality have been sarcomata.

Primary *carcinoma* of the nasal fossæ is very rare.

Pavement-celled epithelioma, starting from the skin of the nose, the cheek, the upper eyelid, the edge of the nostril, or the upper lips often invades the nasal fossæ.

There is a form of cylindrical-celled epithelioma primarily developed in the nasal fossæ, which by the naked eye cannot be distinguished from mucous polypi (see p. 154).

Polypous growths arising in the antrum often project into the nasal fossæ: they usually belong to the class of tubular epithelioma. These polypi are implanted upon a base of morbid tissue, and their prognosis is very grave.

Sect. II.—Larynx.

Congestion, Acute Catarrh, or Catarrhal Laryngitis.—Acute catarrh is primary, as when caused by an impression of cold, or secondary, as when following a febrile exanthema (scarlatina, rubeola, etc.). Congestive and inflammatory redness, accompanied by swelling, is observed by the laryngoscope during life; but at the autopsy the laryngeal mucous membrane is pale, a circumstance which is due to the large quantity of elastic fibres which squeeze the blood from the tissues after death.

The changes in the mucous membrane are the same as in coryza. The sputa from laryngitis, and from the respiratory passages in general, rarely contain normal ciliated cylindrical epithelium. Nevertheless, examined *in situ*, these cylindrical cells exhibit evidence of proliferation (see page 220).

Rindfleisch has indicated the following mode of formation of pus cor-

puscles. The connective tissue corpuscles of the most superficial layers of the mucous corium proliferate, become globular, and animated by amœboid movements travel between the cylindrical cells to the surface of the membrane. It is the same course which, according to Cohnheim, the wandering white corpuscles pursue after escaping from the blood-vessels. It is undeniable that in laryngitis the stroma of the mucous membrane is infiltrated with lymph corpuscles, especially along the vessels. This is seen particularly in the aryteno-epiglotidian folds, in the laryngitis of rubeola.

The glands of the mucous membrane are affected. Their culs-de-sac enlarge, and the cells which they contain are swollen. In the lumen of the culs-de-sac and of the excretory ducts exists an abundant mucous fluid containing pus corpuscles and swollen cells. This state corresponds to a hypertrophy of the glands, appreciable to the naked eye. By pressure a drop of muco-pus can be squeezed from the orifice of the gland. Later, if the suppuration of the gland continues, the duct and the culs-de-sac are destroyed, and there only remains a small erosion or round shallow ulcer.

Chronic Catarrh of the Larynx, or Chronic Catarrhal Laryngitis.—This affection may follow an acute catarrh, or it may be the consequence of a chronic granular or tubercular pharyngitis, or of another disease of the larynx. The mucous membrane is congested, brown, or grayish. It secretes a mucous or puriform fluid. The membrane is thick and its glands are so hypertrophied that the disease has been called glandular angina. This hypertrophy of the glands may be observed as a sequence of the same condition in the pharynx.

In inflammations of long duration, the connective tissue of the mucous membrane proliferates, and there results a thickening with a tendency to the production of vegetations and of papillæ more or less numerous, which may be limited to the inferior vocal cords, for example. In a marked degree of development, these vegetations may constitute small sessile or pedunculated tumors. These modifications of the mucous corium are accompanied by a transformation of the epithelium, which becomes stratified and squamous, not only upon the vocal cords, where it normally exists, but upon the other surfaces, which in health are covered with cylindrical cells. This is the so-called dermoid metamorphosis of Foerster.

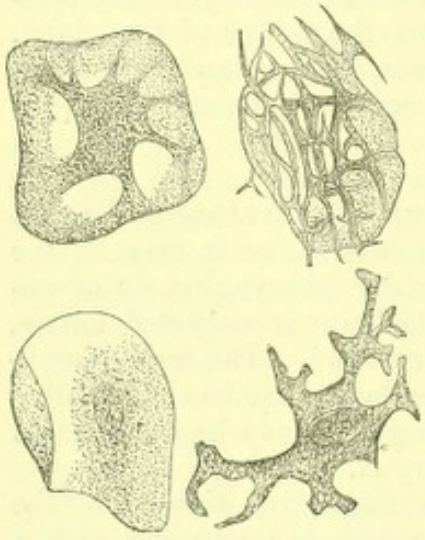
Diphtheritic Laryngitis, or Croup.—It is either primary, or is due to an extension of the lesion first developed in the pharynx, or in the lower portions of the air passages. It is especially met with in children. It begins in a local catarrhal inflammation, which soon is followed by the appearance of false membranes. These false membranes are whitish or grayish, more or less extensive, more or less thick, disposed in superimposed layers. The deepest layer in contact with the mucous membrane is the most recently formed, whilst the superficial layers, the oldest, disintegrate, and are thrown off. The false membrane is more or less resistant. It may be thick, tenacious, and difficult to detach; or, on the contrary, soft and easily reduced to a granular or caseous detritus. These

differences in consistence depend solely upon the age of the false membrane. At the autopsy of children who expectorate a large quantity of tough false membrane, it is astonishing to find almost nothing in the larynx or trachea except some insignificant pulpy detritus.

The explanation of this peculiarity of this false membrane has already been given while describing the modifications of the epithelium in these special inflammations (see pp. 65 and 66). The false membrane expelled by coughing often furnishes a mould of the parts upon which it was located. In the larynx, it may extend over the entire surface of this cavity.

Histologically the false membrane consists of fibrin in the form of filaments, of pus corpuscles, and of epithelial cells. The latter, whether they are derived from the ciliated cylindrical epithelium or from the pavement epithelium of the inferior vocal cords, are modified in form and chemical composition as has been indicated at p. 66. Developed at the expense of the superficial layer of the epithelial covering of the mucous membrane, each layer last formed is pushed forward as new cells and pus corpuscles form under it. They never contain bloodvessels in their interior.

Fig. 221.



Fibrinous degeneration of pavement epithelial cells in diphtheritic membranes. High power. (*E. Wagner.*)

Beneath the false membranes the mucous membrane may be hypertrophied, red, infiltrated, and softened, and often there are found between these two membranes blood extravasations. But most frequently the subepithelial connective tissue is intact, even if the mucous surface appears uneven and ulcerated; nevertheless, this tissue is sometimes inflamed and there may then exist very superficial ulcerations.

We find in the false membranes spores of microscopic fungi, upon the nature and explanation of which there is much disagreement.

Diphtheritic laryngo-tracheitis may exist in the chronic condition.

Erysipelatous Laryngitis.—Erysipelas of the face and of the pharynx, propagated to the larynx by continuity of structure is characterized, as upon the skin, by an intense redness, and a puffiness of the mucous corium. The cellular tissue of the mucous membrane may be distended with serum as in an œdema of the larynx. This condition has been followed by fatal suffocation.

Variolous Laryngitis.—In confluent variola, the larynx and indeed the mucous membrane of all the air passages are the seat of pustules more or less numerous. The pustules of the larynx have, generally speaking, the same form and evolution as those of the skin.

When the pustules are very numerous they unite into groups, and the epithelial layer, degenerating over an extended surface, forms a veri-

table false membrane which in certain cases might be confounded with the false membrane of croup. After the shedding of the epithelium the pustule empties itself; the superficial layers of the mucous membrane may continue to suppurate; there is then formed an ulcer more or less deep and irregular.

More severe inflammations, abscesses, and even perichondrites have been observed toward the end of this process.

LARYNGITIS OF GLANDERS.—The lesion of the mucous membrane is characterized by the presence of small miliary abscesses, and not by granulations such as are seen in the nasal fossæ and air passages of the horse. Groups of these abscesses unite and give rise to ulcerations.

LARYNGITIS OF TYPHOID FEVER.—The laryngitis of typhoid fever is more or less grave. Almost always a superficial catarrh of the larynx accompanies the catarrh of the bronchi and trachea, but sometimes ulcerations, well described by Louis, may be seated upon the aryteno-epiglottic ligaments, upon the epiglottis in the neighborhood of the arytenoid cartilages, at the same time that they are found in the pharynx and in the œsophagus. Perichondritis or an œdematous laryngitis may result.

Syphilis betrays itself in the larynx by catarrhs, mucous patches, deep or superficial ulcerations, and all the accidents which may result therefrom, as perichondritis, œdema, etc. The mucous patches result from a circumscribed irritation of the mucous membrane characterized by a slight elevation and a thickening with proliferation and swelling of the epithelium. All profound syphilitic lesions of the mucous membrane occasion a proliferation and a production of connective tissue usually much greater than in diseases of the larynx due to other causes.

Tubercular Laryngitis also varies in character, according as it may be manifested by a simple catarrh, by laryngeal tubercles, ulcerations, or perichondrites, etc.

ŒDEMATOUS LARYNGITIS; ŒDEMA OF THE GLOTTIS.—This lesion whether it is primary, or is consecutive to one of the affections already mentioned, to general anasarca, or to traumatism, consists in a serous or pruriform infiltration of the submucous connective tissue.

The œdema is most frequently limited to the upper part of the larynx. The aryteno-epiglottic folds, swollen, œdematous, trembling, and semi-transparent, tend to obliterate the opening of the larynx especially during inspiration. The arytenoid region is œdematous, as is also the epiglottis at its base. All the other parts of the mucous membrane may, however, be the seat of a similar swelling. The œdema is usually caused by an ulceration or a perichondritis.

The mucous membrane is livid or rosy red. When incised, a notable quantity of a puriform or a transparent serous fluid escapes. The microscope shows this œdematous connective tissue to be composed of fasciculi of connective tissue separated from each other by a transparent fluid containing granules or a reticulum of fibrin. In this fluid large cells, more or less granular and distended, are also found, as well as pus and blood corpuscles, the quantity of pus depending much upon ulceration, etc.

Ulcerous Laryngitis.—According to their causes laryngeal ulcers vary much in their form and gravity. We have seen an intense catarrhal laryngitis determine the destructive suppuration of a mucous gland—*follicular ulceration*, such as is frequently seen in the laryngitis of phthisis. In typhoid fever, the deeper ulcers with vertical walls and generally filled with a caseous detritus, originate, in all probability, from a typhoid new formation which has for its seat a gland follicle. Ulcerations due to variolous pustules and to syphilis are shallower, and more or less extensive; they result simply from a destruction of the epithelial covering. The exposed corium of the mucous membrane is congested, more or less granular, and moistened with pus.

In *tertiary syphilis*, the bottom of the ulcer is covered with granulations and the submucous tissue is thickened, indurated at times, and very vascular. Syphilitic ulcers may extend over a large area of the mucous membrane of the larynx and even of the trachea. When seated upon the epiglottis, they often cause a loss of the substance of its free border. They frequently give rise to new formations of connective tissue, vegetating in the form of polypi. These ulcers may heal, but the new connective tissue has a great tendency to contract like cicatricial tissue and cause deformities.

Pulmonary phthisis is much the most common cause of laryngeal ulcers.

The ulcers start from a very intense laryngo-tracheitis, and usually extend into the trachea and bronchi. The mucous membrane is usually much congested, and is covered with muco-pus. Upon the non-ulcerated parts the layers of ciliated cylindrical epithelium are still preserved. The lesions which cause the ulcerations are complex: first there form tuberculous granulations, primarily developed under the epithelium, more or less numerous, isolated, and confluent; then follow follicular ulcerations.

In the place of the gland destroyed by ulceration is seen a little cup-shaped circular depression. These ulcers enlarge, and may reach 2 to 3 mm. in diameter. Their floor is grayish or rosy and is slightly depressed. They may unite with each other and form a large ulcer with festooned borders. It is rare that tubercular granules cannot be seen upon the floor or edges of these ulcers. The vocal cords at their point of union, the cords themselves, the arytenoid cartilages, the epiglottis, and the interior of the ventricles of Morgagni, are the most frequent seat of these ulcers. The ulcers extend in depth as well as superficially.

The exposed fibrous tissue of the vocal cords may itself be eroded; the free border of the epiglottis, also, frequently presents loss of substance, involving destruction of the cartilage.

The submucous connective tissue around the ulcerations is much thickened by a new formation of embryonic cells, or it is infiltrated with serum and pus. These lesions affect the function of those portions of the larynx where they are located.

The muscles are also sometimes invaded. The intermuscular connective tissue may be infiltrated, and the fasciculi themselves undergo fatty degeneration.

Deep ulcers and abscesses of the larynx may cause a perforation, when the pus may show itself in the subcutaneous tissue and discharge exteriorly, or it may empty into the œsophagus. These perforations are almost always accompanied by perichondritis.

PERICHONDRITIS.—Suppurative inflammation of the perichondrium of the cartilages of the larynx may arise spontaneously, but it is most frequently caused by extension of the inflammation attending deep ulcers of the larynx. Nevertheless, it appears to have been very frequently observed in typhoid fever.

In severe laryngitis of long duration, when the submucous cellular tissue is proliferated, the tissue which surrounds the cartilage is altered in a similar manner, and the cartilages themselves undergo modifications of nutrition. At one time a calcareous infiltration of their ground substance and of their capsules is observed; at another, a genuine ossification may be seen, with the formation of true bone corpuscles, etc. These lesions of the cartilages are not infrequent in laryngeal phthisis. The epiglottis is often infiltrated with calcareous salts, but it does not ossify.

The irritation of the perichondrium and of the cartilage, which is manifested by proliferations, is of itself an additional cause of suppurative perichondritis.

The latter is characterized by the formation of pus corpuscles between the perichondrium and the cartilage. The pus detaches and separates the perichondrium from the cartilage, which, isolated from its nutrient membrane, must necessarily mortify. In the necrosed cartilages of typhoid fever, we have seen the fundamental substance of the cartilage very granular and the cartilage cells loaded with fatty granules. The abscess by which the cartilage is surrounded spreads among the submucous tissue and the articulations, and points upon the larynx, upon the pharynx, or upon the skin. It is not slow to open and to discharge with the pus, fragments of cartilage, often calcified or ossified.

The cricoid cartilage is most frequently affected, next comes in order of frequency, the thyroid and the arytenoid cartilages. In the first two cases perforation takes place either upon the laryngeal surface, or upon the cutaneous side, and then there may result a subcutaneous œdema or occasionally an emphysema. When the arytenoid cartilage is affected, the perforation is into the larynx, and the laryngoscope will therefore render the diagnosis of this lesion easy during the life of the patient.

TUMORS OF THE LARYNX.—There are a few recorded observations of *myxomata* or mucous polypi of the larynx, resembling small cystic polypi and formed of mucous tissue covered by a thin mucous membrane. They were seated upon the base or the posterior aspect of the epiglottis, and the ventricles of Morgagni.

Fibromata, or fibrous polypi of the larynx, are much less rare. They spring from the connective tissue of the mucous membranes. They are generally small, from the size of a hemp-seed to that of a pea; they increase slowly; they are sessile or pedunculated; their usual seat is upon the inferior vocal cords; they are hard, resistant to the scalpel, and their substance presents all the characters of fibrous tissue. Their

surface is smooth or irregular, and is covered by several layers of stratified pavement epithelium. The nature of this epithelium is always the same. Sometimes the surface of these polypi is ulcerated.

Tubercles of the larynx are, when encountered in autopsies, always found associated with pulmonary tuberculosis, but it is possible that tuberculosis may commence in the larynx. Tubercle granules of the larynx, denied by Louis, have been placed beyond doubt by Rokitansky, Virchow, Foerster, etc., and they are common enough for them to be easily studied in their different stages. At their commencement, they appear as small gray or whitish salient points, and are distinguished from swollen glands by the fact that they have no depression at the centre. A thin section through one of these nodules shows it to be covered by a layer of cylindrical epithelium, and to consist of an agglomeration of elements which characterize all tubercle granules. These granules develop in the superficial layer of the mucous corium. They are discrete or confluent, and are usually less numerous in the larynx than in the trachea. Later, when the granule has become caseous, the epithelial investment is lost. At this time a granulation may sometimes be seen projecting from the midst of an erosion of the mucous membrane. The granule itself may be eliminated in fragments, with the pus which the ulcerating surface secretes. The bottom and sides of a tuberculous ulcer consist of a tissue, more or less thick, composed of tubercle granules.

Primary *carcinoma* of the larynx is extremely rare. There are, however, a few recorded observations of encephaloid carcinoma commencing in the larynx. The tumor shows itself under the form of rose-colored nodules, which lift up the mucous membrane, develop rapidly, invade the submucous tissue, the connective tissue of the muscles, and rapidly cause death.

Ecchondroses and *osteomata* have been met with upon the internal aspect of the cricoid cartilage.

Pavement-celled *epithelioma* develops in the form of granulations and of condylomata which spring from the surface of the mucous membrane, and are covered by a thick opaque secretion. Ordinarily it is easy to see that the tumor springs from the anterior wall of the œsophagus, or from the pharynx, and that it projects into the larynx only after having penetrated its fibro-cartilaginous framework. These growths correspond exactly with the description of lobulated epithelioma (see p. 146). The surface of these vegetations is covered with cylindrical epithelium, or more frequently with the pavement variety. The vegetations may be ulcerated and their epithelial cells disintegrated and mixed with the mucus which covers them, thus forming an opaque fluid.

Epitheliomata must not be confounded with papillomata of the larynx, and in order to avoid this error it does not suffice to examine scrapings, but sections must be made after previous hardening, and must be well studied.

The papillomata, so frequent in the larynx, are covered as we shall soon see by layers of pavement epithelium, and these elements are found in large numbers when one studies the papillomata by the scrapings.

The *papillomata* or papillary polypi of the larynx are growths which are most frequently seen after tubercles. These tumors have a cauli-

flower appearance, and present a mass of primary and secondary granulations. They may consist of a number of fine salient villi. They have a great tendency to spread, but their base is very distinctly pedunculated, and their vegetations are longer and more distinct from each other than in carcinoma and epithelioma. Moreover, neither the connective tissue of the mucous membrane nor the submucous cellular tissue is invaded by the morbid growth, while the contrary is true of the last-mentioned tumors.

The favorite seat of papillomata is at the angle of junction of the inferior vocal cords or upon the cords themselves. Their structure is that of all papillomata, namely, primary and secondary papillæ, consisting of a small quantity of connective tissue with vessels, and of a covering of stratified pavement epithelium.

Adenomata or glandular polypi. Hypertrophy of the glands in the larynx in chronic catarrhal laryngitis has already been mentioned. These hypertrophies are, properly speaking, small adenomata. They may, in very rare cases, grow quite prominent and become pedunculated. The culs-de-sac of these hypertrophied glands are larger than in the normal state, but their epithelium presents the physiological form. At the surface of these tumors we almost always find papillary excrescences, and hypertrophied glands are quite constantly met with at their base, so that polypi of the larynx are very frequently mixed tumors in which it is very difficult to say which predominates, the papilloma or the adenoma.

Secondary *lymphadenomata* or leukæmic tumors have been several times observed as small soft flat nodules seated in the larynx, trachea, and bronchi. Their seat, according to Virchow, is near the mouth of the glands or upon any other point of the mucous membrane.

Parasites.—Young nematode worms have been found, after death, in the larynx and bronchi.

Sect. III.—Trachea.

Inflammation.—The different varieties of inflammations, the acute, chronic, diphtheritic, variolous, syphilitic, and tubercular, which have been described, *à propos* of the mucous membrane of the larynx, present the same anatomical characters in the trachea.

Tuberculous and follicular *ulcers* of the mucous membrane are very common, and often very extensive and serpiginous. They are especially located on the posterior wall of the trachea and in the mucous membrane between the prominence of the cartilaginous rings. Sometimes a deep ulcer communicates by an anfractuous fistula with a caseous abscess of a neighboring tubercular lymph gland.

Perforations of the trachea may result from ulcers of the œsophagus, abscess arising in the adjoining connective tissue, cancerous growths of the lymph glands and of the œsophagus, aneurisms of the arch of the aorta.

Carcinoma never originates primarily in the trachea, but it is not very unusual to see in the cellular tissue of the mucous membrane secondary

carcinomatous nodules which are hemispherical and more or less voluminous.

Secondary *leukæmic* growths have also been met with.

In the aged the tracheal cartilages are sometimes calcified and ossified, and may present exostoses. Even an intimate union of two or more rings may be established by formation of bone.

Sect. IV.—Bronchi.

Congestion; Hemorrhage.—Congestion of the bronchi precedes and accompanies catarrhal and other inflammations of these tubes, and is present in almost all diseases of the air passages and of the heart. It is observed also in many fevers, such as the eruptive fevers and typhoid fever. It is characterized by redness and fulness of the vessels and swelling of the mucous membrane, and most frequently, even in passive congestion, by a secretion of mucus. The inner surface of the bronchi is red, often a dark maroon color. Ecchymoses may appear in the mucous membrane, particularly in the exanthemata, in typhoid fever, in scorbutus, and in asphyxia. Then the bronchial mucus contains a greater or lesser number of red blood globules. Large hæmoptyses arise from ulcerations of the bronchi, from pulmonary cavities, from pulmonary apoplexies, or from rupture of an aneurism into the bronchi.

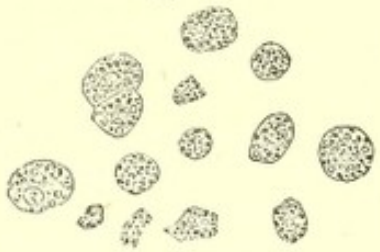
Bronchitis.—Catarrhal inflammation of the mucous membrane of the bronchi, either acute or chronic, is excited by the same causes and presents, in a general way, the same histological changes as does that of the larynx. Limited to the large bronchi, it is not dangerous, but when it invades the small bronchi it is often fatal, especially in children and in the aged. In these grave cases, the bronchitis is rarely simple; it is complicated with lesions of the pulmonary parenchyma, such as congestion, lobular or catarrhal pneumonia, atelectasis, emphysema, and lobular gangrene.

Intense bronchitis of the small bronchi, or capillary bronchitis, may be such that the inflammatory thickening of the mucous membrane, added to the products of exudation, prevent the air from reaching the pulmonary alveoli. In other cases, the diseased bronchi, very red upon their internal surface, which is covered by a puriform mucus, appear to be dilated. The connective tissue of the mucous membrane is thickened and the bronchial tube is more rigid than normal; the natural longitudinal rugæ of the mucous membrane, which result from the contraction of the muscular tunic of the bronchi, become effaced, and the internal surface of the bronchi is smooth. This condition of the bronchial tubes is most frequently seen in broncho-pneumonia. In severe bronchitis, where the secretion is muco-purulent, the cylindrical epithelial cells have desquamated, the glands are filled with embryonal cells and pus corpuscles, and the surface of the mucous membrane, may present an unpolished aspect, due to the formation of microscopic papillæ or granulations.

Diphtheritic bronchitis is seen particularly in children, as a complication of croup. It is then generally associated with pulmonary congestion,

and with more or less extensive areas of broncho-pneumonia. In adults it is not a very rare complication of broncho-pneumonia, or of acute pneumonia.

Fig. 222.



Cells from the sputum of acute bronchitis. Showing the minute granules of pigment within the cells. Some of the cells also contain a few fatty molecules. ×400. (*Green.*)

Chronic bronchitis, often related, as cause or effect, to emphysema or to disease of the heart, is characterized by a violet or slate-gray color of the surface of the mucous membrane. The connective tissue of the latter is frequently thickened by the formation of fibrous tissue, which may vegetate at the surface under the form of small papillary excrescences. The mucus secreted may be transparent, gelatiniform, and small in quantity, or it may be muco-purulent, or a serous fluid may be exuded in great abundance.

Chronic bronchitis may be accompanied by dilatation of the bronchi and by ulcerations.

Dilatation of the Bronchi; Bronchiectasis.—The dilated bronchi, the mucous membrane of which is thickened by acute inflammation, readily return to their normal condition; but under the influence of a chronic process, such as bronchitis, chronic pleurisy, chronic pneumonia, these tubes remain dilated. Almost always the tissue which surrounds the dilated bronchus is indurated and presents the characters of interstitial pneumonia or of peri-bronchitis. The dilatation of the bronchi may be cylindrical and uniform throughout their length—a rare form. One or more bronchi whose diameter is thus increased sometimes terminate near the pleura in an ampulla. There may be several cylindrical or spindle-form dilatations along the course of a bronchus and its branches, as is often observed at the apex of the lungs. The dilatations are connected with one another by bronchial tubes of normal diameter—the *moniliform* dilatation of Cruveilhier. A third and most common form is an ampullar or sacciform dilatation, generally single and frequently very large. Several of these ampullar enlargements may communicate with one another by the intervention of bronchi more or less dilated, whence may result the conversion of a lobe into an alveolar mass, the cavities being separated by shrivelled and indurated pulmonary tissue. The favorite location of these dilatations is at the periphery of the lung, and there always exists in these cases a chronic pleurisy, marked by the fibrous thickening of the pleura. Beyond the dilatation, the bronchus and its terminal branches are atrophied, or some of the bronchi may be converted into cysts. We sometimes find cystic cavities, more or less voluminous, at the apex of the lungs; they are lined with a mucous surface, and contain a mucous fluid. They have been considered as bronchial dilatations, isolated and closed up by the obliteration of the small bronchus upon which they have been formed. Sinuses exist independently of bronchial dilatations. They should not be confounded with certain spaces which may exist between the pleura and the false fibrous membranes, which are due to chronic pleurisy. In the walls of these sinuses

in the lung proper, the pulmonary tissue is readily recognizable. These cavities sometimes reach the volume of a pigeon's egg, and when they are incised, their areolar wall presents the appearance of the lung of a frog.

The internal surface of the bronchial dilatations, in recent cases or when they are not complicated by ulceration or by gangrene, is lined by a mucous membrane which, without interruption, is continuous with that of the normal bronchi communicating with the dilated portion.

The bronchial mucous membrane is in this location rosy, gray, or slaty, smooth, shining, and thin. The glands are small and atrophied; the cartilages are also to be seen, as well as the relief of the muscular bundles, which are far from forming a continuous membrane. By microscopic examination, we learn that the cylindrical epithelium is well preserved. The submucous tissue, usually rich in cells, has lost the greatest portion of its elastic fibres, which have been atrophied and destroyed by the repeated inflammations. The bloodvessels are small and the capillary meshes are large. The muscle fibres are dissociated, but are not destroyed. The disappearance of the elastic fibres here, whilst they are preserved in the neighboring pulmonary tissue, furnishes a possible explanation of the dilation of the tube.

The mucous membrane of the dilatations is not always thin; it may happen, on the contrary, that its connective tissue may be thicker than normal. There is then a hyperplasia and the elastic fibres are destroyed, as in the preceding case.

The absence of elasticity of the bronchial tubes, the induration of the surrounding tissue, interstitial pneumonia, chronic pleurises with adhesions, are the pathogenic causes of dilatation.

Bronchial dilatation is extremely rare in pulmonary tuberculosis.

In old dilatations or when the mucous membrane is the seat of an intense puriform catarrh, at the same time that the secretion changes character the mucous membrane reddens, loses its polish, becomes very vascular, thickens, and, as in chronic catarrh, presents small papillary vegetations.

When the formation of pus is very abundant, the epithelium desquamates and an ulcer of varying extent and depth is the result. The inflammation, the suppuration, and the retention of the pus impress upon the cavity and its contents new characters, which cause the cavity to closely resemble large old tubercular cavities. The mucous membrane no longer exists; and the only remains of the primitive structure of the bronchus is a mass of embryonal tissue. The surface of the cavity sometimes is covered by a grayish adherent layer formed of connective tissue in process of mortification. This is a sort of *superficial* and curable *gangrene*, which may be compared to the death of connective tissue in phlegmon. The purulent contents assume a brownish color, a fetid odor, and a certain fluidity. The pus corpuscles are filled with fatty granules, and crystals of margarin and cholesterin are often found. Mixed with water in a glass, this pus readily dissolves—an indication that it contains little mucin. Similar characteristics appertain to the sputa.

The lesions which belong especially to dilatation of the bronchi, or which are caused by them, have a slow progress. The wall of a dilated

bronchus may calcify. More frequently the bronchi dilated and isolated from the root of the aërial tree, are filled with a brownish nearly solid mass of caseous pus; after having removed the contents, the structure of the bronchial wall is recognizable.

Ulceration of the Bronchi.—Ulcers of the bronchi may be glandular and very superficial, or they may be due to an intense suppurative bronchitis accompanied by points of purulent pneumonia, as in purulent infection, typhoid fever, etc.; at other times they may be caused by variolous pustules, or by pulmonary syphilis of the new-born; but their most frequent cause is pulmonary gangrene and tuberculosis.

These different causes may occasion perforation of the bronchus from without inward, just as well as ulcers may cause perforation from within outward. Aneurisms, malignant tumors, pleurisy, suppuration of the bronchial lymph glands, may also be numbered among the causes of perforation of the bronchi.

Tumors of the Bronchi.—*Lipoma* has been observed by Rokitansky in the submucous cellular tissue and forming a prominence in the left bronchus.

Calcification and true *ossification* of the cartilages is not extremely rare in aged subjects of chronic bronchitis, at the division of the trachea and in the primary bronchi. These tubes then become rigid. A similar process may appear in the small bronchi, but it does not necessarily follow that every osseous spicule, which is accidentally found in the lungs, should be considered as connected with ossifications of the bronchi or their cartilages.

Carcinoma is never primarily found in the bronchi, but it may reach there by extension from a tumor of the mediastinum, the lung, the œsophagus, or the bronchial glands.

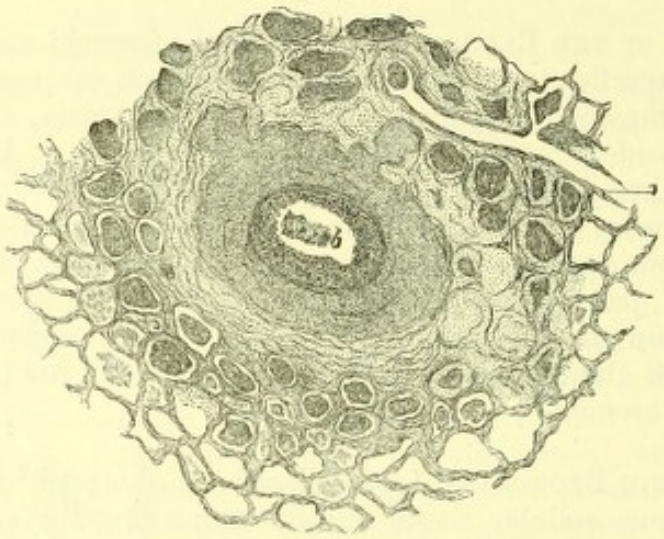
Tubercles of the bronchi are very common, and the lesions which they determine here are very easily studied. Tubercle granules have the same disposition, the same origin, and the same termination as in the larynx and trachea. The alveoli of the pulmonary tissue surrounding this diseased spot, become filled with products of inflammatory exudation, and constitute a small lobule of lobular pneumonia (see fig. 223) which, when the small bronchus is ulcerated and destroyed at any point, will soon become a minute cavity.

Tubercles in the bronchi give rise to an acute puriform catarrh coincident with the suppuration of the nodules of tubercular pneumonia and the rapid formation of a large number of small cavities; or, in the case of nodules or large masses of caseous pneumonia, we may have a caseous bronchitis. Upon section, the bronchi appear completely filled by a dry, gray, or yellowish exudation, which is apparently coherent but is in reality friable.

This caseous mass is composed of granular pus corpuscles and of granular and deformed epithelium, which become reduced to granules or to small fragments. The latter were at one time described as tubercle corpuscles. Examination of thin sections shows the mucous membrane to be reduced to its connective tissue which is diffusely infiltrated with

numerous small cells (tubercular peribronchitis), or the cells may form roundish masses (tubercular granules). The caseous pus and epithelium

Fig. 223.



Acute phthisis. A transverse section of a terminal bronchus (air-passage) and the surrounding alveoli. Showing the lobulated character of the pulmonary consolidation. *b*. Cavity of bronchus containing a little mucus. *v*. A bloodvessel. × 50, reduced ½. (*Green.*)

contained in the lumen of the bronchus in time suffer a molecular disintegration and are eliminated, and the same may happen with the caseous infiltrate in the walls of the bronchus, thus accomplishing the destruction of the latter.

Sect. V.—Lungs.

Anæmia.—Pulmonary anæmia may exist in the general anæmia due to cholera or to systemic cachexias; or it may be caused by compression and atrophy of a more or less considerable portion of the lung. The organ is extremely pale, the vessels are void of blood, but there is no other marked lesion.

Hyperæmia; Œdema.—Hyperæmia of the lung is frequently met with at autopsies. It is present in most of the acute febrile diseases, and in nearly all affections of the heart and lungs, as one of the lesions which precedes and accompanies the agony. It exists nearly always in severe bronchitis, broncho-pneumonia, pneumonia, typhoid fever, measles, emphysema, etc., and in diseases of the heart.

The congested lung is red upon the surface and upon section. Ecchymoses, more or less large and numerous, are frequently observed under the pleura, in all congestions caused by asphyxia. The substance of the lungs is filled with a red or rosy frothy fluid. The capillary vessels which stand out upon the alveolar walls are filled and turgid with blood.

Under the influence of congestion, whether it be active or passive, the pavement epithelium which covers the surface of the alveoli becomes swollen and granular, and undergoes a series of nutritive changes. The

pavement cells become granular or vesicular and often present a yellowish color due to the penetration of dissolved hæmoglobin from the blood plasma which fills the air vesicles. This fluid is soon transformed into hæmatin, thus causing the deposition even in the interior of the cells, of granules, at first red or yellow, but later brownish or black. These cells become spherical, detached, and fall into the fluid which the alveolus contains.

Between œdema and congestion of the lungs there is no sharp line of demarcation. In both cases the lung is distended and larger than normal. After incision of the organ, we can squeeze out from the cut surface a certain quantity of frothy fluid. It is said that there is *congestion* when the color of the surface is red and the escaping fluid is red or pink; that there is *œdema* when the fluid is transparent and colorless and the lung itself is pale. Passive or hypostatic congestion or œdema of the lung is commonly located in the posterior border of the lower lobe. It is often purely cadaveric, when it is due entirely to the gravitation of the blood during and after the moment of death.

The distinction between congestion and true inflammation cannot be sharply drawn at the beginning, for in congestion, in the place of the cells of the alveoli which have desquamated new cells rapidly form; there are then, as in pneumonia, new formation, of elements, and escape from the vessels of white blood corpuscles as well as liquor sanguinis. We also find, in simple congestion, a fine meshwork of fibrin with red and white blood corpuscles; but these elements are not numerous in simple congestion, whilst, on the contrary, they rapidly form in great numbers in the congestion which precedes pneumonia.

When a portion of a much congested lung is at the same time deprived of air it looks like flesh, and the condition has been termed carnification.

Chronic hyperæmia is followed by more profound changes. We have already seen how the epithelial cells may become pigmented; similar alterations may occur here. The distended capillaries of the walls of the alveoli exude into the alveoli and their septa a highly-colored fluid; the connective-tissue cells swell by imbibition, and pigment granules are deposited in and around them. The amount of this pigmentation is the greater the more repeated and persistent the congestion. Its greatest intensity is seen in diseases of the heart accompanied by great impediment to the pulmonary circulation.

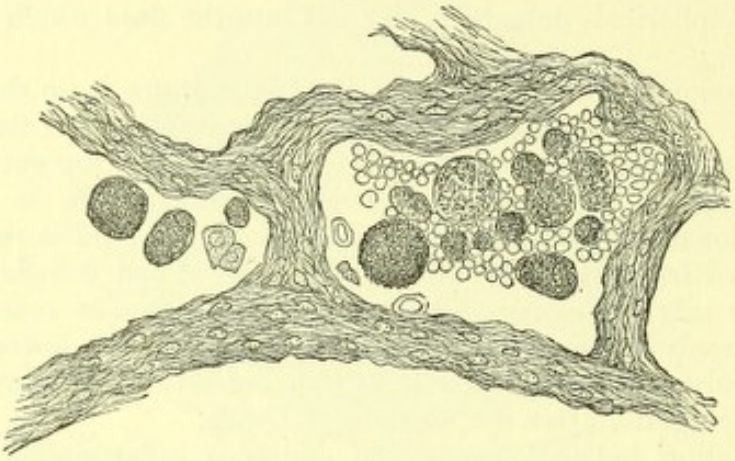
When the hyperæmia of the alveolar walls is very intense or a long time prolonged, the connective-tissue elements have a tendency to proliferate and form new fibrous tissue, principally around the bronchi and the vessels. This thickening of the pulmonary tissue is really the first stage of interstitial pneumonia.

A dark color of the lung may have a cause other than that just described. It may be due to the penetration into the ultimate ramifications of the bronchi and into the parenchyma itself, of fine particles of dust.

Pulmonary Apoplexy.—This lesion is most frequently met with in affections of the heart, above all in those of the mitral valve; it is sometimes connected with the eruptive fevers, with scorbutus, etc.

When the pressure in the capillaries of the lungs is much augmented, especially in passive congestion, besides the elements previously described, we have those of the blood filling the alveoli.

Fig. 224.



Section of lung attacked at the same time with interstitial pneumonia and pulmonary hemorrhage. The walls of the alveoli are thickened; in the alveoli are seen large round pigmented cells, pavement cells, and red blood disks. × 200.

The pigment granules which fill the large granular and vesicular elements, which have been already described *à propos* of congestion, are yellow or red, or, if the apoplexy is old, they are black. We may sometimes find in these cells crystals of hæmatoidin. In the sputa of pulmonary apoplexy we find these same granular elements suspended in a red mucous fluid, in which a large quantity of blood corpuscles is also seen. The alveoli and the terminal bronchioles emptying into them are completely filled with coagulated blood; the air is expelled from them, and the cut surface of the lung presents a mottled appearance, which is due to these small coagula. The distension of the lung by these coagula and the absence of air offer to the naked eye the appearance of a hepatization.

The capillaries and the bloodvessels of the whole of the diseased portion are full of blood. The arteries and veins adjoining the apoplectic spot are also obstructed by a coagulum, which is red if recent, or whitish and hard when old. The extravasated blood probably comes from the capillary network of the alveoli, either by rupture or transudation.

The naked-eye characters of the alterations of the lung in pulmonary apoplexy may present two different aspects.

1st. *Hemorrhagic Infarction of Laennec.*—We find in this case one or more firm points of a brown or sepia tint, generally so well circumscribed that there is a sharp line of demarcation between the hard nodule and the healthy or congested tissue which surrounds it. Cutting into these points, we observe that the surface of section is dark colored and granular, and upon pressure exudes a very small quantity of thick blood, free from air bubbles. The surrounding tissue ordinarily is soft and crepitant, but it may sometimes present a slight sanguineous infiltration.

The most frequent seat of these infarctions is at the centre of the

inferior lobe, or in the neighborhood of the root of the lung. They are also often superficial, and may occupy the sharp border of the lung. When they are located immediately beneath the pleura, they form a slight elevation. The pleural covering is inflamed, and frequently presents a false fibrinous membrane. It then often happens that there is a sero-fibrinous effusion, more or less mixed with blood, in the pleural cavity. This effusion may be so considerable as to compress the lung, thus rendering the discovery of the points of infarction difficult.

2d. *Localized Apoplexy.*—We sometimes encounter in the lung a mass composed of coagulated and fluid blood, surrounded by shreds of torn pulmonary tissue. It is a real apoplectic focus, just as we meet with in the brain. If the apoplexy is located at the surface of the lung, the pleura often ruptures, when the blood escapes into the pleural cavity. This form of apoplexy is rapidly fatal.

ATELECTASIS.—This lesion, which consists in the absolute absence of air from the alveoli, is met with in capillary bronchitis, in broncho-pneumonia, and in compression of the lung by a tumor or by a pleurisy.

The alveoli no longer contain air, their cavity is effaced, and their walls are in contact. The most extensive atelectasis of the lung is that which is caused by the compression resulting from a unilateral pleurisy with great effusion. The compressed lung, in the latter case, is surrounded by a much thickened pleura, which prevents it from fully expanding again, even after inflation. If, however, we remove the fibrous envelope, we can readily assure ourselves that the pulmonary parenchyma is intact, for the alveoli resume their form when the pleura which bridles them has been removed.

In atelectasis, the alveoli may be altogether empty, or they may contain in their interior a fluid holding in suspension large, spherical, granular cells, like those found in congestion.

The affected tissue is flesh-like, and sinks to the bottom when plunged into water; upon section, it presents a violet-red color; it is dry, tough, smooth, uniform, and it is not indented by digital pressure. This condition very well corresponds to that of the lung of a child which has not yet respired. It is most frequently encountered at the periphery of the lung, at its sharp borders, disseminated in points which are frequently small, as in broncho-pneumonia. In this case, the anatomical lesion is the result of the obstruction of a small bronchus or bronchiole by a plug of mucus.

Inspiration is too feeble to cause the air to penetrate; but the expiratory force, which is due only to the elasticity of the lung, remaining unabated, the air is gradually expelled from the alveoli supplied by the obstructed bronchus, and atelectasis follows. The same result can be produced in much the same manner by compression of the lung.

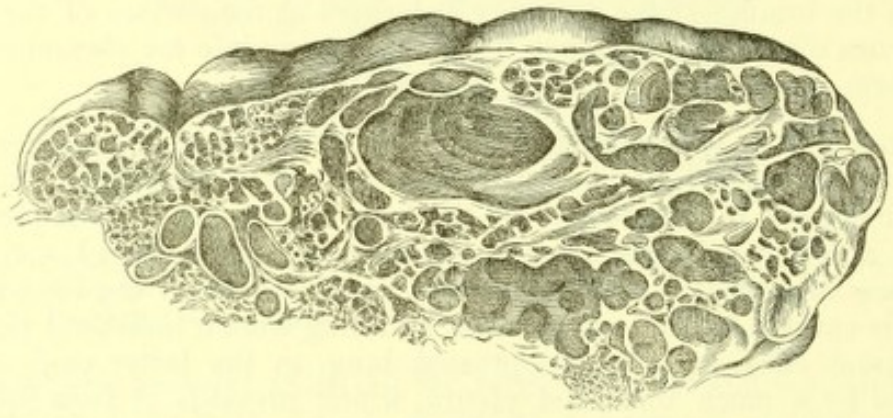
False pleuritic membranes, or induration of the inflamed pleura, render the dilatation of this portion of the lung impossible. The altered portions of the lung may, of course, also be the seat of tubercles, tubercular pneumonia, cavities, etc.

ATROPHY.—Atrophy of the lung, generally limited to one lobe, when it is caused by a pathological lesion, is the consequence of compression

by a tumor, by a pleurisy, or by bronchiectatic cavities. The atrophied part then presents the changes of interstitial pneumonia. This is so also of senile atrophy which is generally limited to the apex of the organ, and is frequently associated with induration and pigmentation. Emphysema should also be considered as a form of pulmonary atrophy.

Emphysema.—It was for a long time believed that, in pulmonary emphysema, the alveoli had simply become enlarged. It is now beyond doubt that, in this affection, there is an atrophy of a certain number of

Fig 225.



Macroscopic view of cut surface of simple chronic emphysema. Advanced stage. (*Reynolds.*)

the alveolar walls, which often leads to the dilatations which are so large in emphysematous lungs.

Upon the walls of large emphysematous dilatations there are to be seen, under the microscope, the vestiges of the septa of those alveoli which have been converted into a single cavity. By examining thin sections of such a lung inflated and dried, or thin pieces of the fresh lung, it is easy to see that the interalveolar septa are often perforated. This is the first stage of the process: the dilatation is limited to the infundibulum, the central cavity of which is enlarged and confounded with the alveolar cavities, of which the walls are more or less atrophied.

When the emphysematous infundibulum is located beneath the pleura, the absence of the resistance of neighboring tissue permits of a greater dilatation. The largest dilatations or vesicles, which may attain the volume of a hazel-nut or walnut, are due to an intercommunication of adjoining infundibula. This is the most advanced stage of the disease.

In certain cases of emphysema, especially in the old, at the apex and on the anterior borders of the upper lobes, the lung is converted into lacunæ which communicate with one another, so extensively that pressure upon one point causes the air to move in the interior in almost every direction.

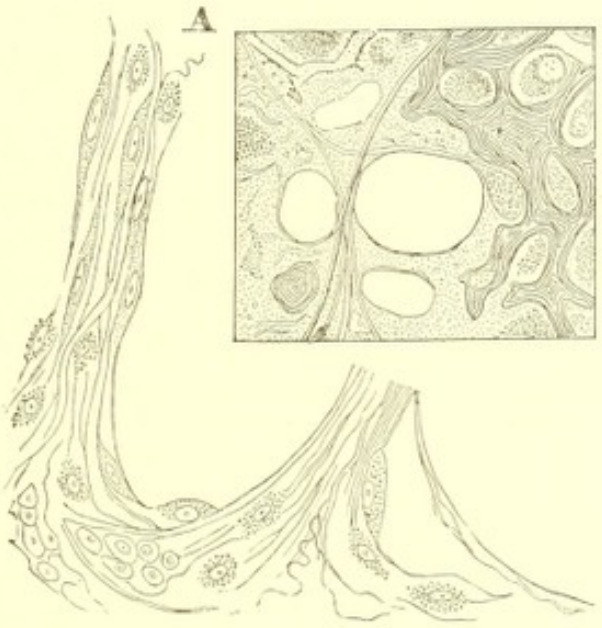
The mechanism of the perforation of the septa has been the subject of various interpretations.

We consider that the employment of silver staining has demonstrated the existence of a pavement epithelium lining the alveoli.

After removing with the scissors the thin wall of an emphysematous

vesicle projecting beneath the pleura, and staining its inner surface with a solution of silver, the pavement epithelium which lines the emphysematous dilatation is very distinctly visible. Examined, *in situ*, in preparations uncolored by the silver, the epithelial cells often exhibit fatty granules in the protoplasm around the nucleus, just as Rindfleisch has figured.

Fig. 226.



The figure to the right and above represents a highly magnified view of the wall of a pulmonary alveolus in a case of emphysema, after Villemin. The preparation shows several perforations.

The figure to the left is from Rindfleisch, and shows fatty granules around the nuclei of the degenerating and atrophying tissue. High power.

The thinned septa also present in their thickness and upon their surface ovoid masses of fatty granules which are derived from a degeneration of those elements, or perhaps of the cells along the capillary vessels. It is probable that this granular degeneration in a great measure causes the small perforations of the cellular septum of the alveoli.

Senile emphysema is especially characterized by nutritive lesions of the lungs. There is no reason why repeated bronchitis, disease of the heart, etc., should not be considered as initial causes of these lesions. While we know that croup, whooping-cough, and broncho-pneumonia of children may undoubtedly give rise to the affection. In these maladies the infundibula may be dilated by efforts of coughing and of respiration. While the process of their formation is acute and the bronchitis remains, the emphysematous vacuoles or vesicles are filled with mucous or muco-pus.

Upon the walls of large emphysematous dilatations, particularly in the old, a pigmentation along the course of the bloodvessels is remarked. We have vainly sought in these cases for atheromatous alterations of the vessels, which have been supposed by several authors to explain the idiopathic production of emphysema.

The wall of the cavities presents ridges formed by the bundles of

elastic fibres which belonged to the effaced alveoli and which are now applied against the internal wall of the dilatation.

If the emphysema exist over a large extent of the lung or of a lobe the circulation is considerably enfeebled; the diseased part is anæmic while in those parts which have remained healthy the tissue is red, œdematous, and gorged with blood.

Emphysema shows itself by preference at the apex and at the anterior and inferior borders of the lung, as whitish or gray prominences, sometimes even as spherical vesicular appendages filled with air. The diseased portions are soft and elastic to the touch.

When the greater portion of the lung is involved, the organ appears hypertrophied; it fills the pleural cavity and does not collapse when the thorax is opened; it may depress the liver and displace the heart.

Emphysema may give rise to pneumothorax by rupture of a vesicular dilatation.

Interlobular emphysema may extend to the mediastinum, to the neck and to the subcutaneous cellular tissue.

Finally, interlobular emphysema by reason of the penetration of air into the subpleural cellular tissue from rupture of the alveolar walls, gives to the vesical pleura the appearance of a membrane uplifted by foam. These vesiculæ are easily displaced by pressure, and moved from place to place under the pleura, a characteristic which distinguishes this form of emphysema.

The most frequent cause of emphysema is asthma, whooping-cough, and in general all the diseases of the chest which are accompanied by cough and by violent efforts at expiration. It is almost constantly coincident with senile atrophy of the lung.

Inflammation of the Lung; Pneumonia.—On account of their different causes and their varying modes of action upon the different tissues of the organ, the forms of inflammation of the lungs are numerous.

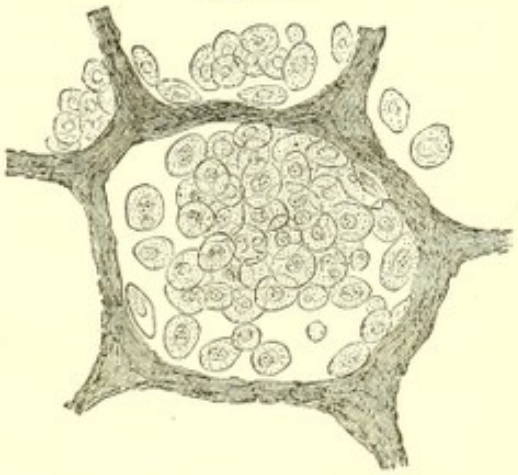
We will first describe those forms of pneumonia which are particularly characterized by an interalveolar exudation. After that we shall consider those forms of inflammation which essentially consist in an alteration of the fibro-vascular framework of the lung.

A. Lobular or Catarrhal Pneumonia.—This form of pneumonia, also described as broncho-pneumonia, is most frequently caused by an extension of inflammation from the bronchi to the bronchioles and the air cells into which they empty. But this extension of the bronchitis is seen only in certain lobules of the lung. It is especially frequent in children, but it is also met with in adults affected with typhoid fever, measles, and in phthisis pulmonalis.

The lesion is generally disseminated in small areas of the size of a hazel-hut or walnut, but nevertheless it may uniformly invade a large portion of a lobe. Under the influence of congestion, the vessels become turgid, and the epithelia of the alveoli swell and present a granular protoplasm which frequently contains two or three nuclei. These cells become globular and fall into the alveolus. Moreover, a considerable number of white corpuscles, with quantities of serum, escape from the

bloodvessels into the alveoli, but the latter are never so distended as in lobar or fibrinous pneumonia. The epithelial elements which are found detached and suspended in the fluid which fills the alveoli, besides suffering the changes above indicated, may experience a division of their protoplasm, thus giving rise to the presence of embryonal cells containing one or more nuclei—changes similar to those described at page 57, *et seq.*, *à propos* of inflammation of the great omentum. But here, the phenomena are more complex, because of the presence of the white blood corpuscles which have escaped from the vessels.

Fig. 227.



Catarrhal pneumonia. From a case of acute phthisis. Showing the large epithelial cells which fill the alveoli. — 200. (*Green.*)

We recognize three stages in this form of pneumonia.

1*st Stage.*—The altered points of the lung are red, prominent, slightly or not at all crepitant, and from their cut surface a red, cloudy, slightly foamy fluid may escape upon pressure. There is no distinct line of demarcation between these points and the surrounding parts which are congested. This is the stage of engorgement or inflammatory hyperæmia, which is only one degree more advanced than congestion already described.

Microscopic examination of the red, turbid fluid which upon pressure escapes from the cut surface will show large numbers of pus corpuscles, and thin sections made after hardening the inflamed tissue will show the alveoli filled with these elements.

2*d Stage.*—The alveoli containing the elements and the fluid previously indicated no longer inclose air; the amount of blood in the vessels is diminished by reason of the equilibrium established between congestion and exudation, between intra-alveolar pressure and the pressure of the blood; coincident with this diminution of the quantity of blood, the affected lobules become less colored; they present a pink or gray appearance. If the lungs are forcibly inflated, a small amount of air can yet be made to enter the diseased alveoli, when the lobule will assume a somewhat normal appearance.

3*d Stage.*—The pus corpuscles which have not been expectorated rapidly undergo a retrograde metamorphosis. At first granular, by reason of the commencement of a fatty destruction, they soon become deformed and broken up, their molecules separate, and are subsequently eliminated in the form of a fatty emulsion, which is probably taken up by the blood and lymph vessels.

When the catarrhal pneumonia terminates by resolution, the pulmonary epithelium re-forms and again lines the alveoli, a further analogy with the inflammation of the great omentum described on page 57.

In certain cases the lobules remain pale yellowish, often appearing as granules of the size of a millet-seed, which somewhat resemble tubercles,

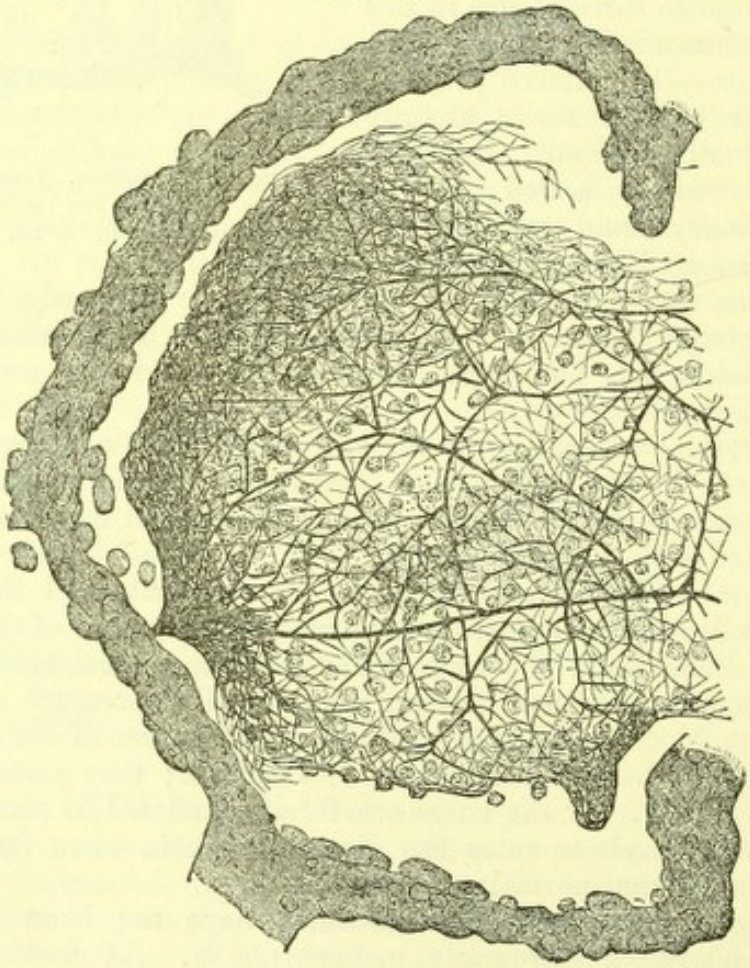
but when they are incised, instead of being solid bodies like tubercles, a fluid escapes from their centre.

There always exists a pleuritic exudation upon the pleural covering of affected lobules.

B. Lobar or Fibrinous Pneumonia; Croupous Pneumonia.—The histological phenomena are much the same as those met with in the preceding form of inflammation; but the exudation, in addition to the other constituents, contains fibrin; the latter is at first fluid, but soon coagulates and holds in its meshes the elements already indicated.

As in the preceding variety, *three stages* are distinguished; 1st, engorgement; 2d, red hepatization; 3d, gray hepatization or purulent infiltration.

Fig. 228.



Croupous or fibrinous pneumonia. Red hepatization. Showing the fibrinous coagulum in one of the pulmonary alveoli, inclosing within its meshes numerous leucocytes, which are already commencing to undergo fatty metamorphosis. A few leucocytes are also seen on the alveolar walls, and the alveolar epithelium is swollen and granular. × 200. (*Green.*)

1*st Stage.*—The first stage, in which there is a very intense congestion, is characterized, in a histological point of view, by fulness and varicose distension of the capillaries of the alveoli, by the alterations in nutrition of the cells already mentioned, by the escape from the vessels of the fluid of the blood together with both red and white corpuscles. The

pulmonary parenchyma, of a brownish-red, is heavier and more compact than in the normal state, it has lost its elasticity, and crepitates but little under pressure. Upon section, there escapes a sero-sanguinolent fluid as yet a little frothy, and portions of the engorged tissue still float when plunged into water. This first stage lasts from twenty-four to forty-eight hours.

2*d Stage*.—The exuded fibrin coagulates, fills, and distends the alveoli; and the lung is converted into a solid mass. The lung seems augmented in volume, and upon its external surface the ribs have left their imprint.

The lung does not crepitate; it is firm to the touch, yet is at the same time very friable; it is heavy and sinks in water. The cut surface presents a granular aspect, which is still more pronounced when the pulmonary tissue is torn. This aspect is due to the relief formed by the infundibula, which are filled with fibrin which, on account of the presence of red blood disks, is red.

If a stream of water is turned upon the cut surface for the purpose of washing away the blood, red as it is at first it soon becomes gray or yellowish-gray, the natural color of coagulated fibrin.

By scraping the surface of section we obtain small grayish granulations, which furnish a complete mould of the infundibulum and alveoli.

When these coagula are examined *in situ*, it is found that they completely fill and distend the alveoli, and that the walls of the latter show no other thickening than that which results from the engorgement of their vessels.

The exudation contained in the alveoli is composed of a reticulum of fibrils of fibrin, which incloses in its meshes altered epithelium and large numbers of white and red blood corpuscles.

Fig. 229.



Cellular elements from the second stage of pneumonia. *f*, *h*, *i*. Pus corpuscles. *a*, *e*. Pavement cells. *d*. Pavement cell with two nuclei. *k*. Vesicular cells. (*Reynolds*.)

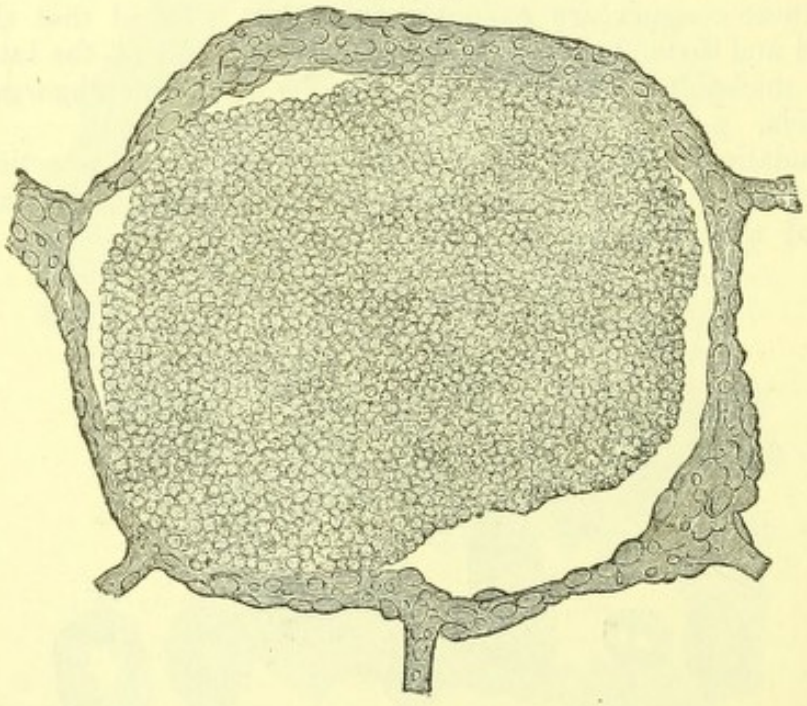
The bronchi contain a transparent, viscid, fluid exudation, and coagulated fibrin similar to the preceding. These coagula do not completely

fill the tubes, they may be found in the sputa, which are also more or less mixed with blood.

The second stage, after having continued on an average from three to five days, terminates by resolution or by passing into suppuration. The fibrin deposited in the alveoli passes from the fibrillar into the granular state, and the cell elements are then freed and easily displaced; the solid exudation has become fluid or semi-fluid. At this time the pus corpuscles or white cells may become granular or vesicular, may disintegrate and be absorbed or expelled with the sputa; this is resolution. But if, on the contrary, the pus corpuscles continue to form, if as often happens they become even more rapidly produced than at the commencement, the pneumonia will pass to the stage of purulent infiltration.

3*d Stage*.—In this stage of gray or purulent infiltration (gray hepatization), the cut surface is pale gray or yellowish, and the granular appearance is less marked. If the lung is squeezed, there oozes out a thick reddish-gray pus. The tissue is very friable, which condition, in the second, and especially in the third stage, is due not only to the friability of the exudation but also to the tense state of the thin walls of the infundibula.

Fig. 230.



Croupous or fibrinous pneumonia. Gray hepatization. Showing the large accumulation of cellular elements within one of the pulmonary alveoli, which in some parts have undergone such extensive fatty degeneration that their distinctive outlines are no longer visible. × 200. (*Green.*)

When acute lobar pneumonia reaches the surface of the lung, it is always complicated with a certain amount of pleurisy. The visceral pleura is covered with a thin layer of false membrane, which is slightly adherent and presents a dull and downy aspect. This false membrane consists of a fibrinous network holding in its meshes pus corpuscles and broad endothelial cells, which are flat, swollen, or proliferating. These

false membranes very rapidly become vascularized. Very rarely do we find any notable quantity of fluid effusion in the pleural cavity; the escape of such a fluid is, in effect, especially characteristic of ordinary acute pleurisy, which may sometimes complicate pneumonia, and we then designate the affection as a pleuro-pneumonia.

The slight thickness of the visceral pleura, scarcely .05 of a millimeter, and the direct connection of its circulation with that of the contiguous alveoli, readily explain this constant complication.

Inversely intense inflammations of the pleura may involve the adjoining pulmonary tissue.

The lymphatics of the surface of the lung are constantly inflamed in pneumonia, and are filled with an inflammatory exudation, similar to that which distends the alveoli. In catarrhal pneumonia they contain swollen endothelial cells, while in fibrinous or croupous pneumonia they are choked with fibrin, white corpuscles, red blood disks, and a few endothelia. In these cases the deep lymphatics are extremely difficult to distinguish under the microscope, because of the identity of their contents to those of the alveoli. But there is not the same difficulty in recognizing the superficial lymph vessels. The whole lymphatic system belonging to the affected portions of the lung, including the vessels of the bronchi and the lymph glands at the root of the lung, always present evidence of inflammation.

In the *new-born* we sometimes meet with a peculiar form of catarrhal pneumonia, which uniformly involves one or more lobes, or which remains limited to lobules. It may involve aveoli which have not yet respired.

In *children a little older* pneumonia is ordinarily lobular or catarrhal, and accompanied with numerous points of atelectasis; nevertheless children may also be attacked with croupous or fibrinous pneumonia.

In *adults* pneumonia is almost always lobar or fibrinous.

In the *aged* we may meet with lobular pneumonia, but the commonest form is that of the lobar or fibrinous or croupous variety, and of all acute diseases which attack man at this time of life it is the most frequent. In the old, croupous pneumonia often follows an unusually rapid course; frequently patients succumb upon the fourth day of a pneumonia while, at the autopsy, the lung shows a gray or purulent hepatization.

In lungs affected with *emphysema*, the large size of the fibrinous granules is remarkable.

Patients suffering with cardiac trouble present a special form of pneumonia. It may be catarrhal or fibrinous, lobular or lobar, but is almost always of slower progress than the ordinary acute pneumonia, and is complicated by an intense congestion, which may even become apoplectic, or result in veritable apoplexiform infarctions of the lung.

Pneumonia may terminate in abscess or gangrene.

Abscess of the Lung.—This termination of the third stage of pneumonia is rare. Abscess is characterized histologically by the destruction of several of the septa, thus causing an intercommunication of several alveoli filled with pus, and the formation of a small anfractuous cavity. Several adjoining infundibula may in like manner form communications.

The abscess is then larger, and if it happens to break into a bronchus and empty itself, a vomica is established.

If the abscess be superficial it may lead to perforation of the pleura, and the establishment of a pyo-pneumothorax; or, as not infrequently happens, the two surfaces of the pleura may adhere at this point, and the abscess break through the intercostal muscles and form an external fistula.

Metastatic abscesses of the lung, such as are commonly seen in purulent infection, in puerperal fever, in ulcerative endocarditis, in typhoid fever, etc., are characterized at the commencement by small congested foci of catarrhal pneumonia, of the size of the head of a pin, seated most frequently under the pleura. As they increase in size a small, at first scarcely perceptible, point of suppuration becomes visible at the centre. This rapidly enlarges as the nodule of metastatic pneumonia, with its surrounding area of apoplectiform congestion, extends. Very soon the pus corpuscles, instead of being compressed within the infundibula, constitute a purulent focus which is due to the destruction of the septa between infundibula.

These nodules of catarrhal or purulent pneumonia instead of being disseminated may become confluent, when they give rise to a larger area of catarrhal pneumonia, the border of which is sinuous and lobulated. If circulation continues in the part thus altered, there forms an abscess; but if the vessels become impermeable by pressure of the intra-alveolar exudation, the entire portion mortifies, and there is thus produced a white infarction of an irregular shape and of a caseous consistence, surrounded by a much congested zone, in which diffuse hemorrhages often occur.

In the caseous spots the contents of the alveoli consist of nothing else than the débris of cells, fatty granules, and crystals of the fatty acids. We can still discern the limits of the alveoli, but their vessels are no longer recognizable. At the border of the caseous areas, the alveoli present the appearances of catarrhal or purulent pneumonia and of apoplexy.

What is the pathology of the pulmonary lesion in purulent infection? Is it an embolus, as Virchow imagines, or is it an inflammation due to another cause? We were the first to disclose that the lesions of purulent infection ought not to be attributed to emboli but rather that they probably depend upon a certain ferment, which in the form of microphytes or bacteria circulating in the blood or lymph passages, determines a local irritation. This view was developed almost simultaneously by two of Virchow's pupils—Klebs and Recklinghausen.

The pneumonia of glanders is a purulent pneumonia, of which the characters resemble those of metastatic abscesses.

Inflammation of the Lymphatics of the Lung.—We have previously seen that, in pneumonia, the lymph vessels are constantly inflamed, and are filled by the same exudation which the alveoli contain.

We may, therefore, recognize, as in pneumonia: 1st, a *catarrhal* inflammation, characterized by swelling and multiplication of the endothelium which lines their internal wall; 2d, a *fibrinous* or croupous inflammation in which the lumina of the vessels are filled with pus

corpuscles and fibrin; and, 3d, a *purulent* inflammation, such as is met with in purulent infection.

Inflammation of the superficial and deep lymphatics of the lung is rarely met with independent of pneumonia and pleurisy. Nevertheless, a few observations have been published. Those lymphangites which are consecutive to cancers of the stomach, to lymphadenomata, to syphilitic disease of the stomach and liver—all lesions which have occasioned alterations of the bronchial lymph glands—are particularly remarkable on account of the enormous distension of the lymph vessels, as well as of the caseous condition of the central portion of the exudation which fills them.

Upon the surface of the lung, the lymphatics, having the appearance of whitish or yellowish moniliform cords, of a diameter from $\frac{1}{2}$ to 1 and 2 mm., mark out the interlobular network; these vessels increase in size as the root of the lung is approached.

In a thin section of the lung, they are seen in the interlobular septa and along the bronchi and bloodvessels. Examined in the fresh condition, two layers of elements are ordinarily visible within the lymph vessel: the one close against the vessel wall, and composed of numerous layers of swollen, polygonal, membraneless, endothelial cells, with a granular protoplasm and large ovoid or spherical nucleus; the other, within the first, consists of a caseous, opaque, yellow coagulum, formed of lymph corpuscles which show a granulo-fatty degeneration.

GANGRENE.—Pulmonary gangrene is sometimes a sequel of pneumonia or of pulmonary hemorrhage. It appears to be most frequently connected with obliterations of the pulmonary or bronchial arteries; or it is caused by infectious diseases—typhoid fever, anthrax, etc.; or it may be the result of a wound or a perforation of the lung. Gangrene, in connection with dilation of the bronchi, has already been mentioned.

Pulmonary gangrene presents two anatomical varieties: it is *circumscribed* or *diffuse*.

1st. *Circumscribed gangrene* usually presents several disseminated foci in one or both lungs.

These gangrened or softened spots are always found to be surrounded by zones of lobular or catarrhal pneumonia. In fact, they are almost always preceded at their seat by a localized catarrhal pneumonia.

Each of these nodules of lobular pneumonia which has terminated in gangrene presents at its centre a smaller or larger anfractuous cavity. If the latter is very extensive, vessels are often observed to project into it. It is filled by grayish, grumous fluid, and it may communicate with a bronchus; both cavity and fluid exhale a very fetid odor.

When one of these indurated foci is cut open, three distinct zones are seen. The 1st or central zone is formed of a grayish débris or a consistent pulp, while the cavernous wall which bounds this softened mass is of a deep vinous red. The 2d zone consists of hepatized pulmonary tissue, gray and friable. In these two zones all the vessels are filled by a fibrinous clot. The 3d or peripheral zone is continuous with the surrounding healthy parts, and presents the lesions of catarrhal pneumonia in the second stage.

The second or intermediate zone, which is about to mortify and be

eliminated, histologically presents the following characteristics: the tissue is bloodless, contains no air, and presents a gray, slightly transparent aspect. Under the microscope, we find in the alveoli large, round cells containing fatty granules, and suspended in a fluid which contains pus corpuscles. These large granular corpuscles usually still contain a nucleus. They give to the alveolar contents their opacity and yellowish color. The vessels are filled with coagulated fibrin. The tissue thus hepatized is distended with fluid and is very friable. It is met with in all the varieties of pulmonary gangrene at the limit of the putrefying zone, and it is often observed in tubercular pneumonia which is going to terminate in an ulcerative destruction.

The solid grayish débris which covers the wall of the ulcerated cavity contains the remains of vessels and elastic fibres which still adhere more or less intimately to the adjoining external zone, and which, under the microscope, may be found to be continuous with the same elements of the hepatized portion.

The loss of substance in this form of gangrene is explained briefly, as follows: Putrefaction and molecular destruction commence at the point where the gangrened pneumonia comes in contact with the external air, namely, at the centre of the lobule which is supplied by a bronchus. This destruction extends from point to point, and the products of cadaveric decomposition, together with the fluid, remain in the ulcerating cavity until expectorated.

The contents of the cavity are now a grumous mass, consisting of a fluid in which float pus corpuscles, large cells infiltrated with fatty granules, filaments of connective or elastic tissue, pigment granules, black, orange, or yellow, derived from the coloring matter of the blood, and, finally, crystals of the ammonio-magnesian phosphates, of margarin, of leucin, and of tyrosin; we may also meet with fungi similar to leptothrix buccalis, and with swarms of vibriones and bacteria.

The sputa have a characteristic odor, are generally gray and puriform, and are slightly colored by blood. They may present all or part of the elements enumerated in the preceding paragraph. Mixed with water they separate into three layers, like the expectoration from bronchiectatic cavities.

The affected lobules, when located under the pleura, excite a fibrinous pleurisy; and, when the gangrenous cavity enlarges, it sometimes opens into the pleural cavity and occasions a pyo-pneumothorax.

Fig. 231.



Fetid pus. Showing common active bacteria amongst the pus corpuscles. × 600. (*Green.*)

2d. *Diffuse Gangrene.*—It may be the termination of the third stage of croupous pneumonia. In the horse it is a frequent sequel of pneumonia, and is the result of a coagulation of fibrin in the bloodvessels. In man this form of gangrene may be the consequence of an obliteration of a large branch to the pulmonary artery by an embolus.

The mortified portion of the lung is more extensive and more irregular in outline than in circumscribed gangrene, but the minute processes, their march, and their results are the same. The ulcerated cavities which result from this form of

gangrene are anfractuous, are very large, are bridged by vascular bands and contain an ichorous, serous, or puriform fluid in which myriads of bacteria swarm.

In certain cases the gangrene has a peripheral location immediately under the pleura, when there very rapidly results a pyo-pneumothorax.

INTERSTITIAL PNEUMONIA.—Under the name of interstitial pneumonia we shall describe several conditions of the lung which have very different causes, and which are far from being the same in an anatomical point of view, but which ought to be considered together because they present a character in common, namely, inflammatory thickening of the fibrous framework of the lung.

What characterizes interstitial pneumonia is, therefore, the multiplication of the connective-tissue elements of the pulmonary septa. The process is generally chronic, most frequently the thickened and indurated pulmonary tissue is at the same time pigmented; it is colored black, or slate gray.

Interstitial pneumonia is *partial*, when, for example, it is occasioned by a limited lesion, by old caverns, by miliary tubercles, by dilated bronchi, by a healed abscess, by a chronic pleurisy, etc. It involves an entire lobe or is *general*, when it is due to an acute pneumonia or to the penetration into the lung of minute particles of carbon, silica, or steel.

In the different varieties of interstitial pneumonia, the anatomical phenomena which accompany the thickening of the interalveolar and other septa, not being the same, we shall be obliged to describe them separately.

Fig. 232.



Interstitial pneumonia. From a case of so-called "cirrhosis" of the lung, in which the disease was unilateral. The bronchi were much dilated, and there was a complete absence of any caseous change. The drawing shows the new fibro-nucleated growth, both in the alveolar walls and in the interlobular tissue, also the pigmentation. At *a* a divided vessel is seen. × 100. (*Green.*)

The phenomenon constant in all the forms of interstitial pneumonia is the fibrous induration of the pulmonary tissue. The alveolar septa are very thick, hard, and of a fibrous aspect. Under the microscope a larger number of small cells are seen in the septa; at the commencement of the morbid process they are round; later they become slightly lengthened

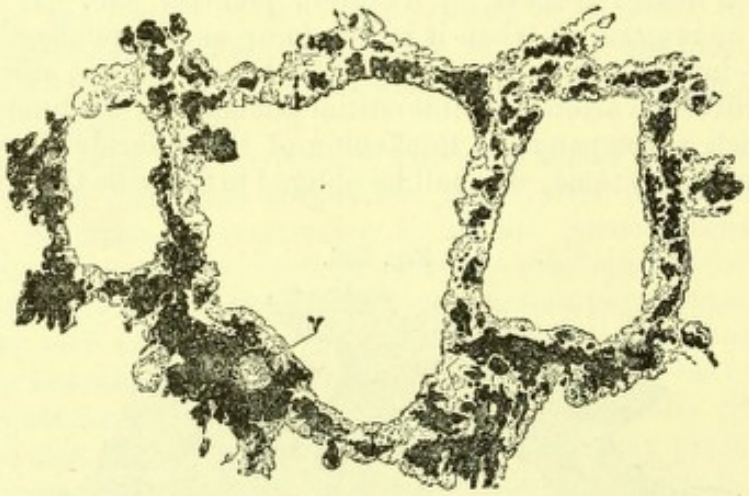
and flattened, and are situated between fasciculi of newly-formed connective tissue.

The cavity of the alveoli, at first only diminished, ends by becoming completely obliterated. The enormously thickened walls are then in contact, and the whole of the affected portion of the lung has undergone a fibrous transformation. This is very often observed in the subpleural portion, and at the apex of the lung in certain chronic pleurites.

This altered tissue creaks under the knife, and, to the eye and the touch, presents all the characters of a fibrous tissue. The microscope reveals a more or less abundant pigmentation of the connective tissue of the alveoli, especially around the vessels. The latter present very much thickened walls, which shade off very gradually into the adjoining fibrous tissue. The arteries are not obliterated; upon section their lumina are gaping.

a. In the *aged* there exists a condition of the lung, so frequent that it could possibly be regarded as physiological; it consists in a *slaty induration* of the apices. The tissue is hard, elastic, non-crepitant, and black;

Fig. 233.



Pigmentation of the lungs. From a woman, æt. sixty-five, with slight emphysema. Showing the situation of the pigment in the alveolar walls, and around the bloodvessel v. × 75. (*Green.*)

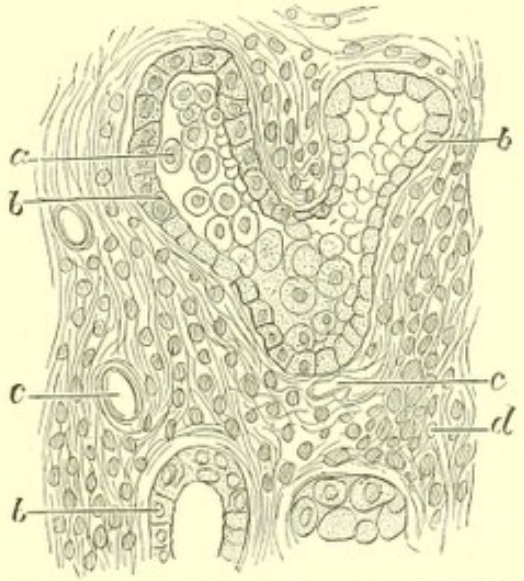
upon the surface it sometimes presents depressed cicatrices of the pleura and dense fibrous adhesions. Upon section we see a dense tissue formed of very much thickened septa limiting retracted alveoli, or on the contrary we observe emphysematous dilatations surrounded by a dense fibrous tissue which is infiltrated with black pigment. Often there also exist, in the midst of this fibrous tissue, caseous or calcareous nodules lodged in minute cystic cavities, which if cylindrical may be continuous with a bronchus. Such cavities containing caseous or calcareous matter, which is nothing else than altered pus, have been regarded by many writers as healed tubercles. If this be true sometimes, it is unquestionable that they may also be the remains of any old morbid process, such as bronchial dilatation, pulmonary abscess, infarction, etc. In this form of interstitial pneumonia, at the apex of the lungs we sometimes meet with spicules of bone, already described at p. 133.

b. Syphilitic Pneumonia.—In this variety, which we find almost exclusively in the new-born, the lung offers no trace of pigmentation. The interalveolar septa are extremely thick, and their cellular elements are round and embryonic. Finally the alveoli, although notably diminished in size, are still permeable, and their walls are covered with a very evident pavement epithelium, which at the centre of the alveolus becomes spherical and is then infiltrated with fatty granules.

The naked eye examination enables us to recognize the density and the resistance of the diseased portion. Upon the cut surface we see tissue, white or grayish, of fibrous appearance, difficult to tear, or to cut with the finger-nail.

In these nodules of syphilitic pneumonia, veritable gummata may be developed. In certain cases they are accompanied by a surrounding bronchitis or catarrhal pneumonia.

Fig. 234.



Transverse section of a hepatized nodule of syphilitic interstitial pneumonia from a new-born child. *d*. Proliferating connective tissue of the lung. *b*. Pavement-cells arranged around the alveoli. *a*. Free spherical cells in the alveoli. *c*. Vessels. × 300.

c. In repeated congestion of the lung following hemorrhagic infarction, in a special form of miliary tuberculosis, and especially in *chronic disease of the heart*, we often find portions of the lung indurated and

Fig. 235.



Brown induration of the lung. Showing the abnormal number of swollen pigmented epithelial cells covering the alveolar walls, the increase of connective tissue around the bloodvessel, *a*, and the large quantity of pigment. *b*. The alveolar cavity. × 200. (*Green.*)

black with pigment, which present the same lesions of the alveolar walls and of the contents of the alveoli as in the interstitial pneumonia of miners or anthracosis.

d. Anthracosis.—The lesions produced in the lungs of miners, metal-founders, etc., by minute particles of carbon are at first those of bronchitis; after that, a special form of interstitial pneumonia which terminates in ulcerations and the formation of cavities.

One or both lungs are altered more or less extensively. The diseased portions are dense and of a slaty or black color; they generally form an elevation upon the surface of the lungs. Upon section of the organ, these indurated portions offer a smooth, shining, solid surface, slate-gray or black, or of a brilliant ebony when the lesion is very pronounced. In the latter case the finger which touches it is soiled black, and by scraping with the scalpel a thick fluid of the same color is obtained. The bronchi contain a dark muco-pus, and the sputa present a similar aspect.

Thin sections examined under the microscope show the interalveolar septa very much thickened and containing minute black particles disposed along the vessels, in their internal coat as well as in the cells and between the fibres of the connective tissue.

In the interior of the contracted alveoli there are round cells of the size of pus corpuscles and larger, which contain dark granules. In the fluid in which these cells are suspended the same dark granules are seen, and they are endowed with the Brownian movement. These granules are either round or irregular and angular. They undoubtedly consist of the dust of carbon introduced by way of the air-passages. This dust cannot penetrate the layer of ciliated cylindrical epithelium which lines the air-passages; having reached the air-sacs, a desquamation of the epithelium is excited by their irritating presence; it is then not difficult for the fine particles to penetrate into the loose connective of the septa. The pus corpuscles absorb some of these particles, thus securing a discharge by the sputa. Others, by an opposite route, enter the lymph circulation of the lungs and reach the bronchial glands. The mesenteric glands may also lodge some of those particles which are swallowed with the sputa, and these glands are usually enlarged.

In the last stage of the morbid process, the black and indurated portions of the lung may ulcerate at their centre. Thus, caverns somewhat analogous to those of pulmonary phthisis are formed.

Artificers in iron and steel are subject to a similar form of pneumonia (*siderosis*), but here the coloration is brown, instead of black.

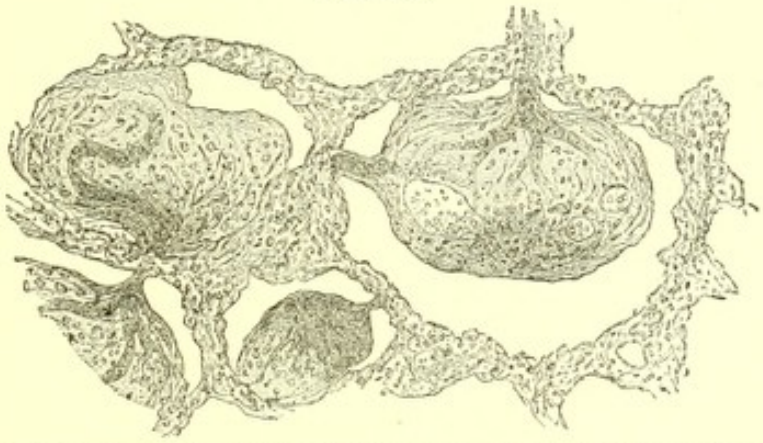
Workmen exposed to the dust of silica may be affected in a similar way.

e. Lobar or croupous pneumonia which has passed into the *chronic state* is extremely rare, but it is sometimes met with in hospitals for the aged. Charcot distinguishes three distinct forms by their color—red, gray, and yellow hepatization. We believe that this difference in color is due, in the one case, to the effusion of blood into the alveoli, and in the others, to the abundance of fatty granules which are contained in them.

In these cases of chronic pneumonia the interalveolar septa are thickened and more or less infiltrated with dark pigment derived from the blood. The alveoli are filled with large spherical cells, containing pigment or fatty granules as well as lymph corpuscles and, in some cases, red blood disks. Cavities have been occasionally met with.

[Green has seen three cases in which, beside the growth of the alveolar walls, the intra-alveolar exudation products were undergoing fibroid metamorphosis. The alveoli were found filled with a fibrinous meshwork containing leucocytes, somewhat similar to those met with in red hepatization. They differed however in this respect—that many of the cells were long and spindle-shaped, and bloodvessels were distributed amongst them, which bloodvessels communicated with those of the alveolar walls (figs. 236, 237). The alveolar walls were also thickened by a fibro-nucleated growth.]

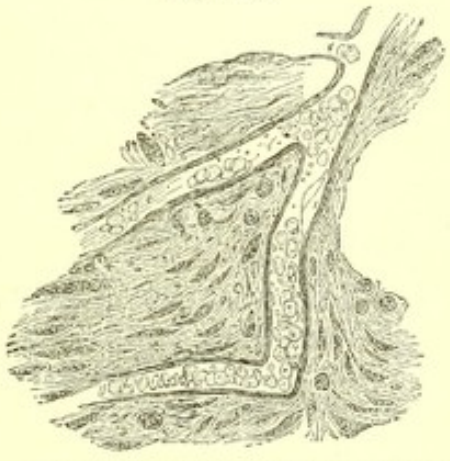
Fig. 236.



Chronic pneumonia. Vascularization and fibroid development of intra-alveolar exudation products. Bloodvessels are seen in the exudation products, which bloodvessels communicate with those in the alveolar walls. The alveolar walls are also thickened by a fibro-nucleated growth. × 100, and reduced ½. (*Green.*)

In all the forms of interstitial pneumonia which we have passed in review, when the lesion is seated at the surface of the lung, it is accompanied by a chronic pleurisy characterized by a considerable fibrous thickening.

Fig. 237.



Chronic pneumonia. A portion of the intra-alveolar exudation products (Fig. 231) more highly magnified. Showing the elongated spindle cells, the fibrillation, and the bloodvessels containing blood corpuscles. × 200. (*Green.*)

TUMORS OF THE LUNG.—Almost every kind of tumor has been observed in the lung, but the most common and the most important are tubercles of this organ. We will describe with tubercle the diverse lesions of the lung which accompany them.

Sarcoma has been met with in the lung only as secondary nodules succeeding primary tumors located elsewhere. In these secondary growths is reproduced the structure of the original tumor. Their development may start in the alveoli or in the interalveolar septa.

In melanic sarcoma the only difference is that the elements of new formation are infiltrated with black or brown granules.

Simple melanic tumors (see page 198), reproduced in the lungs are entirely similar in constitution, both to the naked eye and under the

microscope, to the interstitial pneumonia of miners, except that the black granules are small and round, instead of angular.

A melanic tumor of the lung may invade the bones of the vertebral column in such a manner to destroy the bodies of one or more of the vertebræ, thus giving rise to a variety of Pott's disease.

Fibromata of the lung have been observed by Rokitansky as small hard masses of the size of a pea or hazel-nut, and the same pathologist has seen *lipomata* from the size of a lentil to that of a pea, situated beneath the visceral pleura.

Osteomata are met with in lungs affected with interstitial pneumonia. We have seen an example of osteoid tumor of the lung characterized by the transformation of alveolar septa into osseous tissue.

Enchondromata have been seen in the lung only as secondary formations after the development of an enchondroma in another organ.

Primary *Carcinoma* of the lung is very rare. It is most frequently encephaloid, and is found more often in the right than in the left, but it may invade both lungs, the one after the other.

It commences by nodules which enlarge and form one or more masses, invading the greater part of one or more lobes. The visceral pleura over these nodules always presents a considerable thickening, which is due to a carcinomatous transformation.

Upon cutting into the diseased parts, it is common to observe whitish islands or granulations similar to those of the hepatized lung, separated by pigmented septa of lung tissue. These islands are due to the stuffing of an infundibulum by the carcinomatous elements. In scraping the cut surface with a scalpel these granulations are removed, and a milky fluid is obtained.

A microscopic examination of thin sections shows the alveoli filled by large spherical or polygonal cells containing large usually oval nuclei, with distinct nucleoli. The alveolar walls are very frequently preserved intact, or they may be somewhat thickened by the formation of small round cells between their fibres. Their vessels are gorged with blood. There is therefore no stroma of new formation in carcinoma of the lung, but the fibrous trabeculæ are constituted by the altered inter-alveolar septa.

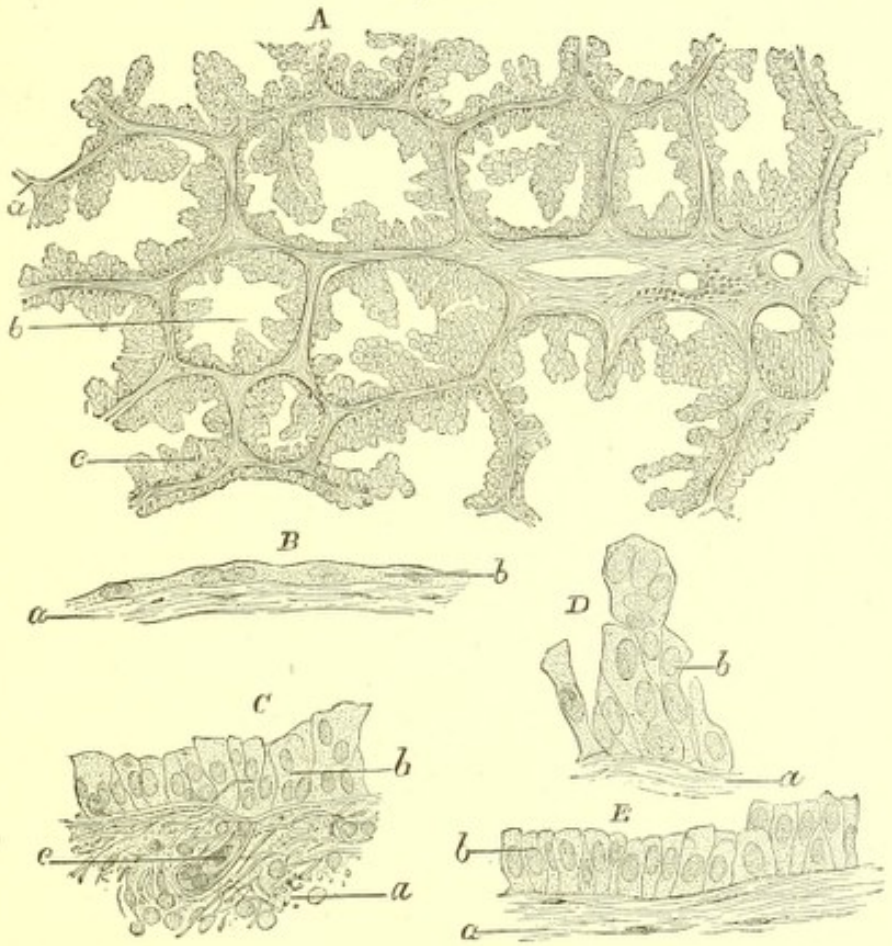
Carcinoma of the lung may give rise to ulcerations or caverns, which are sometimes multiple and in direct communication with the bronchi. Hæmoptysis may then supervene, and the patient expectorate the disintegrated elements of the walls of the cavity with the cancer juice.

Nodules of secondary carcinoma of the lung present the same structure as is found in the primary growth wherever it may be located, and whether it be scirrhous, encephaloid, colloid, melanotic, or any other variety.

Colloid carcinoma, which is comparatively common in the lung as a sequel of a primary tumor of the same nature developed in the mucous membrane of the alimentary or biliary canals, presents itself under the form of small transparent grains, surrounded by the wall of an infundibulum. These grains unite to form small spherical nodules; here also the stroma of the tumor represents the fibro-elastic framework of the lung.

The growth of carcinoma of the lung therefore notably differs from its habitual mode of development (see page 99 *et seq.*).

Fig. 238.



A. Section of encephaloid carcinoma of the lung × 50. *a*. Fibrous stroma consisting of the walls of the pulmonary alveoli. *c*. Epithelial lining of the alveolar walls with their vegetations. *b*. Alveolar cavity.

B. Epithelial covering of flat cells × 300. *a*. Alveolar walls. *b*. Epithelial cells.

E. Epithelial covering of cylindrical cells × 300. Lettering same as preceding figure.

D. Proliferating cells of the lining epithelium × 300. Lettering same as preceding.

C. Section of a bronchial gland × 300. *a*. Reticulated tissue of the follicle. *b*. Cylindrical epithelium lining a space in the cavernous tissue. *c*. A solid epithelial prolongation penetrating into the reticular tissue. (*Malassez.*)

In a certain number of cases of secondary carcinoma of the lung, we have been able to demonstrate a very active participation in the neoplasm of the superficial lymph vessels of the pleura (see below under cancerous granulations of the pleura).

Tuberculosis of the Lung.—However perfectly demonstrated and indisputable the unity of tuberculosis may be, we should not expect to find in tuberculous lungs simple lesions, or those which are always the same. Beside the initial and characteristic lesions, we invariably meet with the ordinary or specific inflammation of the bronchi, of the lung, of the pleura, of the lymph glands. These diverse associated lesions may even become predominant in an anatomical or clinical point of view. Yet

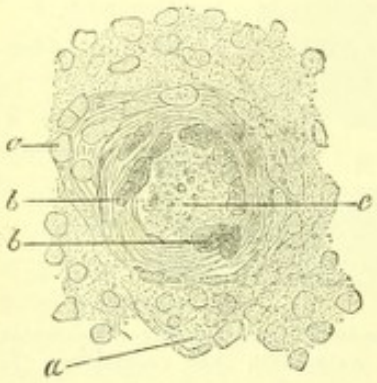
by their progress and their evolution, by their special physiognomy, by their tendency to the caseous state and to mortification, these pulmonary inflammations properly belong to tuberculosis. We shall therefore describe under this head both the tubercle granulations of the lung, and the lesions of this organ which are excited by them.

Tubercle Granulations.—We do not propose to reiterate here the description which has been given at page 112 *et seq.*, but we must consider more in detail the mode of origin and of evolution of the granule in the lung. The seat of the tubercle granule is at the beginning variable. In order to study it we must select a lung which is sown with very fine miliary granules, so small as to be scarcely visible to the naked eye, but which can be better appreciated by the touch.

Studying a properly prepared section we observed that the minute granules may be seated:—

1st. Around the vessels. There is then an accumulation of embryonal elements in their adventitious sheath, and in the adjoining connective tissue, such as is represented in figure 234. As the figure indicates, the lumen of the vessel is obliterated by a granular mass of fibrin, in which some white blood corpuscles can be recognized. The adventitia and the surrounding connective tissue are the seat of an exuberant production of nuclei and of small cells held together by a fibrillar or amorphous intercellular substance. This new tissue is continuous with the thickened walls of the neighboring alveoli, which are lined by swollen pavement cells. These lesions of the walls of the vessels and of the alveoli together constitute a nodule.

Fig. 239.



Transverse section of a vessel filled with granular fibrin. *a*. Tubercular tissue. *b*. White blood corpuscles. There is here a tubercle involving the vessel. × 400.

2d. Around the bronchi. The adventitia of the peribronchial vessels takes as great a part in the neoplasm as does the connective tissue of the bronchus. A very minute granule may occupy only a part of the periphery of a bronchus, or several granules unite around it in such manner that the entire periphery of the bronchus may be surrounded by a zone of embryonal tissue in the midst of which exist several groups of elements which are much compressed and atrophied at their centre.

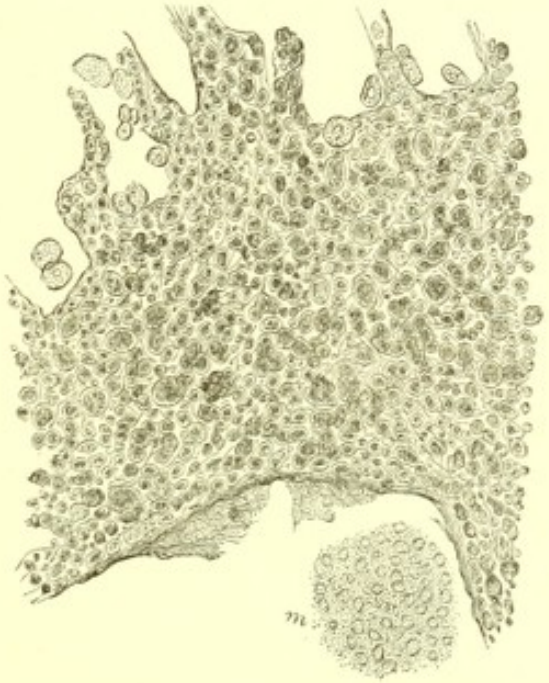
The bloodvessels in tuberculous nodules are always obliterated, and they are very frequently in the same state in the surrounding embryonal tissue (see p. 116). The lumen of the closed vessel is occupied by granular fibrin, and in transverse section between the coagulum and the vessel wall a row of white blood corpuscles and of endothelial cells is often seen (see fig. 239). The white corpuscles may also occupy the centre of the clot. In most tubercles the walls of the vessels are very easily distinguished. But if the centre of the tubercle has undergone caseous degeneration the vessel wall is also altered, and is very indistinct and readily confounded with the caseous mass which surrounds it. If the preceding alterations

are not recognized, one does not know to what the small granular mass containing nuclei, and occupying an ill-defined cavity in the midst of the nodule is due. Schüppel has described these masses as giant cells, which he regards as characteristic of tubercle.

In certain cases the small bronchi are enveloped in a great extent of their course by a cylinder of new embryonic tissue. Such a peri-bronchial cylinder is the almost constant form of the small and recent granulations of glanders in the horse.

The lumen of the bronchus is generally filled with large cells, round or irregularly polyhedric, and a catarrhal or caseous bronchitis complicates the tuberculous peri-bronchitis. The wall of the bronchus shows a tissue containing numerous embryonal cells, which perhaps is continu-

Fig. 240.



Scrofulous inflammation of a bronchus. Section of a small bronchus of a markedly scrofulous child, the subject of bronchitis, which terminated in miliary tuberculosis. The deeper structures of the bronchial wall are seen to be extensively infiltrated with cells, most of which are *larger* than those met with in the less extensive infiltration of healthy inflammation. The infiltration extends to and invades the walls of the adjacent alveoli, which are seen at the upper part of the drawing. The cavity of the bronchus contains a little mucus, *m*. × 200, reduced ⅓. (*Green.*)

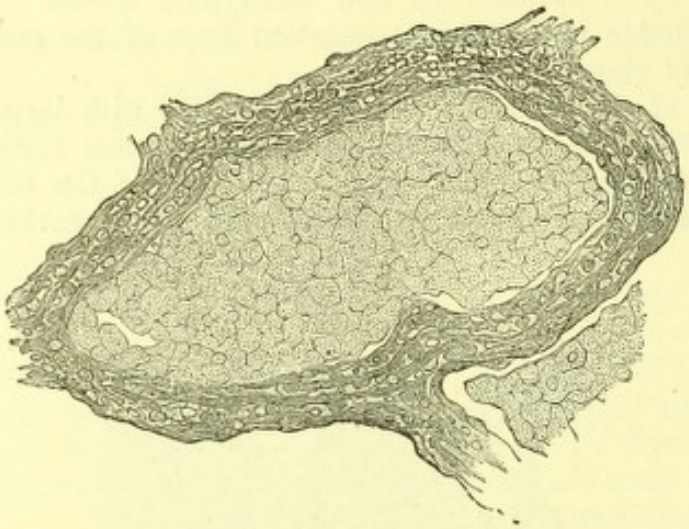
ous with neighboring nodules of similar elements, perhaps with the walls of an adjacent alveolus which have been thickened by a similar new formation.

Figure 223 shows a bronchus, the lumen of which is filled with similar contents, and the walls of which present at different points a tubercle granule surrounded by pneumonia.

3d. The granules may be seated in an infundibulum, all the alveoli of which are filled by the new formation; whilst the interalveolar septa may still be recognized by their elastic fibres. The whole mass forms a little nodule whose centre is already undergoing caseous atrophy, while the peripheral alveoli constantly present the lesions of congestion

and of catarrhal inflammation. Whence come the elements of the granule which fill the alveoli? This is a question very difficult to answer. It is possible that three modes of formation are active. They may come

Fig. 241.



Acute phthisis. Showing one of the alveoli filled with epithelial elements, and marked cellular infiltration of the alveolar wall. × 200. (*Green.*)

from a thickening of the septa, from a proliferation of the epithelium, or they may be derived from lymph corpuscles escaped from the vessels.

In cases of miliary phthisis, tubercle granules also are present at the surface of the lung, and form projections upon it; they are located in the visceral pleura. They are also found in the bronchial mucous membrane.

At the period of eruption of miliary phthisis there exists an intense congestion of the whole lung, a catarrhal pneumonia more or less extensive, and there are soon joined with these, new lesions which consist in ulcerative destruction of small bronchi and of nodules of lobular pneumonia.

All the parts invaded by the tubercle are deprived of their life by the obliteration of their vessels; the cellular elements become granular, the tissue becomes dry, and, like all dead tissue, it is subject to decomposition, which soon manifests itself at the points where the air penetrates. First the contents of the bronchi, next the bronchial walls, then from point to point the altered pulmonary tissue, experience a molecular decomposition which results in elimination.

This complex process is what we understand by tuberculous bronchopneumonia, in which small caverns very soon form at the extremity of the bronchi. These losses of substance are bordered by a zone which contains tubercle granules surrounded by pneumonia, and, since here also the blood circulation is impeded or arrested, this zone offers a yellow or gray aspect, and the inflammatory products undergo caseous degeneration. At the periphery of this zone the pulmonary tissue is congested, and presents the lesions of catarrhal pneumonia in the first or second stage.

When both lungs are invaded throughout by a large number of dis-

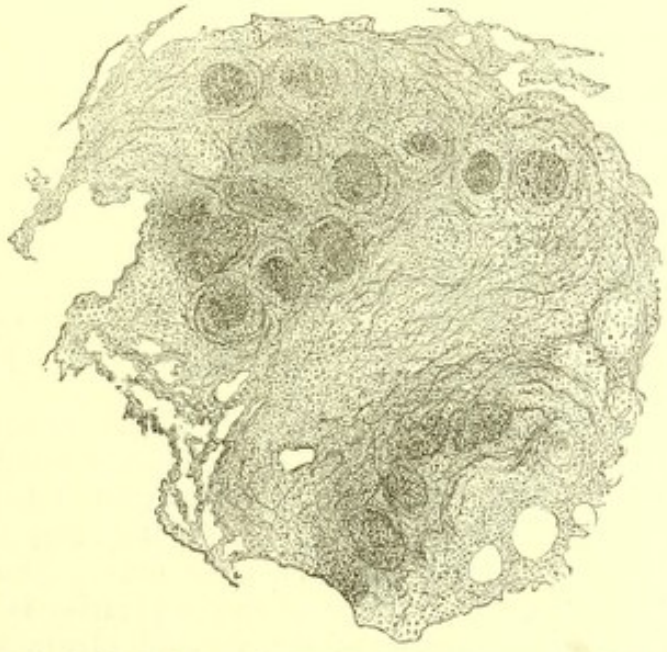
seminated miliary tubercles, death rapidly ensues. But if, on the contrary, the tubercles are much more discrete, a longer duration of the disease permits of the observation of a series of profound alterations of the lung parenchyma, which we shall now pass in review.

TUBERCULOUS OR CASEOUS PNEUMONIA, PHTHISIS.—Pneumonia plays a considerable *rôle* in most cases of pulmonary phthisis, and most of the lesions observed are caused by it. It manifests itself by inflammatory hyperæmia, by catarrhal or croupous pneumonia in the first stage, very soon followed by the caseous metamorphosis of the exudation. It is always present around cavities in process of formation or enlargement. Let us now describe successively lobular pneumonia, lobar pneumonia, and interstitial pneumonia, while indicating their anatomical consequences.

Tuberculous Lobular, or Catarrhal Pneumonia.—The two first stages differ from those already described at page 414 only by the presence around the bronchi or in the infundibula of tubercle granules. Yet these granules, because of the granular degeneration of the pneumonic nodule, may not be recognizable.

The size of these small pneumonic masses is extremely variable; they may be limited to an infundibulum or a primary lobule; they may comprise a secondary or a tertiary lobule; or they may attain the size of a hazel-nut or walnut. In other cases the catarrhal pneumonia is diffuse and more extensive.

Fig. 242.



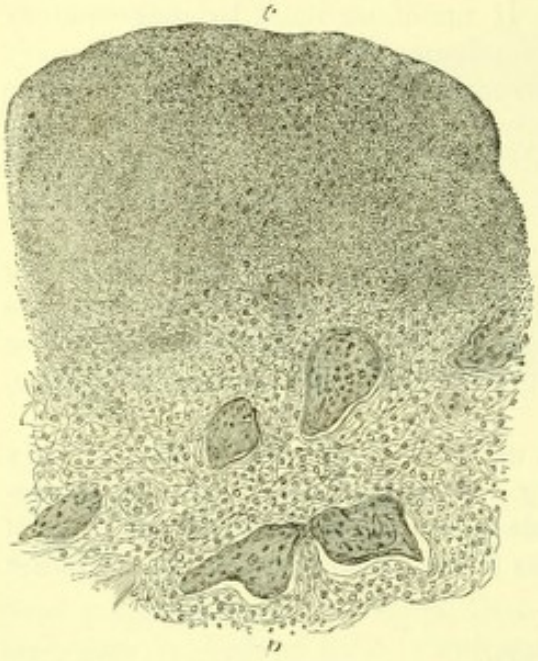
A small soft gray tubercle from the lung in a case of acute tuberculosis. The whole of the tubercle is shown in the drawing, and it is obviously constituted largely of *intra-alveolar* products. × 100 reduced to ½. (*Green.*)

Very soon these pneumonic nodules pass into the caseous state; they solidify and dry up; all the elements of the exudation become granular and agglutinated by a slightly transparent granular substance which

shines like fibrin when acetic acid is added. To the naked eye, these foci appear gray and homogeneous. They are friable. They constitute what Laennec called miliary tubercles.

The elements contained in the alveoli consist of pus corpuscles, round or slightly angular by compression and filled by protein or fat granules, and of round or polygonal cells of variable size, presenting one or more nuclei which have also suffered the same fatty degeneration. The cell nucleus is not wholly visible, for the elements are absolutely inert and dead. These dead elements break up into small fragments often angular, which Lebert has named tubercle corpuscles.

Fig. 243.



A portion of a crude yellow tubercle from the lung in a case of acute tuberculosis. Showing the degeneration of the central portions of the nodule *c*. and the cellular thickening of the alveolar walls and accumulations within the alveolar cavities at the periphery *p*. × 200. (*Green.*)

In these more or less extensive foci of pneumonia, as has already been said, the bloodvessels are obliterated by coagulated fibrin. Sometimes the nodules present, first at the centre or in several points at once and finally throughout their entire mass, a yellow color which is due to a larger quantity of fatty granules; this is the crude yellow tubercle of authors.

The corresponding bronchi almost always present the alterations which have been studied at page 407. (Fig. 223.)

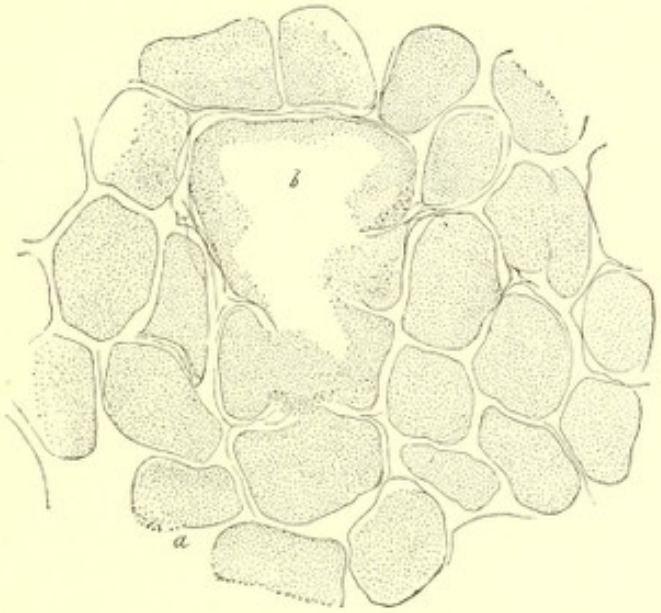
These foci of pneumonia sometimes very quickly pass into the purulent condition. When they are very numerous we have one of the forms of acute phthisis. Upon opening the lung a large number of them are destroyed, thus forming small cavities in communication with the bronchi. In this form of tuberculosis, perforations of the visceral pleura are not infrequently met with.

When these pneumonic lobules are located at the surface of the lung, after having given rise to a localized pleurisy characterized by thin, soft, false membranes, and a thinning of the friable wall of hepatized tissue which separates the pleura from their cavity, they may break through into the pleural cavity and occasion a pneumothorax. The fluid effusion and the air cause atelectasis of a lobe when the pleurisy is so recent that there is not sufficient thickening of the visceral pleura to prevent the retraction of the pulmonary tissue.

In such a compressed lobe multiple lesions are observed: there are tubercle granules and nodules of pneumonia in different stages imbedded in a congested and atelectatic pulmonary tissue. Several times we have seen even recent perforations closed by exudations and pleuritic new formations.

This form of phthisis has been taken as a type for the general description which Laennec, Louis, Cruveilhier, *et al.*, have given of tubercle.

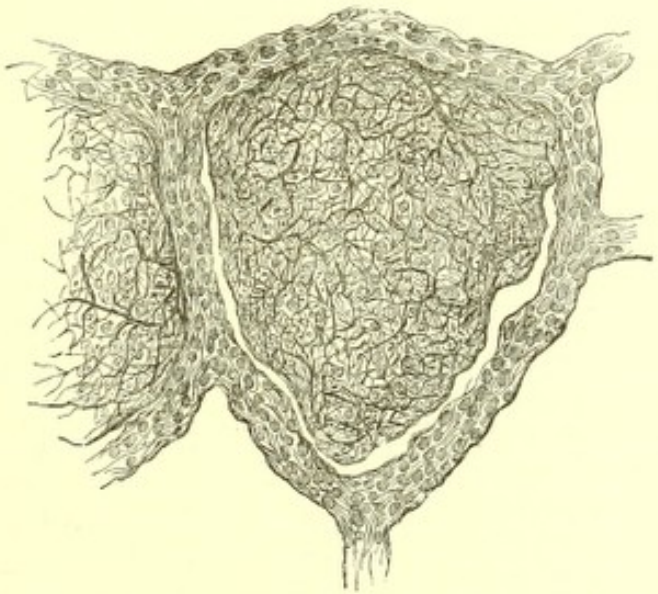
Fig. 244.



Section of a nodule of a lung affected with a caseous lobular pneumonia. *a*. Pulmonary alveoli, filled with an inflammatory exudation. *b*. Terminal bronchus opening into an infundibulum. × 40.

Tuberculous Lobar or Croupus Pneumonia.—This form of pneumonia offers for consideration an evolution very similar to that of common

Fig. 245.



Acute phthisis. Showing one of the alveoli filled with fibrinous exudation and leucocytes, and some cellular infiltration of the alveolar wall. × 200. (*Green.*)

croupus pneumonia. It differs from the latter only by its greater extent; it may involve a large part of a lobe, or an entire lobe, or even almost the whole of one lung. The stage of red hepatization is rapidly reached, but

it is rare to find a fibrinous exudation in the alveoli as solid as in ordinary croupous pneumonia.

In their passage to the caseous condition the diseased portions become decolored, and the cellular elements of the exudation which distends the alveoli become granular and dry. The cut surface of the altered lobe is shining, smooth, uniformly gray, homogeneous, dry and bloodless; the bronchi are filled with the same exudation as that which fills the alveoli, and the vessels are choked with coagulated fibrin. The pulmonary tissue is harder than at the commencement of the hepatization, and notwithstanding that it is easy to tear, moderately thin sections can be cut without hardening. This is the type of the *gray infiltration* of Laennec.

In other cases the hepatized portion presents to the naked eye a colloid aspect; the lung is infiltrated with a trembling gelatiniform material (*gelatiniform infiltration* of Laennec; *colloid*, caseous pneumonia of Thaon). In thin sections under the microscope, the alveoli are seen to contain a colloid substance analogous to that of the thyroid body, readily colored by carmine, besides numerous cell elements some of which are vesicular. This exudation soon undergoes a caseous metamorphosis.

Instead of being gray, caseous pneumonia, which is older and in which the granules are more abundant, offers a yellow color. Save in color, the appearance is the same as in the gray infiltration, and the constitution is also similar.

In certain cases of this kind of pneumonia there are no tubercle granules to be recognized either by the naked eye or by the microscope. It may be that they have been present nevertheless, but in consequence of caseous transformation have become indistinguishable.

According to Grancher there is always in caseous pneumonia a certain amount of interstitial pneumonia in places.

Considerable masses of this tuberculous pneumonia may remain unchanged for a long time, when the lung continues impermeable to the air and to the blood.

Cavities are formed in this variety of tuberculous pneumonia in the same manner as has already been indicated. When the loss of substance has reached the normal pulmonary tissue the destruction is arrested and the surrounding tissue is indurated by a chronic inflammation, accompanied by the formation of connective tissue in the interalveolar septa and even at the surface of the cavity. Upon the latter we find small vascularized granulations beneath the pulpy or puriform covering which lines them.

There sometimes exist also in this layer of granulation, small aneurisms which arise by dilatation of the branches of the pulmonary artery, which softened by inflammation, become distended by the blood. By their rupture, these aneurisms often give rise to fatal hæmoptysis. Vessels and large bronchi often extend across large cavities; such trabeculæ are also covered with a layer of granulation tissue.

Later, the inner surface of the large cavities is smooth, almost as if it were covered by a mucous membrane.

The interstitial pneumonia, aided by the chronic pleurisy, the fibrous induration and intimate adhesions of the two walls of the pleura, when

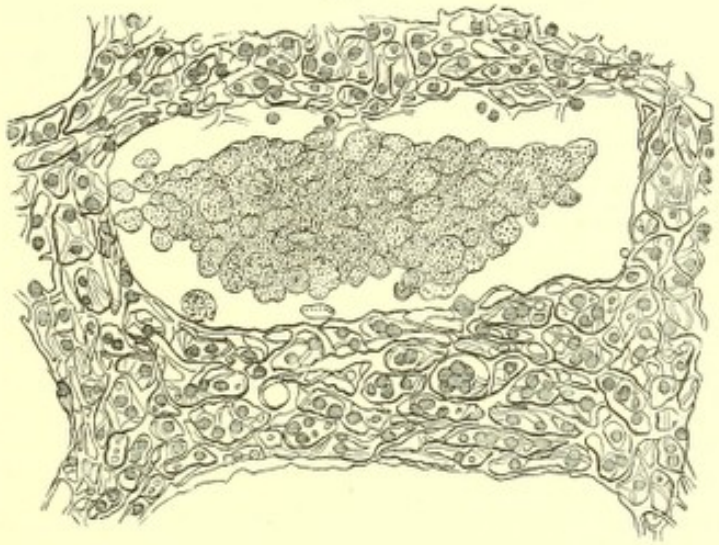
they are located at the apex, as a rule, cause marked subclavicular depressions.

Communications may be established between the cavities and a caseous lymph gland, or between a cavity and a vertebral abscess in Pott's disease. The cavities may even be evacuated exteriorly by a cutaneous fistula.

Because large masses of lobar pneumonia are often found, in which no tubercles are to be seen, the attempt has been made to establish a form of scrofulous pneumonia independent of tubercles. But, when the whole of the lung is examined, we almost always find very distinct granules in other parts of the organ or in the pleura, either visceral or costal, or they may be found in the peritoneum or elsewhere.

Tuberculous Interstitial Pneumonia.—We have previously seen that interstitial pneumonia often is present at the apex of the lung, around

Fig. 246.



Section of lung from a case of somewhat chronic phthisis. Showing the thickening of the alveolar walls by a fibro-nucleated adenoid-like tissue (an interstitial pneumonia); together with an accumulation of epithelial cells within the alveolar cavity. The latter are undergoing retrogressive changes × 200. (*Green.*)

large tuberculous cavities. In those indurated and often slaty or black masses we may find very characteristic tubercle granules, which probably remain a very long time without suffering destruction.

But there exists a form of tuberculosis in which the granules, however numerous they may be, are everywhere surrounded by a pigmented interstitial pneumonia. The tuberculous process is then more or less rapid in its march; but there is no very great tendency to the determination of a lobular or lobar pneumonia.

The general distribution of tuberculous lesions of the lungs is such that it is the apices which are usually first invaded; in the slow form of this disease, the apex of one lung may be attacked a long time before that of the other is involved.

Thus we find, for example, in the right lung, somewhat large cavities at the summit, with interstitial pneumonia, and a pleural membrane very

thick and fibrous; the middle lobe presents extensive nodules of caseous pneumonia with cavities in process of formation at their centre; and the inferior lobe may show a mass of lobar pneumonia in several stages, without there yet being caverns present.

The pleura of the two last lobes is perhaps covered by a fibrinous exudation and may show tubercle granules. In the other lung there may be a few lobules of caseous pneumonia, one or two small cavities in the upper lobe; in the inferior lobe, congestion and some tubercle granules; tubercle granules may be very numerous upon the left pleura. This is a common type, but nothing is more variable than the form and the distribution of the lesions.

Instead of subordinating the inflammatory lesions to the tubercle granules, Niemeyer, Buhl, and several other German writers, regard caseous pneumonia as a possible consequence of every acute pneumonia or pulmonary hemorrhages. Moreover, for them, tubercles are nothing else than the result of an infection following the destruction of the caseous foci.

This theory does not well stand examination, for there are cases where as even Niemeyer and Buhl admit, minute researches made upon the cadaver of patients who died of general miliary tuberculosis of the lung have failed to show a single caseous focus. We are then obliged to admit that the hypothesis of an infection by absorption of a caseous product of inflammatory origin cannot apply to every case.

In chronic phthisis, it seems to us much more natural to accord to tubercle an origin and progress analogous to that of all tumors. In the latter, whatever may be their nature, sarcoma, carcinoma, epithelioma, etc., the tumor grows at its periphery by little masses which are united to the tumor, while the central portions—the oldest—have often undergone an already advanced degeneration. In the development of tubercle, the same march is observed.

We cannot, therefore, subscribe to the idea of the dualism of tubercle sustained by many physicians, in particular by Virchow, according to which tubercle granules, on the one hand, pneumonia on the other, constitute two distinct processes.

[For various opinions regarding the relation of caseous foci to tubercles, see article Tuberculosis, p. 112, *et seq.*]

Sect. VI.—Pleura.

We have sufficiently explained the general pathological histology of the serous membranes (see pp. 248–268) to enable us to avoid repeating here the details of their microscopic lesions *à propos* of the pleura. Almost all that has been said relative to serous membranes in general applies to the pleura, and we shall have to relate here only what especially appertains to it. We shall see that, in most cases, the lesions of the pleura are subordinated to those of the lungs.

Congestion; Ecchymoses; Hyperplastic Pleurisy.—Congestion of the visceral pleura is always present when the lung is congested. The

bloodvessels which belong to the thin transparent layer of connective tissue which forms the visceral pleura are filled and distended with blood. By reason of this transparency of the visceral membrane, the interlobular septa of the lung everywhere permeated by the blood and lymph vessels are distinct. The polygonal spaces, which represent the bases of the pulmonary lobules at the surface of the lung, are, in reality, limited by whitish or pigmented bands. The naked eye very easily recognizes in these bands bloodvessels more or less filled with blood, and lymph vessels which are quite as large as the interlobular veins, and which are very superficial and transparent, and presenting thin flattened walls.

When the pulmonary congestion is very intense and there is dyspnœa, as happens in disease of the heart or of the lung, or there is an asphyxia due to any other cause (disease of the trachea or larynx, submersion, strangulation, etc.), we find at the surface of the parietal pleura small ecchymoses, punctate or having a diameter of one or more millimetres. These ecchymoses are characterized by an extravasation of red blood disks into the connective tissue of the pleura. When the ecchymoses are recent, there oozes from them at the free surface of the pleura a sanguinolent fluid, and they form a slight elevation. Soon after their formation, the extravasated blood disks become modified; they are transformed into red-brown and black pigment granules, and the ecchymotic spot, at first red, subsequently turns slate-brown, and finally black.

In autopsies in cases of heart disease, or in emphysema or an intense dyspnœa, it is rare that we do not find scattered over the visceral pleura a large number of small ecchymoses, some of which are red and recent, while others are dark brown, and still others are slate color or black.

The effects of a *chronic congestion* of the pleura are shown especially in a more or less marked thickening of the membrane, in the formation of vegetations, small villous growths consisting of connective tissue, and often also in a hydrothorax. The pleura is whitish and untransparent. This condition is frequently but slightly marked, and considerable practice is necessary for its recognition, for the visceral pleura thus altered is generally only very slightly thickened and it preserves its pliability and polish. The opacity of the pleura is due to the thickening of its fibrous bundles as well as to the tumefaction and proliferation of the flat connective tissue cells.

Carefully examining the surface of the pleura, especially at the anterior border of the lung and at the sharp edge of the lobes, in similar cases, we often recognize small projections analogous to small red granulations, or long villous growths, or filaments, which unite the two lobes and hold them in contact. The constitution of these papillæ and filaments is that of connective tissue; they are supplied with bloodvessels and are covered by endothelium (page 265).

These slowly-produced lesions should belong to chronic pleurisy rather than to congestion; but the pleurisy cannot be recognized during life, because it does not of itself present distinctive signs. These lesions are produced by congestion with chronic irritation, and there is no doubt that even ecchymoses may become the point of departure of such fibrous growths. In fact, there sometimes exists, besides small ecchymoses, little whitish elevations of the same form and dimensions, which are nothing

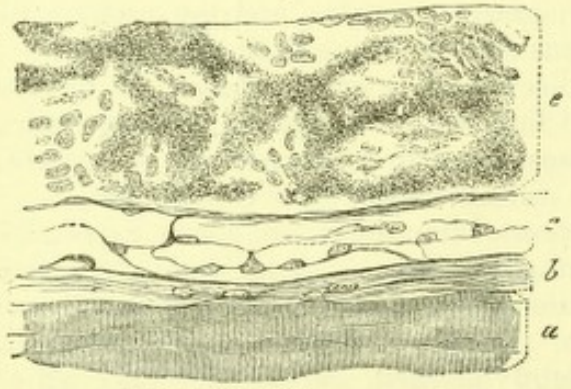
else than small fibromata. They are exactly similar to analogous indurations of the fibrous capsule of the spleen (see page 93) and, like the latter, they may sometimes have the appearance of cartilage.

This chronic congestion, these slow inflammatory growths, may be accompanied by an effusion of fluid into the pleural cavity, a hydrothorax more or less abundant, but generally confined to the lower portion of this cavity. Where the effusion exists, the false fibrous membranes which unite the parietal pleura with the lung are œdematous, and present the usual appearance of connective tissue in that state.

Fibrinous Pleurisy.—In every acute inflammation of the pleura there is a fibrinous exudation and a coagulation of fibrin upon the free surface of the membrane and most frequently also in the fluid exuded. But we designate as fibrinous pleurisy that in which the inflamed membrane is covered with a layer of fibrin at the same time that there is in the pleural cavity a fluid which coagulates into a gelatiniform mass when exposed to the air.

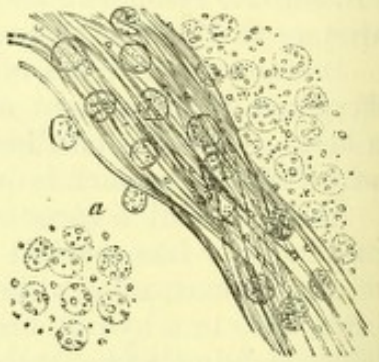
The fibrinous exudation is not found upon old fibrous membranes which

Fig. 247.



Inflammation of the diaphragmatic pleura: showing the adherent fibrinous layer. *a*. Muscular coat of diaphragm. *b*. Subserous tissue. *c*. Serous membrane. *e*. Fibrinous layer. ×400. (*Rindfleisch.*)

Fig. 248.



Lymph corpuscles and filaments of fibrin in a fibrinous exudation upon the pleura: *a*, the corpuscles unchanged by acetic acid. (*Gross.*)

bind together opposite surfaces of the serous cavity. For the deposition of fibrin it is necessary that a considerable part of the pleural surface be free and that the cavity contain some quantity of fluid. For example, in the dry semi-transparent and gray hepatization of tuberculous pneumonia (gelatiniform pneumonia, etc.), one sees upon the surface of the pleura a layer of fibrin which is at one time extremely thin and transparent, and at another time thicker, because formed of several layers. Removing one of these very thin layers and examining it under the microscope, we observe that it is formed of bands of fibrin, forming a meshwork, so arranged that the principal trabeculæ correspond to the pleural vessels situated beneath.

From these principal trabeculæ arise extremely thin filaments, which form a very regular reticulum, inclosing the swollen epithelial cells and pus corpuscles. Beneath this thin layer of fibrin the vessels of the pleura appear swollen, and the pleura itself has a non-transparent appear-

ance. The latter may even be entirely opaque and slightly thickened, a condition which is due to the presence of white blood corpuscles between the fibres of connective tissue. The reticulated appearance of the thin fibrinous false membrane is visible to the naked eye; if the membrane is thicker, this reticulated aspect is no longer marked, and the arrangement described at page 260 is then seen. This fibrinous membrane is very friable. In pleurisy associated with gelatiniform tuberculous pneumonia, the fluid exudation is generally small in amount.

In acute croupous pneumonia, when it is peripheral, there always exists a more or less thick fibrinous exudation which is accompanied by a very small quantity of fluid exudation. The false fibrinous membranes are then sometimes more opaque and yellow than in the preceding case—a fact related to the stage of suppuration or of gray hepatization. In this case the pleuritic exudation contains very many white corpuscles, and the elements are often granular. After detaching the false membrane, upon the surface of the visceral pleura the vessels are found congested and prominent; they may even project above the surface in the form of vascular vegetations. It is upon these vascular loops that the fibrinous exudation is thickest. The pleura is itself thickened and infiltrated with white corpuscles.

In this inflammation, which has extended directly from the lungs, the parietal pleura may escape; but most frequently it shows exactly the same lesions, although the circulation in this part may be altogether different from that of the pulmonary pleura. Perhaps it is the irritating action of the fluid exudation which excites inflammation in the external leaf of the pleural membrane.

The *idiopathic pleurisy* which follows an impression of cold, for example, is variable in its termination and in the nature and abundance of the effusion. It is always characterized by a layer of fibrin deposited upon the pleural surface. It is almost always unilateral. Generally, towards the eighth or tenth day, it has reached the maximum of effusion, the amount of which varies between $\frac{1}{2}$ to $1\frac{1}{2}$ litres.

Both the parietal and visceral pleuræ are at first congested, and very soon (during the first day) they are covered by a thin layer of fibrin; at the same time fluid is effused into the cavity. The effusion increases during the succeeding days, and the layer of fibrin thickens. Frequently flakes of coagulated fibrin float in the fluid.

The visceral and the parietal pleuræ are always affected. Thin vertical sections show a large quantity of white corpuscles between the bundles of fibres, increasing in numbers as the free surface is approached. The bloodvessels project upon the surface in loops. The lymph vessels contain the same elements, as do the spaces of the connective tissue, as well as coagulated fibrin occasionally. The lung itself does not entirely escape the inflammatory process. The superficial alveoli are inflamed; white blood corpuscles, as well as swollen or desquamated epithelium, fill them. Thus we have a secondary pneumonia dependent upon pleurisy, as well as the opposite sequence.

Having reached its state of full development, simple pleurisy enters upon the period of resolution, but the resolution is usually effected very

slowly if the physician does not interfere. The following is what transpires during this period of resolution: little by little the fluid effusion is taken up by the lymph vessels which become permeable; the false membranes undergo fatty degeneration, as also do the white blood corpuscles, whether they be in the fluid or in the false membranes. Occasionally the effusion disappears with great rapidity, as happens often in acute articular rheumatism, and the false fibrinous membranes may also quickly soften and be absorbed without leaving fibrous adhesions, but this is extremely exceptional.

Most frequently the visceral and parietal pleuræ remain thickened. Under the layer of fibrin, formations of embryonal connective tissue and newly-formed vessels constitute small papillæ which project into the false membranes, uniting the visceral and costal pleuræ.

The trabeculæ of embryonal connective tissue, provided with vessels having embryonal walls, push forward into the false membranes until the opposite surface of the pleura is reached, when they unite with similar tissue from that side. These trabeculæ organize and develop into dense connective tissue in proportion as the fibrin disintegrates and is absorbed.

When fibrinous pleurisy remains a long time in resolution, it leaves behind it organized and permanent filamentous or lamellar adhesions of greater or lesser length, or there is almost a direct union of the two pleuræ. The duration of these phenomena consecutive to pleurisy is variable; it may be six months or a year or more. We then say that the acute pleurisy has become chronic.

In certain simple pleurisies with simple serous effusion, lasting for one or two months and terminating in death due to some other cause, we find the visceral pleura thickened and covered with a thin layer of fibrin, without the intervention of a false fibrinous or cellular membrane uniting the two surfaces of the serous membrane. In such a case the effusion is abundant, the lung is compressed (see *Atelectasis*, p. 411), and the visceral pleura, beneath its layer of fibrin, is resistant, and retains the lung in a permanent state of retraction. It is the false membrane which binds down the organ and prevents its dilatation. Sometimes a part of a lobe or of the border of the lung, thus bridled, forms a projection and assumes the shape of an udder or a finger. By incising the thickened pleura, taking care not to wound the pulmonary parenchyma, the latter can again be inflated and made to resume its original form. If a thin slice of the lung, thus compressed, is placed in water, the alveoli take their former size; one may then be assured that, in this compression, the alveolar walls are flattened against one another, but without alteration of their epithelial or other tissues.

Idiopathic fibrinous pleurisy may be accompanied by a very abundant serous effusion which may be poured out so rapidly as to reach three, four, or five litres during the first week, and yet not provoke very pronounced febrile symptoms. Generally the shreds of false membranes in the fluid are in inverse proportion to the amount of the fluid effusion. Those pleurisies in which there is very considerable effusion of serum are sometimes related to the commencement of a tuberculosis whose first manifestations are seen in the pleura.

During the formation and organization of embryonal tissue upon the surface of the pleura accidents may arise from an exuberant formation of vessels both upon the surface of the pleura and in the organized false membranes. The new vessels possess embryonal and consequently very friable walls. The blood tension is high enough to cause extravasation of red blood disks; ecchymoses of the false membranes, and staining of these membranes by the coloring matter of the blood; detachments of the membranes and finally effusion of blood into the pleuritic fluid. These accidents sometimes happen in idiopathic pleurisy, but they are then not very marked. They occasionally occur with greater intensity in the pleurisies which accompany subacute articular rheumatism. But their most common cause is tubercle or cancer of the pulmonary pleura, in which *hemorrhagic pleurisy* is most grave. The pleural cavity is then filled by blood held between successive layers of newly-formed false membrane. These numerous lamellæ are red, consist of fibrin and vascularized embryonal tissue, both of which are infiltrated by the elements of the blood. The blood here undergoes the alterations which are common to it elsewhere.

Another accident to be feared, even in simple pleurisy when it is intense, is *suppuration*. We have seen that the layer of fibrin which covers the inflamed pleura always contains a large quantity of white corpuscles between the filaments or lamellæ of fibrin; that similar cells infiltrate the superficial portion of the thickened pleura; and that large numbers of these are also found in the transparent or slightly clouded serous fluid which fills the pleural cavity. Under the influence of unknown causes, or after repeated punctures, etc., simple pleurisy may become purulent. Then in a short time white corpuscles become extremely numerous in the fluid and in the false membranes. The fibrin breaks up, becomes infiltrated with pus corpuscles, and the fluid effusion becomes cloudy and thick. The latter presents the aspect of serous or phlegmonous pus. This accident, happily rare in simple pleurisy, is much more common in secondary pleurisy. It is sometimes met with in tuberculosis, albuminuria, gout, and almost constantly in purulent infection, etc.

Purulent Pleurisy.—Pleurisy is purulent at the outset whenever there is located upon the surface of the lung a metastatic abscess, a purulent focus or a purulent lymphangitis, that is to say, an infection following a surgical operation, a large wound, confinement, etc. A local pulmonary lesion may also be the starting point; for example, a lobular gangrene seated beneath the pleura, one or more small tuberculous cavities superficially situated. The purulent pleurisy may then be excited provided the pleura be not so thickened and indurated, as to oppose a sufficient barrier to the propagation of inflammation. For the same reason suppurative pneumonia may give rise to an effusion of the same nature. In the preceding examples, the purulent pleurisy is of pulmonary origin. It may also originate in the parietal pleura and succeed, for example, an abscess of the liver opening through the diaphragm.

Wounds occasioning fractures of the ribs complicated by perforations of the thorax, also often give rise to the affection.

A purulent effusion is very often followed by serious disorders and by death.

The pus acquires in infectious pleurisy a repulsive fetid odor due to decomposition, without there necessarily having been either perforation or pulmonary gangrene. Cruveilhier has several times seen gangrenous mortification of the parietal pleura, at one time following a pleurisy from puerperal fever, at other times developed from other causes.

After punctures of the chest, and repeated injections of irritants and antiseptics, the pleura becomes transformed into a pyrogenic membrane. Granulations form and organize, and cicatrization is effected by the union of opposed surfaces, by the process explained at page 71.

Purulent pleurisy often lasts a long time, even months and years. It may terminate by a spontaneous external evacuation of the pus through an intercostal space. This termination is usually preceded by an osteitis with caries or necrosis of one or more ribs, and it is preceded by an œdema of the skin. At other times the pus may discharge into the bronchi, through the diaphragm into the peritoneum, or pass into the mediastinum or along the vertebral column as far as the psoas muscle.

When a tubercular or gangrenous cavity or an abscess has opened upon the pleura, besides the suppuration there is also an escape of air into the pleural cavity, a *pyo-pneumothorax*. The compression of the lung then reaches its maximum.

Chronic Pleurisy.—Chronic inflammation is established at the outstart, or it succeeds an acute pleurisy. The hyperplastic pleurisy previously described is, in reality, a pleurisy which is chronic from the beginning, and which manifests itself by the formation of connective tissue, embryonal at first. The process terminates in fibrous thickening of the pleura, in filamentous or membranous adhesions, or in a complete obliteration of the pleural cavity. We also meet with pleurisies chronic from the first, which follow chronic lesions of the lung or pleura, as, for example, certain cases of tubercular pneumonia, tumors, etc.

The chronic pleurisy which succeeds an acute fibrinous pleurisy and which is marked by the fibrous transformation of false membranes, is most frequently the natural method of healing. It often happens that these false fibrous membranes or the thickened visceral pleura do not much interfere with the expansion of the lung or the movement of the ribs. But, when the effusion has been considerable, when the false membranes have been very thick, and absorption has not for a long time made much progress, the organized false membranes and the thickening of the pleura seriously impede the dilatation of the lung in inspiration. These false membranes form a solid union between the walls of the pleura; and in proportion as the fluid is absorbed and the space which separates the two leaves of the pleura narrows, the contraction of the false membranes draws the costal wall toward the root of the lung. The thorax which had been dilated by the effusion contracts, and the ribs approach and touch each other, especially at the lower part of the chest, so that the diseased side becomes much smaller than the healthy side. The shoulder becomes depressed and the vertebral column may even present a certain degree of scoliosis, with the concavity towards the affected side.

When the pleural cavity is divided into compartments by false membranes, a considerable portion of the effusion remains encysted within a pouch formed by the false membranes.

In chronic interstitial pneumonia, the visceral pleura is always greatly thickened, and whatever be the cause of the pneumonia, the pleural lesion is the same. The pleura forms a fibrous shell, dense, elastic, white or gray, slightly vascular, from $1\frac{1}{2}$ millimetres to 5 or more millimetres in thickness. This inextensible tissue is formed of wavy bundles of connective-tissue fibres, and presents the usual characters of connective tissue. In certain points this tissue may be œdematous.

Fibrous induration of the pleura is generally seated at the apex of the lung where the two surfaces are usually found firmly united. It is impossible to remove the lung without separating the periosteum from the ribs.

When the lung has been removed by separation of the periosteum and costal pleura, white bands are seen which correspond to the position of the ribs, and which consist of the thickened periosteum intimately united with the newly-formed connective tissue of the pleura. The corresponding ribs may even present the characteristics of a condensing osteitis.

In chronic pleurisy we sometimes find more or less extensive calcareous plates, which form a kind of cuirass, now upon the surface of the lung, again at the surface of the parietal pleura.

When a suppurative pleurisy passes into the chronic state, it is associated with lesions similar to the preceding. There may also be caseous metamorphosis of the pus, lesions of the ribs, such as exostosis, periostitis, necrosis, etc.

Tumors of the Pleura.—The commonest tumors of the pleura are *tubercle granulations*. When they are few and recent, they may give rise to a scarcely noticeable pleuritic inflammation; but they are always accompanied by one of the forms of pleurisy already described (pages 265–268).

Fibromata of the pleura present the form of small vegetations, of which we have already spoken. There may be in some of these vegetations enough adipose tissue to justify the name of *lipoma*.

Carcinoma of the pleura very frequently follows its development in the lung or in the breast. In the latter it is propagated by continuity of infection to the pectoral and intercostal muscles, then to the parietal pleura. It is very easy to see upon the surface of the visceral pleura the lymph vessels inflamed and transformed by the carcinomatous neoplasm. These vessels may be generally or only partially affected; their calibre is distended by a more or less solid whitish or yellowish mass, consisting of pavement or spherical endothelial cells. Carcinomatous granulations of the pleura are small and hard in scirrhous, but they are larger and often depressed at the centre when they are secondary to an encephaloid. When these nodules in the costal pleura are deep seated, they may press upon the intercostal nerves and produce neuralgia. All the various forms of carcinoma have been met with in the pleura.

Squamous epithelioma has been observed in the pleura from an extension of the disease in the skin. *Sarcomata* and *enchondromata* have also, but very rarely, been found seated upon the pleura.

SECTION II.

DIGESTIVE APPARATUS.

CHAPTER I.

THE MOUTH AND ITS APPENDAGES.

Normal Histology of the Buccal Mucous Membrane.—The buccal mucous membrane, which is directly continuous with the skin, like the external integument, comprises: 1st, an epithelial covering; 2d, a deeper layer composed of connective and elastic tissue, containing veins, vessels, and glands, and supplied with papillæ; 3d, a deeper layer of loose connective tissue, which is more or less closely connected with the muscles.

The mucous membrane, properly called, or the mucous chorion, is directly continuous with the cutaneous derm. It presents upon its surface numerous papillæ analogous with those of the skin, but presenting peculiar characteristics upon the tongue. Over every part of the mouth, except the tongue, the papillæ are so numerous that they touch at their bases. They are imbedded almost everywhere in thick layers of stratified pavement epithelium. In contact with the papillæ the cells are cylindrical or ovoid, and are implanted perpendicular to the surface of the papilla. Above this layer of cylindrical cells, the epithelium is soft and angular from mutual pressure, while at the surface large flat cells with atrophied nuclei exist. These cells, like those of the skin, are in a continual state of desquamation. The epithelium is very permeable to fluid, an essential for the sense of taste.

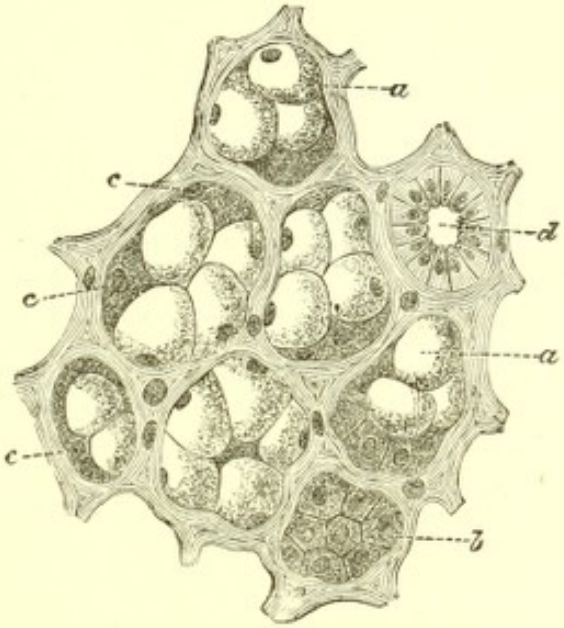
The mucous derm is so closely united with the dental alveoli, and with the bony portion of the palate, that it represents the periosteum of these bones. In the tongue it is in connection with the extremity of muscular fibres through the intermediation of the lingual fascia. Upon other portions of the mouth it possesses a limited mobility.

The glands of the buccal mucous membrane are: 1st, acinous mucous glands of a round and bosselated form, and of a diameter varying from 1 to 5 millimetres. They are found upon the inner surface of the lips, upon the mucous membrane of the cheek, of the roof of the mouth, of the palatine arches, of the base of the tongue, behind the lingual V, and in the vicinity of the calciform papillæ; 2d, glands at the apex of the tongue forming upon either side an elongated glandular island, whose excretory ducts, to the number of five or six, open upon each side of the frænum linguæ.

These glands are formed of an excretory duct, consisting of a base-

ment membrane of connective tissue, lined by cylindrical cells. The subdivisions of this duct which terminate in the pyriform or spherical glandular vesicles or culs-de-sac, are generally paved by large mucous cells similar to those of the sublingual gland.

Fig. 249.



Submaxillary gland of dog. *a*. Mucous cells. *b*. Protoplasm cells. *c*. Crescents of Giannuzzi. *d*. Transverse section of excretory duct with its peculiar columnar cells. High power.

The salivary glands which empty upon the buccal mucous membrane are constructed upon the same model as the mucous glands; their volume is considerable. Their culs-de-sac do not appear to possess a special membrane, but only a delicate cuticle of flat or stellate cells. The cells which line them are of two kinds; in the sublingual gland, and in a part of the acini of the submaxillary, they possess a nucleus and a cloudy protoplasm which are located next to the wall of the cul-de-sac, in such a manner as to leave the rest of the cell clear. The general form of these cells is conical; their base, where the nucleus and granular protoplasm are found, is placed at the periphery of the cul-de-sac, whilst their pointed inner extremity is toward the centre of the acinus. In the parotid and in most of the acini of the submaxillary the culs-de-sac contain granular cells with an oval nucleus. The excretory ducts are lined with cylindrical cells.

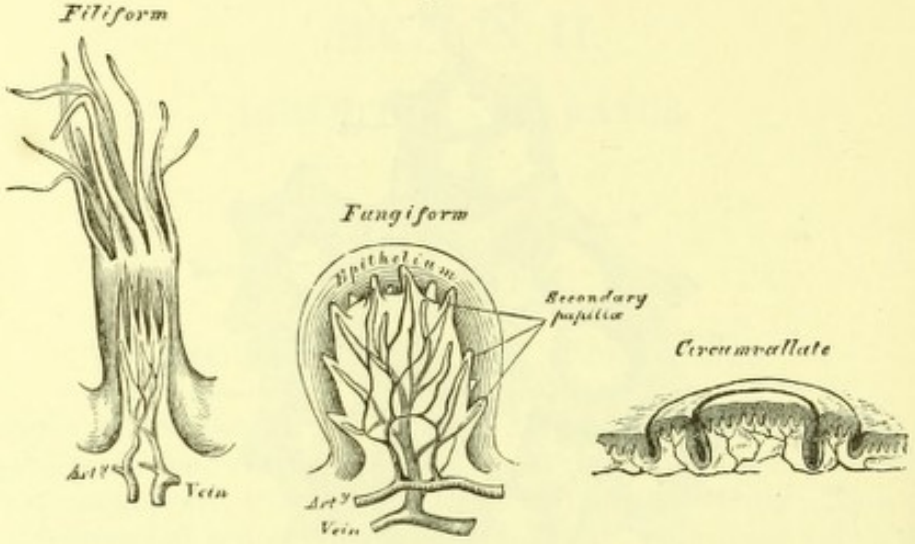
The mucous membrane of the tongue possesses three varieties of papillæ:—

1st. Fungiform papillæ, recognized as little red elevations upon the anterior half, at the apex and at the edges of the tongue, have for their base an elevation of the mucous chorion studded with secondary conical papillæ. They are covered with a soft epithelium, and in their interior vessels and nerves ramify. The latter terminate in special gustatory organs.

2d. Caliciform or circumvallate papillæ, six to twelve in number, which form the lingual V, are composed of a central papilla depressed at the

apex, surrounded by a less prominent ring which circumscribes the base of the papilla. Both are built upon the same model as the fungiform papilla, and consist of secondary papillæ, having the same structure.

Fig. 250.



The three kinds of papillæ of the tongue.

3d. Filiform or conical papillæ consist of elevations of the derm, and they are furnished at the summit with smaller elevations which are thin, elongated, and covered by a common and imbricated epithelium, which, terminating in pointed extremities, gives to the end of the papilla the appearance of a very fine brush.

The buccal mucous membrane presents numerous *lymph follicles*. Upon the base of the tongue simple lymph follicles extend from the limit of the lingual V to the epiglottis. The simple follicles consist of a round prominence, which presents a depression at its centre. The mucous membrane over the surface of the follicle, and in the central depression, presents its ordinary layers. Beneath the mucous membrane the follicles are seen to be formed of a reticulated tissue, such as has already been described (p. 348). The tonsils are composed of the same kind of follicles united in a large mass.

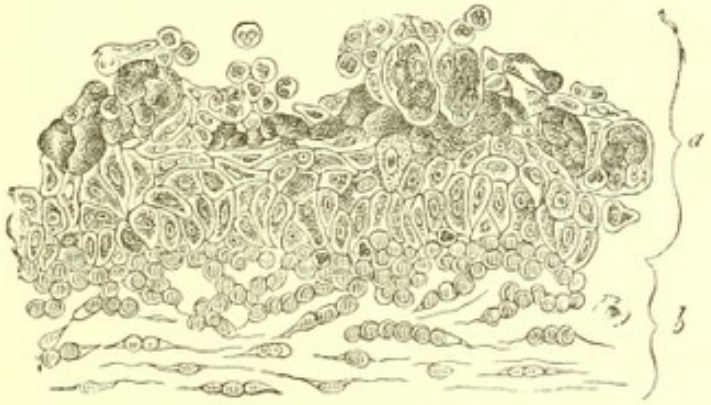
Lymph vessels run throughout the mucous membrane as well as blood-vessels and nerves.

Pathological Alterations of the Buccal Mucous Membrane; Stomatitis.—Stomatitis, or inflammation of the mucous membrane of the mouth, is variable, according to the degree of inflammation, according to its course, according to the depth of the layers affected, and according to the part which is attacked.

Superficial or *catarrhal stomatitis* is characterized, as in other mucous membranes, by a loss of the superficial epithelium, soon replaced by new cells. In the simplest irritations of the mucous membrane there is always a formation of pus corpuscles at the surface. The rapidity of the passage of these corpuscles to the surface of the mucous membrane is such that, in the action of speaking, after a half-hour or an hour's

continuance, the thick and frothy saliva contains a large quantity of these elements. Pus or lymph corpuscles are always found in the mucus which surrounds a carious tooth incrusted with tartar, and there are at the same time large numbers of vibrios, bacteria, etc.

Fig. 251.



Catarrhal inflammation of the conjunctiva, showing changes of the epithelial and sub-epithelial tissue. *a*. Epithelium. *b*. Sub-epithelial connective tissue, showing the proliferation of the epithelium, and the origin of the young elements within the epithelial cells. (*Rindfleisch.*)

Superficial stomatitis, besides the redness of the mucous membrane, is often accompanied by small white superficial patches, which are seen particularly upon the posterior surface of the lips, upon the alveolar mucous membrane, and upon the arches of the palate. This modification of the color of the superficial epithelium is sometimes seen in the stomatitis of typhoid and other fevers. It is almost constant at the commencement of mercurial stomatitis. It is due to the fact that the superficial epithelial cells are swollen, cloudy granular, and opaque. These white patches, which have nothing in common with false membranes or with syphilitic mucous patches, disappear when the diseased cells have regularly desquamated. But if the lesion is more profound, as in mercurial stomatitis, if there are pus corpuscles in large numbers infiltrating the epithelial layers and collecting between the latter and the papillæ, there results a genuine superficial ulcer of greater or lesser extent. At the same time there is profuse salivation.

Mercurial stomatitis, when it is intense, is accompanied by pharyngitis, and, perhaps, by ulceration of the mucous membrane of the pharynx and of the base of the tongue.

In the *stomatitis of typhoid fever*, we sometimes observe round ulcers upon the internal surface of the lips from 1 to 3 mm. in diameter. In the ordinary form of the stomatitis of acute diseases, the tongue is red at its point and edges, as well as in the vicinity of the fungiform papillæ. It may be, on the contrary, dry, dark, and cracked in the middle and in front of the filiform papillæ. The dryness is caused by breathing through the mouth, while the mucous membrane is inflamed, and the corneous cells, instead of being thrown off, accumulate at the surface of the filiform papillæ. The dark color is due partly to the lodgment of foreign particles from the air, and partly to the presence of extravasated red blood

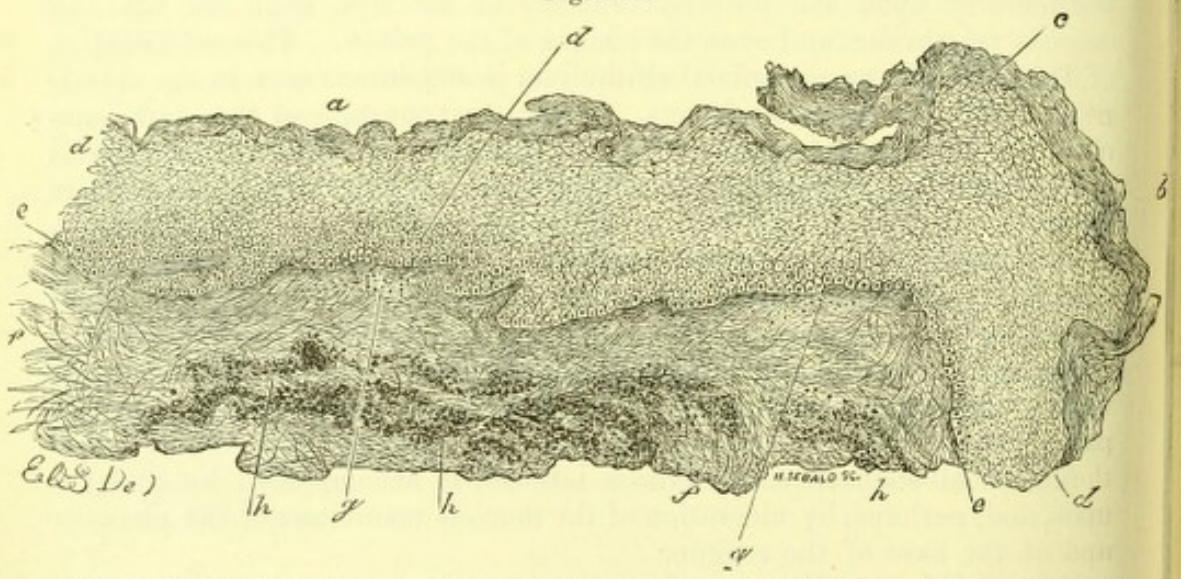
disks. Between these papillæ there are sometimes crevices which contain white or red blood globules. In typhoid fever, the arch of the palate is also congested, dark red, smooth, dry, or covered with strings of mucus. The more or less altered, opaque, and stringy mucus which the patient rejects is characteristic of this form of febrile stomatitis.

Stomatitis due to special causes possesses peculiar characters. Thus labial and buccal herpes begins in the mouth, as it does upon the skin or the lips, as vesicles. But, upon the mucous membrane, these vesicles remain a much shorter time than upon the skin. (For their structure, see Vesicles and Pustules.)

The *lead line* upon the gums around the teeth is due to the presence of fine metallic granules in the cells of the deep layers of the derm. It is visible at this location particularly because of the thinness of the mucous membrane. This deposit always occasions a more or less intense degree of stomatitis.

[*Argyria.*—Prof. W. Pepper, of the University of Pennsylvania, has lately recalled attention to a line at the edges of the gums sometimes seen after the continued use of silver or its salts, and has claimed that the presence of this silver line is a valuable premonition of an approaching saturation of the system by the silver, and a warning to suspend the

Fig. 252.



Section of gum through the colored line, which, according to Dr. Wm. Pepper, is a premonition of argyria, showing silver deposit along the course of the deep vessels. × 150. *a*. Anterior epithelium. *b*. Upper edge of gum near the teeth. *c*. Corneous layer of epithelium. *d*. Rete mucosum. *e*. Layer of cylindrical cells. *f*. Fibrous substance of gum. *g*. A few black granules deposited along the vessels of the papillæ. *h*. Dark granular deposit covering and occupying the vessel walls. (See Trans. College of Physicians of Philadelphia, 1877.)

use of the drug in time to prevent the silver staining of the skin commonly known as *argyria*. This line is caused by the deposit in the deeper portion of the mucous corium of the gums, of metallic silver in the adventitious sheaths of the bloodvessels, and in the neighboring tissue. (See Fig. 252.)]

The *eruptive fevers* manifest themselves upon the buccal mucous membrane by eruptions similar to those of the skin. The redness of the mucous membrane, in the grave forms of scarlatina, often follows a desquamation of the superficial epithelium, under the form of a soft, whitish, pultaceous membrane. When the epithelium of the tongue desquamates, the lingual mucous membrane becomes red and shining and smooth. This desquamation is altogether characteristic of scarlatina.

Cutaneous diseases, such as *eczema*, *pemphigus*, *erysipelas*, are sometimes accompanied by similar eruptions in the mouth and pharynx.

Among chronic stomatites connected with cutaneous diseases, *buccal psoriasis* may be mentioned (ichthyosis of English authors). This lesion is characterized by whitish mammillated patches seated upon the tongue or cheek, the mucous membrane of which is cracked. The epidermic layer upon the diseased part is very thick, the papillæ themselves are hypertrophied, and the derm of the mucous membrane is sclerosed.

The cracks are nothing else than an exaggeration of the normal folds and furrows of the membrane. This lesion is seen around cancroids.

A localized stomatitis with hypertrophy of the papillæ and subacute or chronic inflammation of the mucous corium around the teeth is not infrequently met with.

Scorbutic stomatitis is distinguished by intense congestion of the mucous membrane and a tendency to hemorrhages; fungous surfaces which readily bleed are to be seen upon the gums at their junction with the teeth.

The *syphilitic lesions* of the buccal mucous membrane are the *mucous patches*, and the deeper ulcerations which follow gummata. Recent mucous patches manifest themselves by the white, opaque, or pearly color of the superficial layer of the epithelium; an appearance which is due to causes previously explained. If the mucous patches are old, they determine a thickening of the mucous membrane below the altered epithelium, and they are then slightly prominent. If they are not elevated, they offer to the touch a hardness and a marked thickness of the mucous membrane. Their common seat is at the corner of the lips, where the mucous membrane is white, while the cutaneous portion of the patch is covered with a colored crust; at the borders of the tongue, where they are ovoid or elongated in the direction of the tongue; at the tip or upon the back of the tongue; and upon the tonsils. But they may appear upon any part of the oral cavity. We have often had opportunities to examine, under the microscope, mucous patches from tonsils which had been removed during life. Thin vertical sections, including the patches, showed the latter to be seated upon the mucous membrane which covers this gland. The epithelial layer was thickened; some of the superficial epithelia were swollen and vesicular; the papillæ of the mucous corium beneath were hypertrophied. It is to this hypertrophy that the prominence of the patches is due. The enlargement of the papillæ is due to the presence of a large number of cells.

The more profound syphilitic lesions of the mucous membrane begin by an induration of the corium and of the submucous tissue, by deep nodules or gummata which very soon ulcerate. Their favorite seat is

the roof of the mouth and the arches of the palate, the tonsils, and the tongue. The gummata of the arches of the palate begin by a tumefaction, with induration of the connective tissue, which stiffens the arches; they often cause a perforation, thus effecting a communication between the mouth and nasal fossæ. Gummata of the tongue are very difficult to differentiate from tuberculous ulcers.

Membranous ulcerative stomatitis (diphtheritic of the German authors) is characterized by a diffuse infiltration of the lymph lacunæ of the derm with pus and fibrin. The capillary vessels of the affected part are compressed by the exudation and circulation ceases so completely that the part undergoes an ulcerative elimination which succeeds this mortification. The succeeding ulceration invades the deep layers in such a manner that the edges are vertical. The bottom of the ulcer is gray or dark gray, sanious, fetid, and covered by an opaque gray pulp. If the bottom of the ulcer is cleaned, we see detached from this surface irregular filaments formed of the débris of elastic fibres, connective-tissue fibres, and of vessels. These ulcerations are ordinarily located upon the lips, cheeks, and gums, and sometimes upon the palate or tonsils.

Superficial inflammation of the tonsils or *catarrhal angina of the tonsils* does not essentially differ from a similar inflammation of the buccal membrane. The mucous membrane which lines the depression and the deep crypts being hypertrophied, congested, œdematous, and infiltrated with an inflammatory exudation, there results an enlargement of the whole gland. The desquamated epithelium and the mucous fluid loaded with white corpuscles accumulate in the crypts and form a pultaceous mass which appears at their orifices in the form of gray points. This accumulation often has a fetid odor.

If the inflammation is more profound, the tonsil is much more swollen and the contents of the crypts may form an abscess, which very readily opens of its own accord.

These catarrhal inflammations often repeated in young lymphatic subjects almost always cause a persistent hypertrophy of the lymphoid tissue of the tonsils.

Diphtheritic inflammation, characterized by a false membrane, thin, gray, not very dense, but adherent to the surface of the non-ulcerated mucous membrane (see pages 43 and 65), is not often found upon the mucous membrane of the mouth, except upon the tonsils and the palate. Superficial shreds, which are with difficulty detached, unite to form a hard and adherent layer. The first false membrane being removed or artificially detached, a new layer is soon reformed, or there are stratifications of these diphtheritic lamellæ, the oldest being the most superficial. The uvula is often covered by these productions; the tonsils are more or less invaded by them, and the disease may extend into the nasal fossæ or larynx. These false membranes may occasionally be seen even upon the mucous membrane of the cheeks and the lips. In this affection the lymph glands of the neck are often hypertrophied and inflamed. Usually there is no ulceration beneath the diphtheritic membranes.

Gangrene of the mouth (*noma*) frequently succeeds infectious diseases, such as rubeola, variola, gangrene of the lung, etc. After having commenced in the deep layers of the buccal mucous membrane, it may progressively invade the subjacent layers and terminate in fistulæ of the cheek or in suppurative destructions which compromise even the blood-vessels of the part. Large masses of the tonsil and of the surrounding connective tissue may be destroyed, or the gangrenous ulceration although small may extend deeply. In this manner an erosion and perforation of the external carotid artery may be occasioned.

Gangrene makes its appearance primarily on the lips and on the tonsils in malignant pustule, an extremely infectious disease caused, according to Davaine, by the presence of bacteria.

These diverse anginæ, particularly the diphtheritic, are sometimes accompanied by paralysis of the palate, which is itself followed by more or less extensive paralysis of other parts of the body. According to Charcot and Vulpian, the nerve tubes of the motor nerves of the arches of the palate are altered and present a granular degeneration of their myelin sheath.

TUMORS.—Persistent *hypertrophy* of limited areas of the buccal cavity is not a rarity.

Hypertrophy of the lips and of the tongue (macro-glossia) consist in a thickening with new formation of connective-tissue elements, at the same time that there is a very remarkable development of the lymph spaces. These spaces, lined by a flat endothelium, are filled with serum containing numerous lymph corpuscles (Virchow, Billroth). These lesions exactly correspond with lymph tumors of the skin.

We have met with a hypertrophy of the arch of the palate, caused by a considerable hypertrophy of the acinous glands of this region.

Cysts of the ducts or glandular culs-de-sac are frequently met with in the mouth. Small cysts commonly exist in the mucous membrane of the roof of the palate in the new-born. These are small, whitish, round grains, containing a large quantity of flat lamellated epithelial cells, similar to those of the mouth.

Ranula consists of small cysts situated beneath or upon the sides of the tongue. They often consist in a dilatation of the ducts of the submaxillary or sublingual glands. When the duct becomes cystic the gland atrophies. A few of these tumors belong to a cystic formation developed in the cellular tissue, and they are analogous to pouches of the mucous membrane. These cysts contain an albuminous fluid in which there is sometimes mucin.

Sarcomata are very common in the gums and maxillary bones. Epulis has been described as a variety of ossifying sarcoma (pp. 82, 83).

The tumors of the periosteum and maxillæ which have been described by Robin as myeloplastic, myeloid tumors by Paget (myeloid sarcoma, p. 82), are very common. A benignity had been assigned to them, which their rapid growth and in some cases their reproduction at a distance make questionable. Cystic formations, mucous metamorphosis, effusions of blood are not infrequently met with in these tumors.

Occasionally *fibromata*, hard and spherical or sessile, are found in the

connective tissue of the mucous membrane covering the tonsils. Fibrous polypi springing from the basilar apophysis of the occipital bone may extend in various directions and finally reach the mouth.

Lipomata are sometimes seen under the mucous membrane of the cheek, and sometimes at the tip of the tongue and posterior aspect of the lips.

Angiomata often exist at the free border of the lips, especially in persons who suffer from disorders of the circulation.

Carcinoma is sometimes met with in the tonsils, and in the parotid glands.

Epithelioma with pavement-cells and pearl bodies is very common upon the lips and tongue. It sometimes shows itself at the junction of the mucous membrane and skin, under the form of a horn, from a few millimetres up to a centimetre in length. After their ablation similar growths may return, like genuine cancroids.

Labial cancroid is seated almost always upon the lower lip: the tumor commences at the most superficial part of the derm by a new formation of epithelial cells growing downwards from the mucous layer of the epiderm, from the hair follicles, or from the sebaceous glands, and penetrating deeply between the papillæ of the derm. The tumor spreads both upon the skin and the labial mucous membrane. It is covered upon the exterior by a dark crust which, when it falls, exposes an ulcer or a granulating surface. It extends rapidly in depth and superficially, and from it epithelial lobules arise which penetrate and destroy the inferior maxillary bone in front of and beneath the alveolar processes. Death is the usual sequel.

Cancroid of the tongue much resembles that of the lips both as to its structure and its rapid termination. It usually commences by a swelling of the mucous membrane at the side of the tongue.

Tubular epithelioma has been met with several times upon the arch of the palate and in the antrum (see p. 152).

Tubercle of the buccal mucous membrane commences by one or more small granulations situated at the surface of the derm, which soon become opaque and yellow at their centre. They may be located at the tip or the border of the tongue, or upon the tonsils, the arch of the palate, the base of the tongue, or the posterior wall of the pharynx. These new formations ulcerate, and the ulcer is ragged, and perhaps granulating upon its surface. The edges are irregular or festooned, and show, when on the tongue, a hypertrophy of the papillæ which is very remarkable. The surface and the subjacent tissue are very rich in embryonal cells.

Thaon has seen at the bottom of an ulcer of the tongue, very small and very characteristic tubercle granules located in the connective tissue which separates the muscles. In a case of hypertrophy with ulceration of the arch of the palate in a tuberculous patient, observed by Bernutz, we saw, besides a few but easily recognized tubercle granules, an inflammation of the connective tissue, a hypertrophy of the acinous glands, and a fatty degeneration of most of the cells of their culs-de-sac.

Up to a certain point these morbid growths may be distinguished from gummata of the tongue or palate, because gummata form masses of larger size, the centre of which are caseous, hard, and yellow. Upon a histo-

logical examination of such growths we do not see very minute tubercles like those seated between the muscular bundles of the tongue. It must be avowed, however, that with our present knowledge it would be difficult to make an anatomical diagnosis between gummata and tubercles of the buccal mucous membrane.

Leprous nodules show themselves upon the base of the tongue as upon the skin, and terminate in ulcerations which may extend to the uvula.

PARASITES.—*Leptothrix buccalis* (Robin) exists normally upon the papillæ of the tongue. It vegetates among the epithelium, and is characterized by a felt of very delicate long and straight filaments, arising in a cloudy substance which is their matrix, and which is located among or upon the altered superficial epithelium.

In the mucus and particularly in the dental tartar between the teeth, besides leptothrix we always find vibrios, bacteria, spores of *cryptococcus cerevisiæ* which live and move among softened and decomposing fragments of food. There are always to be found also a certain number of lymph corpuscles. These parasites are swallowed with the saliva and are found physiologically in the gastric juice.

Of all the parasites of the mucous membrane of the mouth the most important and the most common is the *Oidium albicans* (Robin), which constitutes the whitish patches and granulations of *thrush*. Thrush, which is characterized by small whitish grains or soft pulpy patches forming a slight elevation upon the surface of the mucous membrane, is present under different circumstances. In new-born children it is particularly due to the milk taken as food, and is of little importance. In children, as well as in adults, in the course of chronic diseases it is a troublesome indication of profound disturbances of nutrition. According to Gubler, its development is connected with an acid state of the oral mucus, an acidity which is itself due to the presence of fermenting saccharine or amylaceous matter. Under the microscope, there is seen to be imbedded in the midst of a granular epithelium, the elements of the parasite, viz.: 1st, a mycelium composed of trunks and very numerous tubes, fistulous, jointed from point to point, and filled with molecular granules floating in a colorless protoplasm (Quinquaud); 2d, vesicles and spores, which are found at the extremity of the tubes. These oval or spherical spores are very numerous and sometimes of considerable size. The tubes and spores of thrush adhere only to the superficial epithelium.

In many cases patches of thrush are formed upon the pharynx, œsophagus, and even in the stomach.

There are some rare records of cysticerci having been found upon the lip; cysts of these parasites have been met with in the muscular tissue of the tongue. Hydatid cysts containing echinococci have also been seen in the cheek.

CHAPTER II.

PHARYNX AND ŒSOPHAGUS.

Normal and Pathological Histology of the Pharynx and Œsophagus.—The walls of the pharynx and of the œsophagus possess four layers. 1st. At the periphery a fibrous envelope composed of bundles of connective tissue and elastic fibres; 2d. A thick muscular layer composed in the pharynx of the constrictors and levators, all striated; in the œsophagus consisting of two layers, of which the external is longitudinal, the internal circular. The longitudinal fibres of the œsophagus, some arising from the inferior constrictor, others inserted into the cricoid cartilage, are striated in the neck. In the thorax there are added to the circular fibres at first, afterwards to the longitudinal fibres, bundles of smooth muscles which become more and more numerous as the œsophagus is descended. The longitudinal bundles of the œsophagus send expansions to the trachea, the aorta, and left bronchus, etc.; 3d. A layer of submucous connective tissue; 4th. A mucous membrane, the structure of which varies according to the location examined.

The mucous membrane of the pharynx may be divided into two very different regions. Below the posterior pillar of the arch of the palate the pharyngeal mucous membrane possesses rudimentary papillæ and is covered by pavement epithelium like that in the mouth. In the superior portion, on the contrary, that is, upon the posterior aspect of the uvula and arches of the palate, around the orifices of the Eustachian tube, at the posterior orifices of the nasal fossæ, and upon the whole vault of the pharynx, the mucous membrane is invested with a ciliated cylindrical epithelium. Here it possesses no papillæ, but it contains a large number of glands.

The mucous membrane of the œsophagus, like that of the inferior portion of the pharynx, is lined by a stratified pavement epithelium and it is furnished with conical papillæ, which are much more developed than those of the pharynx. Throughout the whole extent of the pharyngo-œsophageal mucous membrane there exist numerous follicular and racemose mucous glands. The first may be simple or compound follicles, and are more frequently met with upon the roof of the pharynx. They form at the orifices of the Eustachian tube a continuous layer several millimetres thick. Considerable numbers of them are formed in the vicinity of the posterior openings of the nasal fossæ, on the posterior aspect of the soft palate, and upon the walls of the pharynx in the neighborhood of the epiglottis.

The mucous glands, which are very easily seen by the naked eye, are met with in the same locations. They are very numerous over the whole

of the posterior wall of the pharynx; they become much less numerous as the œsophagus is approached.

The bloodvessels form in the pharynx a very rich network with elongated meshes. The vascular supply of the œsophagus is much less abundant.

The nerves of the pharyngeal and œsophageal plexus possess ganglion cells.

Lesions of the Pharynx and Œsophagus.

PHARYNGITIS.—Inflammations of the oral and nasal cavities have a great tendency to extend to the pharyngeal mucous membrane, but there are nevertheless numerous exceptions to this rule; for while inflammations of the tonsils and of the arches of the palate like those produced by variola, scarlatina, etc., with the greatest readiness extend to the posterior surface of the palate and to the posterior wall of the pharynx, the same is not true of the aphthous, plumbic, mercurial, ulcero-membranous, and scorbutic inflammations, whose seat is almost solely limited to the lips, cheek, and alveolar mucous membrane. Moreover, pharyngeal inflammations present peculiarities which depend upon the structure of the mucous membrane of the pharynx. In this category are to be placed the lesions of chronic inflammations of the glands in granular pharyngitis.

Superficial or *catarrhal inflammation* of the pharynx most frequently follows exposure to cold, and succeeds a coryza or a tonsillitis; it is characterized by redness and a muco-purulent secretion from the surface.

In *variola*, the pustules formed in the pharynx have not the same solidity as those of the oral cavity; the epithelial cuticle is so easily detached that, instead of well-formed pustules, we usually see nothing else than whitish spots or patches formed of softened and desquamating epithelium mingled with mucus containing pus corpuscles.

In *rubeola* and in *scarlatina*, a punctate redness of the pharynx is almost constant. Scarlatinous pharyngitis is peculiarly grave, and very frequently it gives rise to a superficial pulpy exudation. The surface of the mucous membrane becomes covered with a soft white or gray pulpy layer, which is formed of desquamated epithelial cells and muco-pus. Besides, in scarlatina and in rubeola, a diphtheritic membrane is sometimes observed.

Erysipelatous pharyngitis presents characters similar to those of the same form of stomatitis. It extends to the pharynx from the nasal fossæ or from the mouth; it may descend to the inferior part of the pharynx and reach the epiglottis, the aryteno-epiglottic folds, and the larynx.

Diphtheritic pharyngitis frequently follows the same inflammation of the tonsils and of the palatine arches. Besides covering the posterior aspect of the palate the membranous patches may invade the nasal fossæ and the posterior wall of the pharynx. So also when the diphtheritis extends from the larynx. (For structure of the false membranes, see pp. 65, 66.)

Typhoid fever frequently determines tumefactions of the closed follicles in the lower portion of the pharynx. These swellings which have the

same appearance as the closed isolated follicles of the small intestine are constituted by an infiltration of lymph corpuscles into the follicles and surrounding connective tissue. Their ulceration commences at the pointed portion of the little tumor and spreads over the whole infiltrated mass. These lesions habitually coincide with typhoid laryngitis which has been described.

Syphilis manifests itself in the pharynx by mucous patches and deep ulcerations preceded by induration of the submucous connective tissue, and by gummata. The character of the ulcers has been already described. The disorders caused by these ulcers consist chiefly in a thickening of the whole mucous membrane in their neighborhood, in periostitis, in loss of substance, and in cicatricial contractions, constriction and occlusion of the Eustachian orifices, etc.

Granular pharyngitis, which is sometimes connected with chronic cutaneous disease and often with phthisis, or with the habitual use of alcoholic stimuli, is most frequently a chronic process characterized by alterations of the closed follicles and mucous glands of the pharynx.

Upon the congested surface of the pharynx the glands project more prominently than in the normal state. At the centre of the glandular eminence, the excretory duct of the mucous glands is often surrounded by a whitish rim due to the desquamation and swelling of the epithelial cells; the enlarged duct sometimes contains a puriform mucus. There may be superficial ulceration affecting an entire gland. A similar inflammation attacks the depressions of the mucous membrane situated at the centre of the agminated follicles which exist in the upper part of the pharynx. The tumefaction of the acinous glands is due simply to a hypertrophy of their culs-de-sac, caused by a swelling of their cells and the enlargement of the follicular glands, a hypertrophy analogous to that of the tonsils. When the lesion is older, glandular atrophies are produced by ulcerations limited to a certain number of the glands and follicles. The mucous membrane is irregular, thinned in some places where there are small cicatrices, thickened in others by persistent swelling of the glands. The bloodvessels, particularly the veins, are distended and very visible; they may form genuine pharyngeal varices. We may find cystic dilatations arising from acini or ducts of the glands, small calcareous concretions seated in the glands, and irregular papillary vegetations of the mucous corium.

Chronic pharyngitis is sometimes related to the presence of tubercles which may ulcerate and form ulcers similar to those of the tongue.

The vault of the pharynx, so rich in closed follicles, often presents such an inflammatory swelling of these follicles and of the mucous membrane which covers them, that the orifice of the Eustachian tube is obstructed and a passing or permanent impairment of hearing is the consequence. This happens especially in scarlatina and typhoid fever. Certain cases of deaf-mutism appear to have their essential cause in these obstructions of the Eustachian tube.

Retro-pharyngeal abscess is sometimes produced by an extension in depth of a very intense inflammation of the mucous membrane, as is sometimes seen in scarlatina; occasionally it is caused by the local action of a caustic poison, or by foreign bodies deeply imbedded in the mucous mem-

brane of the pharynx; most frequently its origin is a primary disease of the periosteum and the body of the vertebræ (caries of the vertebræ, Pott's disease). An abscess which lifts up the mucous membrane is more or less large, and has a tendency to extend around the pharyngeal orifice where it may occasion an œdema of the glottis, or along the œsophagus into the posterior mediastinum. It may open spontaneously into the pharyngeal cavity, or it may discharge into the air passages. These abscesses, especially in children, are frequently fatal.

ŒSOPHAGITIS.—The œsophagus is often inflamed from the same causes as is the pharynx, but much less frequently. It is probable that the sensations of *pyrosis* correspond to a slight degree of catarrh or superficial congestion but we cannot be certain of this, for œsophageal congestion is not seen at the autopsy, because of the contraction of the muscles and of the thickness of the pavement epithelium, which is more or less softened and macerated post mortem.

Superficial inflammation occasioned by the febrile exanthemata is much less pronounced in the œsophagus than in either the mouth or the pharynx. Employment of emetics may occasionally cause the formation of small pustules, followed by superficial ulceration.

An inflammation of the œsophagus is sometimes met with in scarlatina or rubeola; it may also be consecutive to a gangrenous pharyngitis. Diphtheritic false membranes may form upon the surface of the mucous membrane. Thrush has also been observed upon the surface of the œsophagus.

Other causes of œsophagitis consist in the effect produced by very warm fluids, such as tea, etc., and by irritants, such as irritant and corrosive poisons. In the first case the inflammation is superficial, and is characterized by vascular redness with tumefaction of the submucous connective tissue, and swelling and desquamation of the layers of epithelium. In the second case, when the caustic agents have remained in contact with the mucous membrane of the œsophagus, after imbibition by the epithelial layers and the connective tissue of the mucous membrane, an eschar is produced and is followed by an eliminating suppurative inflammation. The mortified tissue, after its elimination, leaves an ulcer, the bottom of which may be formed by muscular fibres covered with granulation tissue. The submucous tissue and the connective tissue which separates the muscular fasciculi are infiltrated by embryonal cells. Later, if the patient recovers, the ulcer will cicatrize, and upon the surface of the cicatrix new epithelium will form. Contraction of the œsophageal canal follows with all its consequences.

Foreign bodies arrested in the œsophagus determine not only superficial inflammation of the mucous membrane, but also almost always lacerations and excoriations, and in this way cause an abscess in the submucous tissue of the œsophagus, which may break into the canal of the gullet, into the pleura, the mediastinum, or into the air passages.

Syphilis very rarely affects the mucous membrane of the œsophagus.

All the inflammatory lesions which profoundly affect the submucous connective tissue of the œsophagus are followed by cicatricial contractions of this canal. These contractions are often multiple, yet not very extensive. Opposite these contractions the muscular coat is generally

thickened. Above the constriction the œsophageal canal is dilated. The most frequent seat of constriction is on a level with the larynx, and at the inferior or cardiac end of the œsophagus. All of the above-mentioned lesions may be developed in intra-uterine life.

TUMORS OF THE PHARYNX AND OF THE ŒSOPHAGUS.—*Fibro-myomata*, small and round, originating in the muscular coats of the œsophagus, sometimes form projections upon the surface of the mucous membrane. They may attain the size of a pea, but generally cause no disturbance.

Lipomata have been met with in the œsophagus. They may reach the size of a hazel-nut, and project into the canal under the form of polyps.

Small *cysts* of the mucous glands are met with in the œsophagus. They may occasionally reach a very considerable size without necessarily occasioning serious difficulty in deglutition.

Dermoid cysts have twice been seen in the œsophagus and pharynx.

Tubercles are very rare in the mucous membrane of the œsophagus.

Carcinoma very rarely exists as a primary tumor of the pharynx. In the œsophagus we do not believe that it ever originates as a primary growth. It invades the œsophagus by extension from adjoining parts, such as the lymph glands, cellular tissue of the mediastinum, etc.

Pavement-celled epithelioma appears in the pharynx as an extension from a primary growth in the tongue, or in the œsophagus. It not infrequently occurs in the œsophagus as a primary growth. The favorite location of the epithelioma is at the middle portion of the œsophagus, opposite the lower part of the trachea and its bifurcation. The neighboring lymph glands are early invaded by the epithelial elements, but they preserve their form and their capsule.

By its propagation to adjoining parts, and by the progressive destruction of the growth, œsophageal cancroid ends in a perforation of the trachea or of the left bronchus, or in an opening into the mediastinum, accidents which are rapidly fatal.

CHAPTER III.

THE STOMACH.

Sect. I.—Normal Histology of the Stomach.

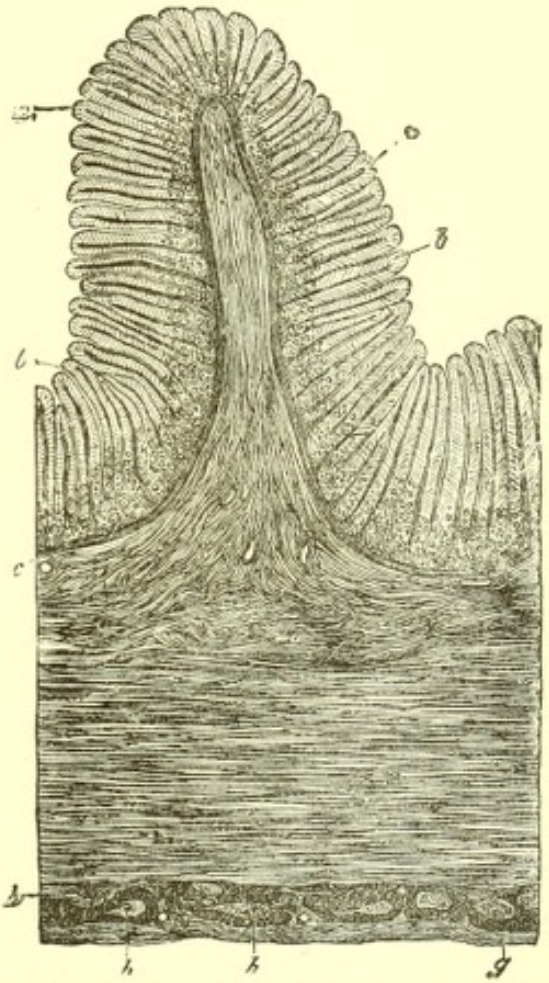
The stomach presents for consideration three tunics, viz.: the mucous membrane, the muscular coat, and the peritoneal covering, held together by connective tissue. The latter is most abundant in the mucous membrane, between the superficial glandular layer and the muscular coat.

The mucous membrane of the stomach is normally pale when inactive, pinkish or red during digestion. When the organ is empty the membrane presents longitudinal folds; during distension it often presents ridges, mammillary elevations, and irregular folds, which are mainly due to contractions of the smooth fibres. Its thickness increases as the pylorus is approached.

The glands of the stomach are of two kinds: 1st, mucous glands, occupy the whole pyloric region, and are also met with, but in smaller numbers, at the cardiac end of the stomach; 2d, peptic glands, which extend over the whole fundus and middle region of the stomach. The first secrete the mucus of the stomach; the second the gastric juice.

Everywhere upon the mucous surface, tubular glands exist parallel to each other, and perpendicular to the surface where they empty into small depressions. Each of these depressions receives the discharges of two or more tubes. These small superficial depressions are separated from each other by circular prominences of

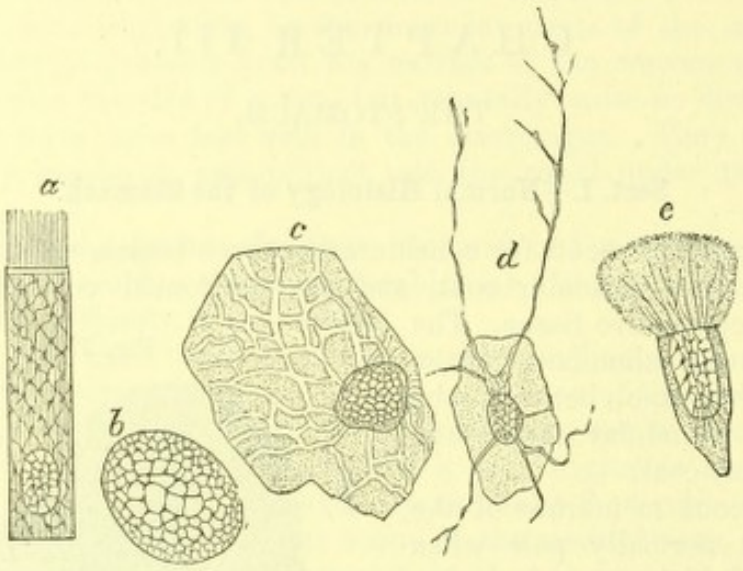
Fig. 253.



Vertical section of the stomach of a child at the fundus. *a*. Columnar epithelium. *b*. Peptic gland tubes. *c*. Muscularis mucosæ, about 1-250th of an inch thick, and chiefly composed of longitudinal fibres. *d*. Submucous tissue. *e*. Circular muscular layer. *g*. Peritoneum. *h*. Ganglia of Auerbach.

the membrane, which in vertical section appear as slightly elevated conical papillæ. These elevations and depressions are covered by a single uninterrupted layer of goblet-shaped cylindrical cells. These cells present a protoplasm and a nucleus situated at their point of

Fig. 254.



Cells showing the reticulum of the protoplasm and nucleus. *a*. Columnar epithelial cell provided with cilia, the latter being prolongations of the intra-cellular network. *b* Nucleus of a glandular epithelial cell from the stomach of a newt, showing the intra-nuclear network. *c*. Endothelial cell of the mesentery of a newt, containing in a hyaline ground substance a plexus of fine fibre bundles —intra-cellular network—in connection with the intra-nuclear network. *d*. Connective tissue corpuscle from mesentery of newt, showing very clearly the intra-cellular network of fibrils and the hyaline ground substance; the former extends into the branched processes, and is also connected with the more delicate intra-nuclear reticulum. *e*. Goblet cell from the stomach of a newt showing the intra-cellular network in connection with fibrils of the intra-nuclear network; the upper part of the cell is greatly swollen by mucus. (*Klein.*)

implantation, whilst the remainder of the cell, moulded into the shape of a goblet, contains a transparent mucus, which is continuous with the thin layer of mucus that usually covers and adheres to the mucous surface; at other times the free extremity of these cells, instead of being hollowed out, is closed by an extremely thin membrane. (*e*, fig. 254.)

The mucus which covers the surface of these cells possesses the reaction of gastric juice (Bernard).

This superficial layer of cells and the subjacent tissue of the mucous membrane are altered with the greatest rapidity after death by the action of the gastric juice, which, by a cadaveric digestion, macerates the elements, renders them transparent, and finally dissolves them. Because of this digestion, the mucous membrane of the stomach is rarely obtained in a fit condition for histological study.

The peptic glands consist of cylindrical tubes which terminate in the depressions above indicated. They possess no independent separate membrane, but they are limited by a layer of flat connective-tissue cells. They possess two kinds of cells: 1st, the peptic cell, described by Kölliker, which is spheroid, granular, and cloudy, and contains at its centre a small round nucleus. These cells, whose granules consist of protein material, are placed along the tube near its limit in such a man-

ner as to produce small enlargements where they are located. They color deeply with carmine and aniline; 2d, the other cells found in the peptic tubes are conical, with their base at the periphery and their apex at the centre of the tube; they are finely granular, and are intimately united with each other.

Fig. 255.



Peptic gastric gland. *a*. Common duct. *b, b*. Its chief branches. *c*. Terminal cæca with spheroidal gland cells.

Fig. 256.



Portion of one of the cæcæ more highly magnified; seen longitudinally at A; transversely at B. *a*. basement membrane. *b* large glandular or peptic cell. *c*. Small epithelial cells surrounding the lumen.

From this disposition of the cells of the peptic tubes, we accordingly see, in a section which passes transversely to one of the tubes, two or more round granular cells at the periphery, while the remainder of the circle is occupied by conical cells whose borders converge towards the centre of the tube, having there a very small central lumen.

Each of the tubes is surrounded by a narrow zone of connective tissue, the fibres of which follow the general direction of the gland. The two or more glandular tubes which empty into the same depression or crypt of the mucous surface are separated from similar neighboring groups of tubes by a greater thickness of connective tissue.

The mucous glands of the pyloric region are also compound tubular glands, with a general resemblance to the peptic glands. They are, however, more voluminous, their tubes are larger, and they contain only a single variety of cells—the conico-cylindrical. These cells approach in structure those of the surface, but their free extremity is not usually goblet-shaped. They are very long and narrow, their nucleus is ovoid

and elongated, and the central lumen is much larger than that of the peptic glands.

The glands which we have just described comprise by far the greatest part of the glandular or superficial tunic of the stomach. They are separated from each other by interlacing bundles of connective tissue, with which, at the lower part of the glandular culs-de-sac, smooth muscle fibres are intermingled. These muscle fibres even penetrate between the glands nearly to the surface of the membrane. This connective tissue is well supplied with a very fine capillary network. The capillaries also form a superficial network immediately beneath the epithelium, around the orifices of the glands, and at the summits of the folds which limit the depression. The capillaries of this superficial network are larger than those between the tubules.

The arterioles which supply these networks of capillaries come from the gastric arteries, from the splenic, from the right gastro-epiploic, and from the pyloric.

The lymphatics form two networks: one situated beneath the culs-de-sac of the peptic glands, the other in the submucous tissue. There exists besides an external network beneath the peritoneum.

Sect. II.—Pathological Anatomy of the Stomach. Lesions of Nutrition.

1st. Anæmia.—Anæmia of the mucous membrane of the stomach is very unfavorable to the normal secretion of the gastric juice. It is probably the usual cause of dyspepsia in chlorosis.

2d. Congestion may be regarded as a physiological phenomenon of normal occurrence in the mucous membrane of the stomach during digestion, and essential to the production of the gastric juice. But it is also, in certain cases, the first stage of a catarrh of the stomach. Under the influence of normal or physiological congestion, we often see ruptures of the capillaries and ecchymoses in the superficial layers of the mucous membrane. The latter are small irregular patches, often difficult to see; sometimes, on the contrary, they are as large as a shilling, red at first, then rapidly passing to red-brown, slate-color, or black. Very dark ecchymoses are not infrequently found at the summit of the folds of mucous membrane; they are elongated in the direction of these folds. The pressure at the base of the folds causes the blood to be retained at their summit. At other times there are small, round, lenticular spots of congestion, situated upon a more elevated plane than that of the anæmic tissue which surrounds them. Localized anæmia is due to contraction of the muscle fibres. Sometimes the spots are seen to be slightly depressed at the centre without there being actual loss of substance; the depression is caused simply by contraction of the muscle fibres.

The change of color which these ecchymoses may undergo is so rapid that they may pass from red to black within twenty-four hours from the time of extravasation. Here also, as elsewhere, the extravasated blood may decompose and give rise to pigmentation or to the infiltration of the elements by blood crystals. In the other tissues of the economy, the

metamorphosis of the blood is never so rapid as in the stomach, where it is subjected to the action of the gastric juice and sulphuretted hydrogen. The digestive action of the gastric juice upon those parts of the mucous membrane which, by reason of pressure of the infiltrated cells and extravasated blood, are no longer nourished by circulating blood, may be considered as a possible cause of the simple ulcers of the stomach.

When death suddenly intervenes during the course of digestion, when the stomach contains not only fluid but also a large quantity of gastric juice, the same digestion of the mucous membrane ensues as is seen in an experimental digestion; this post-mortem digestion is naturally more rapid in a warm than in a cold season. Thus softened, the mucous membrane is reduced to a pulpy detritus under a stream of water. This alteration, which is post-mortem, was for a long time described as an inflammatory lesion, under the name of white, red, or slaty softening, according to the different colors which the membrane presented. This post-mortem digestion of the mucous membrane is met with in the dependent parts of the stomach, particularly in infants who often die while the stomach is filled with milk, an eminently fermentable fluid which very much favors cadaveric digestion. It is possible that in certain cases inflammation may coexist with this softening, but even then the result is certainly due in the main to cadaveric decomposition.

3d. Lesions of the Glands.—We shall describe a species of atrophy and of hypertrophy of the glands when we study chronic gastritis, but we should mention at this point a lesion of the glands which we have had an opportunity of examining several times, namely, a fatty degeneration of the epithelial cells following phosphorus poisoning. We do not refer to the local action of the poison which determines gangrene and ulceration, but it is the effect of the systemic intoxication which results from the absorption of a small quantity of this substance, to which we would call attention. Coincident with the fatty degeneration of the liver, kidneys, etc., the cells of the glands of the mucous membrane of the stomach are filled with fatty granules, and the glands themselves are more voluminous than in the normal state. The mucous membrane is thick, yellow, opaque. Virchow compares this alteration to an adenitis of the glands of the mucous membrane; but the inflammatory nature of this lesion is very doubtful, for we can see only a simple fatty degeneration.

4th. Lesions of the Vessels.—*Atheroma* of an artery of the stomach is not very rare; it may cause ulceration of the mucous membrane. *Amyloid* degeneration of the arteries has been met with, but always in association with a similar alteration of the arteries of the intestine.

Sect. III.—Inflammation of the Mucous Membrane of the Stomach.

1st. Superficial or Catarrhal Inflammation of the Stomach.—In man it is almost impossible to recognize the slight degrees of gastric catarrh which in all probability constitutes the anatomical lesion in dyspepsia. The superficial layer of cells, as we have seen, is very readily

destroyed after death, the lesions of the cells of the glands are rendered very doubtful by reason of similar changes, and there is the same difficulty in studying the histological condition of the superficial connective tissue. It is necessary to resort to the study of inflammation artificially produced in the stomach of animals. We have examined a series of stomachs of dogs, where irritation of the inner surface of the organ had been produced by a venous injection of different substances. The stomach was found intensely congested in various places and covered by a mucous or muco-purulent secretion. The gastric juice, when it is cloudy, contains a large quantity of white corpuscles besides the superficial epithelia, which are almost intact or are filled with mucus.

In the congested areas thin sections show, under the microscope, a very marked distension of the superficial capillary network found at the crests of the interglandular prominences. These prominences are more salient than in the normal state. In the tissue around their capillary vessels extravasations of red and white blood corpuscles are often recognized. When the lesion is not very pronounced, the epithelial covering remains in place, but at other points, where the interglandular folds are more tumefied and the connective tissue around the dilated vessels is much infiltrated with the escaped elements of the blood, the epithelium is completely absent. The depressions of the membrane into which the glands empty are narrowed or even entirely closed by the swelling of the connective tissue which surrouuds them. They nevertheless retain their cellular lining. Neither the mucous glands nor the peptic glands present alterations.

From the foregoing, gastric catarrh artificially produced seems to consist essentially in congestion of the surface of the mucous membrane, in the repletion of the superficial capillary network and the escape of fluid containing red globules and lymph corpuscles, in the œdematous and ecchymotic tumefaction of the interglandular prominences, while the glands of the stomach appear to take no active part in the morbid process.

In man it is impossible to demonstrate all these histological conditions, yet the redness of the membrane, the ecchymoses, and the character of the fluid secretion, indicate with sufficient certainty a superficial catarrh of the stomach.

In a whole series of infectious febrile diseases, such as puerperal fever, variola, etc., we meet with a grayish paleness of the glandular layer of the stomach, which is more or less mammillated. The glandular cells are swollen, cloudy, and filled with fine fatty or protein granules; they are in contact with each other, and their outlines are indistinct. In the salient folds, the glands are enlarged; they are in a state of fatty degeneration analogous to that which we see in the liver and kidneys of the same subjects. It is possible that post-mortem decomposition plays a part in this alteration of the gland cells.

2d. Chronic Catarrh of the Stomach.—The lesions of chronic gastritis extend deeper. They are not limited to the superficial layer of the mucous membrane; they also invade the glands and the submucous connective tissue, even the muscular layers are often altered. In cirrhosis

of the liver, in all affections accompanied by an impediment to the circulation in the portal vein, in some diseases of the heart, etc., the mucous membrane of the stomach is often thickened and of a red, brown, or slate color. The thickening is increased in some places into circumscribed soft gray excrescences, separated from one another by shallow furrows, thus giving to the mucous membrane a mammillated aspect. Upon a vertical section through these places we see in the raised portions dilated glands, filled with a more or less granular epithelium. The thinned parts corresponding to the furrows are, on the contrary, remarkable for the atrophy of the gland whose walls are thickened, and which contain

Fig. 257.

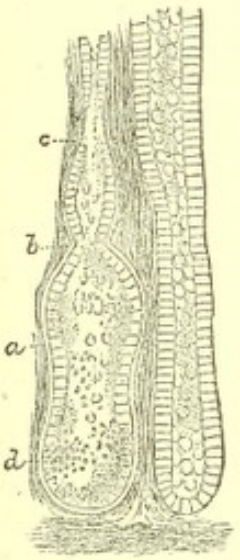


Fig. 258.

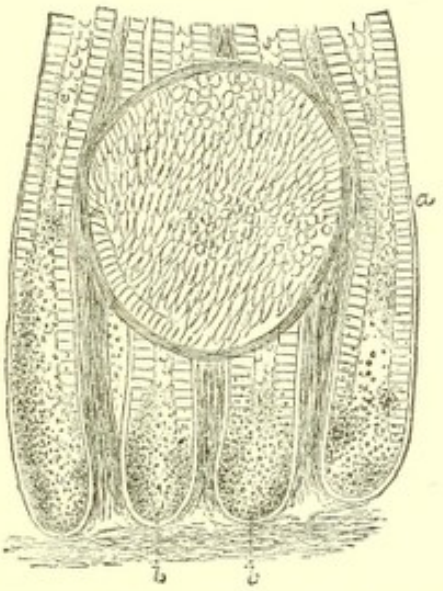


Fig. 257.—Commencing formation of cysts by constriction of tubular glands at *b* and *c*. *a*. Thickened membrana limitans. *d*. Fatty degeneration of contents of tube.

Fig. 258.—Cysts of stomach filled with columnar epithelium. *a*. Adjacent tube, the contents of which are undergoing fatty degeneration. *b*. thickened membrana limitans.

fatty granules and a few granular cells. The elevations are yellow and opaque when the gland cells contain many fatty granules. The submucous connective tissue is everywhere thickened, but especially is this so under the furrows previously mentioned. The color of the mucous membrane is gray, red, or slate color, in spots, according to the congested or pigmented condition of the elevations. In almost all these cases of chronic gastritis, by a careful examination, we find upon the surface of the membrane very transparent shining points resembling small air bubbles. These are cysts formed by distended glands containing a highly refracting viscid mucus. The wall of this dilatation is lined by cylindrical epithelium, and the contained mucus incloses a few spherical vesicular cells. These cysts are habitually surrounded by glands which present one or more dilatations of their culs-de-sac or ducts, so small that they escape the naked eye. At the same time the mucous membrane is covered by a thick layer of gray, viscid, and very adherent mucus.

If the chronic inflammation persists long enough, from the fibro-vascular tissue which separates the glands of the mucous membrane,

vegetations project in the shape of villous growths, at the centre of which are to be found loops of capillary vessels. The cylindrical epithelium is not to be seen upon the surface of these papillary growths, for it falls off within twenty-four hours after death. When these papillary growths have attained an elevation of half a millimetre they give to the internal surface of the stomach the villous aspect of the small intestine. After death, they are often filled with granular corpuscles. They are most frequently found near the pylorus, but they may appear over a great part or the whole of the gastric mucous membrane.

Very often if the chronic inflammation persists, the villosities enlarge and unite at their base, their extremities remaining free upon the surface of the hypertrophied mucous membrane. As a consequence of this condition of the papillæ, the excretory ducts of the glands become obstructed. The glands then suffer a total atrophy, or the epithelium continues to form in the culs-de-sac, while the latter enlarge and present a spherical dilatation which in thin sections has the appearance of a small cyst. The inner wall of these small cysts is lined by a layer of cylindrical cells, while the lumen is occupied by a fluid loaded with spherical cells. In other cases the glands send prolongations deep into the mucous membrane, and the thickness of the glandular layer of the membrane may then be considerably increased in places. These culs-de-sac may also become cystic like the others.

From this partial thickening of the mucous membrane there may result a small tumor sessile or pedunculated. In the latter case we have a polypus whose nature and consistence differ according as it is composed of fibrous tissue and papillæ, or mucous cysts or these different structures united. Mucous polypi are remarkable for their softness and their transparency.

This chronic irritation of the mucous membrane associated with glandular dilatations and with small polypi is more frequent in old persons than in the young.

Tumors developed in the mucous membrane of the stomach determine around them a similar chronic gastritis.

Croupous Gastritis.—It is very rare, and supervenes only in general diphtheritis. The false croupal membranes rarely cover a large extent of the mucous surface; they are seldom seen in small patches.

Pemphigus of the Mucous Membrane of the Stomach.—Superficial ulcers which have succeeded very transient bullæ developed upon the gastric mucous membrane, have several times been met with in general pemphigus. Their color is often very dark, for they are the seat of minute hemorrhages which may become intensely colored. The blood still contained in the vessels is usually coagulated, and dark in color. We have several times had the opportunity of examining these ulcers. In one case they were covered by a brownish pulp containing a large number of spores and tubes of *oïdium albicans* (thrush). These ulcers soon cicatrize.

Phlegmonous Gastritis.—This form of gastritis, ordinarily considered as a secondary or metastatic inflammation, complicating typhus, septicæ-

mia, purulent infection, puerperal fever, and finally general purulent peritonitis, may be excited by the local action of poison, acids, or caustics. It is an extremely rare lesion.

The interglandular and submucous connective tissue of the stomach is the seat of a diffuse purulent infiltration, which usually in a diffuse manner fills the lacunæ of the connective tissue. The purulent infiltrate invades also the intermuscular and subserous connective tissue, and extends to the peritoneal coat which generally inflames throughout its whole extent. The different tissues of the stomach are filled with pus. The thickness of these tissues is so remarkable that often the walls remain rigid and do not collapse.

The mucous membrane finally becomes thinned and at points perforates, giving rise to small openings through which the pus readily escapes into the cavity of the stomach.

Lesions produced by Corrosive and Irritant Agents.—The ingestion into the stomach of corrosive sublimate, of sulphuric acid, of arsenic, of ammonia, of potassa, etc., is followed by the formation of brown or black eschars, surrounded by a vivid areola of injection, and followed by all the phenomena of inflammation. The removal of the eschar reveals a loss of substance or a perforation, which is followed by peritonitis. Phosphorus when swallowed in sufficient quantity produces locally the same effects.

It is probable that the cases of *gangrenous gastritis* cited by authors are all related to poisonings. However, Klebs cites the case of an infant which, consecutive to a gangrenous inflammation of the pharynx with swelling of the cervical glands, presented at the orifice of the stomach several round gangrenous spots surrounded by a purulent eliminative inflammation. The same author states that with malignant pustule of the tongue, in the hog, similar gastric lesions are observed.

Simple Ulcer of the Stomach.—Simple ulcer is characterized by a loss of substance, more or less regularly circular, with edges so sharply cut that the mucous membrane ends at the ulcer without offering a manifestly granulating or everted border. The bottom of the ulcer is pale, fibrous, gray, and is habitually covered by a layer which is in process of molecular destruction through the action of the gastric juice.

These losses of substance are due to a genuine digestion of a limited portion of the stomach in which the circulation is impeded or entirely interrupted. At the beginning, the ulceration involves only the mucous membrane (Cruveilhier). It commences by an erosion of the follicles; later, the fibrous tissue is invaded and destroyed; the bottom of the ulcer is then constituted by smooth muscle fibres. The latter in their turn disappear little by little, and there then remains, of the wall of the stomach, only the peritoneal tunic. When this final coat is eaten away, there is a communication between the cavity of the stomach and that of the peritoneum, or the bottom of the ulcer is bounded by the neighboring organs with which the peritoneum, at this location, has formed adhesions.

When the mucous and submucous tissue, and subsequently the muscular coat, are destroyed by the process of erosion, we have an ulcer of

greater or lesser size, with sloping or terraced sides, the bottom or the apex having a much smaller diameter than the internal orifice.

The shape of the ulcer corresponds to the area of tissue nourished by an arteriole; it forms a cone whose base is upon the mucous surface. Upon the sharply-cut walls of the ulcer small arteries, and at the bottom of it one or more larger arteries are almost always seen with a plug of connective tissue in their lumen. Patients affected with this lesion often die from profuse hemorrhages. The cause of these bleedings is readily appreciated; in the arterial stump which has furnished the blood we see a post-mortem clot.

The extent of these ulcers is extremely variable. When the bottom of the ulcer is formed by adjoining organs, the tissue of the latter may sometimes be eroded to some extent. When the ulcer is located upon the greater curvature of the stomach it may end in a perforation and a general peritonitis, or an inflammation of the peritoneum localized by adhesions. The ulcer may be single or multiple; it may be located upon the lesser curvature, at the pylorus, at the cardiac end, or upon the posterior wall of the stomach; more rarely upon the greater curvature or upon the anterior wall of the organ; it may even invade the lower end of the œsophagus or originate in the duodenum.

When a thin section through an ulcer is examined, the wall of the latter is found to consist of the pre-existing tissue. The connective tissue is only a little thickened, but there is neither juice, as in cancer, nor new products resembling neoplasms. The glandular layer at the limit of the ulcer shows the tubes much lengthened, the interglandular connective tissue richer in cells than in the normal state; the epithelial cells of the gland are not altered. Beneath these glands the connective tissue is thickened somewhat and is rich in fusiform or round cells and fibres. In this tissue, at the border of the ulcer, lesions of the vessel walls, consisting of a sclerotic thickening and contraction of their calibre, are constantly found. The walls of the capillaries are sometimes converted into a thick refracting substance, which stains deeply in carmine. In one case we found some of the lymph vessels of the submucous tissue filled with lymph corpuscles. In this same case the connective tissue showed in spots a colloid metamorphosis; in these spots there were thin reticulated fibres of connective tissue, bounding very small alveoli containing a colloid substance and some large round cells. When the ulcer has invaded and partly destroyed the muscular coat, bundles of smooth muscle project upon the wall of the cavity in the form, as it were, of brushes of irregularly cut filaments, consisting of dissociated contractile elements, which may be normal or be in the various stages of fatty degeneration. The subjacent muscular tissue also sometimes shows fine fatty granules in the smooth muscle fibres. In this tissue, and in the fibrous septa which separate the muscular fasciculi, as well as in the peritoneal connective tissue, the arterioles are altered in the same manner as in the submucous tissue.

In a number of cases, a perforation has formed a communication between the cavity of the stomach and an intra-peritoneal abscess, situated posterior to the stomach, or between the latter and the liver, the spleen, or the diaphragm. Barth has seen a simple ulcer of the anterior

wall of the stomach in which the anterior wall of the abdomen and the posterior face of the ensiform cartilage formed its bottom. The cartilage had suffered a destruction of its perichondrium at this point, and a partial erosion of its substance. Cruveilhier has seen ulcers open into the transverse colon and the third portion of the duodenum. He has also recorded the extraordinary observation of an ulcer of the stomach communicating, through the diaphragm, with the left bronchus.

The anatomical diagnosis of this lesion is easy; the absence of a projecting border, the dryness and hardness of the bottom of the ulcer, and the absence of a lactescent juice in the tissue, which forms the floor and the borders of the erosion, differentiate it from carcinoma and all other morbid growths.

The healing of ulcers is possible. We not infrequently find at autopsies small cicatrized ulcers isolated, or associated with ulcers in process of development, in a quiescent state. The cicatrix which succeeds a small superficial ulcer, which ends by healing, is bordered by a puckering of the mucous membrane, in consequence of the contraction of the cicatricial tissue, but the part destroyed is not replaced by mucous membrane, and presents neither glands nor epithelial covering. If there has been during life a layer of epithelial cells over the spot, they are no longer present twenty-four hours after death. Larger cicatrices may very readily become the seat of a new ulcerative process (Cruveilhier).

Fatal termination of the lesion may be induced by hemorrhage or by perforation of the stomach. These two formidable accidents, and especially perforation, are incomparably more frequent in simple ulcer than in cancer of the stomach.

What is the cause of simple ulcer of the stomach? It is reasonable to refer it to a molecular death of the tissue, to embolism or to thrombosis of one of the vessels. Such is the hypothesis which has been advanced by Virchow, and which is supported by a number of clinical observations and experimental researches. On the other hand, ecchymoses and capillary embolisms, when they accompany ulcerations, give rise to a very superficial mortification, which does not involve the deep tissues. We may admit, as a general law, that the lesion is caused by an arrest of the circulation. Atheroma of the arteries may in some cases be recognized as a cause of the trouble. The quality of food, alteration of the gastric juice, substances which have a local action upon the stomach, as, for example, alcohol, mercury, etc., may also enter into the etiology of this disorder. An ulceration once established, we may suppose that the continuous action of the gastric juice, together with sclerosis of the small arteries, which diminishes the afflux of blood and consequently the nutrition of the part, is sufficient to prevent complete cicatrization, and to occasion the accidents observed.

Ebstein has noted a case of ulcer of the stomach following trichinosis.

Simple or Perforating Ulcer of the Duodenum.—We mention, in this connection, simple ulcer of the duodenum, which resembles in every respect the same ulcer of the stomach. It is much more frequent in man than in woman, in the proportion of ten to one. Its usual seat is in the first part of the duodenum; it is often seated on both sides of

the pylorus, and is more common upon the anterior wall than upon the posterior. It is often accompanied by a partial obstruction to the flow of the bile and of the pancreatic juice. When it terminates in healing and cicatrization, if the cicatrix is located at the pylorus the contraction causes dilatation of the stomach, with hypertrophy of its muscular tissue, vomiting, etc.

Hemorrhage and perforation are to be dreaded in this case as well as in ulcers of the stomach.

Sect. IV.—Tumors.

Lipomata.—They are rare. They may arise in the mucous membrane, or upon the serous covering.

Sarcomata.—Primary sarcoma of the stomach is rare. Virchow mentions a tumor of this kind located at the lesser curvature, and implicating all the tissues. There was in the same case a sarcoma of the ovaries and of the peritoneum.

Papillary or Adenomatous Tumors.—They have already been described in speaking of glandular hypertrophies in chronic gastritis.

Lymphadenomata.—They are sometimes met with in cases of splenic or glandular leukæmia, and in adænia. They have the same aspect as cancer, and form soft whitish granulating tumors, yielding a lactescent juice, and ulcerating at the centre. Microscopic examination alone can reveal their nature. These tumors may have a considerable superficial extent, and may reach a thickness of from 1 to 2 millimeters. When ulceration has not yet taken place, vertical sections show the different layers of the mucous membrane. The glandular layer is still preserved, and the glands seem much longer than normal, an appearance due to development of the connective tissue which surrounds them. This tissue is infiltrated with lymph corpuscles, disposed in longitudinal series between the fasciculi of connective tissue. The epithelium of the glands is preserved. Beneath the glands the much thickened connective tissue is infiltrated with lymph corpuscles, and in thin, pencilled sections, adenoid tissue is very distinctly visible. The muscular coat contains lymph corpuscles between the muscle fibres, but these cells are much more numerous in the interfascicular bundles of connective tissue. When ulceration occurs, the loss of substance affects the glandular layer, and in place of the latter we observe very irregular granulations.

Tubercles.—They are very rare, and are met with only in a general tubercular ulceration extending throughout the intestine. They present the same appearance and follow the same course in the stomach as in the intestine.

Calcareous Infiltration.—Virchow has described under this name, a lesion which consists in an infiltration, by the salts of lime, of a limited

portion of the mucous membrane of the stomach and the corresponding glands. Ulceration may succeed this infiltration, for it occasions a superficial destruction of the tissue of the mucous membrane.

Myo-fibromata.—Tumors constituted by bundles of smooth muscle fibres and connective tissue are sometimes met with in the stomach. They are, both as to their structure and their development, comparable to myomata of the uterus. Arising in the muscular coat of the stomach, they may project either upon the mucous membrane or upon the serous surface.

1st. The myomata which project upon the mucous membrane are more frequently seated in the vicinity of the pylorus. By the movement of the food, they may be drawn into that orifice, and even project into the duodenum. These polypi, covered, as they may be, by hypertrophied mucous glands, may present a mucous or myxomatous appearance.

2d. The polypi, composed of muscular fibres and fibrous tissue, which project upon the peritoneum, are generally hard and small; but they may attain the size of an almond or a walnut, and may sometimes undergo calcareous infiltration.

Syphilitic Tumors and Ulcers of the Stomach.—Pathologists record several observations of ulcers and of hypertrophied thickening of walls of the stomach which they connect with syphilis. But most of the these records are indefinite. This is not so of a case reported by Klebs, where there were ulcers of the stomach and intestine associated with gummata of the liver. We ourselves have seen a case of syphilitic tumor of the stomach accompanied by very characteristic gummata of the liver.

Along the lesser curvature, and in the neighborhood of the pylorus, the mucous membrane of the stomach presented prominences of flattened umbilicated tumors, from 2 to 5 centimetres in diameter. Over them the mucous membrane was preserved, but it was thin and adherent. In a vertical section, the thickened and altered submucous tissue presented a thickness of 8 to 12 millimetres. This elevation, formed of thickened submucous tissue, was perfectly distinct from the muscular layer situated below.

The muscular layers were normal, or scarcely at all thickened, while the submucous connective tissue was hypertrophied. This connective tissue was of fibrous consistence, very dense, and yielded no juice by scraping. Its color was yellow.

The pylorus was constricted. There were no adhesions of the stomach with the liver; but, at the lesser curvature, the peripheral cellular tissue was adherent to the indurated lymphatic glands, and there was a hard, white, stellate cicatrix seen upon the surface of the stomach.

On microscopic examination, the glandular layer was studded with erect and oblique villous or papillary elevations. These villosities consisted of hypertrophic granulations of the connective tissue which surrounds the tubular glands. The glands were separated from each other by thickened and hardened connective tissue. Those gland tubes which were found at the depressed centre of the elevations were narrowed, and

the excretory duct was almost completely replaced by connective tissue. Over the greater part of the tumor the terminal culs-de-sac of the glands were nearly normal. Only at the centre of the tumor were they scarce and less easily distinguished. Under a high magnifying power, the villi appeared to be covered by flat cells, and to be formed of connective tissue, containing between its fibres round embryonal cells and fatty granules. The gland tubes were seen to contain a few small cubical epithelial cells which did not form a complete layer. The terminal dilatations of the glands contained cells which furnished a complete lining and which were conical, having a thin wall with a double contour, and clear or cloudy mucous contents. The tissue which surrounded the glands was dense, and contained elastic fibres, connective tissue fibres, and small round cells, and was permeated by numerous bloodvessels.

The submucous tissue, which, as has been said, constituted the whole prominence of the new formation, was dense and closely felted, and penetrated by arterial, venous, and capillary vessels filled with blood. It contained elastic fibres and connective tissue fibres, among which existed large numbers of small, round, or slightly elongated embryonal cells. In addition to these elements so arranged, there were also found groups of small cells in the midst of a ground substance of small amount and of granular appearance—islands of embryonal tissue. At the depressed centre of the tumors, their submucous tissue, so to speak, reached the surface, for, as we have already seen, in this area the glandular layer was in great part atrophied and converted into connective tissue.

In the muscular tunic the bundles of smooth muscle fibres were separated by bands of fibrous tissue, between which were round embryonal cells; but these cells were not met with in the interior of the bundles of muscle fibres, which latter were in a nearly normal condition.

In the peritoneal connective tissue, we found the same new formation of cellular elements.

This case, in which the lesion was characterized by flat tumors resembling fibrous gummata developed in the submucous connective tissue, leaves no doubt of the syphilitic nature of the neoplasm. It enables us to understand and to acknowledge at the same time the existence, in the stomach, of ulcerations of the same kind.

In this same case, the lymph glands of the lesser curvature were very large, white, and infiltrated with a lactescent juice. The juice when freshly examined contained lymph corpuscles and swollen endothelial cells, some in a state of fatty degeneration. Thin sections of these lymph glands showed the lymph canals extremely dilated and everywhere filled with very large and more or less spherical endothelial cells. The medullary tissue also presented these large cells in its meshes. The same alteration also existed, but in a less pronounced degree, in the reticulated tissue both of the follicle and follicular cords, and there was also a very evident inflammatory thickening of the fibres constituting the reticulum.

The bronchial glands had undergone the same alteration, and the retention of the lymph, and the consequent irritation of the lymph vessels, were manifested by a chronic lymphangitis of the superficial and deep lymphatics of the lung. This is one of the forms of chronic syphilitic adenitis.

CARCINOMA OF THE STOMACH.—Cancerous tumors of the stomach are very common, and, however different in structure their varieties may be, they present to the naked eye much the same aspect, and the same progress. Encephaloid carcinoma, for example, cannot by the naked eye alone be distinguished from cylindrical celled epithelioma, which is very common. The different varieties of carcinoma which appear in the stomach, may be ranked, according to their frequency, in the following order: encephaloid carcinoma, fibrous or scirrhous carcinoma, colloid carcinoma, and melanotic carcinoma. The almost constant location of these tumors is at the pylorus, and the lesser curvature, and they are also occasionally found at the cardiac end. They have a great tendency to extend upon the adjoining portion of the posterior wall; more rarely they advance upon the anterior wall, and sometimes they invade the whole extent of the stomach. Carcinomatous growths begin in the submucous tissue, and in the glandular layer of the stomach. Upon a vertical section it is seen that the glandular layer is thickened, is slightly transparent, and that the principal mass which causes the prominence of the new growth is formed by the layer of submucous connective tissue. Even in very small tumors, by scraping the surface with a scalpel we obtain a milky juice. Microscopic examination of thin sections through the morbid growth, proves that the submucous tissue already shows carcinomatous alveoli filled with cells of a new formation, whilst the glandular layer exhibits its glands much lengthened and filled with cylindrical or cubical cells. The connective tissue which separates the glands contains a large number of embryonal cells between its fibres. From this interglandular embryonal tissue may grow prolongations which extend beyond the neck of the glands in the form of papillary vegetations. This formation of papillary vegetations is common to all new formations in the mucous membrane of the stomach.

In the neighborhood of the cancer, the mucous membrane is usually altered; it is red or violet, sometimes softened or mammillated, and it presents the indications of chronic inflammation, frequently with intense pigmentation. Small retention cysts of the glands are also often met with. It is very rare to find the mucous membrane in a healthy condition around the cancerous nodule.

When there is ulceration, the ulcer is of variable size. If it is seated at the pylorus it may have the form of a ring. Ulceration may momentarily re-establish the course of the food which had been arrested by the contraction of the pyloric orifice. The edges of the ulcer are elevated, and sometimes loosened. Its bottom is habitually fungous, bloody, and covered with detritus; or if the whole cancerous growth is nearly destroyed, the muscular tissue is exposed or partly destroyed, or there may even be a perforation.

Perforation is incomparably more rare in these tumors than in simple ulcer. The muscular tunic adjoining and in the neighborhood of the tumor is always hypertrophied. This hypertrophy may extend far beyond the location of the tumor, it may involve the whole muscular coat, as frequently happens when the new growth affects the pylorus.

The stomach often forms adhesions with the neighboring organs and surfaces. Upon the peritoneal surface miliary cancerous nodules, or

roundish patches of the same nature, and surrounded by a proliferating adhesive peritonitis, are often seen. These adhesions, frequently extensive and sometimes consisting of cancerous tissue, may arrest the extension of the ulceration, in depth, and prevent the discharge of the gastric contents into the peritoneal cavity. Sometimes the stomach contains but little fluid, but most frequently it contains a thick, dark material resembling coffee grounds, which is ejected in the act of vomiting.

The lymph glands of the lesser curvature are always altered. Finally, secondary nodules are often found in the neighboring organs.

Varieties of Carcinoma of the Stomach.—*Encephaloid Carcinoma*, always primary, at one time presents the appearance of a limited ulcer with an irregular granulating surface, everted borders constituted, like the bottom of the ulcer—by a soft, vascular, whitish or pinkish tissue, rich in juice; at another time it extends over the greater part or even the whole of the mucous membrane.

Histological examination shows, as in every carcinomatous tumor, an alveolar stroma, surrounding masses of large flat or globular cells of varied form (see p. 96 *et seq.*). Secondary nodules in the liver form very quickly in this variety of tumor.

Telangiectatic carcinoma, or *carcinoma hæmatodes*, which is only a variety of encephaloid carcinoma, presents in the stomach large dilatations of the vessels, and is remarkable for the facility with which the veins are altered and invaded by the neoplasm. In fact when the peritoneal surface of the tumor is examined we remark opposite the position of the ulcerated portion, large dilated vessels. We have seen two cases in which these veins were filled with a whitish juice, containing cells, similar to those of the tumor, and numerous small red points and lines which were nothing else than minute dilated vessels. These minute vessels projected from the inner wall of the veins. This condition of the veins extended as far as the portal vein. In one of these cases the trunk and the hepatic branches of the portal vein were entirely filled by this singular vascularized new formation.

Primary scirrhous of the stomach is more rare. Even secondary scirrhous is a rarity. The tumor is harder, nodulated, less rich in juice and less vascular than in encephaloid; but in its ulceration, its propagation of nodules to the peritoneum, to the glands, to the liver, to the pancreas, etc., it entirely resembles the latter. It develops in the submucous connective tissue.

Colloid carcinoma is not uncommon in the stomach. It is characterized by the gelatiniform appearance of the tissue of which it is composed.

Many tumors which present a colloid aspect are far from being carcinomata, for frequently cylindrical-celled epitheliomata present a colloid metamorphosis.

Epitheliomata.—Cylindrical-celled epithelioma is the most common of all the primary tumors of the stomach which formerly were termed cancerous. It presents here the same naked eye characters as encephaloid carcinoma, and the same extension, by secondary nodules, to the liver and to the lymph glands of the lesser curvature. Its favorite seat

is at the pylorus, in the region of the mucous glands. Nothing is more easy than to determine its nature by aid of the microscope. Upon thin, vertical sections we find wide depressions having the general form of the mucous glands, and lined by a cylindrical epithelium. These tubes are only less regular, longer and wider than those of the mucous glands. They often present the form of cavities, from the wall of which papillæ or vascular loops covered with the same cylindrical epithelium project into the lumen (see p. 154 *et seq.*). There is no doubt that these tumors originate in the mucous glands, but they progressively invade the deeper layers beneath the mucous membrane. At the borders of the ulcer the mucous glands are much elongated, and there is a new formation of small round cells in the interglandular connective tissue. The lymph glands of the lesser curvature have always been involved in the cases which we have seen. They presented cavities having a form determined by that of the lymph canals: these cavities were everywhere lined by cylindrical epithelium, and showed villous growths springing from their surface, aud covered by the same epithelium.

The secondary nodules in the liver and other organs, sometimes met with, are also constituted by a tissue in which tubes, or small round or cylindrical cavities, always lined with the same kind of epithelium are imbedded.

In the stomach the primary tumor often undergoes, in part or in toto, a colloid degeneration, so that at first sight we may imagine that we have to do with a colloid carcinoma. The points which have a gelatiniform appearance contain cells which are round or of an intermediate shape between spherical and cylindrical. They are filled with a transparent substance, and are more or less destroyed. The cavities which these cells line have at the same time lost their cylindrical form and become spherical. Such tumors are recognized as cylindrical-celled epitheliomata by the structure of the parts of the primary growth which have not suffered the above metamorphosis, or by the fact that the lymph glands or the secondary nodules present the appearance of the typical tumor.

Pavement-celled epithelioma is very rarely met with in the stomach. It is always secondary, and follows an epithelioma of the mouth, the tongue, or œsophagus. In the observed cases the secondary formations in the mucous membrane of the stomach presented histological characters similar to those of the primary tumor.

Hypertrophy of the Muscular Tissue.—We here describe this alteration which is ordinarily caused by chronic gastritis, because it accompanies almost every tumor of the stomach, and because it has very often been mistaken for a tumor. In section the thickened muscular coat presents a pale gray aspect, is hard, semi-transparent, fleshy, and permeated by thickened, parallel lamellæ of whitish connective tissue, which communicate to it a honeycombed appearance. The hypertrophy may be limited to the neighborhood of a cancerous mass, or it may extend more or less throughout the entire muscular tunic.

In a few observed cases, a considerable hypertrophy of the muscles of the stomach, accompanied by narrowing of the pylorus, has been the cause

of death. The lesion may appear to be primary, because at the autopsy neither a tumor nor an ulceration of the surface of the stomach is found. It is probable that in such cases, it is always consecutive to a gastric catarrh, or sometimes to a simple small ulcer which has healed. If it is located at the pylorus, as is frequently the case, it narrows the orifice and an enormous dilatation of the stomach may ensue.

Hypertrophy of the muscular walls of the stomach may result from obstructions and local irritations caused by foreign bodies.

Microscopic examination of the muscular tissue of the stomach, in cases of simple hypertrophy, shows the muscle fibres thicker and much longer than normal. When the hypertrophy is in the neighborhood of a tumor, there is a swelling of the cells of the connective tissue interposed between the bundles of muscle fibres, and at the same time in some numbers, lymph corpuscles are also to be found between the connective tissue fibres. The muscle fibres themselves are hypertrophied. There is an œdematous and inflammatory swelling of the muscular tunics caused by the presence of the tumor and the great vascularization of the part.

CHAPTER IV.

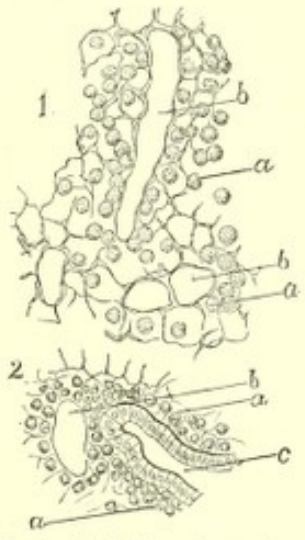
INTESTINE.

Sect. I.—Normal Histology of the Intestine.

Small Intestine.—The small intestine is composed of several layers or membranes which are, from without inwards: the peritoneum, formed of flat cells and connective tissue; two layers of smooth muscle, the most external longitudinal, and the most internal circular or transverse; and the mucous membrane. It is the latter which we have especially to consider.

The mucous membrane of the small intestine, continuous at the pylorus with that of the stomach, forms in the duodenum and jejunum the transverse semilunar folds or valvulæ conniventes, and its surface is covered with villi which give to it a velvety appearance. These villi are extremely numerous in the duodenum and jejunum (50 to 90 to the square line); they diminish in number in the ileum (40 to 70). Throughout the whole extent of the small intestine the mucous membrane contains tubular glands or Lieberkühnian follicles, which have some resemblance to those of the stomach. Moreover, in the upper portion of the duodenum, racemose glands or glands of Brunner, somewhat similar to the salivary glands, are found. In addition from one end of the small intestine to the other, closed follicles are met with; they may be isolated (solitary follicles) or agminated (Peyer's patches).

Fig. 259.



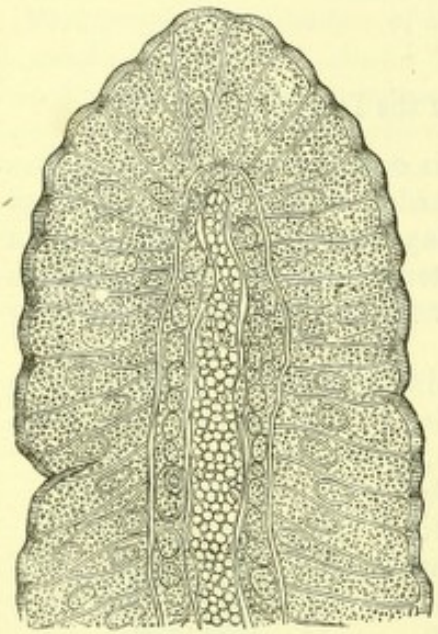
1. Reticulated tissue from a lymphoid follicle of the vermiform appendix of the rabbit, with the system of meshes, and remains of the lymph cells *a*. Most of the latter have been removed artificially. *b*. Lymph vessel. 2. Longitudinal section of a Lieberkühn's gland, showing the surrounding reticular tissue, in the meshes of which are seen the lymph cells *a*. *b*. Lumen of a vessel. *c* Lumen of the gland. (*Frey.*)

The connective tissue of the mucous membrane is a reticulated tissue (His), whether it is located in the papillæ, between the glands, or in the deeper tissue. This connective tissue is covered upon its surface, whether it be of the villi or of the crypts of Lieberkühn, by a layer of flat endothelial cells (Debove), upon which are implanted the investing cells, which are cylindrical epithelia. The cylindrical epithelium which covers the whole of the free surface of the mucous membrane consists of long cells laterally adhering to one another, containing an ovoid nucleus and presenting at their free

border a plate of slight thickness and vertically striated. Besides these cells, goblet cells are met with from point to point. The latter elements, which have been considered as fat absorbents, do not appear to have any other function than the secretion and discharge of mucus.

The intestinal villi covered by the epithelium just described have a variable length. They are traversed by a vascular network forming capillary meshes continuous, on the one side, with one, two, or three arterioles, which penetrate the villus, and on the other, with a vein. The reticulated tissue of the villus also possesses smooth muscle fibres disposed longitudinally. All authors describe chyliferous vessels, in the villi—a single central vessel for the long slender villi, and for the thick villi several lymph vessels, which form anastomoses with each other. Debove denies the existence of the central lacteal, and believes that the flat endothelium described as belonging to the lymphatic is nothing else than the endothelial investment of the villus. The fatty particles first enter the cylindrical cells, then pass into the reticulated spaces of the connective tissue of the villus, and thence are collected and transported by the lacteals. On this account, the villi are the most important agents of intestinal absorption, as well as from the fact that they multiply the absorbing surface.

Fig. 260.



Section of a villus of a rabbit. High power. (*Stricker.*)

The glands of Brunner, situated mainly in the first part of the duodenum, are very numerous between the pylorus and the mouth of the ductus communis choledochus, but are much more rare in the rest of the duodenum. They are visible to the naked eye.

The tubular glands or follicles of Lieberkühn are found throughout the whole of the small intestine, and are situated between the villi. They, as well as the villi, are absent only at the points where the closed follicles are located, around which points they form a corona, so that the projection of the closed follicle is really a depression below the level of the surface. These tubular glands are formed of a simple cylindrical tube, which is sometimes a little dilated at the inferior extremity. They are much shorter and narrower than the tubular glands of the stomach. They do not appear to have a distinct membrane; only a single endothelial layer separates them from the surrounding connective tissue. The tubes are lined by cylindrical epithelium similar to that upon the villi, not always so long, but often goblet-shaped. Their function is to secrete mucus.

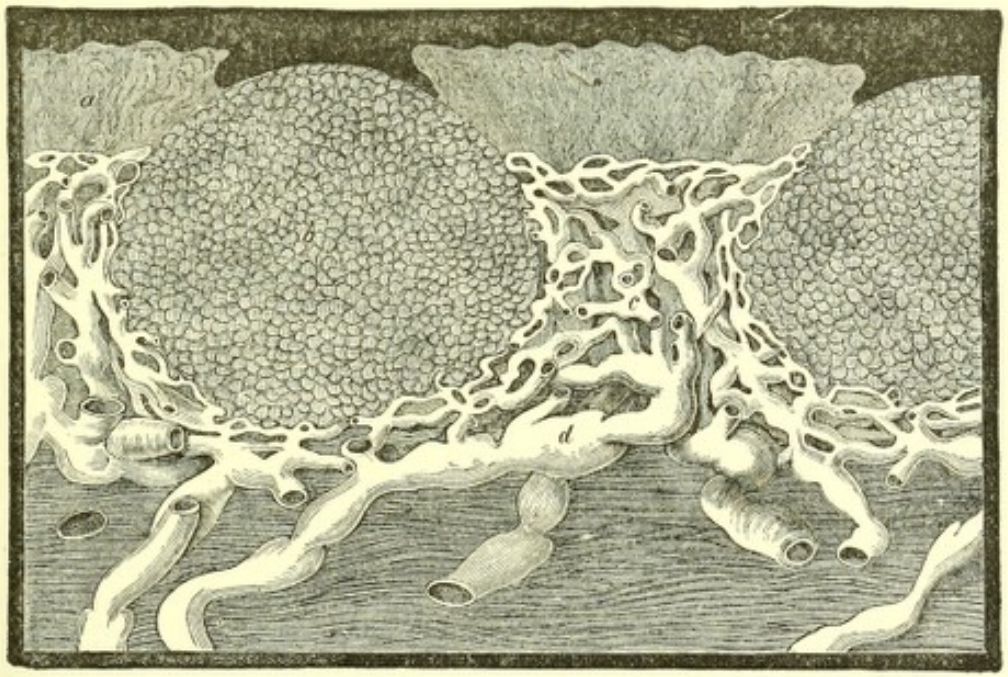
The closed follicles of the intestine are lymphoid glands analogous to those of the base of the tongue and of the tonsils. They consist of reticulated tissue inclosing lymph corpuscles; they are isolated as in the jejunum, the ileum, and large intestine, or they are agminated into

patches which are situated opposite the attachment of the mesentery, and elongated in the length of the intestine (Peyer's patches). The Peyer's patches appear in the ileum and are especially well developed in its lower end.

The solitary follicles reach the surface of the intestine at a point where there are, as a rule, neither tubular glands nor villi; exceptionally, however, the latter may be present. Upon the surface of the Peyer's patches the villi and glands form a corona around each follicle. The form of the isolated follicles is spheroidal; the follicles in the Peyer's patches are compressed against each other in such a way that their long diameter is vertical to the surface of the membrane. These follicles are well supplied with blood capillaries, and are separated from the connective tissue of the mucous membrane by a condensation of the reticulated tissue, but they have no real enveloping membrane.

The fatty particles and the fluids of the small intestine taken up by the villi, are first acted upon by the reticulated tissue of the mucous

Fig. 261.



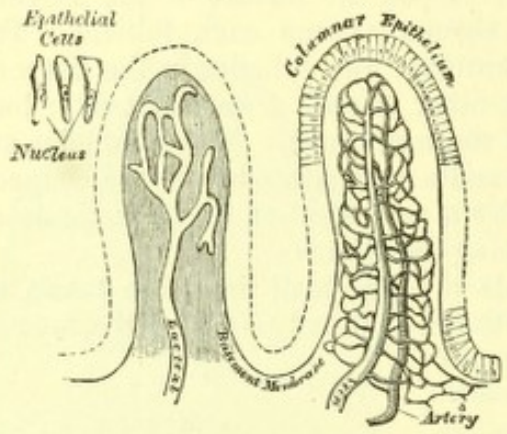
Perpendicular section through the wall of the processus vermiformis (man). *a*. Gland of Lieberkühn. *b*. Solitary lymph follicle, the epithelial investment of its surface is not represented. *c*. Lacteal vessels surrounding but not penetrating the follicles. At *d* are seen the large efferent vessels provided with valves. (*Carpenter.*)

membrane and the closed follicles, and are then emptied into the lymphatic sinuses and vessels. The latter, independently of the lacteals of the villi, form at the surface of the mucous membrane a superficial plexus, which surrounds the tubular glands and the follicles, and communicates with the sinus at the base of the follicles, in which arise the lymph vessels which perforate the muscular wall of the intestine in order to empty into the subserous lymphatics. There exists, besides, a lymph plexus with large meshes, as described by Auerbach, situated between the two

muscular layers. The subserous lymphatics subsequently pass between the two layers of the mesentery at its attachment to the intestine.

The bloodvessels form in the mucous membrane very rich capillary networks, in the villi, around the tubular glands, and in the closed follicles. The muscle fibres are supplied by capillaries forming a plexus with elongated meshes.

Fig. 262.



Two intestinal villi magnified. (*Gray.*)

The nerves which come from the pneumogastric and great sympathetic form two plexuses in the intestine: the first, discovered by Remak and Meissner, and situated in the submucous connective tissue, is formed of ganglia and pale nerve fibres which are distributed to the smooth muscles of the villi and mucous membrane; the second, discovered by Auerbach, is found between the two layers of muscle fibres. It also is formed of ganglia and smooth fibres. The latter are distributed to the neighboring muscles.

In its general plan of construction, the *large intestine* differs little from the small intestine.

In man, the mucous membrane is furnished neither with villi nor Peyer's patches. The closed follicles are less numerous, if we except the ileo-cæcal appendix, which is very rich in these follicles.

Tubular glands or follicles of Lieberkühn are to be found over the whole surface of the large intestine, and their structure here is the same as already described. They are only a little longer than in other portions of the intestinal canal.

Beneath the layer of tubular glands, the connective tissue of the mucous membrane more resembles ordinary loose connective tissue than reticulated tissue, and shows a layer of muscular fibres. This muscular layer, which exists here as in the small intestine, is placed immediately below the tubular glands. The inner third of the solitary follicles is internal to the plane of this muscular layer; the outer two-thirds is external to it.

The solitary follicles, less numerous, but larger than those of the small intestine, are placed in a layer external to that of the tubular glands. The layer of tubular glands is wanting at the position of the closed follicles. There consequently results a depression of the mucous membrane corresponding to the seat of one of these follicles.

The lymph vessels of the large intestine are far from being as abundant as in the small intestine.

The bloodvessels and the nerves present the same general disposition as in the small intestine.

The mucous membrane of the large intestine is directly continuous, at the lower part of the rectum, with the mucous membrane of the anus,

which latter, in its investment of pavement epithelium and its papillæ, is analogous to the skin. The anal mucous membrane possesses sebaceous glands but no hairs.

Sect. II.—Pathological Histology of the Intestine.

POST-MORTEM CHANGES are always met with in the intestine. In the majority of cases the mucous membrane is pale, and is covered by a thick layer of opaque mucus which can be removed by scraping. This mucus is a product of cadaveric decomposition. The cells become detached and mixed with the mucus which at the moment of death normally exists at the surface of the membrane. This fluid is more abundant in those parts of the intestine where the surface is multiplied by the villi, that is, in the small intestine.

The follicles of Lieberkühn are habitually altered; their cells generally have become detached from the superficial part of the gland, thus causing the latter to appear shorter than it is in reality.

The connective tissue itself is softened, and there is often a quite advanced digestion of it, especially in children who die of diarrhœa. Sometimes we meet with perforations, purely and simply post-mortem. In these, neither the thinned and partially destroyed portion, nor the adjoining parts offers a redness or inflammatory infiltration of the connective tissue.

When the vessels are full of blood at the moment of death, they often present a brown or slate color. The ecchymoses and the congestions which accompany ulcerations also show this change of color.

CONGESTION.—Congestion is present in all inflammatory and other affections of the intestine, as well as in the case of stasis of the blood in the portal vein. It is characterized by a more or less abundant secretion of altered intestinal fluid, the composition and the characters of which will be described *à propos* of intestinal catarrh, and by a redness of the mucous membrane which remains after death. On account of the action of the intestinal juice, this color is sometimes brown or slate color; but it is possible that the change of color may be altogether post-mortem. When congested points are examined under the microscope, the capillaries of the villi are seen to be full of blood, which is not the case normally, and the superficial capillaries which describe meshes around the tubes and orifices of the glands are also filled. At the points where the mucous membrane is slate color, the villi, deprived of their epithelium, as they always are twenty-four hours after death, show a large quantity of brown and black pigment granules. This lesion is constant in intense congestions of the small intestine which have continued for a considerable time.

INFLAMMATION OF THE MUCOUS MEMBRANE; INTESTINAL CATARRH.—Catarrh or superficial inflammation of the mucous membrane, associated with an exaggerated secretion, is very common in the intestine. A number of different causes may produce it, and the quality as well as the quantity of fluid varies in different cases.

Purgatives generally excite a local irritation of the intestinal mucous membrane, whether they are administered by the mouth, the rectum, or reach the intestine through the blood circulation. When the mucous membrane of the intestine of animals, under the influence of purgatives, is examined, it is found congested, and covered by a mucus more abundant than normal, rich in lymph corpuscles, and containing also some cylindrical cells with clear and vesicular nuclei.

It is possible also that certain diarrhœas may be due to exaggerated peristaltic movements, which interfere with absorption of the intestinal fluid by causing it to progress too rapidly in its passage downwards.

Fig. 263.

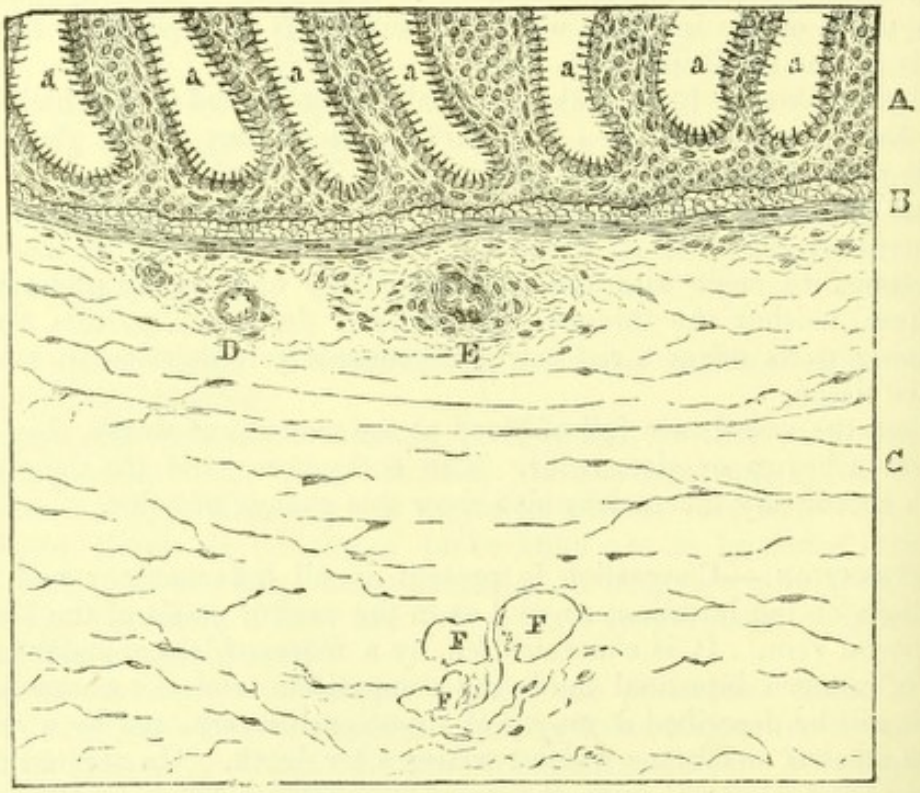


Diagram of a perpendicular section of a colon in a case of acute diarrhœa, showing inflammation of the submucous layer. ×280. A. Mucous membrane; *a*. Follicles of Lieberkühn pushed apart by the swarm of new elements in the adenoid tissue. B. Muscle of Brücke. C. Subcutaneous connective tissue. D. A small artery. E. A small vein surrounded by a swarm of lymphoid elements. F. Accidental rents in the section. (From a photo-micrograph by Surgeon J. J. Woodward, U. S. Army. Copied from the second medical volume of the Medical and Surgical History of the War of the Rebellion.)

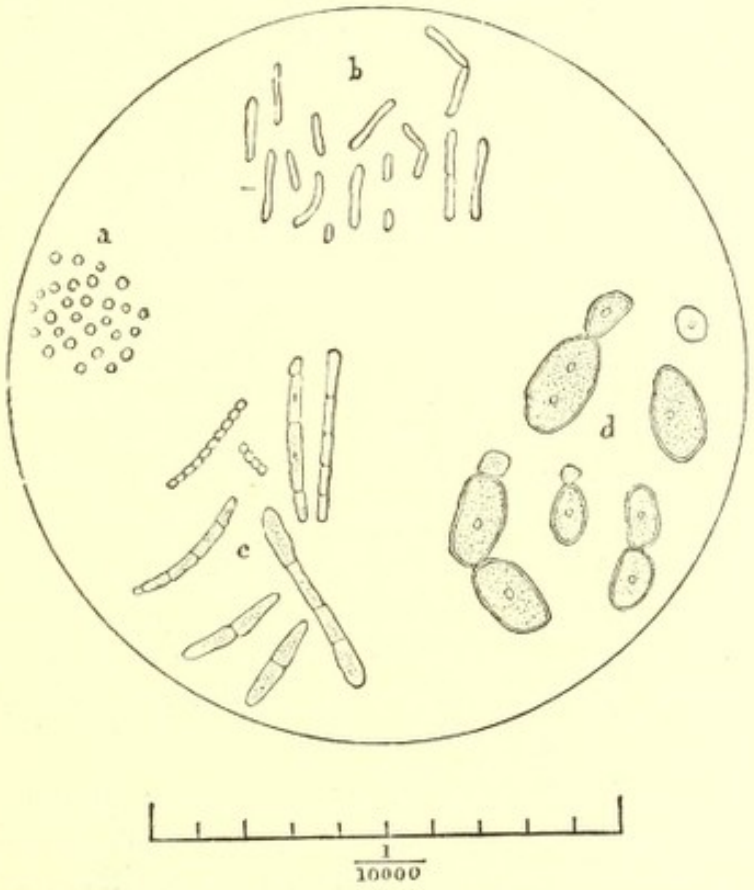
A. Moreau, after having placed two ligatures around a loop of intestine in a dog, cut the nerves supplying this portion of the gut, and observed the included portion of intestine fill up with an abundant fluid. This fluid, which Moreau at first thought to be physiological intestinal juice, differs essentially from the latter; it contains much less organic matter, whilst, on the contrary, it suspends large numbers of lymph corpuscles. It is not normal intestinal juice, but is the secretion from a very intense catarrh. By its sp. gr., by the quantity of organic matter and salts which it contains, it very much resembles the fluid of the diar-

rhœa of cholera. Is this catarrh due solely to the section of the nerves, or is it caused by the wounding of the mesentery and the intestine? This problem does not appear to us to be satisfactorily solved.

It is easy to excite more intense or purulent catarrhs in animals by the injection of irritants into the rectum. In kittens thus injected with a weak solution of nitrate of silver or tincture of iodine, the large intestine was filled with pus at the end of twenty-four or thirty-six hours, yet we found the cylindrical epithelium in position. In some spots most of the cylindrical cells which covered the villi and lined the glands were goblet-shaped. Neither endogenous formation nor division of nuclei was observed in them. It is probable, therefore, that all the lymphoid cells of the purulent secretion had escaped from the vessels and passed through the epithelial layer. These lymphoid cells were numerous in the superficial connective tissue of the mucous membrane.

In *man*, the bad quality of food, the abuse of fruits, or the non-appropriation of aliment, the influence of cold, errors of diet, indiges-

Fig. 264.



Minute vegetable forms from normal feces. ×1900. *a*. Spherical elements (micrococcus). *b*. Rod-like bodies (bacteria). *c*. Filaments composed of both the foregoing. *d*. Torula-like cells. (From a photo-micrograph by Surgeon J. J. Woodward, U. S. Army. Copied from the second medical volume of the Medical and Surgical History of the War of the Rebellion.)

tion, etc., are the most frequent causes of simple catarrhal diarrhœa. Inferior organisms (bacteria, etc.) are often found in the feces in large

numbers, and they frequently exist in the stools physiologically. In the different cases the fluid discharge is watery, is colored yellow or brown by the bile, and contains fluid fecal matter. In this fluid a very small number of cylindrical cells is suspended.

In suppurative peritonitis, and especially in puerperal fever, the small intestine surrounded by the peritoneal exudation is whitened; it has a cloudy or milky aspect. The mucous membrane is whitish and opaque; it appears to be soaked with pus, and it is covered by a thin layer of puriform fluid. We have to do here with a purulent catarrh occasioned by contiguity of structure.

In a succession of chronic catarrhs of the intestine, particularly the large intestine, there is sometimes formed around the hardened substances (fecal matters, scybala) which irritate the intestine, a layer of transparent semifluid mucus; at other times, these matters are invested by a layer of puriform mucus. The more or less tenacious mucus, in the form of false membranes and long filaments, in these cases, may, at first sight be mistaken for fragments of mucous membrane or for parasites. This transparent or opaque mucus always contains many cylindrical cells, as well as a variable number of lymph corpuscles. In these forms of chronic catarrh the abundance of the fluid secreted is not always proportionate to the irritation of the mucous membrane.

Simple catarrh of the mucous membrane is rarely accompanied even by superficial ulcerations.

In chronic catarrh of the intestine, we observe another series of alterations which consist in lesions of the tubular glands, which may be atrophied or hypertrophied, or present the appearance of mucous cysts, as in the stomach. The glands are markedly hypertrophied in portions of the mucous membrane, where, under the influence of an intense irritation of the connective tissue, villous prolongations spring up between the glands. In the large intestine, for example, where villi do not normally exist, we see, in the chronic catarrh of infants, vegetations of the interglandular connective tissue. Here, as in the stomach, increase in the length of the glands is brought about by development of the connective tissue which surrounds them. The portions of the mucous membrane thus thickened at one point may form an elevation, which later may become pedunculated. Thus are produced those papillary glandular polypi so frequent in children, which sometimes become the starting-point of an invagination. The mucous contents of those glands which are dilated and cystic have given rise to the name for these small tumors, of mucous polypi.

Catarrhal inflammation of the intestine has received different names, according to the location of the morbid process, such as duodenitis, inflammation of the ileum, typhlitis, colitis, and proctitis or inflammation of the rectum.

Simple or catarrhal *duodenitis* has rarely been seen independently. The swelling of the mucous membrane of the second portion of the duodenum, and in particular of the ampulla of Vater, causes the closing of the canal of Wirsung, which connects the ductus communis choledochus with

the internal surface of the intestine, and occasions retention of bile and icterus as a consequence.

In *ileitis*, or inflammation of the lower end of the small intestine, besides the common anatomical signs of catarrhal inflammation, we almost constantly observe a tumefaction of the closed follicles, both the solitary and those of Peyer's patches. This lesion is especially marked in cholera, in typhoid fever, and in the infectious maladies, in

Fig. 265.

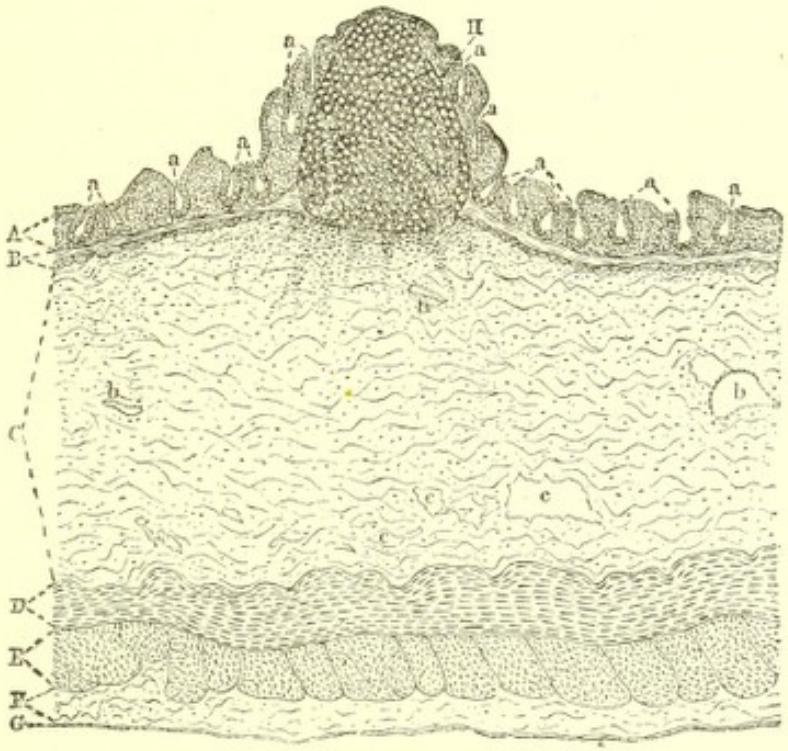


Diagram of a perpendicular section of the ileum, showing enlarged solitary gland, in a case of acute diarrhœa. ×63. A. Mucous membrane, showing the follicles of Lieberkühn, *a*, pushed apart by the abnormal growth of adenoid tissue. B. Muscle of Brücke. C. Submucous connective tissue, showing sections of bloodvessels, as at *b*, and some accidental rents, as at *c*. D. Circular layer of the muscular coat of the intestine. E. Longitudinal layer. F. Subperitoneal connective tissue. G. Peritoneum. H. Enlarged solitary gland. The cells of the epithelium, adenoid tissue and solitary gland in this diagram are much exaggerated in size, and of course correspondingly few in number. (From a photo-micrograph by Surgeon J. J. Woodward, U. S. Army. Copied from the second medical volume of the Medical and Surgical History of the War of the Rebellion.)

the exanthemata, puerperal fever, etc. The isolated follicles, which normally do not form a sensible relief, project upon the surface as little round grains; they are more than twice their normal size, their surface is pale, and their section presents a gray or pinkish semi-transparent aspect. Examining one of these little elevations under a low magnifying power, we see that it is covered, except at the apex, by the villi and the glands of the mucous membrane. The hypertrophy of the follicle is due to the distension of its reticulated meshes by lymph corpuscles. By scraping the cut surface, we often find swollen granular endothelial cells with two or more nuclei.

This tumefaction of the isolated follicles, which is seen in most diarhœas, is more visible at the end of the ileum than in other portions of

the intestine, because these follicles are generally more numerous here; but it is observed nevertheless throughout the whole intestinal canal, in the large as well as in the small intestine. Where the enlargement of Peyer's patches is very marked, as in children, the hypertrophied follicles may end in ulceration. We will study ulcerative inflammations of the follicles under typhoid fever, and caseous degeneration under intestinal tuberculosis.

Typhlitis and Perityphlitis. — Typhlitis is an inflammation of the vermiform appendix. When it is intense it is so often accompanied by an inflammation of the neighboring peritoneum that the two inflammations have generally been described together. No other part of the intestinal canal is more disposed to lodgment of fecal matter or foreign bodies, a circumstance which explains the frequency of inflammatory lesions of this appendix.

When these foreign bodies remain a certain time, they are habitually covered by a coat of triple phosphates, and are converted into small calculi. Whether the appendix is inflamed spontaneously, or, as is more common, the inflammation is excited by the presence of these foreign bodies, the mucous membrane secretes a puriform or mucous fluid; it is thickened, more or less congested, and the thick layer of closed follicles, which it possesses, presents ulcerations. The entire appendix is distended and much more voluminous than in the normal state. The infiltration and thickening of the mucous membrane prevent the contraction of the muscular coat, and render its emptying or change of position impossible. Since the inflammation of the mucous membrane very often is propagated to the serous surface, the congested peritoneum becomes covered with a thin layer of fibrin which is penetrated by vessels, newly formed connective tissue results, and the immobilized appendix forms adhesions with the parts adjoining.

This peritonitis is usually not grave, but is from the commencement limited and adhesive. Most frequently the appendix is bound down to the cæcum, when there is a resulting atrophy. At other times it is united to the uterus, to the bladder, or to the abdominal wall.

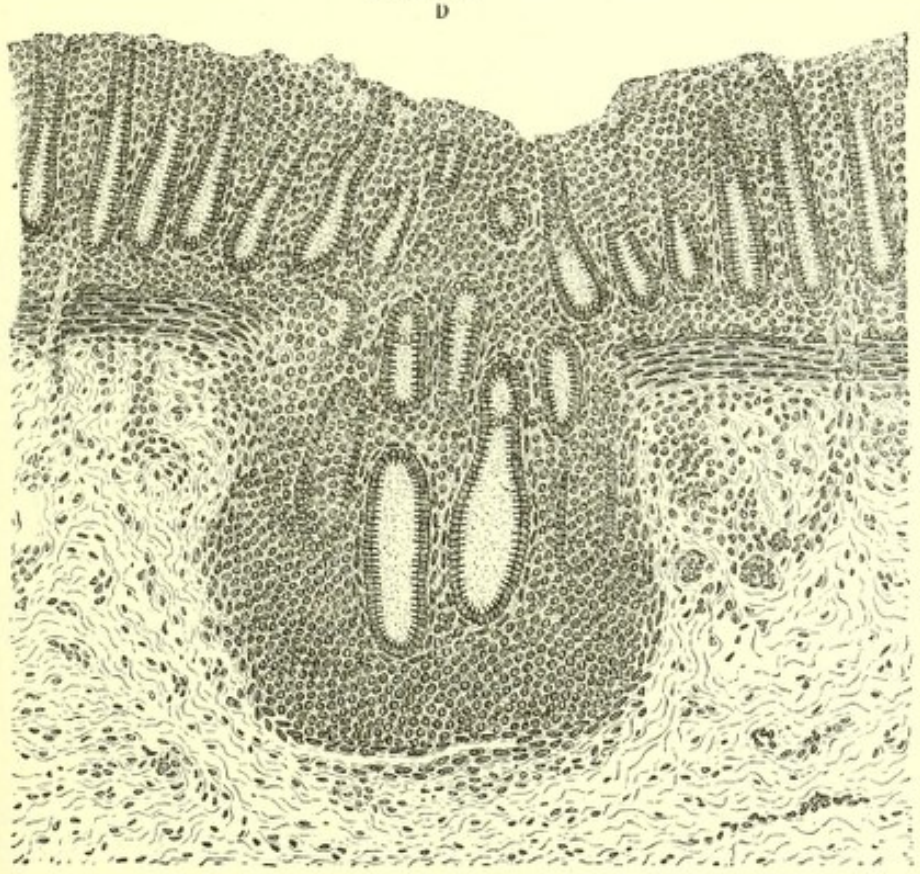
An ulcer starting in the mucous membrane may penetrate the other coats, and extend into the inflammatory tissue which forms the adhesions. It is thus that iliac abscesses are sometimes formed. So also fistulæ may be established, which may or may not communicate with the cæcum.

Inflammation of the large intestine is rarely observed in its whole length. It most frequently originates at the sigmoid flexure or in the rectum. Proctitis or inflammation of the rectum is primary in sporadic or epidemic dysentery, and is then accompanied by ulceration. It often follows hæmorrhoids (hæmorrhoidal catarrhal flux), foreign bodies arrested in the folds of the mucous membrane, syphilitic disease of the anus or rectum, fistula in ano, mucous patches, ulcerations of tertiary syphilis. In cases of cancer of the uterus, even when the walls of the rectum are not invaded by the neoplasm, there is usually an inflammation of the neighboring parts which excites an intense catarrh of the mucous membrane of the rectum.

DYSENTERY.—Dysentery is an ulcerative inflammation of the large intestine. Its favorite seat is the rectum and sigmoid flexure. When it is very intense the lesions ascend and spread throughout the large intestine. The varieties of this affection do not differ much anatomically; they mainly vary in their course and intensity.

ACUTE DYSENTERY.—In the mild form of acute dysentery the surface of the mucous membrane is very red and much congested, and there are small ecchymoses. The lesion which exists throughout the whole extent of the rectum and the neighboring parts of the sigmoid flexure, is particularly marked upon the salient folds of the mucous membrane. The mucous membrane is thickened, and the lymph follicles form a relief

Fig. 266.



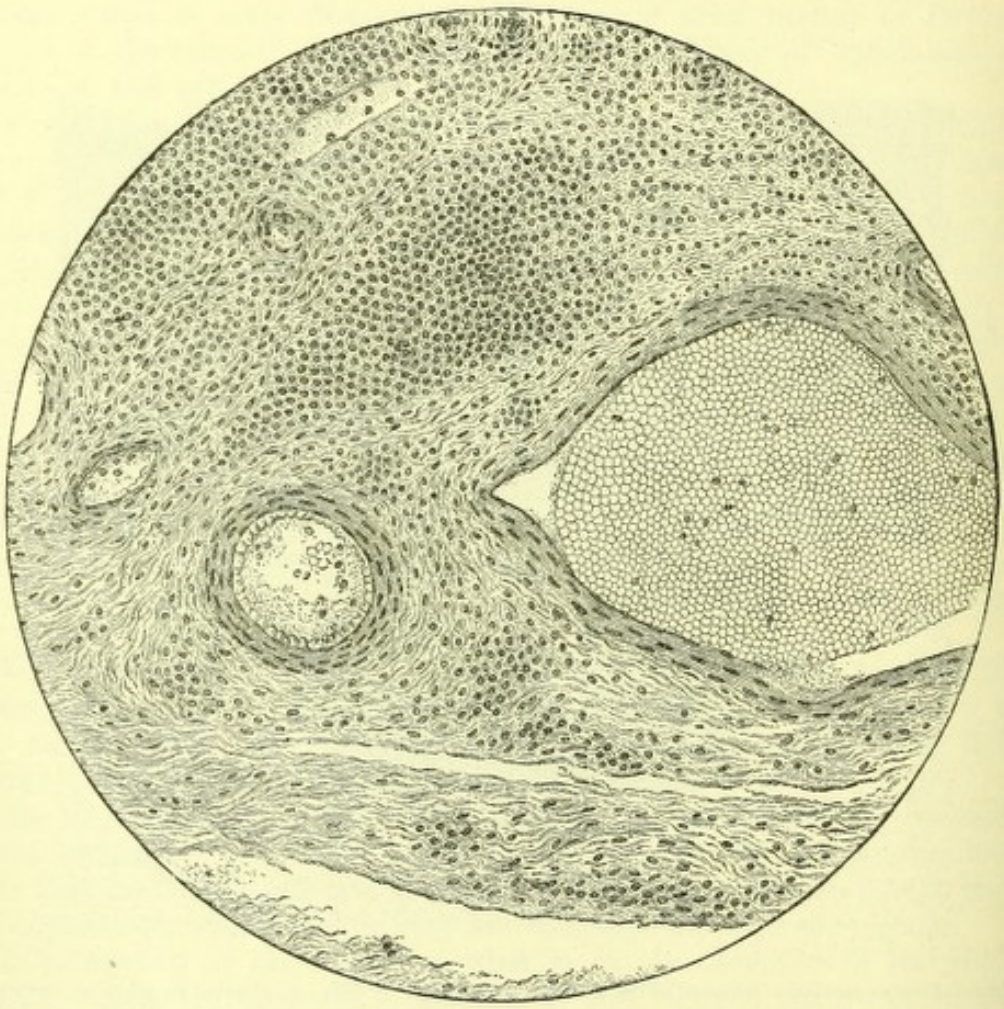
. Perpendicular section of colon of child, cut longitudinally. × 110. A. Mucous membrane, showing the glands of Lieberkühn pushed apart by the swarm of lymphoid cells in the adenoid tissue. B. Muscle of Brücke. C. Submucous connective tissue, with numerous lymphoid elements near the muscle of Brücke. In the centre of the piece (between D and D) is an enlarged solitary follicle, in which several cystic forms appear. The slit-like fissure just below the enlarged gland is a lymph sinus. (From a photo-micrograph by Surgeon J. J. Woodward, U. S. Army, copied from the second Medical volume of the Medical and Surgical History of the War of the Rebellion.)

upon the surface. It is covered by a slight mucous exudation which resembles the white of an egg, or is puriform in spots; this mucous is usually streaked with blood, or colored uniformly red by the latter fluid. This exudation is frequently passed in the stools accompanied by tenesmus and burning of the anus; it constitutes the characteristic sign of dysen-

tery. At the end of a few days small vertical walled ulcers already exist, or there are irregular and shallow losses of substance. These losses of substance are filled with a transparent or cloudy mucus, and have the appearance of being deeper than they really are, by reason of the granulation and thickening of the surrounding mucous membrane. These lesions are very limited in the simple form of dysentery. Microscopic examination of the swollen portions of the mucous membrane shows the following conditions:—

1st. In the glandular layer the turgid vessels are surrounded by connective tissue, infiltrated with lymph corpuscles, and the interglandular

Fig. 267.



Portion of perpendicular section through the submucous connective tissue of the colon in a case of dysentery. × 175. The nearly circular vessel to the left and below the centre of the field is a small artery. The larger elliptical form to the right is a vein. Several smaller vessels are cut across in other parts of the field. The connective tissue throughout is infiltrated with lymphoid elements. (From a photo-micrograph by Surgeon J. J. Woodward, U. S. Army. Copied from the second medical volume of the Medical and Surgical History of the War of the Rebellion.)

septa are increased in length, as well as in thickness, by this inflammation. The glands of Lieberkühn undergo an elongation or a compression with alternating dilatations and contractions, as in the stomach. The epithelium of the glands is preserved *in situ*, and the cells are generally

hypertrophied and cup-shaped. With respect to the surface epithelium, it is useless to look for it twenty-four hours after death, but we may be sure that it is in a state of partial desquamation during life, for it is found in the stools at the commencement of the dysentery.

2d. Around the vessels, in the superficial layer of connective tissue located immediately beneath the glands of Lieberkühn, where the vessels form the plexus from whence the capillaries arise, the lymphoid cells are extremely numerous. (See Fig. 267.) There is an inflammatory infiltration accompanied by thickening of the connective tissue beneath the glands and around the closed follicles. The latter are also swollen and filled with lymph corpuscles, and they project upon the surface of the mucous membrane. They soften and break down in the centre, and their destruction is followed by a follicular ulcer.

In those points where the very abundant inflammatory exudation—consisting of lymphoid cells and a fluid containing fibrin—infiltrates the connective tissue to the point of compressing the bloodvessels, there is produced a genuine mortification of the tissue supplied by vessels.

This is precisely what happens in the layer of connective tissue subjacent to the glands of Lieberkühn and around the follicles. These more or less extended lamellæ of the glandular layer are detached by the suppuration which takes place beneath them, and are thrown off in larger or smaller fragments, which are found in the evacuations.

When the mortification affects a portion of the glandular layer, there results an ulcer whose flat irregular bottom is generally seated at the summit of the fold of the membrane. When the slough affects a lymph follicle and the surrounding tissue, a small circular ulcer follows its elimination.

Ulcers once formed may continue to extend by suppuration of the adjoining infiltrated tissue, and, even when circumscribed, their surface secretes pus during the whole time that the dysentery remains in the acute stage.

This stage may end in repair of the loss of substance, by granulation, cicatrization, and its results, or it may pass to the chronic stage.

Such is the slightest form of the disease, which, in certain cases, is very limited.

Intense acute dysentery exhibits the same general phenomena; but the morbid process is much more active, and the lesions are much more general and extensive, involving the greater part or the whole of the large intestine. At the autopsy of patients who have succumbed during the acute stage of an intense dysentery, the ulcers are deeper, much more extensive, and are scattered over almost the whole surface of the large intestine from the cæcum to the anus. The surface of the ulcers is covered by a débris of the superficial layer of the mucous membrane, infiltrated with pus, and not yet detached; or it is granulating, and red-brown or slate color from the decomposition of putrid blood. The walls of the ulcers are sharp cut, and are bordered by swollen, very congested, ecchymotic, softened mucous membrane. The ulcers may be so extensive that there remain only islands of undestroyed mucous membrane.

In the preserved portions of mucous membrane the glands of Lieber-

kühn are found with their lining of cylindrical cells; but these glands are irregular and deformed, compressed here, distended there. The bloodvessels which surround them are enormous and are gorged with blood. Around them, the connective tissue contains masses of lymph corpuscles and filaments of coagulated fibrin.

The subglandular connective tissue, which forms the bottom of these ulcers, throughout its whole thickness is infiltrated by an inflammatory exudation composed of round cells and fibrin; the bloodvessels are distended with blood, and their walls are in an embryonal condition. The lymph vessels are filled by very large and swollen endothelial cells (Kelsch). All the layers of the submucous cellular tissue are altered to such an extent that we have a genuine phlegmon below the glandular layer. The connective tissue is double or triple its usual thickness, and its most superficial portion beneath the glands is in places transformed into lacunæ of pus, which isolate the glandular layer and render its destruction inevitable. Thus it is not very rare to see patients evacuate, with the stools, considerable fragments of the mucous membrane, either in flakes or in cylinders which may even reach more than a foot in length.

It would seem almost unnecessary to add that those cases of dysentery in which the lesions are so extensive and so profound terminate fatally, by asthenia, or more rarely by perforation of the intestine and peritonitis, or by hepatic abscess.

An *examination of the stools* in acute dysentery is an indispensable complement of the foregoing study relative to the state of the intestine. At the beginning, they are constituted by a small quantity of glairy, gelatinous substance, lumpy or resembling mucous sputa. This mucus has been compared to the spawn of a frog. It is often colored with blood, either evenly or in streaks. Microscopic examination shows in it lymph corpuscles, red blood disks, cylindrical cells, mucous corpuscles, and numbers of infusoria. Such appearances characterize the first period.

When ulceration commences, the evacuations consist of a serous fluid, colored red by the blood, in which float whitish membranous fragments, sometimes actual membranous cylinders, which are composed of the superficial layer of mortified mucous membrane. By a microscopic examination of these flakes or cylinders, we recognize in them fragments of the glands of Lieberkühn, or even series of these glands united together.

When the elimination of these fragments is terminated, the stools consist solely of an ichorous, puriform, or serous discharge of a gray, slate, or sanguineous color. This fluid, secreted from the surface of the ulcerations, contains a large quantity of lymph cells and red blood corpuscles.

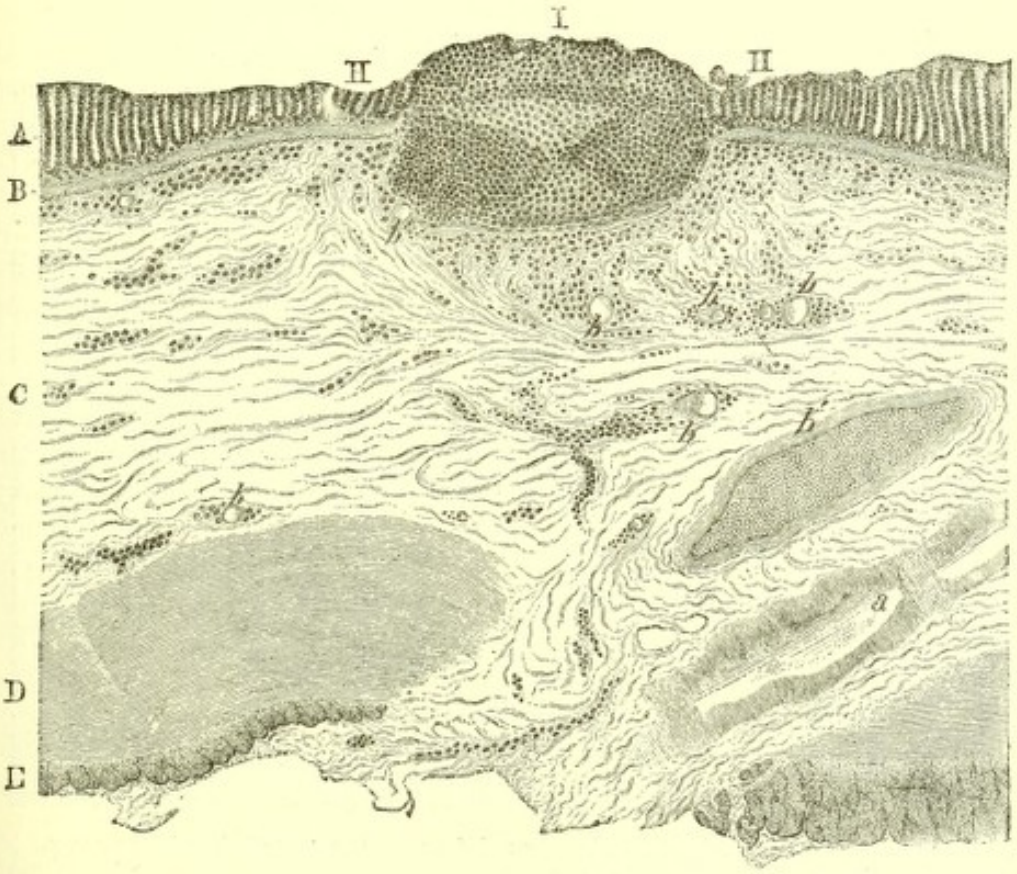
The other organs contained within the abdomen often suffer a secondary involvement: the *bladder* is generally congested, and may be the seat of an acute catarrh; the kidneys are sometimes attacked with catarrhal or interstitial nephritis; the lymph glands in the lumbar region are hyper-

trophied and congested; the spleen enlarged and softened; finally the liver is often affected by congestion and abscess (see Lesions of the Liver).

The small intestine not infrequently presents traces of a more or less intense catarrh, or it, as well as the stomach, may be atrophied from inanition.

CHRONIC DYSENTERY.—Chronic dysentery succeeds an acute dysentery, or the inflammation may follow a chronic course from the outstart. The chronic diarrhœas of warm countries which, by their progress and by certain symptomatic characters can be distinguished from chronic dysentery, do not differ from the latter in an anatomical point of view.

Fig. 268.



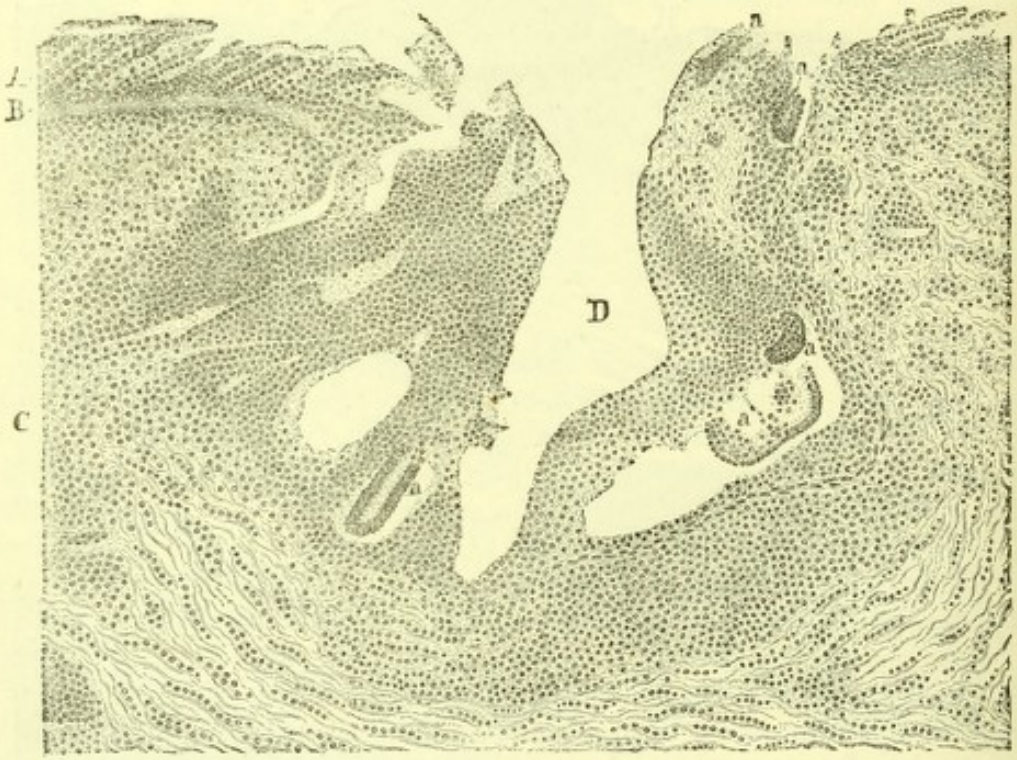
Perpendicular section of colon in case of chronic dysentery, showing a small superficial ulcer H, H, in the centre of which an intact solitary follicle, I, protrudes as a minute nipple-like elevation. Half diagrammatic. × 48. A. Mucous membrane. B. Muscle of Brücke. C. Submucous connective tissue; *b*. Small veins cut across. D. Circular. E. Longitudinal, muscular coats of the intestine; these are divided by the entrance of an artery, *a*, from the mesocolon which is accompanied by a vein of considerable size, and surrounded with connective tissue. (From a photo-micrograph by Surgeon J. J. Woodward, U. S. Army. Copied from the second medical volume of the Medical and Surgical History of the Rebellion.)

At the autopsy, the mucous membrane is found to be swollen in places and congested, very red especially in those parts which border depressions simulating ulceration at first sight. At certain points, in reality, where the naked eye receives the impression of genuine losses of substance, we find the glands of Lieberkühn preserved and a simple prominence of neighboring parts or a granulation of the cellular tissue which

separates the glands. In other cases there is an actual loss of substance by ulceration. These ulcers compromise only a part of the glandular layer, or they penetrate as far as the subjacent cellular tissue. The surface of these ulcers is brown or slate colored, and upon it we recognize by the naked eye more or less regular openings which lead into the follicular depressions which are more deeply seated in the midst of the same submucous connective tissue. From these minute cavities a concrete mucus similar in appearance to frog spawn may be squeezed out by pressure.

This gelatinous mucus when freshly examined shows cylindrical cells, mainly cup-shaped, disposed around the periphery of the mass. The centre of the semifluid mass contains fusiform, elongated, ovoid, or spherical cells which have undergone a colloid metamorphosis. When treated

Fig. 269.



Perpendicular section through a follicular ulcer of the colon in a case of chronic dysentery. × 57. A. Mucous membrane, its surface partly destroyed by ulceration. B. Muscle of Brücke. C. Submucous connective tissue much infiltrated with lymphoid cells. D. Cavity of follicular ulcer; *a*. Glandular and cystic forms derived from the glands of Lieberkühn. (From a photo-micrograph by Surgeon J. J. Woodward, U. S. Army. Copied from the second medical volume of the Medical and Surgical History of the War of the Rebellion.)

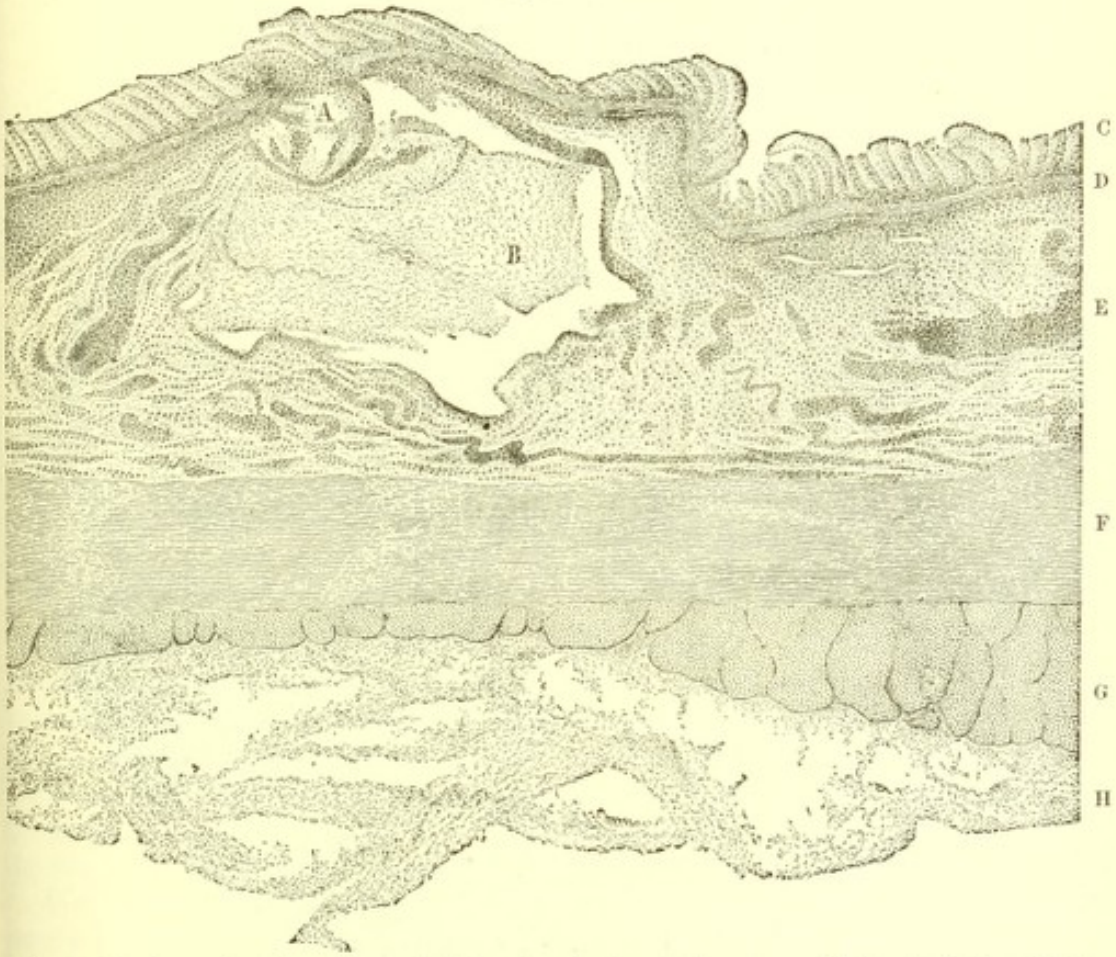
by nitric or acetic acid the mucus gives an opaque precipitate. A thin section comprising at the same time the edge of the ulcers, the ulcers themselves, and the cavities filled with mucus, presents the following appearances:—

1st. In the congested, swollen, and œdematous parts of the mucous membrane which separate the ulcers, the glands of Lieberkühn are very long and wide; they are separated by connective tissue permeated by vessels distended with blood. Below the glandular layer, the superficial muscular layer is normal, and the connective tissue is simply hyperæmic,

while its cells are larger than in the normal state. The sections of follicles present an elliptical or circular outline.

2d. In the ulcers, there are only vestiges of the tubular glands: only the lower third of the gland remains, and in some places the glands are entirely absent. Their remaining culs-de-sac contain cylindrical cells. They are separated from each other by connective tissue infiltrated with lymph corpuscles, and below them the subglandular tissue is equally rich in cells. There is an appearance as if in the ulcerated portion the superficial layer of the mucous membrane has been cut away, while the interglandular connective tissue has been destroyed at the same time.

Fig. 270.

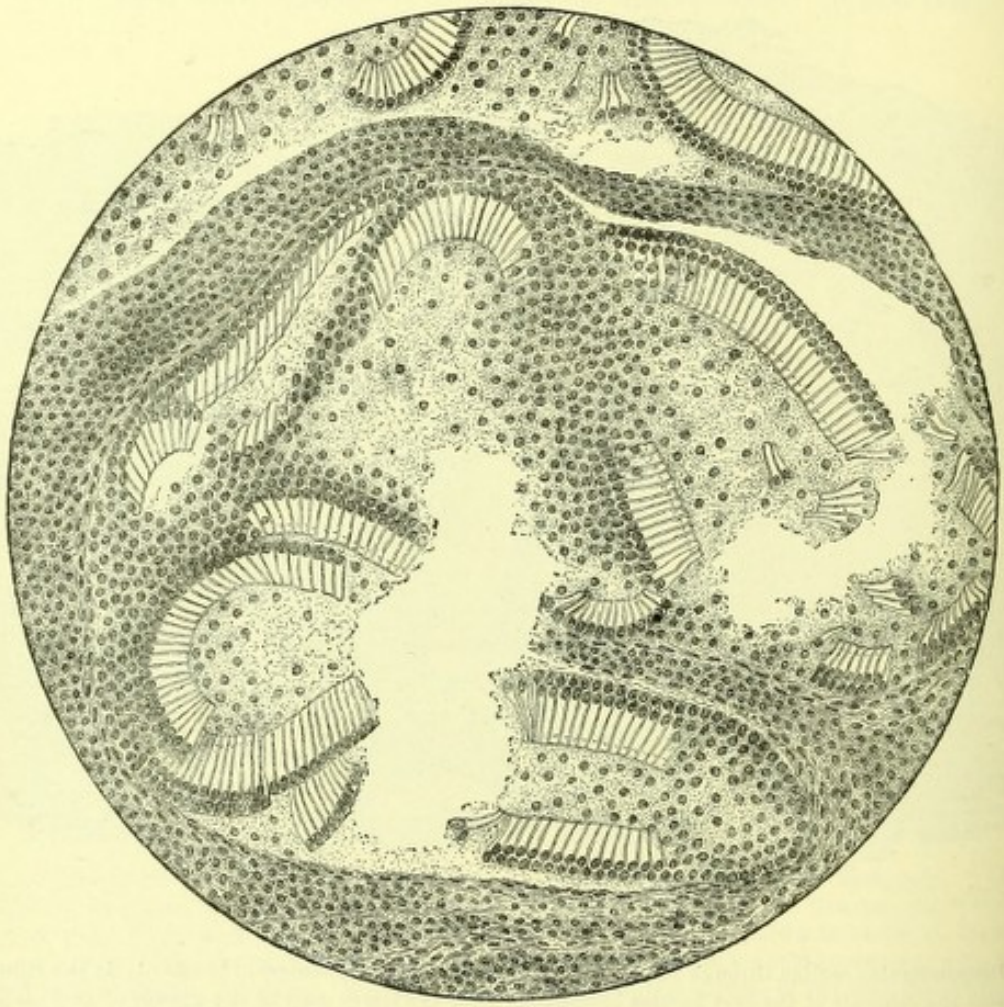


Perpendicular section through a cyst of the colon, in chronic dysentery. × 25. A. Is the point at which the contents of the cyst become continuous with the lower part of the glands of Lieberkühn. B. Glue-like mass filling the greater part of the cyst; the action of alcohol in many places caused it to shrink away from the cyst walls. C. Mucosa. D. Muscle of Brücke. E. Submucous connective tissue infiltrated, especially in the neighborhood of the muscle of Brücke and in the course of the venous radicles, with swarms of lymphoid cells. F. Circular muscular coat of the colon G. Longitudinal muscular coat. H. Subperitoneal connective tissue. (From a photo-micrograph by Surgeon J. J. Woodward, U. S. Army. Copied from the second medical volume of the Medical and Surgical History of the Rebellion.)

3d. There always open on the surface of the ulcer, follicular depressions or losses of substance visible to the naked eye and filled with mucus. They open by an orifice which is often very narrow and irregular. The muscular layer of the mucous membrane is penetrated by their neck, but

otherwise it can be traced above the small cavity, and between it and the mucous surface. There may be a single cavity or there may be several placed together so as to be either entirely or only partially separated by tracts of fibrous tissue. These cavities are filled with mucus which is bounded at the periphery by a layer of cylindrical cells. The contents are readily detached from the fibrous wall. The mucus may retract and form a knob attached near the neck of the follicular cavity, it may then swell up and raise the surface of the mucous membrane. At first sight, this coagulated mucus, with its folds, its depressions, and its elevations, resembles a racemose gland.

Fig. 271.

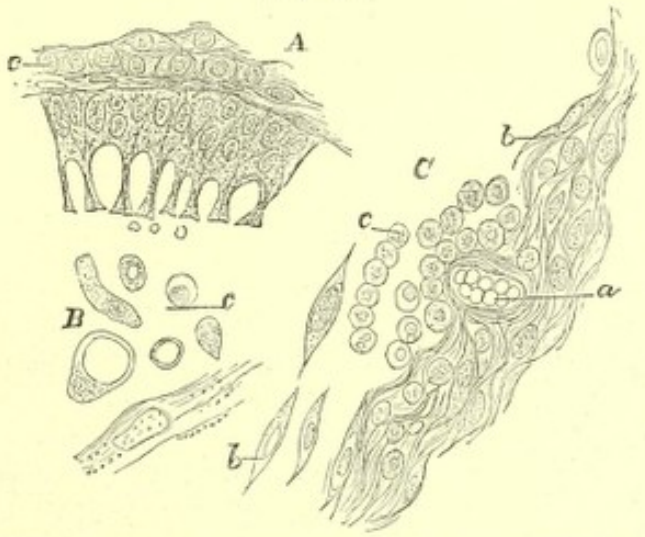


View of part of region marked A in Fig. 270, showing dilated and distorted gland tubules lined by a columnar epithelium similar to that of the glands of Lieberkühn. × 200. The space between the gland tubules is filled with a granular tissue densely infiltrated with lymphoid cells. The delicate granular substance in the interior of the dilated tubules, in which lymphoid elements are less numerously scattered, closely resembles the substance which fills the greater part of the cyst. (From a photo-micrograph by Surgeon J. J. Woodward, U. S. Army. Copied from the second medical volume of the Medical and Surgical History of the War of the Rebellion.)

The wall of the above cavities is formed of connective tissue, between the fibres of which are to be found white corpuscles and swollen flat cells. It is paved with cylindrical cells which form a lining sometimes entire, at other times incomplete. These cylindrical cells are almost

all cup-shaped (see fig. 272). In those cavities where they exist only on a part of the wall, they are seen only at the superior part, nearest the surface of the membrane. In those parts of the wall where the cylindrical cells are wanting, the connective tissue is very abundantly infiltrated with white corpuscles, and there is an intense destructive inflammation which prevents the investing epithelium from reattaching itself (see C, fig. 272).

Fig. 272.



Histological elements of the wall of cystic cavities in chronic dysentery. ×400. A. Goblet-shaped cylindrical cells lining the wall of a cyst. *c*. Embryonic cells of the connective tissue limiting the cavity.

C. Portion of a wall of a cyst from which its cylindrical cells have been detached. *c*. Embryonic cells floating free in the mucous contents. *d*. Free flat cells. *a*. Bloodvessel filled with red corpuscles.

B. Vesicular cells of the mucous contents.

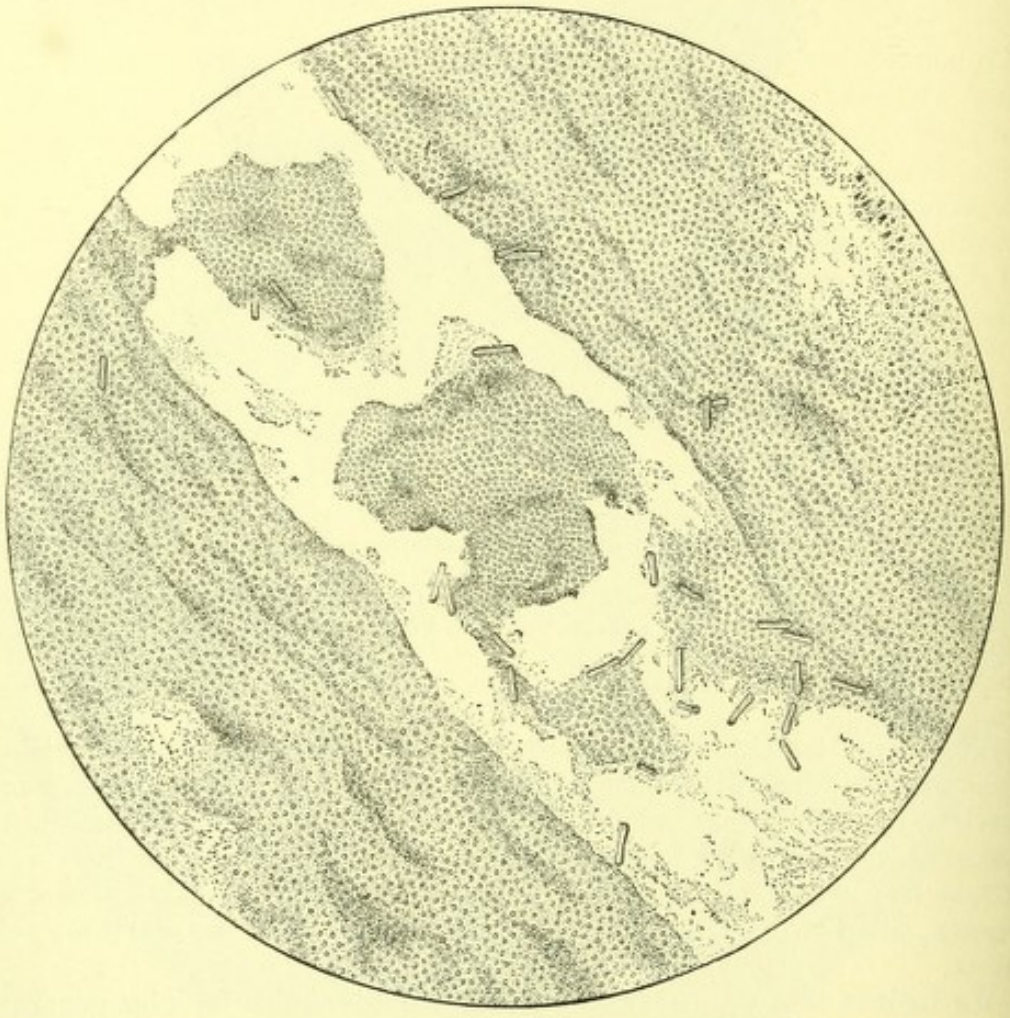
A more or less extensive zone of the connective tissue which surrounds these cavities filled with mucus, is infiltrated with lymph cells or pus corpuscles. Opposite these cavities the glandular tubes have usually disappeared, or they have been reduced to their culs-de-sac, or they have become hypertrophied and dilated in such a way that their inferior extremity, filled with cylindrical cells, has divided into two or three culs-de-sac.

We believe that the previously described glandular follicles generally occupy the place of the destroyed closed follicles. They have the same location, the same relations with the glandular layers and the superficial muscular layer, and the same form as the closed follicles. Moreover, we have seen in our histological preparations closed follicles in process of softening and destruction. When a section of one of these softening follicles has been pencilled and the lymph corpuscles which fill the reticulum have been brushed away, we see that the reticulum is absent in points and that there are large spaces bounded by areas of the reticulum. Should these softened portions of the follicles break open and communicate with the surface, we would have the cavities which have already been described; cavities which would soon be filled by the intestinal mucus and paved by the cylindrical epithelium of the surface, or of the adjoining mucous glands.

Once formed, the follicular cavities enlarge by the destruction of the septa; they may reach a diameter of 4 or 5 mm.

The submucous connective tissue is thickened at the same time; it is fibrous and contains lymph vessels filled with swollen endothelia (Kelcsh). The inflammation is frequently propagated to the connective tissue which separates the muscular layers of the intestine, and it may extend as far as the subserous tissue.

Fig. 273.



Portion of perpendicular section through the eschar in a case of diphtheritic dysentery. ×950. The field is crossed obliquely by a cavity (the former site of one of the glands of Lieberkühn) in which are several micrococcous groups and a number of rod-like forms. The rest of the field is occupied with micrococcus, with a few rod-like elements near the edges of the central cavity. (From a photo-micrograph by Surgeon J. J. Woodward, U. S. Army. Copied from the second medical volume of the Medical and Surgical History of the War of the Rebellion.)

This fibrous thickening of all the layers of the large intestine is the explanation of an apparent hypertrophy of the muscular tissue, and leads to the transformation of the intestinal canal, especially in its lower portion, into a tube with nearly rigid walls.

This condition is met with especially in cases of chronic dysentery, with extensive ulcerations which have been healed and replaced by a dense and solid cicatricial tissue.

Upon these cicatrices, where the mucous membrane has never entirely re-formed, polypous excrescences are often found, consisting of fibrous tissue or of a fibro-mucous structure.

The evacuations observed during the course of these diarrhœas and chronic dysenteries are very variable. When there exists an acute condition, they become mucous and contain blood or a little pus; ordinarily they are serous, abundant, and of a yellow, green, or brown color. The diarrhœa is not always constant during the whole course of the disease; it may be temporarily suspended.

CHOLERA.—Cholera, an infectious disease in which the most of the organs are altered, has for its first manifestation the signs of an intestinal catarrh which correspond to a pathological state of the small intestine. This is why the pathological anatomy of this disease has its place in the chapter on the intestines.

At the autopsy of patients who succumb in the stage of cyanosis, we find the small intestine very much congested throughout its length, but particularly in the ileum. The mucous membrane presents a pink, lilac, or red color. On account of the fulness of the capillaries and small veins, the summits of the folds are especially colored. The mucous membrane is thickened, turgid, and œdematous; the intestine is distended by a large quantity of a whitish, cloudy, odorless fluid, in which are suspended small opaque flakes (rice bodies).

The epithelial coverings of the villi and of the mucous membrane desquamate after death, but an examination of the stools during life does not indicate that there is an abundant loss of the epithelium during the choleraic attack. The cloudiness of the fluid is due not only to lymph cells, but more particularly to the presence, in large numbers, of proto-organisms like those met with in putrefying fluids.

Hayem and Raynaud, in the last epidemic of cholera (1863), verified the observations made by Pacini, Davaine, etc., of the presence of infusoria in large quantity in the stools of cholera, but without finding, among the ten varieties at least which were present, any which are special to cholera. There were varieties of three kinds: bacterium, vibrio, bacteridium (Davaine).

We find besides collections of spores in great numbers, of themselves alone forming the greatest part of the whitish flakes; they probably correspond to the *micrococcus* of German authors, and do not apparently differ from yeast. All these proto-organisms exist in the stools from the first.

The specific gravity of the stools, compared with that of the intestinal fluid obtained by the process of Thiry, is very low; it runs from 1.004, 1.006, up to 1.013 in certain cases.

Chemical analysis shows that organic matter is not very abundant (Becquerel). We find urea or its decomposition product, carbonate of ammonia; it is this which renders the fluid alkaline. The proportion of the alkaline chlorides and salts is sensibly the same as in health. The choleraic stools approach very closely, in chemical analysis, to the fluid obtained by A. Moreau in the experiments above cited.

Very rapidly after the onset of cholera and the commencement of the

algid period, the closed follicles of the mucous membrane of the small intestine, especially those of the lower portion of the ileum, are swollen and look like small pearly grains of a reddish-gray or gray color.

The alterations of the mucous membrane and of the submucous connective tissue, studied under the microscope, are much more profound and more intense than the naked eye would lead us to suppose.

They were described by Kelsch and Renaut in the epidemic of 1873. The connective tissue of the mucous membrane is very thickly infiltrated with lymph cells, while the connective-tissue fibres are quite distinct. This new formation takes place in the interglandular and subjacent connective tissue; it is not limited to the small intestine, but may extend the whole length of the intestinal canal from the pylorus to the anus; it exists also in a variable amount in the intestinal villi. The glands of Lieberkühn usually show epithelium only in the lower part of their culs-de-sac (in part a post-mortem change), and they are often distended by mucus. The bloodvessels which exist in the superficial part of the mucous membrane are distended with blood, and their walls are in an embryonal condition. The same is remarked of the vessels of the submucous tissue.

The lymphatics are filled by round cells or by their swollen endothelium, which is desquamated.

The closed follicles present the lesions already described *à propos* of "psorentérie:" their centre has some tendency to soften, and their cellular elements are fatty degenerated.

The muscular tunic is normal, but the subserous connective tissue is hyperæmic and is infiltrated by lymph corpuscles. There may even be an irritation of the serous covering which shows itself by thin false fibrinous membranes exuded upon the surface.

In a more advanced stage of the lesion, when the autopsy is made during the period of revulsion, we sometimes find follicular ulcers situated at the location of the isolated follicles or at the seat of Peyer's patches. The mucous membrane is less congested, except that at certain points a persistent hyperæmia is observed, and sometimes upon the top of the folds of the small intestine there are even superficial ulcers. These ulcerations may involve the deeper tissues to the extent of perforation (Hamernyck). In other cases the intestine is thinned and atrophied.

The physical characters of the intestinal contents are entirely different from those observed in the first stage. There is no longer a rice-water fluid, as in the first period; the intestinal fluid is colored by bile; often it is strongly tinged by blood. The large intestine contains solid matter or a diarrhœic fluid.

Alterations of the blood are noted in a very high degree during the first or algid stage. The blood, from loss of serum, has become so thick that it does not circulate freely or does not flow at all. From this loss of serum it results that the number of red blood globules is relatively much increased, and the white corpuscles are increased in the same proportion. The red disks are viscous; a large number of them present a volume much less than normal. There do not appear to be any protoorganisms peculiar to the blood of cholera.

This viscosity of the blood in the algid stage appears to be the prin-

cipal cause of the disorder of the kidney, consisting essentially in the diminution or even the suppression of the secretion of urine. The urine contains albumen and casts, and the cells of the tubuli are granular (see Lesion of the Kidney). The cells of the liver suffer a similar alteration.

When reaction is established the serum gradually returns to its normal quantity, and the number of the blood corpuscles in a given volume rapidly diminishes. The deep color of the urine causes the supposition that a large number of the red disks has been destroyed. At this time the blood always contains an abnormal quantity of urea or carbonate of ammonia.

It is during this period that we observe the multiple lesions of the different organs, which are, in part, under the influence of uræmia. Such are pulmonary congestions, bronchitis, laryngitis, pleurisy (sometimes purulent), œdema, congestion, and ecchymosis of the pia mater; and, in rare cases, suppuration of the parotid, cystitis, pyelonephritis, etc.

Uræmic Ulcerations.—There are developed in the large intestine, very rarely in the lower part of the small intestine, ulcerations described by Treitz as related to uræmia. They are preceded by a catarrh and by liquid stools which are alkaline, and contain a large amount of carbonate of ammonia. At the commencement of ulceration, the stools contain a little blood and débris of the mucous membrane. These ulcers follow a mortification of portions of the mucous membrane and the expulsion of the sloughs. It is a species of gangrenous dysentery in which the intestinal mucous membrane is neither materially thickened nor congested. These ulcers which originate in the closed follicles and their surrounding tissue may spread until they reach a diameter of several centimetres. Their long axis is generally parallel with that of the intestine, and they vary in number. They may heal and leave superficial cicatrices, slate colored and smooth upon the surface.

Typhoid Fever.—The intestinal lesions of typhoid fever are located in the lower part of the small intestine; it is seldom that they involve the large intestine. Four stages may be recognized: 1st, the catarrhal period; 2d, the period of swelling and ulceration of Peyer's patches; 3d, the period of abatement; 4th, the period of cicatrization. These four periods correspond more or less closely to the four weeks during which a typhoid fever of medium intensity lasts.

1st. In the first period, which usually lasts four or five days, the mucous membrane is congested, and it secretes a greater or less quantity of diarrhœal fluid; the closed follicles, both the isolated and the agminated, especially those of the lower part of the ileum, are swollen from the beginning. The isolated follicles form small, pinkish, semitransparent, pearly prominences; the Peyer's patches are tumefied, and form slight elevations.

2d. In the second period the hypertrophy of the follicles and of the Peyer's patches increases. At autopsies made on the fifth or sixth day of the disease, we have seen the isolated follicles looking like hard, prominent, conical nodules, from 3 to 4 millimetres in height, while the Peyer's patches were similarly thickened.

During the second week the Peyer's patches nearest the cæcum, that is to say, those which are first affected and now most altered, already begin to ulcerate in one or two points of the same patch, while higher up in the ileum these patches are not yet ulcerated. Upon cutting through an isolated follicle with a scalpel, we see that its tissue is whitish, gray, or slightly pink, of a soft consistence, and is similar to the tissue of lymphatic glands. It yields a cloudy fluid by scraping. To the naked eye there is no sharp limit between the follicle and the surrounding tissue, an appearance which suggests a pathological infiltration both of the follicle and of the adenoid tissue which surrounds it. The follicles of Peyer's patches present similar appearances.

The number of altered patches varies from two or three in the neighborhood of the ileo-cæcal valve to twenty, to fifty, extending up the intestine. In those cases where the lesion is most intense the patch is hypertrophied throughout, and is very much thickened. It may form an elevation of 2–3 millimetres, sometimes even more (hard patches of Louis). When the lesion is less intense the closed follicles do not form so great a relief; the patches then have only a small number of their follicles diseased, and the patch is not swollen over its whole surface (soft patches of Louis).

The hard patches and the very prominent follicles are the most favorable for microscopic examination.

At autopsies made twenty-four hours after death, the cylindrical cells of the surface have been macerated into an opaque, puriform fluid which covers the surface of the mucous membrane. By scraping the cut surface of one of these swollen patches, we obtain small fragments which after treatment with picro-carmine, show a large number of lymph cells, some containing a single nucleus, others several smaller nuclei. There also are to be found in these scrapings numbers of large, swollen, spherical or polygonal or flat cells, with a granular protoplasm, and one, two, or three ovoid nuclei. These large cells are nothing else than the swollen and inflamed endothelial cells of the reticulated tissue of the mucous membrane and of the lymph follicles. These elements are similar to those observed in the leukæmic products of the spleen, and in lymph-adenomata.

These cells, which have been called typhus cells, and regarded as special to typhoid fever, have no really characteristic features.

Thin sections through the now ulcerated patches offer the following details:—

(*a*) The villi, instead of being lengthened and distinctly separated from each other, are increased in width, at the same time that they appear shorter, and have the tendency to fuse together at their bases. This modification of form is due to the fact that the tissue of the villi is infiltrated by small round cells or lymph corpuscles. The fusion of the villi is such that the surface of the patches examined under the microscope appears to be slightly undulated, while to the naked eye it appears altogether smooth.

(*b*) The tubular glands are increased in length and width, as we pass from the normal parts of the mucous membrane over upon the surface of the patches.

On the mucous membrane in the neighborhood of the Peyer's patches, the villi are very distinct and the growth is small. On that covering the patches, the villi are fused together by a mass of embryonal tissue, and they are scarcely separated even at their extremities; the glands of Lieberkühn have double or triple their usual length, and their transverse diameter is increased in the same proportion.

The cylindrical epithelium of the hypertrophied glands is longer than normal. The lumen of the glands contains free round cells, or deformed cylindrical cells.

The inter-glandular and subjacent connective tissue is infiltrated by small round cells: the tissue of the villi is altered in the same manner.

These lesions of the villi and of the glands are the same, whether they are seated in the Peyer's patches or located around the isolated follicles.

(*c*) The profound layer of the mucous membrane, which forms the greatest part of the hardened patch, at first presents a homogeneous appearance. It is penetrated by bloodvessels which are much distended with red and white blood corpuscles, the latter in much greater numbers than normal, and the adenoid tissue which surrounds the follicles is infiltrated with embryonal elements. These embryonal cells are disposed in concentric circles around the vessels.

Such is the structure of the hypertrophied patches in typhoid fever; we see that it consists essentially of a proliferation of the adenoid tissue (villi, closed follicles, and deep adenoid tissue) and of the connective tissue of the mucous membrane, while the tubular glands upon the surface are at the same time hypertrophied. This lesion of the glands of Lieberkühn appears to us simply secondary to alterations of the connective tissue which surrounds them.

During this second period of the disease, the ulceration always begins in the patches and follicles nearest to the ileo-cæcal valve.

In the hard patches it is easy with the naked eye to see the process of ulceration by mortification of a more or less extensive portion of an isolated follicle or a Peyer's patch. It is the most elevated part of the follicle or Peyer's patch which first mortifies and assumes a yellowish tint, due to the imbibition of the intestinal fluid. The mortified part is soon cut off from the rest of the morbid tissue by a narrow border, then by a furrow, and it is subsequently eliminated in small fragments. Alongside of one of these small eschars, still *in situ*, others are seen which are almost completely expelled, leaving in their place an ulcer, the bottom of which is filled up little by little.

The hard patches successively present new points of sloughing, and a total ulceration is thus effected in small islands which are attacked one after another.

The isolated follicles present at the commencement of this ulcerative process a small slough upon their most prominent part. The slough is thrown off, and there results an ulcer which occupies solely the centre of the follicle and which progressively spreads by the invasion of the whole of the diseased tunic. These ulcers often have a great tendency to extend in depth, and notwithstanding that they have a small diameter they

may eat through the muscular walls and perforate the serous membrane.

The inflammation of the mucous membrane and of its cellular tissue is, in fact, propagated to a considerable depth, and we find an infiltration of lymph cells in the connective tissue which separates the two muscular layers and even in the subserous tissue.

The peritoneum opposite a hard patch is reddened; all the vessels, particularly the small veins, are dilated and filled with blood. Opposite patches in process of ulceration the serous membrane is sometimes thickened, and it presents gray or whitish opaque spots, slightly prominent, looking to the naked eye like tubercle granules.

The peritoneum may show a considerable infiltration, and upon the surface of the peritoneum opposite the ulcerations there may exist whitish spots visible to the naked eye, which consist of an agglomeration of embryonal cells imbedded in a fundamental amorphous substance. They are to be distinguished from tubercles because there are no distinct nodules, or points of caseous degeneration. This formation is covered by a layer of endothelial cells, and it seems to be due to a proliferation of the same cells.

It is certain that this cellular infiltration of all the tunics of the intestine, and the consequent softening and friability of the fibrous bundles are conditions which favor ulceration and cause the tendency to the invasion of deep parts and to perforation.

The soft patches and the hypertrophied follicles which accompany them, usually ulcerate in the same manner as the hard patches; only the eschars are less visible, and there is a disintegration and molecular elimination of the superficial parts sooner than the destruction en masse of the more extensive portion.

Partial resorption and removal of the neoplasm of the soft patches may be effected without a genuine ulceration. The fluid mixed with lymph corpuscles, which the previously swollen follicles contained, may be taken up by those blood and lymph vessels which remain permeable; and the follicles may thus become effaced in such a manner as to produce *reticulated patches* (Louis). Upon the surface of these patches the depressions correspond to the follicles atrophied in the foregoing manner, while the reticulum formed by the connective tissue still infiltrated with cells remains elevated. Upon thin sections of these reticulated patches, made during the period of repair of the ulcer, we find in the superficial layer villi and glands of Lieberkühn, the presence of which proves that there has been no ulcerative destruction. Not infrequently we may see one or more follicles transformed into a small abscess from which a drop of serous pus escapes when it is opened. Examining, under the microscope, a thin section through one of these follicular abscesses, it is seen that the pus has been removed by the handling; there exists in its place an empty space in the midst of the follicle. This space is bordered by débris of capillary vessels and fine meshes of reticulated tissue. The walls of these small follicular abscesses consist of a connective tissue the fibres of which are pale and granular, while the peripheral connective tissue contains rows of small cells (fig. 274).

3d. The third period, or third week of the fever, represents the pro-

gress of the ulceration of Peyer's patches which have cast off all the tissue thickly infiltrated with the round cells. The less altered tissue which forms the walls and the bottom of the ulcers is very much congested, and may present granulations. The embryonal state of the vessel walls predisposes to hemorrhages. This is, in fact, the period during

Fig. 274



Section through the periphery of a lymph follicle in a case of typhoid fever. The central portion is converted into an abscess. At the upper part of figure capillary vessels and free cells in the cavity of the abscess are seen. High power.

which profuse hemorrhages take place. It is rare that rupture of the vessels and hemorrhages are met with during the second week, yet they may possibly occur at the commencement of the elimination of the mortified parts.

4th. At the end of the third period, commences the process of repair which continues during the fourth week. At the borders of the ulcer there commences an irregular formation of granulative tissue, which little by little spreads over the ulcerated surface. As this tissue condenses the borders of the ulcer approach, and the cicatrix forms. But complete cicatrization is very slow; quite six weeks or two months or more from the beginning of the disease we still find small ulcerated places. During cicatrization the cicatricial tissue becomes pigmented almost constantly, and this pigmentation remains for years.

Microscopic examination of the cicatrices shows that all the tissue previously attacked by ulceration, that is to say, the whole surface of the mucous membrane of the patches, is replaced by a connective tissue with parallel longitudinal fibres which are separated by a large number of round cells interposed between them. There is here no vestige of the closed follicles, of the glands, or of the villi. The vessels remain dilated with embryonal walls, and are often surrounded with black pigment. If in the cicatrices we sometimes find the remains of a few villi or glands, it is because all the tissue of the mucous membrane had not been attacked by the lesion; in these cases, the patches have been only partially invaded.

The ulcers of typhoid fever do not give rise to constrictions of the intestine.

The *lymph glands* of the mesentery are constantly altered, and in the same manner as are the closed follicles of the intestine.

The *spleen* is always affected; it is hypertrophied, pink or red, most frequently pale, soft, and engorged with lymph corpuscles. The Mal-

pighian bodies, at one time visible, at another time invisible, are generally somewhat enlarged. (See Spleen.)

We have already seen that the *pharynx* and *larynx* are frequently altered in this disease. The *large intestine* is rarely affected; when it is invaded, its lesions, comparable to those of the small intestine, may be located in the cæcum, colon, or rectum.

The *liver* and *kidneys* are almost always the seat of an interstitial inflammation, which will be examined when these organs are studied.

The *muscles* very often, if not always, suffer a fatty or waxy degeneration. This is especially so of the muscles of the abdominal walls, and, on this account, they may sometimes rupture during quick movements in bed. (See Figs. 149, 151.)

The cardiac muscle does not escape. In consequence of this degeneration, which usually happens during the last period of the disease, the cardiac muscle is considerably weakened, and its contractions are intermittent.

We finally mention the hypostatic congestions and inflammations which may occur in most of the organs—the lungs, the brain and its envelopes, the spinal cord and its membranes, etc.

Such are the lesions of typhoid fever, of which the initial lesion is in the intestine. In the primary stages the lesions are congestive and inflammatory, whilst they are retrograde and accompanied by emaciation and anæmia in the later periods.

Lesions of the Intestine in Hernia.—In *inflamed hernia*, the sac may not contain fluid. Under other circumstances, it contains a serous fluid which is transparent, pink, or even dark-red and sanguinolent, and in which false membranes exist. The serous coat of the intestine is almost normal, or it is intensely red, as in acute peritonitis, when it presents a whitish opacity or false membranes and vascular papillæ. The study of the condition of the mucous membrane in such cases has not been thoroughly made, but it is probable that it also is attacked by a more or less intense inflammation. Small abscesses have been found between the intestinal tunics. If the hernia is not reduced, this inflammation of the sac and of the intestine terminates by fibrous adhesions between the two, and by thickening of the sac and of the coats of the intestine.

In *strangulated hernia*, the color of the serous surface of the intestine is of a darker red than in inflammation. It is ecchymotic, brown, approaching violet or black. The strangulated loop is tense, much larger than normal; later, when perforation or gangrene threatens, there may be collapse of the included gut.

The serous covering is stretched, and presents erosions at the seat of strangulation. The subserous cellular tissue is the seat of blood infiltrations and ecchymoses. Later, the serous membrane is covered by a fibrinous exudation, and the sac contains an inflammatory fluid which is colored by blood.

The contents of the strangulated loop consist of a somewhat abundant mucous fluid, often reddened by blood, or altogether hemorrhagic. Gas

may be present in small quantity, but there is very rarely any fecal matter. In fact, the fluid is such as is exuded during a very intense intestinal catarrh.

The mucous membrane is much congested from the beginning; very soon it presents the anatomical signs of a very intense inflammation involving all the structures. The much congested villi are swollen, softened, friable, and shortened; they may even be united together by a pseudo-membrane. The closed follicles, both isolated and agminated, are hypertrophied, infiltrated with fluid, and ulcerated at the centre.

These lesions are especially pronounced at the seat of strangulation, and particularly at the junction of the strangulated loop with the superior end of the intestine. The latter is distended with intestinal matter, especially by gas. The inflammation of the mucous membrane and of the serous covering spreads to the upper end of the gut, and, in certain cases, there results a general peritonitis. The lower end of the intestine is diminished in calibre, contracted, and it also is the seat of inflammatory lesions of the mucous membrane and serous coat which are less intense than upon the superior end of the gut.

When the constriction persists, the impediment or the arrest of the circulation at the point of compression determines a progressive destruction of the intestinal wall, which is effected by a sort of molecular elimination at the points of constriction. This destruction is secured without the gangrene extending beyond the solutions of continuity; the tunics appear as if they had been cut mechanically (Gosselin). The alteration begins at the superficial layer of the mucous membrane, and progressively invades the submucous tissue, the softened muscular tunics, and finally the serous membrane (Nicaise). Save in exceptional cases, section extends from within outwards. The perforation may be very small and difficult to see, or, on the contrary, it may involve the greater part of the circumference of the intestine.

Another termination of intestinal strangulation, much more rare than the preceding, is gangrene, which may appear in superficial spots, or which may affect at once all the coats of the intestine. The gangrene may be located at any point whatever of the strangulated loop.

The lesions of the intestine which are observed in strangulation of the ileum by bridles, by rings, by the accumulation of fecal matter, by invagination, etc., are, generally speaking, the same as those just described of hernia. A strangulation by invagination may terminate by the expulsion of the gangrened intestine, and a union, end to end, of the intestine; or it may end in perforation, peritonitis, pernicious adhesions, and almost always cicatricial contractions of the intestine.

Rectal Fistula.—The fistulæ which follow periproctitis, that is to say, inflammation of the connective tissue around the rectum, may be separated, according to their location, into two varieties: 1st. Those which are seated in the ischiatic fossæ or lower pelvi-rectal space, and which are consecutive to suppurative inflammation of the adipose tissue so abundant in this region. They are almost always complete, that is, they open at one end into the rectum below the levator recti muscle, whilst at the other end, after a more or less tortuous course,

they open upon the skin. 2d. Superior pelvi-rectal fistulæ are almost always external, that is, they open externally and not into the rectum (Pozzi). They habitually present a superior pouch or ampulla which secretes pus, and which is located above the levator recti. They follow a suppurative inflammation of the cellular tissue of this region; the ampulla which remains does not possess a free vent because of the muscle which is situated below it. These fistulæ always ascend very high up along the rectum, from which they are separated by indurated connective tissue.

These different varieties of fistula have a common characteristic in this, that they are chanelled out of connective tissue which is indurated by chronic inflammation. The fistulous channels, when they are recent, constitute irregular sinuses, bounded by suppurating granulations. When they are older the fistulous canals are lined by a mucous membrane with prominent cells, and more or less distinct papillæ which possess vascular loops, and a covering of stratified epithelium, exactly similar to that of the mucous membrane of the anus. These fistulæ are often present in intestinal tuberculosis.

Tuberculosis of the Intestine.—The tuberculous lesions of the intestine, like those of typhoid fever, have their preferred seat in the lower part of the small intestine, but they do not remain confined to that region; they generally extend over a wide extent of the ileum, the jejunum and larger intestine, including the rectum.

These lesions are characterized by tubercle granules and caseous and ulcerative inflammation of the isolated and agminated lymph follicles as well as by inflammation and destruction of the surrounding connective tissue. From the mucous membrane, which is their point of origin, they extend to the deep coats of the intestine, and involve the submucous connective tissue and the lymph vessels of the intestine, as well as those which lead from the intestine to the lymph glands of the mesentery.

We describe together the tubercle granules and the tuberculous inflammations of the closed follicles, because these two varieties of the same process are almost constantly seen associated with the tuberculous inflammations of the follicle, the latter sometimes even preceding the tubercles.

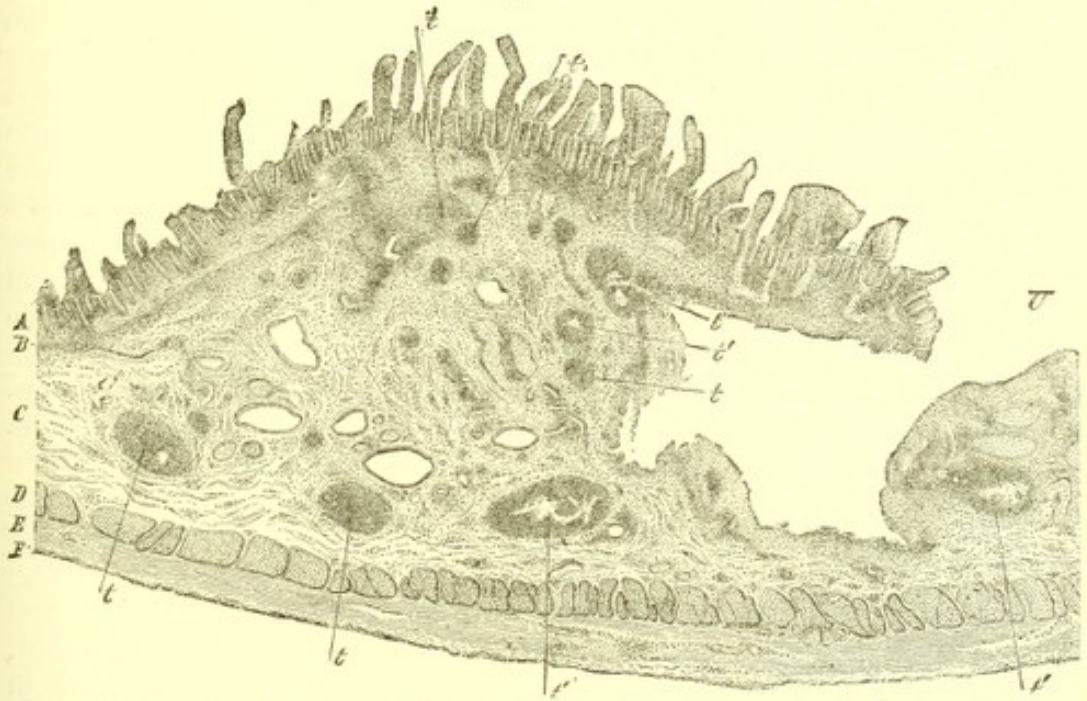
Tubercle granules of the mucous membrane of the intestine begin as small round semitransparent grains which project above the surface, and which may be located in the connective tissue around the culs-de-sac of the glands of Lieberkühn, or in the connective tissue of the villi.

When a thin section passing through such superficial tubercles is examined, we see two, three, or a greater number of villi, with small round cells filling their reticulated tissue. These villi are united together at the base, while they are still separated at their free extremity. They are thickened as well at their free extremity as in the points where they are fused together. From their union and their infiltration by small cells there results a solid excrescence of the superficial portion of the mucous membrane, having to the naked eye and under the microscope the form and the structure of a tuberculous nodule. The tubular glands, compressed and occluded by the neoplasm which surrounds them,

at first still preserve their normal cylindrical cells; they are bent and distorted, and can no longer freely empty their secretory products upon the surface of the mucous membrane. Later the centre of the tubercle granule becomes opaque and caseous, and its elements atrophy and become filled with fine granules. The cells of the tubular glands experience a similar kind of degeneration.

When the tubercle granule begins in the tissue below the tubular glands, the whole is covered by a layer of glands and villi. The latter are, as in the former case, the seat of a hypertrophy and an increase of their transverse diameter. The glands of Lieberkühn are elongated and filled with cylindrical cells, and the villi have the tendency to unite together and form granulation tissue. At the beginning, the special

Fig. 275.



Perpendicular section through a small tubercular ulcer of the ileum. ×15. *A*, mucous membrane, with its tubular glands pushed apart by an accumulation of lymphoid elements; its villi greatly hypertrophied. *B*, muscle of Brücke. *C*, submucous connective tissue infiltrated with lymphoid cells and containing a number of tubercles in various stages; its bloodvessels dilated. *D*, *E*, *F*, respectively the circular and longitudinal muscular coat of the intestine and peritoneum. *U*, cavity of the ulcer; *t*, unsoftened tubercles; the two letters below the lower edge point to tubercles in the centre of which peculiar oval forms are seen (lymph vessels cut across, giant cells). There are, besides, softened tubercles which are not lettered: *t'* tubercles with central softening, in which part of the cheesy mass has fallen out. *t''*, softened tubercles whose cavities form part of the ulcer. [From a photo-micrograph by Surgeon J. J. Woodward, U. S. Army. Copied from the second medical volume of the Medical and Surgical History of the War of the Rebellion.]

inflammations of the closed follicles in tuberculosis do not differ from simple "psorentérie;" but soon the follicle becomes more and more enlarged, and presents at its centre a whitish or yellowish opacity. The follicles thus hypertrophied are longer, less dense, and softer than the tubercle granules. Often, in picking them with the point of a needle, there exudes a little cloudy, whitish or yellowish fluid, holding in suspension granular lymph cells, and large spherical cells containing two or three nuclei and fatty granules. Examining thin sections of these little

tumors, we see that their periphery is more sharply separated from the surrounding tissue than is the case with tubercle, and we sometimes observe the contents of the follicle transformed into a small abscess.

These small follicular abscesses projecting into the lumen of the intestinal tube, possess on that side a thin wall, which readily ruptures, when, the contents discharging little by little, there results an ulcer which enlarges. Several altered follicles located at one time in a Peyer's patch, at another time in another point of the mucous membrane, and surrounded most frequently by a diffuse inflammation of the submucous connective tissue, and at the same time by an inflammation of the villi and glands, unite to form an elevated patch which soon ulcerates in one or more points where the follicles are most diseased. It is in this way that ulcers of the mucous membrane in tuberculosis are formed. When one examines with the microscope the edges of these ulcers, something of the same lesions of the villi and of the glands is seen as is met with at the surface of the swollen patches in typhoid fever. In reality the villi are partly effaced by the swelling of their apices and fusion of their bases. They are infiltrated with embryonal elements, and are transformed into large granulations which unite together. The glands of Lieberkühn are modified in form, in some places compressed, in others dilated, particularly in their culs-de-sac. They are filled with cylindrical cells which are generally larger than normal. Upon the border of some ulcers in full suppuration, we see villi transformed into large, very vascular granulations, separated from each other by deep depressions, the remains of tubular glands, lined by a well-preserved cylindrical epithelium.

Fig. 276.



A number of small tubercular ulcers in a very slightly thickened Peyer's patch. Natural size. (From a photo-micrograph by Surgeon J. J. Woodward, U. S. Army. Copied from the second medical volume of the Medical and Surgical History of the War of the Rebellion.)

When the tubercle granules are confluent, they are surrounded by lesions of irritation of the mucous membrane and submucous tissue, and an ulcer soon appears at the points first invaded or where the circulation is arrested. Ulceration is most frequently effected through the mechanism of molecular gangrene.

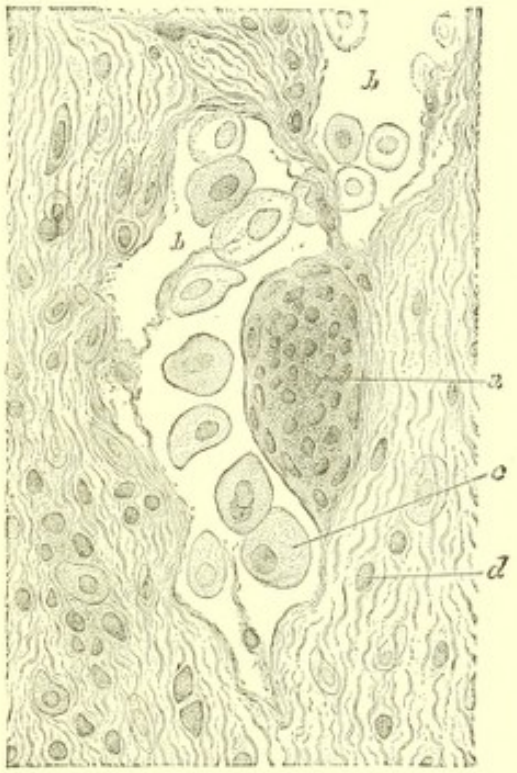
Whatever may be the mode of ulceration, the aspect of the ulcer, its ulterior course, and its consequences are the same.

Tuberculous ulcers of the small intestine have a round or elongated form. Their long axis is longitudinal when in the Peyer's patches; but outside of the Peyer's patches, in the jejunum, in the small intestine, and even in the ileum, it is generally transverse. Rindfleisch regards this predominant transverse form as due to the fact that the granulations follow, by preference, the walls of the blood-vessels and lymphatics, whose course is generally transverse. The sinuous, irregular, and more or less serpiginous borders of these ulcers are thickened and prominent, and contain tubercle granules or altered follicles, caseous in their

centre and surrounded by the above described inflammatory lesions of the villi and glands. Their floor is also covered with gray or whitish nodules, which are mostly tubercles in process of elimination. Klebs considers that these whitish grains are always lymph vessels; it is a fact that the wall of the lymph vessels is often a starting-point of a tubercle granule. (*t*, Fig. 275.)

When we examine the peritoneal surface which corresponds to the location of the ulcer of the mucous membrane, we always see a certain number of minute tubercle granules, semi-transparent or slightly opaque at the centre, forming an elevation upon the surface of the serous membrane. The lymph vessels, which emerge at this point to empty into the lymph glands of the mesentery, appear as large knotted cords, of a whitish or yellowish-white color. At different points they present prominences, due to the tubercles which are developed in their wall, and when they are cut there often escapes from them a whitish caseous, semi-fluid, mass. This growth in the interior of the lymph vessels is composed of swollen, granular, endothelial cells and of lymph corpuscles, which are often granulo-fatty, whence results the opacity of the mass. Thin sections of these vessels made at different points show the vessel walls infiltrated with round cells, and at points in the course of the vessel the sections show one or more granules developed side by side in the walls, which at these points are much hypertrophied.

Fig. 277.



Section through the lumen of a lymphatic in the submucosa of the ileum, in tuberculosis of the latter. × 480. A granular fibrin clot *a*, in which both lymphoid and endothelial elements are imbedded, adheres on one side to the walls of a lymphatic vessel, in whose lumen, *b*, *b*, loosened endothelial cells lie free. Similar elements appear in the connective tissue surrounding the vessel, with a number of lymphoid cells, one of which is indicated at *d*. (From a photo-micrograph by Surgeon J. J. Woodward, U. S. Army. Copied from the second medical volume of the Medical and Surgical History of the War of the Rebellion.)

At the same points the lumen of the lymph vessels is most frequently very much lessened and irregular, and is filled with granular lymph corpuscles.

[Dr. J. J. Woodward believes that in the intestine the tubercles spring from the lymph passages, and that the bloodvessels are rarely, if ever, primarily affected.]

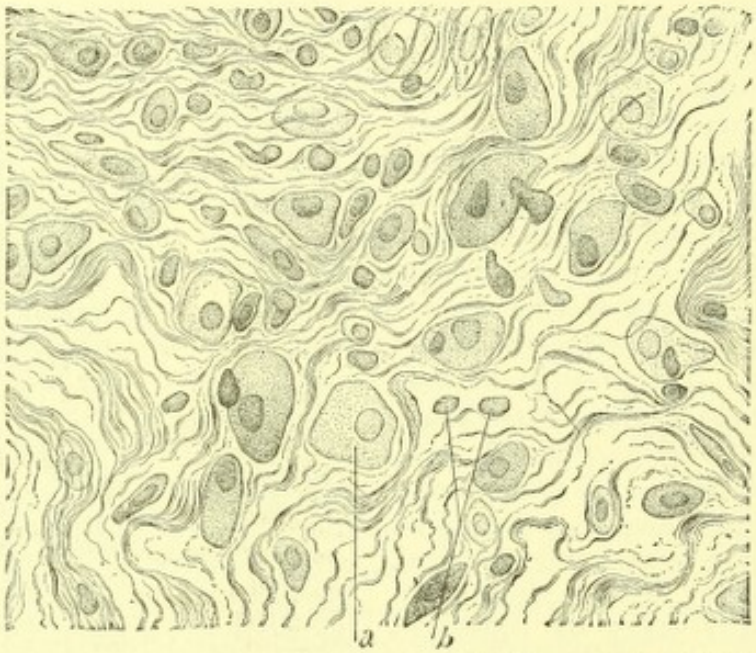
The different layers of the connective tissue of the intestinal wall are the seat of tubercle granules, and ulceration is effected by the process with which we are already familiar. A complete perforation of the intestine may be effected by the spreading of the ulcer, but this accident

is rare, because pulmonary lesions or tuberculous inflammations of the serous cavities occasion death before the intestinal lesions have reached their termination.

Sometimes the inflammatory and tuberculous infiltration of the mucous membrane is so great that there may result in consequence a narrowing of the intestinal canal and its consequences.

Tuberculous ulcers of the rectum may be located at the anus and invade the connective tissue of the surrounding region. It is not necessary to add that in tuberculosis of the intestine the mucous membrane is the seat of a more or less intense catarrh, with hypersecretion of fluid.

Fig. 278.



Portion of the submucosa in vicinity of tubercular ulcer of the ileum. ×480. In the meshes of the fibrillated matrix there are a number of large granular cells (transformed connective-tissue corpuscles, endothelial cells), one of which is indicated by *a*, and numerous lymphoid elements, two of which are indicated by *b*. (From a photo-micrograph by Surgeon J. J. Woodward, U. S. Army. Copied from the second medical volume of the Medical and Surgical History of the War of the Rebellion.)

The tuberculous ulcerations which have just been described are often consecutive to tuberculous ulcers of the lungs, and may be caused by patients swallowing the sputa. They occasion tubercles of the peritoneal lymphatics; but tubercles primarily developed in the peritoneum only very rarely give rise to intestinal tuberculosis and ulceration.

Syphilitic Tumors and Ulcers.—The ulcerations of the intestine which follow syphilitic gummata are not much more frequent than those of the stomach. There exist, however, several very conclusive observations which place their occurrence beyond doubt.

These ulcers are characterized by their thickened edges, which sometimes contain nodules caseous at the centre; by their bottom, which yields but little pus and which consists of a dense tissue, yellowish-gray,

of fibrous consistence, and which corresponds to a cicatricial fibrous thickening and elevation of the serous membrane. This indurated fibrous tissue is infiltrated with small round cellular elements. The beginning of these growths has not been precisely determined; in the small intestine they may be seated in the lymph follicles of Peyer's patches, but if they start in the closed follicles they also invade the neighboring tissue. The lymphatics which emerge upon the serous surface are altered and knotted.

According to the opinion of Gosselin and others, the extensive ulcers of the rectum accompanied by induration of the connective tissue, and sometimes by considerable contractions, are not characteristic of syphilis. These ulcers differ from those of chronic dysentery in this, that they are bordered by a narrow ring, and that they occasion constrictions, whilst, on the contrary, rather a dilatation of the rectum is observed in dysentery. More frequent in woman than in man, they succeed chancres of the anus, mucous patches, or condylomata.

Fibromata.—Fibroma originating at the surface of the intestinal mucous membrane is rare; in the chronic forms of dysentery, we find small fibrous polypi around the ulcerations of the rectum or anus, where they assume the form of papillomata.

A production of fibrous tissue is associated with adenoma in certain mucous polypi which present a development of papillæ at their surface.

Fibro-myoma.—There sometimes exists at the serous surface of the intestine small sessile or pedunculated tumors, composed of fibrous tissue and bundles of smooth muscles. These tumors do not differ from those formed upon the serous surface of the stomach.

Small *lipomata* may form very rare growths beneath the mucous membrane of the intestine.

Vascular Tumors.—Dilatation of the veins or phlebectacy is not infrequent in the large intestine, especially in the hæmorrhoidal plexus around the anus. Varices are often found in the small intestine, forming an elevation of the mucous membrane. The causes of these dilatations are all those which determine a blood stasis of the different branches of the portal vein: cirrhosis of the liver, disease of the heart, abdominal tumors, increase in size of the uterus, efforts of parturition, constipation, the efforts in defecation, etc., all causes which impede the course of the blood in the hæmorrhoidal veins.

Hæmorrhoids consist, at the commencement, in a simple dilatation of the veins at the border of the anus, and which form there a slight projection. At the same time the veins situated beneath the rectal mucous membrane, above and below the sphincter, are dilated. Later these dilatations increase in size and become distended under the form of little lumps by the efforts at defecation. Rupture at some point of the dilatation, consequent hemorrhage and catarrhal irritation of the mucous membrane of the lower part of the rectum are the usual sequelæ. The cellular elements of the altered veins experience the same alterations which have been described *à propos* of varices (see p. 342). The connective tissue around the veins may thicken, so that neighboring veins are united

by an indurated tissue. A section of one of these tumors resembles that of a varix. All the cavities do not communicate directly with the principal vessels (blind hæmorrhoids). Calcareous infiltrations of the walls of the diseased veins are sometimes observed.

Adenomata.—These tumors caused by a hypertrophy of the glandular layer of the mucous membrane are rarely met with in the small intestine, but they are very common in the rectum, where they form *mucous polypi*, which are very frequent in children. Their type is the polypus of the stomach already described (see p. 468). Their constituent parts are only a little more regularly disposed than in the stomach. These polypi may be the cause of an invagination of the large intestine. When they project externally through the anal aperture, that part of the investing layer of epithelium, which is in contact with the air, changes its character; the superficial cells which were cylindrical, like those of the intestine, become flattened and pavement shaped, and the surface of the polypus assumes all the characters of the skin, except in remaining red. This peculiarity is observed of all forms of polypi which project externally.

Lymphadenomata of the stomach and intestine have been studied in the first part of this manual (page 142). It is especially in the lower portion of the small intestine near the ileo-cæcal valve, that these tumors have been observed, but they may be seated anywhere in the length of the gastro-intestinal tube. In two cases of Picot and Rendu the new formation of adenoid tissue had invaded all the layers of the intestine and the mesentery, and there had resulted an enormous tumor. These lesions of the intestine and stomach usually coincide with other adenoid neoplasms of the lymph glands, the spleen, the peritoneum, the lungs, the bones, the skin, etc. Lymphadænic ulcerations and tumors of the intestine to the naked eye, resemble encephaloid growths; their cut surface yields a juice by scraping, and their extent, their thickness, their progressive invasion of the neighboring tissues, their intestinal tunics, and their peritoneum, and the degeneration of the lymph glands very closely assimilate them to tumors which have formerly been called cancerous. Notwithstanding that they may begin in the closed follicles and Peyer's patches, the lymphadenomatous infiltrations and ulcerations present totally different naked eye appearances from those of typhoid fever, for they do not remain limited to the Peyer's patches, but, on the contrary, extend indifferently to all the structures of the mucous membrane. They are habitually transverse, while the lesions in typhoid fever are longitudinal. They cannot be confounded with tubercular ulcers, because there always exist in the latter tubercular nodules or inflammations of the lymphoid organs, which are caseous at the centre. Moreover upon the peritoneal surface, opposite tubercular ulcers, we always find small semi-transparent granules, which are wanting in the disease we are considering.

Under the microscope it would be more difficult than by the naked eye, to differentiate the swollen Peyer's patches of typhoid fever from leukæ-

mic productions. In both cases in effect, previous to ulceration, the tumors show a cellular infiltration of the villi, a lengthening compression and embossing of the tubular glands which contain a mucous or granular epithelium, as well as a cellular infiltration of the reticulated submucous tissue.

CARCINOMATA.—Primary carcinoma of the intestine is incomparably more rare than that of the stomach, but when it occurs it presents entirely the same characters as when found in the stomach. It is often secondary to carcinoma originating in neighboring tissues, the peritoneum, the uterus, the bladder, etc.

The regions most frequently affected by carcinoma are the rectum, the hepatic portion of the transverse colon; the cæcum, the duodenum, and jejunum are very rarely attacked.

Scirrhus and *encephaloid* are met with in the rectum, the first more frequently than the second. The tumor may be developed in the vicinity of the sphincter, or eight or ten centimetres above it. The growth starts in the submucous connective tissue. The submucous infiltration extends in an annular form completely around the circumference of the intestine, and occasions a constriction.

The granulating appearance of the mucous membrane, its ulceration, the extension to the deep layer, the hypertrophy of the muscular coats of the rectum, the infection of the lymph glands, are in every respect comparable to the lesions in carcinoma of the stomach.

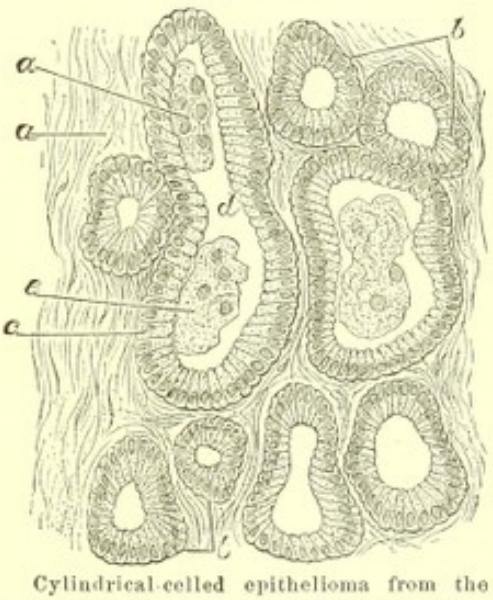
Authors record the frequency of colloid carcinoma of the rectum. It is certain that tumors having a colloid aspect, are not infrequent in the rectum and other parts of the intestine, but we should not consider that every colloid tumor, with large alveoli filled with gelatiniform matter, is carcinomatous. As we have already seen, *cylindrical-celled epithelioma* may suffer a colloid degeneration.

The cancerous tumor may ulcerate, and in this way an obstruction of the lumen of the gut may be partially and momentarily removed as with similar tumors of the pylorus, and the ulceration may cause a perforation of the intestinal wall, an accident which happens more rarely than in the stomach.

Occasionally carcinoma may show itself in the intestine under the form of multiple tumors.

The secondary nodules which originate from carcinoma of the intestine invade the peritoneum, and generally also the liver, with a marked predilec-

Fig. 279.



Cylindrical-celled epithelioma from the large intestine. × 170. *a*. Fibrous stroma. *b*. Small cystic cavities lined with cylindrical epithelium. *c*. Cystic cavity constituted by the union of two adjoining cavities. At *d* there is a constriction, a trace of the original intermediate septum. In the interior of some cavities is an amorphous mass containing cells.

tion. They are also found in the other organs, the lungs, kidneys, etc. The neighboring lymph glands are always altered.

Epithelioma ta.—Cylindrical-celled epithelioma is one of the commonest tumors of the small intestine, the large intestine, and the rectum. It has precisely the same naked eye and microscopic characters as in the stomach, and it has also a similar starting point. (Fig. 279.)

Epithelioma with pavement cells and spherical cell nests, is sometimes met with at the anus.

CHAPTER V.

THE LIVER.

Sect. I.—Normal Histology of the Liver.

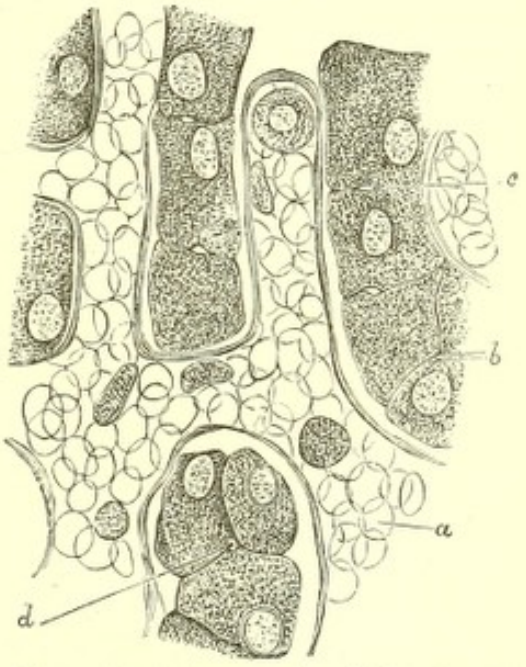
THE liver is composed of lobules in which the hepatic cells are placed in connection with the blood of the portal vein. Large and vascular, designed to elaborate the blood of the portal vein in its passage from the intestines, spleen, and heart, the liver also secretes bile and possesses a system of excretory ducts. It is surrounded by a fibrous membrane, the capsule of Glisson, which is covered by the peritoneum; the connective tissue of this capsule accompanies the vessels as they penetrate between the hepatic lobules.

Although the hepatic lobules are not all of the same size and shape, yet their intimate structure is identical, and a single lobule may be taken as a type for the description of the entire liver.

Structure of a Hepatic Lobule.—The hepatic lobules are spherical or polygonal in shape, of a diameter one to one and a half millimetres; they are appended to the divisions of the hepatic vein as glandular lobules to their excretory ducts.

The principal extra- or inter-lobular branches of the hepatic vein give origin to very short smaller branches each of which enters a lobule, and is named intra-lobular hepatic vein or central vein of the lobule. At the centre of the lobule, the vein divides into capillaries which radiate towards the periphery of the lobule, and anastomose with one another by short transverse branches. The diameter of these capillaries is .010 mm., and they are separated by an average distance of .015 mm., forming a network with meshes elongated in the direction of the radiating capillaries. Communicating at the centre of the lobule with the central vein, the capillaries at the periphery of

Fig. 280.



Liver of child three months old, hardened in chromic acid. The hepatic cells (*b*) with their nuclei are separated from the capillary wall by a small intervening space. The capillaries (*a*) contain closely compressed red blood disks, and a few colorless corpuscles. A few elongated nuclei of the capillary wall are seen. Within the line of junction between the hepatic cells the transverse section of a biliary canaliculus is seen (*c*) (*d*). (*Stricker.*)

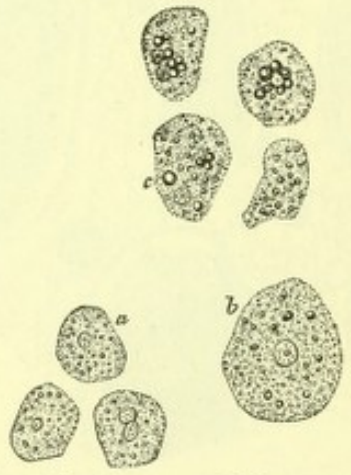
the lobule receive the blood of the portal vein, and are directly continuous with the small inter-lobular portal veins. These latter are placed in the prismatic spaces formed between the lobules, and penetrate the latter at their surface, so that each lobule receives its blood from four or five branches of the portal vein. In the same inter-lobular prismatic spaces which receive the portal vein, run branches of the hepatic artery and inter-lobular biliary canals surrounded by connective tissue in continuity with the capsule of Glisson. The capillaries of the hepatic artery are especially designed for the nutrition of the walls of the portal vein and inter-lobular biliary canals. They are found especially at the periphery of the lobules, where they anastomose with the capillaries of the lobule.

The lobules are in contact one with the other, separated only by the ramifications of the portal vein, biliary canals, and inter-lobular hepatic artery, accompanied by a small amount of connective tissue; their capillaries are intermediate between the portal and hepatic veins.

In the lobules, the spaces between the meshes of the capillaries are entirely filled by the hepatic cells.

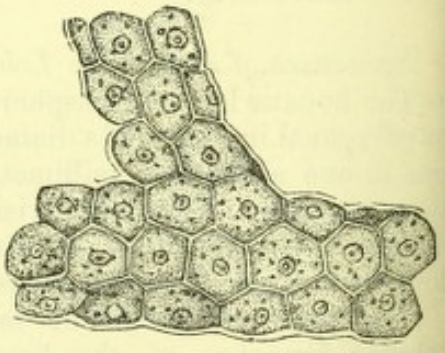
The hepatic cells are small blocks of soft granular protoplasm possessing one or two nuclei, round or oval. The shape of the cells is readily modified by the pressure of the capillary vessels and neighboring cells. When examined isolated, the cells are seen to be flattened, polygonal,

Fig. 281.



Isolated hepatic cells. *a* and *b* normal, but *b* more highly magnified; showing the nucleus and distinct oil particles. *c* Cells in various stages of fatty degeneration. (*Carpenter.*)

Fig. 282.



Portion of trabecula of hepatic cells. Human. (*Carpenter.*)

with four to six sides, or with irregular edges; one of their surfaces is generally notched where it is in contact with a bloodvessel. Examined in thin sections, each one of the hepatic cells is seen to be in contact with five or more of its neighbors, and to touch one or more blood capillaries.

The granular, semi-fluid, protoplasmic mass of the hepatic cells frequently contains fine yellow granules of biliary pigment or red-colored granules which are derived from the blood. They also inclose glycogenic

granules, which may be colored by tincture of iodine. During digestion, the cells at the periphery of the lobule contain fat.

The cells do not possess a separate membrane, but their granular substance is denser at the surface of the biliary canals, and forms a thin cuticle, serving as a wall to the canals.

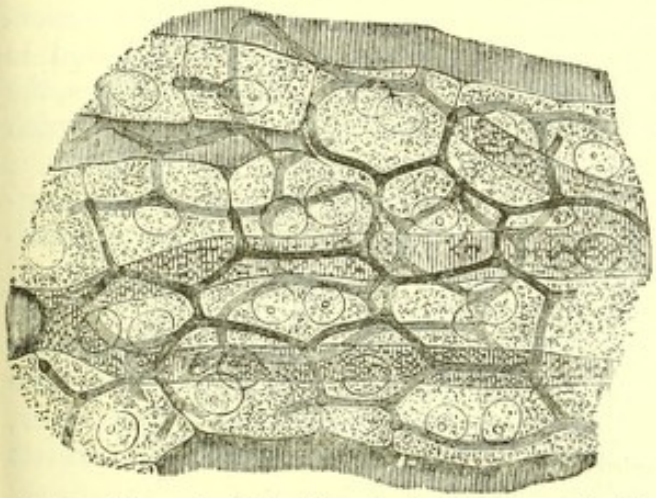
Considered in their mutual relations in the lobule, the hepatic cells, according to Eberth, appear to form series or columns radiating from the centre to the periphery, and anastomosing transversely.

These networks or *trabeculæ of hepatic cells* are compared to the tubes containing hepatic cells which are met with in some animals (fishes and reptiles). This appearance of trabeculæ is due to the general configuration of the capillary network, as demonstrated by Héring and Kölliker. In man and the higher mammiferæ, there is no membrane comparable to a glandular sac which incloses the hepatic cells and separates them from the capillaries. In the rabbit (Héring), the hepatic cells adhere to the capillaries, and do not separate from them when a piece of the liver is placed in alcohol or chromic acid, reagents which cause the elements to shrink. In man and dogs, the hardening action of these fluids separates the cells from the walls of the capillaries.

The hepatic lobule should then be considered simply as a continuous mass of cells channelled by a capillary network, the cells being arranged according to the form of the vascular meshes.

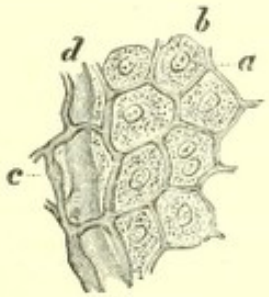
The biliary vessels have their origin in the hepatic lobule by a network of fine canaliculi, which form narrow meshes, and are in contact with all the hepatic cells. This network connects with the inter-lobular biliary canals which accompany the branches of the portal vein.

Fig. 283.



Injected liver of rabbit. The slender biliary canaliculi form a plexus, each of the meshes of which incloses a hepatic cell. The much wider blood capillaries are also seen. (*Stricker.*)

Fig. 284.



Injected biliary canaliculi of rabbit. *a*. Biliary canaliculi. *b*. Hepatic cells. *c*. Small biliary ducts at border of lobule. *d*. Blood capillary. (*Carpenter.*)

The biliary intra-lobular canaliculi or capillaries have a rectilinear and regular course; their diameter is .0015 mm., while that of the meshes of the network varies from .014 to .017 mm. in the rabbit. They have no cells in their interior, and their wall is formed solely by the hepatic cells,

the surface of which becomes condensed at this point and forms a sort of cuticle. The meshes of the biliary canaliculi are elongated somewhat like the blood capillaries. The canaliculi pass between the hepatic cells in such a manner that they do not come in contact with the capillary blood system, from which they are separated by at least half the surface of a hepatic cell. The meshes of the biliary canaliculi are polygonal, following the shape of the hepatic cells. Each cell is consequently in contact with a blood capillary by its angles, and by several of its surfaces with the biliary capillaries.

At the periphery of the lobule the biliary capillaries unite to form somewhat narrower networks, which empty into the peri-lobular biliary canals.

The peri-lobular biliary canals have an entirely different structure. They are formed of a thin enveloping membrane, in the interior of which is found a complete lining of cubical epithelial cells provided with a round or oval nucleus. At the centre of the canal exists a narrow lumen for the flow of the secreted products. These are true excretory ducts which are in connection with the biliary capillaries, which latter have no cellular lining in their interior. It is the hepatic cells which represent the secreting cells of the bile, which, being secreted by the hepatic cells, first enters the small intra-lobular canaliculi, then passes into the peri-lobular canals.

Such are the essential elements which enter into the composition of a hepatic lobule. It remains to consider the connective tissue and lymphatics of the lobules. The connective tissue which comes from the capsule of Glisson, and the fasciculi which accompany the inter-lobular vessels, penetrate into the interior of the lobule as very fine fibrillæ. It is connected with the wall of the capillaries, forming in places a kind of adventitia, or it is spread out between the capillaries, forming a reticulated tissue. The existence of flat connective-tissue cells applied to these fibres is questionable. By its union with the blood capillaries, the reticulated connective tissue forms in the lobule the framework which supports the hepatic cells.

The peripheral connective tissue of the lobule does not always constitute a complete covering; at times, two lobules are joined at their periphery without any prolongation of the capsule of Glisson being interposed between them.

Upon the surface of the liver, the capsule of Glisson can be demonstrated to consist of two layers: one serous, formed of loose connective tissue covered by the endothelial cells of the peritoneum; the other, deeper and thicker, is in connection with the hepatic lobules and consists of a close and dense fibrous tissue.

The existence of lymphatic vessels in the lobule has been admitted by MacGillavry, who, in injecting the biliary vessels, produced extravasations located around the blood capillaries, between them and the hepatic cells. In similar cases, the injected substance has been seen by Kölliker to flow into the peri-lobular lymphatic vessels which accompany the portal vein. It is certain that in the cat, dog, and man, the hepatic cells are easily detached from the capillaries, and it is these peri-vascular spaces which MacGillavry regards as the lymphatic lacunæ. Héring is

opposed to this view and says that in the rabbit nothing of a similar nature exists, the hepatic cells adhering always to the wall of the vessels.

The peri-lobular lymphatic vessels consist of trunks or networks, which accompany the portal vein and are united upon the surface of the liver with the superficial network situated under the peritoneum.

Nerve filaments have not been met with in the hepatic lobules, and in the latest investigations they have only been followed into the walls of the inter-lobular portal veins. [Pflüger has thought that he could trace fine nerve filaments into the periphery of the lobules, and occasionally could even see a communication with an hepatic cell.]

The biliary excretory ducts.—The biliary capillaries of the hepatic lobule empty, as we have seen, into the interlobular canals. The latter accompany the ramifications of the portal vein, and join to form larger trunks which follow the principal branches of the portal vein. As they pass out of the liver, two principal trunks unite in the transverse fissure to form the hepatic canal, which is continued partly as the *ductus communis choledochus* (common biliary duct) to the internal surface of the duodenum, and partly as the *cystic duct* to the gall-bladder.

Besides these principal divisions, there exist accessory ramifications which unite with the two branches of the hepatic canal in forming a network in the transverse fissure. At different points upon the surface of the liver, the biliary canals divide and anastomose in the connective tissue; those entering the left triangular ligament extend to the diaphragm.

The interlobular biliary canals are composed of a membrane of connective tissue. The smallest have a lining of cubical epithelial cells, while the larger canals are lined by cylindrical cells; in the smallest interlobular canals it is difficult to see a membrane, and their cells are frequently flattened; the fibrous membrane of the large and medium size canals contains smooth muscular fibres. All these canals are provided with small simple or compound glands, formed by round or elongated vesicles which open into the biliary duct, and have a lining of cells similar to those of the duct.

The epithelial lining of the hepatic, cystic, and common biliary ducts, and of the gall-bladder, consists of a single layer of long cylindrical cells, the nuclei of which are oval and elongated in the direction of the cells. The sub-epithelial connective tissue has a very abundant network of capillary bloodvessels.

The gall-bladder has, beneath its mucous membrane, a layer of connective tissue traversed by fasciculi of intersecting smooth muscular fibres, giving rise to an alveolar appearance. It is covered by the peritoneum upon its external surface, and possesses a network of subserous lymphatics.

Sect. II.—General Pathological Anatomy of the Liver.

We commence the study of lesions of the liver by a general observation upon the pathological anatomy of this organ. General pathological

anatomy is one of the most important branches of general pathology, and each organ may be looked upon as having a general pathology which properly belongs to itself.

The situation of the liver with respect to the course of the blood loaded with the materials of digestion, its consequent relation to intestinal diseases, and the large amount of blood which continuously passes through it, render it very liable to lesions secondary to intestinal and splenic diseases, and to the alterations of the blood in all general diseases which greatly derange the organism, or which change the conditions of the circulation of the blood.

Therefore, excepting traumatic affections, it may be said that the great majority of hepatic affections are secondary to other general or local affections.

In warm countries, where derangements in the functions of the liver are so common, the more intense follow intermittent fever, yellow fever, dysentery, alcoholic excesses, etc. In our climate they are secondary to intermittent fever and dysentery, but are always less serious than in tropical countries; the most intense hepatic affections here met with are due to alcoholism, low types of fevers, typhoid fever, variola, scarlatina, etc., and to purulent infection; or they are occasioned by affections of the biliary canals, the lobules being sometimes secondarily affected. Finally, parasites may also cause secondary diseases of the liver. Affections of this organ are found to be almost always deuteropathic.

In order to have a general idea of the lesions of the liver, it is necessary to study the anatomical alterations which its elementary parts undergo; that is, first, those of the hepatic cells which make up the greater part; next, the cellulo-vascular tissue, and finally the biliary canals.

1st. *Changes in the Hepatic Cells.*—It has been seen that the shape of the hepatic cells is polyhedric; that they contain a nucleus, and exceptionally two nuclei; that their granular protoplasm contains albuminous and glycogenic granules; that sometimes, in the normal state, they are pigmented and fatty; but under the influence of the several morbid states, their constitution is greatly modified.

Their shape is very easily altered by pressure; in the normal condition they are frequently moulded upon a capillary, by one of their excavated surfaces. From the pressure of tumors developed in the liver, the cells may be flattened in one direction, so as to have a resemblance to connective tissue with lamellæ and flat cells, like those of the internal coat of arteries or the capsule of the spleen. Seen in profile each such cell resembles a fusiform cell a little thicker at the position of its nucleus. The hepatic cells assume such an appearance when compressed by the tissue of a gumma, by a tubercle, by a scirrhous nodule, by a hydatid cyst, etc. All the cells of a compressed lobule take the same shape; this results in the entire lobule being flattened and spread out around the tumor.

In consequence of the softness of the protoplasm of the hepatic cells, the entire liver may be changed in its form by the compression of an abdominal tumor, or of an effusion of fluid into the peritoneal cavity.

External pressure from corsets also changes the normal shape of the liver. In this case, the base of the thorax being contracted by the constriction, the entire liver is pushed downwards, its superior surface becomes anterior; this surface, smooth in the normal condition, is indented, and presents depressions corresponding to the ribs; the inferior border of the liver, which now extends below the false ribs, is at times turned up beneath the ribs in following the convexity of the abdominal wall. These deformities become permanent in consequence of the atrophy of the lobules compressed in the folds of the hepatic surface, and from the thickening of the capsule of Glisson at the same points. Similar deformities are very frequent in old persons, in whom the back is arched, and in whom the inferior border of the thoracic cavity compresses the anterior surface of the liver.

The shape of the cells is also frequently modified by blood pressure, as in diseases of the heart and lungs with increased blood pressure in the right auricle, and consequently in the inferior vena cava. The pressure in the inferior vena cava is directly transmitted to the hepatic vein and to the central vein of the lobule. The capillaries are necessarily distended, and consequently the hepatic cells are compressed and flattened. At the same time, from the influence of the surrounding blood pressure, they are infiltrated with fluid containing coloring substance, and have in their protoplasm red-brown granules of hæmatin. The pressure continuing, they become more granular, gradually thin and atrophied, and may even completely disappear, so that, in points of the hepatic lobule, the distended vessels are not separated by cells. These are the essential lesions observed in cardio-pulmonary affections, and particularly in lesions of the mitral valve.

In some hepatic congestions not accompanied by any impediment to the blood circulation of the liver, the cells are hypertrophied at the beginning. This occurs especially in the hepatic congestion observed at the commencement of diabetes. The liver is now uniformly congested, and the cells are larger than in the normal state; they also contain numerous granules of glycogenic material. The entire organ is hypertrophied. Later, the cells are loaded with fat granules of medium size, and the liver remains hypertrophied or returns to its normal size.

In all cases of increased blood pressure, the cells experience analogous lesions; increase of nutritive activity, when the blood circulation is simply accelerated; atrophy, on the contrary, when the cells are compressed, when there is an obstruction of the flow of blood through the hepatic vein, while the pressure is the same in the portal vein; pigmentation of the cells occurs in both cases. The nuclei of the hepatic cells are usually unchanged, at least there is no atrophy even when the compression exists in a high degree.

Another series of modifications of the cells occurs in all acute and febrile infectious diseases of great intensity, as typhoid fever, puerperal fever, variola, particularly hemorrhagic variola, scarlatina, measles, erysipelas, etc., as well as in acute tuberculosis, in certain poisonings, and in fatal jaundice or acute yellow atrophy of the liver. This last lesion has received from Virchow the name of *parenchymatous hepatitis*, cer-

tainly not a good term, since the signs of inflammation are but slightly evident, and the term parenchymatous is open to criticism.

There occurs in all these affections, a change in the nutrition of the cells, in consequence of which they become clouded, more spherical, and larger than normal. The contained granules obscure the nucleus of the cell. However by staining with picro-carmine, or employing acetic acid the nuclei may be made evident. Examination of the cells very often proves half of them to possess two nuclei, some even containing three or more. If the cells of a normal liver present two nuclei it is exceptional, while here it is very common, and therefore abnormal. Besides these large cells in a state of *cloudy swelling*, there are seen, in the fluid obtained by scraping, others without a nucleus and small, the protoplasm of which is soft and permits the nucleus to escape; free nuclei are also found. It is very probable, that the protoplasm of the cells, after swelling and softening, becomes fragmented.

Fig. 285.



Liver from a case of acute rheumatism with high temperature; showing the swollen and granular condition of the liver-cells. In many of the cells the nucleus is so much obscured as to be almost indistinguishable. ×200. (*Green.*)

Such is the lesion found in the first stage of fevers of low type, although it is not known to what actual change in the blood it corresponds, yet it is evident that it is related to the infectious nature of the disease, and to the elevated temperature of the blood, and that it should be considered as adding to the gravity of the disease. At a more advanced period of the disease, there are found in the cells numerous fatty granules, and a true fatty degeneration of the liver, as observed at the termination of typhoid fever. In other diseases of this group, especially in hemorrhagic jaundice, the cells are atrophied, and broken down, they are infiltrated with yellow granules of biliary matter in connection with albuminous and fatty granules. Lobules, or portions of lobules are replaced by the débris of cells. Post-mortem decomposition very probably plays an important part in the softening of the entire organ, which is so very extensive in this lesion.

Acute yellow atrophy of the liver is not the only form of parenchymatous hepatitis in which the cells are infiltrated with biliary pigment. In the liver of persons dying from hemorrhagic variola, there is found a similar lesion. The organ is now large, soft, and of a uniform grayish-yellow color. Nearly one-half of the hepatic cells have two nuclei, and are clouded with albuminous, fatty, and pigmentary granules.

The numerous general febrile diseases all cause a parenchymatous hepatitis. Although in them this lesion may present an evolution, and an intensity slightly different in the several diseases, yet they may all be connected with a similar nutritive derangement of the hepatic cells. This series of nutritive alterations of the cells in parenchymatous hepa-

titis is connected with a change of the blood in infectious fevers, which is as yet little known.

An analogous granular change, followed by destruction of the cells, is observed at points where the blood circulation is interrupted (by emboli or thrombi), and when the cells are compressed by suppuration.

A second series of nutritive changes is seen in chronic cachectic diseases, in pulmonary phthisis, prolonged suppurations, scrofula, cancer, etc., and is characterized by *fatty infiltration* or *amyloid metamorphosis* of the hepatic cells.

Fatty infiltration consists in a surcharging of the cell by small oil drops. Very frequently in these chronic cachectic diseases, the nucleus of the cell is preserved, and therefore the hepatic cell is not destroyed. It is simply surcharged with fat. The protoplasm of the cell contains either several small drops of oil or a single large drop, which occupies almost the entire cell, and it is seen as a circle of protoplasm surrounding the fat. In a part of the protoplasm the nucleus is seen well preserved. The appearance now very much resembles adipose cells of the subcutaneous tissue. This is termed an infiltration of fat, since the nucleus is intact, and since the cell is not destroyed, while, on the contrary, the degenerated cells filled with albuminous and fatty granules in parenchymatous hepatitis are broken down and reduced to débris followed by a death of the cell. Each fatty infiltrated hepatic cell becomes enlarged, consequently there is a hypertrophy of the entire liver. A physiological infiltration of fat in the hepatic cells occurs during digestion, and at the end of parturition.

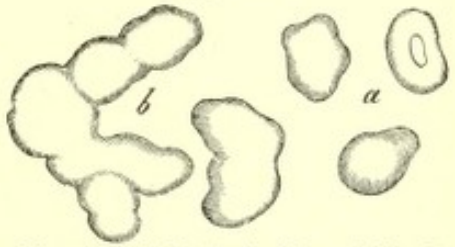
Fig. 286.



Liver-cells in various stages of fatty infiltration. × 300. (*Rindfleisch.*)

Amyloid degeneration, which is found in analogous pathological conditions, also affects the hepatic cells, transforming them into small blocks of a transparent, refracting substance, easily broken into small cubes. The granules and nucleus of the cells have disappeared. These small masses of refracting material are colored brown by tincture of iodine, and frequently after the action of iodine, when treated with sulphuric acid, they are colored violet, blue, green, and garnet-red.

Fig. 287.



Liver cells infiltrated with amyloid substance; *a*, single cells; *b*, cells which have coalesced. × 300. (*Rindfleisch.*)

Besides these two great series of general causes, infectious febrile diseases and chronic cachectic diseases which so greatly modify the hepatic cells in consequence of changes in the blood, the elements undergo other lesions secondary to a disease of the liver which does not have its beginning in the cells. Thus, in retention of bile there is found an accumulation of pigment in their interior; in acute suppurative inflammations, they are destroyed after having

become granular; in chronic cirrhotic inflammations and in tumors, they may present all the series of nutritive changes.

2d. *Lesions of the Cellulo-vascular System.*—It is difficult to separate the lesions of the connective tissue of the capsule of Glisson surrounding the interlobular branches of the portal vein and hepatic artery and penetrating with the capillaries into the lobule, from those of the wall of the vessels. It is around the lobules and in the neighborhood of the portal vessels that the changes of the connective tissue begin. They are usually due to the presence of foreign substances in the portal vein, which do not exist in the normal state, or of normal elements, which are found in abnormal quantity. These substances occasion, by their contact with the vascular walls, an irritation which is transmitted to the neighboring connective tissue.

In leucocythæmia, for example, the blood is loaded with numerous white corpuscles, which interfere with the circulation in the vessels and cause an increase of pressure and a resulting diapedesis of the leucocytes into the connective tissue. Thus occur true infarctions of white corpuscles in the connective tissue surrounding the small interlobular veins of the portal vein and around the capillaries in the hepatic lobule.

In chronic intermittent fever with cachexia, when the swollen and indurated spleen is attacked by interstitial splenitis, when the white corpuscles contained in the lacunæ of splenic tissue are loaded with black pigment granules (melanæmia), the blood of the portal vein contains many of the same pigmented lymph cells. The wall of the small interlobular portal veins soon presents a black pigmentation of its cellular elements, and the pigmented lymph cells pass out of the vessels and infiltrate the connective tissue surrounding the interlobular vessels as well as that accompanying the capillaries of the lobule. There is also generally found a thickening of the interlobular connective tissue; it is inflamed and infiltrated with lymph cells, some of which are filled with pigment. This is a variety of cirrhosis or chronic thickening of the connective tissue of the liver.

The most frequent cause of cirrhosis of the liver is alcoholism, the irritant probably acting directly upon the vascular walls and upon the connective tissue surrounding them. Alcohol is found in the blood, and especially in the blood of digestion. The liver is always congested after eating, particularly when large quantities of alcohol have been imbibed, and it is very probable that the presence of alcohol in the blood acts upon the wall of vessels and through them upon surrounding connective tissue, producing a chronic inflammation. In alcoholic cirrhosis as in malarial cirrhosis, the hepatic connective tissue is inflamed, there are found in the developing stage of the disease numerous lymph cells, situated between the fibres of the connective tissue. There soon occurs a new formation of fibrous fasciculi and a sclerosis of the vascular walls which blend with the fibrous tissue. This stage of cirrhosis continues a varying length of time, and terminates in a cicatricial contraction of the new tissue.

In purulent infection following traumatism, when small metastatic abscesses appear in the liver, not only do lymph cells occur in greater

number than in the normal state, but there are also microscopic germs, vibrios, spores coming from the part first affected and carried away in the blood. In autopsies made a very short time after death, during the war and under special conditions, in a very low temperature, below the freezing point, we have seen small metastatic abscesses containing besides the lymph cells coming from the vessels, the previously mentioned microscopic germs. Moreover there occurred during life a true putrid fermentation in these abscesses, demonstrated by the presence of gas bubbles in their interior.

Lesions of the Vessels.—The vessels are altered either primarily or secondarily. Among the primary lesions is inflammation of the portal vein, in which the vascular trunk is found, at the autopsy, filled with pus or coagulated fibrin. This affection also occurs as a sequence of intestinal lesions: dysenteric ulcerations of warm countries are frequently their source of origin; at other times they follow general affections, and often it is impossible to find any primary lesion which has given rise to the pylephlebitis. Upon opening a liver affected with this lesion there are often found a varying number of small purulent collections, true canalicular abscesses which have the shape and direction of the branches of the portal vein.

In cirrhosis and other chronic affections of the liver the walls of the portal vein are changed as well as other parts of the organ; the cellular coat shows a very manifest cirrhosis.

Vascular tumors seldom occur, yet aneurisms of the portal vein have been met with. Induration of its internal coat and atheroma have occasionally been seen.

More frequently are observed what are designated as *hæmic tumors* of the liver—small red nodules which form in the hepatic tissue an island of cavernous tissue.

Sect. III.—Special Pathological Anatomy of the Liver.

Post-mortem Changes.—At autopsies, the liver is generally pale, and more or less bloodless—the large vessels only containing blood, particularly the branches of the hepatic vein. The small vessels and branches of the portal vein contain very little blood. If a large quantity of blood is found in the vessels, the liver has been congested during life.

The absence of blood in the small vessels of the liver is explained by the circumstance that the bile destroys the red corpuscles of the blood. This disappearance of the red globules explains the apparent anæmia and paleness that is so frequently met with at post-mortem examinations.

The liver may also be found *softened;* sometimes after the death of an animal, the protoplasm of the hepatic cells becomes solid, so that one or two hours after death, the liver is rigid; but this condition disappears after a few hours, and when an autopsy is made twenty-four hours after death, the liver is soft.

The diffusion of bile occasions another phenomenon, which consists eventually in a yellow-greenish staining of the parts in proximity to

the gall-bladder, particularly the intestine. There has not necessarily been any rupture of the gall-bladder or any other lesion before death. After death the surface of the gall-bladder and canals is green; under the microscope the epithelial cells are also colored green, but this is never seen in living animals, for they are normally transparent

Putrefaction also causes changes in the hepatic parenchyma which may lead to error in pathological investigations.

There are produced in the fluids of the economy, particularly in the blood, constant metamorphoses. Putrefaction develops sulphuretted hydrogen which unites with the iron of the blood, and causes a greenish or blackish dotting of sulphate of iron, which has been taken for pathological lesions. This error however may very readily be avoided by the use of ferro-cyanide of potassium, which forms the characteristic color of Prussian blue.

Another cause of error, which has been described as a pathological lesion, is that in some cases of putrefaction there is a formation of gas, which collects in the tissue of the liver, and is accompanied by serum; upon making an incision into these little cavities the gas escapes, and only the fluid contents remain; these little cavities have been incorrectly described as cysts.

Congestion of the Liver.—Congestion is a very frequent lesion, since it is met with at the beginning of almost all diseases of the liver, and in diseases of the heart and lungs it is almost the only anatomical change observed in the organ. Notwithstanding the frequency of congestion, every enlargement of the liver is not necessarily due to an increase of blood. The initial congestion is often followed by very diverse lesions, fatty degeneration, cirrhotic hypertrophy, etc. etc. We make two divisions of hepatic congestions: in one the initial cause is an overfilling of the portal vein; in the other an increased blood pressure in the hepatic vein.

1st. After eating, the portal vein contains more blood than at any other time during the day. After a large dinner, during which considerable wine has been imbibed, the blood of the intestinal and splenic veins, loaded with the absorbed fluids, is emptied into the liver, which is congested and enlarged. There is now felt a sensation of fulness in the right hypochondrium, or at times an uneasiness, or actual pain. From this filling of its vessels the liver may increase one-third its normal size, which may be demonstrated by percussion. There is here an exaggeration of a physiological function, the elaboration of the intestinal blood by the hepatic gland. These errors in diet, when repeated, or when they become habitual, may, by the continual congestion, lead to cirrhosis or gout. Writers upon gout have pointed out that in many cases the disease is preceded by a hepatic congestion. Congestion of the liver from a too nitrogenous and too alcoholic diet is an important factor in the general alteration of the blood which Murchison terms uricæmia (uric acid diathesis).

Great heat is a cause of hepatic congestion, and sometimes of exaggerated secretion of bile. In warm countries, this is a common condition; but heat alone is not the most energetic agent; alcohol has also an important influence, and so also has malaria.

Intermittent fever, dysentery, zymotic diseases which exert their special action upon the organs supplied with the blood of the portal vein, are the most general causes of hepatic congestion in warm countries, congestions which there precede either pigmentary cirrhosis, especially melanæmia, abscesses of the liver or the various degenerations of this organ. In pernicious fevers a section of the liver is uniformly red; at times ecchymoses beneath the capsule are seen. Hepatic congestion occurs at the beginning of ictero-hæmaturic fever of warm countries, of bilious intermittents described by Dutroulau, of diseases in which the secretion of bile is so great that the patients vomit, and void by the rectum one to two litres of bile during twenty-four hours, while the biliary coloring matters infiltrate the hepatic tissue, skin, etc., and altered red blood corpuscles are passed in great numbers with the urine. The congestion of the liver is so extreme that the tissue of the gland is ecchymosed, and frequently small effusions of blood are seen beneath the capsule of Glisson. A section of the liver shows a tissue uniformly red; the blood flows from the small vessels and distended large trunks. The histological appearances are nearly the same as those observed by Griesinger in Egypt in bilious typhoid fever: congestion at the beginning, followed by biliary and granulo-fatty infiltration of the hepatic cells. In the latter stage the liver is normal or diminished in size, its color is yellowish-gray and opaque as in yellow fever.

Something of a similar nature is met with in our climate, although of less intensity, during extreme heat and from other causes, such as improper diet, alcoholism, etc. There may occur with jaundice, bilious gastric derangement, vomiting, bilious stools, coincident with an increase in the size of the liver and a febrile state of short duration. This is an increased secretion of bile with hepatic congestion, and should be distinguished from another variety of simple jaundice, also frequently accompanied with congestion, which is due to an intestinal catarrh, with catarrh of the biliary passages, and obstruction of the latter by plugs of mucus.

Most of the low infectious fevers of our climate, variola, typhoid fever, erysipelas, etc., are accompanied at the beginning by a hepatic congestion which precedes the cloudy swelling of the cells, and their fatty degeneration. This is a transient state, soon marked by the degeneration of the cells.

2d. When the cause of hepatic congestion is an increase of the blood pressure in the hepatic veins, it generally manifests itself by a distension of the central veins of the hepatic lobules and the capillaries of the lobule nearest to the vein, so that the inner half or the inner two-thirds of the lobule is red, while the periphery is gray. All cardiac diseases, but particularly those affecting the right and left auriculo-ventricular valves, stenosis or insufficiency, aortic aneurism, chronic diseases of the lung, emphysema, pulmonary induration, chronic pleuritis, tuberculosis, etc., in which the cardio-pulmonary circulation is interfered with, have the same result. Yet if the asphyxia is very rapid, as occurs in poisoning by carbonic acid, the congestion, instead of being limited to the central part of the lobule, is general.

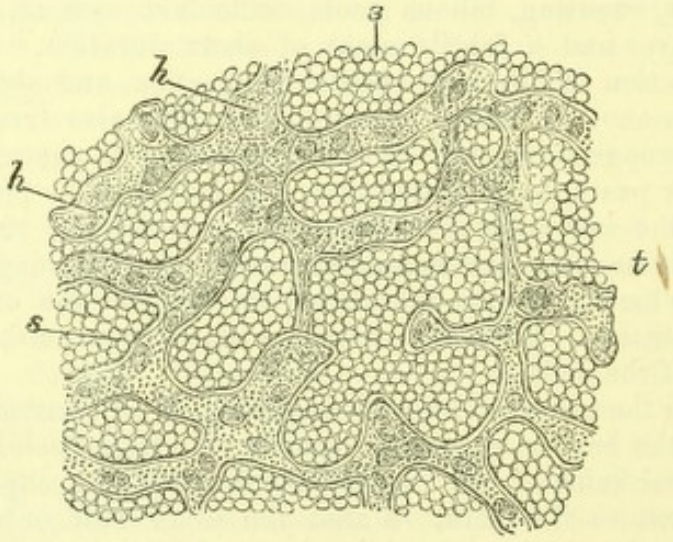
Congestion of cardiac origin continues as long as the cardiac disease;

from it follows a series of nutritive lesions of the liver, beginning with a hypertrophy, and terminating in an atrophy of the organ.

Hypertrophied and congested *cardiac liver* presents at first a smooth surface; the capsule of Glisson is thinned by distension; upon making a section of the organ, the lobules appear larger than normal; in their central zone, occupying one-half or two-thirds of the lobule, they are of a very uniform deep red color, resembling mahogany red, while their peripheral zone is gray and opaque. At the points where the section passes through and parallel with the divisions of the hepatic vein, there is seen a leaf-like figure with red branches surrounded by gray zones. If the section is made perpendicular to the direction of the hepatic veins, there are seen regular circles having red centres, while the periphery is gray. This distribution of red and gray in the same lobule is evidently what caused M. Andral to believe in the normal existence of two different substances in the liver. The coloration has been compared to that of the nutmeg, and the lesion has been named *nutmeg liver* or *cardiac liver*. The latter name is not absolutely correct, since the lesion also occurs in pulmonary diseases.

An examination of a thin section of such a pathological liver shows at the centre of the red part the central vein much dilated. Sometimes its opening may be seen with the unaided eye. The remainder of the red region of the lobule has the capillaries very much dilated, two or three

Fig. 288.



Section of a portion of a hepatic lobule in a case of congestion due to cardiac disease. The hepatic cells, *h*, are atrophied, whilst the capillary vessels, *s*, are greatly dilated and filled with blood corpuscles. The hepatic cells have entirely disappeared at some points, as at *t*. × 250.

times larger than normal, and filled with blood. The hepatic cells between the dilated capillaries are flattened and atrophied. They possess a nucleus, but their protoplasm is finely granular, and very frequently contains brown pigment granules of hæmatin. Crystals of hæmatoidin have been met with, and some cells contain yellow granules of bile pigment. These may be found in the centre as well as in the peripheral region of the red portion of the lobule.

At its peripheral gray portion the lobule consists of capillaries, normal in size or smaller than the preceding, and of fatty infiltrated cells. The cells contain large granules or one or two oil drops which distend and give them a spherical shape.

Such is the first stage of the lesion; the hepatic blood distends the central vein and central capillaries of the lobule, the cells are infiltrated with the coloring matter of the blood, and atrophied, while the portal blood stagnates at the periphery and surcharges the peripheral cells with the fat derived from digestion.

Other lesions soon follow; the dilated capillaries, after the more or less atrophic destruction of the cells separating them, may come in contact with one another; their walls are separated only by the normal connective tissue surrounding them, and perhaps by flattened hepatic cells still possessing a nucleus. These dilated capillaries, filled with blood, form in the red portion, at its centre or irregularly disseminated, small foci which very much resemble hæmic tumors of the liver, but, in the latter, the vascular cavities are much larger.

Upon section of the nutmeg liver, the red points appear as distinctly reticulated spaces, whose meshes are filled with blood corpuscles.

Later, the liver, originally hypertrophied, becomes smaller; it is atrophied (red atrophy). Its surface is now a little granular. Upon section of the organ, the lobules appear smaller than normal. The red substance seems at first more unequally distributed, although it is still in reality always limited to the centre of the lobule; but the lobules being smaller, the difference in the color of their centre and periphery is more difficult to appreciate by the unaided eye; again, there is now always a new formation of connective tissue around the central veins of the lobules and the sub-hepatic vein; this tissue is also uniformly colored red. Sections of these livers, examined microscopically, present a zone of newly-formed connective tissue around the central dilated vein. In this zone of fibrillar tissue there exist cells with an oval nucleus. The hepatic cells are atrophied, finely granular, and often reduced to a mass of albuminous and fatty granules. The capillaries are not always so much dilated as in the preceding stage. This state constitutes a sclerosis around the hepatic vein, or, better, a peri-phlebitis, a thickening of the external coat of the vessel.

In such cases a true cirrhosis is said to exist, comparable to cirrhosis of alcoholic origin; the lesion is not frequent. Recently, however, at the autopsy of a woman who died with stenosis and double insufficiency of the mitral and tricuspid orifices, we found the peri-lobular vessels also surrounded by a zone of sclerosis. There was around some (not all) of the interlobular branches of the portal vein, fibroid connective tissue containing cells of this tissue and forming, upon section, small circles inclosing both the hepatic arterioles and small branches of the biliary canals which accompany the portal vein; but the new connective tissue did not form perfect circles around each hepatic lobule, as seen in well-marked cirrhosis. This red atrophy of the liver has been differently interpreted by writers. Rokitansky considers it a method of recovery from acute yellow atrophy of the liver. This does not seem probable, since recoveries from acute yellow atrophy seldom occur, and an examination

of the changes in the liver of animals poisoned by phosphorus shows a complete regeneration of the hepatic cells after their destruction by fatty degeneration.

As a consequence of hepatic congestion, from stasis of the blood either in the heart or in the venous branches and capillaries of the liver, there is always great interference with the circulation of those organs, the venous blood of which flows into branches of the portal vein. There result sanguineous engorgements of the spleen, stomach, intestines reaching the rectum, often producing varicose dilatations of the veins of these parts, varices of the inferior portion of the œsophagus, of the several parts of the intestines, hemorrhoids, etc. At times ecchymoses are seen, particularly in the mucous membrane of the stomach. When these pathological occurrences exist, there is present during life chronic catarrh of the stomach and intestine, a condition characterized by loss of appetite, vomiting, diarrhœa, at times by a yellowish coloration of the sclerotic, and finally by a certain amount of ascites. These symptoms are always present, in a varying degree, in patients affected with cardiac lesions and red atrophy of the liver.

A very curious and unfrequent phenomenon is sometimes observed in similar cases, which consists in a pulsation of the liver. These pulsations, synchronous with the venous pulse of the heart, were referred by Potain to an insufficiency of the tricuspid valve.

Congestion of the liver may be due to traumatism. Sometimes the injury is so severe as to cause a bruising of the hepatic substance, with ecchymoses, and even resultant abscesses. In the rare atheromatous lesions of the portal vein, infiltrations of blood are met with after perforation. There may be an aneurismal dilatation and rupture of the hepatic artery of which Lebert has reported an example.

Thus, it is found that congestion of the liver occurs at the beginning of all nutritive lesions of that organ, inflammations, cirrhoses, tumors, etc., and it may constitute of itself a permanent morbid state, particularly in cardiac diseases.

Hepatitis.

Three principal varieties of hepatitis are recognized: *parenchymatous hepatitis*, especially characterized by lesions of the hepatic cells, *suppurative hepatitis*, and *interstitial hepatitis or cirrhosis*.

A. Parenchymatous Hepatitis.—The word hepatitis although objectionable because suggestive of inflammation, which in reality may perhaps have no existence in some of these cases, has been long used by writers. It is on that account that we retain it.

Of all the varieties of parenchymatous hepatitis, the best determined is that known as *acute yellow atrophy of the liver* which corresponds in symptoms to grave or hemorrhagic icterus, typhoid icterus. The symptoms of this affection, which frequently begins as a simple jaundice, and afterwards breaks out with fever, hemorrhages, delirium, and coma, soon terminate in death.

These symptoms, however, do not always correspond to acute yellow

atrophy of the liver. They are seen in a number of liver diseases accompanied with retention of bile. According to some writers, sometimes in idiopathic icterus followed by grave symptoms, there are found at the autopsy none of the characteristic lesions of acute atrophy. In our own observations, however, we have always found the characteristic lesions, when a fatal idiopathic icterus had been the cause of death.

In patients, observed during the short duration of their disease, it may be demonstrated that the liver, of normal or increased size at the beginning of the malady, diminishes in volume during the course of the affection. At the autopsy, the liver is more or less atrophied, according to the duration of the disease; it is softer than normal; the greater the atrophy the more the softening. The capsule of Glisson may be pinched up between the fingers. When the liver is taken in the hands, its softness and flabbiness can be best appreciated. It feels like a semi-fluid mass. The color of its surface is like yellow ochre; upon section the same color and softness are found, and it presents a homogeneous surface owing to the hepatic lobules being uniformly colored.

The gall-bladder and biliary canals contain very little bile, or bile which is slightly colored, or at times even colorless. Microscopic examination of the fluid obtained by scraping, shows a small number of hepatic cells of normal size and shape, containing fine albuminous, fatty and numerous yellow biliary pigment granules. Most of the cells are very much smaller than normal; their edges are thin; they are broken into fragments, and the granular protoplasm of the fragments contains fatty and biliary granules. In places where the softening is very great, none of the hepatic cells have retained their physiological shape or size. The fluid scraped from these places contains only small masses of granulo-fatty and pigmented substance, in the centre of which there is not always a nucleus. The latter has been set free through the softening of the protoplasm of the cell as well as by the mechanical force employed in the method of preparation.

According to most pathological anatomists, the peripheral connective tissue of the lobules and that accompanying the capillaries of the lobules undergoes an albumino-fibrinous infiltration, in which are found escaped lymph cells. This inflammation of the peripheral connective tissue of the lobule is the initial lesion of atrophy, according to Winiwarter, who has seen a patient who died twenty-four hours after the beginning of the disease. He also thinks, with Holm and Hüttenbrenner, that the segmentation of the hepatic cells leads to their transformation into connective-tissue cells. This we believe to be an error. We have never seen thickening or notable inflammation of the peri-lobular connective tissue in this disease.

At the autopsy of one case, we observed around the hepatic lobules the network of biliary canals penetrating into the external third or half of the lobule. In this case the acute yellow atrophy was chronic and had reached to a very advanced stage in the destruction of the hepatic cells. Thin sections showed the canals in the midst of a fibroid tissue. The hepatic cells had entirely disappeared, and there remained only the capillaries and fibrous framework of the lobule. The larger interlobular biliary canals were characterized by the existence of a structureless mem-

brane lined by small cubical epithelial cells. From these canals smaller canals had their origin, in which the membrane was more difficult to see, and which were lined and entirely filled with the same cubical or more flattened cells. These canals formed a very distinct network in all those parts of the lobule from which the hepatic cells had disappeared, and their cells, which neither contained pigment nor fat granules, were distinctly stained with carmine. They could not be mistaken for hepatic cells or bloodvessels. This demonstration of intra-lobular biliary canals in man was of importance, since up to that time they had not then been injected in the normal state, and their structure had been unknown, although it had been believed that they did not differ from those in the same location in animals. Were these canals normal, and visible only in consequence of the disappearance of the hepatic cells, or were they altered canals dilated and filled with epithelial cells which do not normally exist there? We are inclined to accept the latter view.

Another examination of a liver from a case of acute yellow atrophy, showed the cells, although granular, to be infiltrated with pigment and partly atrophied, but not destroyed. The biliary canals did not present any alteration; the peri-lobular connective tissue was neither thickened nor inflamed.

The blood in this affection is very much richer in corpuscles than in the normal condition; it not only contains a larger quantity of urea than physiological blood, but also a quantity of the less completely oxidized albuminous products, leucin, tyrosin, and xanthin. These substances exist in considerable amount in the blood of the veins of the liver as well as in the general circulation. The liver does not perform its hæmatopoietic functions, the incomplete combustion of albuminoid substances leaves a residue—leucin, tyrosin, and xanthin.

These same substances are found in the urine, which is sometimes albuminous, contains less urea than normal, and is loaded with bile and the coloring substances of the blood. The urine, tinted by the coloring matter of the blood, does not always contain distinguishable red blood corpuscles.

The spleen is constantly swollen and softened.

The heart is flabby, its muscular tissue is in a state of fatty degeneration.

The kidneys are always altered in icterus; the epithelial cells of the tubules are, in places, infiltrated with biliary granules, and the tubules contain hyaline casts, in which are inclosed biliary granules, and which are covered by pigmented cells. Again, in many cases in which albuminuria may or may not exist, during life, the cells in some of the tubules of the cortical substance are found in a state of fatty degeneration. In other words, there exists a slight catarrhal or parenchymatous nephritis.

These lesions of the solids and fluids may seem to explain the symptoms observed in grave icterus. They consist especially in the alteration of the blood. The latter is poor in red corpuscles, and it contains biliary coloring matter, and a quantity of imperfectly oxidized albuminous products, whose presence is due to the fact that the liver does not perfectly perform its functions, and also that the products resulting from the destruction of the hepatic cells are taken up by the liquor sanguinis.

The lesions of the spleen, kidneys, and heart, are the result of this changed composition of the blood.

The symptoms of grave icterus have been attributed to uræmia, but they are very different from the latter. They have been attributed to cholæmia or choletoxæmia, or poisoning by the bile, a theory based upon the hypothesis that bile does not pass into the biliary passages, and that its materials accumulate in the blood. But, if this were true, every retention of bile should give rise to the same phenomena. Finally they have been attributed to poisoning of the blood by cholesterin (A. Flint). The cholesterin, a product produced from the nutrition of the brain, is eliminated by the bile ; in consequence of the suppression of the function of the liver, it accumulates in the blood. But the same objection may be applied here as in the case of cholæmia. Vulpian regards grave icterus as the result of a poisoning of the blood by numerous products, due to the derangement of the hæmatopoietic function of the liver, to the presence in the blood of several principles resulting from the decomposition of nitrogenized and biliary substances. These changes in the composition of the blood account for all the nervous phenomena of icterus and the hemorrhages, as well as for the anatomical lesions of other viscera. In regard to the initial lesion of the liver, we are without a satisfactory explanation of its cause.

Grave idiopathic icterus may be connected with acute yellow atrophy as we have seen, and with parenchymatous hepatitis, observed in certain poisonings and in grave typhoid fever. By a number of its symptoms and anatomical lesions, phosphorus poisoning is closely related to grave icterus. But in this poisoning, fatty degeneration of the cells predominates. In poisoning by antimony and arsenic, the change in the hepatic cells is comparable to that produced by phosphorus, but is less intense.

The infectious diseases, the icterus, with hæmaturia, of warm countries, the febrile diseases, such as pneumonia, tuberculosis, present different degrees of parenchymatous hepatitis, which vary according to the disease and its intensity. The lesions of parenchymatous hepatitis are comparable to those of acute yellow atrophy, but they are less intense and less perfectly marked. Thus in icterus with hæmaturia, the liver, after having been congested and ecchymosed, passes to a state of fatty degeneration of its cells, characterized to the unaided eye by a yellowish tint. The same is the case in yellow fever.

In the liver of typhoid fever, there is frequently observed at the middle or end of the second week a condition of softening, which coincides with the cloudy swelling and lesions of the cells previously described. Later the fatty degeneration predominates, and sometimes, at the end of the disease, instead of the surface being uniform, the lobules are red at their central part and gray at the periphery, in consequence of a stasis of the blood in the hepatic vein, due to the feeble contractions of the cardiac muscle. Parenchymatous hepatitis, as met with in our climate, generally presents a state analogous to that seen in the liver in typhoid fever, with a greater or less intensity. In many cases the blood is more or less altered in the same manner as in grave icterus, by the retention of imperfectly oxidized albuminous substances.

At the autopsy there is found a catarrhal or a slight parenchymatous nephritis, perhaps accompanied by albuminuria, and there are parenchymatous lesions of the muscular tissue of the heart and voluntary muscles.

B. Purulent Hepatitis.—This variety of hepatitis is characterized by the presence of purulent foci, seldom numerous, either small and multiple, as is most frequently observed in our climate, or large, as met with in warm countries. In warm countries abscesses of the liver frequently are the terminations of hepatic congestion and derangement of the biliary secretion; they accompany dysentery and intermittent fever.

Metastatic Abscesses of the Liver.—Purulent infection, severe traumatism, surgical operations, puerperal fever, dysentery, sometimes typhoid fever, and variola in the suppurative stage, etc., are recognized as causes of this lesion. In the latter diseases small miliary abscesses coexist with parenchymatous hepatitis. Their beginning is characterized by a blood-red ecchymotic coloration, or by a yellowish color limited to a hepatic lobule. In the deep red part, due to a filling of all the capillary vessels of the lobule with blood, there soon appears in the middle of the lobule a small white point, which is a small drop of pus scarcely visible to the unaided eye. The pus increases, and suppuration soon invades the greater part of the lobule. Thin sections show the capillary vessels filled with red and white blood corpuscles. Around the capillaries in the accompanying connective tissue are seen escaped white corpuscles. These cellular elements surround and compress the hepatic cells, and cause them to become granular and atrophied, and to break up into granular fragments. Their nuclei become free, or remain surrounded by a small amount of protoplasm, in the midst of pus-corpuscles which fill the spaces between the capillaries. The latter soon undergo alteration, soften and disintegrate within the suppurating focus, and no trace of them is found when the process has involved the entire lobule.

The suppurating foci increase in size by union with neighboring foci, so as to form larger cavities filled with pus. Around the suppurating points the liver is generally fatty, yellowish, and opaque.

Such are the changes which indicate the beginning of metastatic abscesses. An investigation of the anatomical cause and manner of formation of these abscesses may now be considered.

During the past fifteen years the theory of embolism advanced by Virchow has sufficed for most writers. This theory of embolism supposes that in consequence of fibrinous coagulations formed in a vein, and subsequently transported by the circulation, small fragments are arrested in the arterioles and capillaries, and an abscess ensues. But, in this hypothesis, local anæmia, by the interruption of the passage of the blood, should precede the suppuration in the part affected, yet according to the previously described anatomical facts there is no such condition. The congestion was explained by an increase of the pressure in the collateral vessels; but this collateral congestion was insufficient, and scarcely proven. Again, a coagulum is seldom found in the nutritive vessel of the suppurating part; moreover, the coagulum may be a thrombus,

caused by the suppuration, instead of an embolus. Where a vessel, arterial or venous, is found in a purulent focus, the wall of the vessel is inflamed, infiltrated with lymph cells, and its calibre is filled with coagulated fibrin. The demonstration of the presence of an embolus is, therefore, doubtful and difficult.

In the doctrine of embolism applied to metastatic abscesses of the liver there arises another difficulty, the explanation of the formation of the migrating clot. When, for example, there is a wound of a limb as a point of purulent infection, it is in a peripheral vein that the primary fibrinous clot forms to be carried into the right auricle, then into the pulmonary artery and vein, then into the left heart, and finally into the liver by means of the hepatic artery; but in this long course would the fibrinous particles not be arrested in the capillaries of the lung? How explain the formation of abscesses in the liver when none are found in the lung? The theory of embolism as the cause of hepatic abscesses can only be applied to the branches of the portal vein in supposing that the abscesses have their origin in a lesion of the organs from which arise the radicles of this vein.

The theory of diapedesis, or the passing of the lymph cell through the walls of the vessels in suppuration, has given a fatal blow to the doctrine of capillary embolism considered as the cause of metastatic abscesses.

More recently, the view has been advanced that in peripheral suppurations there exist microscopic germs, which are carried away by the blood which contains more than a normal amount of white corpuscles. These inferior organisms and white corpuscles are arrested in the organs and occasion small suppurating foci.

No organ of the economy is so much predisposed to purulent infection as the liver, and especially when the primary seat of suppurating foci is in the bones, particularly the bones of the cranium. Magendie has attempted to explain this marked tendency to suppuration of the liver in wounds of the head, by saying, that in wounds of the head there is, through the communication of the blood with the superior and inferior vena cava, a possibility of a reflux of blood into the superior vena cava as far as the hepatic vein. This hypothesis is contrary to our knowledge of the circulation; but it may be admitted that purulent infection is favored by the arrangement of the osseous veins. It may also be inferred that the diapedesis of the lymph cells and microcytes contained in the blood occurs more easily at points where the circulation is slow. The hepatic circulation, comprising two venous systems, must necessarily be a slow one, and perhaps this is the cause not only of the frequency of metastatic abscesses in the liver, but also of all secondary infectious carcinomatous, sarcomatous, or syphilitic growths. Such is the explanation proposed by Klebs.

Thrombosis and inflammation of the external and internal walls of the branches of the portal vein should not be overlooked in the study of hepatic abscesses, since they are very frequent and very important occurrences. They are met with under the following conditions:—

1st. Thrombosis and phlebitis of the portal vein are observed consecutively to the formation of metastatic abscesses. For example, an abscess

of the liver about as large as a pea or hazel-nut, formed by the union of several miliary abscesses, has its wall limited by connective tissue, and at several points connected with one or more large interlobular branches of the portal vein. Here the connective tissue which forms the external coat of the vein is infiltrated with pus corpuscles; at this point the periphlebitis, by continuity of the inflamed tissue causes an endo-phlebitis and a coagulation of the blood in the interior of the vein—a thrombus. This infiltration of the peripheral connective tissue of the interlobular veins and the resulting suppuration, explains the extension of the abscesses to the neighboring parts; but the thrombosis and periphlebitis are purely secondary lesions.

2d. The thrombosis of a branch of the portal vein may be primary, for example, in consequence of a phlebitis of a branch of the mesenteric vein, in intestinal ulceration and the migration of a fibrinous clot into the branches of the portal vein. When this clot is arrested in one of the hepatic branches of the portal vein, it occasions, by the obstruction of the vessel, an interference of the blood circulation in a number of lobules. It acts as an embolus and is followed by thrombosis of the portal vein. There occurs in the part where the circulation is arrested, neither intense congestion, nor hemorrhage, nor pus, as seen at the beginning of miliary metastatic abscesses, but a local anæmia of the part which is drier, grayer, and whose cells have undergone a granulo-fatty degeneration. There is simply an infarctus, similar to those observed in the spleen and kidney of old persons, or seen in the course of valvular diseases of the heart. In the liver, these infarcti are not followed by suppuration any more than they are in the kidney. Similar infarcti of the liver are very unfrequent, a circumstance explained by the fact that in the liver, when the portal vein is obliterated, the hepatic artery may continue to nourish the affected part, while in the kidney and spleen there exists only one kind of nourishing vessels, the renal and splenic arteries. At least in our climate emboli of the portal vein seldom seem to cause abscesses in this way. In warm countries, however, several writers believe that the large abscesses may be due to softening and molecular destruction of a part of the liver in which the small portal veins have been obliterated, for example, in the same manner as large pulmonary cavities follow the mortification of a considerable amount of lung in caseous pneumonia. We have had no personal experience relative to this mode of formation of large abscesses of the liver, and the observations collected in warm countries are not exact enough to convince us upon this point.

3d. Purulent inflammation of the portal vein, or *suppurative pylephlebitis*, is better known to us. This is a disease quite common in our climate, and we have been able to study several examples. In this affection the suppuration takes place within the portal vein, the internal coat of which is inflamed and suppurating. This lesion is the origin of abscesses found in the liver in these cases. The abscesses do not arise by emboli, but by a suppurative phlebitis.

The cause of these suppurative inflammations of the portal vein is well known since the labors of Dance, Cruveilhier, Frerichs, etc., have

been published. We know that almost always pyle-phlebitis is secondary to ulcerations of the intestines, especially of the large intestine, in typhlitis and dysentery. Sometimes it has been secondary to an abscess of the spleen and a phlebitis of the splenic vein. In one case it was provoked by a fish bone, which came from the stomach or duodenum and lodged in the portal vein. A phlebitis of one of the afferent branches of the trunk of the vein extends to the trunk and hepatic branches of this vein.

When the trunk of the portal vein is opened, it is found filled by a fibrinous coagulum or by a puriform fluid which is continued into the hepatic branches of the portal vein. In the more serious cases, the majority of the large branches of the vein are filled with thick pus mixed with granular fibrin; the calibre of the diseased vessels appears enlarged; and in several parts of the liver, along the branches of the middle and small sized veins, true oval, round, or irregular abscesses are found, the walls of which, instead of being formed by the coats of the vein, are constituted by the hepatic tissue after the suppurative destruction of the vascular wall.

Thin sections perpendicular to the direction of the portal vein, at a point where it is filled with pus, including the vein and neighboring parts, show the internal coat of the vein thickened, roughened, and infiltrated with lymph cells. The middle coat is equally changed, as is also the external coat. The peri-phlebitis extends to the peripheral connective tissue, the fasciculi of which are separated by lymph cells. The swelling of the venous walls and surrounding connective tissue causes the vein to be considerably increased in size and to compress the neighboring hepatic lobules, which are flattened, as well as their cells, in a direction perpendicular to that of the pressure.

In the parts where the abscesses are larger in diameter, the suppurating focus, having first destroyed the internal coat of the vein, forms a cavity filled with pus. The middle coat resists a longer time, but is ultimately destroyed by a continuation of the suppuration, which is now limited by the inflamed connective tissue of the external coat and the indurated hepatic connective tissue which surrounds it.

By this suppurative and destructive process of the walls of the vein, the pyle-phlebitis may occasion abscesses which for a time are limited by the neighboring hepatic lobules. This is especially seen in the small branches of the portal vein, since here the venous walls are less resisting than in the large trunks.

Around the abscesses, where the venous wall is partly or completely destroyed, and further along the course of the diseased venous branches, there is always a new formation of embryonic connective tissue, which accompanies the small divisions of the portal vein and surrounds them like a sheath. When, therefore, a thin section of a liver containing abscesses is examined, the prismatic spaces which separate the lobules are seen to be replaced by a circular zone of connective tissue infiltrated with round cells, in the middle of which pass the inter-lobular portal branch, the inter-lobular biliary canaliculi, and the branch of the hepatic artery.

4th. The portal vein is not the only vessel of the liver which may be the seat of thrombosis and inflammation. Recently we studied a specimen of metastatic abscesses of the liver secondary to a fatal paronychia (whitlow). The abscesses measured from 5, 10 to 15 millimetres in diameter. They contained a yellowish-gray detritus formed of granular hepatic cells and pus corpuscles. Surrounding them were lobules, which, to the unaided eye, appeared yellowish in color, and infiltrated with pus. These lobules retained their shape; the blood capillaries and hepatic veins, the central vein of the lobules and interlobular veins, were filled and distended by white corpuscles and coagulated fibrin. The hepatic cells of the lobules were somewhat atrophied, and, in places, the trabeculæ of hepatic cells were represented only by cells compressed and flattened between the neighboring capillaries. There were lymph cells and fibrin in the capillaries, yet there was no suppuration of the surrounding connective tissue of the capillaries. This was readily appreciated because of the preservation of the capillary walls and their endothelial lining, which separated the vascular contents from the hepatic cells. Between the wall of the capillaries and the atrophied hepatic cells there were also lymph corpuscles which had passed out of the vessels, as well as granular fibrin. The intra-lobular veins and the enlarged small branches of the hepatic vein were also distended and filled; their walls were also infiltrated with lymph cells. There was then a phlebitis and thrombosis of the hepatic vein. The perilobular branches of the portal vein and the hepatic artery were normal. If we admit, which is very probable, that the initial lesion of the abscesses has been the same as that of the neighboring parts, we recognize as a cause of these abscesses a thrombosis of the capillaries of the lobules and of the hepatic veins, followed by atrophy of the hepatic cells and a suppurative destruction of all the parts deprived of blood.

5th. *Biliary Abscesses.*—Almost the only cause of inflammation of the mucous membrane of the biliary passages is the presence of biliary calculi in their interior. The small calculi resembling sand or fine gravel, calculi which are irregular, angular, formed of pigment, cholesterin, and calcareous salts, and which exist in the hepatic canals and their interlobular branches, appear alone to have the power to excite catarrh of these canals.

Catarrhal inflammation of the biliary passages in the liver varies in intensity; sometimes it is limited to the secretion of a slightly turbid mucus, colored by the biliary material, and is accompanied by a certain amount of dilatation of the canals which frequently have ampullar enlargements along their course. The fluid contains lymph cells, cylindrical cells, biliary pigment, and fine granules. It is in inflammations of this kind that biliary abscesses of the liver most frequently occur.

In other cases, the inflammation of the biliary passages is very intense, and the dilated canals are completely and uniformly filled with a thick, whitish, opaque fluid, like muco-pus or pus. Only pus corpuscles might be expected to be found in this fluid, but these round cells are very much less numerous than are the cylindrical cells of the biliary passages.

These cells are frequently altered; they are infiltrated and distended with a mucous fluid, or they contain several nuclei.

In some livers thus altered, the hepatic ducts are filled with pus, and are frequently as large as the finger, at first sight appearing like abscesses developed in the parenchyma, but upon opening them carefully, it is seen that the pus has not passed beyond the walls of the biliary passages. It is in the less intense and slower inflammations rather than in these last cases of intense inflammation, that we have met with biliary abscesses. The cavities are formed by dilatations of the biliary ducts, and are filled either with mucus or muco pus or pus. Their wall is either smooth and consists of the mucous membrane of the duct; or it consists of connective tissue of new formation, the wall of the duct having been destroyed by suppurative inflammation, while the neighboring connective tissue is infiltrated with lymph cells.

The fluid within the abscesses always contains, besides the lymph cells and biliary pigment of a sandy nature, a varying number of cylindrical cells. It is these free cylindrical cells in the fluid of the abscess which are characteristic of it. In true purulent abscesses of the hepatic substance, atrophied, granular and fatty, hepatic cells may be met with, but cylindrical cells are not found. Another anatomical characteristic of these abscesses is, that they communicate with the biliary canals.

Large Abscesses of the Liver.—Idiopathic abscesses of the liver of a large size, are seldom seen in this climate. Whether they arise from an embolus or thrombus of the portal vein which completely interrupts the circulation, is not yet sufficiently known. The necrosed tissue is subsequently softened, and is surrounded by a purulent inflammatory zone, in such a manner that the necrosed and bloodless part is ultimately transformed into a large abscess.

Any of the acting causes which have been previously mentioned may, in warm climates, be followed by the formation of large abscesses; even intermittent fevers, long-continued congestions, or imperfect secretion of bile may in warm countries develop abscesses of the liver.

These abscesses have irregular walls which are formed of hepatic tissue. The thick pus contained in them is yellowish in color and granular, is composed of lymph corpuscles, and altered hepatic cells. A few pulpy, softened fragments of hepatic tissue infiltrated with pus are found adhering to the wall of the abscess. This is the first stage in the formation of the abscess. Later the surface of the cavity becomes smoother, when all the suppurative parts of the liver are softened and detached; the internal surface of the abscess is then formed of embryonic connective tissue, which surrounds the abscess and extends, for some distance, along the branches of the portal vein and inter-lobular tissue. This wall of embryonic tissue is more or less vascular, and its surface is more or less irregular; at times its surface presents true granulations; it then constitutes a soft pyogenic membrane, analogous to that which covers ulcers. The abscess may subsequently increase in size from the suppuration of the pyogenic membrane and surrounding inflamed connective tissue. As this tissue is continuous with the peripheral connective tissue of the portal vein, there is always a peri-phlebitis, and generally also an endo-

phlebitis, with the formation, at the inflamed point, of a fibrinous clot. All this tissue may be entirely destroyed by the suppuration, in such a manner that the abscess may be enlarged by a lateral extension along the branches of the portal vein. It is also readily understood how a phlebitis may be excited secondarily in a branch of the portal vein, and become the starting point of one or more secondary abscesses in the proximity of the primary abscess.

The internal wall of the abscess is gray, or pinkish-gray, in color. Cruveilhier has seen gangrenous abscesses. It is possible that a true gangrene due to interruption of the circulation of the blood may be present at the beginning and in the later stages of the abscesses; but the changes of color in the connective tissue and glandular tissue surrounding the abscesses, described by writers, should be mistrusted. The slaty or greenish colorations are almost always the effect of post-mortem decomposition which occurs so rapidly in tropical climates.

When the abscess ceases to enlarge, the pyogenic membrane becomes smoother, more fibrous, and the neighboring connective tissue is thickened and becomes more dense. There is now a true fibrous membrane, which is frequently quite thick and tough, formed of layers of connective tissue; we have in this case a true encysted abscess.

In the more chronic abscesses the pus varies in color from yellowish-brown to chocolate, depending upon the amount of blood, and the fatty, granular infiltration of the lymph cells.

These large abscesses may be located in any part of the liver; but they are more frequently found in the right lobe, and especially in its thicker part—that is, at its right extremity, or upon its superior surface, near the diaphragm. They have, like all collections of fluid with equal pressure upon their walls, a tendency to assume a spherical shape when they are chronic. The hepatic tissue is easily pushed aside and flattened by the pressure of the abscess.

The amount of fluid, as well as the size and number of abscesses, varies very much. The largest are generally single; they may contain from 100 grammes to one or even two litres of fluid.

By its development and progress, an abscess at the periphery of the liver has a tendency to open spontaneously; most frequently it points upon the superior surface of the liver at the diaphragm, or at the border of the true or false ribs, or a little below upon the abdominal wall. When the abscess is covered only by the capsule of Glisson, and is thus connected with the peritoneum, there occurs a local peritonitis, and the presence of the abscess is soon made known by the œdema of the abdominal or thoracic walls, and by the sensation of fluctuation. If the abscess now breaks into the connective tissue surrounding its wall, it may occasion the formation of purulent sinuses, which may pass along the false ribs and extend upon the side as far as to the axilla, or anteriorly to the middle of the thorax. These collections of pus should be soon opened, or if the diagnosis of abscess of the liver is well established, an adhesive peritonitis and opening of the abscess should be caused by the application of Vienna paste.

When the abscess points at the diaphragm, it may occasion beneath the latter an adhesive peritonitis, and an adhesive pleuritis above it, with

a pneumonia at the same point, so that the cavity of the abscess may, after the destructive suppuration of the diaphragm, inflamed pleura and lung, communicate with the cavity of a bronchus. This termination, as well as that externally through the abdominal wall, is one of the most fortunate, not more than one-half being fatal.

But instead of causing an adhesive pleuritis, the hepatic abscess may occasion a pleuritis with considerable effusion, when the abscess perforates the diaphragm, and is emptied into the pleural cavity. This purulent pleuritis may occasion a pneumonia and a perforation of the lung, through which the abscess may be evacuated. But this method of evacuation of the pus is not so favorable as the preceding, since it leaves behind a pleuritic cavity which is only imperfectly emptied, and often a purulent collection, between the diaphragm and the liver, remains. In these several cavities are contained a sanious fluid and gases, which give the same physical signs as pyo-pneumo-thorax.

The abscesses may also open into the peritoneum and excite a fatal peritonitis; or into the stomach, the duodenum, or colon. They have very rarely opened into the pericardium, causing immediate death; or into the biliary canals and bladder, which is very fortunate, since from here the pus may escape into the intestine.

Finally, the liver may be ulcerated when it forms part of the base of a gastric ulcer. From the effects of the gastric juice the hepatic tissue is broken down, and there results a loss of substance. The trabeculæ of connective tissue, which extend from the base of the ulcer around the neighboring hepatic lobules, are hypertrophied, thus constituting a kind of localized cirrhosis in the proximity of the ulcer.

Interstitial Hepatitis or Cirrhosis.—Interstitial hepatitis or cirrhosis is characterized histologically by a new formation of embryonic or adult connective tissue. To the unaided eye it is seen as an induration with hypertrophy or atrophy of the organ, generally accompanied by a granular condition of the surface.

The lesions in interstitial hepatitis are very variable both as to extent and cause. Different cases of cirrhosis, at first sight, may have little resemblance one with another, especially if judged from the shape, color, and size of the organ. This, however, is so of all chronic diseases, which develop slowly from different or variously acting causes.

Partial Cirrhosis.—Interstitial hepatitis is associated with a number of tumors and lesions of the liver. It is then often limited in extent. Thus all tumors consisting of fibrous tissue, such as tubercles, gummata, fibrous cysts developed around hydatids, abscesses, angiomata, etc., are surrounded by a new formation of connective tissue which is continuous with the interlobular connective-tissue septa. When, as at times occurs, an eruption of miliary tubercle or of small gummata in newborn children is diffused throughout the liver, there naturally follows a variety of cirrhosis, which extends through the greater part of the organ. Sometimes, in chronic inflammations of the biliary canals or portal vessels, the connective tissue which accompanies them is also seen to be inflamed and thickened. This occurs in inflammation from the presence

of calculi in the biliary canals, in pyle-phlebitis, etc. We have several times observed cases of pigmented liver, in consequence of malarial cachexia and melanæmia in children. In two cases the blood in the portal vein was loaded with white corpuscles containing black pigment. In one the wall of the interlobular branches of the portal vein was thickened, especially the external coat, in which were seen flat or stellate cells containing black pigment. The connective tissue around the lobules was almost everywhere more marked than normal, and was also pigmented. In another case, all the branches of the portal vein were surrounded by a zone of embryonic connective tissue containing pigment in a few of the cells. Upon section of the liver, small islands, rich in round cells, were seen. In the middle of these islands was found the section of a small vein. This may be explained by the irritation of the vascular walls which was caused by the black pigment carried by the blood, and which extended by continuity of tissue to the neighboring connective tissue. The pigmented embryonic cells which were found in this tissue may also be considered as pigmented white corpuscles escaped from the portal vessels.

By reviewing the cases in which chronic inflammation of the connective tissue occurs sometimes around the biliary canals, sometimes around the branches of the portal vein, in pyle-phlebitis, in malarial cachexia, sometimes around the hepatic vein, as has been mentioned under red atrophy of the liver, it is seen that there exists a variety of cirrhosis in which the zones of new connective tissue surround the branches of the different vascular systems of the liver. The portal veins, biliary canals, and hepatic veins may thus be accompanied by sheaths of fibrous tissue, either in a portion or throughout the whole of the liver. These partial cirrhoses are very frequent, and upon section of the liver are characterized, to the unaided eye, by small grayish points or zones which surround the vessels; but a more minute examination is necessary in order to determine whether it is the biliary canals or the bloodvessels which are the seat of the lesion.

General Cirrhosis.—The cirrhoses which involve the entire liver are generally due to alcoholism or to syphilis. Sometimes they follow intermittent fevers, or a residence in warm climates, in patients in whom alcoholism has had considerable influence in connection with fever or with dysentery.

From the effects of repeated congestions, and of the irritation caused by the passing of alcohol through the branches of the portal vein during digestion, there results a permanent inflammatory state of the connective tissue in contact with the vascular walls. Around the interlobular vessels, in the prismatic spaces which separate the lobules, there are now seen areas of tissue rich in white corpuscles; this tissue is continued around the entire lobule. This alteration takes place at the beginning of all the different varieties of cirrhosis.

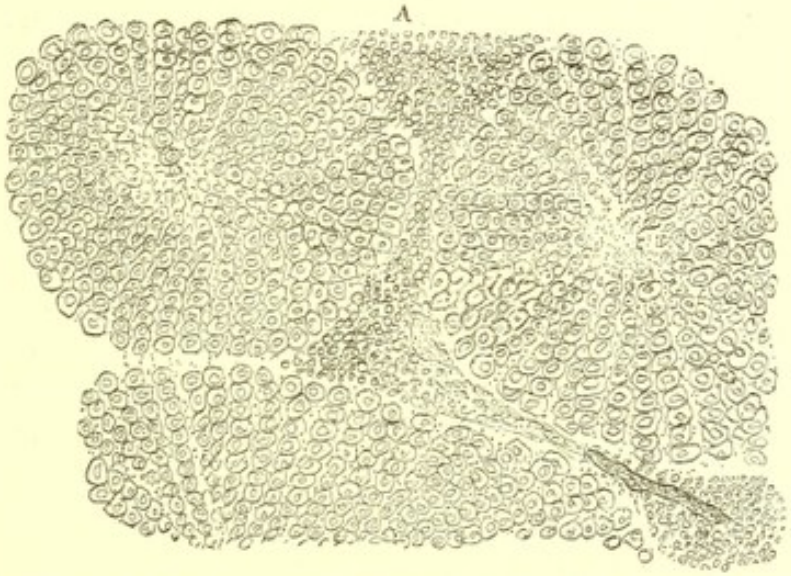
It is difficult to believe that the lesions of all cirrhotic livers follow the same regular course. In a number of cases the liver is smooth upon its surface (*hepatitis glabra* of Klebs), and is either hypertrophied or normal in size. In other autopsies, the organ, either much hypertrophied or of ordinary size, has a granular surface. Finally in cases which

serve as a type for the first descriptions of cirrhosis, the gland is both atrophied and granular.

To these differences in size and shape of the liver, are to be added the changes in the hepatic cells, which are sometimes fatty, sometimes infiltrated with bile or blood pigment, causing a red, yellow, or greenish coloration of the liver.

A. Cirrhotic Liver with a smooth surface.—The liver may have preserved its normal size and shape. The surface is smooth, and, upon section, it presents varying appearances; sometimes it is of a uniform yellowish-brown, or it offers yellowish or gray points, or the periphery of the lobules presents reddish lines which become gray and semi-transparent after washing. The resistance to the pressure of the nail is variable, at times the tissue is firm, or it breaks down quite readily. In examining thin sections with the microscope, the prismatic spaces which separate the

Fig. 289.



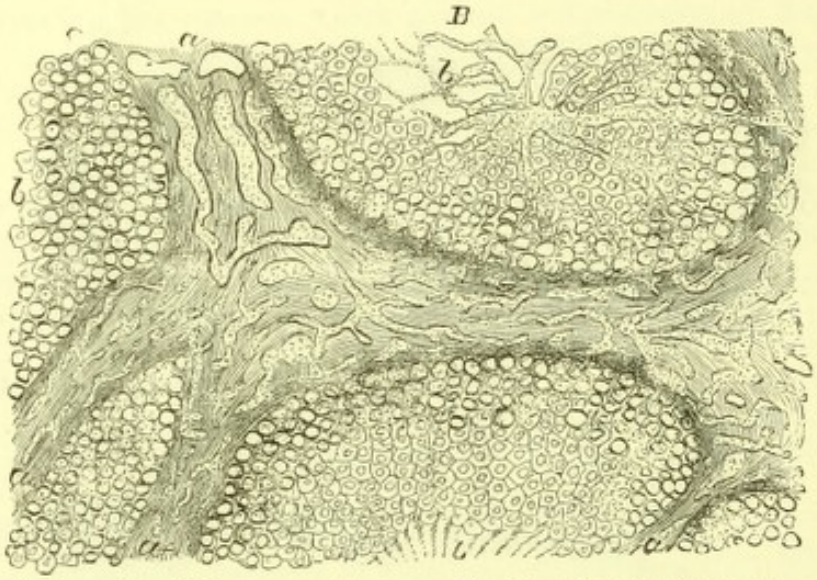
Indurating inflammation of the liver, first stage. *a*. Lumen of interlobular vessels in whose environs there is a small-celled infiltration. *b*. Lumina of intralobular vessels. × 300. (*Rindfleisch.*)

lobules are thickened and show round embryonic cells. When the process is recent, as in newly born syphilitic children, or in adults where death has resulted from some other cause than the liver lesion, the peri-lobular tissue is slightly resisting, since it is composed mostly of cellular elements and contains few fibres. We have examined several cases of this kind in children, and have seen embryonic tissue following the capillaries of the portal vein in the interior of the lobules between the hepatic cells. There is now a diffused hepatitis involving to a certain extent the lobules as well as the interlobular tissue. In the variety of syphilitic liver described by Gubler (miliary interstitial hepatitis), the small semi-transparent or yellow granulations, which are seen by the unaided eye, consist of a collection of small embryonic cells. They are small gummatous nodules. Frequently there is seen in the liver of newly born children a similar

naked-eye appearance, which is due simply to a fatty degeneration of the hepatic cells.

The cirrhotic liver with a smooth surface occurring in adults, may or may not be hypertrophied. It is generally indurated and resists pressure by the nail. This is owing to the new connective tissue which separates the lobules, being dense, and consisting of fibres. While the friable tissue of recent cirrhosis is embryonic, composed of vessels with embryonic walls, and round cells with a soft fibrillar intercellular substance, the tissue of chronic cirrhosis consists of a dense, fibrous substance, composed of longitudinal fibres or of a laminated network of fibres. Between the fibres are found flat cells, and frequently also numerous round cells analogous to lymph corpuscles are seen, possessing a single nucleus, and situated between the fibres, or in round, oval, or elongated spaces with the fibres arranged in a network between them (Hayem). In this dense tissue run the bloodvessels belonging to the interlobular

Fig. 290.



Indurating inflammation of liver, second stage. *a*. Broad bands of interlobular fibrous connective tissue, which is very rich in vessels without distinct walls, and is bounded towards *b* by an interrupted layer of young connective tissue. *b*. Groups of lobules of the liver with their periphery infiltrated with fat. × 200. (*Rindfleisch.*)

branches of the portal vein; their wall blends with the sclerosed tissue. This kind of tissue is very abundant in cirrhosis with hypertrophy, it more or less regularly surrounds the hepatic lobules, in such manner that upon section wide bands of it are seen between the lobules. The latter are frequently thus separated and their cellular parenchyma encroached upon, either at the edge of the lobules, where groups of hepatic cells are isolated from the rest of the lobule, or even in the middle of the lobule where such isolated groups may be formed. It generally follows the course of the intra-lobular capillaries, and, by compression, causes an atrophy with flattening of the hepatic cells, which are thin and granular. At other times the lobule is divided by one or two bands of thick fibrous tissue, and the groups of hepatic cells which remain have a spherical outl ne.

In cirrhosis with hypertrophy, the liver is frequently smooth and is considerably increased in size; but in other cases, it is somewhat irregular, lobulated, or granular upon its surface, while the organ is also enlarged and granular.

B. Granular Liver; Hobnail Liver.—The granular state, which always indicates a certain amount of contraction of the newly-formed tissue also always coincides with an excess of fibres and a density of the tissue.

As has been demonstrated by Cruveilhier, the granulations of cirrhosis have at times the size of normal lobules; at others, they are larger or smaller. He thought that cirrhosis consisted essentially in an atrophy of numerous lobules, occasioned by pressure from thickening of the fibrous tissue, while some lobules were hypertrophied in order to take the place of those which were atrophied.

The atrophy of the hepatic lobules is only apparent. When a large lobule is examined, its cells are always changed and most frequently distended by oil drops. Upon section of the liver, the cirrhosed granulations—that is, the hepatic lobules—when they are in a state of fatty infiltration, have a yellowish-fawn color, from which Laennec has named the disease cirrhosis. They are surrounded by bands of a semi-transparent, gray, or pink tissue, the color depending upon the amount of blood and the fibrous structure which constitutes the essential lesion. If the hepatitis is diffused, extending throughout the entire lobule, the perilobular connective tissue is continuous with that of the interior of the lobule and cannot be separated from it; but, if the lobule is not implicated in the fibrous thickening, and especially if it is infiltrated with fat, it may easily be enucleated from the surrounding fibrous tissue. This condition has been fully described by Gubler, who remarked that the larger granulations are most readily separated from the fibrous tissue around them. But these large granulations, which to the unaided eye appear homogeneous and formed of a single lobule, are constituted by a number of hepatic lobules, which have their connective tissue almost normal, while the entire group is surrounded by a thick fibrous envelope.

Cirrhosis with Atrophy.—The cirrhosed liver atrophies in proportion to the duration of the disease and to the organization and contraction of the newly-formed fibrous tissue. It may contract to two-thirds, one-half, or one-third its normal size. The granulations seen upon its surface or upon section of the organ are generally regular and small, yet at times they are quite large. The fibrous connective tissue separating the lobules is very resisting; it is impossible to tear the hepatic parenchyma by pressure with the nail, and the new tissue is also elastic, so that the organ may be stretched without rupturing. Connective tissue fibres predominate in the new tissue, and between these fibres no collections of embryonic cells are found. All the cellular elements interposed between the fasciculi of fibres are flat or stellate and provided with a flat nucleus. The liver is usually anæmic; its lobules are fatty infiltrated, and yellow, or they are colored by bile or blood pigment.

When cirrhosis due to malaria reaches the atrophied stage, the thick-

ened connective tissue, and especially that around the branches of the portal vein, is the seat of black pigment granules situated in the connective-tissue cells.

From the preceding description, it is seen that the structure, the distribution and amount of sclerosed tissue vary very much according to the condition of the liver at the beginning of the cirrhosis, whether in the smooth, hypertrophied, granular, or atrophied liver. Since the diseased organ is seen but once and only at a certain period of the evolution of the disease, it cannot be positively affirmed that the condition found at the autopsy has been preceded or would have been followed by certain different stages, yet what is known regarding the changes of connective tissue authorizes us to believe that this tissue in the liver is at first embryonic, and afterwards becomes dense and fibrous and tends to contract. It may also be inferred that cirrhosis with hypertrophy, characterized by a great abundance of embryonic connective tissue, represents the first stage of cirrhosis.

The *fibrous covering* of the liver is always thickened and difficult to detach in cirrhosis. To the unaided eye the projections of the capsule of Glisson, penetrating deeply between the granulations, have a whitish or pink color. Upon the surface there are seen extensive cicatricial depressions, both in syphilitic and non-syphilitic hepatitis; but they are never so deep, so hard and puckered as those occurring in syphilitic gummata.

The hepatic peritoneum is exceptionally intact in well-marked cirrhosis with hypertrophy or atrophy. Sometimes, and in cases where there is a slight peritonitis, there are seen, upon the surface of the liver, especially in the depressions between the lobes, small granulations or villous filaments scarcely visible to the unaided eye; sometimes there are fibrous, laminated, false membranes, which float free upon the surface or which are attached by adhesions to the diaphragm or neighboring organs. Occasionally these false membranes are covered with fibrin. The peritonitis, when it is somewhat acute, may be general and may frequently occasion slate-colored or blackish ecchymoses.

When a thin section, perpendicular to the surface of the capsule of Glisson, and including the small vegetations upon the peritoneum, is examined microscopically, there is seen a thickening of the capsule which is formed of horizontal layers of connective tissue; upon its surface the vegetations of the serous membrane are observed to be continuous with the connective tissue of the peritoneum which covers the capsule of Glisson. The vegetations are sometimes sessile, sometimes long and thin; they may divide and sub-divide at their free extremity, or unite with a neighboring filament to form an arch.

These vegetations are composed of fasciculi of connective tissue, separated by flat cells, or at times one is formed of a single fasciculus, very fine, very long and slender. Most of the large vegetations contain blood-vessels, the smallest do not always possess them; all are covered with endothelial cells, which are collected in thick layers upon the surface of the vegetations. These cells are swollen, their protoplasm is increased and more granular than in the normal cells of the peritoneum; they resemble the enlarged endothelial cells of the inflamed peritoneum.

The vessels of these vegetations and adhesions are filled with the injecting fluid when it is thrown into the portal vein. These vegetations often form the adhesions with the neighboring organs and thus favor the return of the blood from the portal vein to the heart by a collateral circulation.

Condition of the Vessels and of the Circulation of the Liver in Cirrhosis.—In acute cirrhosis with embryonic tissue, the interlobular branches of the portal vein are surrounded by round cells, which are thought to be leucocytes, and numerous round cells infiltrate the external coat of these veins. In the lobules, the connective tissue which accompanies the capillaries is infiltrated with the same elements. The capillaries and small bloodvessels experience the same change as in inflammation; the cells forming their wall are swollen; they become embryonic, and the tissue has a softness and friability which it did not previously possess.

The peri- and intra-lobular portal vessels and small branches of the hepatic artery found in the connective tissue or embryonic tissue of acute cirrhosis, may be greatly dilated, and cause a large portion of the liver to resemble erectile tumors.

In the cirrhosed portions, in some places there exists a true cavernous tissue, the irregular lacunæ of which are, like the capillaries, dilated and filled with blood. The walls of these vascular sinuses are formed by the neighboring connective tissue and their internal surface is lined by a layer of flat cells. The same lesion is found also in a number of hepatic lobules; the capillaries of the lobules being enlarged and filled with blood, atrophy and fatty degeneration of the hepatic cells by compression from the dilated vessels follows. It seems that the presence of soft embryonic tissue favors the dilatation of the vessels. The branches of the portal vein and hepatic artery are permeable to blood, while, on the contrary, the circulation in the capillaries of the lobules is impeded; the pressure of the blood dilates the smallest vessels which remain permeable, especially when they are seated in a soft embryonic tissue. It is under such conditions and in such a tissue that cavernous angiomata of the liver are developed.

Later, when the cirrhotic tissue has become dense and resisting, the bloodvessels are still very numerous and large in diameter, with walls formed only of the neighboring connective tissue. There are a few sinuses which are channelled in the indurated connective tissue, the walls of which are blended with the neighboring tissue. In the wall of the interlobular branches of the portal vein there are no contractile or elastic elements to force the blood into the capillaries of the lobules; their external and middle coats are wanting, there remains only a layer of endothelial cells lining a canal which is neither contractile nor elastic.

It is easily understood how insufficient is the circulation of the blood with the portal vein in this condition. The cardiac impulse and *vis a tergo* are scarcely present in the veins from the intestine and spleen which unite in order to form the trunk of the portal vein. When the hepatic branches are deprived of elasticity and contractility, it is evident then that the blood must pass with difficulty through the capillaries of the

lobules. This is what occurs during life, and causes the interference of the circulation in the portal vein.

The causes of ascites are: 1st, the preceding structural alterations of the wall of those branches of the portal vein included in the cirrhotic tissue; 2d, the obstruction of a number of capillaries of the lobule by extension of the cirrhosis to the cellulo-vascular tissue of the lobule; 3d, the obstruction of a number of interlobular branches. Thrombi have been found to a greater or less extent in the portal vein in cirrhosis. According to Rindfleisch, the blood of the hepatic artery has a pressure evidently very much above that of the blood of the portal vein, and takes the place of the latter in all parts of the sclerosed tissue where it is obliterated, so that the system of blood canals of the cirrhotic tissue is mainly supplied by arterial blood. It is from this arterial blood that the bile is elaborated. This proposition seems to us too positive, after having studied several injections which we have made into the portal vein in such cases. The injected fluid passed very rapidly through the vessels at the periphery of the lobules, and from thence it passed into the accessory portal veins, and into the veins of the adhesions which united the liver to the diaphragm; but frequently the capillaries of the lobules were injected through the portal vein. In the later stages of cirrhosis, that blood of the portal vein which does not pass through the hepatic lobules, escapes partly by the vessels which traverse the adhesions formed between the liver and diaphragm (Kiernan), and partly by the greatly dilated system of accessory portal veins described by Sappey. Sappey, from his investigations, concludes that the blood of the portal vein is, in cirrhosis, returned into the inferior vena cava by the greatly dilated accessory portal veins, after having occasioned dilatation of all the anastomosing veins, subcutaneous abdominal, internal mammary, etc. A small vein in the suspensory ligament of the liver, and in the atrophied umbilical cord, is of special importance. It extends from the sinus of the portal vein to the femoral artery, sometimes following the subaponeurotic veins, sometimes the subcutaneous abdominal veins. The direct current beneath the skin is evident by a sensible thrill given to the hand, and a murmur perceptible by the stethoscope (Sappey). The manifest insufficiency of this collateral circulation for the blood of the portal vein explains the ascites, which gradually increases notwithstanding the aid of the accessory portal veins.

In a case of cirrhosis examined by us, there were found between the hepatic lobules, large, cylindrical, lymphatic canals, measuring from .2 to .5 mm., situated in the middle of the sclerosed tissue, and filled and distended by lymph cells.

The *biliary passages* are not always changed in cirrhosis; especially is this the case with the large vessels. The bile is normal in appearance; it is, however, generally more watery and less colored than in the physiological state. It is secreted in sufficient amount, a fact which was remarked by Bichat in tumors of the liver, which he described by the name of steotomata, and which have been carefully noted by every writer who has studied the pathological anatomy of cirrhosis. The

biliary canals visible to the unaided eye do not usually present any notable change; yet they may be dilated in places. Gubler insists upon this dilatation, which he compares to the dilatation of the bronchial tubes in cirrhosis of the lung or interstitial pneumonia. The canals, instead of being dilated, may be contracted by the cicatricial tissue, and a retention of bile occasioned in the small interlobular canals and in the hepatic cells.

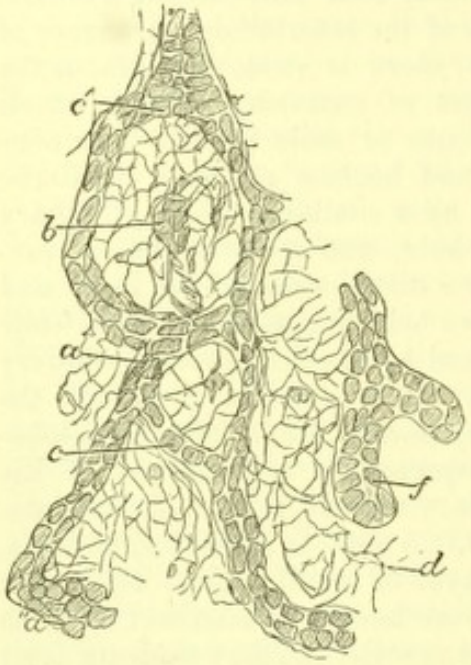
In cirrhosis with an abundant formation of sclerosed tissue, the interlobular biliary canals, with their lining of small cubical cells, are well preserved. Instead of finding, in the cellular zone surrounding a lobule, a single biliary canal accompanying each of the interlobular branches of the portal vein, as in the normal state, there is seen, throughout the breadth of the sclerosed zone, a system of numerous biliary canals forming a network. In portions where one or more lobules have completely or almost entirely disappeared and become replaced by dense connective tissue, the latter is traversed by a similar network of biliary canals, forming fine meshes within the lobule, and at the periphery presenting larger canals, calling to mind the distribution of the inter- and intra-lobular biliary vessels. Therefore we believe that in cirrhosis, while the hepatic cells are atrophied and replaced by fibrous tissue, the biliary canals remain, and become very distinct. It is possible then that the biliary canals seen in cirrhosis are only normal inter- and intra-lobular canals made more distinct in consequence of the atrophy of the parenchyma. Only the interlobular biliary vessels in man are well understood; they measure from 0.020 to 0.025 mm. in diameter, and possess a basement membrane lined by a layer of small cubical cells. In animals, the intralobular biliary canals have been well studied; in them they consist of delicate canals not possessing cells, and they measure from .0013 mm. to .0028 mm. in diameter (see *ante*). This system has not been satisfactorily studied in man. The biliary canals so numerous in cirrhotic tissue in which they form a network, are very similar in diameter and constitution to the interlobular canals, and do not correspond to the description of intralobular canals of animals. The meshes which they form in the new sclerosed connective tissue, are also larger at times than the narrow meshes of the intralobular canals of animals. It is not a question simply of normal canals made apparent by the disappearance of the hepatic cells; but it is also possible that, at the beginning of the cirrhosis, the pre-existing canals, situated in an inflammatory tissue, increase in length and number by an extension of the epithelium, which nominally exists in the peri-lobular canals with which they communicate.

When the thickened connective tissue which separates several lobules in cirrhosis with hypertrophy is examined, there is frequently seen, in the centre of the area occupied by the connective tissue, one or more large biliary vessels surrounded by zones of embryonic tissue consisting of round cells. There is now a true inflammation around the canaliculi. In the interior of the latter there is found a row of cylindrical cells and similar desquamated cells filling the lumen of the vessel. The vessel is generally dilated, and there is a true catarrhal inflammation of the

interlobular biliary ducts, very probably secondary to the inflammation and embryonic state of the connective tissue of the liver.

Examined with a high power, the network of biliary canaliculi situated in the newly formed connective tissue, is seen to be very regularly arranged. In the centre of fibrous tissue bands, run one or two canals having a diameter of 0.020 to 0.040 mm., completely lined with cubical or cylindrical cells leaving a central lumen, empty or filled with detached cells. These canals have a distinct wall, and are surrounded either with round cells or flat cells placed between the fibres of the dense connective tissue. From these principal canals proceed either a smaller network of canals which still retain their complete epithelial lining and a distinct hyaline wall, or of very small canals filled with elongated cells placed end to end. The canals lined with a complete epithelial lining and measuring 0.020 mm. in diameter, can readily be followed into the canals measuring not more than 0.010 to 0.005 mm. in diameter and possessing elongated cells. These cells consist of protoplasm and an oval nucleus. In the smaller canals, they are placed end to end; their protoplasm and nucleus completely filling the lumen. Seeing these canals filled either with rows of elongated cells or by a single row of the same elements, their nature may be mistaken for blood capillaries. But the facility with which their continuation with the large canals lined with cubical or cylindrical epithelium can be demonstrated removes all doubt. The smallest of these canals running around the circumference of the lobules form a very fine meshed reticulum, much narrower than that of the large biliary ducts completely lined with epithelial cells.

Fig. 291.



Network of biliary canaliculi in the newly formed connective tissue of cirrhosis. *f*. Interlobular biliary canal. *c*. Very small canaliculus communicating with other canaliculi also minute and lined with cells placed end to end. These canaliculi empty into larger canals, *a*, *c'*, *a''*. *d*. Connective tissue corpuscle. × 300.

From these facts it may be concluded, in regard to the development of these networks, that by the formation of embryonic connective tissue around the canals, and in consequence of the new formation of cells in the interior of the interlobular biliary canals, newly formed epithelial cells penetrate into the intralobular canalicular networks, which in the normal state do not contain them. (Fig. 291.) There is then a transformation of the smallest canaliculi; they are dilated and filled with epithelial cells. The canals nearest to the healthy part of the lobule have only one row of the cells which fill them, while those canals in the most altered parts have a complete epithelial lining.

In regard to the circulation of the bile, the catarrh of the interlobular canals, the filling of their lumen with cells, as well as the extension

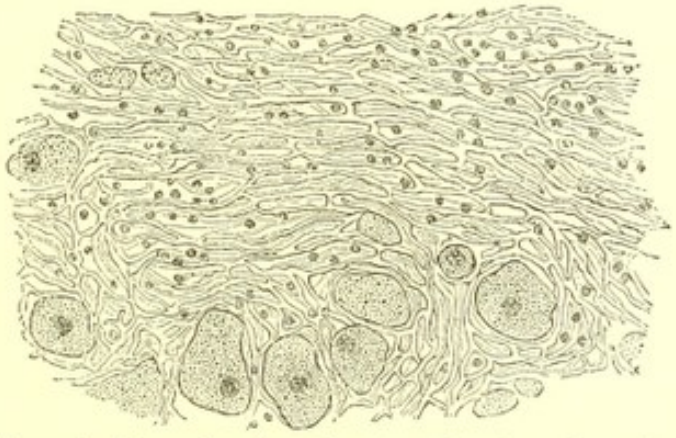
into the biliary canaliculi of cells which do not normally contain them, offer an obstacle to the discharge of the bile. Therefore an icterus, more or less intense, at times sufficient to occasion an infiltration of the cells of the lobules with bile, is observed almost always in cirrhosis with hypertrophy.

The preceding lesions of the biliary canaliculi are also frequently seen at points where there is local cirrhosis from any cause. They have also been observed in syphilitic cirrhosis.

In the hepatic lobules colored a deep olive green, such as are met with in some cases of cirrhosis, with retention of bile, there are seen in the small intralobular canals dark-green contents, while the extralobular canals have a pale greenish-yellow color. A thin section of these lobules, examined under a high power, shows in the interior of the straight and anastomosing canals small cubical fragments, hard, resisting, and of a deep green color. We believe these canaliculi to be intralobular biliary canals containing small calculi of coloring matter, very probably deposited in the cells. As to the interlobular canals, their cubical cells are sometimes faintly colored green from post-mortem imbibition, for the cells of the biliary canals are colorless during life, but become impregnated with bile after death.

Condition of the Hepatic Cells in Cirrhosis.—The hepatic cells present alterations which are very variable, and are evidently secondary to the changes in the connective tissue. In fact the connective tissue changes are always of the same nature, whilst, on the contrary, the liver cells may be at one time normal, or only slightly granular or flattened and atrophied by compression; or the cells may be infiltrated with biliary granules; but most frequently they are filled and destroyed by oil globules. They may contain red or black pigment, or may have undergone amyloid degeneration.

Fig. 292.



Cirrhosis of the liver. A thin section from the external portion of one of the hepatic lobules, showing the new growth of connective tissue, and the way in which it involves the intercellular network and causes atrophy of the liver cells. × 200. (Green.)

The hepatic cells may be found normal not only at the commencement of cirrhosis, which shows that they have but little to do with the origin

of the disease, but the same healthy state of these cells may also be present in very advanced and very intense atrophic cirrhosis. In the latter case, although many of them have disappeared, and some of them have become isolated either singly or in groups among the sclerosed connective tissue, yet those which remain may have a normal nucleus and protoplasm. While undergoing atrophy from the pressure exerted by this perilobular and intralobular connective tissue, the hepatic cells often preserve their original form. In other cases, when the pressure is exercised only in one direction, they become flattened against each other. We have already seen the facility with which entire lobules may change form under pressure.

When the lobules are colored green, as is the case in retention of bile and general icterus which sometimes accompanies atrophic cirrhosis, and not infrequently also hypertrophic cirrhosis, the hepatic cells contain bile pigment under the form of minute granules, and in certain cases the entire cell is colored bright yellow. In carefully treating the preparation with nitric acid the cell becomes more intensely colored and assumes a greenish-yellow tint. The same result is obtained with the solution of iodine. In these colored cells there may be at the same time an accumulation of colorless oil drops, which distends them more or less. It is in these cases of retention of bile that we find the intralobular biliary canals filled with the small greenish concretions which we have previously described.

The alteration of the cells most commonly met with in cirrhosis is fatty infiltration. At the same time there are cells more or less infiltrated with bile or blood pigment. It is the latter alteration which gives to the entire lobule the yellowish or brownish color regarded as characteristic.

The red pigment is often predominant. The cells then contain brown granules and hæmatin, and the lobules present a mahogany-brown color. This condition of the hepatic cells is analogous to what is seen in nutmeg liver, due to increase of blood pressure in the right cavities of the heart, and in the subhepatic veins.

In cirrhosis we sometimes find portions colored black. We should not, however, mistake a cadaveric change for such an alteration in color, for the red pigment readily turns black after death. Many observers have spoken of the presence of black pigment in the connective tissue, or in the hepatic cells in subjects who have or have not suffered during life with intermittent fever. As we have seen above, in chronic malarial poisoning the pigment is especially found in the white blood globules and in the more or less abundant connective tissue which surrounds the vessels.

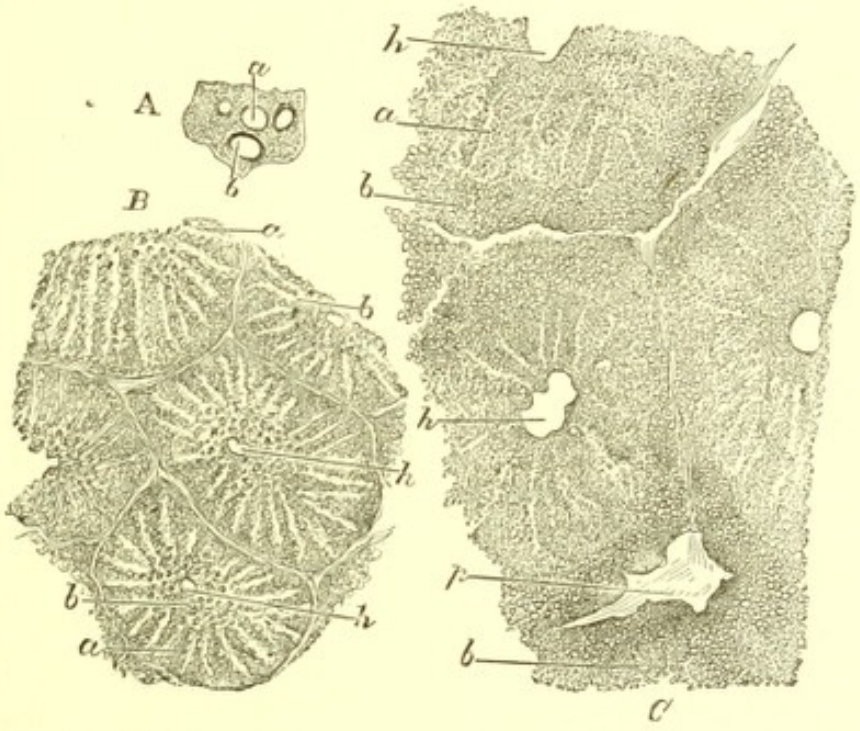
The complication of cirrhosis of the liver with amyloid degeneration of the cells and of the vessels is infrequent. It may occasionally be met with in diseases which lead to amyloid degeneration of the visceræ, particularly in syphilis and in prolonged suppurations, whatever may be their cause. The spleen is generally hypertrophied in cirrhosis of the liver; sometimes it is even indurated and affected with chronic inflammation of the connective-tissue trabeculæ and of the splenic capsule.

DEGENERATION OF THE LIVER.—We have already studied the alterations of the hepatic cells in amyloid and in fatty degeneration. We will now attempt the description of the macroscopic distribution of the lesion with respect to the hepatic lobule.

Fatty Infiltration.—The accumulation of fat in the liver has no connection with the undue development of the panniculus adiposus, or obesity. On the contrary, the subjects who present at the autopsy a fatty infiltration of the liver are generally emaciated from the effects of a long chronic disorder, such as pulmonary phthisis, caries, scrofula, or they are a prey to cardiac disease.

We shall see, in fact, that impediments to the circulation, diseases of the chest, etc., have a great influence upon the production of the hepatic lesion which we are now considering; and that, instead of the accumulation of fat in the liver indicating a richness of the economy, it suggests an inability to consume the hydrocarbons which come from digestion.

Fig. 293.



Fatty infiltration of the liver (Sinéty). *A*. A hepatic cell containing several fat drops, *b*, and granules of the same nature; *a*, normal nucleus. × 300. *B*. Fatty infiltration of hepatic cells during lactation; preparation treated by osmic acid. The cells, *a*, of the periphery of the lobules are normal; the cells of the centre of the lobule are filled with drops, *b*, stained black with osmic acid; *h*, central vein. × 40. *C*. Fatty infiltration of the cells at the periphery of the lobule; *h*, central vein; *p*, portal vein; *b*, cells of the periphery fatty infiltrated; *a*, normal cells in the central portion of the lobule. × 40.

There is, however, an exception to this rule, namely, the physiological accumulation of fat in the liver before and during lactation in mammiferæ. In women in particular, from the establishment of lactation to its cessation, the hepatic cells of the centre of the lobule are filled with large fat drops (Ranvier, de Sinéty). In the central half of the lobule the

cells which surround the central vein are loaded with fat, whilst those at the periphery contain scarcely any or none at all. This considerable quantity of fat, evidently held in reserve for the fabrication of milk, is deposited as near as possible to the blood which will go directly to the heart. (B, Fig. 293.)

In most of the other partial fatty infiltrations of the liver, the fat is located at the periphery of the lobules. Thus, in the physiological processes of digestion, only a very thin peripheral zone of the lobules is infiltrated. (C, Fig. 293.)

In all pathological cases, fatty infiltration is secondary, and it may occupy to a greater or lesser extent the periphery of the lobule, or it may involve the whole hepatic lobule. Thus, for example, in the external half of the lobule, the cells here, instead of retaining their normal polyhedric form, have become spherical and voluminous; their nucleus, still preserved, has been displaced to the periphery of the cell. The cells thus altered very much resemble an ordinary fat vesicle of adipose tissue. The periphery of the lobule infiltrated in this way, after death, appears anæmic, gray or yellow, and opaque; whilst in the centre of the lobule, on the contrary, the hepatic tissue preserves its brownish or rosy color, and the cells are normal or contain a few scattered fatty granules, or some brown or yellow pigment granules.

Fig. 294.



Liver-cells in various stages of fatty infiltration. × 300. (*Rindfleisch.*)

The distribution of the lesion is determined by the impediment to the circulation of the blood in the liver, by stasis in the capillaries of the portal vein, and, at the same time, by an insufficient hæmatosis. Pulmonary and cardiac affections work the same result, which is the arrest in the liver of the fatty material carried by the portal blood in digestion.

In the nutmeg liver which is met with in cardiac diseases there is a new element added, as we have seen—dilatation of the central vein and capillaries, and a pigmentary infiltration of the cells at the centre of the lobule.

In chronic pulmonary diseases, and especially in phthisis, the entire hepatic lobule is most frequently in a state of fatty infiltration. The same condition is observed in the cachexias with chronic suppurations. In the latter cases, we have the most complete type of fatty infiltration. To the naked eye the organ appears hypertrophied, because all its cells are increased in size by the accumulation of fat. Its color is uniformly gray or yellowish; its edges are obtuse and thick; its consistence is doughy, for it contains a large quantity of oily fluid; and the capsule of Glisson is stretched and shiny. It greases paper, and, with the naked eye, we can see oil globules in the scrapings from a cut surface. An anatomical diagnosis is very easy.

The circulation is still carried on in these fatty infiltrated livers, but it is evidently impeded in the capillaries by the pressure of the swollen cells.

The biliary secretion is sometimes vitiated, according to Frerichs. In fact, the hepatic cells are not placed in normal conditions for the

secretion of bile. The large biliary canals may be found empty or containing only mucus, and the gall-bladder filled with a mucous and pale bile. In the bile thus decolored and impoverished the coloring matter is wanting, but the biliary acids still exist. Finally, in these enlarged fatty infiltrated livers a sacciform dilatation of the biliary canals and a catarrhal condition of their mucous membrane have been noted.

Fatty Degeneration.—Besides these fatty infiltrated livers observed in the course of chronic cachectic diseases, there is a totally different series of hepatic lesions which terminate in *fatty degeneration;* it is the series of parenchymatous hepatites. In these, the cells are filled with minute protein or fatty granules, and they tend to fragmentation and destruction. We have already called attention to the distinction between fatty infiltration which does not kill the cells, and fatty degeneration or necrobiosis which results in the death of the elements. Among the parenchymatous hepatites, those which follow poisoning by phosphorus, by arsenic, and by antimony, etc., are characterized by a marked fatty degeneration of all the hepatic cells. At a certain stage of phosphoric poisoning, the liver does not much differ from this organ in the state of fatty infiltration of the entire lobule. The cells are completely filled with granules and small oil drops. The organ is of normal size, or is slightly tumefied, gray, and opaque on the cut surface; is frequently congested, and of a doughy softness. The kidneys are almost always in a complete state of fatty degeneration at the same time.

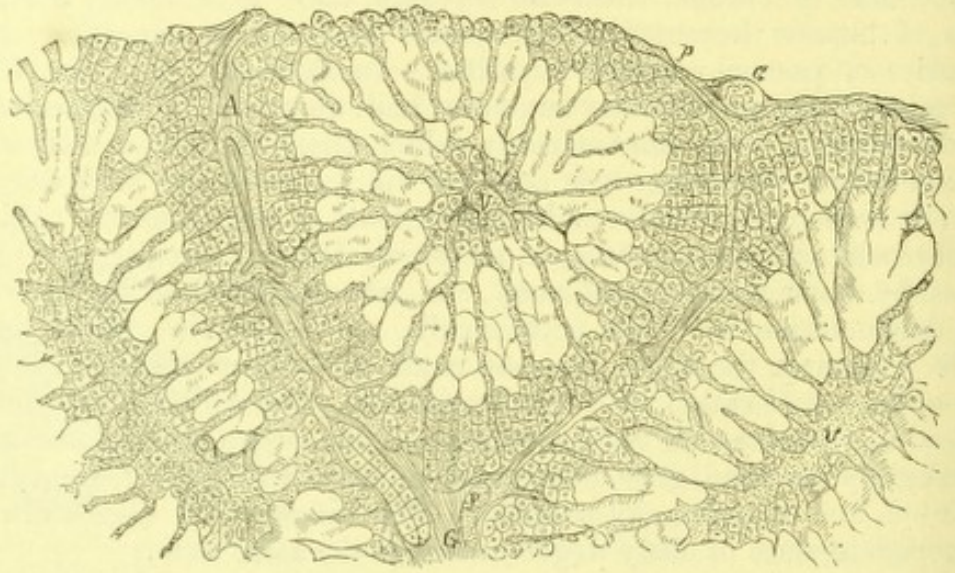
Amyloid Degeneration.—Amyloid degeneration of the hepatic cells (see *ante*) consists in the more or less complete infiltration of the cells by a peculiar translucent, refracting substance, which possesses the property of fixing iodine, and of staining mahogany-brown by a weak solution of iodine. This dark-brown mahogany color is sometimes altered by sulphuric acid, which may successively cause a change to green, blue, violet, or red, or to only one of these colors. The hepatic cells become transformed into small vitreous blocks with obtuse angles, or into spheroids. The cells thus altered are united together into small masses, which may present irregular fissures. In these cells nothing remains of their normal structure, neither nucleus, nor fatty granules or drops, nor pigment granules, nor glycogenic matter.

This amyloid degeneration commences in the liver, in the terminal branches of the hepatic artery, and the capillaries belonging to them. The interlobular branches of the hepatic artery penetrate the periphery of the lobule, and break up into capillaries which anastomose with those from the portal vein. The amyloid degeneration of these arterioles transforms them into canals, with hard refracting walls, constituted by cellular and muscular elements infiltrated by the amyloid substance. The adjoining hepatic cells are those first attacked. It results, therefore, that the lesion is limited at first to a middle zone of the lobule, yet nearer to the periphery than to the centre. At this stage the lobule is divided into three zones, a very narrow peripheral zone, the cells of which are in a state of fatty infiltration; an intermediate zone in a state

of amyloid degeneration; and a central zone, of which the cells may be normal, may be filled with fatty granules, or may be infiltrated with red or yellow pigment.

When the lesion is older and more advanced, the whole hepatic lobule is degenerated. But it is rare that the whole of the liver has undergone amyloid degeneration. There are nearly always parts of lobules or entire lobules which are simply in a state of fatty infiltration.

Fig. 295.



Amyloid liver. *A*. Interlobular artery with amyloid walls. *G*. Biliary ducts; *p*, portal vessels. *V*. Intralobular veins. The liver cells in the central zones of the lobules are infiltrated with amyloid matter. × 300. (*Rindfleisch.*)

The lesion may extend to the hepatic veins and to the branches of the portal veins, in which case the lobule is entirely transformed.

In the last three examples of amyloid liver which we have examined, the lesion was limited solely to the vessels. In one of these, a case of splenic leucocythæmia, only the capillaries of the hepatic lobules were affected by the amyloid degeneration. The hepatic cells were a little atrophied from the thickening of the capillary walls. In the two other examples all the vessels of the liver, the branches of the portal vein, of the hepatic vein, as well as the capillaries, were simultaneously affected. When a thin section of such an altered liver is stained with the two varieties of Lauth's methylaniline, the violet color decomposes into two tints, a red violet, which is fixed by the amyloid elements, and a blue violet, which is imbibed by the normal cells and fibres. Hoffmann's violet presents the same reaction. Upon preparations thus obtained it was easy to assure one's self that the hepatic cells were normal in these three cases, or were simply atrophied. The endothelium of the vessels also almost always escaped the amyloid alteration.

To the naked eye the amyloid liver presents nearly the aspect of the fatty liver; it has a doughy consistence; is anæmic, gray or yellowish-gray; its edges are rounded; its size is normal, or is slightly or sometimes greatly increased. But when one makes a large, moderately thin

section, and examines it upon a glass plate by transmitted light, it is seen that it presents more or less considerable areas which are vitreous and transparent. Moreover, when tincture of iodine, or even a weak solution of iodine, is poured over such a section, portions of lobules or entire lobules assume a characteristic dark mahogany brown color.

Most frequently, when the liver is invaded, the spleen and the kidneys are also similarly altered. If the kidneys are not amyloid, they always present a granulo-fatty degeneration of the epithelium of the secretory tubes.

The etiology of amyloid degeneration offers many points of resemblance to that of fatty infiltration of the liver. Amyloid degeneration may be met with in all the cachectic diseases with chronic suppuration, in tuberculosis, scrofula, syphilis, in cancer sometimes. It offers this point of resemblance to simple fatty infiltration, that inanition or emaciation are the sole clinical symptoms.

TUMORS OF THE LIVER.—We have already spoken of tumefactions of the organ occasioned by acute suppurative inflammation, by chronic inflammation (hypertrophic cirrhosis), and by certain degenerations, hypertrophies, limited or general, which have not infrequently received the clinical designation of tumors.

Angioma.—Cavernous angioma is a tumor not infrequently observed, but which only very rarely attains a notable volume. Most frequently one observes at the surface of the liver a small, spherical, salient tumor beneath the capsule of Glisson. It is dark-red upon the cut surface, and blood escapes while the small tumor contracts. It consists of an areolar cavernous tissue, the cavities of which were filled with blood. For their minute examination they should be placed in some hardening agent before they are opened. Upon thin sections the cavities are seen filled with blood; they are limited by thin trabeculæ, which separate adjoining caverni. These trabeculæ are formed of dense fibrous tissue, and are covered by a layer of endothelial cells. The tumor is everywhere surrounded by a zone of embryonal connective tissue, in which course the dilated vessels which communicate with the previously mentioned caverni. These caverni intercommunicate with one another; they originate by a dilatation of the capillaries of an embryonal tissue of new formation. These tumors may be injected from the hepatic artery.

Tubercles.—Tubercle granules are very common and often very numerous in the liver of patients who have succumbed to an acute miliary tuberculosis. These granules are so minute that they are seen with difficulty by the naked eye. The liver is anæmic, yellowish, and it is only in examining it attentively in a favorable light that the small semi-transparent grains are seen between the lobules. Granules located in the capsule or upon the peritoneum are more easily distinguished. The miliary granules in the substance of the liver are seated in the connective tissue which accompanies the portal vessels. Upon a thin section, these vessels are found either in the centre or near the periphery of the granule. They are accompanied by a new formation of embryonal tis-

sue which envelops the granule, and which, where the latter is very recent, is not easily distinguished from it. There is consequently a sort of interstitial hepatitis, which accompanies tuberculosis of the liver. Later, when the granule is older it consists, at the centre, of atrophied cellular elements, and is very readily distinguished from the surrounding embryonal tissue. They do not then differ from miliary tubercles elsewhere; they rarely exceed 1–10 millimetres in diameter. Those of the largest size are formed by an agglomeration of several smaller ones, and are caseous and soft. Tubercles in the liver are sometimes associated with tubercles of the peritoneum in children.

Gummata.—When considering cirrhosis we briefly gave the characters of interstitial syphilitic hepatitis. In the tertiary period of syphilis the liver is often the seat of gummata. These morbid growths are constituted by an agglomeration of two, three, or more small neoplasms from the size of a millet seed to that of a small pea, of an angular or irregularly spheroid form, of a yellowish color and very firm consistence. These small yellowish masses are bound together and surrounded by a thickened zone of dense connective tissue, which forms a common capsule. There thus results a spheroid tumor from the size of a hazelnut to that of a walnut, or greater, which is usually located at the bottom of a cicatricial depression of the surface of the liver. There often exist several of these colonies of minute gummata, surrounded by their fibrous capsule, either upon the superior face or, as is more common, upon the inferior aspect of the liver, or in the depth of the organ. In the cicatricial depressions the capsule of Glisson is thickened, and almost always also there are fibrous adhesions which unite these points with neighboring surfaces. When one examines a section passing through such a cicatrix and the group of gummata which are found at the bottom of the depression, one sees a cirrhotic thickening of the interlobular connective tissue around neighboring lobules, of such a nature that one recognizes a partial cirrhosis as always accompanying gummy tumors. What characterizes gummata to the naked eye and differentiates them from all other products is their dryness, their yellowish caseous condition, joined to their great hardness and to their elasticity, so dense that they cannot be torn by the finger nail.

Fig. 296.



Gummatous growth from liver. *a*. Central portions of growth, consisting of granular debris. *b*. Peripheral granulation tissue. *r*. Blood-vessel. ×100.

The volume of the liver affected with gummata is usually found much diminished at the autopsy, because the lesion is then old and the peri-hepatitis, as well as the cicatrices following the embryonal formations, have caused an atrophy of the organ. But at the commencement of syphilitic hepatitis things may be altogether different. The liver may be much hypertrophied in the congestive and acute inflammatory period of syphilitic hepatitis. According to Lancereaux, Klebs, and some other authors, hepatic gummata may be reabsorbed while leaving in their

place cicatricial depressions. There is no doubt that caseous nodules may be partially absorbed. We described (page 111) lacunæ filled with fatty granules around the caseous centre of gummata, which was regarded as lymph vessels acting as absorbents: but it is difficult to believe that the new formations can disappear completely. The connective tissue which surrounds them cannot, in any case, disappear.

Concerning their structure, old gummata present in their caseous central portion small cellular elements closely packed together and filled with minute granules; the vessels in this portion are obliterated. Around the yellowish caseous portion lacunæ exist in the connective tissue similar to the lymph spaces and filled with granules. In the peripheral fibrous zone are bundles of tough connective tissue, between the fibres of which are cells sometimes roundish, sometimes flat, and in which sclerosed vessels course.

The more recent gummata of the liver, of which we have given a description (p. 109), are constituted by small microscopic nodules (*a*, fig. 296), the centre of which has already undergone an atrophy and a fatty degeneration of the cells, whilst the round cells of the periphery are confounded with the neighboring embryonal tissue. A large gumma is composed of colonies of these minute nodules.

Lukæmic Tumors.—In leucocythæmia we may find in the liver several varieties of lesions associated with a considerable swelling of the organ. At first there are small extravasations of white blood corpuscles into the hepatic tissue, caused by an obstruction of the capillaries by the white corpuscles which distend them. Moreover, in lymphatic or splenic adenitis, new formations of lymphatic reticulated tissue are often met with. These new formations of reticulated tissue appear between the lobules, around the perilobular vessels, and especially along the course of the branches of the portal vein.

Sarcoma.—Sarcoma is rarely met with in the liver. It is always of secondary formation, especially following melanotic sarcoma.

Up to this point, the tumors of the liver which we have passed in review—tubercles, gummata, leukæmic tumors, sarcomata—are all secondary, cavernous angioma being the only exception.

Carcinoma.—Carcinomata and epitheliomata are very rarely met with as primary tumors of the liver; they usually follow similar tumors of the stomach, of the intestine, of the rectum, of the peritoneum, of the lymphatic glands, of the uterus, the testicles, the breast, etc., or of the gall-bladder. The gall-bladder and biliary passages may be the seat of primary growths which secondarily involve the whole liver. Because of a considerable development of the cancerous formations of the liver, while the lesion of the gall-bladder is of small extent, or is not even suspected or sought for, an inexperienced observer might readily believe that he had to do with a primary growth, whilst, on the contrary, its real nature is that of a secondary tumor.

Secondary carcinomata of the liver are peculiar in the fact that they

are often of very considerable size, while the primary tumor, in the stomach, for example, may consist of an ulcerated encephaloid, scarcely as large as the hollow of the hand.

Of all the organs of the economy, the liver is the most frequent seat of secondary carcinoma. And, since it is a law that the secondary formations reproduce more or less closely the structure of the primary growth, it follows that we should expect to find in the liver all the varieties of carcinoma.

Primary carcinoma of the liver presents a homogeneous mass of considerable size, at the centre of which there is no vestige of hepatic tissue. The central portion uniformly degenerated, is yellow and opaque. Around the tumor secondary carcinomatous foci are developed by infection. These tumors yield a milky juice upon section, and present, under the microscope, the typical structure of carcinoma.

In *secondary carcinoma* of the liver, instead of finding a considerable homogeneous mass, completely supplanting the structure of the organ where it is found, as in the preceding example, we find usually a large number of islands of the morbid growth, nearly of the same age, and very uniformly scattered through the entire organ. These secondary nodules of spherical form have a volume which varies between that of a millet seed and that of a hazel-nut or walnut. If the primary growth is very near the liver, in the stomach or gall-bladder for instance, that part of the organ adjacent to the original tumor will be, as a rule, most altered.

The nodules developed at the surface of the organ form a hemispherical projection, the half of the tumor being covered by the capsule of Glisson, whilst the other half is imbedded in the substance of the liver. The centre of the projection is generally umbilicated, because of the fatty degeneration and atrophy of the central elements of the tumor.

A liver affected with primary or secondary carcinoma is generally very much enlarged, especially when the growth is encephaloid. It extends much beyond the inferior border of the ribs, and by palpation we may often feel the inequalities upon the anterior surface, and the inferior border of the organ if the peritoneal cavity be not too much distended with fluid.

We will study here some of the peculiarities of carcinoma which belong to its location in the liver and to its development there.

One very remarkable character of cancer of the liver is that the tumor may invade and fill the different branches, the trunk and neighboring divisions of the portal vein. We have several times seen associated with a telangiectatic cancer of the stomach, a carcinomatous formation of the same nature in the portal vein.

In this variety of carcinoma the net work of telangiectatic capillaries, and the isolated spherical aneurismal dilatations are very easily recognized by the naked eye as sinuous lines and isolated red points. In those cases which we have seen, the ulcerated tumor of the stomach seated near the pylorus presented upon its peritoneal surface lines or tortuous cords of the size of a crow or goose quill, which were nothing else than the afferent branches of the portal vein, which could be easily followed up to the trunk of the vein. When opened, these veins appeared

filled with a soft carcinomatous growth, like that of the primary tumor, in which ecstatic capillaries could be seen. These vessels projecting into the lumen of the vein, were often quite long. The wall of the vein although infiltrated with new elements was still recognizable on the peritoneal side, but on the side towards the ulceration it was confounded with the carcinomatous tissue, in fact it was totally transformed into alveoli, filled with cells. The alteration of the veins was not limited to this location. The trunk of the portal vein and all of its afferent branches running into the liver were filled by a similar growth.

In other cases a carcinoma of the lymph glands, whether primary or secondary, or of other tissues in the vicinity of the portal vein, invades the wall of the vein and thus reaches the lumen of the vessel into which it sends projections. At the point of invasion the endothelium of the inner tunic proliferates, and the cancerous tissue projects more and more into the lumen. Later this cancerous tissue may soften and break down under the influence of the blood, and become detached and form genuine emboli. These cancerous emboli, arrested in an interlobular branch, may become the point of departure of secondary tumors.

The neoplasm occupying the portal vein may, at a given moment, ulcerate, and there may thus result a complete loss of substance in the wall of the vein.

In several observations of melanotic carcinoma of the liver, reported by German authors, the capillaries of the hepatic lobules were filled with the cellular elements of the tumor (radiated carcinoma of Rindfleisch).

Lastly, we have met with an example of secondary melanotic carcinoma of the liver in which the new formation at first sight appeared to be irregularly infiltrated throughout the entire organ. Upon thin sections, examined under the microscope, it was seen that most of the vessels belonging to the portal vein had a much larger diameter than normal, and were of cylindrical form. Their wall was the seat of a large-celled infiltration; their inner membrane presented connective tissue elevations infiltrated by the same large cells. These regular elevations filled the whole calibre of the vessel, or left a central lumen occupied by free cells and blood. The cellular elements were more or less pigmented. Almost all the vessels were altered in this manner. The hepatic arteries were not the seat of so intense a carcinomatous endarteritis, but they also showed in their inner membrane layers of endothelial cells, some of which were pigmented. Some of the lobules were entirely transformed into carcinomatous islands; the corresponding interlobular portal vessels, although recognizable, were affected with the previously described endophlebitis. The central vein and its radiating capillaries were nearly healthy. But the network of hepatic cells was replaced by nests of cells with large nuclei, large nucleoli, and a protoplasm for the most part pigmented. The thickened connective tissue which accompanied the vessels formed the stroma of the carcinomatous alveoli. The interlobular biliary canals were also to be recognized, but their swollen cubical cells were replaced by large cells with large nuclei and highly refracting nucleoli, and their calibre was increased. It would be difficult

to see a more beautiful example of the participation of all parts of the liver in the development of a tumor.

We need not necessarily conclude, however, that the usual development of carcinoma is effected by the filling of the veins and capillaries of the liver. In the greatest number of cases, indeed, the recent miliary nodules are seated in the perilobular connective tissue, around the small divisions of the portal vein, and they arise from a new formation of cells between the bundles of connective tissue fibres. The veins, then, sometimes present an inflammation characterized by the formation of numerous endothelial cells upon their internal surface. This alteration of the vessels may also be recognized as a secondary lesion.

Rindfleisch looks upon the hepatic cell as the starting-point in the usual development of carcinoma of the liver. We do not believe that this mode of development is so common.

While we are cognizant of some facts concerning the development of carcinoma of the liver, many questions yet remain unsolved. In particular, the role of the lymph vessels at the commencement of these growths has never been thoroughly studied. It has been said that the cells of hepatic cancer are a reproduction of the structure and the form of the normal cells of the liver. We have been unable to recognize such an analogy. The cells of carcinoma of the liver possess the same characters as they do in other locations, and resemble the hepatic cell in nothing.

Cylindrical-celled Epithelioma.—Cylindrical-celled epithelioma (see p. 154) is not infrequently met with in the liver as a secondary formation which follows a primary growth of the same nature in the stomach, the small intestine, the rectum, the gall-bladder, etc.

To the naked eye, this variety of tumor offers the same characters as encephaloid, that is to say, it consists of nodules more or less voluminous, and of a soft consistence yielding an abundant lactescent juice. It may also assume the appearance of colloid cancer, by reason of a partial or a very extensive colloid metamorphosis of its cells—an appearance which the primary growth also presents. In order to determine the nature of these tumors it is necessary to harden them, and subsequently examine thin sections. The alveoli are found to be lined by a single layer of cubical or cylindrical cells. These elements and their arrangement faithfully reproduce the structure of the primary tumor. It is not possible to demonstrate an isolable membrane around these tubular formations. They are simply limited by the neighboring connective tissue. The centre of the tubes shows a distinct lumen or cavity. The colloid portions of the tumor present the same tubes and the same cavities, but they are lined by a layer of cells which have undergone a colloid metamorphosis.

This epithelioma with cylindrical cells has been described under the name of adenoma by several authors, particularly Rindfleisch. In our personal experience, these tumors of the liver have always been secondary. We readily admit the possibility of a primary epithelioma of the liver, but this is no reason for regarding as an adenoma a growth which is absolutely identical in structure with a cylindrical-celled epithelioma.

It would be more logical to consider the formation as an epithelioma developed from the budding and the new formation of biliary canals. In most of the observations published in France under the name of adenoma, when the anatomical details are clearly given, one recognizes a case of hypertrophic or atrophic cirrhosis with large granulations on the surface of the liver. A genuine *adenoma* of the liver should reproduce the structure of the hepatic lobules. Then how can we distinguish the lobules of new formation from the normal lobules? This at first sight does not, to us, seem possible to do, and we lack undoubted examples of such tumors for study. Those which have been published under the name of adenoma by Rindfleisch and several other German authors are cylindrical-celled epitheliomata primarily developed in the liver, or are examples of carcinoma in which the cells of the tumor have appeared similar to those of the liver. For those isolated nodules upon the surface of the liver projecting beneath the capsule of Glisson, which present the structure of a hepatic lobule, they are less to be considered adenomata than vices of development and conformation, and possess only a purely teratological interest.

Serous *cysts* of the liver are very probably never anything else than dilated diverticula of the bile ducts, which may become isolated from the ducts wherever they have arisen. We have several times examined cysts located upon the surface of the liver, and containing minute biliary calculi. The internal covering of these cysts consists of a single layer of flat epithelial cells. The connective tissue which surrounds them is continuous with the periphery of the adjoining lobules, and constitutes a sort of local cirrhosis. In this sclerosed tissue the biliary canals show the same lesions as in cirrhosis. Serous cysts of the liver are very rare. They are surrounded by connective tissue, and are lined by a prominent epithelium. We should not commit the error of regarding as cysts of the liver the cavities which are sometimes found in the centre of cancerous tumors, or those which succeed abscesses. Advanced putrefaction, leading to the development of vesicles under the capsule of Glisson, containing air and a little fluid, might at first view occasion a mistake.

Hydatid Cysts.—Cysts containing echinococci, which are not uncommon in the liver, usually constitute a voluminous tumor, commonly projecting upon the convex surface. Sometimes they are seated in the depth of the organ. We find in proceeding from without inwards: 1st, A thick fibrous envelope or adventitious membrane, the structure of which is the same as that of lamillated fibrous tissue. This fibrous membrane is continuous with the connective tissue surrounding the lobules, which is increased to such an extent that there is a localized cirrhosis at the periphery of the tumor, and the lobules here are flattened by pressure. 2d, Internal to the fibrous envelope, is a perfect hydatid membrane, in recent formations, spherical and tense; in old cysts, shrunken, wrinkled and ruptured. This membrane is characterized by its regular lamellæ, parallel with each other, formed of a hyaline amorphous substance, without any cellular elements interposed between the layers. Within this membrane, of which the sharp fracture, the separation into lamellæ, the

vitreous and trembling aspect can be confounded with nothing else (see pp. 192 and 193), are found daughter vesicles, also having a similar but thinner membrane, a volume varying from that of the head of a large pin to that of an egg. These daughter vesicles are very regularly spherical. They contain non-albuminous aqueous fluid, and small granules which are nothing else than echinococci. Often these vesicles contain nothing—they are then sterile. 3d. The echinococci are small vesicular worms, formed of a caudal vesicle adherent to the germinal membrane. In the midst of this vesicle the body and head of the animal is found. The head shows a proboscis, four suckers, and a double row of hooks (see p. 193).

Echinococci are the vesicular worms of *Tænia echinococcus*, which does not live in the intestines of man, but is common in the dog. The Tænia echinococcus is remarkable for the small number of its rings. The eggs of these worms, discharged with the fecal matter of the animal in which they live, are swallowed with the water and food, and arrive in the stomach of man where they lose their enveloping membrane. The embryo thus set free perforates the membranes of the stomach in order to lodge itself in the neighboring organs, and to undergo there the second phase of its development.

When the hydatid cysts reach their full development, and still remain in the liver, they contract, and the hydatid membranes rupture. The fluid is then thick, opaque, and rich in the salts of lime; it is rendered yellow or reddish by the presence of the coloring matter of the bile and of blood. The echinococci no longer exist, they are broken up and destroyed; yet we may still recognize the hooklets in the fluid. It is not uncommon to find at the autopsies of patients who have not presented any symptoms of hepatic disorder—at least in the latter years of their life—such cysts of the size of a fist, or greater. Their fibrous membrane is contracted. In one case which we examined it had undergone a genuine ossification, with bony trabeculæ, bone marrow, and osteoblasts, etc.

A variety of hydatids of the liver, described latterly by Friedreich, Virchow, etc., consists of a *multilocular hydatid tumor*. These tumors are composed of small hydatid cysts disposed in a fibrous stroma. Each cyst contains a characteristic membrane which sometimes incloses a perfect echinococcus, sometimes only its hooks. Such tumors very much resemble, at first sight, colloid carcinoma, with which they had been a long time confounded. Microscopic examination will immediately remove all doubt.

Hydatid cysts in process of growth, instead of atrophying and shrivelling up, may reach a volume so great as to require surgical interference. At other times, they may cause adhesions between the surface of the liver and the diaphragm, the walls of the stomach, the small intestines, etc.; and they may open into the pleura, the lungs, the bronchi, the stomach, the intestine, the gall-bladder, etc. One case has been observed of a perforation into the portal vein. When the opening takes place into the peritoneal cavity, there results a fatal peritonitis.

Biliary Vessels and Gall-Bladder.

Inflammation.—Catarrhal inflammation of the gall-bladder frequently is caused by the presence of biliary calculi, which act as foreign bodies. Yet calculi do not always, or usually, occasion irritation of its mucous membrane; in old women, with whom calculi are so frequent, the internal membrane of the gall-bladder is often intact. At other times, it is injected and contains a pale, stringy, mucous bile with pus corpuscles. This is especially seen in connection with inflammation of the biliary canals. The mucous membrane is thickened, roughened, and œdematous, instead of having its ordinary thinness and delicate villous surface. In a more intense degree of the lesion, there are found one or more ulcers upon the mucous membrane, especially at the inferior portion of the gall-bladder. These ulcerations, when they are rapidly produced by a purulent infiltration of the connective tissue of the mucous membrane which extends to the muscular layers, may occasion fatal perforations of the peritoneum and an escape of the calculi into its cavity; but this, however, is a very uncommon accident. The ulcers, when they exist, are accompanied only with a local irritation of the peritoneum, which is seen upon the external surface of the gall-bladder opposite the point of disease, where are found fibrinous false membranes, or a fibrous thickening of the serous membrane with adhesions. Local peritonites with adhesions have resulted in communications of the gall-bladder with the duodenum, with the colon, and even in biliary fistulæ, opening externally through the abdominal wall, calculi having been discharged by these several passages. In all these cases the inflammation extends to the cystic, hepatic, and common biliary ducts, causing an icterus. While the presence of calculi seldom occasion, these fatal results, they frequently cause a thickening of the mucous membrane of the connective tissue and muscular fibres, comparable to the hypertrophy of the urinary bladder caused by calculi in that organ.

Louis, Andral, Rokitansky, etc., have described an infiltration and gangrenous ulceration of the mucous membrane of the gall-bladder occurring in cholera, typhoid fever, and purulent infection.

Catarrhal inflammation of the common biliary, cystic, and hepatic ducts, frequently occurs either spontaneously or in consequence of an inflammation of the duodenum, when it causes catarrhal or simple icterus. At other times, it is due to biliary calculi coming from the gall-bladder or formed in the hepatic canals. Biliary gravel or small fragments of calculi are the most active causes of this inflammation. Every stage has been observed between the swelling of the common biliary duct limited to the ampulla of Vater, or to the neighboring portions of the duodenum, where it arrests the flow of bile, in simple icterus, and acute suppurative inflammation. It is easily understood that the œdematous swelling of the ampulla of Vater and connective tissue around the common biliary duct at its duodenal extremity, may be an obstacle to the flow of bile capable of producing jaundice. It is seldom that an autopsy demonstrates this lesion in simple icterus, but the observations by Virchow and Vulpian are such as to leave no doubts as to the patho-

logical condition. With the congestion there is observed an exudation of mucus, a mucous plug. More intense inflammation, from the presence of biliary calculi, extends to most of the biliary canals in the liver. The mucous membrane of these canals is covered with a transparent mucus, or the latter is rendered cloudy by the presence of desquamated epithelial cells and pus corpuscles. The canals are dilated, their mucous membrane thickened, as is also the connective tissue surrounding them ; in such cases ampullar dilatations are seen lined with mucous membrane, and filled either with a mucous or puriform fluid. The dilatations, which very much resemble small abscesses, are found through the entire organ, are lined with a mucous membrane, and contain many cylindrical cells, mixed with lymph cells and blood pigment, or grains of bile pigment.

In the most intense inflammations, the contents of the much dilated biliary vessels consist of opaque and whitish muco-pus, but possess a certain viscidity due to the mucus, as in muco-purulent sputa. The amount of this pus is sometimes so great that, upon making a section of the liver at the autopsy, there is the appearance of an abscess. The numerous cellular elements in this pus consist of cylindrical epithelium and lymph cells. In intense inflammation of the biliary canals, there are always observed during life, febrile symptoms which are intermittent in type. The inflammation may terminate in suppuration or a perforation of the portal vein, and may occasion perforations, peritonitis, etc., when the calculi act as foreign bodies.

It is probable that, in consequence of intense inflammation of the canals, narrowing and even complete obstruction of the hepatic and common biliary ducts are produced; sometimes, as in the case referred to by Andral, fibrous cords have replaced these canals.

At times, papillary excrescences of the mucous membrane of the ducts are found, in consequence of inflammation; this, however, is unfrequent.

When a large calculus passes into the cystic duct, thence into the common duct, it may be arrested in the latter at its entrance into the duodenum where the duct is narrow. If it experiences any difficulty in its passage, the contractions of the ducts and gall-bladder give rise to hepatic colic. It may also result in more serious inflammatory accidents if it remains fixed in the canal or if it is encysted. The bile may be arrested in its passage, occasioning jaundice; and, again, the inflammation of the mucous membrane and submucous tissue caused by contact of the calculus, may extend to the neighboring organs, especially to the peritoneum. There frequently results suppurative inflammation or limited sloughing, which terminates in perforation. If the calculus has been arrested near the duodenum, from the mortification of a portion of the mucous membrane and wall of this part of the intestine there occurs, as a favorable termination, the passage of the calculus into the intestine; but if the perforation is into the peritoneum, a fatal peritonitis is the result.

The biliary ducts, and particularly the small interlobular canals, experience in many of the diseases of the liver, lesions due to hepatic disease or to irritation by contiguity. Such are the alterations described in cirrhosis ; in acute yellow atrophy ; such are the inflammatory irritations occurring in the large and small canals included in carcinomatous

masses, or situated in their neighborhood; such are the moderate catarrhal irritations, pointed out by O. Wyss, in poisoning by phosphorus, and in parenchymatous hepatitis, and which exist, with good reason, in suppurative hepatitis. In the parenchymatous hepatitis of puerperal fever, smallpox, etc., we have seen an infiltration of the peri-vascular connective tissue with lymph cells, and at the same time a catarrh of the small biliary canals included in the inflamed tissue.

These inflammatory lesions of the biliary canals, which end in an abundant secretion of mucus, and the formation of cells which fill them, interfere with the passage of the bile from the hepatic cells to the common biliary duct. In hepatic tumors the inflamed biliary canals are tortuous, flattened, and compressed, causing complete retention of bile, and icterus.

Another result of inflammation of the biliary ducts—which is, however, infrequent—is hemorrhage from their mucous membrane, occurring occasionally in cirrhosis, carcinoma, or simple inflammation of the liver. Hemorrhage may also occur in consequence of abscesses of the liver. In a case reported by Lebert, hemorrhage followed the rupture of an aneurism of the hepatic artery into the gall-bladder.

Tumors of the Gall-bladder.—According to Rokitansky, a new formation of adipose tissue is found in the subperitoneal connective tissue of the gall-bladder in obesity; this is, however, infrequent.

The tumors developed in the mucous membrane of the gall-bladder are carcinomata or cylindrical-celled epitheliomata. The history of carcinoma of the gall-bladder is relatively of recent date, yet it is not a very unusual affection. It may be primary or secondary; in the latter case it follows a carcinoma of the liver, stomach, intestine, or neighboring glands. Primary carcinoma of the gall-bladder is most frequently a colloid carcinoma; at other times it has the appearance of encephaloid, and more rarely it belongs to scirrhus. Its anatomical form is very similar to that occurring in the intestine. Generally, indeed fourteen times in fifteen, the gall-bladder contains one or more calculi; the fewer in number the larger the calculi. The bile is sometimes colorless, or it is thick and brown; it may contain small fragments detached from the tumor. The surface of the gall-bladder at the diseased point is uneven and granulating, for new formations assume the villous form in the gall-bladder, just as in the urinary bladder. The tumor invades a part or the entire mucous surface, which is increased in thickness, and upon section shows colloid tissue, or a whitish tissue infiltrated with a milky juice. The lesion of the mucous membrane and submucous connective tissue may extend to the muscular tissue, which latter is always somewhat œdematous and hypertrophied. The cavity of the gall-gladder is generally increased, but may be diminished. The tumor frequently extends into the cystic duct and common biliary duct, the mucous membrane of which is infiltrated, and the calibre contracted, occasioning retention of bile in the hepatic canals and interlobular biliary ducts. Biliary cysts may result from this condition, which is always accompanied by jaundice. Generally the hepatic tissue, in contact with the altered gall-bladder, is invaded by the carcinoma, and the entire liver may be studded with

nodules having the structure of the primary carcinoma of the gall-bladder. In some autopsies, in examining the liver invaded throughout by such spherical nodules, varying in size, there may be some hesitation in believing that the nodules are secondary to the ulceration of the gall-bladder; but what occurs in hepatic carcinoma, secondary to that of the stomach, should make us admit that the same connection may exist between the hepatic nodules and the ulceration of the mucous membrane of the gall-bladder.

The neighboring lymph glands are always altered and transformed, and the duodenum, colon, and even the stomach may be invaded by a carcinoma which has its beginning in the gall-bladder. These several organs are then united by carcinomatous and fibrinous adhesions. The patches in the stomach and intestine are smaller and more recent than the ulcers of the gall-bladder.

The question whether the carcinomatous ulcer precedes the formation of the calculi, or whether the latter exist primarily, and produce the tumor by irritation, is doubtful. We are inclined to believe the first hypothesis.

Histologically, the superficial non-ulcerated granulations are covered by the cylindrical cells of the mucous membrane, and are most frequently constituted by a simple, very vascular embryonic tissue. Sometimes they show the alveolar structure of scirrhous, encephaloid or colloid carcinoma. The ulcerated portion of the tumor is deprived of all epithelial covering. The alveolar structure of carcinoma is best seen in the very thick submucous tissue. In the muscular tissue there is first seen an infiltration of embryonic cells, afterwards a true carcinomatous tissue.

Cylindrical-celled epithelioma of the gall-bladder, to the unaided eye, does not differ from encephaloid; the histological characters of the tumor are absolutely the same as those previously described under cylindrical-celled epithelioma of the liver. It gives rise to secondary nodules in the liver, as does carcinoma, and has the same symptoms and prognosis (see p. 154). In the published observations of epithelioma there were also found calculi in the gall-bladder.

CHAPTER VI.

PERITONEUM.

THE remarks made in Part First concerning experimental inflammation of the peritoneum, and those in relation to alterations of the serous membranes in Part Second, may be applied to much of the pathological histology of the peritoneum.

PERITONITIS.—Peritonitis is acute or chronic, general or local.

Acute peritonitis, seldom primary (rheumatic), is almost always the result of traumatism, a contusion or wound, or of a lesion of one of the organs covered by this serous membrane—such as perforations of the intestines or of the stomach, foreign bodies entering the peritoneal cavity, the opening of abscesses into its cavity, superficial inflammations of organs covered by this serous membrane, lymphangitis and phlebitis of the uterus and its appendages, metastatic abscesses of the liver, etc.

In *acute general peritonitis* the vascular injection of the visceral peritoneum is very intense, and is accompanied from the beginning by a fibrinous purulent exudation, more or less abundant between the meshes of the great omentum, in the connective tissue of the serous membrane between its layers and upon its surface. The parietal peritoneum is also implicated, as are also the different layers of the omentum and mesocolon. Fibrous adhesions very rapidly form between the parietal and visceral layers, and between the different organs contained in the abdomen.

Fig. 297.

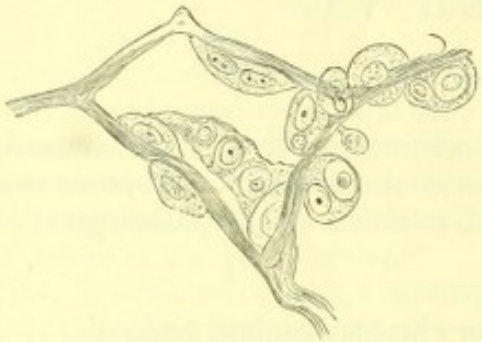


Normal omentum, stained with nitrate of silver, showing the outlines of the endothelial covering of the connective tissue trabeculæ. × 250.

In puerperal peritonitis, when the autopsy is made two or three days after the beginning of the disease, the parietal layer of the peritoneum is found thickened and infiltrated with pus, it is gray and opaque in color, and united in places, either to the great omentum or to the intestines, by soft fibrous false membranes, infiltrated with pus. The pus escaped into the cavity of the abdomen usually collects in certain localities, as in the pelvis around the appendages of the uterus, etc. The injected and thickened great omentum, at the points where lobules of fat are found, is sometimes adherent to the surface of the intestines, or folded upon itself; it presents the appearance of a fleshy, red, irregular mass covered with pus. When the great omentum is exposed, it is found adherent to the intestines, especially to the small intestine, from which it is with difficulty detached; it almost always also adheres at several points to the abdominal wall by its free border. Beneath the omentum, the intestinal loops, swollen and distended by gas, are united to one

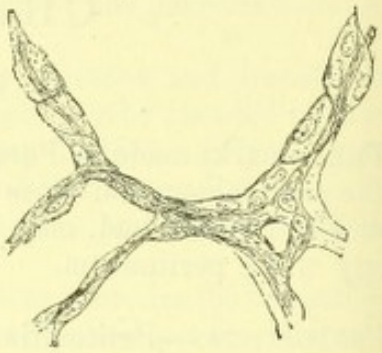
another by fibrin infiltrated with pus, forming either a thick layer or a gray or yellowish-gray mass, which fills up the spaces between the neighboring loops. This thick, semi-solid exudation varies in amount. It is difficult to separate the united intestinal loops without rupturing

Fig. 298.



Omentum artificially inflamed and silver treated. It shows the epithelial cells in process of proliferation and in the act of detaching themselves from the trabeculæ. Pus cells are imbedded in the fibrin, and thus remain connected with the fibrous trabeculæ. × 250.

Fig. 299.



Omentum artificially inflamed and examined the eighth day after the operation: the endothelial cells have again become applied to the fibrous trabeculæ. Their protoplasm is less granular than in the preceding figure, and they form an almost complete epithelial investment. × 250.

some of their walls, since the intestinal coats themselves are infiltrated with fluid, and are pale and softened. This serous infiltration of the intestine also extends to its mucous surface, which is at times anæmic or congested, and perhaps covered with a puriform mucus. The surfaces of the liver and spleen equally present an intense superficial inflammation; here the peritoneum is infiltrated with pus, and the capsules of these organs are thickened and opaque. There always exists, either upon the appendages of the uterus, upon the surface of the liver or other organs, lymphangites, phlebites, or superficial abscesses, which are the starting-point of the purulent peritonitis.

The peritoneal exudation instead of being small in quantity, opaque, and fibrino-purulent, as in the preceding example, may be more abundant, sero-purulent, with flakes of free fibrin in the fluid, or entirely serous; in the latter there are also always fibrinous flakes present.

A histological examination of the great omentum demonstrates the same appearance, as described in Part First, under artificial peritonitis (see p. 56), that is fibrillæ of fibrin, lymph cells and large, swollen, granular cells, with one or more nuclei, located in the meshes of the omentum. There is an infiltration of lymph cells and fibrin between the fibres of the connective tissue throughout the thickened and opaque membranes. Accumulations of these lymph cells are particularly seen around the vessels. The same increase of round cells is observed around the vessels in the adipose nodules of the great omentum.

The liver and kidneys are pale upon section, and their cells are generally fatty.

The fluid exudation into the peritoneal cavity may contain blood associated with fibrinous serum and pus, and there are generally at the same

time ecchymoses, with infiltrations of blood into the subperitoneal cellular tissue. But this variety of peritonitis usually has a special cause, such as cancer, tubercle, or cirrhosis of the liver, and it is not acute in the same sense as the preceding variety.

The termination of acute peritonitis varies. When it does not rapidly end in death, the escaped fluid becomes absorbed, embryonic connective tissue forms upon the surface of the peritoneum, and vessels of new formation having embryonic walls penetrate into the fibrinous false membranes. These false membranes thus organized form adhesions between inflamed surfaces, and, at times, cause digestive troubles, by the intestines becoming immovable, contracted, or fixed in an abnormal position; the bands of adhesion formed between the visceral and parietal peritoneum may be the cause of internal strangulation.

In other cases acute purulent peritonitis terminates, after the absorption of a portion of the exudated fluid, by a kind of cascation or inspissation of the pus which collects in one or more points upon the peritoneum. These collections become encysted within false membranes. An evacuation of this purulent fluid may be effected by a perforation of the intestine from without inwards, or it may even be discharged through the walls of the abdomen. When the suppuration causes an opening both of the intestine and of the abdominal wall, there results a fecal fistula.

Acute local peritonitis is traumatic or idiopathic. In the latter case, it generally follows an inflammation of an organ covered by the peritoneum. When an inflammation reaches the surface of such an organ, the peritoneum is always inflamed; therefore, a local peritonitis is frequent in lesions of the liver, gall-bladder, spleen, in diaphragmatic pleuritis, in metritis, in inflammations or tumors of the appendages of the uterus, in cystitis, in typhlitis, etc.

General chronic peritonitis follows acute peritonitis, or it is chronic from the beginning. In the latter case, it is seldom that it cannot be referred to a chronic peritoneal or intestinal lesion: tuberculosis, carcinoma of one of the abdominal organs, cirrhosis of the liver, disease of the heart, malarial cachexia, etc.

As carcinomatous peritonitis is superficial at its beginning, as well as in its subsequent development, there are found upon the surface of the peritoneum large cells with large nuclei and enormous nucleoli, which are mingled with the lymph cells and fluid exuded into the peritoneal cavity. Therefore, sometimes a carcinoma of the peritoneum may be suspected after a microscopical examination of the fluid obtained by an exploratory puncture.

The lesions of chronic peritonitis vary much. Thus, in chronic peritonitis following acute peritonitis, there are found adhesions between the intestinal loops, or between the loops and neighboring organs or abdominal wall, consisting of filamentous or lamellar fibrous tissue. Complete obliteration of the peritoneal cavity may occur, just as obliteration of the pleural cavity often happens in pleuritis. That life may be prolonged even when the intestines are contracted by the interference and retraction of the new fibrous tissue, is seen in the autopsies of old per-

sons who, for a number of years, have lived with this lesion. At other times, the membranes consist of a few unimportant bands or cellular adhesions, in which case there is usually no fluid found in the peritoneal cavity.

In cardiac diseases, in cirrhosis of the liver, and in malarial cachexia with hypertrophy of the spleen, a true peritonitis does not occur, but there is a serous effusion or ascites instead. Yet, in pure ascitic effusion, there are constantly observed some lesions, which may depend upon a chronic inflammation which is secondary and which consists in thickenings of the capsule and peritoneal covering of the liver and spleen, and in excrescences or granulations of the peritoneum of the liver in cirrhosis, of the peri-splenic peritoneum in malarial cachexia and cardiac diseases. These new formations of connective tissue may justly be considered as traces of chronic peritonitis. Again, the parietal peritoneum may be thickened, and frequently there may exist other evidences upon the omentum and intestines of chronic peritonitis. In cirrhosis of the liver there is very often a true subacute or chronic peritonitis, with the presence of fibrinous flakes in the effused fluid, as well as blood. The surface of the peritoneum, either upon the surface of the liver, or the mesentery, or intestines, is covered by fibrinous false membranes, or very vascular organized membranes, which are accompanied with subperitoneal ecchymoses. Frequently there occurs a peculiar hemorrhagic peritonitis in hypertrophic cirrhosis. Abdominal punctures do not appear to develop or aggravate inflammations of the peritoneum.

Hemorrhagic peritonitis, which is chronic or subacute, as seen in hypertrophic cirrhosis, in articular rheumatism, in tuberculosis, in Bright's disease, etc., is characterized by vascular new membranes, which at first sight resemble spots of blood, and are similar in appearance to the new membranes of pachymeningitis. These new membranes cover a part or the whole of the parietal peritoneum, the peritoneal surface of the intestines, and in a general manner the whole peritoneal surface of the pelvis. The membranes are simple and thin, forming a single layer, or they consist of superimposed layers separated by effused blood; the embryonic tissue composing them may also be infiltrated with red blood corpuscles. When these membranes are thick and ecchymotic, the fluid effused into the abdominal cavity always contains blood in considerable quantity. The connective tissue subjacent to the new membranes is also sometimes the seat of infiltrations of blood. In this variety of peritonitis, now and then the entire surface of the peritoneum has a dark brown color, and the effused fluid has a chocolate hue.

Tubercles of the Peritoneum and Tuberculous Peritonitis.—Nothing is more varied than the distribution and consequences of tubercles of the peritoneum. Tubercles of the peritoneum may be discrete and numerous, or there exist only a few, very small, semi-transparent granulations upon the intestinal peritoneum, opposite tuberculous ulcers of the intestinal mucous membrane. The lymphatics, ramifying under the peritoneum, are seen to be inflamed and tuberculous (see p. 511); at this point there are sometimes found traces of peritonitis, fibrous false membranes, and weak adhesions.

But when the entire peritoneum, or a greater part of this serous membrane is covered with miliary granulations, we have a very different appearance. Sometimes there results a peritonitis characterized by considerable ascites, the effused fluid being lemon-colored, transparent, aqueous, and now and then containing flakes of fibrin. This occurs when the granulations are small, and when they are seated upon the surface of the serous membrane.

At other times the peritonitis is more intense, especially when the granulations are found deep in the connective tissue of the peritoneum and in its folds. The mesentery, great omentum, and mesocolon have tuberculous granulations not only upon their surface, but between their several layers; this causes a thickening of these membranous folds, for the granulations are surrounded by an embryonic tissue with which they are continuous without any line of demarcation. These membranes may acquire a very great thickness. The great omentum or mesentery, instead of being a thin membrane, may measure one to one and a half centimetres in thickness. The great omentum is shrunken and drawn towards the transverse colon. The mesentery is also drawn towards its fixed insertion, carrying with it the mass of small intestine. The loops of this intestine are agglutinated to each other, and, as the abdomen contains a considerable amount of serous fluid, upon palpation of the belly, the impression is obtained of a very large elastic tumor situated below the umbilicus, and formed by many intestinal loops united together.

The effused fluid in this variety of tuberculous peritonitis is of a changeable nature; at first lemon color, it may become puriform, and contain flakes of lymph, while fibrinous false membranes are formed upon the peritoneum. The fluid may be absorbed and the abdomen diminished in size without losing its elasticity. The effused pus at times collects in one or more points at the dependant parts, becoming encysted by false membranes, and eventually becoming caseous.

In some varieties of tuberculous peritonitis the intra-abdominal effusion is bloody, and the tuberculous granulations of the surface are usually surrounded by ecchymoses. There are also frequently seen, in this hemorrhagic form, vascular new membranes which contain tuberculous granulations.

Tubercles upon the surface of the peritoneum in children, rarely in adults, may, by the union of several granulations, reach the size of small peas, or be as large as almonds. These large tubercles scattered over the surface of the mesentery, omentum, parietal peritoneum, etc., upon section, appear yellowish and caseous.

The lymphatic glands, either those of the mesentery or those above the lesser curvature of the stomach, or the pelvic glands, are always more or less implicated in the tuberculous process. They contain tubercle granulations, or they are in a condition of caseous infiltration. When the glands are very large and caseous, the lesion is named *tabes mesenterica;* this disease is observed in scrofulous children.

Chronic local peritonitis is generally the result of a chronic inflammation of an organ contained in the peritoneal cavity. For example,

inflammations of the appendages of the uterus occasion the adhesion of the Fallopian tube to the uterus, by fibrinous formations in the ligaments around the tube and ovary, etc. Foreign bodies in the peritoneum coming from the alimentary canal, after a perforation limited by adhesions, uterine fibrous polypi becoming free in the abdomen, pedunculated or detached lipomata or papillomata of the omentum, extra-uterine pregnancies, etc., are also causes of chronic local peritonitis. It is especially characterized by fibrinous adhesions.

Tubercles, when they are developed only at one part of the peritoneum, also at first occasion a local peritonitis.

Carcinoma and Carcinomatous Peritonitis.—Primary carcinoma of the peritoneum generally begins in the omentum. It may be encephaloid, scirrhous, or colloid. The latter occurs most frequently, and at times constitutes a large tumor, involving the entire peritoneum, the omentum, mesentery, mesocolon, and the peritoneal covering of the superior surface of the liver. The size of the tumor filling the abdomen is such that it has been frequently taken for a very large cyst of the ovary. The structure of these colloid carcinomata does not materially differ from the description given on page 104; there are seen in the older portion of the tumor large alveoli filled with spherical and large transparent vesicles having several concentric circles. But in the more recent portions there is a very remarkable abundance of extremely fine fibrillar fibrous tissue, inclosing between the fibrillæ a colloid substance with or without free cells.

Secondary carcinoma of the peritoneum occurs in consequence of similar tumors of the stomach, intestine, liver, or of the uterus and its appendages.

At first it is usually seen as a diffused nodular thickening of the connective tissue of the peritoneal covering of the diseased organ. In a carcinoma of the stomach, the gastric peritoneum shows either nodules of a similar nature or a diffuse infiltration; generally, the lymph vessels or veins proceeding from the tumor of the stomach, and passing to the liver or neighboring lymphatic glands, may be seen ramifying under the peritoneum at the seat of the lesion. An invasion of the entire serous membrane by the carcinoma follows; it is seen covered with numerous granulations or small tumors, varying in size from a millet seed to a small pea or larger. The smallest of these granulations, especially when the primary carcinoma is a scirrhus, to the unaided eye very much resembles tubercles; a microscopical examination, however, will remove all doubt. These new formations resemble the primary tumor in structure.

Secondary carcinomata of the peritoneum are always accompanied by a variable amount of peritonitis. Sometimes there is simply an abdominal effusion, the fluid being lemon color and varying in amount; or it contains flakes of fibrin, while fibrinous exudations are found upon the surface of the peritoneum. At other times carcinomatous formations of the peritoneum are accompanied by the development of vascular new membranes, consisting of embryonic connective tissue; hemorrhagic peritonitis may now occur. These new formations of connective tissue occasion adhe-

sions between the organs; the adhesive bands themselves finally undergo carcinomatous metamorphosis.

Finally, carcinomatous peritonitis may develop into an acute purulent peritonitis. This occurs when the diseased organ opens into the peritoneum, or when the destruction by purulent softening of the carcinomatous tumor in an organ occasions the formation of a purulent focus located near the surface of the organ; this is especially observed in carcinoma of the uterus and its appendages.

Other new formations or tumors of the peritoneum are very unfrequent; they are *lipomata*, having their origin in the epiploic appendages or in the adipose tissue, situated under the parietal peritoneum, or they consist of various forms of cysts, proliferating, dermoid, etc.

At the autopsy of an old woman, we found upon the peritoneum of the diaphragm *Pacinian corpuscles* projecting in great numbers. They measured one, two, and three millimetres in length, and were arranged in an arborescent manner, several being united to a single pedicle.

Hydatid cysts containing echinococci sometimes exist in the peritoneum. They may come from the spontaneous opening of a similar cyst of the liver, or they may be primarily developed in the great omentum, or any other part of the peritoneum.

CHAPTER VII.

PANCREAS.

Sect. I.—Normal Histology.

The pancreas, analogous in its structure and functions to the salivary glands, is situated transversely in front of the vertebral column, between the spleen and duodenum. It consist of acini which empty their product of secretion, the pancreatic juice, through the canal of Wirsung, into the ampulla of Vater, in the second portion of the duodenum. There exists a second excretory canal coming from the head of the pancreas, and opening separately near the former. The acini or glandular culs-de-sac are from .045 mm. to .090 mm. in diameter; they have a very thin membrane lined by pavement cells, the protoplasm of which becomes granular by the action of acetic acid, and is dissolved by an excess of this acid. The excretory ducts, the thin wall of which consists of connective tissue and elastic fibres, are lined by a single layer of small cylindrical epithelial cells.

When these ducts are injected with a solution of Prussian blue, with continuous and slight pressure, the injection at first penetrates into the central lumen of the culs-de-sac, then into a system of canals forming a complete network around the glandular cells. This network of canaliculi is comparable to that of the intralobular biliary canaliculi.

The acini of the gland are imbedded in a mass of adipose tissue, which contains the bloodvessels and nerves. The bloodvessels and lymphatics have the same arrangement as in the salivary glands. The nerves come from the great sympathetic, consist mostly of fine fibres, and accompany the vessels.

The pancreatic juice is clear, limpid, slightly viscid, alkaline, contains albuminous materials, and possesses as an essential property the power to emulsify fats; it also acts like the saliva transforming into sugar the amylaceous substances; finally it assists in the digestion of nitrogenous substances. Therefore the pancreas is one of the most essential glands in intestinal digestion, if it is not positively necessary to life. When the pancreatic juice does not reach the intestines, the fatty substances are incompletely digested, and they are found in the feces, which are generally liquid (fatty diarrhœa).

Sect. II.—Pathological Anatomy of the Pancreas. Parenchymatous Inflammation.

According to Hoffmann the pancreas is always altered in typhoid fever in the same manner as the liver. There is seen during the first week of the fever a very intense hyperæmia of the connective tissue, while the

glandular cells are hypertrophied. In the second week, the cells contain several nuclei; their protoplasm becomes filled with fatty granules, which obscure the nuclei; the contour of the cells is not very decided. The hypertrophy of the acini, which results from this lesion, causes pressure upon the bloodvessels, and an anæmia of the interstitial connective tissue. It is very probable that a similar lesion exists in a number of infectious diseases.

Suppurative inflammation of the pancreas seldom occurs; it is met with in the form of disseminated metastatic abscesses or diffused suppuration of the gland, or as an inflammation extending to the surrounding connective tissue and lymphatic glands The pancreas may be surrounded by an abscess, which may open into the peritoneal cavity, into the duodenum, or into the stomach. These abscesses should not be confounded with cysts containing a whitish pulp, which are sometimes found in this organ.

Interstitial inflammation may occur in the connective tissue of the pancreas. The few cases of this lesion which have been reported show that the head of the pancreas joins in the chronic inflammatory thickening of the connective tissue which surrounds it and the duodenum. This is often seen when a biliary calculus is arrested in the ductus communis choledochus near the duodenum and causes a chronic inflammation of all the surrounding connective tissue. In cases of tumors of this region, or in simple ulcers of the pylorus or duodenum, etc., the pancreatic duct is either normal or contracted.

Induration of the Pancreas.—We have frequently examined pancreases, hard and of a gray color, in which the glandular acini were perfectly marked out. This condition has been taken for scirrhus. In our examinations we found no very appreciable lesion of the organ. Its appearance would suggest to a beginner only the idea of cancer. According to Klebs, it is possible that there may be a parenchymatous inflammation similar to that of typhoid fever, or a new formation of acini (an adenoma), or, as Vulpian believes, a thickening of the connective tissue of the organ. In cases of induration seen by us, the acini were large and well developed, and appeared normal, as did also their cells and connective tissue, yet the latter presented no adipose tissue; on the other hand, when the pancreas is soft, and the acini are small and atrophied, a soft and very abundant adipose tissue takes the place of the glandular parenchyma.

Fatty Degeneration and Infiltration.—Fatty infiltration of the epithelial cells of the glandular acini, and a new formation of adipose tissue, should not be confounded with one another; they are distinct changes which have nothing in common.

Granular *fatty degeneration* of the epithelial cells of the acini is seldom seen, and the conditions under which it is found are not well determined. We have seen one example in senile marasmus. It is probable that it may be found in a number of cachexies. When there is an obstruction to the discharge of the pancreatic juice, the glandular acini

are atrophied, and their cells filled with fatty granules. Atrophy of the pancreas may be a consequence of the fatty degeneration of its acini.

Fatty infiltration of the connective tissue which invests the pancreas, and penetrates with the vessels between the lobules, is a quite frequent lesion. When from alcoholism, from chronic diseases of the heart, from diabetes, from hindrance or arrest to the flow of the pancreatic juice, the glandular parenchyma has partially or entirely disappeared, it may be replaced by adipose tissue, which is developed in the fibrous stroma of the organ around its vessels and glandular ducts. The newly-formed adipose tissue resembles very closely the shape of the gland, and at the autopsy there may be found a mass of adipose tissue having the size, seat, and configuration of the pancreas, presenting at its centre the canal of Wirsung, without there being a single normal acinus.

Atrophy of the pancreas may occur from various causes: 1st, from pressure from without, exercised upon the gland by neighboring tumors; 2d, from pressure from within, by distension of cysts, caused by concretions in the excretory ducts of the gland; 3d, from granular fatty degeneration of the epithelial cells of the acini; 4th, from interstitial inflammation, and, according to Kolb, especially by stasis of blood in the gland in consequence of chronic diseases of the heart, liver, and lungs. Munk and Sylver have each seen a case of atrophy of the pancreas in diabetes. Sometimes the atrophied acini are replaced by adipose connective tissue, which forms around them; sometimes there is no increase of fat, but the acini are found in the midst of a loose connective tissue, and the pancreas is much atrophied both in appearance and reality. This condition is frequently associated with calcareous concretions, or with a whitish pulp contained in the ducts.

Amyloid Degeneration.—According to Rokitansky, the cells of the acini may undergo amyloid degeneration. These cases are very rare, and even doubtful. The vessels of the pancreas have several times been found in a state of amyloid degeneration in connection with similar conditions of the liver and spleen.

Tumors of the Pancreas.—*Tuberculosis* of the pancreas so seldom occurs that Cruveilhier was inclined to doubt its existence, and believed that the cases regarded as such are only a caseous alteration of the neighboring glands. The tuberculosis of the pancreas is always secondary to that of the lungs and peritoneum; the miliary tubercle granulations are developed in the connective tissue separating the acini. In a case reported by Aran there was a tuberculous caseous mass in the acinus itself.

Syphilitic gummata are very seldom met with. Klebs has seen gummata in the pancreas of a fœtus of six months which had syphilitic lesions of the lungs, liver, and kidneys.

In a case of *lymphoma* of the stomach and corresponding lymphatic glands reported by Lépine, the right half of the pancreas was enlarged and compressed, but not included in the tumor formed by the glands. Instead of normal glandular pancreatic tissue, a section showed a soft, whitish tissue resembling an encephaloid. The pyloric region, liver,

diaphragm, and right lung were involved, as well as the pylorus, pancreas, and lymphatic glands. The morbid tissue of the stomach, liver, and pancreas was formed of reticulated lymphatic tissue.

Carcinoma.—Carcinoma of the pancreas is infrequent. It may be primary or secondary. From the statistics of Willigk, of 467 cases of carcinoma, 9 were carcinoma of the pancreas, the majority being secondary. Primary carcinoma is most frequently developed at the head of the pancreas, very seldom at the left extremity or middle. As primary carcinoma of the pancreas very soon extends from the head of this organ to the neighboring parts, to the duodenum, lymphatic glands, ducts, etc., it is very difficult to determine its origin when a tumor including these organs is found at the autopsy.

Primary carcinoma may be either scirrhous, encephaloid, or colloid. It may begin by one or more tumors which are united, when a portion of the gland is soon transformed into a uniform cancerous mass. When the tumor is limited to the head of the pancreas, the canal of Wirsung is contracted; it leads from the duodenum into an indurated tissue which compresses it, and the discharge of pancreatic juice is prevented. If the left half of the pancreas is not included in the lesion, but continues to secrete somewhat altered juice, the excretory ducts are dilated in this portion of the gland, and form cysts. The subserous connective tissue, the muscular layers, and the submucous connective tissue of the duodenum, as well as the ampulla of Vater, and ductus communis choledochus, soon become involved, and there frequently results a narrowing of the duodenum, perhaps considerable, followed by an icterus, etc. The extension to the lymphatic glands may occasion pressure upon the vena porta; the infiltration of the subperitoneal connective tissue terminates by compressing and narrowing the aorta. The stomach is very seldom secondarily invaded by the tumor. Klebs and Lücke have reported a primary colloid carcinoma of the pancreas in which a secondary dropsical and cystic dilation of the omentum was found projecting prominently below the transverse colon. This secondary tumor of the peritoneum had been punctured during life.

Secondary carcinoma of the pancreas, due to an extension of the carcinoma from surrounding parts, the stomach, the duodenum, the liver, the lymphatic glands, is seldom seen in the form of isolated nodules, at least when it is not a melanotic tumor; generally the new formation of the pancreas is directly continuous with the primary cancerous mass. The head of the pancreas is almost always the first region invaded, and it is unusual for the entire organ to be degenerated.

Cylindrical-celled epithelioma of the pancreas has been once seen by E. Wagner. It probably followed a similar epithelioma of the mucous membrane of the duodenum.

Sarcoma of the pancreas has been met with only in the form of a melanotic tumor.

Cysts.—The only cysts of the pancreas are those which result from a dilatation of the excretory ducts of the gland. A tumor, such as carcinoma of the head of the pancreas, or of the duodenum, or an encysted

biliary calculus, obstructing the ampulla of Vater and causing an inflammatory induration of the surrounding connective tissue, or pancreatic concretions obstructing the excretory duct of the pancreas, occasion obstructive cystic dilatation of the duct. These dilatations, somewhat regular, with protuberances along the principal duct, have the form of sacculated or spherical dilatations, in the secondary ducts which penetrate as far as the surface of the gland. There develop in the left or middle portion of the pancreas prominent tumors, which appear to be spherical cysts bounded by a membrane; but, upon section, there is always seen a communication with the principal duct by a narrow passage. The sac-like dilatations and the irregular dilatation of the canal of Wirsung contain either a whitish chalky mucus, rendered opaque by the salts it contains, or true concretions, usually friable and white.

These cysts of retention and calculi are not unfrequently met with. In a case recently observed, the large dilated excretory canals contained an opaque, thick, white pulp, white and irregular friable calculi consisting of phosphate and carbonate of lime. The internal surface of the canals was lined by a single layer of very thin flat cells with irregular edges, provided with an oval flat nucleus. The wall of the canals was thickened, formed of superimposed layers of laminated connective tissue separated from one another by flat nucleated cells. These modifications in the structure of the wall and the shape of the epithelial cells were evidently due to the pressure exerted by the solid concretions. To the unaided eye, no traces of the glandular acini were seen; the secreting structure of the pancreas was replaced by adipose tissue. Microscopically, there were seen in the fibrous trabeculæ of this tissue, only the small excretory canals unchanged and provided with their cubical epithelial cells.

The size of pancreatic concretions is very variable. Their presence may cause an acute inflammation and even the formation of an abscess.

SECTION III

CHAPTER I.

THE SPLEEN.

Sect. I.—Normal Histology of the Spleen.

The spleen, an asymmetrical vascular blood gland, consists of a fibrous envelope (capsule) covered by the peritoneum, of a soft red parenchyma containing special bodies named Malpighian corpuscles, of vessels, and of nerves. The splenic pulp is formed of reticulated tissue. The fibrous membrane (capsule) of the spleen is very resisting and dense, formed of parallel laminæ of connective-tissue fibres and elastic fibres; between these elements a few flat cells are interposed. Fibrous tissue trabeculæ arise from its inner surface and form numerous partitions traversing the splenic tissue. This fibrous tissue also accompanies the vessels, arteries, and veins, forming a fibrous sheath for them. These trabeculæ constitute the fibrous stroma of the organ. They contain smooth muscular fibres in those animals which have them in the capsule (many mammiferæ). In man, the presence of smooth muscular fibres is affirmed by some histologists (Frey, Meisner), and denied by others (Kölliker, Gerlach, Henle).

The splenic artery and vein enter the organ at the hilus, surrounded by a fibrous sheath provided by the capsule. This sheath is thinner than the arterial wall, but thicker than the venous wall. Each of the principal branches of the splenic artery divides and forms branching tufts, which do not anastomose with those formed by the neighboring arteries. When these branches have a diameter of .2 mm. to .4 mm. they are separated from the veins, and have along their course the Malpighian bodies.

The Malpighian bodies or corpuscles of the spleen are spherical or oval in shape, surrounding an arteriole; their diameter varies from .2 mm. to .7 mm. They are always intimately connected with an arteriole, which passes through their centre, or near their periphery, and which sends into their interior small arterioles and a network of capillaries. These corpuscles consist of a reticulated tissue, similar to that seen in the closed follicles of the intestine. The meshes of this tissue are connected with the sheath of the arterioles and capillaries: the meshes at the periphery of the corpuscles are narrower and the fibrils are nearer together, but there is no true membrane separating them from the splenic pulp. The reticulum of the pulp is continuous with the reticulated tissue of the corpuscles.

The cellular elements contained in the meshes of the reticulated tissue are lymph cells, both small and large, provided with a nucleus; the largest contain pigment granules, or even red blood corpuscles.

The Malpighian corpuscles of the spleen do not inclose veins, while the splenic pulp is traversed by a very dense and abundant venous network. A thin section of the splenic pulp shows sections of small veins very close together, forming the essential element of the pulp, and separated from each other by a reticulated tissue, with very fine meshes and filaments (intervascular cords of Billroth). The veins have no distinct wall, and are limited by a thickening of the reticulated tissue; they are lined by large flat endothelial cells.

The cellular elements contained in the meshes of the reticulum of the splenic pulp are the same as those in the reticulum of the Malpighian corpuscles. From the above description the corpuscles may be compared with the follicles of the intestine and of lymphatic glands. The whole spleen may be compared to a lymphatic gland in which the medullary substance is replaced by a cavernous tissue; the veins replacing in the spleen the peri-follicular spaces and the lymphatic canals of the glands. It is evident that the lymph cells are able to pass from the reticulated tissue into the blood, and from the blood into the reticulated tissue.

The mode of connection of the arterioles and corpuscles with the venous network of the pulp is not yet accurately understood. Histologists have not yet agreed upon the manner of communication: some believing that the arteries are directly continuous with the veins; others admit the existence of an intermediary capillary network; and, finally, others think the communication takes place through the spaces bounded by the fibrous network of the splenic pulp. The blood in the splenic vein contains a greater number of red corpuscles than the blood in the artery (Malassez); therefore it has been inferred that the most essential function of the spleen is the formation of red corpuscles, although the blood pigment found in the lymph cells, indicates the destruction of a number of these elements.

The lymphatics of the human spleen are not very abundant; they are found in the capsule of the organ, and also follow the arteries into the substance of the spleen. It is very probable that the lymphatics of the arterial sheaths penetrate as far as the Malpighian corpuscles, but their relation with the reticulated tissue of the spleen is not known.

The nerves of the spleen, consisting of large medullated fibres and numerous fibres of Remak, come from the splenic plexus, and penetrate the organ in company with the arteries. They may be followed upon the arterioles as far as the corpuscles, and, according to Ecker, terminate in free extremities.

Sect. II.—Pathology of the Spleen.

Atrophy of the spleen is frequently seen in old persons; it generally is associated with a fibrous thickening of the splenic capsule. The parenchyma of the organ may also be indurated, but usually it is of normal consistence. It is generally pale, anæmic, at least when there has been,

during the life of the patient, cardiac disease accompanied with interference of the circulation of the blood. The thickening of the capsule of the spleen consists in the formation of laminæ of connective tissue, separated by flat cells. This tissue is remarkably hard and resisting; frequently it is like cartilage and infiltrated with calcareous salts. A chronic inflammation of the peritoneum upon the surface of the capsule is always seen, and new formations in the shape of granulations are present; they are hard and non-vascular, are in the form of patches or floating filaments.

HYPERÆMIA OF THE SPLEEN.—Congestion of the spleen occurs in a number of very different morbid states, and also is the first stage of the majority of diseases of the spleen. No organ is more prone to congestions; but the structure of its trabeculæ and capsule, which contain elastic fibres and smooth muscular fasciculi, is such that it generally returns to its normal condition. When, however, the cause of the congestion is frequently repeated or permanent, it is not the same, there is then a permanent increase in size. The hyperæmia may be acute or chronic.

An acute temporary congestion occurs in all infectious febrile diseases, such as eruptive fevers, pyæmia, erysipelas, etc., and in a number of pyrexiæ. There occurs in this congestion not only a filling of the vessels with blood, particularly the veins of the splenic pulp, but very probably also an interruption of the blood-making function of the spleen, and the formation of white corpuscles and the destruction of red ones, beside the changes peculiar to each disease. The precise alteration of the splenic blood following each infectious febrile disease is not known. In most cases of acute congestive hypertrophy seen in infectious diseases, the spleen is soft, and its pulp is not of a deep red color, but is pink, because of the numerous white corpuscles contained in the blood.

In *intermittent fevers* the spleen is tumefied during the fever. At first, the hyperæmia passes off during the apyrexia to return with each access of the fever. Soon, however, the tumefaction becomes permanent. Splenic congestion in these fevers is always accompanied with destruction of the red blood corpuscles in the spleen, and pigmentation of the splenic tissue. When the disease has continued for some time, and a malarial cachexia supervenes, the spleen is not only congested, but is also indurated, a cirrhosis with pigmentation.

Typhoid fever is one of the infectious febrile diseases which most frequently implicate the spleen. This organ is almost always hypertrophied, reaching at least twice its normal size. The congestive hypertrophy varies: it may increase to four or six times its usual volume. In the adult, the increase in size is less than it is in children, for in the former the capsule of the spleen is denser, thicker, and consequently less extensible. The capsule is thin and tense. A section of the organ shows it to be infiltrated with blood, brown in color, or more often pink. The Malpighian corpuscles are sometimes very apparent and large, or they are invisible, a fact due very probably to post-mortem softening. The consistence of the spleen is generally less than normal. When examined

microscopically in the fresh state, the cellular elements of the splenic pulp are found surrounded by red corpuscles, on the tenth or fifteenth day of the disease; the swollen lymph cells, with granular and soft protoplasm, frequently have several nuclei. Many of the lymphoid cells contain one or more red corpuscles. The nuclei of these lymph cells are very distinct. The red corpuscles within the protoplasm are sometimes normal in size, and easily recognized by their shape, their color, and the homogeneous appearance of their structure; sometimes they are small, measuring only .003 to .004 mm.; sometimes they are granular and are only recognized by their color. The large endothelial cells of the veins always appear normal to us; but Billroth has described a proliferation of their nuclei in typhoid fever.

The number of lymph cells containing red corpuscles is considerable in typhoid fever; from a drop of the pulp obtained by scraping, at least one hundred may be counted.

When the fever terminates in recovery, the spleen diminishes in size; its cut surface is brown in color and not much congested. Microscopic examination does not show the cells in a state of proliferation; but the lymph cells contain fatty granules (Fœrster) and red pigment.

The lesion of the spleen in typhoid fever is therefore not a simple congestion; it seems more like a parenchymatous inflammation, as there is a proliferation of the lymph cells. On the other hand, it is not a simple inflammation, since there is, as an essential phenomenon, a destruction of the red corpuscles which are taken up by the lymph cells.

In very intense congestions due to intermittent fever and typhoid fever, there are also found true hemorrhagic foci, and in many cases ruptures of the spleen. In typhoid fever sometimes splenic infarcti are met with.

A chronic congestion is always observed in diseases of the liver accompanied with interference of the portal circulation, and in diseases of the heart with obstruction to the venous circulation. The pressure of the blood is increased in the splenic vein in these diseases, and there results a blood stasis with congestive hypertrophy of the spleen. Diseases of the heart are not so apt to cause intense hypertrophy of the spleen as chronic diseases of the liver, particularly cirrhosis. Generally, chronic congestion is accompanied with some amount of interstitial splenitis with induration and thickening of the capsule, with or without pigmentation of the elements of the splenic tissue.

In *chronic disease of the heart* the spleen almost always has its capsule indurated and thickened, and upon its surface exist small vegetations with free extremities, or fibrous cartilage-like patches. The size of the spleen is normal or is increased. In old persons it is smaller than in middle age. The splenic tissue presents the color of venous blood; it becomes paler upon exposure to the air. The cut surface is smooth and somewhat firm; by scraping it yields some splenic pulp. By closer examination there are seen upon the deep red surface fibrous trabeculæ and vessels much more distinct than normal. The trabeculæ are thickened and have a greater number of connective-tissue fibres, than in the normal state. The arterioles are firm and their wall thick; their internal coat is frequently the seat of an endarteritis, especially when there are atheromatous lesions of the aorta; their external coat is also thickened. The reticu-

lated tissue of the pulp and corpuscles is usually not thickened. The capillary and venous systems of the organ are filled with blood.

In diseases which cause an interference with the circulation of the vena porta, especially *cirrhosis*, the spleen is much hypertrophied, and is at least double its normal size; as in the preceding case, the capsule is thickened, and sometimes covered with numerous vegetations; there is also ascites with the subacute peritonitis which so frequently accompanies the cirrhosis. The color of the cut surface is blood red; the fibrous trabeculæ are thickened.

Microscopic examination of the splenic pulp obtained by scraping the fresh spleen, frequently shows lymph cells containing brown or black pigment surrounding the nucleus. The endothelial cells of the veins of the pulp often have pigment granules in their protoplasm. In thin sections these veins are found larger than normal. The trabeculæ of the capsule and reticulated tissue are normal or slightly thickened. In these cases, therefore, the hypertrophy of the spleen is especially due to a distension of the veins and a slight thickening of the fibrous trabeculæ. The lymph cells are not more numerous than normal.

Interstitial Splenitis.—Chronic congestions of the spleen terminate, as above stated, in a new formation of connective tissue, which may be considered as indicative of an inflammation or slow irritation similar to that of cirrhosis of the liver or interstitial pneumonia. This lesion is seen in a more advanced and intense degree in *malarial cachexia* than in any other disease. The spleen of persons who die with this cachexia varies very much in appearance. Sometimes it is red or pink upon section, or it may be of a brown or slate color, and the trabeculæ as well as the splenic pulp may be dark brown. The differences in color depend upon the amount of pigment contained in the connective tissue and in the blood of the spleen. An almost constant lesion in intermittent fever which has lasted for some time is a fibrous thickening and induration of the capsule, which is also covered upon its surface by inflammatory productions. These consist of prominent, very dense, frequently cartilage-like granulations, and of fibrillar-like vegetations or fibrous floating false membranes. The false membranes are vascular, while the fat granulations forming small fibromata with laminated layers (see p. 92) are non-vascular or only have very few vessels. The size of the spleen is almost always increased. A pigmented spleen may reach 20 to 25 centimetres in its largest diameter. These spleens are indurated, but not to such a degree as is a cirrhotic liver. On examination of the pulp obtained by scraping from a red or pink spleen, there are found a small number of lymph cells containing pigment granules; in a spleen indurated and pigmented there are found many lymph cells infiltrated with the pigment granules. These granules are either small, brown and brilliant when they are examined with high power, or they are large and dark, or perfectly black. They are contained in the lymph cells, but are also sometimes free in the blood. The lymph cells generally have only one nucleus. The large endothelial cells of the internal coat of the veins also frequently contain brown or black pigment, but in the form of fine granules and not large grains.

Microscopic examinations of thin sections show the fibrous trabeculæ,

coming from the capsule, thickened to a varying degree. There is a new formation of connective tissue fibres in these bands. The Malpighian corpuscles are usually very distinct. The reticulated tissue of the corpuscles and pulp undergoes changes, which essentially consist in a pigmentation of the lymph cells contained in the meshes of the reticulum. The cells, however, within the reticulum of the corpuscles are less pigmented than those in the bands of reticulated tissue between the veins of the pulp. In this portion of the spleen, the splenic veins have upon their internal surface slightly pigmented or normal endothelial cells, and in their lumen numerous lymph cells deeply pigmented among the white blood corpuscles. These veins have their lumen dilated, if the process is recent, and if the organ is slightly indurated; they are normal or even contracted, if the spleen is indurated and the lesion chronic. The reticulated connective tissue separating the veins from the pulp is very deeply pigmented. Examining this tissue with a high power, it is found that the color is due to the lymph cells within the reticulum. These cells are generally black. When the cellular elements are removed from the reticulated tissue, the filaments which compose the reticulum are usually not thickened to any notable extent, but have upon their surface very fine pigment granules. In spleens which are greatly indurated, these filaments may be two or three times thicker and more rigid than in the normal state. Yet they are always composed of fibres, and have no nuclei at their intersections if the section is very thin and well pencilled.

The enlarged arterioles, arteries, and veins of the spleen have their walls thickened, indurated, and infiltrated with pigment, especially in their peripheral zone. The connective tissue forming the large fibrous trabeculæ also have a large amount of black pigment in the protoplasm of the cells and around them.

The lesion of the spleen in intermittent fever is such as to essentially consist in a destruction of the red corpuscles, and in the formation of black pigment from them. This change is not confined specially to malarial fever; as has been seen, there is an absorption of the red corpuscles by the white blood corpuscles in other infectious febrile diseases, typhoid fever, for example; besides, chronic congestions of the spleen, particularly in cirrhosis, terminate in induration and pigmentation of the cells. But the exaggerated pigmentation is especially marked and constant in malarial cachexia, and it is in miasmatic infection that melanæmia or black pigmentation of the white blood corpuscles occurs.

In repeated congestions of the spleen, and in interstitial splenitis, it has been seen that there occur a thickening of the capsule, and a new formation of connective tissue upon its peritoneal surface. The folds of peritoneum forming the gastro-splenic omentum, the phreno-diaphragmatic and pancreato-splenic ligaments are inflamed, resulting in an intimate union of the spleen with the neighboring organs by false membranes which become organized connective tissue. This *fibrous peri-splenitis* is most frequently the consequence of primary changes in the spleen, but it may also be the evidence of a general or local peritonitis from any cause. In intermittent fever it is always present to a varying extent.

Suppurative Splenitis.—Large abscesses in the spleen are very seldom seen; they may be caused by contusions of the splenic region, by fracture of the ribs, etc. In a few cases the cause of splenic abscesses found at autopsies, is not known, yet, during life, they may have occasioned very intense febrile symptoms. In other cases, also rare, abscesses of the spleen have been seen in debilitated persons who have had fevers or have lived in a malarial country.

Suppurative splenitis occurs in three forms:—

1st. As a diffused infiltration, so that a considerable part of or the entire splenic parenchyma is softened, grayish-white or pink, reduced to a pulp or pus; the blood and the débris of the tissue of the organ are mixed together. Lesions of this kind have been described as *gangrenous spleens*.

2d. One or more abscesses of varying size have formed in the tissue of the spleen. These abscesses are a result of traumatism, of phlebitis of the splenic vein, or they are metastatic abscesses, or a consequence of fevers of low type (typhoid especially); they may unite and form purulent foci, which are separated from the normal tissue of the spleen by a pyogenic membrane. Abscesses of this kind may attain considerable size; they are generally encysted, and their pyogenic membrane becomes fibrous. In some cases the capsule of the spleen is thickened when they are superficial. In other cases—the capsule being itself invaded by the suppuration, and fibrous adhesions being established with the neighboring organs—an abscess of the spleen may open into the stomach, or through the diaphragm, into the pleura and lung, or it may discharge through the abdominal or thoracic walls. In some cases the abscess communicates with the splenic vein, and, finally, it may work its way into the sub-peritoneal cellular tissue as far as the pelvis and open into the vagina.

3d. Metastatic abscesses occur frequently in the spleen as well as in other organs; they are met with in pyæmia, in puerperal fever, in acute endocarditis, in phlebitis, etc. They are located especially at the periphery of the spleen, their base towards the capsule. Their number is generally limited; their size varies from a hemp-seed to a hazel-nut or larger. They begin by a small dark-red-colored spot; pus is soon seen in the centre of this area, which gradually softens, becomes fluid, and forms a small abscess.

The pathogenetic conditions for the formation of these metastatic abscesses frequently occasion at the same time suppurative peri-splenitis or general peritonitis.

Infarction of the Spleen.—The spleen is an organ in which infarcti are very frequently met with. This is explained by the fact of the splenic artery having its origin from the aorta, not far from its arch, and by the absence of anastomoses between the branches of the splenic artery. When, therefore, the aorta is atheromatous, and fragments of fibrin enter into the branches of the artery, the portion of the spleen receiving its blood from the obstructed artery is the seat of an infarctus. It is not possible for the circulation to be re-established by collateral vessels. Infarcti should be carefully distinguished from metastatic

abscesses. Splenic infarcti are seen in atheromatous changes of the aorta, of the aortic valves, of the splenic artery, in endocarditis, etc. Their size and number vary. A spleen may be entirely invaded by the lesion, or there may be only one, two, or three small infarcti, the size of a hazel-nut or walnut. Their form is characteristic, and usually resembles a cone, the base towards the surface of the organ and the apex towards the hilus. When a large extent of the spleen is involved, the splenic artery or several of its branches are completely obstructed by an adherent clot. At the beginning, the cut surface is deep red, almost black, owing to the blood having coagulated in all the small veins and in the arteries, giving to the whole the color of venous blood. Later, when the fibrin has become granular, when the corpuscles and fibrin are transformed into a granular fatty substance, the color of the section is grayish or yellowish and opaque. The consistence of the infarctus is at first much greater than that of the normal spleen; later, the part becomes softer, semi-fluid, and yellow, and has a doughy feel. The softening may occur in such a manner that a portion of the infarctus is surrounded and partly separated by fluid. The healthy part of the spleen limiting the region where the circulation is arrested is congested and inflamed, but suppuration never occurs.

From the complete obstruction of the arteries, from the coagulation of the blood in all the vessels of the altered region of the spleen, and from the resulting necrotic softening, this process may be compared to that of gangrene. The mortification is owing to the arrest of the circulation of the blood. But here, as in the liver and kidney, the mortification occurs without any communication with the atmosphere, and there is no putrefactive or gangrenous odor. Anatomical lesions of the spleen comparable to putrid gangrene may occur, but only when a portion of the mortified spleen is surrounded by the pus from a peri-splenitis.

Microscopic examination of recent infarcti shows the vessels simply distended with coagulated blood. Soon the lymph cells contained in the reticulum of the fibrin of the clot become fatty degenerated. The fat separates and forms round collections of crystals of fat acids, which, with a low power, appear as opaque bodies. The lymph cells contained in the reticulated tissue of the spleen undergo caseous degeneration, while the elements of the blood in the vessels pass through the changes previously described.

The trabeculæ of the reticulum in time experiences a molecular destruction, as do also a number of the lymph cells, and there results a partial or extensive softening of the infarctus, and the formation of a pulpy mass, in which are found granular cells and albuminoid and fatty granules. The infarctus is at first swollen, later it contracts, and there is seen a depression upon the surface of the spleen.

The capsule of the spleen is almost always affected in this lesion. At first it is congested, afterwards it presents villi and vegetations, is thickened, becomes denser, and may even undergo a kind of calcification.

As the infarctus softens, the fluid portion is absorbed by the healthy peripheral portions of splenic tissue. The loss of substance is, in part, replaced by new-formed connective tissue from the capsule, which is here

depressed, and in part by a fibrous growth of the neighboring splenic tissue. Finally, a fibrous cicatrix replaces the infarctus.

In these cicatrices of the spleen, recognized by a depression upon the surface with thickening of the capsule, there is generally calcification. Examination of the calcified tissue does not show true osteoblasts with their canalicular prolongations. A decalcified section shows small cavities, which represent the spaces containing pre-existing connective tissue cells.

Especially in infarcti, but also in the majority of indurated spleens, either from cirrhosis of the liver, or diseases of the heart, the splenic arteries are indurated, and their walls considerably thickened, due to endarteritis and periarteritis, with or without calcareous incrustation.

Ruptures of the Spleen.—Traumatic or spontaneous ruptures of the spleen sometimes occur. When this accident takes place, it almost always happens in spleens swollen from congestive or inflammatory lesions, as in intermittent fever, typhoid fever, cholera, syphilis, etc. They are met with as superficial or deep fissures, varying in size, and are seated in all parts of the organ, particularly upon the external surface, in the large longitudinal fissure. A clot of blood is found at the seat of rupture; this clot is sometimes continuous with a cruoric mass which surrounds the entire organ as a large clot. Hemorrhage into the peritoneal cavity at times occurs, resulting in rapid death when the amount of blood is considerable, or symptoms of peritonitis if the escape of blood occurs gradually during several days.

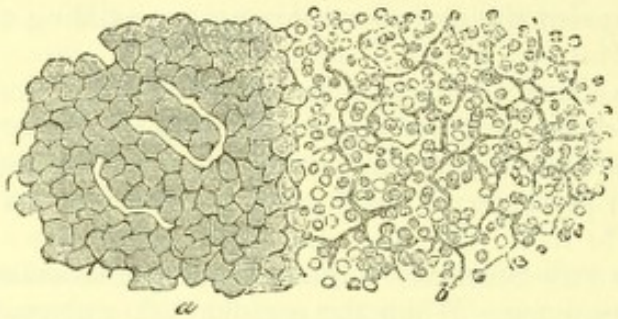
Amyloid Degeneration.—Amyloid degeneration of the spleen is seen in two forms: in one, it is limited to the Malpighian corpuscles; in the other, the amyloid degeneration is diffuse. In both varieties the spleen is hypertrophied, spherical, and of doughy consistence; its capsule is stretched, and is frequently thickened by new formation of connective tissue upon its surface; its edges are thick and rounded.

In the *first variety* the Malpighian corpuscles are seen, upon section, to be increased in size, measuring from one to two millimetres or more in diameter; they are semi-transparent, consisting of a hyaline substance, which is colored mahogany-red by a solution of iodine. The appearance of these large numerous corpuscles resembles boiled sago grains, and the lesion is termed a *sago spleen*.

Sections of an amyloid spleen, colored by iodine and examined with low power, show that the diseased parts are appended to the arteries, or arranged around these vessels. The degeneration is best studied by staining with the violet of methylaniline, which colors the amyloid infiltrate violet-red and the normal parts blue. (See p. 933.) The wall of the arteries which pass through the diseased corpuscles is infiltrated or normal. In two cases we found the arterial wall unchanged, while the walls of the capillaries and most of the elements of the splenic corpuscles, the lymph cells and reticulated tissue, were infiltrated by the amyloid substance. The degeneration of the lymph cells is seen by tearing the corpuscle with needles in the fresh state; in thin sections, the lymph cells of the corpuscles are vitreous in appearance, spherical or

transformed into small irregular blocks, or are united to one another and have lost their nuclei. When examined with high power, most of the fibrils of the reticulum, in the diseased corpuscles, are seen infiltrated with the amyloid substance; the capillary walls are also in the same con-

Fig. 300.



Amyloid degeneration of the spleen—"sago spleen." A portion of one of the infiltrated Malpighian corpuscles *a*, with the adjacent normal splenic tissue *b*. Showing the increase in size and, in many parts, the coalescence of the cells, of which the corpuscle is composed. × 200. (*Green.*)

dition. As all these parts, lymph cells, reticulum, and walls of the capillaries, have a tendency to blend together, they form homogeneous masses, which are channelled by narrow clefts forming a network; this is a network of capillaries which have their lumen increased, in which the endothelial cells and corpuscles of the blood are preserved intact. In recent investigations made with the violet of methylaniline the endothelium of the capillaries was always found to be normal.

The altered Malpighian corpuscles are much enlarged, and in some places are almost in contact with one another, only separated by bands of normal splenic tissue. Very frequently it is not only the corpuscles which are infiltrated with the amyloid substance, but the veins of the pulp near the corpuscle also have their wall slightly thickened and diseased. The endothelial cells of these veins are always normal. The calibre of the veins is not changed; the reticulated tissue surrounding them, and the lymph cells of the reticulum of the pulp are generally unaltered.

The *second variety* of amyloid degeneration, general and diffuse infiltration of the spleen, is very probably only a more advanced stage of the lesion which began in the capillaries of the corpuscles. The spleen is much hypertrophied, and upon section is homogeneous and vitreous in appearance, according to the amount of infiltration. In portions where the lesion is at its acme, large masses of the spleen are pale, anæmic, and waxy. The circulation, although interfered with, is never entirely interrupted. In very advanced amyloid infiltration there may be foci of suppuration.

In three cases of complete amyloid infiltration, that we have recently studied, all the vessels were altered in a very high degree, although permeable to the blood. The capsule and trabeculæ of the organ were thickened; they were traversed by a few capillaries, the walls of which were diseased. The Malpighian corpuscles were small and imperfectly colored red, in such a manner that a zone of normal lymph cells was always found at the centre of the corpuscle surrounding the artery.

The veins of the pulp were implicated, their walls were much thickened by the degeneration, although their calibre remained normal; a very distinct and normal endothelium was seen in their interior which latter contained blood corpuscles. The reticulated tissue which united the veins of the pulp was sometimes normal, or in part amyloid. The lesion, therefore, affected alike the fibrillar network, which was very thick, and the cells contained in its meshes.

In diffused infiltration, the splenic pulp, and especially the walls of the small veins of the pulp, appeared to be the essential seat of the degeneration. The two varieties are not always distinctly separated, and nothing varies so much as the intensity and seat of the lesion, according to each particular case.

Tumors of the Spleen.

Leucocythæmia.—Generally in leucocythæmia and lymphadenitis, the spleen is infiltrated with numerous white blood corpuscles, and is very notably hypertrophied. But this hypertrophy is never so great in splenic leucocythæmia. In this form of the disease the spleen may acquire a diameter of twenty-five to thirty centimetres.

The increase in size is due to the hypertrophy of the Malpighian corpuscles, which may become as large as a hazel-nut or walnut. A section of the organ shows numerous gray or whitish nodules, sometimes yellow at their centre, and yielding a juice by scraping. The nodules, formed of a homogeneous tissue, are separated from each other by red zones, frequently so narrow that they appear to touch at their periphery. The cellular elements obtained by scraping the gray portions are lymph cells, the majority containing a single nucleus; some, however, are large, measuring .015 mm. to .020 mm., granular, and containing several round or oval nuclei.

In large and thin sections of these spleens, examined with the microscope, the whitish nodules are found to correspond to the Malpighian corpuscles; while the red zones which surround them correspond to the tissue of the pulp. The hypertrophied Malpighian corpuscles consist of a reticulated tissue, with fine meshes filled with lymph cells and large proliferating cells. The arterioles passing through these corpuscles have an excessive infiltration of white corpuscles into their walls, so that a transverse cut of the arterioles shows their lumen surrounded by a circle of embryonic tissue. There results a series of small embryonic nodules around the arteriole which traverses the new-formed reticulated tissue of the corpuscles. The meshes of this reticulated tissue are formed of fibrils, mostly thickened. In the central portions of the corpuscles, which are yellow and opaque to the unaided eye, the lymph cells have undergone a granular fatty degeneration.

At the periphery of the hypertrophied corpuscles, in the red zone which separates them from one another, the network of small veins is seen which characterizes the tissue of the pulp of the spleen. This portion of the spleen is evidently atrophied from the compression exerted by the Malpighian corpuscles. The small veins are slightly enlarged,

they contain many lymph cells, and their endothelium is small. There are found only a very few lymph cells which contain brown pigment.

Tubercles.—Tubercles of the spleen are frequently met with as secondary granulations in children, but they are very seldom seen in adults. Sometimes numerous large disseminated miliary granulations are found in the splenic parenchyma with their usual characters; sometimes large masses, the size of a small pea, are met with, formed by the union of several caseous tubercles. Tubercles of the spleen are never primary. The point of beginning of the miliary granulations, according to Billroth and Virchow, is the reticulated connective tissue of the pulp. The bands of thin reticulated tissue separating the veins become thickened, and present new elements; at the same time the endothelial cells of the veins show a multiplication of their nuclei. Fœrster, however, has seen the granulations develop from the fibrous tissue which forms the trabeculæ departing from the capsule of the organ; he has also seen them in the Malpighian corpuscles. The difficulty of anatomically diagnosing tuberculous granulations, is on account of their shape and size. These, with the lymph cells which they inclose, give them a resemblance to the Malpighian corpuscles. But in tubercles the centre becomes caseous, and the cells are infiltrated with fine granules, and atrophied. Again, the small vessels and capillaries which pass through the granulations are filled with granular fibrin, lymph cells and large endothelial cells, and they are obliterated, as has been mentioned under tubercles in general. The elements contained in these obliterated vessels have been taken in Germany for giant cells of a special nature, and characteristic of tubercle. Some German writers, however, are reconsidering this wrong interpretation; yet, without any reference whatever to the description we have given of them, or notice of the criticisms upon giant cells by Thaon and Grancher in their thesis upon tubercle.

Syphilitic Tumors.—It has previously been remarked that the spleen was hypertrophied in syphilis, at the period of syphilitic infection. This tumefaction of the spleen is especially evident in new-born children suffering with syphilis. The organ may also be indurated and cirrhotic, with the capsule much thickened, and covered by fibrous formations; or the spleen may be in a state of amyloid degeneration. Finally, true gummata may be met with, which, however, are infrequent; they should not be confounded with infarcti, which are also found in syphilitic persons.

Carcinoma of the Spleen.—It is doubtful if the spleen is ever primarily affected with carcinoma. We will not positively deny it, but the cases reported as *primary carcinoma* are wanting in histological details sufficient to convince us of their carcinomatous nature. It cannot be diagnosed by the naked eye or by a microscopic examination of scrapings. The stroma of carcinoma, and details of the structure of secondary formations in the glands and other neighboring organs are necessary to support and demonstrate the anatomical diagnosis. We have never seen primary carcinoma of the spleen. Secondary carcinoma, on the contrary, has certainly been met with, following tumors of the stomach,

mammary gland, liver, brain, etc. These formations are seen as nodules or infiltrations, which resemble the tissue and cellular elements of the primary tumor.

Cysts.—Mucous cysts of the spleen are extremely infrequent. Andral reports a case where there existed several visicles, which he compared to cysts of the neck of the uterus; Leudet saw a large cyst divided into four or five compartments by fibrous partitions lined with a pavement epithelium; Magdelain reported a case where the internal wall of a unilocular cyst was smooth and covered with hard patches, formed of carbonate and phosphate of lime and magnesia. The fluid was estimated to be about 3 litres, of a yellowish-brown color, albuminous, and contained lymph cells, red blood corpuscles, and crystals of cholesterin. Fœrster mentions, in the collection at Würtzburg, a serous cyst of the spleen, as large as a hazel-nut, with cartilage-like walls. The mode of development of these tumors is not known.

Andral reports having seen a *dermoid cyst* of the spleen, containing fatty material and hairs.

Parasites.—Single or multiple cysts in the spleen containing echinococci have been very rarely met with. The hydatid sac may be the seat of daughter hydatids, as in the liver. They are most frequently developed in the peritoneum, which covers the organ, and are pedunculated, projecting into the peritoneal cavity. They are generally seen in connection with analogous productions of the liver and peritoneum. E. Wagner has seen an example of Pentastomum denticulatum, surrounded by a calcified cyst, in the human spleen.

CHAPTER II.

THYROID GLAND.

Sect. I.—Normal Histology.

THE thyroid gland, the function of which is unknown, is constructed very much like the racemose glands, except that it possesses no excretory ducts. It consists of closed spherical or oblong glandular vesicles, which join to form round or oblong lobules, separated by bands of connective tissue, thicker than those separating the vesicles. The lobules grouped together form larger lobes surrounded by a capsule which is continuous with the fibrous capsule of the gland.

The vesicles have a diameter of .045 mm. to .110 mm., and consist of a hyaline membrane, lined with a layer of finely granular polygonal epithelial cells measuring .009 mm. to .013 mm. The centre of the closed cavity is occupied by an albuminous fluid. A colloid substance is so frequently found, instead of this fluid, that it may be considered as a normal condition. The colloid degeneration of the cells in the thyroid gland is very easily followed. Between the central colloid mass of the vesicle and its epithelial lining are seen one or more layers of cells, which are round, have lost their nucleus, have a vitreous appearance, and which gradually blend with the mass of colloid substance which occupies the centre of the follicle.

The bloodvessels of the gland are very numerous, and come from the thyroid vessels. They break up into a rich plexus of capillaries around the follicles.

Sect. II.—Pathological Histology.

The lesions of the thyroid gland are extremely rare, with the exception of goitre or hypertrophy of the thyroid body.

GOITRE.—Hypertrophy, commonly known as goitre, consists in a hypertrophy and new formation of the glandular substance. The follicles show a more abundant formation of epithelial cells than in the normal state; they are enlarged and send off prolongations or lateral buds which form new follicles (Billroth). The hypertrophy of the isolated follicles, and the new formation of follicles is sometimes uniform throughout the entire gland, or it is limited to a few lobules. In the latter case there results a tumor united to the gland, and situated upon one of its sides, or a tumor which has a tendency to separate from the gland. The gland is frequently lobulated by the great hypertrophy of some of its superficial lobules.

Frequently the vesicles do not appreciably differ from the normal state; although they are increased in size, yet their lining of epithelial cells and their fluid or colloid contents is very similar to that in the physiological state.

The distension and hypertrophy of each of the glandular vesicles causes the formation of small cysts, and gives a certain softness to the hypertrophied gland (*soft goitre*). A superficial examination of these goitres, by the unaided eye, would lead one to consider them as large cysts; but a microscopic examination shows the presence of vesicles, somewhat enlarged, the partitions of which are distinct. The formation of the cells and of the fluid or colloid substance continuing, the thyroid body is transformed into a multitude of large cysts and the entire gland becomes very voluminous (*cystic goitre*).

In many other cases, the capillary vessels and small arteries are dilated; the large arteries also undergo a change analogous to that seen in cirsoid aneurisms, giving rise to a pulsation in the tumor; the capillaries project into the cavity of the follicles, and hemorrhages occur therein; these are termed *aneurismal goitres*. The vessels are sometimes incrusted in places with calcareous salts.

At other times, the connective tissue of the gland is very evidently thickened and the gland is mostly formed of fibrous tissue, which presses upon the follicles and finally takes their place; this is termed a *fibrous goitre*. In old persons the fibrous goitre gradually becomes harder in consequence of the calcification of the connective tissue. This calcification is limited or it invades the entire tumor (*calcified goitre*).

Tubercles.—Tubercles of the thyroid gland have been described in Part I. The development of the new formation from the epithelial cells and connective tissue of the gland has been pointed out. These tubercles are of very unfrequent occurrence, and do not differ from tubercles of other organs.

Carcinoma.—Secondary carcinomata of the thyroid body are seldom met with, and we know of no histological description. Primary tumors, described as encephaloid cancer, are also very unfrequent. They are large, and by their invasion of the neighboring connective tissue, they have a tendency to project into the cavity of the trachea and œsophagus, giving rise to the same symptoms as a cancerous tumor of these cavities. Their histological description has not been given. The following case seen by us, leads to the belief that the primary tumors of the thyroid gland are epitheliomata and not carcinomata.

A patient, in whom an epithelioma of the œsophagus had been diagnosed during life, presented at the autopsy soft granulations infiltrated with a milky juice, arising in the connective tissue of the neck, and projecting under the mucous membrane of the œsophagus, which over their surface was raised and thin. The connective tissue, infiltrated with large cells, having large nuclei and brilliant nucleoli, resembled the tissue of an encephaloid carcinoma, except that there were no regular alveoli of new formation, it being simply an infiltration of the pre-existing tissue by large cells. The thyroid body presented a similar alteration of its tissue which was infiltrated with a milky juice and contained the same large cells.

An examination of a section, after hardening, showed that the degenerated portions of the thyroid body had the same general arrangement as the normal parts, and that the new formation consisted of a transformation, *in situ*, of the epithelial cells of the follicles into large distinct cells provided with large nuclei and nucleoli. In most of the changed follicles the cells were arranged in a single layer; they were implanted immediately upon the cellulo-vascular tissue which surrounds the follicles, and their nuclei were oval in shape. In some of the follicles the cells formed several layers, and there was a desquamation of the large cells into the cavity of the follicle. The wall of the follicles frequently had one or more fine cellulo-vascular vegetations projecting into their cavity and covered by a layer of cells similar to those above described. The vegetations contained embryonic cells, as did the peri-follicular connective tissue. This infiltration was not very abundant, and the interfollicular partions were not thickened. At the boundary of the implantation of the epithelial cells upon the cellular tissue a layer of flattened cells with flat nuclei were seen, which in thin sections had the appearance of fusiform cells.

The change from the normal follicles to those most altered was easily followed. The cells in the normal follicles were hypertrophied, the colloid substance contained in the cavity of the follicle gradually diminished and finally became absorbed, when the epithelial cells had become very large and were detached from the wall and set free in the cavity. These altered follicles formed islands, in which the degeneration was visible to the unaided eye; but even in those islands which were most diseased, almost normal follicles could be found which still contained the colloid substance, and in which the cells were slightly hypertrophied. The septum of cellulo-fibrous tissue separating two alveoli frequently had upon one side a row of normal or almost normal cells, and upon the other side a row of large cells.

This mode of development of the tumor is allied to carcinoma of the lung, in so far as concerns its origin from the pre-existing epithelial cells in the normal cavities of the organ. The vegetations which project into the interior of the follicles, and which are covered with new cells, are analogous to those observed in the galactophorous ducts included in tumors of the mammary gland.

In regard to the nature of the tumor, we consider it an epithelioma, in which the hypertrophied pre-existing and abundant cells are cylindrical when in place, but irregularly polyhedral or round when free. As the neoplasm of the connective tissue does not form tubes lined with cylindrical cells, but consists simply in an infiltration of large cells between the connective-tissue fibres, it cannot be considered a cylindrical-celled epithelioma. On the other hand, it is difficult to class the tumor as a carcinoma, since the new formation of connective tissue does not have the regular appearance of the stroma of carcinoma. It is a variety of epithelioma intermediate between the types which we have used to establish the classification of tumors. It is well known that some isolated cases of tumors cannot be placed under the description of a definite type; they establish the connecting links between one variety and another.

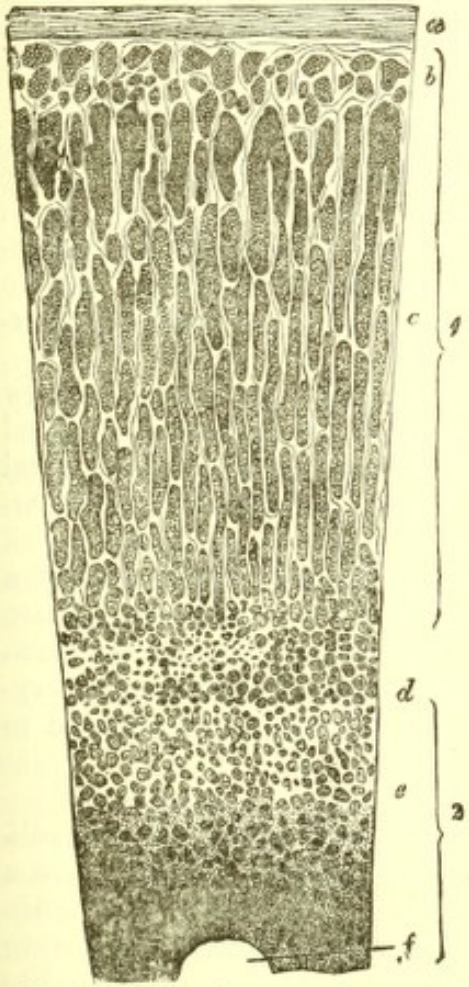
CHAPTER III.

SUPRA-RENAL CAPSULES.

Sect. I.—Normal Histology.

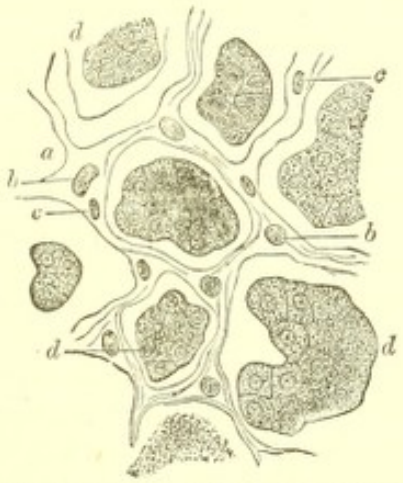
THESE organs are allied to the vascular blood glands which have no excretory ducts; their function is entirely unknown. They consist of a fibrous envelope continuous with the fibrous stroma of the gland, and of a cortical and medullary substance. The cortical substance in man is usually yellow and opaque, due to the presence of fat in the cells; it is composed of cylinders running from the periphery towards the centre, and formed of cylindrical or polygonal cells. These cortical cylinders have no basement membrane, and are limited only by the connective tissue which forms the stroma of the gland. At the internal boundary of the cortical substance, the cells are large and filled with fatty granules, giving here a more marked yellow color, which extends to the whole cortical substance when the cells are infiltrated with fat.

Fig. 301.



Vertical section of supra-renal capsule of man. 1. Cortex. 2. Medulla. *a*. Capsule. *b*. Layer of external cell masses in cortex. *c*. Columnar layer. *d*. Layer of internal cell masses. *e*. Medullary substance. *f*. Section of vein.

Fig. 302.



Transverse section through cortical substance of the supra-renal body (human). *a*. Framework of connective tissue. *b*. Capillaries. *c*. Nuclei. *d*. Gland cells.

The medullary substance also possesses a connective tissue stroma composed of thin fasciculi which form a network of round and narrow meshes. In this network is found a fine granular substance with pale angular or branching cells, provided with a nucleus and nucleolus somewhat resembling nerve cells, from which however they ought to be discriminated. Between the cortical and medullary substance, cadaveric decomposition frequently causes a softening, thus separating the two substances by a brownish fluid containing blood and large cells filled with fat.

The numerous bloodvessels derived from the phrenic, cœliac, and renal arteries, at first form a plexus upon the capsule, then penetrate into the medullary substance, and form capillary plexuses in the medullary and especially in the cortical substances where they surround the cortical cylinders. The veins follow the same course. The lymphatics have not as yet been sufficiently studied. The nerves, very important on account of their number and the size of their trunks, come from the semilunar ganglion and renal plexus. They are accompanied by nerve ganglia consisting of bipolar and multipolar cells which are found in the medullary substance.

Sect. II.—Pathology of the Supra-Renal Capsules.

Hyperæmia and Hemorrhage.—*Congestions* of the supra-renal capsules frequently occur in newly-born children and in early life, but are met with in the adult only in chronic diseases of the heart, with considerable hindrance of the venous circulation.

Hemorrhages of the supra-renal capsule are not very frequent; they occur always in the medullary substance, which is softer than the cortical substance. The escaped blood collects in foci in this portion of the gland and may be considerable in amount. In a case reported by Rayer occurring in an old woman, the capsule was transformed into a sac filled with a brownish fluid weighing two kilogrammes. Several other cases of a similar character have been reported, but generally the hemorrhages are not larger than a pea or hazel-nut. These collections of blood may, when the latter is absorbed, develop into a cyst containing a serous fluid varying in color. There are no special symptoms which may be referred to this lesion.

Thrombosis.—Klebs reports a case of thrombosis of the cortical substance of the supra-renal capsule in a case of pyæmia occurring in a woman in consequence of a resection of a bone. The cortical substance presented spots of a brownish-yellow color, in which the capillaries were obstructed by fibrinous coagulations. The epithelial cells of the cylinders were completely fatty degenerated.

Fatty and Amyloid Infiltration.—The infiltration of the epithelial cells of the cortical substance by small drops of fat is normal in man, therefore it is difficult to appreciate a pathological infiltration. The amyloid infiltration does not often occur, it involves only the vessels of the medullary substance and not the epithelial cells. It has been ob-

served only in connection with similar lesions of the spleen, kidney, and liver.

Inflammation of the Supra-Renal Capsule.—Purulent inflammation of the supra-renal capsules very seldom occurs. The suppuration may involve the entire organ, the cellular elements participating in the inflammation, or it may be circumscribed. The caseous metamorphosis which results from this process has been taken for tuberculization. The abundant new formation of connective tissue, true cirrhosis or formative subacute or chronic inflammation of the gland, occurs more frequently than suppuration.

Tumors.—*Sarcoma* has been met with in children as a primary tumor. Ogle, cited by Klebs, has described a case of sarcoma as a whitish mass in both supra-renal capsules. Primary melanotic sarcoma has been seen by Küssmaul. The tumor was as large as an adult head, metastatic nodules followed, and death resulted from an embolus in the pulmonary artery.

Carcinoma is primary or secondary. These tumors generally have the characters of encephaloid, and may be very vascular. The primary carcinomata are very rare. The proximity of the kidney to the supra-renal gland predisposes it to the invasion by a cancer which has its origin in the kidney; a cancer of the rectum may also extend to the gland.

Klebs reports a case of *epithelioma*, which invaded, at the same time, the thyroid body and supra-renal capsule, very probably beginning in the thyroid body. The cell nests of the new formation in the capsule had, at their centres, stratified calcareous concretions.

An example of syphilitic *gumma* of this organ has been reported by Bærensprung. It consisted of patches of connective tissue with embryonic cells, the centres of which were in a state of caseous degeneration. These patches were seated in the medullary substance, which was but slightly modified. The surface of the gland was smooth and lobulated, the consistence firm, and the thickened capsule was adherent, not only to the cortical substance of the organ, but also to the surrounding parts.

A section of a gland very much altered, presents no trace of its normal structure. There exists in its place a firm and hard tissue, in the midst of which are seen caseous masses varying in size. The cortex is frequently transformed into a firm semi-transparent grayish tissue, while the central portion is yellow and opaque. Sometimes the caseous portions are distributed irregularly through the entire gland.

Microscopic examination of the gray and semi-transparent portions shows only a connective tissue infiltrated with round lymph cells. The fibrous stroma also contains connective tissue cells. The yellow and caseous parts show atrophied lymph cells filled with fine albuminous and fatty granules; no trace of the gland elements can be found.

The further metamorphoses of gland so changed are various: sometimes the caseous portion is softened into a pulpy detritus; sometimes the softened focus forms a cyst containing caseous pulp, or a fluid which, to the unaided eye, resembles pus; at other times calcareous points are

found. The absorption of the fluid parts and the calcification coincide with the formation of dense fibres around the calcified parts.

Associated with chronic inflammation terminating in the caseous state, and which in many points resembles tuberculization, there are also seen acute and subacute inflammations terminating in foci of suppuration. These abscesses should not be confounded with caseous softening; they contain pus characterized by numerous and free lymph cells.

Tuberculosis, Chronic Inflammation, and Caseous Degeneration (Addison's Disease).—We class together tubercle of the gland and chronic interstitial inflammations which terminate in caseous degeneration, because these lesions present, among other general and important points, a symptom which accompanies the anatomical lesion most frequent in Addison's disease—pigmentation of the skin.

Tubercles—either as miliary granulations, or as collections of granulations the size of a hemp seed or a small pea, and completely caseous—are not unfrequent. They are consecutive to a pulmonary or other tuberculosis, and occur in one or both supra-renal capsules. The miliary granulations, whether in the cortical substance beneath the capsule, or disseminated through the gland, do not differ from those found in other organs. They generally begin in the cortical substance, becoming larger by uniting together; their centre becomes caseous; they may invade the medullary substance; they are surrounded by an embryonic tissue. When large masses exist, the entire gland may be transformed into a yellow caseous tissue, at times softened and pulpy; or, while the centre is yellow and soft, the periphery may be hard, fibrous, and gray. In this complete transformation of the gland there remains no trace of the normal structure. This condition is frequently found at autopsies of patients who died having the bronze color described by Addison.

The lesion most frequently observed at autopsies of *Addison's disease* consists in a *fibro-caseous metamorphosis* of the gland, or a chronic interstitial inflammation, characterized by the new formation of connective tissue, the central part of which is in a state of caseous degeneration. It is difficult, from the cases, to say whether we have to do with a tuberculous lesion or not. By their appearance and degeneration, the glands so changed are similar to scrofulous lymphatic glands; but doubts still exist concerning the nature of the disease.

In this state the gland is increased in size; it may reach twelve centimetres in its greatest diameter; its shape is oval. The softened portion may be transformed into a serous cyst.

Tuberculosis, and chronic inflammation with caseous degeneration, a lesion closely allied to the former, constitute the great majority of affections of the supra-renal capsules associated with Addison's disease. The two capsules are usually affected in a different degree; sometimes one is found normal.

We will not attempt to explain why the lesion of the capsules produces the characteristic symptoms of Addison's disease, that is, the pigmentation of the rete mucosum of the skin and mucous membranes, the

anæmia and the digestive disturbances. The physiological explanations which have been given are far from satisfactory. The lesions of the nerve centres of the supra-renal capsule and of the great sympathetic probably in part account for the phenomenon of pigmentation. It is also to be remembered that, very frequently, lesions of the capsule are found, such as cancer, tuberculosis, and even a caseous inflammatory state to an advanced degree, without the skin being pigmented. According to Klebs, in 141 cases of lesions of the supra-renal capsule, the skin was colored in 100, and in the remaining 41 no coloration was present.

But, on the other hand, Addison's disease—when it has been carefully distinguished from the melanæmia of intermittent fevers, and from the cachexias with cutaneous pigmentation of tubercle and cancer—is associated almost invariably with a very decided lesion of the supra-renal capsule.

The changes in the other organs, observed in Addison's disease, are very varied and multiple ; but pulmonary tuberculosis and scrofula are most frequently met with.

SECTION IV.

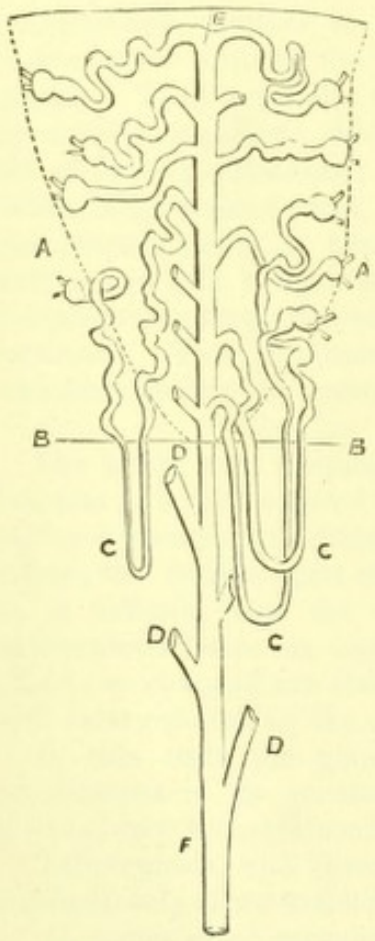
GENITO-URINARY APPARATUS.

CHAPTER I.

THE KIDNEYS.

Sect. I.—Normal Histology of the Kidney.

Fig. 303.



A, A. Diagrammatic sketch of a pyramid of Ferrein. B, B. Margin of medullary substance. C, C, C. Loops of Henle. D, D, D. Straight tubes cut off. E. Commencement of straight tubes. F. Termination of straight tube. (*Gray.*)

THE kidney, the function of which is the secretion of urine, has for excretory passages and receptacles the pelvis, ureter, bladder, and urethra. When its fibrous envelope is removed, the surface appears mammillated in the child, but in the adult it is smooth. A section made in the long diameter of the organ shows it to consist of two substances differing in shape and color: the cortical and medullary. The latter, also termed tubular, forms the pyramids of Malpighi. The cortical substance is gray or grayish-pink, translucent, and in greater amount than the medullary substance. In it are seen the Malpighian tufts as small bright points. The pyramids or cones of Malpighi are redder, and terminate in a point at their free extremity, where they are covered by the mucous membrane of the calyces. From the apices of these cones the urine flows into the pelvis.

An examination of a kidney in which the bloodvessels are injected red and the uriniferous tubules blue, shows to the unaided eye that the cortical substance is most colored by the red injection. The Malpighian bodies are seen as small red points in this part. The uriniferous tubules filled with the blue injection radiate from the apex of the Malpighian cones in the pyramids, afterwards pass into the cortical substance and constitute the *pyramids of Ferrein or medullary rays*. Their course is as follows. (Fig. 303.)

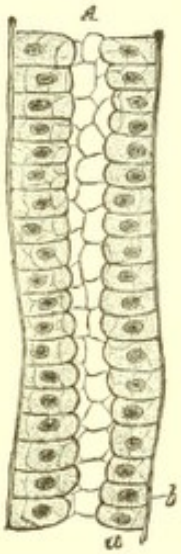
They have their origin in the cortical substance around a Malpighian glomerulus, the capsule of which is directly continuous with the membrane of the tubule. The Malpighian glomerules, as will be soon seen, consist only of a tuft of small vessels arising directly from the intertubular arteries of the kidney, and are entirely surrounded by a capsular membrane. Opposite the entrance of the arteriole into the capsule, there is seen a narrow orifice by which it communicates with the uriniferous tubule. At its origin, the uriniferous tubule is winding and large (convoluted tubules of the cortical substance). After forming a number of tortuosities, it narrows, takes a rectilinear course, and is directed towards the substance of the pyramids (descending limb); after proceeding in this direction for some distance it forms a loop (loop of Henle), the convexity of which is turned to the apex of the pyramids; it now ascends (ascending limb), following a direction parallel to that of

Fig. 304.



Longitudinal section of Henle's descending limb. High power. *a*. Membrana propria. *b*. Epithelium. (*Gray*.)

Fig. 305.



Longitudinal section of straight tube of kidney. High power. *a*. Cylindrical or cubical epithelium. *b*. Membrana propria. (*Gray*.)

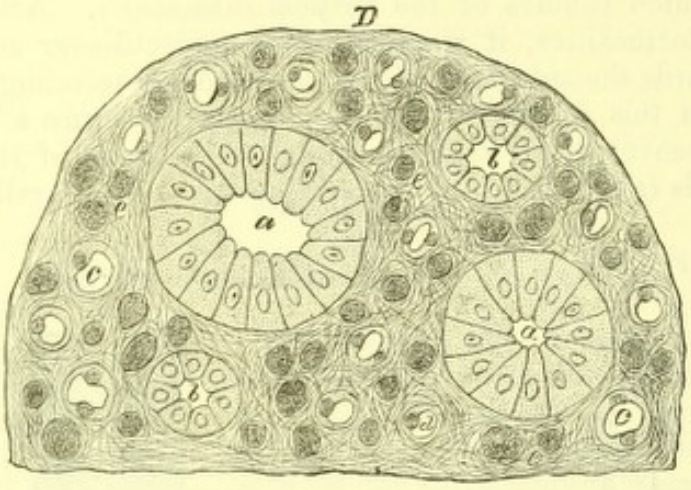
its descending portion, enters again into the cortical substance, again dilates, becomes convoluted, and is again contracted before passing into a straight tubule. This latter (collecting tubule), the direction of which is rectilinear, and which at first runs in the cortical substance, then in the medullary substance, receives by the way several isolated or united tubules; these branches become gradually more numerous as the apex of the Malpighian pyramid is approached. The collecting tube finally opens at the renal papilla into the pelvis; the opening is large enough to be seen with the unaided eye.

The diameter and structure of the tubule vary in the different parts of its course from the glomerulus to its termination in the renal papilla. The glomerulus measures from .13 mm. to .2 mm., its shape is spherical; the convoluted tubules of the cortical substance measure from .040 mm. to .050 mm.; in the loops of Henle the tubules are not more than .015 mm. to .020 mm.; most of the straight tubules measure only .030 mm.

to .040 mm.; by their union at the terminal extremity of the collecting tubule they acquire a diameter of .180 mm. to .200 mm.

The capsule of the glomerulus is a thin hyaline membrane which is easily wrinkled by the action of water and diluted acids. It is lined upon the internal surface by a layer of flat pavement cells which are directly continuous with the cellular lining of the convoluted tubules.

Fig. 306.



Transverse section of pyramidal substance of kidney of pig, the bloodvessels of which are injected. *a*. Large collecting tube cut across, lined with cylindrical epithelium. *b*. Branch of collecting tube cut across, lined with epithelium of shorter cylinders. *c* and *d*. Henle's loops cut across. *e*. Bloodvessels cut across. *D*. Connective tissue ground substance. High power. (*Gray*.)

The convoluted tubules, the loops of Henle, and the straight tubes also possess a hyaline membrane which may be wrinkled like that of the glomeruli, and which, according to Ludwig, possesses nuclei placed at intervals. In the large collecting tubes of the medullary substance Ludwig says this separate membrane does not exist, but is blended with the neighboring connective tissue.

The epithelial lining of the tubules is modified according to the different points of their course. In the convoluted tubules the pavement cells approximate the form of a cube, having around their oval nucleus a clouded and granular mass of protoplasm. The separations between these cells are scarcely visible. The cells show, especially where they are implanted upon the hyaline membrane, fine striations perpendicular to the hyaline membrane which have been considered as small minute canaliculi. These special cells, the description of which has been given by Heidenhain, have, according to this author, the function of elaborating and separating from the blood the solid substances which enter into the composition of the urine. By their striation they very much resemble the cells in the excretory ducts of the salivary glands. They do not present any distinct enveloping membrane. Their protoplasm, which contains very fine albuminous granules, becomes more clouded when acted upon by water. The cells are regularly arranged within the hyaline membrane, so as to leave a central lumen, through which the urine flows. They adhere one to the other more than to the membrane of the tubule, so that in preparations from a fresh kidney they are often seen as cylin-

ders having the form of the tubules. The hyaline membrane of the tubule is then seen folded and adherent to the renal tissue. In the loops of Henle the epithelium becomes thin, flat; the protoplasm is much reduced, and the nuclei of the cells project into the lumen of the tubules.

In the convoluted tubule connecting the loops of Henle with the straight tubules, the epithelium again becomes swollen and granular; the epithelium has the same character in the straight tubules. In the collecting tubes the pavement and cubical cells gradually become very long and cylindrical; they are implanted perpendicularly upon the wall; their large base is attached to the membrane, while their free thin extremity projects upon the lumen of the tube; their largest diameter is 0.02 mm. At the small papilla they are directly continuous with the cells of the mucous membrane of the calyces and pelvis.

Such is the course of a uriniferous tubule. The relations between the cortical and medullary substance of the kidney may now be considered. The collecting tubules emptying at the papilla ascend and divide as far as the cortical substance, where they send off the straight tubules known by the name of *medullary rays* (pyramids of Ferrein), which receive the convoluted tubules emanating from the glomerulus, after these tubules have formed in the medullary substance the loops of Henle. Each medullary ray is composed of straight tubules emanating from the collecting tubules and the ascending and descending branches of Henle's loop. The convoluted tubules and the glomeruli in continuity with the straight tubules of the cortical substance, form in this substance as many secondary pyramids as there are medullary rays, the base of these pyramids being turned towards the periphery of the kidney.

The bloodvessels present a special distribution. The renal artery enters at the hilus, and there divides; its divisions run between the pyramids, and give off branches at the boundary between the cortical substance and the pyramids, at the base of the latter. The intertubular arteries arise at this point, pass directly into the cortical substance perpendicular to the surface of the kidney, in their course giving off at intervals arterioles which enter into the Malpighian tufts. The afferent vessel of the glomerulus divides into a number of secondary branches, each presenting free loops upon the surface of the glomerulus. The vessels proceeding from these subdivisions are united into a single trunk (efferent vessel), which passes out of the glomerulus alongside of the afferent vessel.

In the glomerulus the small vessels possess a membrane containing nuclei like the capillaries. These vessels are covered upon their external surface by flat cells, so that the cavity of the glomerulus is a closed cavity lined throughout with cells.

The efferent vessel, after passing out of the glomerulus, is separated into capillaries, which as a fine network surround the glomeruli and uriniferous tubules. In the same region that the intertubular arteries are given off to the cortical substance at the base of the pyramids, the renal arteries give off other very small arterioles, which pursue an opposite course, and descend into the pyramids. These arteries are straight, having loops with the convexity turned towards the papilla of

the pyramids, and separating into capillaries which accompany the straight tubules and collecting tubes.

The blood of the capillary vessels nearest to the surface of the kidney is collected by venous trunks, which come from the surface of the kidney, where they form the stellated veins (stars of Verheyen); these uniting form an intertubular trunk, which descends into the cortical substance parallel with the intertubular arteries. The intertubular veins receive the blood from all the capillaries of the cortical substance, and empty into large veins situated at the boundary of the medullary and cortical substance. The veins arising in the substance of the pyramids have a course parallel to that of the straight arteries, and also form loops with the convexity towards the papilla. The veins of the medullary substance are always more developed, and generally more turgid, than the arteries of this portion of the kidney; at autopsies the pyramids almost always are found of a deep red, even when the cortical substance is pale.

The most important part of the circulation of the blood in the kidney is the glomerulus; it is here that the pressure of the blood is the highest (Ludwig), and that the greatest amount of fluid material from the liquor sanguinis passes from the interior of the vessels into the uriniferous tubules. It is in the cortical substance that the convolutions of the tubules are more marked, and consequently the urine remains a longer time in this region; here alone the glomeruli are located; in the tubules of this substance are elaborated the materials which are swept away by the current of fluid coming from the glomerulus. Thus is explained the physiological function of the kidney: it is almost always affected by pathological modifications of the organ, which in the cortical substance acquire their greatest intensity and frequency. Although it is simply a structure for the passage of the urine, the medullary substance participates in the functions and pathology of the excretory tubes with which it is immediately continuous.

The *lymphatic canals* of the kidney are readily injected and demonstrated in the fibrous capsule and hilus. An injection made through these canals penetrates into the entire organ, even into the connective tissue surrounding the uriniferous tubules. In the kidney, as in connective tissue in general, it is difficult to separate the study of the lymphatic system from that of the connective tissue. The connective tissue of the kidney is unequally distributed; the fibrous capsule is formed of fasciculi of interlacing fibres, and sends fibrous prolongations, which accompany the vessels of the capsule into the cortical substance of the organ. The capillary vessels of the connective tissue offer little resistance to the separation of the capsule from the kidney. At the apex of the Malpighian pyramids the connective tissue is quite thick, and easily demonstrated; here the wall of the collecting tubules is formed by this tissue, not having any interposed membrane between it and the lining epithelium. Surrounding the glomeruli, there is also a very distinct layer of connective tissue. Throughout the remaining portion of the organ the structure supporting the vessels and surrounding the uriniferous tubules is very delicate, and is blended with the vessels. The connective tissue in the kidney is, as everywhere else, permeated by spaces containing flat cells, and communicating with the lymphatic vessels.

The pelvis, calyces, and ureter, excretory canals of the urine, are lined by a mucous membrane without glands. The lining epithelium is formed of several layers, the most superficial of which is pavement, the middle cylindrical, and the deepest formed of flat cells. The pelvis and ureter are furnished with muscular and fibrous layers.

Sect. II.—General Pathology of the Kidney.

The most essential lesions of the kidney and the most extensive are those which occur in the tubules, and particularly in their epithelial cells.

Alterations of the Epithelial Cells.—Lesions of the epithelial cells of the uriniferous tubules vary according to the region under consideration. The granular and striated pavement cells of the convoluted tubules of the cortical substance are those which are most frequently affected. They, and the renal connective tissue also, are swollen and saturated with urinary fluid, when the latter is retained in the kidney, in consequence of an obstacle situated at some point along the course of the urinary passages. They become larger, more spherical, swollen, and granular (clouded swelling), in renal congestion, in the first stage of Bright's disease, and in every transient albuminous nephritis. If the elements are now examined in water, their nuclei are concealed by the fine granules. By the addition of acetic acid, the albuminous granules disappear or clear up, and the nucleus of the cell appears; at times two nuclei are present, and there frequently remain small fatty granules in the cell. Fatty granules in the renal cells do not exist in the normal state either in the child or adult, although they are found physiologically in great numbers in some animals, as the dog. Frequently in old persons fatty granules are found in some parts of the uriniferous tubules of the cortical substance without any renal disease having existed. With these exceptions the presence of fatty granules is pathological. Frequently, especially when these granules exist with the cloudy swelling and albuminous infiltration of the cells, there is present one of the forms of a catarrhal or albuminous nephritis, of varying intensity, which involves the escape of albumen into the urine. In certain poisonings (phosphorus, sulphuric acid, arsenic, icterus, etc.), and in some cachexias (pulmonary phthisis, etc.), the cells of the kidney may be loaded with granules and fat drops without any albumen having been present in the urine.

These albuminous and fatty granular renal cells may be seen in all parts of the kidney, but it is in the large and convoluted tubules of the cortical substance that they are generally found. This lesion also affects Henle's loop. In the straight tubules of the medullary rays and in the collecting tubules, the lining epithelial cells are less frequently the seat of a fatty granular change, for these are especially the excretory ducts of the urine, but their lumen is often filled with altered, spherical, and granular cells, which come from the cortical substance and are eliminated with the urine.

As a consequence of repeated congestions, the coloring matters of

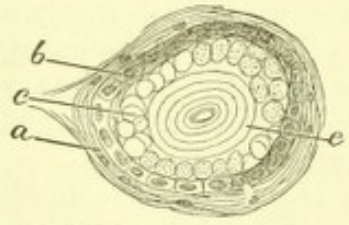
the blood may pass into the interior of the uriniferous tubules and cause a pigmentation of their cells. There are then seen yellow or brown granules infiltrating the pavement epithelium of the convoluted tubules; the cells may be detached from the wall and fall separately or in fragmented cylinders into the lumen of the tubules.

In renal inflammations, indicated by the presence of albumen in the urine, the epithelial cells are cloudy, contain two or three nuclei, and are said to be in a state of proliferation. The renal cells in the normal state, however, sometimes contain two nuclei. In inflammation accompanied by a desquamation, there is constant reproduction of new cells, as in desquamative nephritis, for the hyaline wall of the tubule is always regularly lined with cells. It must be admitted, therefore, that there is a constant cellular formation the mechanism of which has escaped us. We will again refer to cellular proliferation of the kidney when considering sarcoma and carcinoma of this organ.

By virtue of these elementary lesions, which belong to the inflammatory process, there is a series of modifications which result from changes in nutrition of the cells, or their infiltration by different substances. Thus, in every case of icterus, whatever may be the cause, there are found in the kidney some of the uriniferous tubules whose cells contain yellow or greenish-yellow granules possessing the reactions of biliary coloring matter. The cells thus altered remain *in situ* or are free in the interior of the tubules, or they form elongated masses moulded in the cavity of the tubules. When bile is present in large amount in the kidney, crystals of bilirubin are found either in the cells or in the connective tissue. Under other circumstances, salts infiltrate the renal cells; the latter become centres of crystallization and of microscopic or larger calculi. This occurs, for example, in newly-born children, when the renal parenchyma is obstructed with urate of soda, or when, in the gouty diathesis, the same salt infiltrates the cells of a number of tubules and is deposited in the form of needle-like crystals.

The calcareous salts, alkaline carbonates and phosphates, also may be deposited in the epithelial cells of the capsule of the glomeruli. The latter appear in the shape of small opaque and hard granules upon the surface of the kidney, where they are scarcely visible to the unaided eye. Further there are found upon the surface of free cells in the uriniferous tubules, crystals of the tribasic phosphates or of the oxalate of lime.

Fig. 307.



Colloid degeneration of the epithelial cells of a uriniferous tubule in interstitial nephritis. *a*. Connective tissue. *b*. Epithelial lining of the tube. *c*. Colloid cells. *e*. Colloid cast with concentric layers. × 300.

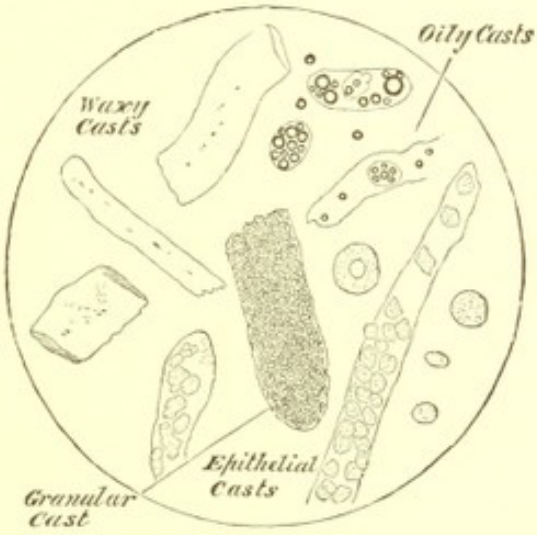
The cells of the kidney may atrophy and be destroyed. For example, in a renal infarctus, when the circulation of the blood is arrested in a part of the organ, as in a metastatic abscess, the cells become fatty and break up into granular molecules. When a portion of the kidney is compressed by a pelvic calculus, or in chronic pyelitis with retention of urine and distension of the calyces and pelvis, the atrophied tubules contain only small or granular cells.

Frequently in advanced stages of Bright's disease, especially in colloid cysts, but also in the open uriniferous tubules, cells are seen which have become colloid, refracting, round, or with the angles and edges blunted (Fig. 307). These cells are deeply colored by carmine, but they do not give the special color by iodine and sulphuric acid which is characteristic of amyloid degeneration.

Finally, the cells at times present an amyloid infiltration, and are transformed into small vitreous blocks, which give the characteristic color with iodine and sulphuric acid.

Hyaline and other Casts which are formed in the Uriniferous Tubules.—In most of the cellular alterations, which will be considered, there occurs a secretion of an albuminoid, hyaline, vitreous substance, in the interior of the uriniferous tubules; this substance encloses, or has upon its surface, cellular elements more or less changed. The shape of this albuminoid coagulated substance is cylindrical, so that the name casts or cylinders has been given to them. They are found by microscopic examination of the sediment of urine passed during life, and therefore they are very important in a diagnostic and prognostic point of view of diseases of the kidney.

Fig. 308.



Urinary casts. (*Bryant.*)

We must, however, not exaggerate the importance of casts. As Charcot has correctly remarked, casts formed in the convoluted tubules, where the lesion is generally the most important, pass with difficulty into the urine if they are somewhat large, it being necessary for them to traverse the narrow tubules of Henle's loops. It is certain that casts formed in Henle's loops sometimes pass into the urine, and it is probable that narrow casts formed in the convoluted tubules of the cortical substance may also be washed out by the secretion of urine.

There are found in urinary sediment collections of granular epithelial cells, containing fatty or transparent and colloid granules. These cells are joined together by a homogeneous or slightly granular substance diffi-

cult to see, but nevertheless obvious, since the cells do not separate one from the other: these are *epithelial casts.*

In urine nearly normal, or when the kidney is affected by a congestion or slight catarrh of the tubules, there exist very pale, narrow casts, formed of a fine granular, soft, amorphous material, the edges of which are not bounded by a dark line. Frequently upon their surface there are renal epithelium or lymph corpuscles. For a beginner these casts are difficult to recognize, owing to their delicacy and transparency. They are generally very long, and formed by an albuminoid material, analogous to mucin. These are *mucous casts.*

The majority of casts seen in diseases of the kidney with albuminuria, are formed by a homogeneous, hyaline, colloid material, without granules in their interior. Their edges are well marked and shaded; they are not flattened beneath the glass slide, and retain their cylindrical shape. Their ends are rounded and their edges are dark. Their shape varies, as also their length and diameter; frequently they are not more than .050 mm. to .100 mm. long, but they may reach one millimetre in length; at times they resemble a cork-screw, having the shape of the convoluted tubules in which they were formed; some are very narrow, a fact readily explained when sections of the diseased kidney are examined, for they are frequently found in the interior of the tubules of Henle's loops; others, very large, are formed in the collecting tubules. Their diameter varies from .005 mm. to .040 mm. Sometimes vitreous casts are seen with transverse fissures. These are *hyaline casts;* their substance is somewhat hard and resisting. When they are numerous, they always indicate a serious form of Bright's disease; if they are hard and dark-bordered, they indicate a chronic Bright's disease. They are not changed by acetic acid; they are readily colored by most coloring materials, by carmine, or by the coloring material of the blood, so that when blood is mixed with the urine in Bright's disease, they are yellowish-brown in color; they are also colored by iodine, which, however, is not so marked as in parts of the kidney which have undergone amyloid degeneration. Casts in amyloid degeneration are not colored violet-red by the violet of methyline, which demonstrates that their substance is not amyloid material.

Hyaline casts are mostly covered either with granular cells, or transparent and colloid lymph corpuscles, or a few colloid epithelial cells. In granular fatty degeneration of the epithelial cells of the tubules, the cells are also granular upon the surface of the casts, and fine fatty granules may form a complete cortical covering to a hyaline cast.

These casts may at times present upon their surface, or in their interior, granules of urate of soda, or crystals of tribasic phosphates, or oxalate of lime, or uric acid.

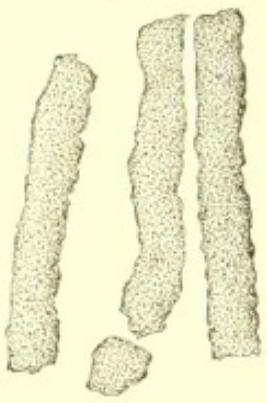
In regard to the chemical nature of these productions, it is known that they are composed of albuminoid matter, but it is not definitely known of what this substance consists. Their homogeneous state, the absence of fibrillation, their resistance to acetic acid, separate them from fibrin, although they are frequently termed fibrinous casts. This name is the more inappropriate, since true fibrinous casts are sometimes found.

The casts present in amyloid degeneration do not differ from the preceding hyaline casts.

According to some authors, hyaline casts are formed by a simple exudation coming from the serum of the blood, filtered through the membranes of the vascular walls and tubules. According to Rindfleisch, there occurs a colloid transformation of the cells, which are agglutinated one to the other in the form of casts, or the colloid substance escapes from the cells. This opinion is opposed by Klebs. It seems to us improbable that hyaline casts have this origin in the majority of cases of recent Bright's disease, since they are found without any colloid change of the cells being discovered when the kidney is directly examined. But we have seen, in several cases of chronic Bright's disease, colloid metamorphoses of the cells around colloid casts, and the participation of the cells in their formation seemed to us very evident (see fig. 307), especially in the colloid cysts of an atrophied Bright's kidney.

In jaundice from whatever cause, there are found in the urinary sediment hyaline casts colored yellow, and covered with yellow granules and with epithelial cells containing bile pigment, or, as we once saw, crystals of biliverdin. The hyaline casts, in cases of jaundice, are numerous, yet not any or but very little albumen is present.

Fig. 309.



Fatty casts in albuminous urine from a case of phosphorus poisoning.

In poisoning by phosphorus the casts in the urinary sediment are peculiar in being composed of a granular mass consisting of fatty molecules, consequently differing from the usual casts of Bright's disease. These are *fatty casts*. In intense congestion and hemorrhage into the interior of the uriniferous tubules, there is a coagulation of fibrin which is carried out with the urine, and a true fibrinous cast is formed, characterized by fibrillar fibrin which swells by the action of acetic acid, and which contains in its interior red and white blood corpuscles. Instead of being in the form of small cylinders, the fibrin may present small masses, with indistinct edges. Red corpuscles are seen in these masses of fibrin. The urine preserves the red corpuscles, but changes their shape; they become granular or crenated upon their surface or excavated.

Alterations of the Hyaline Walls of the Tubules.—The hyaline wall of the convoluted tubules and Henle's loops is usually preserved in renal diseases. In Bright's disease, with granular fatty degeneration of the cells, when the hyaline walls are isolated, albuminous and fatty granules are seen upon their surface; these granules are not in the substance of the membrane, it remains intact beneath them. According to Rindfleisch, the hyaline wall of the tubules is thickened in chronic albuminous nephritis.

This membrane in suppurative nephritis, and in tumors developed in the renal parenchyma, disappears; in interstitial nephritis it also completely disappears at points where the lesion is far advanced, when the boundary of the cylindrical cavity of the tubules is formed by the thickened con-

nective tissue of the kidney. Rindfleisch believes that the hyaline wall, in the normal condition, is pierced by pores, which permit the lymph cells coming from the vessels to pass through, either to constitute the epithelial cells of the tubules in the normal state, or to form the cellular elements of pus in renal suppuration. These pores have not yet been satisfactorily demonstrated.

In amyloid degeneration, the hyaline walls of the tubules, in some cases, become very thick, and are infiltrated with the amyloid substance.

The pathological changes of the cells in the tubules, those of their hyaline wall, and the exudations into their lumen, have been considered. We now pass to the changes undergone by the uriniferous tubules as a whole.

The uriniferous tubules may be uniformly distended; this occurs in retention of urine, and a urinary infiltration of all the elements of the kidney is the consequence; a similar distension is seen in the first stage of Bright's disease, when the epithelial cells are swollen and cloudy, and the lumen of the tubules contains a hyaline exudation, desquamated cells, blood, etc., when the entire organ is increased in size. But soon, in Bright's disease, there occurs either obstruction of a number of tubules by their contents which escape with difficulty, or interstitial inflammations which occasion at a part of the tubule an obliteration or a permanent narrowing, when the tubule presents above the obstacle irregular dilatations or true cysts of retention. These cysts are generally formed from the uriniferous tubules; from the same cause a distension of the capsule of the glomerulus may take place.

Total obstruction and even complete atrophy of the uriniferous tubules is observed in compression of the kidney from within outwards by distension of the pelvis and calyces, in the several varieties of pyelonephritis. There is almost always associated with this condition an interstitial nephritis characterized by thickening and induration of the connective tissue.

Lesions of the Connective Tissue of the Kidney.—The connective tissue of the kidney is not very abundant, yet it is certainly present, especially in the parts that have been mentioned.

The lesions which this tissue undergoes in nephritis are varied, according to the cause of the disease. In simple congestion, the cells of the connective tissue consume a greater amount of nourishing fluid than in the normal state; their nucleus becomes larger; the protoplasm of the cell is granular and distinct; the entire cell is enlarged. If the congestion is intense and persistent, as occurs in cardiac diseases, especially in lesions of the mitral valve, an extravasation of the coloring material of the blood may be manifested by pigment granules around the cells in the fibrous stroma of the kidney. Almost always, in these cases, the connective tissue cells proliferate and increase in number. The intertubular septa are therefore increased in thickness. The cellular elements which compose them belong to the cells of the connective tissue. The cellular stroma of the kidney is thickened, more resisting than normal,

and the entire organ seems denser. Such is the essential lesion of nephritis in heart diseases, the congestive and interstitial nephritis causing an organization of new elements in the connective tissue.

In well-marked Bright's disease with congestion and renal inflammation, the connective tissue presents inflammatory lesions, which at first consist in the presence of numerous round cells (embryonic or lymph cells) in the lacunæ or lymph system of the connective tissue. These cellular elements are seen in the septa between the tubules, and in the tissue surrounding the glomeruli. This lesion is not always present, and it varies in different portions of the kidney.

Do these elements come from a proliferation of the fixed flat cells of the connective tissue, or are they white blood corpuscles or lymph cells? This is difficult to determine otherwise than by forming a hypothesis based upon analogy. It is possible to suppose that there occurs here a diapedesis similar to that observed upon the peritoneal serous membrane. Later, when the kidney is atrophied and contracted, in the last stage of Bright's disease, the embryonic tissue is organized, and becomes very fibrous and dense.

In advanced stages of Bright's disease, and in renal atrophy due to chronic pyelo-nephritis, the interstitial induration of the connective tissue reaches its highest degree. A true dense fibrous tissue at this time separates the atrophied secreting elements. The fibrous capsule closely adheres to the surface of the kidney, which is granular and mammillated like a cirrhotic liver.

Small metastatic abscesses, or diffused suppuration of the kidney, should also be ascribed to a primary lesion of the circulation and connective tissue. Consecutive to capillary emboli, or to the transportation of putrid or fermenting materials by the blood, there are seen one or more red miliary ecchymotic points, the centre of which soon becomes whitish and puriform; afterwards the entire small mass is transformed into a miliary abscess. During this process the vessels are at first turgid, next the intertubular connective tissue is infiltrated with white corpuscles and softened; at the same time, the epithelial cells of the tubules become granular; as soon as the small abscess is formed, there are found mingled together in the puriform fluid white corpuscles and granular epithelial cells.

Such are the lesions of the renal connective tissue in the different varieties of inflammation. This tissue may be infiltrated by the urine, and in a manner become œdematous from retention of this fluid. The urine then distends the meshes of the connective tissue as well as the lumen of the renal ducts.

Tumors of the kidney, fibromata, tubercles, syphilitic gummata, carcinomata, have their origin and are developed in the connective tissue of the organ; their beginning is marked by a thickening of the intertubular partitions, which are infiltrated by the new cellular elements.

Alterations of the Bloodvessels of the Kidney.—The renal arteries are frequently the seat of obstructions caused either by a migrating clot (embolus), or by vegetations due to a chronic arteritis with atheroma. These lesions are located either in the renal artery itself, or, which is more

common, in one or more of its principal branches, at the boundary between the cortical and medullary substance. The result of these several processes is one or more infarcti.

Acute, subacute, or chronic arteritis may occur in the kidney at the same time that there exists a similar state of the whole arterial system, on account of senility or from any other cause, or it may be consecutive to an embolus which occasions an irritation limited to one or more branches of the renal artery. It does not differ from an arteritis occurring elsewhere.

Acute inflammation of the renal arterioles is developed in consequence of certain forms of albuminuric nephritis; for example, that which follows scarlatina. The wall of the small arterioles, particularly those which supply the Malpighian glomerules, shows a considerable increase of the nuclei.

In chronic albuminous nephritis, the walls of the arterioles are thickened, as is also the cellular tissue of the organ; this change occurs in every interstitial nephritis, whatever may be the cause.

Chronic arteritis, characterized by thickening, induration, tortuous state of the wall and narrowing of the calibre of the arteries, ultimately exists in every case of interstitial nephritis, as well as in general senile atheroma. In a section of the kidney, the lumen of the arteries remains open, and the course of these vessels is marked to the unaided eye by opaque lines. The same characters are observed under a low power of the microscope, when a transverse or longitudinal section of the vessels is examined. The external coat and the most external part of the middle coat present an opaque appearance. This opacity sometimes is due to the presence of fatty granules, but more often it is owing to a great number of elastic and connective-tissue fibres, which intercept the direct rays of light. The internal coat almost always undergoes a notable thickening, which is seen in transverse cuts of the arteries. This thickening, caused by a new cellular formation, narrows the calibre of the vessels to a varying extent. Endarteritis is always well marked in the arteries obstructed by thrombi or emboli, occurring with old infarcti of the kidney, and it is always present in parts of the kidney which have become fibrous in consequence of interstitial nephritis. The arteries are the favorite seat of amyloid degeneration of the kidney.

Alterations of the Malpighian Glomeruli.—The small vessels which arise from the division of the afferent artery, frequently exhibit in Bright's disease, and especially in scarlatinous nephritis, a multiplication of their nuclei. Generally, in albuminous nephritis, the flat cells which line the wall of the capsule are swollen, granular, and even converted into true granular bodies. Upon the surface of the vessels of the glomerulus, granular spherical cells, or nuclei also filled with fat granules, are seen. These elements remain upon the vascular loops when the glomeruli are removed by teasing; by washing, the vascular wall is seen to contain numerous fine fatty granules. (Fig. 311.)

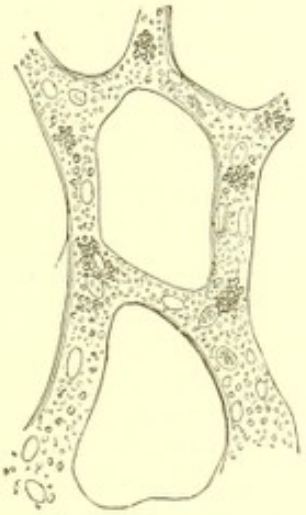
In renal atrophy following a compression which in points arrests the circulation of the blood, or in an interstitial nephritis, the glomeruli are atrophied; the blood does not enter them, and their vessels are atrophied

and form a small fibrous ball. When the capsule is distended by urine or by a colloid substance, the entire glomerulus is transformed into a cyst.

The glomeruli are generally the first portions of the renal vascular system which are attacked by the amyloid degeneration.

The renal capillaries are with difficulty separated from the connective-tissue stroma, and in order to study their lesions thin sections of the

Fig. 310.



Fatty degeneration of the intertubular capillaries of the kidneys. ×250.

Fig. 311.



Fatty degeneration of the capillaries of a Malpighian tuft. ×250.

kidney are examined. In regions which are the seat of infarcti, the capillaries are completely obstructed, either by fibrin and blood, or by their metamorphosed products. In albuminous nephritis in the stage of fatty degeneration, their walls as well as the interfibrillar lacunæ of the connective-tissue stroma, present cells and nuclei infiltrated with fatty granules. (Fig. 310.) Finally in interstitial nephritis their walls become thickened by the formation of new elements. In lymphadenitis, the capillaries are sometimes filled with white corpuscles, and a rupture of their wall, or a simple diapedesis, may cause an infiltration of these elements into the connective tissue.

The lesions of the veins of the kidney are thrombosis and acute phlebitis; both cause the escape of albumen with the urine. Chronic phlebitis is characterized by a thickening of all the coats of the vein, by a new formation of connective-tissue elements; in interstitial nephritis, in the last stage of Bright's disease, in pyelo-nephritis with renal atrophy, and in old infarcti which have become fibrous, it may occasion a complete obliteration of the veins.

Sect. III.—Special Pathological Histology of Kidney Diseases.

Anæmia.—Anæmia frequently occurs in all chronic cachectic diseases, particularly in cancer and the last stage of tuberculosis. The kidneys are pale, and of a grayish color, the cortical substance more so

than the pyramids, which indeed are pinkish. They are smooth upon their surface, and are generally small. Frequently, when there is general anasarca, the kidneys are infiltrated with urine, and are normal in size, or distended. When an obstacle to the escape of urine exists—for example, when a cancer of the bladder or uterus compresses the ureters or infiltrates their wall and causes a narrowing of these passages at a given point—they become dilated above the obstruction by the continued accumulation of the urine, which is thus dammed up in the kidney and infiltrates the lymphatic connective tissue of the organ. The kidney becomes tense, the capsule smooth and stretched, while the organ is pale, very anæmic, and infiltrated with urine; the uriniferous tubules, especially those of the cortical substance, are larger than in the normal state. The cells of the tubules are not changed.

Congestion; Hemorrhage.—Renal congestion is seen, in the acute state, in poisoning by cantharides, in the first period of fevers, etc., and in the chronic state, in all diseases which are attended with a difficulty of the return of the venous blood to the heart. It is also always present at the beginning of the several varieties of nephritis.

Congested kidneys are generally larger than normal; yet they may not be perceptibly increased in size. Their capsule is easily detached. The surface is red, and the much dilated stellate veins of Verheyen are prominent. The cut surface of the organ exhibits a diffuse redness of both substances, the medullary more so than the cortical. In the latter, there are seen, with the unaided eye, red points which are due to a filling of the vessels of the glomeruli. The pink or red color of the cortical substance depends upon the amount of blood in the capillary vessels. The deep red color of the medullary substance is owing to the fulness of the renal veins.

When the blood pressure has been considerable during life, rupture of the vessels, or a diapedesis of the red corpuscles from the vessels of the glomeruli may have happened. There then results a true renal hemorrhage, having its origin in the interior of the glomeruli. The blood escapes between the vascular tuft and the capsule of the glomerulus, which is slightly distended; from thence it passes into the lumen of the convoluted tubules of the cortical substance, then into the loops of Henle, into the straight tubules of the medullary rays, into the collecting tubules, and finally into the pelvis of the kidney. The congestion having reached this intensity, the kidneys are found increased in size and weight; upon section the glomeruli are very distinctly seen as small red spots, and surrounding them red tortuous vessels, which, at first, are taken for enormously dilated capillaries, but they are only the convoluted uriniferous tubules filled with blood, as can be seen by microscopic examination, which shows the lumen of the convoluted tubules filled with red blood corpuscles. At the periphery of the tubule the epithelial cells are seen, either normal as to shape and structure, or flattened by the pressure exerted by the blood. The flattened cells form a bright border in uncolored sections, and in carmine stained sections, their nuclei, instead of being round, are seen flattened and elongated parallel to the wall of the tubule. The glomeruli which are the seat of the blood effusion are surrounded by

convoluted tubules which, at times, are enormously distended with blood. In other glomeruli, instead of blood corpuscles, there is found a coagulum of a hyaline substance colored yellow by the blood, and arranged in concentric layers. These are true fibrinous concretions in the interior of the capsule, similar to certain cysts existing in interstitial nephritis. The blood escaped in the interior of the tubules undergoes several changes after it coagulates, forming hæmatin granules, brown pigment which infiltrates the desquamated epithelial cells. The blood is discharged with the coagulated fibrin in the form of fibrinous casts containing red corpuscles, or covered with pigmented epithelial cells. These casts are sometimes yellow from the presence of the coloring matter of the blood.

Congestion with renal apoplexy or hemorrhage is sometimes observed at the beginning of a nephritis, and in other rare circumstances where the blood pressure is very high.

Prolonged passive congestion of the kidney, due to cardiac disease, almost always occasions more serious lesions than does simple congestion. The kidneys are seen to be very red, indurated, and by microscopic examination present the characters of interstitial nephritis—that is, increase in the size and number of the cells of the connective tissue, and a fibrinous thickening of the stroma. At times in such a kidney the epithelial cells of the tubules are also filled with albuminoid and fatty granules. Passive congestion is generally accompanied by the presence of a small quantity of albumen in the urine.

Infarction of the Kidney.—The infarcti described as rheumatic nephritis by Rayer, are associated with valvular lesions of the heart, and with aortic endarteritis, lesions which frequently occur in rheumatism. The infarcti of the kidney are very similar, both in frequency and cause, to those of the spleen; they are found upon the surface of the organ, at first deep red in color, and slightly elevated. Soon they lose their redness, and become yellow; their periphery is surrounded by a zone of congestion. Upon section of the cortical substance, the infarctus is seen to be conical in shape, with the base toward the periphery of the organ, and it occupies the entire vascular territory of an arteriole.

Microscopic examination of the altered part shows that the capillary vessels of the kidney are filled with an opaque substance rich in granules of hæmatin and fat, elements which come from the fibrin and blood corpuscles. The epithelial cells are granular and opaque; they are also infiltrated with fat granules, and are disintegrating.

Gradually the materials resulting from the molecular destruction of the affected part are taken up by the circulation and absorbed, the infarctus shrinks; instead of being elevated, it is now contracted, and in its place there is found a depressed, fibrous cicatrix. A microscopic examination of the cicatrix shows a dense fibrous tissue, the vessels of which are in a state of chronic atheromatous inflammation; no trace of the glandular parenchyma remains in this fibrous mass.

Albuminous Nephritis.—Renal lesions which occasion the presence of albumen in the urine are various, and the quantity of albumen escaping from the kidney is also very variable. The word nephritis, by which these

several conditions of the kidney are usually characterized, is not entirely satisfactory; for, while there is a nephritis with congestion, with exaggerated formation and desquamation of epithelial cells in catarrhal nephritis and in the first stage of parenchymatous nephritis, it is difficult to see any traces of inflammation in the further stages of this disease. It is the same in amyloid degeneration, which is always accompanied by the presence of albumen in the urine. The renal lesion associated with albuminuria which best merits the name of nephritis, is interstitial nephritis (renal cirrhosis, or gouty kidney).

Varieties of albuminous nephritis, comprise *catarrhal nephritis*, *parenchymatous nephritis*, *amyloid degeneration*, *fatty degeneration*, and *interstitial nephritis*.

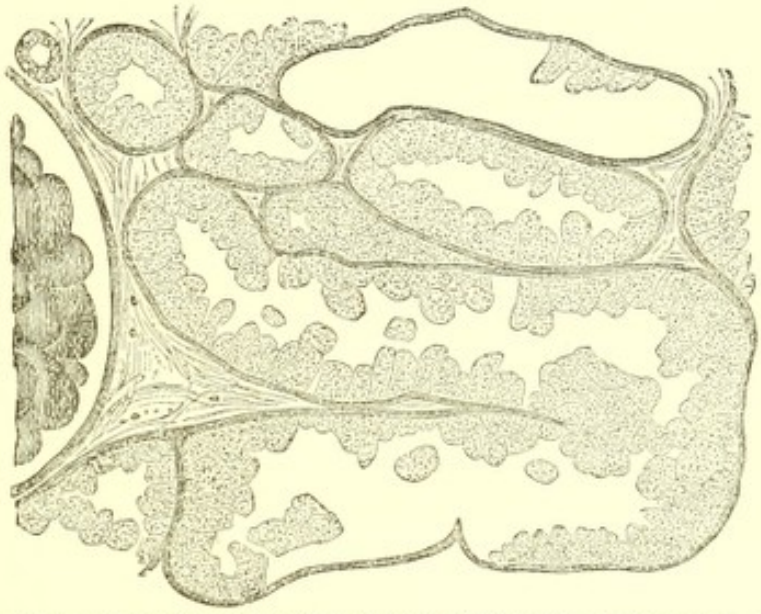
Until recently, interstitial nephritis was considered to be simply a late stage in the evolution of parenchymatous nephritis. Such was the teaching of Reinhardt, Virchow, and Frerichs, who placed the changes of the renal epithelium in the first rank. Beer, and afterwards Traube, however, have drawn attention to the participation of the connective tissue of the kidney in the inflammation of acute or chronic albuminous nephritis; and Traube regards the latter as essentially an interstitial process. The English writers, Wilks, Handfield Jones, Todd, etc., have insisted upon the clinical and anatomical differences which separate parenchymatous nephritis (large white kidney) from interstitial nephritis (granular contracted kidney). The most recent works upon this subject published in France by Lécorché, Kelsch, and Charcot retain the division made by the English writers, whether separating interstitial nephritis from Bright's disease, as Léchorché; or with Charcot, making it a special variety of Bright's disease.

A. Catarrhal Nephritis (*Transient Albuminous Nephritis*, *Superficial Nephritis*).—This renal lesion is met with under a number of different circumstances: from the effects of cantharides, in low types of fevers, in typhoid fever, in cholera, in pneumonia, etc. It may be more marked in the excretory ducts of the kidney—for example, in poisoning with cantharides when it is accompanied with pyelitis and catarrhal redness of the pelvis and calyces. In this case, even when the nephritis succeeds an inflammation of the bladder and ureter, by pressing upon the summit of the Malpighian cones a considerable quantity of turbid fluid may be forced out. This fluid contains fatty granular epithelial cells, mucous or hyaline transparent and soft casts, and lymphoid cells. The inflammation of the mucous membrane of the pelvis and calyces is also characterized by a turbid mucous fluid, containing lymphoid cells. In other cases, the elements of the kidney particularly affected are the cells of the convoluted tubules of the cortical substance, which have undergone cloudy swelling; sometimes in the convoluted tubules and in Henle's loops a granular fatty degeneration is found. This latter state is more especially seen in the low types of fevers.

To the unaided eye, the kidney is but little changed: it is somewhat larger than normal; its cortical substance is pale, gray, or yellowish-gray, and slightly opaque; its consistence is soft; the capsule is tense,

and easily detached; the surface of the organ is smooth. In the stellate veins of Verheyen, and in the glomeruli, the vessels are generally full of blood.

Fig. 312.



Catarrhal nephritis; the earlier stage of the process, showing the swelling of the tubular epithelium. In some of the tubes the epithelium has fallen out during the preparation of the section. × 200. (*Green.*)

This variety of renal lesion is usually secondary, is accompanied with a very small quantity of albumen, and terminates in rapid recovery.

B. Parenchymatous Nephritis (*Diffused Nephritis, Profound Nephritis, Large White Kidney*).—Parenchymatous nephritis affects especially the cells of the uriniferous tubules of the cortical substance. They become swollen, and granulo-fatty; they desquamate, are eliminated, being replaced by others, and numerous hyaline casts escape with the urine.

The cases which are classed as parenchymatous nephritis are very different from one another. Recovery is the rule; their course is very rapid, lasting from eight days to three weeks, as in scarlatinous albuminuria. In them, besides the infiltration of the connective tissue and glomeruli with lymphatic cells observed by Klebs and Kelsch, there are always cloudy swelling and fatty degeneration of the epithelium of the tubules of the cortical substance.

The albuminous nephritis, more or less persistent but generally curable, occurring during pregnancy or at the time or after delivery, accompanied or not with eclampsia, consists in a fatty degeneration of the epithelium, comparable to the changes seen in scarlatina.

From the effects of excessive drinking, or the action of moisture and cold, there may result either an intense albuminous nephritis which terminates in recovery after a week or several months, or there may arise a fatal albuminuria terminating in death in several months or years. The same causes may, in consequence of a different intensity of action or in

consequence of special predispositions of each person, produce lesions varying in intensity and general character, but still comparable with one another.

There are some diseases in which, if albuminuria occurs, there is almost always a similar condition of the kidney found. Thus, in the parenchymatous nephritis of diabetic patients, as we have several times seen, the kidneys were normal in size, smooth, and presented a slight fatty degeneration of their epithelium, but it was diffused uniformly throughout the entire cortical substance. In the albuminous nephritis of phthisis, the kidney is generally smooth upon its surface, white, and opaque ; its size is normal or slightly increased ; the fatty degeneration of the cells is very decided, either uniformly or in patches ; moreover, there frequently occurs, at the same time with the lesion of the cells, an amyloid degeneration of the vessels and walls of the tubules.

In very intense albuminuria, terminating in death, and caused by moist cold, there is usually found a *large white kidney* (waxy kidney), smooth upon its surface, considerably increased in size ; upon section, one sees opaque yellow lines formed by the convoluted uriniferous tubules, which are filled with a fatty detritus ; there are sometimes seen, upon the surface of the kidney and scattered through the cortical substance, yellow and opaque spots, varying in size from a millet- to a hemp-seed.

Finally, in lead-poisoning, in gout, and in some chronic heart diseases, the kidneys are small, and are granular upon their surface, as also upon a section of the cortical substance. Associated with the fatty degeneration of the cells of a varying number of tubules, atrophy and interstitial nephritis are often encountered.

From the above descriptions, it is evident that—although related by a common symptom and a common lesion, namely, the presence of albumen in the urine, and the fatty degeneration of the cells—parenchymatous nephritis is far from being always the same. A similar diversity is also observed in all the chronic diseases due to a variety of causes.

After Bright's discovery (1827), pathologists were inclined to regard as one disease all renal changes found at autopsies of albuminuric patients. According to Rayer, the lesions presented six distinct varieties ; the first two belonged to acute albuminous nephritis, and the others to chronic albuminous nephritis. Frerichs admits only three stages of Bright's disease : the first stage consists in hyperæmia and cloudy swelling of the cells ; the second in fatty degeneration of the epithelium ; and the third in the destruction of the epithelial cells and atrophy of the tubules and of the entire kidney.

The effect of such a classification of albuminous nephritis is to cause the erroneous impression that the several anatomical states regularly succeed one another, while in reality we have to do with a class of cases distinct from one another by their cause as well as by their pathological anatomy, but nevertheless somewhat similar.

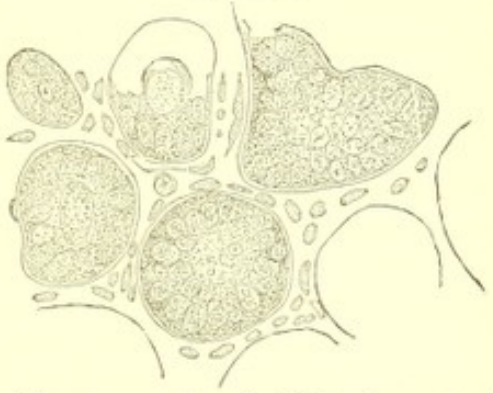
1st. *At the beginning* of every albuminous nephritis, the kidneys are congested and increased in size at the expense of the cortical substance. The capsule is easily detached ; after its removal, the renal surface ap-

pears red-brown or yellowish-gray, congested uniformly or in patches. The portions which are not reddened by the distension of the vessels are gray or yellowish-gray; hence we have a marbled appearance. By making a section of the organ and washing it to remove the blood, the traces of congestion are noticeable; small red points indicate the fulness of the vessels of the glomeruli; the remaining portion of the entire cortical substance is thickened and yellowish-gray in color.

When the lesion is more advanced, the congestion of the cortical substance is diminished, and the yellow-gray color predominates; Rayer correctly terms this state inflammatory anæmia when the part is cleared of blood by washing. The Malpighian glomeruli are seen by the unaided eye, as brilliant and translucent points, for they generally remain normal in the midst of a tissue which has become opaque.

Microscopic examination with low power demonstrates, as in catarrhal nephritis, numerous opaque and distended uriniferous tubules of the cortical substance. The glomeruli sometimes contain small blood effusions between the vessels and capsule, as in all intense congestions of the kidneys.

Fig. 313.



Transverse section of a kidney in a case of Bright's disease. The cells lining the tubes appear granular, owing to the presence of albuminous and fatty particles. At the centre of the tubes, hyaline casts are seen in section. × 420.

Examination with higher power shows the tubules filled with cells clouded by albuminous and fine fatty granules, and containing in their lumen hyaline casts. (Fig. 313.)

The altered cells of the convoluted tubules are usually *in situ;* the lumen of the enlarged tubules contains hyaline casts. The cells, however, may not retain their normal connection with the wall of the tubules; and they may accumulate and distend the uriniferous tubules into the form of varicose dilatations. The term desquamative nephritis is employed by Johnson and most English writers; the word is not good, since it seems to indicate that the uriniferous tubules possess fewer cells than in the normal state, while they are, on the contrary, distended by altered epithelium.

The large number of hyaline casts and their supposed fibrinous nature induced Reinhardt to compare Bright's disease to pneumonia; and Virchow gave it the name of croupous nephritis; but the fact that the casts are not chemically composed of fibrin opposes these views.

The autopsies of persons dying after delivery or scarlet fever, in which albuminuria has existed for a short time, usually do not show all the convoluted tubules changed to the same degree. Some are normal, others have a granulo-fatty epithelium, and a few tubules of the cortical substance are filled with cells entirely fatty. In scarlatinous nephritis, the glomeruli and connective tissue forming the wall of the capsule and the intertubular partitions are infiltrated with lymph cells. In the same conditions, if the albuminuria is considerable and has lasted a long time,

the whole of the cortical substance presents, to the unaided eye, a marked opacity, and most of the tubules of the region show some epithelial degeneration. This stage of the disease may terminate in recovery.

2d. When a persistent and more serious albuminuria exists, such as seen in *phthisis*, in *alcoholism*, *from cold*, etc., the preceding lesions are more pronounced. The kidney is generally increased in size, but may be normal, smooth upon the surface, as well as upon section; the cortical substance is yellowish-white in color and very evidently opaque; the consistence is soft and doughy, but never so flabby as in catarrhal nephritis. The cortex of the kidney, at first view seems anæmic, but the stellate veins of Verheyen however are filled with blood and the glomeruli are congested; this appearance is caused by the opacity of the tubules. The red medullary substance is traversed by yellowish and opaque lines, following the direction of the straight tubules, the loops of Henle and the collecting tubules. The mucous membrane of the pelvis and calyces is thickened, slightly opaque, anæmic, or presents a varicose distension of the veins.

The histological examination of these kidneys should be made in the fresh state, if the lesions of the epithelium are desired to be well seen. In thin sections examined in water with low power, almost all the convoluted tubules appear opaque and dark by transmitted light, white and also opaque by reflected light, because of the fat that they contain. These tubules are frequently varicose and larger than normal. The loops of Henle are likewise filled with granular fatty cells. The condition of the straight tubules of the medullary rays varies; some are normal, others contain free fatty cells. The collecting tubes are generally normal, and their cells unchanged. The Malpighian glomeruli are usually clear, yet sometimes they present in places an opacity, due to a granulo-fatty degeneration of the epithelium which covers them and lines their capsule. With a higher power, the epithelial cells of the convoluted tubules appear filled with fine and larger fatty and albuminous granules. They contain a nucleus seen by coloring with picro-carmine. Their shape is frequently changed; some are large and spherical, separated from the hyaline membrane, and occupy the lumen of the tubule as large granular bodies; others are irregular without any definite shape, consisting of masses of fat and albuminous granules surrounding a nucleus. Free fat and albuminous granules are found in the lumen of the tubules with hyaline casts. These casts, the substance of which is usually perfectly homogeneous and vitreous, are covered upon their surface with cells or fragments of granular fatty cells, or with a granular layer which completely conceals them. Very rarely granules are found in the albuminous masses which form the casts. Numerous casts are found throughout the whole course of the tubules. The hyaline membrane of the uriniferous tubules is still recognizable, it has experienced no change, but when isolated it is seen to have upon its inner surface fine fatty granules.

The arterioles and capillaries are generally normal, but it is not unusual to see upon the surface of the small vessels of the glomerulus, and between them, a manifest multiplication of the nuclei and cells, be-

longing either to their wall, or to the connective tissue interposed between them in the tuft of the glomerulus. The endothelial cells, which line the internal surface of the capsule of the glomerulus and the surface of the vascular loops, are granular, fatty, degenerated, and swollen, frequently detached and spherical as granular corpuscles; they also contain a nucleus. By pencilling a section, the capillaries and cells of the vascular tuft are frequently found containing fine fat granules. The connective tissue is generally intact. Yet when thin sections are examined in the fresh state, and pencilled to remove the epithelium, very fine fatty granules in the protoplasm surrounding the nucleus are often seen in the connective tissue cells, or in the cells of the external coat of the small vessels.

3d. In examinations of very intense albuminuria, especially that resulting from the effects of cold, the cells of the kidney are found in a state of most decided fatty degeneration. The organ is tumefied, attaining double its normal weight or more; it is smooth upon its surface, and is yellow or gray in color with lines and spots of a deeper yellow and more opaque (large fatty kidney). All the previously described lesions are intensified. For example, the convoluted tubules of the cortical substance are dilated and filled with fat, at some points appearing to the unaided eye as small yellowish opaque lines; by their union these form small spots of the same color (opaque non-elevated granulations of Bright's disease). The kidney is flabby and soft; its vessels, particularly the stellate veins of Verheyen and the glomeruli, are filled with blood. The cortical substance is extremely thick, and it is to this thickness that is due the increase in size of the organ. By microscopic examination, the convoluted tubules, varicose, dilate, and opaque, are seen to be filled with a fatty emulsion, with large free granular corpuscles, derived from the epithelial cells, and with granular casts. The capsules of the glomeruli contain the same elements; the walls of the vessels of the glomeruli are generally found to be in a state of fatty degeneration. The connective tissue of the kidney, which is not in a state of proliferation, is infiltrated with very fine fatty granules. A thin section from a fresh kidney pencilled, shows that the very fine fatty granules are located upon the surface of the fibrils and capillaries of the stroma; by continuing the pencilling they are almost all removed. The small lacunæ of the connective tissue between the fibrils and capillaries, constituting the connective tissue lymphatic system of the kidney, are filled with very fine fatty granules; the cells of the connective tissue are also filled with the same kind of granules. The employment of osmic acid is useful in studying this variety of fatty degeneration.

The hyaline casts have the same characters as those previously described. The tubules of Henle are fatty degenerated. A few of the straight tubules of the medullary substance escape the granulo-fatty change. The cylindrical cells of the collecting tubules are found in the same unaltered state; nevertheless the lumen of these tubules is occupied by round granular cells filled with fat, by fragments of cells, by free fatty granules, and by hyaline or granular casts. This variety of fatty degeneration of the kidney in Bright's disease differs very much, in regard to the fatty degeneration, from that caused by phosphorus poisoning.

This large, smooth, and white kidney is with difficulty distinguished from some amyloid kidneys by the unaided eye.

4th. In a small number of *cardiac diseases*, in a few cases of *arthritis deformans*, of *gout*, of primary albuminous nephritis from moist cold or alcoholism, at the autopsies, kidneys are found which by their essential histological lesions resemble both of the preceding varieties, but which differ in regard to size and shape, being normal or slightly atrophied, and presenting upon their surface prominent and well defined granulations.

This pathological lesion of the kidney may be classed between typical parenchymatous nephritis, that is, smooth and large kidney, and interstitial nephritis or granular contracting kidney.

The capsule of the kidney may be easily detached, or, more frequently, it carries with it a thin layer of the cortex of the organ; the surface of the kidney stripped of its capsule presents slightly prominent, sharply raised small granulations, the size of a millet seed; their color is yellow or yellowish-white and opaque. There exists at their circumference a depression, in which the much congested stellate veins of Verheyen are found. Upon section the surface of the cortical substance presents granulations analogous to those seen upon the surface of the organ; they are hemispherical or elongated, yellowish in color, and anæmic, while the vessels and glomeruli which surround them are congested.

The prominent and opaque granulations upon the surface, and the round or elongated spots, also opaque, seen upon the cut surface in the cortical substance, are the pyramids of Ferrein or medullary rays, the tubules of which, both straight and convoluted, are filled with fatty granular degenerated cells, and are distended or normal in size. The contracted tissue surrounding them upon the surface of the kidney is composed of atrophied and fibrous glomeruli, and of a few atrophied convoluted tubules near the glomeruli. The connective tissue enveloping these glomeruli and tubules, on the contrary, is thickened, as in interstitial nephritis. The atrophied glomeruli have sometimes undergone fibrous degeneration, sometimes they are filled with fat and calcareous granules. The atrophied tubules contain small cells infiltrated with fine fatty granules.

The granulo-fatty lesions of the convoluted and straight tubules which retain their normal size, and the hyaline casts, have the same characters as in the preceding pathological condition.

When the atrophy is very decided the thickened fibrous capsule of the kidney is always observed to adhere closely to the surface of the cortical substance, which in some places presents depressions, with a very finely granulated surface. At other points exist elevated yellow granulations. The cortical substance is partially or entirely atrophied. It is very difficult to say in such cases whether there is a parenchymatous nephritis in an advanced stage, in which the convoluted tubules, originally dilated and filled with fat, have afterwards become empty and contracted, or whether there is a primary interstitial nephritis.

The atrophy of numbers of tubules and glomeruli, the fibrous transformation of the latter, the fibrous thickening of the capsule of the glomeruli, the lesions of the arterial vessels, etc., are the same in both

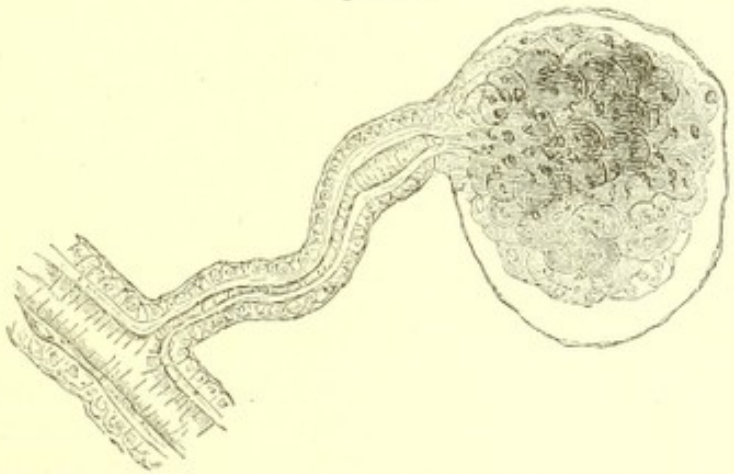
cases. These lesions will be studied in more detail when considering interstitial nephritis.

C. Albuminous Nephritis with Amyloid Degeneration.—In the numerous cases of amyloid degeneration of the kidney, that we have examined, we have always seen the same granular fatty alterations of the epithelial cells of the tubules as in parenchymatous nephritis; there were also always hyaline casts, generally hard and waxy, and the amount of albumen in the urine was considerable. In other words, there was always an association of parenchymatous albuminous nephritis, with special lesions of the vessels and walls of the tubules which characterize amyloid degeneration. We are, moreover, convinced that parenchymatous nephritis precedes amyloid degeneration. We have never met with amyloid degeneration of the kidney, without there being parenchymatous nephritis, while we have frequently seen in tuberculosis, for example, an amyloid spleen, with parenchymatous nephritis without amyloid change of the kidney. There was in these cases an amyloid lesion of the spleen, and as amyloid degeneration always begins in the spleen, there is no doubt that the kidney would have been attacked later, if the patient had lived long enough.

The shape and size of the kidney vary: at times it is very large, and its surface is smooth; its capsule is easily detached, leaving a surface white or yellowish-white, and, to the unaided eye, resembling a large white kidney. In this case, the amyloid degeneration is not far advanced, only a few, or, perhaps, a considerable number of the Malpighian glomeruli being altered.

At other times the kidney is normal in size, resembling, macroscopically, the smooth and white kidney upon its surface. It is now usually much

Fig. 314.



Amyloid degeneration of a Malpighian tuft and small artery of the kidney: showing the thickening of the walls of the vessel, the enlargement of the cells of the circular muscular coat, and the homogeneous layer formed by the intima and longitudinal muscular fibres. × 200, reduced one-third. (*Green.*)

altered; all the glomeruli, most of the arterioles, small veins, and basement membrane of the tubules are infiltrated by the degeneration. Finally, in rare cases, the kidney is atrophied, its surface granular, its capsule

adherent. The organ is changed in the highest degree by infiltration of the amyloid substance. It is very probable that atrophied amyloid kidneys are only an advanced stage of a lesion which begins by a hypertrophy more or less marked, due to a parenchymatous nephritis.

The amyloid lesion may be recognized by the unaided eye only when it is very marked, that is, when the glomeruli are large and vitreous in appearance, when the medullary substance, and especially the apex of the Malpighian pyramids, presents a similar hyaline aspect, accompanied by a certain density of tissue. But it may always be recognized with the naked eye when a solution of iodine is poured upon the surface of a section, the diseased parts becoming immediately reddish-brown in color.

Amyloid degeneration has been studied generally (page 46), and also under lesions of the liver and spleen (pages 557, 591).

When the lesion is slight it is limited, as above mentioned, either to a part, or to all the loops of the glomerulus; almost all of the glomeruli are more or less attacked. In these cases, the reaction of sulphuric acid employed after the coloration by iodine, gives the most decided effects, yielding a series of colors—green, blue, violet, and finally red-brown.

We have recently studied six specimens of amyloid kidneys, having colored them with the violet of methylaniline, after preservation in alcohol.

In three of these kidneys, the amyloid change was very extensive; all the arterioles, the glomeruli, the small veins, the hyaline wall of some of the convoluted tubules, nearly all the tubules of Henle, and the straight tubules were infiltrated with the amyloid substance, and colored red, while the parts remaining normal were colored blue. In the glomeruli, the walls of the vessels were very thick and stained red. The lesion attacked their inner layers; the connective tissue uniting these vessels showed its fibrils and cells colored blue. The flat cells which covered the vascular loops of the glomeruli were normal and blue. The cells lining the capsule of the glomerulus were normal and very distinctly blue. The capsular membrane itself was generally normal.

Transverse sections of the arterioles showed their endothelium very distinct, normal, and blue in color. In all the endothelial cells of the altered vessels, the nucleus was plainly visible; its edge was marked by a blue line, and the nucleoli and granules of the protoplasm were also blue. The internal coat, the laminæ of elastic fibres, and the smooth muscular fibres of the middle coat were colored red; the former were swollen. When the lesion was not so far advanced, only the internal coat was degenerated. The external coat is usually not implicated; its connective-tissue cells and fibres were colored blue. Yet sometimes a few fibres colored red were seen, while the connective-tissue cells retained their blue color. The lesions of the small veins of the pyramids are analogous, and are well marked. Their endothelium is preserved intact; the red blood corpuscles and lymph cells are blue in color. In the convoluted tubules of the cortical substance frequently the hyaline membrane is seen thickened and red; but this thickening by amyloid degeneration is much more decided in Henle's loops, and particularly in the straight and collecting tubules. In a transverse section of the latter, where the hyaline membrane is of doubtful existence, there is seen, as in the others, a thick zone, colored

red, limiting their lumen. Within the hyaline membrane, the epithelial cells of the different tubules are found in their normal position and colored blue. Their blue color is lowered by a dark tint which is probably due to the cells being granulo-fatty, as in every albuminous nephritis. In the preparations from the three much degenerated kidneys, none of the epithelial cells had experienced the amyloid transformation.

The epithelial cells of the convoluted tubules were frequently flattened by the pressure exerted upon them by the highly refracting hyaline casts contained in the central lumen of the tubules. Many of Henle's tubules, and most of the straight and collecting tubules also contained hyaline casts in their lumen. The casts were always blue in color, more deeply tinted than the cells. A section of a tubule, therefore, presented three very decided colors; the red color of the membrane and neighboring connective tissue, the modified blue color of the epithelial lining, and the deep blue color of the central cast. Among the collecting tubules were seen red stained sections of Henle's tubules, and loops of small veins containing blood corpuscles and cells colored blue. The connective tissue which separated the transverse sections of tubules was colored blue, but was traversed by capillaries with red walls. The sections of kidneys which we have made, lead us to believe that the hyaline casts, which are formed as in chronic albuminous nephritis, are not constituted by the same substance that infiltrates the walls of the tubules and vessels. We can also say, that, in these cases at least, the endothelium of the vessels, as well as the epithelium of the uriniferous tubules and of the membranes of the glomeruli, are not involved in the amyloid degeneration.

D. Fatty Degeneration.—Simple fatty degeneration of the epithelial cells of the kidneys is not generally accompanied with albuminuria; yet there are cases where a small amount of albumen is present in the urine. Thus, in some cases of poisoning with phosphorus, albuminuria is observed, while in others it is not. Frequently there is in old persons, in tuberculosis, and in several other cachectic states, a partial fatty degeneration of the epithelium of the tubules, without the quality of the urine being changed. This may have some analogy with the physiological fatty condition of the epithelial cells of the renal tubules in several animals, particularly the dog and cat. Poisoning by arsenic or sulphuric acid produces a fatty change similar to that of phosphorus, but less intense.

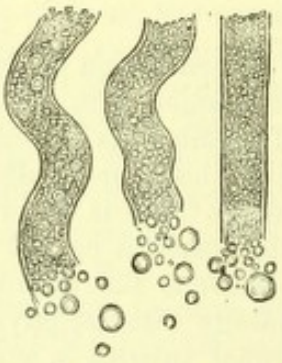
The kidneys of a person poisoned by phosphorus are typical fatty kidneys. The organs are somewhat larger than normal, in consequence of an increase of the cortical substance; the capsule is easily removed; the surface is smooth, opaque, and yellowish-gray in color. Sections show the same uniform, opaque color throughout the cortical substance, which latter is frequently congested at the same time. The medullary substance is deeper red, and presents a certain opacity when its blood is removed by washing. The mucous membrane of the pelvis is normal.

Preparations studied under the microscope, show in all the tubules of the cortical substance a filling up of the protoplasm of their cells and the lumen of the tubules, with numerous fatty granules, generally larger

than those observed in parenchymatous nephritis. The lesion is uniformly extended through all the convoluted and looped tubules; the straight tubules of the cortical substance are also altered, but their epithelium contains less fat than does that of the convoluted tubules; the lumen of these tubes gives passage to numerous free granules, granular fatty cells, and granular casts, which come from the tubules higher up. The lining of the collecting tubes is almost normal. In the midst of the much changed cortical substance, the glomeruli are absolutely normal; their vessels, and the flat cells covering them, do not show any fatty degeneration; neither have the endothelial cells of the capsule experienced any change. The connective tissue surrounding the tubules and capillaries is also quite normal in the cortical substance, differing in this from the fatty degeneration occurring in parenchymatous nephritis, where there is always an increase of this tissue. In parenchymatous nephritis it has also been seen that the connective tissue, the walls of the capillaries, and the glomeruli were always infiltrated with very fine fatty granules.

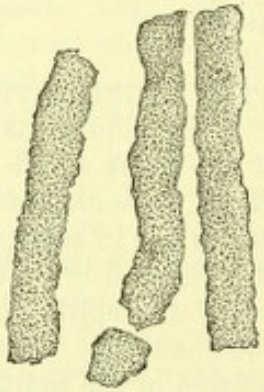
When poisoning with phosphorus occasions the presence of albumen in the urine, the protoplasm of the epithelial cells is infiltrated with albuminoid granules in connection with the fat granules, and the cells are generally smaller than in the fatty condition without albuminuria. In phosphoric albuminuria the connective tissue and vessels of the glomeruli are normal, as in the fatty form without albuminuria.

Fig. 315.



Uriniferous tubes of the cortical substance from the kidney of a non-albuminuric form of phosphorous poisoning.

Fig. 316.



Fatty casts in albuminous urine, from a case of phosphorous poisoning.

Casts found in the sediment of the albuminous urine, due to phosphorus, are peculiar in being composed of a granular mass, containing fatty granules, while in Bright's disease this form of casts is very rare. The fatty granules seen in the latter affection are only upon the surface of the casts which are hyaline beneath.

In fatty kidneys found in phthisis, in alcoholism, and in old persons, this pathological change is almost always complicated by some other lesion. In phthisis and in alcoholism, parenchymatous nephritis generally exists; in old persons there are seen, with atrophy, a dense state of the connective tissue and atheromatous lesions of the arterioles of the kidney.

In every variety of *icterus*, the coloring matter of the bile passes into the uriniferous tubules. When the elimination of biliary pigment is very great, there is produced a special parenchymatous inflammation of the kidney, which we will describe here, since the epithelial cells show a partial fatty degeneration. Jaundiced kidneys are slightly larger than normal, smooth and yellow upon their surface. The yellow color is varied with greenish lines; the cut surface presents a similar appearance; to the unaided eye the tubules are seen to contain biliary pigment; they appear as greenish-yellow lines. These yellow tubules are found both in the cortical substance and in the substance of the pyramids. By pressure upon the pyramids, there flows out an icterous urine, containing yellow casts covered with epithelial cells infiltrated with biliary pigment.

Sections of the renal substance show, in some of the tubules of the cortical substance, not in all, a granulo-fatty degeneration of the cells; the fatty granules may be very large, as in poisoning by phosphorus; the same cells contain biliary pigment; sometimes crystals of bilirubin are seen within the cells. The intertubular connective tissue also shows biliary pigment and bile crystals. The lumen of the tubules at times contains free cells, and hyaline casts. The circumstance that the urine of the patient while living shows these elements, is an evident proof that the renal cells contain biliary pigment during life. This lesion of the kidney is seldom accompanied by marked albuminuria.

Interstitial Nephritis.—Interstitial nephritis, characterized by the formation of new connective tissue, embryonic or fibrous, by fibrous atrophy of the glomeruli, and by fibrous and inflammatory induration of the vascular walls, with atrophy of the renal tubules, is a lesion met with in many different conditions. It may be general or partial; it may or may not be accompanied by albuminuria.

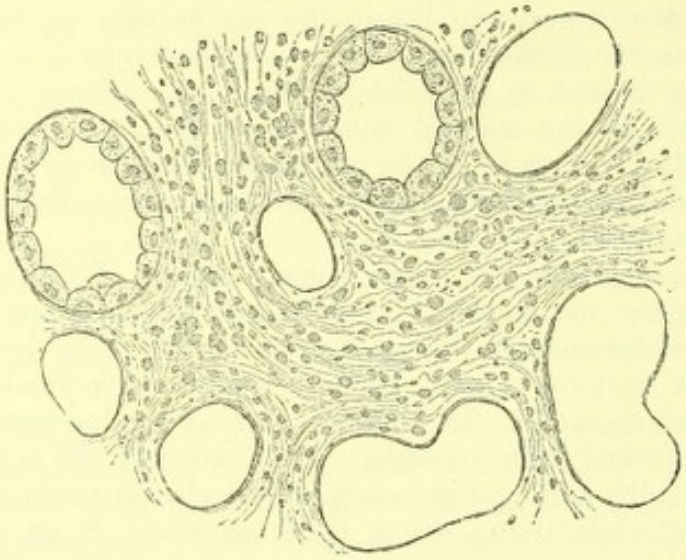
Albuminous Interstitial Nephritis. 1st. *Acute or Subacute.*—We have previously seen that in some cases of parenchymatous nephritis there is a new formation of small cells and nuclei in the vascular tuft of the glomerulus, either at its centre or upon the vascular loops. When this formation is very abundant, the vascular loops are not separate; they form a compact ball, in which the small vessels of the glomerulus are fused together by an embryonic connective tissue infiltrated with lymph cells. This condition has been well described by Klebs in scarlatinous albuminuria.

Kelsch has reported several cases of scarlatinous nephritis, in which the glomeruli, the connective tissue surrounding them, and that separating the convoluted tubules of the cortical substance, were infiltrated with numerous embryonic cells or lymph corpuscles. This lesion is accompanied with a granulo-fatty degeneration of the epithelial cells of the tubules.

The infiltration of the renal connective tissue with white corpuscles may be considered, from our knowledge of the evolution of connective tissue, as the first stage of an interstitial nephritis, which after continuing some time terminates in the formation of a sclerotic tissue; but we lack

positive evidence of this change. Scarlatinous albuminuria ends in recovery, or terminates in death in the first stage, so that we do not know of any example where an albuminuria of this kind has terminated in chronic interstitial nephritis with atrophy of the kidney.

Fig. 317.



Interstitial nephritis. The earlier stage of the process. Showing the cellular infiltration of the intertubular connective tissue. The epithelium has fallen out of some of the tubes during the preparation of the section. × 200. (*Green.*)

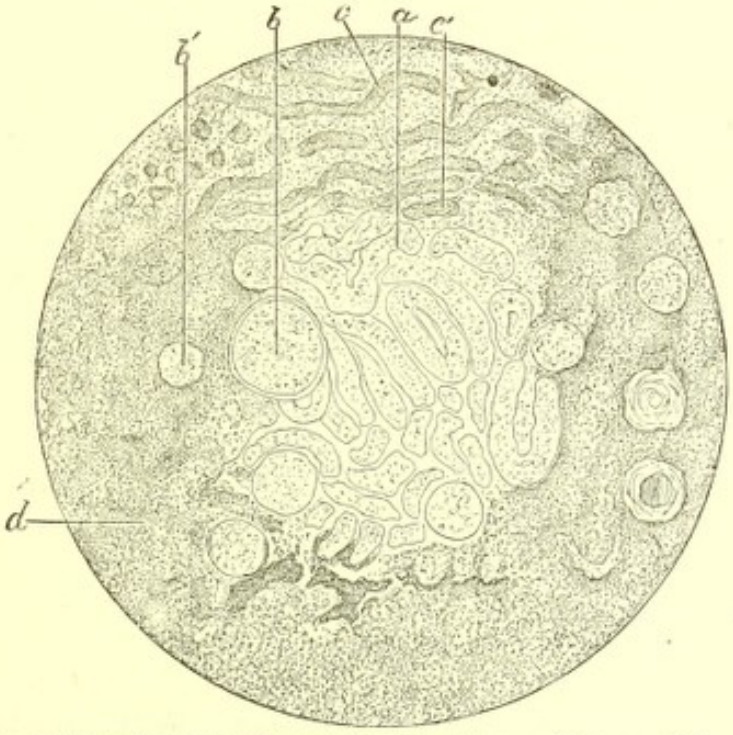
2d. *Chronic Variety.*—In this form of albuminous nephritis the kidney is generally smaller than normal; the amount of atrophy, however, varies; at times it is scarcely observable, or the organ may be reduced to one-half or one-third its ordinary size. Both kidneys may be equally atrophied, or one may be half as large as the other.

The fibrous capsule is thickened, dense, and adherent. In removing it, a thin irregular layer of the cortical substance is always separated with it, which, notwithstanding its thinness, always contains many altered glomeruli. Beneath the capsule, the surface of the kidney is granular. The granulations are formed by the bases of the pyramids of Ferrein; they vary in size—the more atrophied the kidney, the smaller the granulations; they measure from one to one and a half millimetres in diameter. When the kidney has reached the last stage of atrophy, its surface is finely granular. The central part of a granulation, examined in section, is either opaque or translucent; the latter condition is usually seen in very much atrophied kidneys. The cortical substance, both upon the substance of the kidney and between the Malpighian pyramids, is lessened in thickness. When the atrophy is not very great, it presents, upon section, round spots, which are differentiated by the color of their centre differing from that of their margin. These spots are analogous to the granulations upon the surface, and represent transverse sections of the pyramids of Ferrein. When the cortical substance is greatly atrophied, the granulations are visible only upon the surface. They are always separated, upon the external part of the kidney, as well as in the prolongations of the cortical substance between

the pyramids, by a tissue which is more vascular than the centre of the granulation. The atrophy may be such that the thickness of the cortex is reduced to one millimetre or less. The medullary substance is always less than normal, but experiences a diminution in size relatively much less than that of the cortical layer; it is generally congested. The mucous membrane of the pelvis and calyces is congested, the submucous tissue is dense and thickened; sometimes the pelvis and calyces are dilated. There almost always exist cysts, visible to the unaided eye, in the cortical substance. The consistence of the kidney is firm and dense. Such are the most important macroscopic lesions.

In an extreme degree of atrophy, a varying extent of the kidney is atrophied and in places the cortical substance has almost disappeared, the corresponding pyramids are also reduced in size. At these places the cortical substance is finely granular upon the surface, of a doughy consistence, of a regular pink color, and by careful examination with obliquely incident light it is seen to be semi-transparent. This semi-transparency is due to a formation of numerous small cysts, some of which are visible to the unaided eye. Let us glance now at the histological details of the foregoing description.

Fig. 318.



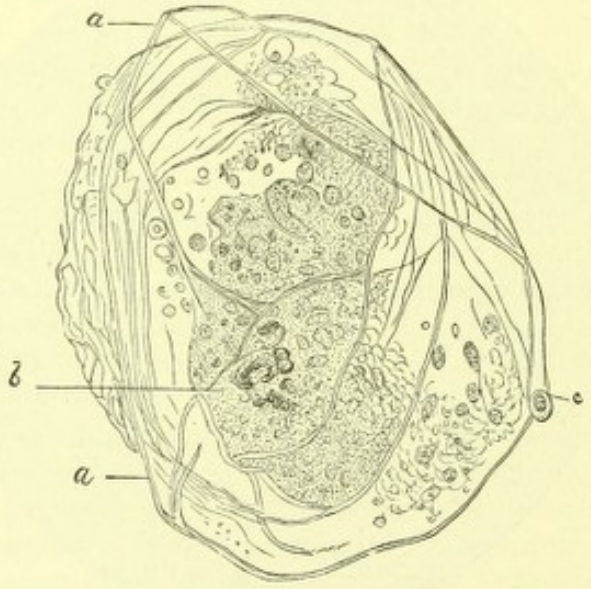
Section through a granulation in a kidney of Bright's disease. The granulation corresponds to the whole of the light portion of the centre of the figure. *a*, tubules; *b*, glomeruli in the granulation. *c*, *c'*, *b'*. Atrophied tubules and glomeruli of the surrounding renal parenchyma. × 40.

The granulation is due to the fact that the uriniferous tubules occupying the centre are normal in size or even dilated, while those at the periphery are atrophied, as are also most of the glomeruli; at the same time, between these atrophied elements, the connective tissue shows numerous cellular elements and newly-formed fibres. In order to fully understand the atrophied portions, it is necessary to turn to the normal

structure of the kidney. The collecting tubules divide and subdivide while passing into the cortical substance; the resulting straight tubules then go to the centre of each small pyramid, giving off laterally convoluted tubules, which, after forming Henle's loops, terminate in the last convolutions of the tubule which enters into the capsule of a glomerulus. Each of these small pyramids (of Ferrein) of the cortical substance possesses at its centre straight and convoluted tubules; its periphery contains the convoluted tubules, which are continuous with the capsules of the glomeruli. It is these last elements, the glomeruli and convoluted tubules, which are atrophied and surrounded with thick connective tissue, and it is here that occurs the atrophy with contraction.

When a section is examined with the microscope, there are seen, around the glomeruli, laminated concentric zones of connective tissue, between the lamellæ of which exist flat, stellate, or small round cells. Within this connective-tissue envelope, the glomerulus has undergone changes. Its diameter may be only one-third its normal size. The superficial portions of kidneys affected with interstitial nephritis generally exhibit numerous glomeruli located very near together, owing to the atrophy of the tubules which separate them. There is no part of the kidney where the lesion is more marked than it is immediately beneath the renal capsule. The capsule of the glomerulus is usually wrinkled

Fig. 319.



An isolated glomerulus from the surface of a kidney affected with interstitial nephritis. *a*. Membrane of the capsule wrinkled and folded by the action of acidulated water. *b*. Vestiges of vascular loops of the glomerulus. The contents of the capsule of the glomerulus show, besides vessels, some cells and fatty and calcareous granules. × 240.

and thickened; sometimes it presents concentric folds which may be taken for concentric and parallel layers of connective tissue. But if, by teasing, the glomerulus is isolated while still surrounded with its capsule, it is seen that the latter becomes distended, unfolded, and has the appearance of a rumpled membrane, which has been contained in a space

too small for it This membrane is made very distinct by the action of acetic acid, which causes it to swell. Figure 319 represents a glomerulus isolated and treated by acetic acid. The membrane which formed the concentric layers and circular folds around the granular mass in its interior is distended and presents irregular folds, while within it are seen granular cells and calcareous granules. At times, in very thin sections of kidneys attacked with chronic interstitial lesions, the structureless capsule of the glomerulus is seen to be distinctly thickened, having upon its internal surface flat cells with oval and prominent nuclei. The hyaline membrane is not always preserved in interstitial nephritis; frequently the wall of the cavity is formed by the neighboring connective tissue. This occurs where the new formation of connective tissue is most abundant.

The arterial tuft of the glomerulus is distorted; its vascular loops are united by a thick connective tissue containing cellular elements. It gradually atrophies, and represents at times an almost homogeneous mass, irregular at the periphery, and in which the vessels cannot always be recognized. As the atrophy increases, the vascular tuft contains less embryonic elements; it consists mainly of a few stellate cells in a mass of fibrous tissue. Upon the surface of this mass which represents the glomerulus, and upon the internal surface of the membrane of the glomerulus, there exist granular cells containing some fatty or calcareous granules. Frequently the entire cavity of the capsule is distended and filled with granules of this nature.

The whole of the glomerulus now appears, to the unaided eye, as a small, yellow or gray, and opaque point; to the microscope, as a small, round, dark, and opaque mass, which effervesces upon the addition of acetic acid.

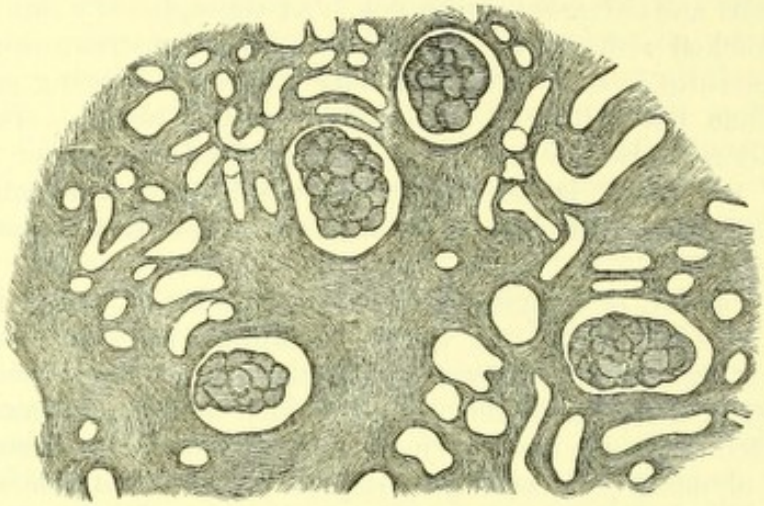
Almost all the glomeruli are more or less altered, and the tubules proceeding from them undergo an analogous atrophy, while the connective tissue surrounding them is notably thickened by the formation of cells and connective tissue fibres. The shrinking and even total disappearance of the convoluted tubules near the glomeruli, in the peripheral zone of the granulations, causes the latter to come almost in contact one with the other.

Sometimes glomeruli are seen, the vessels of which are atrophied, while the capsular cavity is filled by a colloid substance. These are colloid cysts developed in a glomerulus. In these cysts there still remain, upon the internal surface of the capsule and upon the surface of the vascular tuft, a few flat cells.

The tubules, which retain their normal diameter in the centre of the granulations, contain normal cells, or fatty, granular, or colloid cells, and their central lumen incloses hyaline or colloid casts. At other times they contain numerous blood corpuscles. In the first case, the centre of the granulation is semi-transparent; in the second, it is opaque and yellow or red. In the atrophied tubules the cells are small, they have lost the characters of secreting cells, and they are also somewhat granular. Generally some of the cells of the tubules are filled with blood pigment, and, with a low power, give a characteristic yellowish-brown color. The membranous sheaths of the tubules are normal at the

centre of the granulations. In the atrophied tubules the membrane is at times absent or blended with the neighboring connective tissue, or it may be thicker than in the normal state.

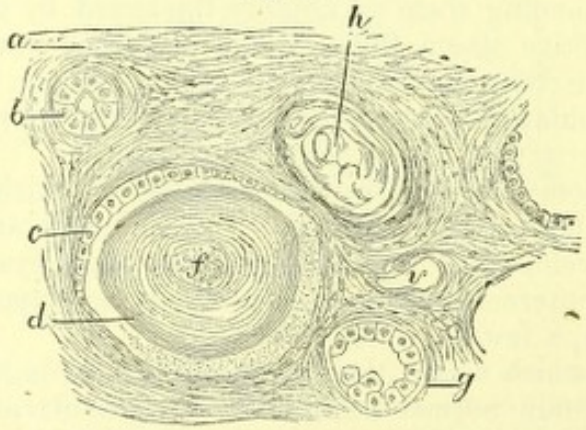
Fig. 320.



Interstitial nephritis. A very advanced stage of the process. Showing the large amount of fibrous tissue between the tubes of the cortex, and the extensive atrophy of the tubes. The degenerated epithelium which was contained in some of the tubes has fallen out in the preparation of the section. × 50. (*Green.*)

The Malpighian pyramids do not present such marked lesions; the atrophy of Henle's loops and of the collecting tubules, and the thickening of the connective tissue, are not so great. At times there are found, as in the cortical substance, numerous hyaline casts which more or less fill the collecting tubes and loops of Henle.

Fig. 321.



Section of kidney in an advanced stage of interstitial nephritis. *a*. Connective tissue formed of fibres and flat cells. *h*. Section of an atrophied uriniferous tube containing in its lumen a colloid cast. *b*. A uriniferous tube lined with flattened epithelium, and also containing a colloid cast. *g*. Uriniferous tube. *c*. Flat cells lining a cyst formed by a dilated tubule which contains a colloid substance, *d*, with concentric layers and a central granular mass, *f*, consisting of granules of hæmatin. *v*. Bloodvessel. × 200.

In a more advanced stage of interstitial nephritis there is seen, as above mentioned, a homogeneous semi-transparent tissue. Examination

with the microscope shows only atrophied glomeruli, many of which have no characteristics by which they can be recognized, some cysts, seen only with the microscope, and a few uriniferous tubules containing colloid casts.

The glomeruli are reduced to small spherical balls of fibrous tissue; the microscopic cysts are at times so close together, that a section through the surface of the kidney shows them covering the surface as small clusters in contact one with the other. They are filled with a yellowish or colorless refracting colloid substance. They are undoubtedly developed from the uriniferous tubules. By the sides of these cysts are seen sections of greatly atrophied uriniferous tubules filled with colloid casts. The cysts frequently contain in their centre a colloid or granular cast; and by examining a section, not too thin, and varying the focus, the casts in the interior of the cysts are seen to extend into a uriniferous tubule. (Fig. 321.)

The atrophied uriniferous tubules and the cysts which remain in the midst of the new connective tissue have a very similar structure. In transverse sections very narrow tubules are seen with a thin hyaline membrane, upon the inside of which is found attached a single layer of cubical or pyramidal cells, provided with a round or oval nucleus which is colored by carmine. In the lumen of the tubule there almost always exists a colloid cast. (Fig. 322.)

Fig. 322.



Colloid degeneration of the epithelial cells of a uriniferous tubule in interstitial nephritis. *a*. Connective tissue. *b*. Epithelial lining of the tube. *c*. Colloid cells. *e*. Colloid cast with concentric layers. × 300.

The colloid cysts have the same structure. There is found a hyaline membrane applied against the connective tissue which has grown thick around it. In this tissue, the cellular elements are flattened and placed in the direction of the fibres, following the concentric form of the capsule of the cyst. Upon the interior of this capsular membrane there is seen a complete lining of cubical cells in the small cysts, and in the more distended cysts the cells are slightly flattened, but in both always containing a nucleus. Within this first layer one or two other layers are seen in which the cells have no nucleus, are spherical, transparent, and are transformed into small round masses of colloid substance. We think it is by the fusion of these elements that the colloid substance filling the cyst is formed. This substance is sometimes homogeneous, sometimes granular, or it forms slightly yellow, refracting, transparent, concentric layers (*d*, *f*, fig. 342, fig. 343). Acetic acid swells the mass, causing the concentric circles to disappear. In the centre there is seen either a true colloid cast—older, more refracting, and yellower than the peripheral layers—or a small collection of yellow granules which are derived very probably from altered red blood corpuscles. This description warrants the belief that, after the inflammatory destruction of the normal cells of the convoluted tubules, there are developed cells, not having the characters of secreting cells, but assuming the cubical or flat form; and that these cells undergo colloid transformation and fuse into a colloid mass, which is increased by

the deposit of successive layers, while at the same time new cells at the periphery become colloid. In this conception of the formation of the colloid contents of the cysts, the centre and central layers are necessarily the oldest formed.

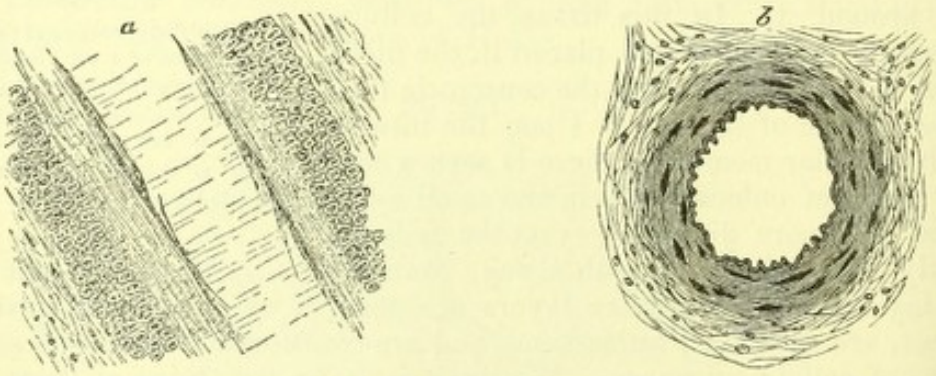
These cysts are not always constituted by the distension of a single tubule; several cysts may unite to form one, when the connective tissue surrounding several tubules develops into a thick envelope common to them all.

In an atrophied kidney we once observed a cyst, nearly one centimetre in diameter, situated in the midst of a tissue filled with small colloid cysts. The walls of the large cyst were formed of thick layers of very dense flat lamellæ of connective tissue, resembling that formed in the fibrous thickenings of the capsule of the spleen, and having a cartilaginous appearance. The fluid contained in the cyst was thickened by lime salts.

By teasing and tearing the renal tissue transformed into colloid cysts, the small cysts are obtained united together by narrow bands of fibrous tissue resembling a string of beads. It is very probable that they are developed one below the other in the course of the same uriniferous tubule, but the fibrous tissue uniting them does not always have the characters which belong to an atrophied tubule.

Frequently, in granular and atrophied kidneys, there are found small concretions of the urates; they are seated in the substance of the pyramids rather than in the cortex. The white concretions are characteristic of *gouty nephritis*, and are formed of acicular crystals of urate of soda.

Fig. 323.



Arteries from contracted kidney of advanced chronic Bright's disease. *a*. Longitudinal section, showing the great thickening of the internal longitudinal and external circular muscular coat, also of the outer fibrous coat. *b*. Transverse section of another vessel less diseased. Here is seen the thickening of the circular muscular and external fibrous coat. × 200. (*Green.*)

The red concretions are due to amorphous urates. Both have the same location, and at first fill either the collecting tubules of the Malpighian pyramid, or the straight tubules of the cortical substance. The deposit, continuing to increase, invades the neigboring connective tissue, and the larger concretions include a group of adjacent uriniferous tubules which are filled while the connective tissue is at the same time infiltrated by the same salts.

The vessels in this variety of nephritis constantly experience very great

anatomical changes. To the unaided eye, the arteries are seen manifestly thickened and rigid, not collapsing when a transverse section is made, generally tortuous if the section is longitudinal. These lesions have been pointed out and known for a long time, but within the past few years they have been the subject of discussions among several English writers. Johnson refers the induration of the arterial walls to a hypertrophy of the muscular coat, while Gull and Sutton regard it as a deposit of a hyaline fibroid or hyaline granular mass infiltrating the walls of the arterioles and capillaries. We cannot accept the opinion of either, for, in the cases we have seen, the arteries were only affected by chronic arteritis. When thin sections are examined with low power, the arterioles show their wall thick and rigid, presenting in their external and middle portions a dark coloration due to the great abundance of elastic fibres. The external and middle coats possess the numerous cellular elements seen in arterial sclerosis, and there is usually also an endarteritis characterized by the proliferation of the cells included between the last elastic lamina and the internal surface of the vessel. The calibre of the arterioles is diminished; at the same time their wall is thickened by chronic inflammation. The wall of the capillaries returns to the embryonic state, and the veins are attacked with chronic phlebitis.

Such are the anatomical characters of this disease, which is slowly developed, is accompanied with variable and slight albuminuria, with the voiding of large quantities of urine, with little or no œdema, and is generally associated with hypertrophy of the left ventricle occasioned by the difficulty of the circulation in the kidneys and a consequently increased pressure in the aorta. In all the cases of atrophied kidneys that we have examined, we have always seen in some of the tubules less atrophy than in others, and a granular fatty degeneration of the epithelium, similar to that observed in parenchymatous nephritis. Consequently in these two varieties of albuminous nephritis there is an alteration of the renal epithelium common to both. To distinguish between interstitial nephritis and parenchymatous nephritis (large white kidney), it must be remembered that in the latter, the connective tissue is normal, the epithelium of the tubules is primarily granulo-fatty, and the surface of the organ is smooth. The symptoms differ also, for in the latter the course of the disease is more rapid, the albuminuria is very abundant, the quantity of urine is less than normal, and the œdema is always very decided.

The preceding facts appear to be well established, and the two distinct groups of symptoms correspond with two well-established distinct lesions. But before concluding from these syndromes two distinct diseases, or even two distinct varieties of the same (Bright's) disease, it is necessary to be certain that the granular contracting kidney never begins in parenchymatous nephritis. Now it is precisely this question which does not seem to be certainly established. The last stages of interstitial nephritis, the atrophy, the fibrous thickening, etc., are well characterized; but what changes does the kidney undergo previous to these stages? This is difficult to understand from the descriptions of autopsies given by writers. There is only seen at autopsies one anatomical phase of the disease, and it cannot always be said what were the preceding changes or what will be those which follow. The first stages of granular contract-

ing kidney given by writers are, especially: 1st, congestion, accompanied by a slight hypertrophy and induration of the organ, a lesion common to both, and we will not consider it; 2d, congestion and infiltration of the cellular tissue and lymphatic spaces by white blood corpuscles or embryonic cells. This is observed in scarlatina, where the epithelium of the tubules is fatty granular, while the cellular tissue is inflamed, although atrophied intestinal nephritis may not be the consequence; 3d, there is a fibrous organization of the connective tissue; the autopsies cited as belonging to this stage, showed the induration of the kidney of cardiac diseases. In this case the connective tissue is thickened, and organized as a consequence of the blood stasis in the kidney. But is this lesion one of those which may be followed by the atrophied and granular kidney of Bright's disease? We doubt it, since, in nearly every autopsy of cardiac lesions there is found this cyanotic induration of the kidney, which evidently has existed a long time, while the atrophied and granular kidney is relatively rare as a direct result of a heart affection. But in acknowledging the probability of the existence of established lesions corresponding to symptoms in the group of albuminous nephritic diseases, we will not venture to say, that granular interstitial nephritis never follows an initial parenchymatous nephritis. It appears to us that the difference in the types of albuminous nephritis depends especially upon the intensity of the producing cause and of the lesions which are the consequence of it. For example, as the result of cold, there is produced an albuminuria which develops quickly and terminates in death. At the autopsy there is found a large white and smooth kidney; the intensity of the lesion has killed the patient. Would this same kidney later have been atrophied, if the patient had lived long enough? The pathologist who would judge without having before his mind the evolution of the lesions, would very certainly separate the recent infarction of the kidney, which is prominent, red, or yellow, and the chronic infarctus which is represented by a depressed and fibrous cicatrix.

When the exciting cause is slow in its action, for example alcoholism, we may have either a smooth kidney or an atrophied and granular kidney; the lesions being limited, and slower in their changes, the connective tissue is irritated at the same time as the cells of the tubule. When the cause is constitutional and very slowly developed, as gout, the lesions will be limited, and at first not very intense, and a typical granular contracting kidney will be found at the autopsy. But it should be remembered that there always occurs, in every case of albuminous nephritis, a greater or lesser change in the renal epithelium; when it is questionable if the lesion of the tubules is primary or secondary, we do not believe an answer can be arrived at, except in the two extremes of these varieties of Bright's disease.

The kidney may be attacked with interstitial nephritis at the same time that the liver is affected with cirrhosis. Such a complication is not rare in alcoholism and gout. The English writers insist upon this coincidence; it is probably more common with them than upon the continent. Grainger Stewart observed cirrhosis of the liver fifteen times in a hundred cases of interstitial nephritis, and Dickinson once in seven. Charcot in citing these cases reports that in five or six cases of interstitial pneu-

monia (fibroid phthisis of Sutton) he has twice seen interstitial nephritis with albuminuria.

E. Non-albuminous Interstitial Nephritis.—General or partial interstitial nephritis is frequently seen without albuminuria, which is evidence that an inflammatory lesion of the connective tissue of the kidney has no direct connection with the presence of albumen in the urine.

General interstitial nephritis without albuminuria is observed in the senile state with chronic arteritis, and in chronic calculous pyelo-nephritis.

In senile cachexia with atheroma of the aorta, more or less general, the kidneys are usually hard and small; their capsule is more adherent than in the normal state; their surface is finely granular; sometimes it presents infarcti in different stages of evolution; the cortical substance is atrophied and pale, while the medullary substance is congested and nearly normal in amount. The renal arteries are sclerosed and hard, as in interstitial nephritis. Examined with the microscope, the connective tissue of the cortical substance is seen a little thickened; a few groups of glomeruli are sclerosed and atrophied as in the preceding lesion; there is an interstitial nephritis, but it is chronic, not very intense, and the tubules are generally normal. There is no albumen in the urine. In calculous pyelo-nephritis, the atrophy of the cortical substance is still more marked; the inflammation of the tissue of the capsule and neighboring organ is such, that there may occur a peri-nephritis, either acute and purulent or chronic, with the new formation of connective tissue. The surrounding cellular adipose tissue may adhere so intimately to the capsule, that the whole forms a single mass, in the midst of which the kidney is found almost completely atrophied, compressed from without inwards by this chronic inflammation, and from within outwards by distension of the pelvis and calyces filled with calculi and pus. A microscopical examination of these kidneys shows the vessels sclerosed, and the renal connective tissue dense and thicker than normal. The uriniferous tubules and glomeruli are very much atrophied; the latter are transformed into small fibroid masses, as in granular interstitial nephritis of Bright's disease. The most extreme degree of atrophy of the kidney is seen in some cases of pyelitis and calculous hydro-nephrosis, in which the entire renal substance simply forms the wall of the cyst, while the pelvis and calyces are enormously dilated. These varieties of very chronic and atrophied interstitial nephritis by their causes, by their lesions, by their symptoms, and especially by the absence of albuminuria are very far removed from those forms which are included in Bright's disease.

In interstitial nephritis without albuminuria, the tubules contain neither hyaline nor colloid casts; the epithelial cells are seldom fatty degenerated, and do not exhibit colloid degeneration so frequently as in albuminous interstitial nephritis.

Partial *interstitial nephritis* is seen surrounding most tumors, and especially those of a connective tissue type. For example, around gummata, the tissue of the gumma, which is primarily developed from the fixed elements of the renal connective tissue, extends from the tumor as

thick partitions which separate the tubules and glomeruli. Again, tuberculous granulations of the kidney are, at their beginning, only a collection of embryonic corpuscles arranged in the connective tissue of the kidney—elements which, accumulating, occasion atrophy and granulo-fatty destruction of the cells of the tubules, and disappearance of the latter. Around tubercular granulations, the renal connective tissue septa are thickened by an infiltration of similar embryonic or lymph corpuscles.

Small fibrous tumors (fibromata) are rarely found in the human kidney, but they are more frequent in the dog.

Contracted cicatrices, which are characterized by considerable depression of the cortical surface of the kidney, and which follow old infarcti occasioned by an embolus or thrombus or by atheroma of a renal arteriole, are very distinct examples of partial interstitial nephritis. In this case, after all the elements within the infarctus have become degenerated and absorbed, a true fibrous cicatrix takes their place.

Suppurative Nephritis.—There are two forms of suppuration of the kidney; it may be diffuse or in the form of metastatic abscess.

1st. *Diffuse Suppuration.*—This occurs after contusions, traumatisms, inflammations extending along the tissue of the excretory ducts, caused by calculi of the pelvis or ureters, retention of urine, in uterine carcinoma, during the course of spinal disease, etc. The lesion varies in extent, it may affect one or both kidneys.

The organ is at first congested and swollen, a considerable amount of blood escapes upon making a section of the kidney; by washing, the redness generally diminishes, but true ecchymoses remain, either as red or as slate colored spots, due to blood extravasations into the connective tissue of the kidney, into the capsule of the glomerulus and into the uriniferous tubules. In corresponding points, the fibrous capsule of the kidney is deeply injected, presenting vascular arborescences, and even red or slate colored ecchymoses. When there is found such a decided congestion of the kidney at autopsies, there is usually at the same point a collection of pus, either in the form of one or more abscesses, or of purulent collections within the pre-existing cavity of a renal cyst. Frequently the suppuration is an acute condition complicating a chronic lesion of the kidney, especially a calculous affection or retention of urine.

The general shape of the kidney is retained; it is increased in size, and it may be completely infiltrated with pus; when the capsule is removed the surface appears yellow and opaque. The cut surface also is yellow and opaque; upon pressure, a thick pus exudes. After washing the surface of a section, the renal tissue is seen infiltrated with pus and is very friable. A microscopic examination of a thin section shows the pus corpuscles in the cellular tissue, and in the interior of the tubules of the kidney. The puriform infiltration most frequently affects the cortical substance.

2d. *Suppuration in Foci.*—At some autopsies, pus is seen collected into small and disseminated foci, and care must be exercised in discriminating them from metastatic abscesses. When these abscesses are recent, they contain a thick yellowish pus; the wall of the sac is formed by the

intensely congested renal tissue. When the foci are chronic, the pus is more or less decomposed, thickened by the presence of calcareous salts, or it is serous and fetid. The sac may consist of a true membrane of connective tissue. In kidneys which are the seat of these chronic foci, there are almost always found other lesions, as partial atrophy, irregularities of the surface, cysts, etc. It is possible that these purulent foci

Fig. 324.



Surgical kidney. At the lower part of the figure is seen the cellular infiltration of the intertubular tissue, and the blocking of the tubes with epithelium and leucocytes. At the upper part, there is the commencing formation of an abscess. × 100. (*Green.*)

may, after the absorption of the pus, give place to serous cysts; but attention should be directed to the fact that in kidneys in which serous cysts have existed for a long time, one or more of the cysts may become filled with a turbid puriform fluid. This occurs in retention of urine followed by an inflammation of the kidney.

A very frequent error consists in mistaking a distension of the pelvis and calyces by pus for one or more abscesses of the kidney. The distension of the pelvis and ureter may secondarily occasion an atrophy of the entire kidney, whose substance then forms the wall of a sac filled with pus. When abscesses of the kidney are very large, they are generally connected with a suppuration of the pelvis. True abscesses in the kidney are, however, quite frequent in suppurating pyelitis, which is an occasional cause of nephritis.

The suppurating foci of the kidney have variable terminations. When only the apex of the pyramids is involved, the foci may ulcerate and form irregular ulcers, which freely discharge into the pelvis. Cysts or cicatrices, followed generally by atrophy with a condensation of the organ, are the consequences of small abscesses which have healed.

Large abscesses of the kidney may open: *a*, into the pelvis and be evacuated with the urine, a comparatively favorable termination; *b*, into a portion of the intestines; *c*, upon the exterior, passing through the

abdominal walls, especially in the lumbar region; *d*, into the peritoneal cavity, causing a peritonitis rapidly fatal; *e*, through the diaphragm, into the lungs, and bronchi. Rayer saw a case in which the liver was ulcerated and formed the wall of an abscess, which involved both the liver and the kidney. A splenic abscess, communicating with a purulent sac in the kidney, has been reported.

In several cases suppurating nephritis seems to have terminated by a true gangrene of the kidney; but it should be remembered that post-mortem decomposition of the kidney is very rapid, and ought not be confounded with gangrene.

3d. *Metastatic Abscesses.*—These are usually found with analogous lesions of the lungs, liver, etc.; but they may occur solely in the kidney, as often happens in affections of the genito-urinary passages, and sometimes in typhoid fever.

They can usually be studied in different stages of development in the same kidney, especially when they are recent. After removing the fibrous capsule, there are found upon the surface of the kidney small, circular, miliary, prominent agglomerations, some deep red, others white or yellow in their centre or throughout their whole mass—the latter being surrounded by a zone of congestion. The small foci are best for studying under the microscope the beginning of the suppuration. A section passing through the midst of an agglomeration of small miliary foci demonstrates that they extend into the cortical and medullary substance, assuming an arrangement which recalls the distribution of a renal arteriole, or, better, one of the pyramids of Ferrein. These agglomerations of small abscesses have in general the shape of a cone with the base towards the periphery of the kidney.

We class metastatic abscesses with the *parasitic nephritis*, described by Klebs, because the most recent writers upon purulent infection consider that the bacteria come from a sanious suppurating focus instead of being conveyed by the blood, as occurs in purulent infection; the small algæ and spores pass along the urinary passages in this form of nephritis. Starting from the bladder or pelvis, the infecting particles ascend into the cortical substance by way of the uriniferous tubules. Their presence occasions irritation, and fatty degeneration of the epithelial cells, and the escape of lymph cells either into the uriniferous tubules or into the connective tissue of the kidney. The abscesses which are the result of this inflammation have the same seat and shape as metastatic abscesses.

We readily acknowledge that, among the many causes of metastatic abscesses of the kidney, the presence of parasites coming from the bladder in catarrh of its mucous membrane, or carried by the blood in infectious diseases, may be recognized as one.

The hyaline casts in parasitic nephritis, represented by Klebs, and observed during the life of the patient, present upon their surface spores and parasitic algæ. The great abundance of bacteria adhering to the casts coming from the kidney would suggest that they are formed in the kidney during life, and that they are not deposited at the time of the entrance of the hyaline casts into the bladder.

PYELO-NEPHRITIS.—There are many varieties of pyelo-nephritis, between a superficial and temporary catarrhal pyelo-nephritis, such as seen after vesication by cantharides and a suppurative pyelo-nephritis, or a chronic pyelitis caused by the existence of calculi found in the pelvis, calyces, ureters, and kidneys.

Catarrhal pyelo-nephritis is characterized by a redness of the mucous membrane lining the excretory passages of the urine, by a desquamation and very abundant formation of the epithelium of the mucous membrane of the pelvis and calyces, and by a notable thickening of this membrane. The urine contained in the pelvis holds in suspension desquamated epithelial cells and lymph cells. The collecting and straight tubules of the pyramids participate in the inflammation.

When the lesion is more intense, the fluid exuded upon the surface of the mucous membrane contains fibrin which coagulates and forms a membrane or fibrinous patches upon the surface of the pelvis and calyces (*pseudo-membranous pyelitis*). These cavities are now dilated to a varying extent.

Acute *purulent pyelitis* may be met with during the course of chronic diseases of the bladder and urethra, hastening their fatal termination. It is also frequently met with in uterine cancer when the ureter and bladder are invaded, and in purulent infections. The amount of pus accumulated in the pelvis, when there exists an obstacle to the escape of the urine, may be considerable. The connective tissue of the mucous membrane is infiltrated with lymph cells. If the disease has lasted for some time, the mucous membrane of the pelvis is irregular, and its surface presents small vascular granulations, formed of embryonic tissue and villi, which float, when examined, under water.

The apices of the pyramids also suppurate, and ulcerate. This condition is usually complicated with abscess or diffuse suppuration of the kidney.

Chronic purulent pyelitis is sometimes accompanied with considerable effusion into the cavity of the pelvis, causing large cystic tumors when an obstruction exists in the ureter. These large sacs contain, with the fluid pus, ammoniacal products, inspissated pus, soft white calcareous matter, and calculi. The submucous tissue is thickened, and the tumor contracts adhesions with the surrounding organs. The secreting structure of the kidney is naturally atrophied, spread out, and flattened, so as to form the wall of the cyst. The pyramids are always flattened, and do not form elevations. Notwithstanding the fibrous thickening of the wall, the latter may ulcerate and cause an opening either into the intestine, or into the lung after passing through the diaphragm, or into the subperitoneal connective tissue, when the pus appears under the crural arch. Abscesses of the liver may be developed in the neighborhood of the sac, if the right kidney is the one affected. Peritonitis or pleuritis may be the ultimate termination of the disease.

Calculous pyelitis, which is essentially chronic, is occasioned by the presence of calculi in the pelvis, calyces, or ureter. Multiple calculi are

generally small; when there exists a single calculus, it either is simple or is formed by the union of several. The shape of the calculi is that of the cavities which they fill.

These calculi are most frequently composed of uric acid, urates, oxalate of lime, ammonio-magnesium phosphate or phosphate of lime, cystin, etc. Sometimes they consist of several substances.

In calculous pyelitis the kidneys are always affected by interstitial nephritis, cysts, very marked atrophy, etc.

The mucous membrane of the pelvis and calyces is also always much changed: it is thickened, fibrous, infiltrated upon its surface with calcareous salts which form a sort of superficial incrustation, or it may be ulcerated.

From the effects of calculi, or any other obstacle to the passage of urine, there may be developed a *hydro-nephrosis*, that is, an accumulation of urine in the pelvis and considerable distension of this reservoir.

Tuberculosis of the Kidney.—Tuberculosis of the kidney is primary or secondary. Primary tuberculosis is not of very frequent occurrence; it may affect one or both organs, but one always to a greater extent than the other. In kidneys but little altered, whether in primary or secondary tuberculosis, the histological structure of the tubercle can be best studied where the granulations are miliary. They ordinarily begin in the cortical substance, along the arterioles which separate the pyramids of Ferrein, or upon the surface of the kidney. There are seen along the arterioles of the cortical substance, longitudinal rows or groups of tuberculous granulations. Each of these fine granulations consists of a portion of changed kidney structure; in it the intertubular cellulo-vascular tissue is thickened and infiltrated with small round cells. The epithelial cells of the tubules become granulo-fatty, and the tubules are compressed by the abundant cell formation in the fibrous partition which surrounds them. The centre of the small granulation becomes caseous. Neighboring granulations fuse together, forming larger masses, which are usually located at the union of the cortical with the medullary substance. For a more minute description of tuberculosis we refer to part first (see p. 112).

Persons who die of primary tuberculosis of the kidney, always present a very complex morbid condition of the genito-urinary organs. The cortical and medullary substances are the seat of large caseous tuberculous masses. The greater part, or even the whole of the kidney, may be invaded by this new formation. The pelvis and calyces are dilated and filled with caseous pus, or with a semi-fluid pulp containing masses coming from the destruction and elimination of the ulcerated parts at the extremities of the Malpighian pyramids.

When the distended cavities of the pelvis and calyces are washed there are seen upon their surface elevated tuberculous granulations, either discrete or forming a continuous layer. A section of the mucous membrane shows that the mucous and sub-mucous connective tissue is very thick, often measuring one or more centimetres. It is transformed into an embryonic tissue, in which exist one or more super-imposed layers of tuberculous granulations. The mucous membrane so altered is frequently ulcerated, the pus and the detached fragments, which are the result of the ulceration, fall into the cavity of the pelvis.

When the ureter is permeable, the urine carries away the products of suppuration, and has an appearance characteristic of renal tuberculosis: it is intimately mingled with caseous pus and flaky opaque débris, which are deposited in a thick cloudy layer at the bottom of the vessel in which it is received. Examined with the microscope, there are found lymph cells loaded with fatty granules, a few blood corpuscles, and débris of connective tissue infiltrated with small and fatty granular cells. The urine contains albumen, as does all purulent urine; but it is impossible to confound it with ordinary albuminous urine, which is clear, and contains numerous hyaline casts, while in tuberculous urine tube casts are almost always absent; if they do exist, they are few in number. These characters of the urine, with the pain and renal tumor, afford a means of diagnosis.

The ureter is generally affected with the same tuberculous lesions as is the mucous membrane of the pelvis, but instead of being dilated, its lumen is frequently contracted, permitting the urine to pass only with great difficulty; it may be completely obstructed.

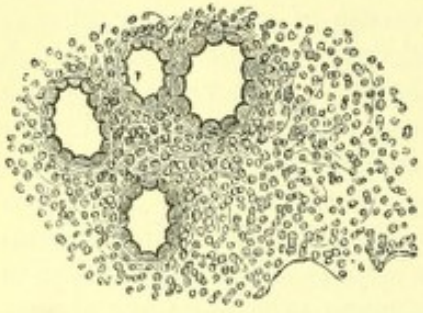
In the further stages of renal tuberculosis most of the lesions of chronic purulent pyelo-nephritis are observed: calcareous incrustations at some parts of the mucous membrane of the pelvis, abscesses of the kidney which have a tendency to become caseous, a tumor varying in size due to the distension of the pelvis, perforations opening into the peritoneal cavity and intestine in consequence of tuberculous ulcerations of the mucous membrane.

In man, renal tuberculosis is very often extended to all the excretory ducts of the urine: the ureter, the bladder, and the mucous membrane of the urethra. The granulations are seated in the connective tissue of these mucous membranes, under the epithelium, and deeper in the submucous tissue. It is accompanied with a purulent catarrh. The prostate, the seminal vesicles, the vas deferens, and the testicles are also sometimes rapidly invaded by tuberculosis. A special variety of tuberculosis limited to the genito-urinary organs may therefore be recognized. In the female renal tuberculosis is much more rare; it may also be complicated with granulations of the bladder and tuberculosis of the Fallopian tubes and uterus.

Finally, the patients usually die from a general tuberculosis in the lungs and intestines.

Gummata.—Gummata of the kidney very seldom occur. The kidney of syphilitic patients may, however, be affected with albuminous nephritis and amyloid degeneration. We have reported a marked example of gummata of the kidney occurring in connection with amyloid change of this organ and with gummata of the liver. The gummata of the kidney were numerous, twenty in number, isolated or grouped, varying in size from a hemp seed to a small pea, very characteristic to the unaided eye, by their fibrous density, by their caseous degeneration and by hardness. They were all located in the cortical substance. Examined with low power, they were transparent at the periphery and opaque and caseous in the centre. The new formation consisted of embryonic

Fig. 325.



The peripheral portion of a gummatous growth in the kidney, showing the small-celled granulation tissue in the intertubular tissue. × 200.

connective tissue developed from the pre-existing fibrous partitions of the kidney. The glomeruli were very easily recognized both in the peripheral fibrous tissue, and in the central caseous zone of the tumor. In the peripheral zone the new embryonic connective tissue surrounded the still visible but atrophied uriniferous tubules. The tissue of the gummata did not differ from that of similar formations seen in the liver of the same case.

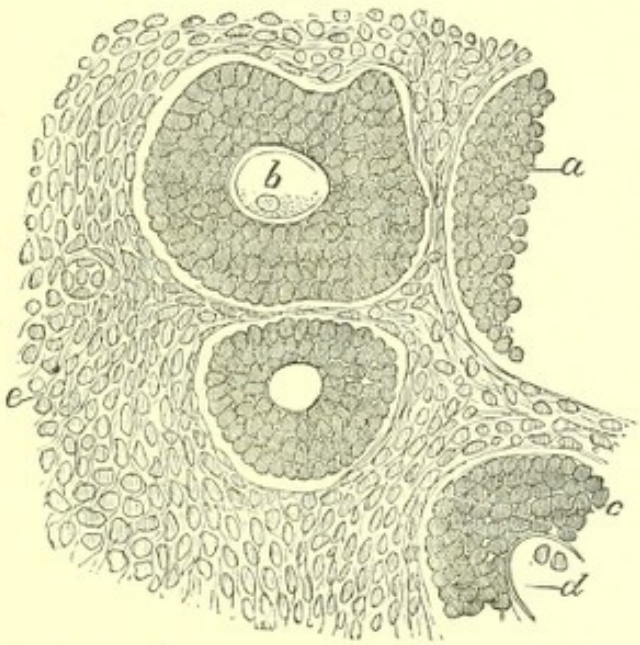
Lymphadenoma.—The kidneys may be the seat of secondary formations consisting of adenoid tissue. These small tumors do not differ from those seen in other organs, especially in the liver. They are developed in the connective tissue. Independent of these tumors there exist cases where an accumulation of white blood corpuscles is seen in the vessels of the glomeruli, in the capsule of the glomeruli, in the capillaries of the intertubular connective tissue, and between the fibres of the latter. In a word, there is an accumulation of lymph cells in all the small arterioles of the glomeruli, also in all the capillary vessels of the kidney, and a diffused infiltration of these same elements into the cellular framework of the organ. At the same time, the epithelial cells of the tubules undergo a granular fatty degeneration; the lumen of the tubules sometimes contains collections of lymph cells, or hyaline casts.

Sarcoma.—We know of only two cases of sarcoma of the kidney. These cases were tumors of considerable size, occurring in young children. The centre of these enormous spherical tumors was softened in one case; there was considerable infiltration of blood into the substance and into the lacunæ of the sarcomatous tissue. The renal capsule which everywhere surrounded the tumor was thickened. The kidney was flattened upon the surface; under the capsule, at some points it showed to the unaided eye and to the microscope the appearance and structure of the cortical substance. The sarcoma was certainly developed in the substance of the pyramids, at the point of union with the cortical substance. The central part was soft and friable, showing all the characters of round celled sarcoma, with vessels having embryonic walls in one of the cases, and fascicular (spindle-cell) sarcoma in the other. In both cases the development of the sarcoma could be followed from the centre to the periphery. In the fascicular sarcoma it had extended into the cortical substance along the course of the arterioles. The circumference of the vessels and the neighboring connective tissue around the uriniferous tubules exhibited a new formation of round or elongated cells, with fusiform nuclei, interposed between the fibres.

In the second tumor, the participation of the cells contained within the uriniferous tubules, in the formation of sarcomatous tissue, could very easily be studied. The elements of the tumor were developed both in the connective tissue and in the interior of the uriniferous tubules. Upon

thin sections made from the peripheral portion where the kidney was not destroyed, uriniferous tubules could be seen in different degrees of alteration, some retaining their normal size, their hyaline membrane, and a single layer of epithelial cells, with a central empty lumen. Alongside of these normal tubules others were seen having a diameter two or three times enlarged, or even more; the hyaline membrane could still be recognized in those not greatly dilated, but it was wanting in the much enlarged tubules. In the first the epithelial cells formed two or three

Fig. 326.



Section across four altered tubules in the midst of sarcomatous tissue. The tubule (*a*) is seen only in part. The three others present an empty lumen (*b*, *d*) and several layers of epithelial cells. The intertubular tissue is seen to consist of closely crowded spindle cells. × 200.

superimposed layers. The layers of newly-formed cells consisted of elements smaller than normal; they had lost the characters of secreting cells of the kidney, having only an oval nucleus, surrounded with a small amount of protoplasm; it was necessary to add acetic acid in order to distinguish the nucleus from the protoplasm. The small cells, arranged in thick layers, were oval or elongated, having their long axis perpendicular to the wall of the tubule. The centre of the tubule showed an open lumen. In other parts, the tubules were only represented by large, irregular spaces, without any trace of a hyaline membrane; these spaces were filled with round nucleated cells, having the diameter and all the characters of embryonic cells.

Both the normal and the enlarged tubules were separated by thick bands of a tissue composed mostly of cells generally oval, seated in a fibrillar tissue parallel and concentric to the border of the tubules, the whole constituting a tissue very characteristic of sarcoma. The peripheral sarcomatous tissue of the small uriniferous tubules was relatively dense and close; but where the tubules were enlarged, and filled with round cells, the surrounding sarcomatous tissue was much more friable. Its cells were round, and its fibrils formed a much looser network.

These two cases very clearly establish the existence of primary sarcoma in children. It is very probable that some of the tumors of the kidney in children, published as cancers, may have been sarcomata.

Carcinoma of the Kidney.—Renal carcinoma may be primary or secondary. The latter is developed in nodules, most frequently located in the cortical substance beneath the capsule, and has the structure of the primary tumor.

Primary carcinoma is of infrequent occurrence. Located generally in one kidney, the tumor may constitute any of the varieties of carcinoma; the most common is encephaloid, especially hematoid carcinoma. Colloid carcinoma is more frequent than scirrhus. The invaded kidney enlarges to a varying extent, and its weight may be four or five times greater than normal. The shape of the organ is generally retained, so that the cortical and medullary portions may be recognized; yet when the entire kidney is not involved, it is mostly in the cortical substance that the lesion appears to have originated. The morbid growth is diffuse and uniform, or it has the form of irregular nodules, separated by the altered, but still recognizable renal parenchyma. The pelvis and calyces are invaded by extension of the tumor. The tissue of the kidney, alongside of the cancerous nodules, is at times the seat of a fibrous thickening and atrophied interstitial nephritis; if compressed by the tumors the glomeruli undergo the same atrophied fibrous transformation as in interstitial nephritis. At other times the epithelial cells of the uriniferous tubules are fatty degenerated, and the bloodvessels are greatly congested. Renal hemorrhages, a frequent symptom of these tumors, occur on account of this extreme congestion of the renal substance, as well as from the carcinomatous new formations upon the surface of the pelvis and calyces. In portions where the tumor invades the normal tissue by extension, Waldeyer has isolated cylinders of epithelial cells growing from the uriniferous tubules, and extending by diverticulæ. Robin had indicated the method of development of epithelioma by a new formation of renal epithelium; but he confounded, under the name of epitheliomata of the kidney, not only carcinomata, but also other lesions of the kidney, particularly Bright's disease. After the investigations of Waldeyer, observations published by Neumann and others, have confirmed the mode of development and extension of the tumor by budding of the epithelial cells of the uriniferous tubules. What we know of the development of tumors in glands, and what we have described relative to the origin of renal sarcoma, incline us to believe that the epithelial cells, as well as the connective tissue, participate in the development and extension of carcinoma.

The structure of the tumor does not differ from the descriptions given of the several varieties of carcinomata. A peculiarity of hæmatoid encephaloid of the kidney is marked by the presence of very numerous, enormously dilated capillary vessels. The renal vein is sometimes the seat of cancerous thrombi, which may extend into the inferior vena cava.

Cysts.—Cysts of the kidney are very frequent, and their varieties are numerous. Colloid cysts occurring in the cortical substance during

advanced interstitial nephritis have already been considered. Cysts of the same nature following the distension and filling up of the capsule of the glomeruli by the same colloid material, may also be met with under the same circumstances, but they are not so frequent as the preceding. Cysts containing fibrin coagulated and laminated upon the interior of the capsule of the glomeruli in kidneys greatly congested are observed, where there has been primarily an escape of blood into the cavity of the glomerulus. In Bright's disease cysts may form by dilatation of the tubules in the medullary substance. The histological characters of these varieties of cysts have been already sufficiently studied, and it only remains to describe congenital and serous cysts.

Congenital cysts are at times so numerous that the kidney is filled with them; their size and that of the organ may be so great as to offer an obstacle to the delivery of the child; they contain a clear fluid, which is urine, prevented during fœtal life from escaping by the excretory ducts. These cysts have their origin in the glomeruli; the capsule of the latter is much dilated, the vascular tuft is atrophied, and flattened against the wall of the cyst.

Serous cysts frequently occur either in perfectly normal kidneys or in the kidneys of old persons, especially in senile atrophy of these organs. They contain a clear fluid, and are small and numerous, or larger and fewer in number. Their mode of origin and development is more difficult to determine than in the preceding variety; they may be surrounded by perfectly normal renal tissue, and in them there is no trace found of the atrophied vascular tuft of the glomeruli as there is in the congenital cysts; they are lined with a layer of flat epithelium. It is probable that they are developed in the connective tissue by the enlargement of a lacunar lymph space of this tissue.

Dilated calyces which penetrate between the pyramids, should not be taken for cysts of the kidney.

Angioma.—There are found in the kidneys small tumors constituted by capillaries, dilated in such a manner that the entire tumor represents an erectile tissue, with cavities filled with blood. These tumors are analogous to similar formations seen in the liver, but never acquire so great a size, and are without any pathological importance.

Parasites.—In Europe, the most important parasites are the echinococci, which, however, seldom occur in the kidney; when found in this organ, they resemble both in structure and details those described under the liver. Sometimes they break into the pelvis. A very few cases have been reported of cysticerci and strongyli existing in the kidney; the latter live in the pelvis.

The distoma is a variety of renal parasite frequently met with in Africa. It exists in the embryonic state in the urinary passages, in the urine, and in the renal vein. It occasions in the kidney pyelo-nephritis, and afterwards, very probably, the hæmaturia endemic in that country.

CHAPTER II.

EXCRETORY URINARY PASSAGES. URETER. BLADDER. URETHRA.

NORMAL HISTOLOGY.—The ureter consists of a peripheral fibrous membrane, of a muscular layer of external transverse and internal longitudinal fibres, and of a mucous membrane. This membrane is thin, and destitute of glands; its epithelium is laminated, the deep cells are small and round, the middle cylindrical or conical, and the superficial polygonal or flat. The bladder has beneath its peritoneal layer of fibrous tissue muscular fasciculi, the most superficial running longitudinal, and the internal having a transverse or circular direction. The former are partly continuous with the urachus. The latter do not form a perfect layer, the fibres interlacing form a network, which causes a slight unevenness of the mucous membrane; and at the neck of the bladder they are continuous with the internal sphincter. At the inferior part of the bladder is the trigone, bounded in front by the urethra, and behind by the openings of the ureters; here the fibrous connective tissue and thick elastic fibres, which exist in the rugæ of the mucous membrane, also have mingled with them many muscular fibres. The mucous membrane of the bladder, pink in color, is composed of epithelial cells, forming several layers, more numerous than in the ureters; the most superficial are flat and laminated, the deeper cylindrical or conical and round. At the neck of the bladder and towards the fundus there are found small, pyriform, simple or aggregated glands, lined by cylindrical epithelium. There are no papillæ upon the mucous membrane of the bladder.

The mucous membrane of the urethra is red and vascular; its epithelium is similar to that of the bladder; it has, both in males and in females, numerous large glands, the *glands of Littre*, about one millimetre in diameter; their oblique ducts are from two to four millimetres long, and are lined with cylindrical cells, which secrete mucus. The submucous connective tissue forms a membrane rich in elastic fibres; this membrane, in the prostatic portion, is intimately united to the prostate, and to the cavernous body in the spongy portion.

PATHOLOGICAL HISTOLOGY.—*Hyperæmia* of the mucous membrane of the bladder is observed in certain poisonings, by cantharides for example; it also exists in all acute and chronic inflammations of the bladder, whatever may be the cause. In old persons, in diseases of the spinal cord, or as a consequence of tumors of the neighboring parts, there are seen ecchymoses in the submucous connective tissue, at the base of the bladder, and especially at the orifice of the neck. This same region of the bladder, is, in some persons, the seat of varicose dilatations of the

veins, which may be the occasion of abundant and repeated hemorrhages. Hæmaturia, however, occurs more frequently from fungous or papillary tumors.

Catarrhal inflammation of the bladder, caused either by cantharides, or by an extension of urethral catarrh, by atony of the bladder, by stricture of the urethra, by swelling of the prostate, by affections of the spinal cord, by calculi, etc., may be either acute or chronic; it presents the same histological changes, which have been several times described in connection with catarrhs of the mucous membranes. The presence of numerous lymph cells in the urine gives the latter a milky or turbid appearance, and there is always an abundant muco-purulent deposit in it. In intense inflammation limited to the base of the bladder, there are seen, with the unaided eye, small prominent vesicles, resembling small pearls, which contain a transparent or slightly turbid, or muco-purulent mucus, they are the small glands distended by an abundant mucous secretion. These hypertrophied glands are spherical in shape and from one to two millimetres in diameter; they are located either in the inferior part of the trigone, immediately behind the orifice of the urethra, or in a circle around the neck of the bladder. The mucous membrane surrounding them may be deeply congested. At other times intense inflammation of the bladder causes the formation of prominent papillæ upon its surface. When the catarrh has lasted for some time, the irritated submucous connective tissue becomes denser and thicker, while the muscular fibres of the wall are hypertrophied. The elevations of the transverse folds form crypts into which the mucous membrane sinks. The bladder cannot now be easily or completely emptied; the urine remaining is mingled with pus corpuscles and soon undergoes alkaline decomposition. Bacteria are developed, and urinary calculi are formed.

Intense acute inflammation of the bladder may occasionally terminate by suppuration of the submucous connective tissue; by ulceration of the overlying mucous membrane, this submucous abscess may communicate with the interior of the bladder, which fortunately is a very unfrequent lesion. As a consequence of this process there may result a perforation of the bladder, a peritoneal peri-cystic inflammation, a communication of the bladder with the vagina or with the intestine.

In other cases, the violence of the inflammation, the paralysis of the bladder, the retention of urine which results, may occasion a gangrene of the mucous membrane. The membrane is brown or in patches black; its surface is irregular, and covered with a débris incrusted by the salts of the urine; the bladder contains a brownish fluid consisting of pus, mucus, fragments of breaking down mucous membrane and blood corpuscles. The consequences of this lesion are destruction of a portion of the mucous membrane, infiltration of urine into the neighboring connective tissue, urinary abscesses, local or general peritonitis. Pyelonephritis also is frequently a consequence of severe cystitis.

Chronic cystitis is often accompanied by vesical calculi. The latter come from the kidney, from the pelvis, or they may form in the bladder. They vary in size, are free or are inclosed in one of the crypts formed by the folds of the mucous membrane. The calculi consist of uric acid and urates, of ammonio-magnesium phosphates, or of carbonate

of lime; very seldom they are composed of xanthin. They are attended by a chronic catarrh of the bladder, and a pyelo-nephritis is frequently present in the kidney and pelvis.

Ulcerating cystitis occurs in pyæmia, typhoid fever, low types of eruptive fevers, etc. A limited and superficial portion of the mucous membrane infiltrated by an exudation composed of extravasated lymph cells and fibrin, is softened and destroyed by an ulcer with a grayish base (diphtheritic ulceration of the Germans). Variolous pustules have been noticed both upon the mucous membrane of the bladder and urethra.

Urethritis.—The catarrhal inflammation of the *urethra* consecutive to herpes, to the passing of instruments, or to an infecting coition, is generally acute. In the latter (true blenorrhagia), it may continue several months, and it is accompanied with a series of accidents, the most serious being stricture of the urethra. The blennorrhagia is localized in the anterior region, the fossa navicularis for example, in the bulbous portion, in the prostatic region, or it is general.

The formation of lymph cells, the desquamation of epithelial cells, the presence of blood corpuscles, the vascular congestion, etc., are the same upon the urethral mucous membrane as upon all mucous membranes. When the inflammation is very intense, it extends in a varying extent to the submucous connective tissue, and may spread to the erectile connective tissue of the corpus spongiosum. Sometimes there results an inflammation of the lymphatic vessels of the dorsal region of the penis, when beneath the skin are seen the lines and cords of lymphangitis. When the much inflamed submucous connective tissue is infiltrated with lymph cells, and the tissue of the spongy body is also involved, these parts are not distended by the blood during the erections, which are so frequent and painful in acute blenorrhagia (gonorrhœa). The erection gives rise to an enlargement of the cavernous body and glans, while the mucous membrane of the urethra remains unchanged. There then results what is termed blenorrhagic cordée, in which the cord is formed by the urethra, the arch by the tumefied cavernous body and glans.

A very intense blenorrhagic inflammation of the urethral mucous membrane is at times limited to the glands, and the surrounding connective tissue, causing an abscess either in the fossa navicularis, or in the glands of Cowper. If these abscesses, containing a varying quantity of pus, open through the skin externally, they do not occasion such serious results as when they rupture into the urethra. In the latter case, there occurs an infiltration of urine, which may extend to the connective tissue of the perineum, if a counter-opening through the skin is not early made.

Strictures of the urethra are generally caused by fibrous organization and contraction of a part of the inflamed submucous connective tissue. Chronic blenorrhagia occasions vegetations analogous to granulation tissue, which cause a sinuous or irregular urethral canal, and a chronic catarrhal inflammation at the point of disease. Hard fibrous nodules, creaking under the knife, are sometimes found around the urethra, at the base of the glans or fossa navicularis; they compress the canal and constitute strictures.

Tumors.—*Tuberculosis* of the bladder and urethral mucous membranes is sometimes observed, especially associated with the previously

described tuberculosis of the genito-urinary organs. It presents the same characters as upon other mucous membranes. The tuberculous granulations developed upon the surface of the mucous membrane, and in the connective tissue, occasion a puriform catarrh, with purulent and caseous secretions. The tubercles may be grouped into patches, and united by an embryonic tissue; molecular mortification of the parts which have become caseous gives rise to ulcers varying in size and depth.

Enchondromata have been reported by Ordonez and Landetta in the walls of the bladder. In the case of Landetta, the tumor was due to an extension to the wall of the bladder, of an enchondroma from the bones of the pelvis.

Papillomata (vesical fungus) of the bladder occur frequently, and may be of considerable size. Although the mucous membrane of the bladder does not normally possess papillæ, there is a very great tendency to the new formation of vascular papillæ in every irritative process. The favorite seat of these papillæ which form true tumors of variable size, is around the neck (fundus) of the bladder. At times they form upon the surface of the mucous membrane a single mass, or several disseminated tumors; they are very vascular. When examined under water, long or short hair like fibrils and wavy papillæ, anastomosing or free, are seen floating freely in the fluid. They consist of connective tissue, in small amount, forming a support for the capillary vessels, which traverse the papillæ. The capillaries and small vessels having a thin, embryonic and easily torn wall, terminate in loops at the top of the papillæ. The papillæ are covered with a thick layer of epithelial cells. These same cells, formed in great abundance, fill up the spaces remaining between the divisions and subdivisions of the papillæ of the new formation. The epithelial cells break down into a turbid, muco-purulent fluid which infiltrates the centre of the tumor. Papillomata spring from the submucous connective tissue with which they are directly continuous. This tissue does not present much pathological change, in this respect differing from carcinoma and sarcoma; it is sometimes slightly thickened, and contains more connective tissue and lymph cells. An examination of the base of the tumor and of the connective tissue from which it was developed is necessary in order to diagnose between a papilloma and a carcinoma, for the latter has a tendency to become villous upon the surface of the bladder. These growths occasion a catarrh of the bladder, as well as abundant and persistent hemorrhages produced by the rupture of the capillaries from very slight mechanical causes, such as the effects of micturition, for example.

Instead of having the papillary form with long hair-like filaments, the papillomata may be more compact and dense; they may be seen as single or multiple nodules, consisting of embryonic connective tissue, forming a compact and prominent mass upon the surface of the mucous membrane.

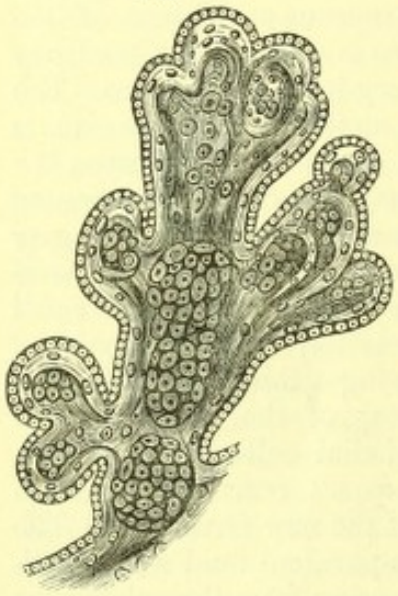
Carcinoma of the bladder is primary or secondary; the latter results from a direct invasion of the layers of connective tissue and muscles of the bladder by a neighboring carcinoma, developed primarily in the uterus, rectum, or in the prostate. The mucous membrane is afterwards invaded, and there are then developed either sessile carcinomatous buds with large and prominent hemispherical base, or dendritic papillary vege-

tations implanted upon a carcinomatous base; these vegetations are somewhat similar to those of papilloma.

In the vesical tumors occurring so frequently by the extension of uterine carcinoma, the mucous membrane of the bladder is much inflamed, especially where it is not the seat of cancerous productions. Its surface is intensely red, in consequence of vascular congestion, and there are frequently seen prominent vesicles formed by the vesical glands filled with transparent mucus or muco-pus.

Primary carcinoma of the bladder is usually encephaloid, very seldom is it scirrhus. The form it assumes is variable. When primary it sometimes infiltrates the entire mucous membrane, or its greater part, especially the fundus and neck. The mucous membrane may have a thickness of one-half to one centimetre; the muscular fibres are hypertrophied and the connective tissue is also thickened. The whitish or pinkish surface of the mucous membrane is ulcerated in patches of varying size, and covered by small villous processes. A section of the diseased portion presents a whitish tissue rich in a milky juice. At other times the mucous membrane may be changed only at one point, particularly in the trigone. Generally carcinoma of the bladder is villous, that is, patches of the degenerated mucous membrane are covered with tufts of elongated vascular villi, covered with epithelium, and traversed by capillaries, which do not differ from the villi found in papillomata. But in carcinoma the basis of mucous membrane upon which the villi are implanted, is formed of carcinomatous tissue, which extends deeply and causes a thickening of the wall of the bladder at the seat of the lesion; the new tissue is almost always white, soft, encephaloid.

Fig. 327.



Carcinomatous papilla of the bladder.

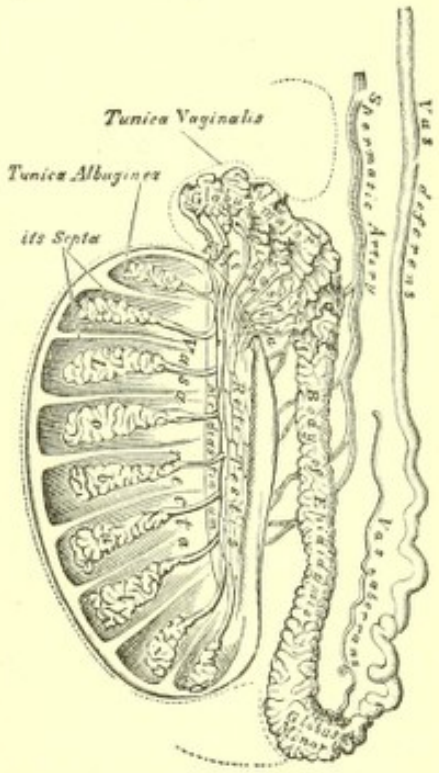
CHAPTER III.

TESTICLES.

Sect. I.—Normal Histology.

The testicles, surrounded by the tunica vaginalis, which constitutes their serous covering, present for consideration a fibrous membrane or tunica albuginea; and a parenchyma which essentially consists of winding canals, termed spermatic tubes which excrete the spermatic fluid which passes into the epididymis; finally, vessels and nerves.

Fig. 328.



Vertical section of testis, showing the arrangement of the ducts. (*Grey.*)

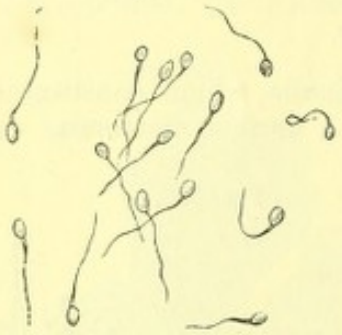
The tunica *vaginalis* consists of two layers: the one parietal, in connection with the scrotum; the other visceral, covering the tunica albuginea and epididymis. It is formed of connective tissue lined with a layer of flat cells.

The visceral layer of the tunica albuginea is a thick, dense, fibrous membrane, which sends fibrous prolongations into the testicle to unite directly with the fibrous trabeculæ of the organ. The most important and thickest of these prolongations is the corpus Highmorianum or mediastinum testis, a thick layer of close connective tissue which exists at the posterior part of the testicle, and through which pass the tubes going to the epididymis.

The parenchyma or glandular substance of the testicles is composed of tubes which divide and subdivide, anastomosing with each other, in such a manner that when a number are collected together they form cones, the small end of which enters the corpus Highmorianum, while the enlarged extremity is placed at the periphery of the gland, where the tubes terminate by a free extremity or loop. At the small end of the cone the tubes become rectilinear, unite together in order to form a network in the corpus Highmorianum (*rete testis*). In this network seven to fifteen *vasa efferentia* are formed, which perforate the tunica albuginea, and pass into the epididymis. These efferent vessels, becoming narrow and tortuous, form another series of cones (coni vasculosi), which constitute the head of the epididymis. They unite into a duct, the canal of the epi-

didymis, which runs tortuously along the posterior border of the testicle, and after being reflected from below upward becomes continuous with the vas deferens. The *seminiferous tubes* consist of a thick, dense, fibrous membrane, composed of laminæ of fibrous tissue, separated by flat connective tissue cells. Upon the internal surface of this membrane there exists a layer of polygonal cells, which may be considered as an epithelium. In the lumen of the tube there are spherical cells, seminal cells, and vesicles, containing one or more nuclei, and which give origin to the spermatozoids. But the spermatozoids seldom become free in the testicle; it is in the vas deferens that the spermatic fluid reaches its maturity.

Fig. 329.



Spermatozoids (high power). (*Gross.*)

The spermatozoids present a swollen portion or head, flat and pyriform, when seen in profile; and a tail which is extremely thin, and which terminates at its free extremity in a filament scarcely appreciable with the highest powers of the microscope. The tail is connected to the head by a middle piece. The movements of spermatozoids are very lively, and they may continue for several days in the genital organs and uterus of female animals. Water arrests their movements; they are accelerated or may be re-established by alkaline solutions, by concentrated solutions of sugar, albumen, urea, etc. Acids, on the contrary, stop their movements. Cold paralyzes them, but after being exposed for three or four days to 0° (C.), they may be revived by heat. The epithelial lining of the efferent vessels of the epididymis consists of cylindrical ciliated cells. These cells become extremely long and narrow; their cilia also are very long in the epididymis, and in the beginning of the vas deferens.

In the efferent canals, in the epididymis and in the vas deferens, thick layers of muscular fibres are seen.

In a portion of the epididymis, generally at its inferior part, there is frequently seen a small, elongated, cylindrical body, with a free extremity, which has been named by Haller the *vasculum aberrans*.

Giraldès has described a small organ situated at the superior border of the testicle, between the body of the epididymis and the vas deferens (organ of Giraldès), which consists of several loosely connected whitish nodules; each of the latter is composed of the convolutions of a tube in the form of a glomerulus. The interior of these tubes is lined with a pavement epithelium; they represent the remains of the Wolffian body.

The arterioles of the testicle come from the spermatic artery which follows the cord; at the head of the epididymis, one of its branches enters the corpus Highmorianum, while other branches pass to the anterior part of the testicle or pass along its surface, and penetrate into the testicle with the fibrous trabeculæ of the tunica albuginea. The veins follow the course of the arteries. The nerves, not numerous, come from the spermatic plexus, and reach the testicle with the arteries. Their termination is not known. The lymphatics, in which the subvaginal network is very abundant, penetrate, according to the investigations of Ludwig and Thoma, into the testicle, forming a network of large canals,

which surround the seminal canaliculi. They are lined with an endothelium. The *vas deferens*, a cylindrical rectilinear tube with thick walls, a continuation of the tail of the epididymis, is composed of an external or fibrous membrane, of layers of smooth muscular fibres, and of a mucous membrane. The muscular fasciculi form several layers, a middle layer of circular fibres, between an internal and an external longitudinal layer. The mucous membrane presents a number of longitudinal folds. The connective tissue of the mucous membrane has in its external part a network of numerous elastic fibres. The epithelial lining consists of a single layer of pavement cells, containing some pigment granules, which give a yellow color to the surface of the mucous membrane.

The *seminal vesicles* are nothing else than appendages of the vas deferens, which terminate in a blind extremity. They are constructed upon the same general type. They consist of a fibrous membrane, containing smooth muscular fibres, which penetrate between the different convolutions of the mucous membrane, and unite them. This membrane is thinner than the thick envelope of the vas deferens. The ampullæ and depressions which form the mucous membrane of the seminal vesicles contain a transparent, viscid fluid, in which exist the spermatozoids. The mucous membrane secretes a special fluid which enters into the composition of the spermatic fluid. In old persons there are found in these organs colloid concretions formed of an albuminous substance.

The *ejaculatory ducts* have thin muscular walls, which are thinner in the prostate. Their mucous membrane is wrinkled like that of the vas deferens.

In old age, or from the effects of disease, such as advanced tuberculosis, diseases of the spinal cord, with marked emaciation, etc., the spermatic canaliculi become atrophied, and then contain in their interior fatty degenerated cells. A section of the testicle now presents a yellowish-gray color and an opacity due to the presence of fat, instead of the usual pinkish-gray appearance. Yet Duplay has seen living spermatozoids in the spermatic fluid of old men, eighty years and older. Atrophy of the spermatic tubes, and the fatty degeneration with atrophy of their cells, are constant occurrences in the majority of lesions of the testicle in which the tubes are compressed, as occurs in chronic orchitis, where there is a formation of new connective tissue, and in tumors which press upon the parenchyma of the testicle. Similar degenerations are seen when the spermatic vessels, especially the epididymis or the vas deferens, are compressed in such a manner that the excretion of spermatic fluid is interfered with by an impediment to its ejection.

Sect. II.—Pathological Histology.

Inflammation. Acute Orchitis.—An opportunity to anatomically study the acute orchitis which follows blennorrhagia or traumatisms seldom occurs. It is probable that the testicle presents an œdematous infiltration of its connective tissue, followed by all the consequences of this condition: that is, irritation of the cells of the connective tissue and inflammation of its lymph passages. The prominent lesion, and that which

can be seen during life, is the epididymitis and acute inflammation of the tunica vaginalis which constantly accompany orchitis. When there occurs a blennorrhagic orchitis, the inflammation extends by the vas deferens and epididymis, and readily reaches the tunica vaginalis. The epididymis is first affected; it enlarges and fluid escapes into the tunica vaginalis. This tunica presents all the characteristics of inflammation of a serous membrane, that is, an escape of fluid with fibrin, lymph cells, red blood corpuscles, and a proliferation of its endothelial cells.

Simple orchitis often disappears without leaving any traces; but, indurations of the cellular tissue which surrounds the head or other parts of the epididymis not unfrequently remain. These indurations, formed of hard and contracting cicatricial tissue, compress the excretory duct; there results a narrowing or an entire obliteration of the duct, and consequently a suppression of the function and an atrophy of one of the testicles. A similar lesion may be produced simultaneously in the other organ, when impotency must necessarily occur. Secondary to inflammation of the tunica vaginalis, there are found fibrous vegetations upon its surface, in the shape of villi or granulations, which may be well marked. These will be considered under hydrocele.

Suppurative inflammation of the parenchyma of the testicle seldom occurs. It is, however, observed in traumatisms, being either local or general. Pus is formed in the cellular tissue, probably in the lymphatics of the gland. Sometimes suppurative inflammations of the lymphatics or veins of the cord occur.

Chronic Orchitis.—There are several varieties of chronic inflammation of the testicle. It may invade at the same time both the testicle and epididymis, which are increased in size. According to the description of Fœrster, the lesion consists of an enlargement of the seminiferous canals by the cells forming in greater abundance than in the normal state, and by an infiltration of all the cellular tissue with an inflammatory exudation. The fibrous trabeculæ are thickened; the testicle and epididymis are indurated and bossellated. Upon the cut surface the thickened fibrous trabeculæ are visible, and between them a yellow homogeneous caseous mass (*caseous orchitis*) is seen, in which traces of the seminiferous tubes are only occasionally found. This lesion has some resemblance to tuberculosis, with which it is frequently confounded. According to Virchow, it has no connection with tuberculosis, but follows a traumatic inflammation or an extension of a catarrhal inflammation of the urinary passages.

Another variety of chronic orchitis consists in a chronic inflammation of the interstitial tissue of the testicle. The size of the organ is sometimes increased, sometimes normal or even diminished. Seldom is an atrophy of the substance of the testicle observed. Sometimes this chronic inflammation is accompanied with a suppuration which occasions the formation of one or more abscesses. The abscesses may remain stationary and be surrounded with a fibrous or calcified encysting membrane; or they may extend and open spontaneously.

By a solution of continuity, a hernia of the testicle may occur externally as a spongy, vascular, and granulating mass, in which the altered

seminiferous tubes are found surrounded by granulation tissue. The granulations consist of embryonic tissue. The lesion is termed *benign fungus of the testicle*. The mass gradually diminishes through suppuration, and recovery takes place by the formation of a cicatrix.

The surface and connective tissue of the epididymis, as well as the serous membrane of the testicle, may be the seat of chronic inflammation with an abundant formation of embryonic tissue; the latter may proliferate and form elevations like the granulations of fungus of the testicle.

The granulations of embryonic tissue formed upon the tunica vaginalis after gangrene of the scrotum should not be confounded with benign fungus.

Benign fungus, that is, hernia of the inflamed substance of the testicle, in which the connective tissue of the testicle is changed into granulation tissue, occurs under various circumstances: in acute purulent inflammation when an abscess has been opened; in tuberculous orchitis, and at times in syphilitic orchitis.

Syphilitic chronic orchitis consists in a new formation of fibrous tissue between the seminiferous tubes. The tubes are separated from one another by embryonic or fibrous tissue, and are atrophied by pressure. In some cases they are almost reduced to their enveloping membrane, and have in their interior only a few atrophied granular fatty cells. This lesion may affect either the entire testicle or only a few lobules. A thickening of the tunica albuginea and tunica vaginalis is also observed. The tunica vaginalis may present either vegetations or adhesions. This variety of orchitis usually coexists with syphilitic gummata, but may occur without them.

Hydrocele. *Hydrocele of the Tunica Vaginalis.*—Although hydrocele of the tunica vaginalis has been placed among the dropsies, it should be considered as a chronic inflammation. The lesion seldom occurs in general dropsy, and the fluid in the tunica vaginalis contains a considerable quantity of fibrin, as occurs in all inflammatory exudations; frequently there are formed fibrous productions, new membranes, and excrescences upon the internal surface of the serous membrane. This disease is characterized by a serous or fibrinous exudation into the tunica vaginalis, resulting either from an acute or a chronic inflammation of the whole serous membrane or from a varicocele. The amount of fluid varies; it is generally clear; at times colored yellow by a few blood corpuscles; there may be present crystals of cholesterin, swollen endothelial cells, and enough lymph cells to give it a turbid appearance. In some cases of hydrocele there exists a cyst of the epididymis, which may rupture into the tunica vaginalis; in the latter case, spermatozoids are then found in the fluid of the hydrocele.

The internal surface of the tunica vaginalis in recent cases is smooth, but the connective tissue of the membrane is always thickened. In chronic hydroceles there are always found very evident signs of chronic inflammation; there are superimposed, upon the surface of the tunica vaginalis, either the parietal or the visceral, layers of new vascular membranes. These formations usually consist of a dense, hard connective

tissue, similar to that covering the surface of the spleen in chronic perisplenitis. These dense fibrous formations also, as upon the surface of the spleen, form elevated patches with a cartilaginous appearance, or flat, sometimes elevated nodules, or even villous projections; they consist of parallel layers of laminated connective tissue separated by flat cells. Ecchymoses are frequently seen beneath them, between the normal connective tissue and the new fibrous formation. Vegetations and round elevations, having the shape, semi-transparency, and density of small pearls, may become free in the serous cavity, in the same manner as such foreign bodies are formed in the articulations. These bodies in the cavity of the tunica vaginalis are formed of concentric layers of laminated connective tissue separated by flat cells. These different varieties of new formations may be infiltrated with calcareous salts. The testicle surrounded by such a thickened and contracted tunica vaginalis atrophies.

Hydrocele of the tunica vaginalis is frequently complicated either with cysts, or other varieties of hydrocele, or with a scrotal hernia; it may be the origin of a suppurative or intense inflammation of the tunica vaginalis; it may also be complicated with a hæmatocele, that is, an escape of blood into the cavity of the tunica vaginalis.

Congenital Hydrocele.—The peritoneal sac which accompanies the cord and testicle in its descent into the scrotum, instead of being obliterated above the testicle, to form the tunica vaginalis, remains open, and the serous membrane surrounding the testicle communicates during life with the peritoneal cavity. Therefore fluid in the peritoneal cavity may pass into the tunica vaginalis, and fluid in the tunica vaginalis may also pass into the peritoneal cavity. Frequently in these cases there is an inguinal hernia.

Cystic Hydrocele.—It sometimes happens that the peritoneal sac which accompanies the cord is not obliterated throughout its entire extent, but remains open in some part of its course, being closed above and below. If these parts become filled with fluid, there is formed a cystic hydrocele of the cord. Several cysts may thus occur along the cord.

It happens, at times, that an old hernial sac is obliterated, and the prolongation of the peritoneum constituting it, instead of remaining collapsed is filled with fluid. There then results a dropsy of the hernial sac, which should not be confounded with a cystic hydrocele. Cystic hydrocele of the cord, or hydrocele of a hernial sac, frequently complicates simple hydrocele of the tunica vaginalis.

Other cysts which have been for a long time confounded with simple hydrocele, are *spermatic cysts* (spermatic hydrocele), generally located at the superior part of the testicle. These cysts, sometimes very large, are filled with a turbid fluid, containing with the living or altered spermatozoids, epithelial cells similar to those of the normal spermatic canals.

These cysts may open into the cavity of the tunica vaginalis which is frequently at the same time the seat of a hydrocele. In regard to their mode of formation, the hypothesis of a new and independent formation of the cysts has been advocated by Paget. According to the investigations of Gosselin, Luschka, etc., it is more probable that they have their

origin from a dilatation of pre-existing ducts. Their seat is exactly the point where the tubes of testicle and those of the epididymis are separately developed during the embryonic period, although afterwards united; here also are found the useless tubes coming from the Wolffian body which constitute the *organ of Giraldès*.

Independent of all the foregoing varieties of cysts met with in hydroceles, there is often found an œdematous infiltration of the connective tissue of the vasculum aberrans of Haller and organ of Giraldès, or a true cystic dilatation of the canals of the latter.

HÆMATOCELE.—It has been seen that, in chronic hydrocele, the tunica vaginalis is covered by new membranous formations, arranged at times in superimposed thick fibrous layers supplied with vessels whose rupture causes the ecchymoses often found in this formation. From the frictions or contusions, to which these large tumors are exposed, there may occur an escape of blood into the cavity of the tunica vaginalis. The tumor formed by this blood is dense, hard, and non-fluctuating; the cavity of the thickened fibrous tunica vaginalis is filled with a chocolate or brown fluid, a color due to the presence of disintegrating blood corpuscles. Upon the surface of the membrane and in the sac, blood clots and coagulated fibrin are seen. Microscopic examination of the fluid shows fibrin, red blood corpuscles, swollen endothelial cells containing blood pigment, fatty granules, and frequently also crystals of cholesterin. If the escape of blood occurs when there has previously been a large amount of the serous fluid of a hydrocele, there is no coagulation of the fibrin in the fluid of the hæmatocele. The testicle is generally atrophied beneath the thick layers of new membrane. An escape of blood may also occur in a cyst of the cord.

Infiltrations of blood into the connective tissue of the testicle are of unfrequent occurrence. They sometimes, however, give rise to a hæmatocele within the testicle. This rare lesion has not yet been minutely described. With Coyne we have had the opportunity of studying two cases. There was a very old large hæmatocele in the tunica vaginalis. At the central portion of the testicle an old, partly discolored clot was found, about the size of a small apple; the clot was traversed by vessels with thick walls. In the peripheral layers of the clot were found separated seminiferous tubes. The neighboring substance of the testicle presented the lesions of parenchymatous and interstitial orchitis, characterized by an abundant formation of round embryonic elements.

TUMORS OF THE TESTICLE.

ENCHONDROMA.—Enchondroma of the testicle is not very rare; it generally follows traumatisms. The hyaline cartilaginous tissue is easily seen, both with the unaided eye and the microscope, in the form of nodules of variable size, or as a diffused infiltration. It generally occupies the gland, but it may involve the epididymis, either primarily or secondarily. The testicle is increased in size, sometimes it is very large, but in this case the cartilaginous tissue is usually found in the midst of a fibrous or

sarcomatous tissue, while cysts exist in the substance of the gland. Enchondroma does not always consist solely of cartilaginous tissue.

From the observations of Paget and Virchow, it has been ascertained that cartilage may develop in the interior of the lymphatics of the testicle and present the ramifying shape of these passages. In one case, reported by Paget, the tumor extended along the spermatic cord, into the iliac lymph glands, into the lymphatics of the inferior vena cava, into the lumen of which a cartilaginous mass protruded as far as the pulmonary artery; and the lung also presented secondary tumors of the same nature. [Secondary formations are not extremely rare. The most favorite seat of the secondary deposits is the lungs.]

Fibroma. — Except the hard, often calcified fibromata, which are formed upon the surface of the tunica vaginalis, or which originate in a fibrous hypertrophy of the tunica albuginea in hydrocele, fibromata of the testicle are very rarely seen. However, Fœrster reports a case in which a fibrous tumor developing in the tunica albuginea projected into the substance of the testicle.

Sarcoma.—Sarcoma without cystic degeneration is not often met with. It occurs in the testicle or epididymis; the gland is uniformly enlarged, not lobulated; the tunica albuginea is not involved, a small amount is found in the cavity of the tunica vaginalis. Upon section the tissue is soft, fleshy, vascular, homogeneous, and infiltrations of blood are frequently seen. Examined with the microscope, these tumors sometimes approach the myxomata in their fundamental substance, which imbeds large fusiform cells, or small round cells. Fatty degeneration, and blood extravasations at times give a caseous appearance to portions of the tumor. In a case of Lebert there was a reproduction of the neoplasm in the lymphatic glands of the neck and in the pleura.

In another variety of sarcoma, which is frequently combined with enchondroma, the tumor contains cysts varying in size. These are *cystic sarcomata*, which, after remaining localized for a time, at length break through the tunica albuginea, and become generalized, and malignant in type. Cystic sarcomata have been, up to the present, confounded with malignant cysts of the testicles belonging to a group of tumors differing in structure, nature, and prognosis. An anatomical examination of malignant cysts of the testicle demonstrates that they are unlike sarcomata. Malassez concludes from his investigations, that they are a peculiar variety of epithelioma, and he names them myxoid epitheliomata.

In a large cystic sarcoma, a fibrous or sarcomatous tissue, in places spindle celled, in other parts round celled, frequently having small areas of cartilage disseminated through it, is interposed between the seminiferous tubes and cysts. The cysts vary in size from a hemp seed to a hazel-nut, and are filled with a serous or colloid fluid. The tumor is at first limited by the tunica albuginea, and there are found portions of the testicle unchanged. Occasionally the growth begins in the epididymis. From the histological descriptions, particularly that by Fœrster, the cysts appear to originate by an enlargement of the seminiferous tubes: the latter are lined by an epithelium, which becomes detached, filling the

cavity with cells; these cells undergo mucous degeneration, and are transformed into a homogeneous mucoid fluid. Papillary excrescences covered with epithelium grow from the walls of the cysts into their interior. The contents of the cyst, instead of being mucous or serous, sometimes resemble the caseous matter of dermoid cysts. The epithelium of the serous cysts is formed of flat, cylindrical or ciliated cylindrical cells. Associated with the sarcomatous and cartilaginous tissue, there are often found in the stroma, new formations of striated muscular fibres.

In several cases of sarcoma and cystic sarcoma, complicated with enchondroma, Nepveu has followed the process of enlargement of the seminiferous tubes, and has pointed out the presence of small pearly globules (cell nests) situated in the cavities of the enlarged tubes. These globules were formed of corneous epithelial cells.

It seems to us that the neoplasm termed a cystic sarcoma has often been classed with tumors which differ from it in their course and histological structure. It is probable that clinical and anatomical investigations will, in the future, determine a distinction between them.

Malassez has recently published some observations upon this subject, in which the cystic formations, situated in the centre of the testicle, were separated from the parenchyma of the testicle, which was pushed to the periphery in contact with the tunica albuginea. The cysts surrounded by an almost normal connective tissue, which contained a few lymph cells between its fibres, varied in size from a pea to a hazel-nut. Smooth muscular fibres were found in this connective tissue. The internal surface of the cysts, either smooth or presenting villous projections, was lined with cells varying in form; polygonal and flat, cylindrical or ciliated and goblet-shaped. These several varieties of cells were found united into groups in the same cystic cavity. The cells found in the serous or mucous fluid of the cysts resembled those lining the internal surface; many had become spherical and undergone a fatty degeneration. In no part could Malassez discover a change of the normal seminiferous tubes into cysts; moreover, the cysts had no similarity to the seminiferous tubes. Hence he concludes that there is a new formation of epithelium and of cavities filled with mucous epithelium, and he proposes to call the neoplasm a *myxoid epithelioma*.

Tubercles.—Tubercles in the testicle may be the first manifestation of tuberculosis of the genito-urinary organs, previous to a deposit occurring in the lungs. It may begin in the testicle, but more frequently it is the epididymis or vas deferens which is first affected.

The testicle at times presents very small gray miliary granulations, scarcely visible to the unaided eye, which are seated upon the tunica vaginalis and in the connective tissue of the testicle, surrounding the spermatic canaliculi. The miliary granulations, at first gray, become caseous at their centre, and form lobulated groups, the centre upon section appearing like a caseous ulcer. There is no doubt that the development of the granulations commences around the spermatic canaliculi. In examining the canaliculi of the periphery of a nodule, the lamellæ of the fibrous walls of the canaliculi are found separated by an abundant de-

posit of small lymph cells, so that there is considerable thickening of the wall at this point.

It is this accumulation of small cells in the connective tissue of the wall which causes the limited swelling of the granulation. At the same time the lumen of the tube is enlarged at this point, and not diminished, as might be expected, by a formation of granular epithelial cells united to each other by a granular substance. This mode of development of a tuberculous granulation of the testicle, investigated by Malassez, is comparable to the development of a granulation around a vessel of the pia mater (see pp. 116, 379). The wall of the tube is externally in relation with the lymphatics, and in a limited portion of its length is infiltrated with lymph cells, while the corresponding intra-canalicular epithelia accumulate and become caseous. A thin section of a testicle infiltrated by tuberculous granulations in process of development, presents an accumulation of small lymph cells forming a circular zone around a seminiferous tube, the lumen of which is enlarged and filled with caseous epithelial cells. The lumina of the lymphatics and bloodvessels included in the tissue of the granulation, are filled with fibrinous coagulations inclosing in their granular substance, lymph corpuscles and endothelial cells. Around the granulation the connective tissue trabeculæ separating the tubes, also are infiltrated with cells.

In a section of a larger granulation there is always seen in its centre a caseous area, which corresponds to the lumen of a canaliculus filled with cells; only the centre of the granulation is caseous, while in the peripheral zone of proliferation the seminiferous tubes are atrophied by pressure, and narrower than in the normal state.

In a recent work on tuberculosis of the testicle by Tizzoni and Gaule, they conclude that the affection begins by a new formation of the epithelium of the tubes. They describe fibrinous coagulations uniting the cells of the lymphatic vessels, and the collections of caseous epithelial cells of the tubes in the granulation as giant cells; this error of interpretation we have several times previously explained.

When tubercles of the testicle become still larger, they are united into groups, the centre becoming caseous and softened. The softening and suppuration in the centre always correspond, at the beginning, to the lumen of an enlarged seminiferous tube; but when the cavity extends by ulceration, all the tissues, without distinction, become caseous in the central part of the nodules, and undergo a molecular destruction. There are frequently seen upon section several caseous centres united in a common destruction, so that the cavity is surrounded by several granulations.

Tubercles are frequently localized primarily in the epididymis, rete testis, or vas deferens. In the vas deferens and in the epididymis, tubercles are seen generally as multiple nodules arranged along the tube. The large nodules, which are two or three times the diameter of the canal, and oval or spherical in shape, consist in an infiltration of the wall of the tube by small lymph cells, while at the same time the epithelial lining of the mucous membrane proliferates, and numerous granular cells fill the dilated lumen of the canal. The same lesions occur in these large ducts as in the seminiferous tubes of the testicle. The yel-

lowish caseous contents of the duct at the point of disease are softened, and a destructive suppuration, with caseous ulceration of the wall, takes place at the same time. A portion of the wall may be destroyed, and a chronic inflammatory process occurring in the neighboring connective tissue causes adhesions of the diseased parts to the skin. There are seen fistular cutaneous openings of the scrotum, communicating either with the epididymis and cord, or with the testicle; they consist of a fungous, embryonic tissue, generally pale, and discharge a small quantity of grumous pus. Tuberculosis of the epididymis and cord is frequently complicated with tuberculosis of the seminal vesicles, prostate, bladder, or the entire genito-urinary system. The lesion also frequently extends to the neighboring lymphatic glands, and finally to the lungs, which are generally affected secondarily.

Syphilitic Gummata.—Interstitial syphilitic orchitis has been previously described; it remains to study gummata of the testicles, which are always accompanied with an interstitial and peri-orchitis—that is, a fibrinous thickening of the tunica albuginea and vaginalis, frequently ending in intimate union of the two serous surfaces.

According to the description of Virchow, gummata begin by the formation of dense, fibrous, callous fasciculi from the tunica albuginea and surface of the gland, penetrating between the lobules of the testicles as conical fasciculi, or large masses having a spherical or lobulated shape. This fibrous tissue taking the place of the seminiferous tubules, which are completely atrophied at the surface, becomes later the seat of yellow gummatous tumors, located either in the thickened tunica albuginea or in the fibrous tissue developed in the testicle. These yellow gummatous masses are nothing more than the caseous degenerations of the pre-formed fibrous tissue.

Syphilitic gummata are very easily recognized and differentiated from other lesions; they have been described by Curling as chronic orchitis. The hardness of gummata, even when they have become caseous, the great fibrous induration of the substance of the testicle where the seminiferous tubes are atrophied and separated by fibrous tissue, distinctly discriminates this lesion from the tubercles in which the caseous foci are soft, suppurate, and have a tendency to open externally by fistular tracts. Again, the induration of the epididymis is less frequent than that of the testicle; also gummata of the epididymis are more rare. The large tubercles of the epididymis and vas deferens, which are very characteristic, are more common than tubercles of the testicles. Syphilis of the testicle, in consequence of the complete atrophy of the seminiferous tubes by the pressure of the connective tissue, entirely arrests the function of the gland. There is no positive evidence of suppuration or an external opening of gummata of the testicle. This establishes an essential difference between these formations and tubercles.

Lymphadenoma.—We know of but one case of lymphadenoma of the testicle. It was described by Malassez. The tumor of the testicle was formed of a typical reticulated tissue, the meshes of which were filled with lymph cells.

Carcinoma.—Carcinoma is one of the most frequent new neoplasms of the testicles. It is primary; almost never secondary. It occurs only in one testicle; it begins by separate nodules, or by a diffused infiltration, which rapidly extends, and acquires a large size. The tumor generally begins in the testicle, but the epididymis is almost always soon involved. The new tissue begins around the seminiferous tubes in the connective tissue of the gland, which is transformed into a carcinomatous stroma; in the diseased portion the seminiferous tubes are atrophied, and filled by the new formation. In the centre of the tumor, the oldest and most diseased part, there are no traces of the tubes remaining. When the tumor has had its origin from the central part of the testicle, or from the rete testis, or from the corpus Highmorianum, there is always seen at the periphery of the growth opposite to the place of its development, under the tunica albuginea, a gray and opaque, or pink layer, which consists of the seminiferous tubes pushed aside and compressed by the new tissue. These tubes are atrophied, surrounded by new very vascular connective tissue, and they cannot be drawn out. The distended tunica albuginea is intact. Later, however, this tunic is invaded by the tumor, and presents excrescences of the same nature; the epididymis, the cord, the pelvic and retro-peritoneal lymph glands are also involved. From our investigations the seminiferous tubes do not seem to be the point of origin of carcinoma; yet Birch-Hirschfeld has isolated seminiferous tubes, which presented new-formed protuberances, increasing rapidly as they penetrated into the morbid mass. According to this writer, carcinoma of the testicle has its origin in a new formation of epitheloid elements in the interior of the seminiferous tubes. We have not been able to verify this mode of development, and do not believe that carcinoma is developed in the tubes, but in the connective tissue, by the swelling of the connective tissue cells, and the new formation of large cells, which occupy the connective tissue spaces between the fasciculi of the fibres and the lymphatic cavities.

The most frequent variety of carcinoma of the testicle is encephaloid; the surface, upon section, is white, doughy, and, upon pressure, exudes a large quantity of milky juice. To the unaided eye, it is impossible to confound this tumor with a sarcoma, which contains juice only when it is undergoing cadaveric decomposition. Sometimes an encephaloid presents a great development of capillary vessels, and is then termed a hæmatoid-carcinoma; it is then very friable, and the connective tissue small in amount. Histological examination of this variety of carcinoma of the testicle presents very distinctly all the characteristics of such new formations.

Scirrhus of the testicle is extremely rare; several writers deny that it ever occurs. Nepveu has studied and published one case of this variety.

Melanotic carcinoma (or melanotic sarcoma) has been noticed as a secondary tumor of the testicle.

Many cases of tumors published as cancer of the testicles, with insufficient histological details or even without microscopic examination, mention the presence of cysts; others report the coexistence of carcinoma

with cystic sarcoma, and admit that a sarcoma may be transformed into a carcinoma. These are very interesting points, and as yet remain unexplained.

The testicle is sometimes the seat of dermoid cysts and cysts of fœtal origin.

Both striated and non-striated muscular fibres have been found in connection with sarcoma of the testicle.

There are reported some very rare cases of hydatid cysts with echinococci developed in the epididymis and tunica vaginalis.

CHAPTER IV.

PROSTATE.

Sect. I.—Normal Histology.

The prostate is an organ composed mostly of smooth muscular and connective tissue fibres; this tissue is traversed by glands which open at the sides of the veru montanum in the folds of the urethral mucous membrane. At the inferior portion of the prostate, in the depressions of the gland, pass the ejaculatory ducts, which open in the inferior part of the prostatic portion of the urethra. The veru montanum or prominence, shaped like a crest, directed from above downwards in the middle of the prostatic portion of the urethra, presents besides at its middle part a slit-like depression or canal, named the utriculus prostaticus or male uterus.

The glands of the prostate, which open by ten or twelve orifices on each side of the veru montanum, are remarkable for the length of their canals, for the small number and the slenderness of the glandular vesicles constituting them. These vesicles are lined by a layer of cylindrical or polygonal epithelial cells which contain brown pigmentary granules. The excretory ducts are lined with the same variety of epithelium as the urethral mucous membrane. The mucous membrane of the male uterus has an analogous lining of stratified epithelium.

Sect. II.—Pathological Histology.

Inflammation.—Inflammation of the prostate occurs most frequently with blennorrhagic catarrh of the urethra and neck of the bladder, but it may also be spontaneous or traumatic. It is acute and slight or chronic, and is associated with the formation of abscesses. The latter variety is more often seen at autopsies. Patients seldom die of non-purulent prostatitis; therefore, a hypothesis of its nature must be formed. The gland is supposed to be congested and œdematous; it secretes an abundance of mucus with pus corpuscles; and its ducts and glandular acini take an active part in the inflammatory process.

Prostatic abscesses occur most frequently as a result of chronic inflammations of the mucous membrane of the urinary passages; they are either small and numerous or of considerable size. The entire prostate may be transformed into a large sac filled with pus, which becomes thick and caseous if the lesion is of long duration. These abscesses may become surrounded by a dense cystic wall infiltrated with calcareous salts, or they may open into the urethra, which is the most frequent termina-

tion. But an opening may take place into the bladder, the seminal vesicles, the surrounding connective tissue, or into the peritoneal cavity.

Tumors. *Hypertrophy.*—The increase in size of the prostate is a physiological fact occurring in advanced age. The venous vessels of the gland and perineum are dilated; the fibro-muscular tissue becomes thicker and denser; the glandular vesicles are hypertrophied and multiplied; and the prostate is enlarged either uniformly as a whole or in some of its parts—the right, left, or middle lobe.

Prostatic concretions or calculi are also frequently met with in old persons. They are formed in the interior of the glandular acini or ducts. Their size varies from .004 mm. to .005 mm. up to a half millimetre or one millimetre in diameter. The smallest are round or oval, refracting, and colorless; they consist of a hard colloid substance difficult to crush; with tincture of iodine and sulphuric acid they offer the same reaction as do parts affected with amyloid degeneration, and have been described by Virchow as due to amyloid degeneration. The larger calculi are more resisting, yellow, yellowish-brown, or darkish-brown in color, and present concentric layers; oxalate or phosphate of lime may be deposited upon them in laminæ, when they become very large. The glandular acini and ducts dilated by the calculi are filled with a mucous fluid, so that when the prostate is the seat of numerous concretions, which is often the case, the gland is transformed into a series of cavities which give it the appearance of cavernous tissue. These cavities are lined with a cylindrical and polygonal epithelium, several layers thick. The calculi remain in position and do not produce any symptoms, or they are passed through the dilated excretory ducts, and give rise to inflammatory troubles either in the prostatic ducts or in the urethra.

General or partial hypertrophies should be placed among myomata of the prostate, due to the new formation of a very dense, grayish-white or pinkish tissue, consisting of smooth muscular fibres and newly formed connective tissue. The glands of the prostate also increase in size at the same time that the cellulo-muscular tissue is developed, and there is seen a new formation of glandular acini. Such a growth might be considered as a mixed tumor or adeno-myoma.

A *general* hypertrophy of the prostate due to the formation of new fibro-muscular tissue, is not usually uniform, but commonly forms nodules or elevations, which frequently project into the urethral canal and offer an obstacle to micturition and catheterism. The enlargement is not always symmetrical, and there may result a lateral displacement of the urethra in the prostatic portion. The consequence of hypertrophy of the prostate is an increase in the calibre of the prostatic region of the urethra, but it occasions at times great difficulty in the passing of instruments into the bladder, because of the development of nodules projecting into the urethra and often uplifting the neck of the bladder.

Partial hypertrophy is characterized by the nodules which form upon the surface of the prostate, very similar in structure to the preceding, and generally developed around hypertrophied glandular acini.

Tubercles.—Tuberculosis of the prostate often accompanies that of the other genito-urinary organs. The tuberculous granulations developed in the connective tissue, in the proximity of the ducts and glandular acini, are diffused or grouped together, and they do not differ from those found in other organs. Caseous softening, ulceration of the glandular ducts, and central softening give rise to cavernous foci which sometimes, by the medium of fistular passages, open into the bladder and rectum.

Carcinoma.—Carcinoma of the prostate seldom occurs; it may be primary, or secondary to a primary tumor of the rectum. The most frequent variety is encephaloid. The diseased gland projects into the urethra or neck of the bladder, as in simple hypertrophy. The walls of the bladder may be secondarily involved. According to O. Wys, carcinoma begins by a new formation of epithelial cells springing from the epithelium of the glandular tubes, the stroma of the gland remaining almost passive.

CHAPTER V.

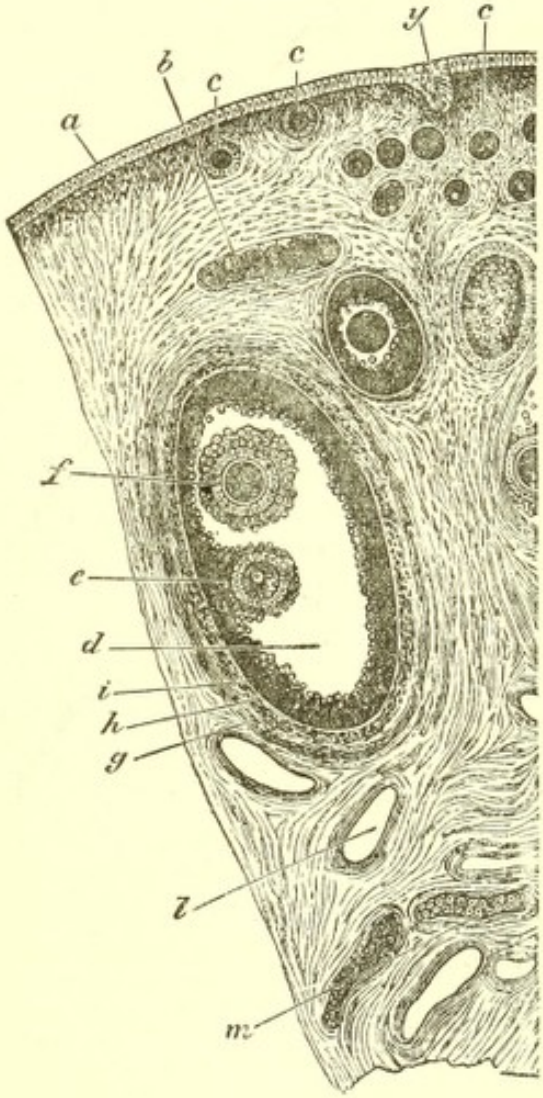
OVARIES.

Sect. I.—Normal Histology.

THE ovary consists of a cortical and medullary substance.

The *cortical substance* is limited externally by a peritoneal covering, which is lined upon its surface with a layer of cylindrical cells and a connective tissue layer belonging to the peritoneum. The latter layer, however, cannot be separated from the tunica albuginea, a dense fibrous membrane, which completely surrounds the organ, and accompanies the vessels entering the hilus. Beneath the tunica albuginea is seen a grayish layer, absent only at the hilus; it contains the ovisacs. The latter are so numerous in children and young women that Sappey estimates them at about a million; they consist of a membrane lined with epithelium, and at the centre of this vesicle, which is spherical in shape, there is found a large cell, which is the ovule. The smallest of the ovisacs contain a single ovule surrounded by a mass of cells which are in immediate contact with it. As the ovisacs approach the cortical substance, they become larger, and in their further evolution they are filled with a fluid, and are visible to the unaided eye, when they receive the name of *Graafian follicles* or vesicles.

Fig. 330.

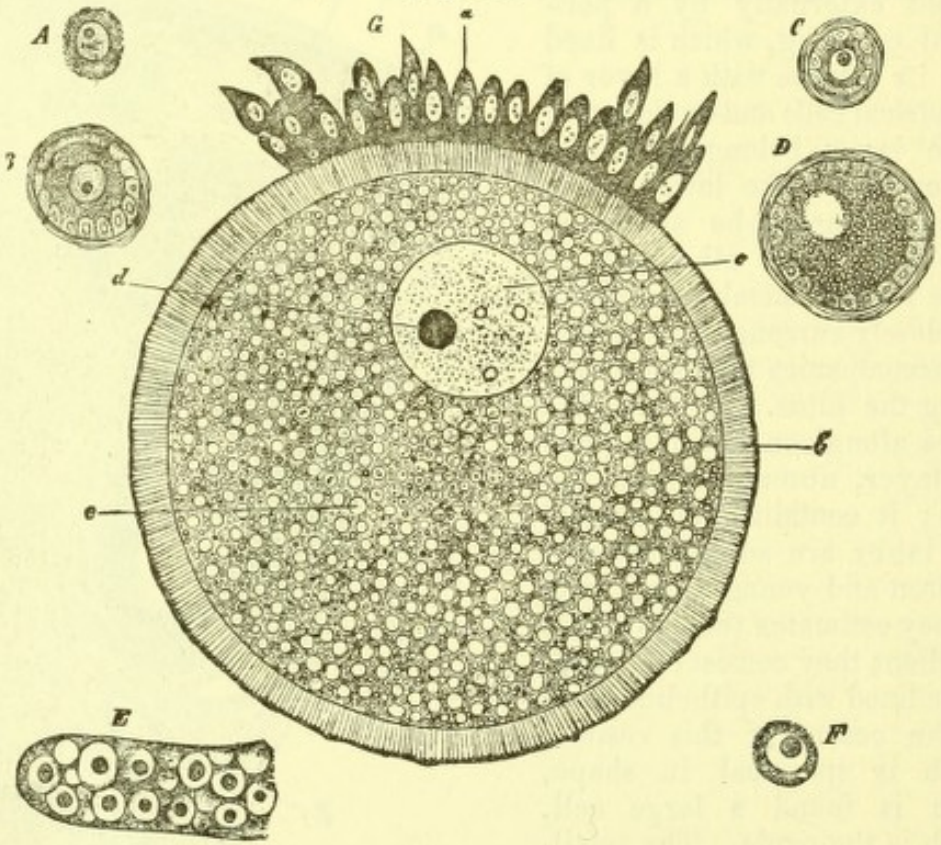


From an ovarium of an old bitch. High power. *a*. Germinal epithelium. *b*. Ovarial tubes. *c*. Younger follicles. *d*. Older follicle. *e*. Proligerous disk, with egg. *f*. Epithelium of a second egg in the same follicle. *g*. Tunica fibrosa folliculi. *h*. Tunica propria folliculi. *i*. Epithelium of the follicle (membrana granulosa). *l*. Vessels. *m*. Cell tubes of the parovarium in long section. *y*. Tubiform depression of the germinal epithelium into the ovarian tissue. (*Stricker*.)

The Graafian follicles are always found in great numbers in children, young girls and women; they consist of an internal tunic and an epithelial lining. At a point of the epithelial lining, the cells forming it are collected together in a larger mass (*the proligerous disk*), enveloping an ovule which has acquired its complete development.

The wall of the follicle consists of two layers of loose connective tissue: the first (*fibrous membrane*) contains the ramifications of arterioles and veinules; the second, more internal (*internal membrane*) supports the capillary bloodvessels. The two layers composed of reticulated connective tissue possess numerous connective-tissue cells. Within this is seen a membrane consisting of a single layer of large endothelial cells (Slavjanski). This membrane is lined with a layer of pavement epithelial cells (granular membrane). The pavement cells are small, measuring

Fig. 331.



A. Primordial egg (human) from a fœtus at the eighth month. *B*. Primordial follicle from a rabbit; *C*, from a pigeon; *D*, a somewhat older one from same. *E*. Cæcal extremity of ovary of ascaris nigrovenosa. *F*. An egg of this animal. *G*. An egg from a follicle of a rabbit, 2 mm. in diameter: *a*, epithelium of the ovum; *b*, radially striated zona pellucida; *c*, germinal vesicle; *d*, germinal spot; *e*, yolk. High power. (*Stricker.*)

only .006 mm. to .012 mm. in diameter, and are provided with nuclei. Where the layer of cells is thickest, that is at the proligerous disk, there is found a completely developed ovule. The ovule is situated in the part of the follicle most removed from the ovarian surface. The rest of the cavity of the follicle is filled with a fluid holding a few cells in suspension.

Upon examination of the ovule after separating it from the cells of the

proligerous disk, it is found to be a very large spherical cell measuring .1 mm. to .2 mm. and can be seen by the unaided eye. It consists of a capsule or vitelline membrane. This membrane is very thick, homogeneous in women, but in some animals traversed by canaliculi. The mass of the cells termed vitellus is a viscid mass containing albuminous and fatty granules. The nucleus of the cell or germinal vesicle (vesicle of Purkinje) is also spherical, from .020 mm. to .048 mm. in diameter, and incloses several nuclei named germinal spots.

Independent of this nucleus there always exists a second nucleus, discovered by Balbiani, and named by him embryogenous vesicle, because before the fecundation of the ovule it is the centre of nutritive changes which take place in the vitellus, and because it remains after fecundation. Balbiani has also seen the germinal spots change their form, and he regards them as contractile vesicles.

When the Graafian follicle has reached a centimetre in diameter, and projects from the surface of the ovary, it ruptures and empties its contents into the Fallopian tube during the tubulo-ovarian congestion which accompanies menstruation. It is, however, an error to believe, that every Graafian follicle ruptures upon the surface of the ovary, for numerous follicles undergo involution and atrophy before the evolution of the menses and after their cessation. It also appears to be demonstrated that ovulation may occur without menstruation, under the influence of an ovarian congestion occasioned by a grave type of fever (typhoid fever, variola). Again, it has been proved that fecundation and gestation have occurred in some cases after the menopause and without any return of menstruation. But notwithstanding these facts, which are exceptions, it is determined that, as a general rule, menstruation corresponds with the passing of an ovule by the Fallopian tube into the uterus.

The ovisacs, or primordial follicles containing the ovule, come from distinct glandular tubes which exist in the ovary of the embryo. According to Pflüger, they are formed by an envelope lined with a layer of small epithelial cells, which represents the granular membrane of the Graafian follicle, and inclose at their centre a series of rudimentary ovules. By the growth of these ovules and their surrounding connective tissue, the tubes are partitioned by the connective tissue, and divided into separate very small segments. Each segment now contains an ovule surrounded by a zone of epithelial cells, and constitutes an ovisac.

When the Graafian follicle has emptied its contents into the oviduct, it undergoes a series of changes, being transformed into what is known as the *corpus luteum*. These bodies differ according to whether the follicle corresponds to a fecundated egg or to a simple menstruation. The first or the corpus luteum of gestation is large in size, and very slowly undergoes modifications. It appears as a prominent point upon the surface of the ovary, where is seen the cicatrix which follows the rupture of the follicle. Upon section there is seen an oblong or spherical cavity, which acquires its greatest size two or three months after fecundation, and is filled with coagulated blood or a bloody mucous fluid. This cavity is lined by a wrinkled yellowish or whitish, very vascular thick zone; outside of this limit between the corpus luteum and the stroma of the ovary, there exists a whitish and very thin fibrous mem-

brane. The yellowish and wrinkled inner zone comes from a thickening of the internal layer of the fibrous membrane of the Graafian follicle. The thickening, in which the epithelium does not appear to participate, is due to an immense number of cells resulting from the proliferation of the connective-tissue elements. Among these cells many become very large, containing a large nucleus and a great quantity of fatty granules. It is the latter which have given the folded membrane its yellow color and opacity. The thin fibrous membrane of the corpus luteum represents the fibrous membrane of the follicle. This new formation of embryonic tissue continues during gestation; at the same time the blood is absorbed, as also are the fatty granules of the wrinkled membrane. The corpus luteum diminishes in size, and becomes denser. At the time of delivery it measures about nine millimetres. Later it gradually atrophies, and is transformed into a yellowish-white or dark pigmented fibrous cicatrix, which never entirely disappears. The various colors it presents are due to the transformation of the hæmatin which it contains.

When the corpus luteum comes from a simple menstruation, it is generally small from the beginning; the phenomena occurring in the follicle are the same as above described, but the changes are very rapid, so that the corpus luteum disappears completely in the course of one and a half or two months.

The *medullary substance* of the ovary consists of a dense, fibrous tissue, which is continuous, in the hilus of the ovary, with the ovarian ligament, and sends prolongations as far as the fibrous capsule of the organ. Here are found the largest bloodvessels and lymphatics which enter through the hilus. The arteries, which are spiral, first run in the central connective tissue, afterwards pass to the surface of the ovary, following the fibrous fasciculi of the organ; veins traverse the connective tissue, as also do lymphatic trunks. The external fibrous membrane of the Graafian follicles has a very abundant network of lymphatic vessels.

The connective tissue of the medullary substance contains some fasciculi of smooth muscular fibres.

The nerves come from the ovarian plexus, penetrate into the organ, and follow the course of the arteries. Their termination is not known.

The broad ligament beneath the ovary is traversed by winding and ramifying tubes. These ducts have a membrane and are lined by an epithelium. They are considered as the remains of the Wolffian body, from which the ovary is developed. The winding ducts are named Rosenmüller's organ.

Sect. II.—Pathological Histology of the Ovary.

Hyperæmia; Hemorrhage.—Congestion and hemorrhage of the ovary are monthly physiological occurrences; each menstruation and opening of a Graafian follicle, as has been seen, necessitates a very intense congestion followed by a hemorrhage. Ovarian congestion also always exists during the acute periods of low forms of fevers. (Gubler.)

Congestion of the ovaries is excited by the causes of congestion of the genital organs of the female, by excesses in coition, by gestation, by labor

and its consequences, by metritis, etc. Traces of chronic congestion, caused by impediment to the flow of venous blood in cardiac diseases, are met with, and in the same cases there may exist an induration of the ovary due to the new formation of indurated connective tissue.

From a very intense congestion of the ovary during menstruation or between the menses, there may occur an escape of blood into one or more Graafian follicles. The ovary is then enlarged, and upon section, there are seen, in its indurated parenchyma, several follicles which are filled with coagulated blood. These follicles vary in size from a pea to a cherry; the coagulated blood which distends them is dark brown or black, and undergoes the usual changes. These pathological products are easily distinguished from corpora lutea; in the normal state there is never more than a single follicle which contains blood, and it is that of the last menstruation, the cicatrix is also easily seen which corresponds to it upon the surface of the ovary. Pathological hemorrhage, on the contrary, occurs in two or three follicles of one ovary or in both ovaries, as well in the deep as in the superficial follicles. Follicular hemorrhages sometimes occur with chronic peri-ovarian adhesive peritonitis, or with pathological adhesions of the Fallopian tube which prevent the normal rupturing of the follicles. In such cases there is at the same time a callous thickening of the ovary and retrograde changes of the Graafian follicles, which are sometimes filled with a mucous tissue, or have become dropsical. When the ovary is free from adhesions and when hemorrhage occurs in a superficial follicle, there may result a rupture of its wall and a more or less abundant hemorrhage into the peritoneal cavity.

Inflammation of the Ovary, Ovaritis.—During gestation, the phenomena which occur in the ovary are inflammatory, and constitute, what may be termed, a physiological inflammation. The parenchyma is tumefied, and the circulation more active, owing to which the corpus luteum of gestation is of unusual size; the cells of the connective tissue are large and cloudy; there is also a greater number of migrating lymph cells; the smooth muscular fibres are more swollen and longer, and comparable to the same elements in the wall of the uterus during gestation.

From these nutritive changes the organ is disposed to a more or less intense pathological inflammation after delivery or after an abortion. Thus it is almost exclusively in women recently delivered, that acute inflammations are met with, or they may occur in connection with metritis and peri-ovarian peritonitis. The lesions vary in intensity. In a slight form, the ovary is saturated with fluid, and there is an infiltration into its connective tissue of numerous lymph cells. The fully developed Graafian follicles have in their interior a turbid fluid, sometimes colored by blood, and containing a great number of epithelial and lymph cells, there is in fact a true catarrh of the capsule of the follicle. When the inflammation is more violent, as in pelvic peritonitis following delivery, at the same time that there is found a very intense congestion and new fibrinous membranes upon the surface of the ovary, there is a more abundant formation of lymph cells collected into whitish lines or small abscesses in the stroma of the ovary. At the same time the Graafian

follicles frequently contain a sero-purulent fluid. Finally in severe puerperal metro-peritonitis, the ovary is found in the midst of pus and false membranes; its tissue is much congested and its follicles are always filled with pus.

When ovaritis is accompanied with a peritonitis limited to the true pelvis by fibrinous and connective-tissue adhesions, the ovary may be found in the middle of a circumscribed abscess, the contents of which may be absorbed or open into the rectum, bladder, etc. Later, the ovary forms firm intimate or filamentous adhesions with the neighboring organs, and its function is destroyed.

The formation of the hard and dense fibrous tissue which follows repeated ovarian congestions, and the retrograde evolution of the Graafian follicles, may be considered as results of a chronic interstitial ovaritis. In old women the ovary is almost always hard and callous; its fibrous capsule is thickened and indurated, like the capsule of the spleen; its cortical layer is absent, and the Graafian follicles or corpora lutea of previous pregnancies are seen only as cysts with hard and contracted fibrous walls. These ovaries are small or atrophied.

Tumors.—*Enchondroma* of the ovary has been twice observed by Kiwisch; in one of the cases, the right ovary had acquired the size of the fist, and was transformed into a hyaline and hard cartilaginous mass. Scanzoni has seen one case of an enchondroma in the middle of a fibrous tumor of the ovary.

Tubercles of the ovary are seldom seen; sometimes they occur with tuberculosis of the other genito-urinary organs, especially in children. The seat of the tuberculous granulations is either in the peritoneal covering or in the parenchyma of the ovary, more frequently in the former, the parenchyma being relatively less affected. They present their usual characters.

Gummata are also very rare. Lancereaux cites two examples, without histological details. He considers as syphilitic, a dense fibrous state of the ovary which he has several times observed in women still menstruating.

Lymphadenoma has been seen once by us as a secondary tumor.

Fibro-myomata of the ovary are comparable to those of the uterus, but they occur much less frequently than the latter. They are sometimes seen as small spherical tumors located either upon the surface, or in the substance of the ovary. Sometimes they form large hard tumors, the size of the fist or larger. A very large cystic myoma has been examined by us.

Sarcoma.—Several ovarian sarcomata have been reported; they varied much in size. Villard has reported a round-celled sarcomatous tumor of the ovary, with cysts containing a bloody fluid. In other cases serous cysts have been developed in the sarcomata.

Carcinoma.—Carcinoma of the ovary is either primary or secondary; it may follow a carcinoma of the neck and body of the uterus, of the rectum, or of a more distant organ. The new formation is then generally small and nodular. Yet we have several times seen a diffuse and complete

infiltration of the entire organ by secondary nodules which emanated from a carcinoma of the uterus, and extended to the neighboring organs.

Primary carcinoma, in some cases, attains a very large size, as large as an adult's head or larger; most frequently it belongs to the encephaloid variety. One ovary only is the seat of a large tumor; but the other may be in a less degree diseased. Ovarian medullary carcinoma is a tumor varying in consistence; it is usually firmer than in other organs, because of the fibrous structure of the ovary. By scraping, an abundant milky juice is obtained. The cut surface is white or grayish-white, and opaque. The fibrous capsule of the ovary is generally involved if the carcinoma is not very recent, and there are then found upon the capsule vegetations consisting of carcinomatous tissue. The peritoneum, either in a limited part or throughout its entire extent, very soon participates in the degeneration of the ovary. We have several times seen enormous tumors with cancerous peritonitis in young persons. The structure of encephaloid carcinoma of the ovary does not much differ from that of typical encephaloid; besides the connective-tissue fibres, the trabeculæ limiting the alveolar spaces sometimes contain smooth muscular fibres; the epithelial cells are arranged without order in the cavities of the stroma, or they are placed perpendicular to the wall of the cavities. The vessels are sometimes of large size, constituting a hæmatoid cancer. In carcinoma, as in other tumors of the ovary, cysts are found, which have formed with the tumor, or have preceded its development. Usually, vegetations formed of carcinomatous tissue project into the cavity of these cysts.

Primary carcinoma may be colloid in character; this variety, however, is not so frequent as scirrhus.

Secondary tumors of the ovary offer the same structure as the primary formations. For example, cylindrical or pavement-cell epithelioma of the ovary, occurs secondary to tumors of the same nature developed in the uterus.

Cylindrical-celled epithelioma may, according to the investigations of Rindfleisch and Klebs, be developed primarily in the ovary. In a case reported by the latter, a reproduction in the cutaneous wound followed the extirpation of the tumor. An examination of the cutaneous tumor showed it to consist of gland-like tubes.

Ovarian Cysts.—Of all the new formations and diseases of the ovaries, cysts are the most common, and the most important in view of their development and their results. The ovary and kidney are organs in which these formations have the greatest tendency to be developed. It has already been seen that cysts may form in tumors of the ovary, and it now remains to describe cysts proper, which vary much in their development and nature.

1. *Dropsy of the Graafian Follicles.*—Rokitansky has shown that the Graafian follicles may be so distended by a serous and limpid fluid as to form small cystic cavities, the size of a small bean or hazel-nut. In an ovarian tumor composed of cysts of this size, this author has shown that each one still contained an ovule. The cysts from distension of the follicles are generally small, and the tumor is seldom larger than the fist.

2. *Unilocular Cysts.*—A single ovarian cyst is sometimes seen of very large size, and limited simply by a wall consisting of the peritoneal covering, and of a layer of laminated connective tissue, which is invested internally by an epithelial lining. These tumors are considered as the result of a dropsy and dilatation of a single Graafian follicle; but we have no positive proof of it. On the contrary, they appear to result from the fusion of several cysts into one. This occurs in a peculiar manner, by means of the cystic degeneration of the ovary, of which we have given a description in part first (p. 169). Every variety of cysts may suppurate—that is, they may have in their interior a sero-purulent or purulent fluid, caused either by puncturing or by other traumatisms, or occurring in the course of general septic diseases or uterine inflammations, especially after delivery.

3. *Proliferous Cysts; Gelatinous or Multilocular Cysts; Myxoid Epithelioma.*—These cysts are multilocular, and generally contain a mucous fluid. They are very large, and formed of several cysts contained in a common envelope, or united by a dense and abundant connective tissue. The walls of the cysts are also formed of connective tissue, in which spiral arteries and very large veins course. The layer of connective tissue nearest to the surface is formed of lamellæ, like those of the cornea, separated by layers of flat cells. The inner membrane, which is almost always the seat of papillary or warty vegetations, is lined with a cylindrical epithelium. According to Malassez, the epithelium is implanted upon a membrane formed by an endothelial layer. The cylindrical epithelium very frequently experiences a partial or complete mucous degeneration. Some of the cells become goblet shaped, being reduced to a cup with thin walls, containing a nucleus at the point of implantation, while the cavity of the cell contains and continues to secrete a mucous fluid. Other cells become spherical, and are filled with mucus. These cells may be destroyed, and fall into the cavity of the cyst, thus increasing the amount of mucous fluid. Sometimes ciliated cells have been met with.

After the action of nitrate of silver, there are seen upon the internal surface of these cysts, markings which indicate the open extremities of the goblet cells; after removing these cells by pencilling, the large endothelial cells which are placed beneath are made visible by the silver solution. By this process the endothelium of the capillaries in the wall of the cysts is displayed, and the superficial position of these vessels is rendered very evident.

The contents of the cyst consist of a mucous or gelatinous fluid, which coagulates by the addition of alcohol, swells and is made transparent by water. Striæ are seen concentric with the surface of the cavities. The cells which are found either have no definite order of arrangement, or they are in rows parallel to the striæ of the mucous mass. These rows consist either of goblet cells arranged in layers, as if they had been desquamated, or of epithelial cells, or of branching cells with many prolongations, resembling the cells of mucous tissue, although there may be no formation of mucus in the interior of the tumor. Collections of fatty degenerated cells are also seen.

Chemical analysis of the fluid, according to Méhu, shows a large quan-

tity of albumen, metalbumen, and paralbumen; it is the latter which gives the fluid its gelatinous consistence. Eichwald has found also albuminous peptone, mucin, and mucous peptone. These different substances are products of the filtration of the albumen of the blood, and of the elaboration of the calice-like cells.

The contents of cysts lined with very vascular villi are frequently mixed with blood, which gives them a brown or chocolate color. There may also be present in them numerous lymph cells, or even pus, especially as a result of traumatisms.

The cysts may communicate with each other by a spherical opening which is found opposite to the place where the principal bloodvessels are situated, that is, where the wall was primarily thinner and less vascular. There is no evidence that a single primary cyst divides, forming two or more; while, on the contrary, the appearances of communicating cysts show that two neighboring cysts have opened one into the other, in consequence of a thinning and rupture of the separating partition.

The connective tissue which separates several cysts, usually itself contains smaller cysts, which are in the process of development, and present the same structure as the preceding cysts; as these cysts increase in size they project into the cavity of the principal cysts.

In none of the cysts, even the smallest in course of development, can ovules or proligerous disks be recognized; therefore the hypothesis of a formation of the cysts by the distension of pre-existing Graafian follicles cannot be accepted. Neither is there found any trace of ovisacs or Graafian follicles, the ovary being completely transformed into cysts analogous to those we have described. The entire absence of ovarian follicles serves as an argument for writers who, like Virchow, Waldeyer, etc., explain the genesis of multilocular cysts by changes of the ovarian tubes, which are described by Pflüger in fœtal life. There are some points of analogy of structure, and the comparison is ingenious; but there is no proof that the large or the more recent cysts have their origin from the ovarian tubes of fœtal life.

We have described in part first the structure of vegetations upon the wall of cysts. We admitted the possibility of the development of secondary cysts according to the method indicated by Wilson Fox, that is, by the union of villi, which in uniting form closed cavities. The more recent investigations by Malassez weaken this view of the mode of formation. He has seen secondary cysts form in the villi, appearing at first as a small collection of cells, the most central of which become mucous, and are destroyed in forming a cavity, around which the parietal cells become epithelioid. This mode of formation is comparable to that which has been described by Fœrster. From a later investigation Malassez was led to believe that there occurs in these tumors a new formation, a true epithelial heterotopia, a peculiar epithelioma, and from the fact that the epithelium has the property of forming a mucous secretion, he names it, as in the corresponding cystic disease of the testicle, a *myxoid epithelioma*.

When the cysts are old or during their period of growth, they may, in consequence of peritonitis, be intimately united to the neighboring parts, rendering the operation of ovariotomy very difficult and dangerous.

Generally a single ovary is diseased and forms the large tumor; but the other may present a few small cysts in process of development, so that the larger ovary being removed, the second ovary becomes in its turn the seat of a large cystic tumor. Very old tumors have a fibro-cartilaginous thickening of their walls, which latter are frequently incrusted with calcareous salts, either in the connective tissue forming them, or upon the internal surface of the cyst, or there may be found upon this internal surface a whitish pulp formed of degenerated fatty cells, calcareous granules and crystals of cholesterin.

Tumors of this kind are not generalized. In adopting the name of myxoid-epithelioma, proposed by Malassez, this circumstance should be remembered, as it is different with other varieties of epithelioma. Secondary formations of these cysts in the glands or elsewhere have never been met with.

Dermoid Cysts.—The ovaries are one of most frequent seats for the formation of dermoid cysts of the third variety of Lebert; they are at times very large, as large as an adult's head, and have in their interior hair, teeth, etc. We have nothing to add to the description given in part first. (See p. 166.)

CHAPTER VI.

FALLOPIAN TUBES AND UTERUS.

Sect. I.—Normal Histology.

Oviducts or Fallopian Tubes.—These are the temporary ducts of the ovaries, serving for the passage of the ovule. The fimbriated extremity is applied to the surface of the ovary at the time of the rupture of the Graafian follicle, and it receives the ovule which passes along the tube to the uterus. The ducts consist of a peritoneal covering, which surrounds them, of a layer of fibrous and muscular tissue forming their wall, and a mucous membrane. They present for consideration a fimbriated extremity which is attached to the ovary by a short ligamentous cord, an inferior and narrow part traversed by a canal which passes through the muscular tissue of the uterus at each lateral cornua, and opens into the cavity of the uterus by a very small orifice scarcely large enough to receive a fine bristle.

The lumen of the tube in its free portion is large, and its mucous membrane is longitudinally folded like that of the vas deferens. From its free extremity to its uterine orifice, the mucous membrane of the tube is lined with a ciliated cylindrical epithelium. The movements of the cilia cause a current in a direction from the free extremity towards the uterus, assisting the progress of the ovule, but not that of the spermatozoids. There are no glands in the mucous membrane of the oviducts.

Uterus.—The uterus presents for consideration the body or superior part, and the neck opening into the vagina. It has a cavity passing through it from the fundus to the os, which is narrowed at the union of the body with the cervix. The uterus is covered by a layer of connective tissue and cells belonging to the peritoneum: it possesses a very thick wall consisting of smooth muscular fibres and connective tissue. The muscular fibres are difficult to separate. The superficial layer is composed of fibres running longitudinally and transversely; the first form a thin layer extending over the fundus and the anterior and superior surface of the uterus; the second a thick layer which extends partly into the round ligament, the broad ligament, and the oviduct. The middle layer, which is the thickest, consists of longitudinal, transverse, and oblique fasciculi. The most internal, like the external, is very thin, having intersecting fasciculi which form circles at the orifices of the oviducts. The transverse fibres of the cervix constitute a true sphincter. In the cervix there are also found some very superficial fibres in the folds of the arbor vitæ. The muscular fibres of the uterus and Fallopian tubes are short except during pregnancy; they are separated by a large quantity of dense connective tissue containing oval cells.

The mucous membrane of the uterus is intimately united with the muscular layer, from which it may be distinguished by its lighter color. The deep layer of the mucous membrane is formed of a connective tissue containing connective tissue corpuscles having oval nuclei, and smooth muscular fibres; there are no elastic fibres. The lining epithelium consists of a single layer of ciliated cylindrical cells.

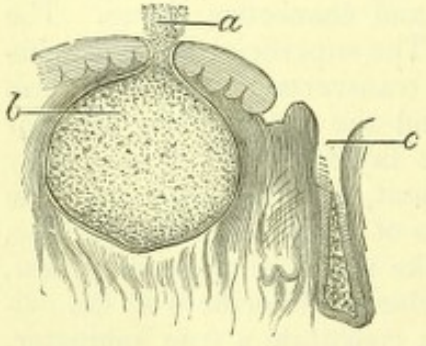
The movement of the cilia is in a direction from without inwards. The glands of the mucous membrane of the cavity are simple or bifurcated tubular glands, analogous to the glands of Lieberkühn. They are lined with a cylindrical epithelium, and open upon the mucous membrane, either singly or two or three together.

The mucous membrane of the cervix of the uterus, instead of being smooth as in the body, presents folds which unite to form the arbor vitæ. These folds, and the entire mucous membrane of the cervix, are covered with villi. Between the folds are seen crypts, which, as well as the cavity of the cervix, contain a viscid and transparent mucus. Upon the surface of the folds are found utricular depressions situated between the villi. In the bottom of the crypts are the openings of acinous glands (Sappey) of considerable size, and comparable from their shape to sebaceous glands. The acini of these glands are lined with elongated cylindrical cells, and they are filled with a viscid mucus.

The superficial epithelium of the cavity of the uterus is a single layer of cylindrical cells. Some writers describe them as ciliated; others deny the existence of cilia. Sinéty has seen goblet-shaped epithelium upon the surface of the mucous membrane of the cervix in a fœtus at term, and examined immediately after death. In this case the epithelium of the cavity of the uterus did not possess cilia. It is probable that the mucus in the cervix of the uterus is secreted by the cylindrical cells of this cavity; just as in the intestinal lining, the cells which secrete mucus always appear as goblet cells, and are especially found in the folds of the mucous membrane, in the crypts, and in the glands. Renaut has found goblet cells in the layer of cells lining the ovula Nabothi.

There are frequently seen in the normal state in young persons, but more often in advanced age, spherical cystic dilatations of the glands in the cervix of the uterus, containing a mucous fluid; they are named eggs of Naboth (ovula Nabothi). The fluid contents of the ovula Nabothi, as also the mucous fluid of the cavity of the cervix, consist of mucin and striæ, which are apt to be taken for fibrils. Cylindrical, oval, and spherical cells in a state of mucous degeneration are found in the fluid, either in rows parallel to the striæ or irregularly arranged. Irregularly shaped cells with ramifying prolongations are also seen, and Renaut believes that he has been able to follow here the development of mucous tissue.

Fig. 332.



Egg of Naboth of the vaginal mucous membrane of the cervix uteri. *b*. Spherical dilation of a gland, the orifice opening at *a*. *c*. Tubular gland. × 20.

The mucous membrane of the cervix completely changes in appearance and structure at the point where it is reflected over the intra-vaginal prominence, forming the os uteri. In this intra-vaginal portion of the cervix, the mucous membrane consists of connective tissue forming papillæ, which lie beneath a laminated pavement epithelium.

A similar arrangement of the mucous membrane and epithelium exists over the entire surface of the vagina. The hard excrescences found upon the surface of the vagina are nothing more than prominent papillary formations covered with laminated epithelium.

The arterial vessels of the uterus run in the muscular substance and form capillary networks, which ramify in the mucous membrane and muscular layers. The veins are without valves, very large, have thin walls, and follow the same course as the arteries. The lymphatics are very numerous; they probably originate in the mucous membrane, and form upon the surface of the uterus beneath the peritoneum a close network which communicates with the pelvic and lumbar glands.

The cellulo-vascular tissue of the broad ligaments contains smooth muscular fibres (Rouget).

During menstruation, the very notable increase in the size of the uterus is due to the considerable afflux of blood into its tissue, and to a swelling of the mucous membrane. This membrane during menstruation experiences great hypertrophy; it becomes softer, and the glands are readily isolated, measuring from two to six millimetres long and .070 mm. to .090 mm. wide; the connective tissue of the mucous membrane is swollen and contains numerous lymph cells. The vessels are dilated and very abundant. At the same time that the menstrual blood is discharged, the epithelium of the cavity of the uterus is almost entirely cast off. Elimination of the glands and of shreds of exfoliated mucous membrane during menstruation are pathological lesions.

We have frequently had an opportunity of examining the products discharged during menstruation, coinciding with symptoms known as *pseudo-membranous dysmenorrhœa*. They vary, at times consisting simply of coagulated fibrinous clots, which are with difficulty passed through the orifice of the os uteri when it is very small, as is frequently the case in females who have never borne children. Microscopic examination shows the fibrin in a fibrillated state, inclosing in its reticulum numerous lymph and epithelial cells.

In other cases there are found irregular shreds containing capillary vessels with embryonic walls, in the midst of connective tissue infiltrated with lymph cells. There are also frequently seen fragments of uterine glands, or entire glands. This is a genuine discharge of exfoliated mucous membrane. The mucous membrane may be expelled entire; this, however, is not a frequent occurrence.

In a third and larger series of cases the products consist of the débris of the decidua, which are recognized by the villi of the chorion. The surface of the discharged membrane presents villi, which are easily demonstrated by placing it in water; the villi are formed of branching cylinders containing vessels in their interior, and covered upon the surface with epithelium. There is also found, if the membrane is discharged entire, a smooth portion or a cavity containing the embryo. We are of

the opinion that these cases of villous dysmenorrhœa are always associated with the products of conception, and with the membranes corresponding to an embryo of two or three weeks, or to the interval which separates two menstrual periods.

The changes which the uterus undergoes during gestation especially affect the smooth muscular fibres, the vessels, and the mucous membrane. The great hypertrophy of the muscular layers is caused by the increase in size of the pre-existing muscular fibres, and by the formation of new fibres; the old fibres become ten times longer and five times wider than normal. The formation of new fibres occurs particularly during the first months of gestation in the internal layers of the muscular coats.

Immediately after conception the mucous membrane thickens, becomes looser and redder, and the folds are more prominent; it is infiltrated with embryonic cells, and its glands are hypertrophied (true decidua). Where the ovum is located, the mucous membrane is transformed into the uterine placenta. The placental portion of the mucous membrane forms granulations which surround the ovum, and constitute the decidua reflexa. The cylindrical epithelium of the mucous membrane of the cavity of the uterus completely disappears upon the decidua. The mucous membrane of the cervix takes no part in this process; it preserves its epithelium, and secretes a mucous plug which fills the cervical canal during pregnancy. The bloodvessels of the uterus undergo a parallel growth with the muscular walls. After delivery the true decidua is completely cast off; the expulsion of the placenta leaves a granulating surface which breaks down, and is also discharged. The internal surface of the uterus no longer contains a trace of mucous membrane, but consists of a soft, pulpy tissue, in which, among embryonic connective tissue, are found hypertrophied muscular fibres, vessels and cells. The latter, which are connective tissue corpuscles, are swollen, flat or spherical, oval or stellate, frequently very large and granular, containing one or more nuclei, and are often in a state of fatty degeneration. The histological phenomena constituting the regeneration of the mucous membrane, have not as yet been sufficiently studied; it is very probable that the regeneration is a slow process, since the wound, which corresponds to the placental insertion, remains visible several months after delivery. Slavjanski has recently described papillary vegetations analogous in structure to granulation tissue, and an infiltration of the superficial layer of the mucous membrane with lymph cells, in a young woman three months after delivery. The surface of the mucous membrane and that of the vegetations was destitute of epithelial cells. The utricular glands, well formed and presenting their normal arrangement, were filled with round cells.

The muscular fibres rapidly return to their ordinary size after having presented numerous fatty granules. It is probable that some of them are destroyed by fatty degeneration.

Sect. II.—Pathological Histology of the Fallopian Tubes and Uterus.

Congestion; Hemorrhage of the Fallopian Tubes.—*Hyperæmia* of the Fallopian tubes, occurring at the same time in the several tissues

which compose them, is observed during menstruation, after excessive coition, and in acute affections of the uterus.

Hemorrhages of the mucous membrane of the Fallopian tubes, and effusions of blood into their lumen, are sometimes a result of hyperæmia, and other morbid conditions. Thus Rokitansky reports two cases of hemorrhage of the Fallopian tubes during the course of typhoid fever; another in a recently delivered woman who died of pleuritis and hepatitis; a fourth, due to retroversion of the uterus. Barlow has seen it in purpura hæmorrhagica; Scanzoni in menstrual congestion; Puech in a young girl with measles, who died of a hemorrhage from the Fallopian tube rupturing into the peritoneum, and causing a fatal general peritonitis. To these may also be added rupture of the tube in extra-uterine tubular pregnancies (see Peri-uterine hæmatocele).

Inflammation of the Fallopian Tube, Catarrhal Salpingitis.—Catarrhal inflammation of the Fallopian tube occurs frequently in consequence of inflammatory and catarrhal affections of the genital passages during inactivity or after delivery. The tubes are filled and distended by turbid mucus or pus; they are tortuous, with irregular dilatations. This lesion is frequently accompanied by a congestion of the ovary, and almost always by an irritation of the neighboring peritoneum, by a true subacute or chronic pelvic peritonitis with adhesions; sometimes by an acute and suppurative peritonitis. The tube now generally adheres to one of the neighboring organs; usually it is the uterus, rather to the inferior part of the body, or cervix than to the fundus. The tumors formed by the hypertrophy and adhesion of the tube are generally recognized by vaginal examination.

In acute inflammation of the tube it is increased in size, its mucous membrane is very much congested and thickened, its longitudinal folds are effaced, the fimbriæ are obliterated, and its lumen is filled with a muco-purulent or opaque fluid. This fluid, examined microscopically, is seen to contain only distorted, granular, cylindrical epithelial cells and lymph corpuscles. The connective tissue of the mucous membrane is infiltrated with lymph cells.

Inflammation of the Fallopian tube is most intense in puerperal metritis; it is always accompanied with phlebitis, lymphangitis, general or local peritonitis, false membranes infiltrated with pus, and purulent effusions.

In chronic inflammation, the adhesions of the tube to neighboring organs is always observed, the connective tissue of the mucous membrane is thickened, the fluid in the canal is either clearer and more serous, or more opaque and more caseous than in the preceding case.

Chronic dropsy of the tube should be considered as a species of inflammation. The tube may become as large as a child's head, and the more or less numerous sacs situated one after the other along the tube, convert the canal into a series of distinct cysts, that portion of the duct between the cysts being obliterated.

The fluid from a dropsy of the tube may be discharged by an opening of the duct into the uterus, from which it passes out by the vagina. This, however, is a very unfrequent termination.

Tumors of the Fallopian Tubes; Tubercules.—Tuberculosis of the genital organs of females is not an unfrequent disease. The tuberculous granulations of the peritoneum, which covers the tube, are accompanied by tuberculous nodules upon the surface of the mucous membrane having their origin in the submucous connective tissue. At the same time there is produced an intense catarrhal inflammation of the mucous membrane. The duct is dilated and filled with pus, which at first is mucous or muco-purulent, but soon becomes caseous. The surface of the mucous membrane also now presents a caseous degeneration of the nodules, with embryonic tissue uniting them. The somewhat thickened layer of embryonic tissue studded with tuberculous granulations which occupies the submucous tissue, is in a condition of caseous degeneration. The tissue of the wall of the tube situated between the tuberculous peritoneum and thickened submucous connective tissue is also infiltrated with lymph cells. Thus results a considerable thickening of the wall which remains rigid after division. The tube so changed is large, nodulated, frequently tortuous, and adherent to the uterus and neighboring organs. Tuberculosis may begin in the tube, and frequently, through a vaginal examination, the time of its onset may be recognized by tumors of the tube and by the pelvic peritonitis which accompanies it.

Carcinoma.—Carcinoma of the Fallopian tube is never primary, it especially follows a primary lesion of the wall of the uterus, when the carcinoma is diffused throughout the internal wall. In carcinoma of the neck of the uterus, the most frequent location, the tube almost always remains intact. In a case of secondary carcinoma of the tube, we found the peritoneal coat much thickened; the fimbriæ, also infiltrated with carcinoma, were open and filled with a milky fluid. There was also peritonitis, from which the patient died It was very evident that the carcinoma of the tube had been in this case the cause of the peritonitis. Generally carcinoma of the tube developed by an extension from the uterus is complicated with a similar lesion of the ovary. Rokitansky has seen cancerous vegetations in the lumen of a tube already dropsical.

Cysts of the Fallopian Tube.—Cysts developed in the wall of the tube are very common, but usually small. Their mode of formation is not yet entirely known. Yet there is one frequently found at the fimbriated extremity, which is regarded as developed in the closed extremity of Müller's duct, the fœtal organ from which the tube is developed. Another cyst is often found by the side of the preceding; it is attached to the broad ligament, representing, according to Virchow, the remains of the primary excretory duct of the Wolffian body. These two cysts become as large as a cherry. Besides these cysts, others are found developed in the tubes of Rosenmüller's organ; finally, there are some which seem to have their origin simply in the subperitoneal tissue of the tube and broad ligament.

Peri-uterine Hæmatocele.—It has been seen that by the rupture of a Graafian follicle there occurs an effusion of blood, but the amount of blood is very small. More abundant hemorrhages take place from the

rupture of large varicose venous vessels of the broad ligaments, by a hemorrhage from the Fallopian tube during a menstrual flux, or by a hemorrhage in consequence of delivery, or from a rupture of the tube in extra-uterine tubular gestations. In the latter the hemorrhage is caused either by a rupture of the varicose tubulo-ovarian veins, by a rupture of the ovary, or by a solution of continuity of the tube, or even by the rupture of a fœtal cyst. If the hemorrhage is very great death is rapid, either by the amount of blood lost in the peritoneal cavity, or by a subacute peritonitis which results. But if the intra-peritoneal effusion is less, and is repeated at several menstrual periods, the blood collects in the lower part of the pelvic peritoneal cavity, and occasions an inflammation of the peritoneum, circumscribed by a false membrane (a blood tumor). This tumor may be felt through the vagina, and constitutes a peri-uterine hæmatocele, which is of much importance clinically. Bernutz believes that the Fallopian tubes have considerable to do with the production of hemorrhage into the peritoneum. According to him, blood coming from the Fallopian tube escapes into the serous cavity whether there may have been a primary hemorrhage in the tube, or from both uterus and tube, or whether there has been retention in the uterus of the catamenial blood during several months, as occurs in cases of imperforate hymen in young girls. It must, however, be remembered that the lumen of the tube, especially where it passes through the uterine wall, permits the passage of fluids from the cavity of the uterus into the tube with difficulty, yet that it may occur has been demonstrated beyond doubt in several observations.

Virchow, on the other hand, has stated, that vascular new membranes, due to primary or secondary inflammation, may form upon the surface of the peritoneum, and that these new membranes may themselves be the origin of blood effusions upon their surface, or in the loose connective tissue constituting them, as occurs in the new membranes of pachymeningitis.

Whatever may be the origin of the hæmatocele, it constitutes a tumor located posteriorly, upon the sides, or all around the uterus, and which may be felt through the vagina. The envelope of the tumor at first consists of fibrinous false membranes, afterwards cellular, which separate the tumor from the peritoneal cavity. It contains coagulated or fluid blood, varying in color according to the age of the effusion and the chemical changes it has experienced. In time, the blood is absorbed and the sac contracts by means of the organization of the connective tissue which surrounds it. During the escape of blood, inflammatory and even purulent foci are sometimes seen, so that peri-uterine abscess and hæmatocele are very similar in their seat, causes, and symptoms, and may complicate one another.

A. Lesions of the Mucous Membrane of the Uterus.

Congestion, Hemorrhage.—Congestion of the uterus due to venous stasis is very common in diseases of the heart and lungs with dyspnœa. The mucous membrane of the cavity of the uterus is bluish-red, and the cavity itself contains a very small quantity of bloody mucus. This lesion

is frequently seen at the autopsies of old persons; it also occurs from pressure upon the uterine venous plexus by tumors, especially fibrous tumors of the uterus and its appendages. Physiological hemorrhages of menstruation are not included here, but we should mention menstrual hemorrhages of the uterus, which cannot be discharged fast enough, or are retained in consequence of a narrowing or obliteration of the orifice of the cervix, or by an imperforate hymen. In these cases the Fallopian tube is also filled with blood, and sometimes the blood escapes into the peritoneal cavity through the tubes (see *Peri-uterine hæmatocele*).

Catarrhal Inflammation (*Internal Metritis*).—Acute catarrhal inflammation of the mucous membrane occurs, either in consequence of a vaginitis, and particularly with blennorrhagic vaginitis, or in consequence of a local eruption in the cervix of the uterus, or it occurs in certain general acute diseases, as typhus, or it is more commonly associated with a number of pathological conditions, scrofula, tuberculosis, syphilis, etc. In many cases, the only cause is chlorosis, or disorders of menstruation, or the remote consequences of parturition. Catarrh of the mucous membrane of the cervix causes the formation of a fluid having the mucous constitution of the secretion of the cervix, but instead of being transparent, is puriform, resembling muco-purulent sputa. Catarrh of the mucous membrane of the cavity of the uterus is characterized by an abundant fluid secretion, more serous than that of the cervix, and of an opaque and puriform appearance. In these lesions, there is an abundant formation and desquamation of the epithelial cells, as well as an escape from the vessels of lymph cells and also of a few red blood corpuscles, contributing to the morphological elements in the catarrhal fluid. A turgescence of the vessels of the mucous membrane, and an infiltration of its tissue with serum and even with lymph cells, accompany the secretion.

Chronic inflammation follows an acute attack, or it is from the first chronic especially in anæmic, tuberculous, or scrofulous persons. The secretion of puriform mucus, with its differences in the cervix and cavity of the uterus, the state of serous infiltration and of vascular congestion of the mucous membrane are the same as in acute inflammation; but there is in addition a series of more profound changes in the mucous membrane, such as the formation of ovula Nabothi in greater number than normal in the cervix, hypertrophy of the papillæ, polypous excrescences of the cervix which are formed of vascular connective tissue, sometimes of mucous tissue, having the elongated shape of the cavity of the cervix, or remaining small and sessile. The former are frequently seen projecting from the os uteri, and may reach several millimetres in length. Among the small polypi, a few contain, scattered throughout their tissue or only at their extremity, eggs of Naboth, produced by the accumulation and retention of a mucous fluid in the glands in the folds of the arbor vitæ.

Small fibro-mucous polypi occur much less frequently in the cavity of the cervix; yet they may be developed here, but are then small and sessile. We have sometimes seen upon the mucous membrane of the cavity of the uterus small ovula Nabothi scattered over its entire surface.

In intense chronic catarrh of the mucous membrane of the cavity, there

is a very decided brownish-red color of this membrane, and upon pressure, there is seen to exude a puriform fluid from the glandular orifices.

Consecutively to these several pathological conditions of the uterine mucous membrane, the mucous membrane of the vaginal portion of the cervix within view is always altered to a varying extent. Thus in catarrh of the cervix or cavity, when the catarrhal fluid flows in abundance from the uterine orifice, it remains in contact with the lips of the os uteri, especially the posterior, and there results at first a superficial erosion, afterwards a true ulceration, which destroys the epithelial covering, particularly in the middle of the posterior lip. In chronic states, there is at this point a growth of the papillæ of the mucous membrane, in the form of small granulations composed of embryonic connective tissue traversed by vessels.

These granulations are pink or red. When repair takes place they are covered with epithelium, and contract, on account of the embryonic tissue becoming fibrous, finally becoming buried under the epithelium. In those cases favorable for the study of their development, it is seen that these granulations have their origin in a proliferative inflammation of the papillæ which normally exist under the laminated epithelium of this portion of the mucous membrane of the cervix.

The mucous membrane of the os uteri may be the seat of numerous eruptions, such as vesicles of herpes similar to those occurring upon the vulva and prepuce, bullæ of pemphigus, eruptions in connection with eruptive fevers, simple or indurated chancre, mucous patches, vegetations developing upon the surface of mucous patches, etc. In secondary syphilis there are almost always found a redness of the cervix and a uterine catarrh, the latter particularly when there are several mucous patches upon the surface of the cervix following erosions.

In chronic catarrh of the cervix, the mucous membrane of the intra-vaginal portion frequently contains eggs of Naboth. The catarrh of the uterus quite often extends, as has been previously mentioned, to the mucous membrane of the Fallopian tubes, and, by extension along the latter, there may occur a subacute pelvic-peritonitis.

An unfrequent result of inflammation of the mucous membrane consists in a narrowing of the internal os and cervix. The puriform or sero-mucous catarrhal fluid then accumulates in the cavity of the uterus and distends it. The mucous membrane atrophies from pressure, and the muscular coat is generally thinned. We have seen this lesion very often in old women, and it is probably the result of a senile atresia of the cervico-uterine orifice.

When the inflammation of the mucous membrane is very violent, there is an infiltration of its mucous membrane with lymph cells and fibrin, in such abundance that superficial mortification or ulceration may be the result; this is observed in typhoid fever and low types of eruptive fevers, but not in every case, it being an unfrequent complication.

These inflammatory lesions involve only the mucous membrane, and do not extend to the fibro-muscular tissue. Yet it is possible, from the severity of a chronic catarrh of the cervix, that it may, by the congestion of the deeper parts of the mucous membrane, by the formation of fibro-mucous polypi, cause also a more intense nutritive activity of that part

of the muscular parenchyma in connection with the mucous membrane. This seems to be one of the causes of hypertrophy of the cervix in women who have not had children, but the abuse of coitus must also be taken into account.

Puerperal Inflammation.—Puerperal endometritis beginning immediately or a few days or several weeks after delivery (post-puerperal metritis) is never simple; it extends to the parenchyma, to the venous sinuses, to the lymphatics, to the peritoneal covering, to the Fallopian tubes, etc.

The uterus, as has been already mentioned, is in all its parts very much altered by parturition, and, by this increase of physiological activity of all its elements, it is predisposed to acute inflammation, which in reality is only an exaggeration of this activity. All parts, then, are liable to participate in the puerperal inflammation. The muscular contractions, traumatisms, manipulations, and operations during delivery, especially the wound resulting from the removing of the placenta, are the principal concurring and exciting causes of the inflammation. The putridity of the contents of the uterus, the phlebitis, the lymphangitis, the condition of the blood which carries infecting zymotic germs, are the causes of the febrile phenomena so rapidly terminating in numerous metastatic abscesses, general peritonitis, and death.

At the autopsies of women dying soon after delivery from metro-peritonitis, the uterus is found relaxed; its walls are flabby and saturated with fluid, while pus or a fibrino-purulent coagulation always fills to a greater or less extent the venous sinuses which traverse them. The mucous surface of the uterus is dark red, and a pulpy softening of the uterine decidua or a puriform sanious fluid saturating the softened mucous membrane is seen. At the point of placental attachment a vegetating surface is found formed by villi of the mucous membrane. At the projecting portion of the villi frequently exist small fibrinous clots. The entire placental disk is soft, pulpy, infiltrated with sanious blood mixed with a puriform fluid, and has a very offensive odor. Frequently this portion of the mucous membrane is gangrenous, dark-brown in color, and is detached in shreds from the membrane by a small stream of water. Sometimes, at the same location, there is a grayish false membrane which separates into lamellæ, and beneath which the tissue of the mucous membrane is red-brown. This diphtheritic or gangrenous false membrane at times extends over the entire uterine mucous membrane.

When the fluid obtained by scraping the surface is examined with the microscope, there are found numerous lymph cells. From the deep layers of the infiltrated mucous membrane we obtain, by scraping, a small quantity of fluid which contains, with lymph cells, large, swollen, and granular fatty cells of the connective tissue. The neck of the uterus is softened, reddish-blue, pulpy; also often covered with the same gray mortified false membrane, beneath which the tissue is greatly congested. The same gangrenous lesion frequently exists in patches upon the vaginal mucous membrane and upon the vulva.

The cavity of the venous sinuses is free, or it contains a puriform fluid, or a coagulated, soft, or pulpy semi-fluid substance, mixed with

lymph cells, and swollen, granular, endothelial cells. The wall of the venous sinuses in the uterine muscular tissue has the appearance of an endo- and peri-phlebitis.

The large veins are frequently filled with pus or fibrin, and the broad ligaments always contain a varying amount of pus, collected into purulent foci, situated in the connective tissue or in the veins.

The superficial lymphatic vessels of the uterus are sometimes filled with pus. The peritoneum which covers the uterus is always the seat of an intense inflammation, with redness, vascularization, and formation of false fibrino-puriform membranes, and with a purulent infiltration of its connective tissue.

The Fallopian tube and the ovary are similarly affected. Finally, a general rapidly fatal peritonitis occurs; metastatic abscesses are formed in the lungs, liver, kidney, etc. In the metritis which occurs some time after delivery, the phenomena do not have the same intensity. The uterus is contracted—at least so far that it does not contain large clots or fragments of placenta; the venous plexuses have had time to contract, and the decidua is in greater part eliminated. All the parts of the uterus and its appendages are less vulnerable. Metritis under these circumstances, however, is always more intense than in the non-gravid organ, and is frequently accompanied with peri-metritis. There results a local peritonitis, circumscribed by false membranes containing a purulent collection, varying in quantity, which is frequently absorbed when the amount is small. Sometimes there occurs a phlegmonous inflammation of the broad ligament or of the cellular tissue of the iliac fossa.

Phagedenic ulcer, characterized by a progressive destruction, with a gangrenous appearance of the cervix, causes a loss of substance, so that the inferior portion of the neck, and even of the body of the uterus, and neighboring portion of the vaginal mucous membrane are destroyed to such an extent as to form a fetid cavity with gangrenous walls, and cause a perforation of the bladder and rectum. This ulcer, we think, should always be referred to carcinomatous tissue or epitheliomatous ulcers of the neck.

Tumors developed in the Mucous Membrane of the Uterus.—*Mucous cysts*, formed by the retention of mucus in the glands, and known as eggs of Naboth, have previously been described; at times they may become as large as a pea or cherry. *Villi*, which may exist upon the internal surface of the mucous membrane of the cavity of the uterus, have also been mentioned; they also occur very frequently as vegetations and *fibrous polypi* upon the surface of the cavity of the neck. These polypi are very vascular, and generally contain in their substance or upon their surface eggs of Naboth, which cause them to be named *mucous polypi*.

Tubercles of the Mucous Membrane of the Uterus.—Tuberculosis of the uterine mucous membrane sometimes occurs in connection with tuberculosis of the other female genital organs. The lesions of the uterine mucous membrane are in everything comparable to those of the mucous membrane of the Fallopian tubes. The surface of the mucous membrane of the neck is the seat of a profuse catarrh, with the production of a

thick, grumous, opaque, and caseous pus; more rarely the cavity of the uterus is affected in a similar manner. The mucous membrane of the cavity presents granulations at first semi-transparent, later becoming yellow and opaque, and uniting in patches varying in size. The sub-epithelial connective tissue is the initial seat of the lesion, but the deep tissue of the mucous membrane is invaded by an abundant formation of embryonic connective tissue and tuberculous granulations. There results a general thickening of the submucous connective tissue. The same lesions may be seen in the neck of the uterus, and at its orifice; but they are always more limited. The gelatinous mucous fluid secreted by the cervix in this disease is loaded with a grumous, opaque, yellowish, semi-solid débris, due to the caseous degeneration of the pus coming from the tuberculous portions of the cavity or neck of the uterus.

Syphilis frequently attacks the cervix in the form of chancre and mucous patches, as also in the form of indurations and deep ulcers of the tertiary period.

Carcinoma.—Primary carcinoma of the neck of the uterus is very frequently met with; the variety is almost always encephaloid. Thus, in thirty-four specimens determined histologically by us in 1863 and 1864, all belonged to this variety. Some pathological anatomists, however, mention isolated cases of scirrhous and colloid carcinoma. But it must be remembered that carcinoma, which at the beginning seems hard, becomes soft, and has the appearance of encephaloid when the tumor extends.

Carcinoma of the neck begins upon one of the lips of the os uteri, which is indurated, hypertrophied, and soon presents upon its surface, especially upon the side of the orifice, and at the free border of the lip, soft and vascular vegetations. The opposite lip, in its turn, becomes hypertrophied; there results a dilatation of the orifice of the neck, permitting the finger to enter; and the whole surface of the cervix is covered with vegetations. The infiltration of all the vaginal portion of the cervix produces a peripheral excrescence of the neck in the shape of a fungus, the end of which projects into the vagina. The subjacent cellular tissue of the vaginal mucous membrane which surrounds the os uteri becomes indurated to form, with the cervix, nodules and granulations.

The carcinoma always appears to have its origin in the submucous connective tissue, so that the mucous membrane of the cavity of the neck and of the vaginal portion remains for some time normal upon the surface of the tumor. Soon, however, this membrane ulcerates, and the cancerous nodules cause the formation, upon the surface of the vagina, of a fetid fluid, which accumulates in the folds, where it is mixed with the vaginal secretion.

The carcinoma extends to the muscular wall of the neck at the same time as to the peripheral connective tissue and to the sub-vaginal tissue. The ulceration, which is accompanied by putrid moist gangrene of all the primarily invaded parts, is followed by a loss of substance limited by a portion of retained carcinomatous tissue. There is now seen a complete interruption of continuity of the vaginal mucous membrane and a transverse section of the inferior portion of the neck. If this ulcerating cavity is examined under water, there floats into view a considerable

quantity of whitish or gray filamentous tufts of gangrenous connective tissue. These are the vessels of the ulcerated part of the tumor, which remain attached to the portion not yet ulcerated. Upon the walls of these vessels, the microscope shows cells implanted perpendicular to their axis. In the gray or slate-colored filaments the cellular elements of the vessels are in a state of fatty degeneration, and their walls are infiltrated with brown or black pigment, due to the metamorphosis of the coloring matter of the blood. In dissecting and separating these vessels at the point where they penetrate the mass of the tumor not yet ulcerated, it is found that they contain in their interior a deposit of fibrin, or a thrombus formed by large cancerous cells. The veins, large in size, very often contain vegetations or similar formations which partly fill them. These thrombi are evidently the cause of the mortification of the new tissue, which is hastened by the putrid decomposition of the fluids accumulated in the vaginal culs-de-sac.

By the new formation continuing to extend to the neighboring parts, the whole wall of the neck and a great part of the wall of the body of the uterus are involved, thickened, infiltrated, and softened, and contain the milky juice of encephaloid. The walls of the bladder and rectum are also invaded; a perforation of one or both of these cavities may result. A fistular opening between the bladder and vagina is always a special cause of rapid putrefaction of the parts invaded by the carcinoma. The surface of the ulcer may sometimes be covered with phosphatic and calcareous deposits from the salts of the urine. At other times the floor of the ulcers of the uterus and vagina is, at the time of death, formed of normal tissues, all that portion infiltrated by the carcinoma having been destroyed by a gangrenous slough. The erosion now has the appearance of a simple phagedenic ulcer, unless there are found villous granulations or nodules saturated with milky juice, projecting from the surface of the perforated bladder or rectum. When the latter organs are not perforated, but have their deep connective tissue infiltrated or only congested, their mucous membrane presents the characteristic signs of a very intense catarrh. The destruction of the uterus may be so great that the fundus and cornua only remain; but the portion of tissue left may be normal, and the Fallopian tubes unaltered.

If instead of beginning only at the neck, the carcinoma begins there, and at the same time infiltrates the whole muscular tissue of the uterus, the ulceration of the cervix does not present the same characters: the uterine tissue, thickened and infiltrated by new formations, measures two, three, or more centimetres, and not unfrequently the Fallopian tube and ovary are also degenerated. The latter organs, on the contrary, escape when carcinoma begins at the neck alone.

In these two varieties of the lesion, when it is chronic, the sub-peritoneal connective tissue of the true pelvis is generally thickened and indurated, and in places very closely adherent to the osseous wall. This hardened fibrous tissue, without any trace of carcinomatous degeneration, is especially thick and hard at the postero-lateral wall, and compresses the sciatic and pelvic nerves. The fibres of the latter are in a state of fatty degeneration. Pain is experienced in the thighs, in almost all cases of uterine carcinoma. Sometimes the cellular tissue is degenerated, as

well as the pelvic and lumbar lymphatic glands. Metastatic deposits are frequently found, especially in the lungs and liver. Invasion of the ureters occasions a retention of urine, and urinous infiltration and anæmia of the kidneys. The cellular tissue of the broad ligament and iliac fossa is frequently the seat of purulent collections, and finally before the death of the patient a general peritonitis may occur. In these cases we have observed a phlebitis and a carcinomatous lymphangitis. Histological examination of the changed uterine tissue shows, as in every carcinoma, a stroma of small alveoli, filled with polymorphous cells, generally arranged without order; sometimes those at the periphery are implanted regularly upon the wall of the alveolus. The stroma, composed of connective tissue, frequently contains also smooth muscular fibres.

Epithelioma.—There are two distinct varieties of primary epithelioma of the mucous membrane of the uterus; the pavement-celled epithelioma, with or without epithelial pearls, and the cylindrical-celled epithelioma. The first variety occurs much more frequently than the second. From what we know of the localization of these tumors in general, they appear to have their origin only in mucous membranes which possess a covering of cells similar to those constituting the new formation. Thus, upon the vaginal portion of the cervix is normally found a covering of laminated pavement cells, while there is a layer of cylindrical cells upon the mucous membrane of the cavity.

These two varieties of epithelioma having their origin in the cervix, cannot be distinguished from carcinoma in the same locality, either by their physical signs during life, by their color, by their course, or by their severity.

At autopsies it is very difficult, and frequently impossible, with the unaided eye, to make an anatomical diagnosis between the varieties of epithelioma or between them and carcinoma. *Cylindrical celled epithelioma* is a tumor generally very soft and infiltrated with juice, resembling a very soft encephaloid; it also has lacunar cavities filled with a milky juice, which are visible to the unaided eye. The alveolar spaces contain cylindrical cells, and their walls have numerous capillary loops projecting into the spaces covered with cylindrical cells. In the three cases which we have seen, and in which histological examinations were made, there was an extension of the tumor to the neighboring parts—to the glands, to the bladder and rectum in one case, to the sciatic and crural nerves in another. In one all the tissue of the uterus was invaded, as were also the lymphatic vessels upon the peritoneal surface. There was no secondary propagation to more distant parts, but a number of well studied cases of generalization have been reported.

Pavement-celled epithelioma, which in about one-half the cases possesses pearly bodies, presents characters by which it may sometimes be recognized with the unaided eye at autopsies. Portions of the tumor are slightly vascular, having the opaque, waxy, and apparently firm appearance, which is in contrast with its friability. Upon section its surface is dry; and by pressure small grumous, vermiform, opaque, white plugs, consisting of collections of pavement epithelial cells, are squeezed out.

Microscopic examination shows a tubular or lobular type of epithelioma with pearly bodies. In the first variety the tubes filled with epithelium

are either very large or very small, and the cells are also small. It is probable that the tubes are developed from the culs-de-sac of the glands of the neck of the uterus, but this is not certain. The tissue separating the tubes consists of the fibro-muscular tissue of the uterus. These epitheliomata are reproduced with their characteristic structure in the glands, in secondary nodules, located in the fibro-muscular tissue of the uterus, or upon its peritoneal surface, and in nodules developed in the layers of the bladder and upon its mucous surface. But metastatic nodules of these epitheliomata, situated in organs distant from the uterus, seldom occur. We have never seen them, but they have been reported by other pathologists, especially Virchow.

Ulceration with its several consequences, especially gangrene of the altered part, is the same in epitheliomata as in carcinomata. In pavement-celled epithelioma, the diseased part of the neck may entirely disappear. The neighboring organs are neither so frequently nor so extensively infiltrated with the new formation as in carcinoma. Epitheliomata are apt to be taken for a simple phagedenic ulcer. The latter should always be carefully examined for traces of epitheliomatous structure, both upon the vaginal surface of the ulceration and in the pelvic and lumbar glands.

The different varieties of carcinoma and epithelioma are usually developed at the time of the menopause or a few years later; yet they have been observed in young women from twenty to thirty years of age. The tumor of the cervix does not prevent fecundation, parturition, or delivery. After delivery the lesion of the uterus progresses with great rapidity.

B. Lesions of the Fibro-muscular Wall.

The fibro-muscular wall of the uterus generally escapes involvement in catarrhal inflammation, and it is markedly affected only in puerperal inflammation. The veins are attacked with inflammation, and abscesses may be developed in their wall.

Lesions of the uterine wall mostly consist in a new formation of smooth muscular and fibrous tissue, which occasions either a general or a local hypertrophy of the wall. A local hypertrophy when sharply limited may be regarded as a myoma. The different forms of diffused fibro-muscular hypertrophy of the wall are included by many writers under the name of parenchymatous metritis, which is certainly not a good term, since they arise generally by a slow process, consisting simply in a new formation of smooth muscular fibres. Virchow considers this growth as a hyperplasia of the uterine fibro-muscular tissue, which is a much better name; and he describes it with the myomata. There are according to this author two varieties: the one soft and resembling the uterine wall shortly after delivery, a condition due to its vascularity and abundance of muscular fibres, and the softness of the connective tissue; the other hard, compact, not very vascular, and containing numerous fasciculi of dense fibres.

These varieties of local hypertrophy often follow delivery, especially when the neck has been torn. The subacute inflammation succeeding such a traumatism, the new formation of connective tissue, and the active

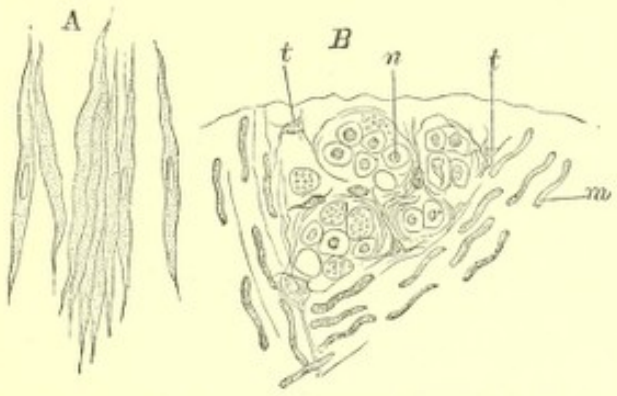
nutrition of the part, all retard or prevent the fatty degeneration, and atrophy of the muscles, and occasion a fibro-muscular hypertrophy of the neck.

Simpson considers the changes of the muscular fibres during and after gestation of great importance in the explanation of general and local hypertrophies and atrophies of the uterus. In the former, the small fibres hypertrophied by the gestation remain so, or, at least, their atrophy or involution is impeded; in the latter the physiological atrophy continues, causing a pathological, general, or local atrophy. This ingenious view may explain a certain number of cases, especially in general or local hypertrophies following delivery. It is also true that pre-existing myomata of the uterus may increase very rapidly after a pregnancy. Uterine myomata, however, are observed in young girls, or in women who have never had sexual connection, or have never borne children. West regards the formation of myomata as a result of activity of the uterus while the organ is deprived of its physiological function, which is gestation; for example, when married women do not have children. Yet local and general hypertrophies of the uterus are also seen in women who have had children. Local hypertrophy of the vaginal portion of the neck is very frequent in multipara. The lips of the neck are large, irregular, and bosselated upon their surface. The hypertrophy may occur upon either lip, giving various shapes to the neck. The mucous membrane of the cavity of the neck is changed; it has lost its cylindrical epithelium and is covered by laminated pavement cells. Generally there are seen, upon the altered lips, ovula Nabothi, or folds, depressions, and small cavities, or sacs with elevated partitions, which give the appearance of a hypertrophied tonsil (Virchow). The mucous membrane of the neck assists in the formation of this hypertrophy by the development of the ovula Nabothi; but hypertrophy of the lips has also been seen, in the shape of elongated fleshy prolongations, projecting even from the orifice of the vagina, and covered by a thin mucous membrane with pavement cells. The vaginal portion of the neck may be generally hypertrophied to such an extent as to cause a prolapsus into the vagina as far as the vulvar orifice. But prolapsus is more frequently caused by a hypertrophy of the entire cervix, the supra-vaginal portion as well as its vaginal part. This mode of hypertrophy of the neck frequently occurs; the cervix is then very long, and projects into the vagina either by an elongated or by a club-shaped extremity. In these cases, the uterus may remain in position, and be of normal size, or its body may be hypertrophied as well as the neck. When, however, the body of the uterus is normal in size, it may be drawn into the prolapsus by the weight of the neck. This hypertrophy of the entire neck has been met with in women who have never carried children. General hypertrophy of the whole uterine wall is not so frequent a lesion as local hypertrophy.

Myomata are the most frequent, almost the only, tumors which have their origin in the muscular wall of the uterus. They consist of fasciculi of smooth muscular fibres, intersecting each other in every direction. A general description of this class of tumors has been given in Part First, which we will not again repeat, as it is equally applicable to the uterine

myomata under consideration. We will give only the peculiarities of their development, seat, and anatomical consequences in the uterus.

Fig. 333.



Muscular cells from a leio-myoma. *A*. Cells separated by the action of nitric acid, 20 per cent. *B*. A hardened section colored with carmine and treated with acetic acid. *m*. Longitudinally cut, *n*, transversely cut nuclei. *t*. Connective-tissue corpuscles. High power.

They begin in the muscular wall. They are generally at first very vascular and soft, later becoming indurated in consequence of the fibrous organization of their connective tissue. Sometimes the intra-parietal tumors are very small, round, and quite hard. At the beginning the fibres of the tumor are directly continuous with the neighboring fibro-muscular fasciculi of the uterine wall. By their development, these tumors project either upon the external surface of the uterus, when they are covered by the peritoneum (subparietal tumors); or upon the internal surface of the uterus, when they are covered by the mucous membrane. Frequently they are pedunculated in such a manner as to be united to the wall, either by a large and vascular or very narrow pedicle. Myomata projecting into the uterus are frequently called fibrous polypi. The subperitoneal tumors, not being impeded in their growth, acquire a very large size. They are usually multiple, even when of considerable size, and very often there are, at the same time with subperitoneal tumors, intra-parietal tumors and polypi projecting into the cavity of the uterus; at times they are so numerous as to cause a change in the shape of the organ. It is also sometimes difficult to find the cavities of the uterus, owing to the cavity of the neck being entirely cut off from that of the body, by intra-parietal myomata projecting at the point of separation of the two cavities. The several degenerations which have been mentioned in Part First, as occurring in myomata, may also occur in this class of uterine tumors, especially the subperitoneal. A carcinomatous metamorphosis of a uterine myoma has been seen by us in a case of carcinoma of the peritoneum. Virchow has also observed carcinoma in a myoma.

Myomata projecting into the cavity of the body of the uterus are either hard and fibrous, or formed of a softer muscular tissue, redder, more vascular, and having large vessels; their ablation gives rise to hemorrhages difficult to arrest. The former of these intra-uterine polypi sometimes occasions considerable and repeated hemorrhages of the mucous

membrane. It is seldom that a polypus of this variety is developed in the wall of the cervix. When a polypus having its origin in the body of the uterus projects into the neck and passes through the lips of the os uteri, its mucous membrane is changed, becomes thicker, and is covered with pavement epithelium. The projecting portion covered by mucous membrane sometimes is red, inflamed, and ulcerated. The mucous membrane is entirely destroyed in spots varying in extent, exposing the muscular tissue. The neighboring mucous membrane forms a sharply cut border to the ulcer; it is red or red-brown, and much inflamed by contact with the irritating fluids of the vagina.

CHAPTER VII.

MAMMARY GLAND.[1]

[NORMAL HISTOLOGY.—The mammary glands are organs common to both sexes, but it is only in the female, and at the end of gestation, that they reach their perfect physiological development. In the male these organs remain—except in very rare instances—as rudimentary structures, never attaining that physiological or histological perfection met with in the female.

The group of glands to which the mammæ belong is the racemose, or it is better to describe each gland as consisting of several racemous glands, since it does not empty itself by a single duct, but there are found opening upon the summit of the nipple fifteen to twenty minute canals or *galactophorous ducts*, which are the outlets of as many racemous glands. This collection of glands or lobules is surrounded by a mass of adipose tissue, and the nipple is the only point where the glandular structure is in immediate connection with the skin. Here and under the areola there is an absence of fatty tissue, and instead of it there is found a layer of smooth muscular fibres.

Following the course of the excretory ducts into the gland from their opening upon the nipple, they are seen to dilate, at a point corresponding to the base of the nipple, into sacculated receptacles known as the *sacculi lactiferi*. Occasionally recurrent branches are given off under the areola, which collect the secretion from the small glandular bodies in this location; these glands, however, may have their own excretory ducts which open within the areola (Glandulæ aberrantes of Montgomery). Below the dilated portions, the excretory ducts again become narrow, divide and subdivide until they ultimately terminate in the vesicles or acini. Separating the lobules we have the stroma of the gland or the peri-lobular and peri-acinous connective tissue. This connective tissue is a continuation of the subcutaneous connective tissue, and like the latter contains in its meshes the adipose tissue of the gland.

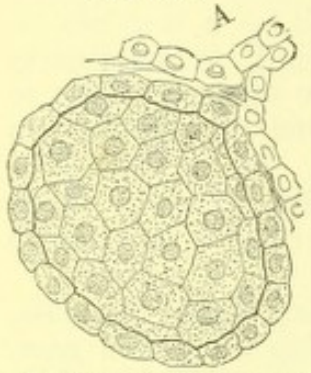
The histological structure of the excretory ducts is distinctly seen in a transverse section. Externally the wall of the duct consists of fibrillar connective tissue, the fibres having a circular direction, and interwoven with this layer are elastic tissue fibres; no proper muscular layer is present, but scattered, smooth, muscular fibres are described as existing in the connective tissue; implanted upon the wall of the duct is seen the lining epithelium, consisting of columnar shaped cells, and separated

[1] On account of the importance of this organ in pathological histology, we have written a more extended description of its histology than that given by Cornil and Ranvier.

from the surrounding connective tissue by one or more layers of endothelial cells.

Passing to the secreting portion of the gland, the glandular vesicles or acini are spherical or pyriform in shape, separated one from the other by the peri-acinous connective tissue, and are surrounded by the membrana propria common to glandular structures. A section across an acinus demonstrates the floor to be lined by a layer of polyhedral epithelial cells, containing a central nucleus, averaging about one-third of the entire breadth of the cell. In a profile view, as may be seen at the periphery of the section, the cells are found to be oblong or cubical, having a height about one-half their breadth. As the cells approach the outlet of the acinus they gradually assume the columnar shape, resembling to a certain extent the cells lining the excretory duct. The cavity of the acinus is filled with fat globules and débris of cells. Examined during lactation the acini are found to contain the elements of milk deposited between and within the epithelial cells. By removing the lining epithelial cells of the acini, there is seen a regular arrangement of delicate fibres, forming polyhedric spaces in which the bases of the epithelial cells were placed. Between the lining epithelium and the membrana propria is a single layer of very thin endothelial cells. Immediately outside of the membrana propria is seen a very delicate clear zone, in which the cells are very few or very indistinct; external to this structure exists a second layer, consisting of a tissue in which the cells are more numerous and arranged concentrically to the acini, having the appearance of a second membrana propria to the acini. The connective tissue nature of this layer is evident from the circumstance that there is observed a gradual intermingling of its tissue with the fibrous trabeculæ, which form the framework of the gland.

Fig. 334.



Fully expanded acinus of mamma, showing mosaic of polyhedric epithelium. ×300. (*Creighton.*)

A varying number of acini are grouped together into lobules. The latter are separated from each other by more or less thick bands of fibrous tissue, usually containing fat.

The blood supplied to the mammary gland comes from the subcutaneous connective tissue vessels, entering at the under surface of the organ; the largest pass upwards towards the nipple, giving off branches to the several lobules and ducts. Both the acini and ducts are found to be surrounded by a capillary system, which is particularly distinct during lactation.

The lymphatic system of the mammary gland is represented by a number of lacunæ or lymphatic spaces. These lacunæ are situated in the peri-acinous connective tissue, separated from the acini by the dense zone of connective tissue previously described; they communicate with lymph spaces and vessels running in the interlobular bands of connective tissue; their shape is irregular, triangular, oval, or elongated, frequently appearing as a separation of the connective tissue fibres, but, upon close examination, they are seen to have an external wall of connective tissue,

a middle layer consisting of very delicate elastic tissue fibres forming a reticulum, and an internal lining of endothelial cells. By means of an interstitial injection with Prussian blue, the form of the lymphatics may be demonstrated. When the section is made in the direction of the principal vessels, the irregular lacunar spaces are seen filled with the injected fluid. Other sections show canals filled with the fluid which present a beaded appearance, the constrictions representing a modified form of valves.[1]

The nipple and areola are peculiar in being erectile and of a darker color than the surrounding skin, and containing in their structure numerous unstriped muscular fibres. The direction of the fibres in the former is chiefly longitudinal, with intersecting bands; a few longitudinal bundles are also seen. In the areola the course of the fibres is mostly circular. Numerous papillæ are found in the skin of the nipple, some of which belong to the variety known as tactile papillæ. Sebaceous glands and hairs are present in the areola.

No satisfactory investigation of the nervous system of the mammary gland has yet been made.

The first indication of the mammary gland is seen about the third month of intra-uterine life, consisting of an ingrowth of cells of the *rete mucosum*, surrounded by the fibrous tissue of the skin. At about the fifth or sixth month, by a process of gemmation or budding, the rudimentary ducts of the lobules are apparent, springing from the central collection of cells. These buds are increased in size by a continuation of the cell proliferation, but as yet there is no attempt at the development of the secreting acini. During childhood, and until puberty, the increase in the number of ducts is very slow. But at puberty, in the girl, there is a rapid increase in their number; while in man, on the other hand, there is no further development, except, in extremely rare cases, there may even be an atrophy of the existing ducts. The beginning of the formation of the secreting structure of the gland, the acini, is noticed in the female at puberty. Yet it is only during the supervention of the first pregnancy that the gland attains its full development. The gland retains this structural development during the child-bearing life of the woman, becoming somewhat smaller in size and losing a few of its acini during the periods of physiological rest. When the menopause is reached there is an entire disappearance of the secreting acini, and the gland returns to its embryonic state, fatty tissue being substituted for the glandular tissue.

This view of the histogenesis of the mammary gland, from the *rete mucosum*, has been accepted by most histologists. Recently, however, Charles Creighton, of Cambridge, England, in his work upon the *Physiology and Pathology of the Breast*, advances the opinion that it is not the epithelial but the connective tissue layer of the embryo from which this organ takes its origin. His conclusions, drawn from many investigations upon the subject, are as follows:—

"1st. That the mammary acini of the guinea-pig develop at many separate points in a connective-tissue matrix; that the embryonic cells

[1] Labbé and Coyne, "Tumeurs benignes du sein."

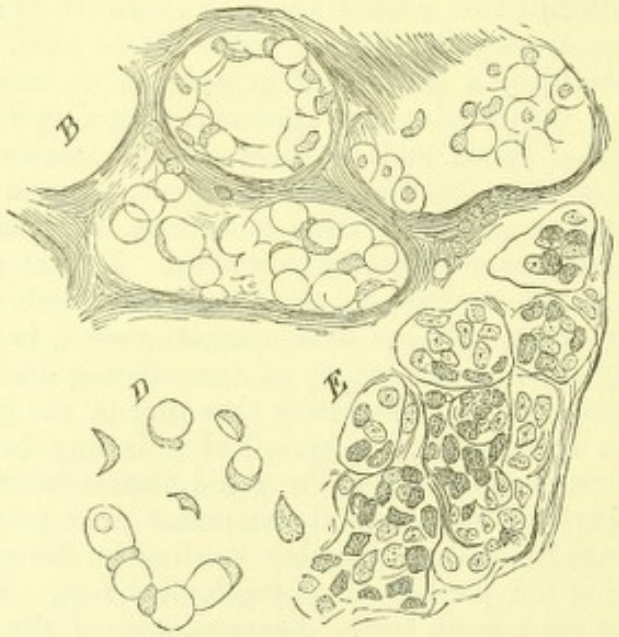
from which they develop are of the same kind that give origin to the surrounding fat tissue; and that the process of development of the mammary acini is step for step the same as that of the fat lobules.

"2d. That the ducts of the mamma develop from the same matrix-tissue by direct aggregation of the embryonic cells along pre-determined lines; that the ducts develop in the individual guinea-pig before the acini, whereas, in the phylogenetic succession, the ducts are a later acquisition."

From the same writer we have made the following extract of his views upon evolution and involution of the mamma:—

"An examination of a gland in the state of well-advanced involution, or resting period, always presents the ducts and bloodvessels very distinctly, because of the retraction of the glandular substance. The minute structure of the acini is of a very definite character, and occurs with great uniformity. Their size is about one-fourth that of the acinus during lactation. Instead of the cellular elements lining the acini being 15 to 20, there are only about half a dozen, and, instead of forming a

Fig. 335.



B. From udder of ewe shortly after the end of lactation, vacuolation of the epithelium *in situ*. × 300. *D.* Cells from the mamma of a cat nine days after lactation; the lobule containing them still retained its full expansion, but its epithelial cells presented the alteration as seen in the cut. × 300 *E.* Appearance of an involuted lobule. × 300. (*Creighton.*)

mosaic of polyhedric cells, they constitute an irregular collection of naked nuclei varying in shape—a certain number are oblong, others crescentic or triangular, and the more round or oval show a nucleolus. (*E*, fig. 335.)

"The examination of a gland in an intermediate state, that is, during the interval between full evolution and complete involution, will give us the steps of the process through which involution is reached. A mamma of a cat that had suckled its young for sixteen days, and had then been kept apart from them nine days, upon examination, showed most of the

lobules to be as large as in the condition of full evolution. The acini were also of much the same shape and size as in the secreting gland. But their cellular contents were very different. In each acinus were found variously shaped cellular bodies, usually corresponding in size to that of an epithelial nucleus; also, a number of ring-like forms of a grayish unstained granular appearance, with the variously shaped cellular bodies placed on their periphery, were seen. (*D*, fig. 335. *C*, fig. 336.)

Fig. 336.

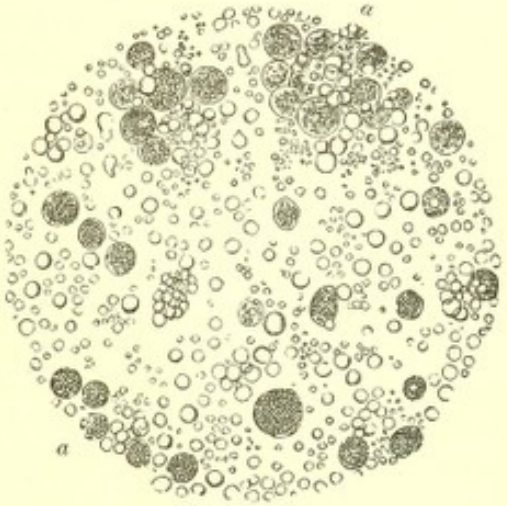


Characteristic appearance of cell occupying the cavities of acini in an early stage of involution. × 300. (From the same specimen as *B*.) (*Creighton*.)

"The significance of these appearances is better comprehended from another preparation. (*B*, fig. 335). Here the acinus presents a profile view of the epithelium, which shows the cells arranged as a complete circlet adhering to the circumference of the acinus. In many of the acini were seen irregular collections of cells free in the lumen of the acinus. In other parts of the same preparation were observed cells of which *C*, fig. 336, is a drawing. The cells *in situ* are vacuolated cells, usually possessing the thin and mostly uncolored ring of the vacuole (signet-ring type). Other cells undergoing the process of vacuolation are found. There is thus a gradual transition from the perfect mammary epithelium to the forms that characterize the various stages of the involution processes."

The secretion of the mammary gland formed during its physiological activity is milk. Anatomically considered, it is a fluid in which are suspended vast numbers of fatty globules, in other words, an emulsion.

Fig. 337.



Microscopic appearance of human milk, with colostrum corpuscles.

Examined with the microscope, there are seen numerous, distinct, and separate oil-globules, varying in size from 0.0023 mm. to 0.0090 mm. By the addition of acetic acid, the globules lose their individuality and coalesce, forming large oil-drops; therefore, each globule may be considered as a minute drop of oil inclosed in a delicate membrane of some albuminous substance, probably casein.

The microscopic appearance of the fluid secreted during the last days of gestation, or immediately after labor, the *colostrum*, contains, in addition to the fat globules, other bodies, spherical in shape, from the 0.0151 to 0.0564 mm. in diameter, composed of a collection of oil globules, held together by a cement, and sometimes containing a nucleus; they are also said to possess the power of contractility to a slight extent. These bodies are known as the *colostrum corpuscles*.

Frequently the mammary gland of new-born children secretes a milky

fluid, in which are found globules of oil. The histological phenomenon is the same as in the secretion of milk in women (Sinéty).

Milk is supposed to be either a metamorphosis of the lining cells of the acini, or a product of these same cells without their destruction. The latter view is most probably the correct one.]

Pathological Histology of the Mammary Gland.

Acute Inflammation or Mastitis.—Inflammations of the mammary region are extremely varied; they occur after delivery, during the first weeks of lactation, or as a result of contusions or tumors.

Inflammations of the areola of the nipple, chapping of the skin, subcutaneous abscesses of the areola frequently occur during the first days of nursing.

Erysipelatous inflammations of the skin covering the gland are frequently seen either during lactation or in consequence of ulcerating tumors, and in the latter it occurs especially in the lymphatics, recognized with the unaided eye by redness along the course of the subcutaneous network of lymphatics. The erysipelatous inflammation may be followed by true subcutaneous phlegmonous abscesses. Recurring subcutaneous lymphangitis, due to an ulcerated carcinoma of the breast, sometimes terminates by a carcinomatous degeneration of the wall of the lymphatics, which are then transformed into hard and tortuous cords.

Parenchymatous or glandular inflammations of the mammæ are deeper, and begin either by a retention of the milk, or by a purulent inflammation of the connective tissue which separates the lobules. These purulent inflammations are generally seen in nursing and recently delivered women, very seldom in pregnant women.

The abscesses which form in the gland are at times very numerous and often recurring. They contain the elements of milk, mixed with lymph cells, and, when opened, may result in a milk fistula, if a sinus or large galactophorous duct is included in the suppuration or cut with the knife. Deep or submammary abscess may be produced from the same causes as the preceding, by the extension of the purulent inflammation to the loose connective tissue which separates the gland from the fibrous fascia. It is certain that these submammary abscesses are produced by inflammation of the lymphatic sinuses and mucous bursæ; pus rapidly collects in a sac beneath the gland, and raises it up.

Occasionally submammary abscesses follow the course of cold abscesses, and instead of having for a cause an acute inflammation extending from the breast to the deep connective tissue, they follow lesions of the ribs or sternum, from scrofulous or tuberculous caries, or from abscesses of the same nature which are developed upon the internal surface of the ribs or sternum, and which subsequently perforate the intercostal spaces, and project into the inflamed submammary connective tissue.

Chronic Inflammation.—When mammary abscesses recover, they give rise to indurations consisting of organized connective tissue of new formation, which may increase in amount, and constitute fibrous tumors.

The causes of general chronic inflammation or chronic mastitis are very obscure. There is formed an abnormal amount of fibrous tissue, and a general induration of all the new-formed tissue which separates the acini. This anatomical alteration is often confounded with general hypertrophies or with fibromata of the glands.

Tumors of the Mammary Gland.

The essential histological characters of tumors of the mammary gland have been described in Part First, under tumors. We will here consider their general history, and complete their description macroscopically and microscopically. Tumors of the breast occur almost exclusively in females, but may also exceptionally be met with in males.

General Hypertrophy of the Mammary Gland.—There sometimes occurs, although seldom, considerable hypertrophy of the mammary glands in young girls after puberty, or in young women consecutive to parturition. Both breasts may be affected at the same time, or only one. The left, more frequently than the right, may attain an enormous size. The consistence of the gland is normal, moderately firm in young girls or during gestation; when the hypertrophy has existed for some time in young women, the gland becomes soft and flabby; to palpation it gives a sensation of lobules which are movable. The skin is normal, or slightly thickened, but not adherent. The glands in the axilla are not enlarged. Upon section of the gland, there is seen a gray tissue, with yellowish lines or lobules; but there is no juice. Microscopic examination of the tissue shows an abundance of connective tissue, which is dense around the lobules of the gland. Elastic tissue also is found. The canals and acini of the gland are either lined, as in the state of rest, with small cells forming a single layer, or, as in the first months of gestation, their cells are larger and granular. In every case the canals are elongated, in order to keep pace with the hypertrophy of the connective tissue, but the alteration is principally a fibrous thickening of the connective tissue, and not a lesion either primarily or principally of the epithelium. Sometimes there are lobules of fat in the gland, but generally they are not present. Manse observed that the galactophorous ducts were much dilated, so much so as to receive the extremity of the finger. Hypertrophy of the mammary gland consists mostly of a new formation of fibrous tissue. In most connective-tissue new formations, the glandular ducts and acini are dilated; this dilatation is analogous to that of the biliary ducts in cirrhosis of the liver. By the same process, small cysts may form from the retention of the glandular products, when a galactophorous duct is isolated in the middle of fibrous tissue.

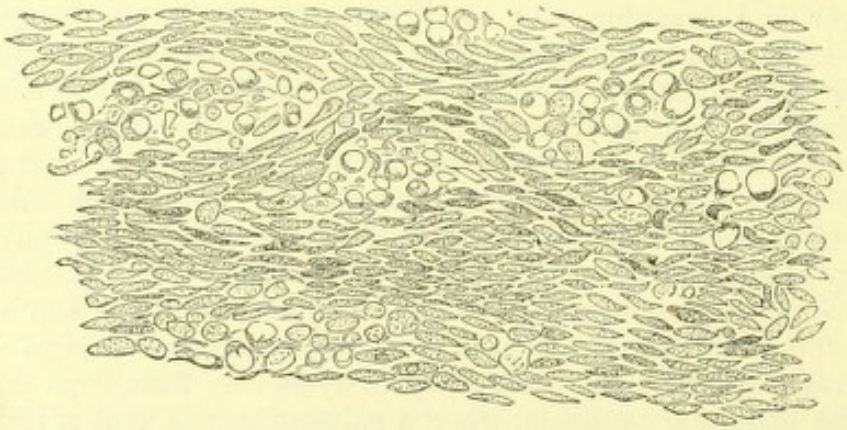
Galactocele.—Galactocele is a tumor caused by the accumulation and retention of milk in a part of the mammary gland, either at its centre or periphery. Its development coincides with lactation, and it may spontaneously disappear after the cessation of this function. The milk is either normal, or curdled and creamy; it is contained in a single sac, or partitioned by bands, giving it an alveolar appearance. The sac com-

municates with a number of secreting lobules. From the description of these tumors which have been published, especially that by Forget, it seems that the cystic sac is nothing more than a dilated galactophorous canal, which cannot discharge by the nipple the milk it contains.

Sarcoma.—Tumors of this class vary in size. They do not at their beginning adhere to the skin, but later they become attached, and, as a rule, they do not infect the neighboring lymphatic glands. The entire mammary gland may be implicated, and there is a very large tumor, or, for a long time, only a limited portion is affected. In the former case the development of the tumor is uniform, the skin is stretched over it, sometimes adherent; in the latter, there exist one or more tumors, which give the gland a lobulated appearance. A section of the tumor, after its removal, presents a solid, uniform, gray mass, with some vascular portions scattered here and there; older parts are yellowish in consequence of a fatty granular degeneration. There are also seen several distinct masses, separated from each other by less changed portions of the gland. In the more altered portions, the glandular tubes and acini are often preserved; they are hypertrophied, but not cystic; frequently the acini are wanting in those portions, which are developed only from the connective tissue and peripheral adipose tissue of the glands.

When the entire gland is involved in the new formation, there is an increased formation of epithelial cells, a distension and filling of the ducts or galactophorous sinuses with fatty degenerated cells,having the appearance of milk corpuscles. More frequently there is found a mucous fluid. Cysts are often observed in such cases, or rather arborescent clefts representing cavities and acini into which the neighboring sarcomatous tissue buds (for Histology see Part First, page 81).

Fig. 338.



Inter-acinus spindle-celled sarcoma of mammary gland, showing the distorted acini filled with vacuo'ated glandular epithelium. High power. (*Creighton*)

Sarcomata of the breast are very easily distinguished from carcinomata by the entire absence of the cellulo-adipose tissue—it has been transformed into sarcomatous tissue—and by the lymphatic glands of the axilla not being infected.

The most frequent variety of sarcoma of the mammary gland is encephaloid; the fascicular sarcoma is also of frequent occurrence. These

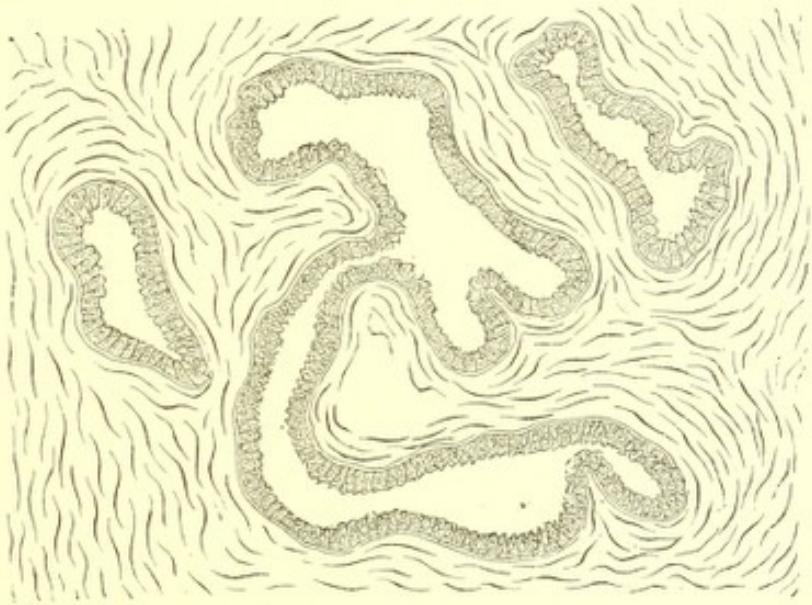
tumors often return after ablation. When a cystic sarcoma has been removed at the first operation, with the entire breast, the recurrent formation is found to be a sarcoma without cysts. This is explained by the whole of the gland being removed at the first operation.

Secondary sarcomatous nodules of pleura, lungs, bones, and other organs are sometimes met with at autopsies of persons who had been operated upon for sarcoma of the mammary gland.

Myxoma.—Myxomata of the mammary gland are not unfrequently seen; they differ from sarcomata only by the nature of the tissue composing them, for their situation in relation to the glandular acini and canals is the same. Cystic myxomata are the most frequent (for Histology, see Part First, page 89).

Myxomata of the breast are essentially benign tumors; they do not contract adhesions with the skin, and at times may be completely enucleated, appearing as if contained in a serous membrane which separates them from the surrounding tissue. In a case recently seen by us, the large tumor, a papillary myxoma, presented in its deeper portion large masses situated in a serous cavity, one wall of which covered the nodules. We

Fig. 339.



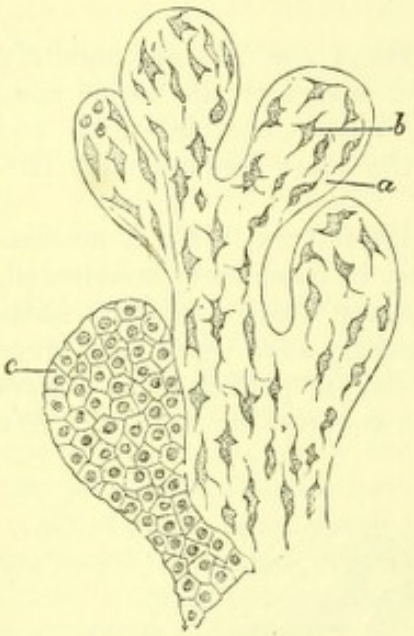
Fibroma of the mamma, showing a dilatation of the galactophorous ducts and endo-canalicular vegetations. High power. (*Labbé* and *Cogne.*)

had here to do with a large serous bursa, the anterior wall of which belonged to the tumor, while the posterior wall was in connection with the connective tissue situated behind it. The cells upon the surface of this cavity were thin and flat. From this arrangement we were led to think that this serous membrane was the serous cavity or large lymphatic lacuna situated beneath the breast, for it was impossible from its location to suppose that it was formed by galactophorous canals or glandular acini. It is very probable that the clefts and cavities into which the new formations of fibromata, sarcomata, and myxomata project, are not only the

galactophorous ducts and mammary acini, but frequently also the lymphatic lacunæ described by Giraldès and Coyne (see page 157).

Fibroma.—Among fibromata may correctly be classed general hypertrophy of the mammary gland, since the whole of the new formation is fibrous tissue. There also exist fibromata in which the breast is of considerable hardness, and but little enlarged. Instead of being general, fibroma of the breast may be limited to a part of the gland, and form a tumor varying in size, generally small, hard almost stony, and having no intimate adhesions to the neighboring tissues. These tumors have the same arrangement as sarcomata and myxomata in regard to the glandular ducts and acini. (For Histology see Part First, page 91, and figs. 339, 340.)

Fig. 340.



Papillary fibroma of the breast. Fibrous vegetations projecting into the galactophorous canals which have become cystic; they are covered by their epithelium at *c*, and are denuded of it at *a*; *b*, connective tissue corpuscles. × 300.

Syphilis.—Apparent syphilitic indurations of the breast have been met with, which have disappeared with antisyphilitic treatment, there have been no histological examinations of these lesions. We know of no example of *tubercles* occurring in the mammary gland.

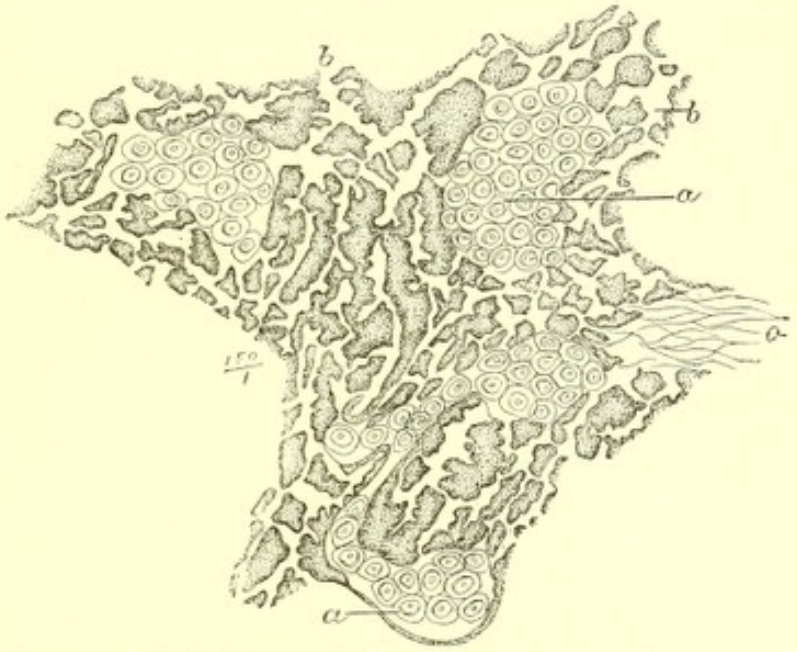
Carcinoma.—The several varieties of carcinoma are met with in the mammary gland, occurring as a primary lesion: scirrhous, encephaloid, and colloid carcinoma.

Fibrous or scirrhous carcinoma begins by a hard generally small tumor following a different course according to the case. Thus, it may extend with great rapidity, becoming adherent to the skin, invading it and presenting branching processes, or it may extend in ramifying and anastomosing lines which are due to the consecutive change of the superficial lymphatic vessels; at other times there are seen small nodules developed in the subcutaneous cellular tissue and in the skin. We have twice seen very large and hard lymphatic vessels raising the skin, and extending from the tumor to the axillary gland. A microscopic examination in one of the cases proved that the periphery of the lymphatic vessels throughout their entire course consisted of a carcinomatous tissue with alveoli and characteristic cells. We have already indicated the connection between the lymphatics and the alveoli of carcinoma (see p. 101).

In rapidly growing fibrous carcinomata, the skin is not only indurated in small patches, but also as dense bands; the opposite breast in its turn may be invaded (*cancer en cuirasse* of Velpeau), and generalization of the tumor gradually occurs in the pectoral muscles, in the fibrous tissue of the axilla, in the ribs, in the intercostal muscles, in the pleura, lungs, etc. In a number of cases, especially in old women, the scirrhus is atrophied.

The tumor remains small, the breast shrivelled, the nipple retracted; the axillary glands are involved, but only after four or five years or longer, and there are observed neither secondary nodules of the skin nor generalization in the internal organs. It is the secondary formations which cause death. The cancerous nodules found in the organs and tissues are remarkable for their smallness and hardness, and which by a careless naked-eye examination may be confounded with tuberculous granulations.

Fig. 341.



Carcinoma of mammary gland—the ground substance of the section stained with nitrate of silver. *a*. Alveoli of the carcinoma filled with cells. *b*. Lymph spaces shown in the fibrous tissue after treatment by nitrate of silver. *c*. Lymphatics showing silver staining of the endothelium.

When atrophied scirrhus ulcerates, which frequently happens at the sunken, retracted, central portion of the tumor, there are seen, upon section through the borders and base of the ulcer, the phenomena described in part first under inflammation of carcinoma. (See p. 106.) The ulcerated and inflamed part shows a large mass of inflamed tissue. Its borders and base present alveoli, thickened connective tissue, and cell-clumps of carcinoma.

Fully developed mammary scirrhus, upon section presents, instead of a smooth, white, and slightly juicy tissue, the sinuses of large galactophorous ducts filled with a yellowish-white fluid, or with an opaque yellowish or brown caseous material consisting of fatty granular cells. The ducts of smaller calibre are also filled with granular epithelial cells, and are recognized by the unaided eye as arborescent lines, which can be followed as far as the periphery of the tumor. Upon thin sections examined when fresh, it is seen that the glandular acini are filled with large cells provided with a large nucleus and nucleolus. In hardened tumors, sections of the central or oldest portion of the formation show the ducts, distinguished by their enveloping membrane, containing upon their internal surface large epitheloid cells arranged in several layers, and at the centre of the duct, in its lumen, a collection of fatty cells distinct from

the lining epithelium. The pre-existing mammary acini and connective tissue are transformed into carcinomatous alveoli containing large cells. At the periphery of the tumor, in the parts more recently attacked, the changes in the glandular and connective tissues may be followed. Thus, alongside of a normal glandular lobule, the cells of which are only slightly swollen, and the acini larger than when in a state of rest, are seen lobules the acini of which are distended by large finely granular cells possessing large nuclei and nucleoli. These acini still retain their enveloping membrane. The lobule, so changed, becomes much larger than the surrounding lobules. At the same time the peripheral connective tissue has its cells more distended and more numerous than normal with proliferating nuclei, and the lymph spaces are filled with cells of new formation or lymph cells. The connective tissue is transformed into carcinomatous tissue, by the new formation of cellular elements in its cavities. In time the membrane of the acini disappears, and all the preëxisting tissue is riddled with alveoli filled with large cells. The lymphatic vessels are in their turn involved and contain the same elements. (Fig. 342.) When the scirrhus is old, the fibrous tissue is

Fig. 342.



Development of carcinoma in the mamma. *a*, Lymph spaces which enlarge by the multiplication of their cells; at *c*, they have preserved their angular form; at *d*, they have become spherical and form there the alveoli of carcinoma. × 150.

Fig. 343.



Scirrhous carcinoma of the female breast. The fibrillar stroma of the breast is occupied by rows and fusiform groups of nucleated cells. × 300. (*Creighton.*)

very thick and the alveoli are small. In the central part of atrophied carcinoma there exists a fatty degeneration with atrophy of the cells; the dense fibrous tissue also contains fatty granules.

In this variety of carcinoma the lymphatic glands of the axilla are always indurated. They are frequently changed into fibrous tissue (see page 175); the connective tissue in the axilla, which accompanies the nerves and vessels, is also extremely hard, and presents at points carcinomatous alveoli, and especially a new formation of dense fibrous tissue,

which compresses the vessels and nerves, interrupting the circulation in the arteries, which are filled with organized thrombi; the membrane of the arteries is folded longitudinally, their calibre is contracted, and sometimes entirely obliterated; thus an œdema of the arm is caused. The peripheral end of the compressed nerves is in a state of fatty degeneration. The axillary lymphatic glands, attacked with carcinoma, show that the tumor is developed in the meshes of the reticulum; in the small meshes of this reticulum the cells are much larger than lymph corpuscles, and there are two or three cells in a mesh. These cells possess a distinct granular protoplasm, saturated with fluid and contain oval nuclei, resembling the cells of the tumor; they are very probably the flat cells of the reticulated tissue, swollen and proliferated.

Encephaloid carcinoma forms, in the breast, tumors generally larger than the preceding, and growing more rapidly. The skin, in time invaded and thickened by a new formation of embryonic or carcinomatous tissue in its deep layers, shows upon its surface enlarged papillæ, infiltrated with lymph cells, and containing large vessels. These changes of the skin precede the ulcerations. The ulcers, covered with very vascular granulations, and spreading to a varying extent, frequently give rise to repeated hemorrhages, at times considerable. Hemorrhage may also occur in the hard variety of carcinoma, but is always more frequent and more abundant in the soft (encephaloid) form.

A section of the tumor presents a soft, vascular, grayish-white tissue, and yields a very large quantity of milky juice—possessing, in a word, all the characters of encephaloid. The development, the extension to the neighboring tissue and to the lymphatic glands, are the same as in scirrhus, with this difference only, that the new tissue always has the same characters as the primary tumor.

Colloid carcinoma is not so frequent as the preceding varieties.

Villous Carcinoma.—We have several times seen a tumor of the mammary gland, which resembled a carcinoma in its mode of extension, its infection of the lymphatic glands, and its generalization, but which, however, differed from the preceding varieties in its histological structure. To the unaided eye its appearance does not perceptibly differ from encephaloid carcinoma; upon section there flows an abundant milky fluid, and there are seen cavities and cysts which are quite large, measuring one-half to two or more millimetres, which are filled with a milky juice, and contain dendritic filaments. Some of these open cavities are only galactophorous ducts filled with vegetations, which may be easily detached with a needle. These dendritic vegetations, removed and stained with picro-carmine, show under the microscope a very beautiful branching arrangement. The principal trunks divide, forming long divided papillæ, terminating by free, elongated, or club-shaped extremities; all are traversed by capillary vessels, which terminate in loops at the extremity of the papillæ, and are surrounded by a very small amount of connective tissue. They are everywhere covered with prismatic or cylindrical cells, forming one or more layers; the first layer is implanted perpendicularly upon the surface of the papillæ, and the cylindrical cells forming it are pressed one against the other, elongated, granular, distinct, and provided with an oval nucleus. The more superficial and detached cells are larger,

prismatic, or polygonal, more distinct, and have a more swollen and larger nucleus, and one or more large nuclei. The latter cells become free in the fluid contained in the cavities, and undergo fatty granular degeneration. By studying sections from hardened specimens, the villous vegetations are seen implanted upon the fibrous wall of these cavities, and growing into their interior. The internal surface of the cavities is lined with the same variety of cells as the vegetations. The majority of the cavities are dilated galactophorous ducts, filled with vegetations which grow from their wall, and extend along the canal, which they partly fill. The glandular acini experience a cystic enlargement, their walls covered by epithelial cells arranged as in the canals; and there also frequently exist vegetations projecting from the wall into the cavity.

The galactophorous canals have a distinct wall, and the neighboring connective tissue has its fibres arranged concentric around them. But it is not the same with the acini, the hyaline membrane of which disappears; they are surrounded by a connective tissue transformed into alveoli which are filled with large swollen cells having a large oval nucleus.

These tumors may be considered as epitheliomata. This opinion is based upon their probable origin from the surface of the galactophorous canals, and from the shape of the cells resembling those of the cylindrical-celled epitheliomata. Yet the infiltration of the neighboring connective tissue, changed into alveoli containing large cells, resembles carcinoma more than cylindrical-celled epithelioma, in which the epithelial formations, when they invade the connective tissue, have the form of cylindrical tubes containing regularly arranged cylindrical cells. For these reasons we have placed these tumors among the carcinomata. However, this variety, like several other mammary tumors, is not yet satisfactorily understood, and further investigation is necessary to determine their exact nature. We cannot too strongly recommend to those making a classification of mammary tumors, the examination of the tumors which return in the cicatrix after the complete removal of the gland, for they give most important information of the nature of the primary tumor. The degenerated neighboring connective tissue and lymphatic glands should also be carefully examined.

From the foregoing descriptions it is seen, that in fibromata, myxomata, sarcomata, and carcinomata, the initial lesions in the gland and excretory ducts of the breast, have a great analogy; for example, in all these tumors vegetations grow into the interior of the galactophorous ducts, and cysts have their origin by the distension of the ducts and acini. These cysts and vegetations are not, therefore, characteristic of any particular tumor, and in order to determine the nature of the new formation, examination of other portions must be made—that is, of the connective tissue, which is in each changed into a special tissue.

Enchondroma.—The enchondromata of the mammary gland are very rare tumors; a few only have been reported. In a specimen met with by Wagner, there were found cartilaginous masses in a carcinoma.

Calcareous or osteoid indurations may be met with either in an enchondroma or in nodules of fibrous tissue.

ADENOMA.—The characters of adenoma of the breast have been given in Part First (see p. 161). They were for a long time considered by

Fig. 344.



Adenoma of the mamma. × 300. (*Rindfleisch.*)

Velpeau as synonymous with benign tumors of the breast, among which were confounded fibromata, myxomata, sarcomata, and true adenomata.

MELANOTIC TUMORS OF THE BREAST.—See Part First, pages 329, 330.

EPITHELIOMATA, with pavement cells and pearly bodies, are seldom met with in the mammary gland. They occur especially as a new formation, having its origin from the skin in the region of the nipple, where are found numerous and large sebaceous glands. These tumors do not differ in their mode of development or extension from epitheliomata of the skin, and especially those of the lips.

CYSTS.—The cysts occurring in adenomata, sarcomata, fibromata, myxomata, and carcinomata, have already been described. We have now to consider cysts due to the retention of the secretion of the galactophorous canals and acini. Their causes, as yet not well understood, have been associated with the partial obliteration of a duct from the fibrous atrophy of involution of the gland, from cicatrices following an operation upon the breast. The majority of sero-sanguineous cysts are associated with tumors, such as sarcomata or myxomata; yet they may follow contusions.

Several cases of *dermoid cysts* have been reported, especially that by Velpeau, which should be classed among the dermoid cysts of the first variety (see page 304); another, reported by Albers, contained hairs in the midst of a sebaceous mass.

Hydatid cysts, with echinococci developed in the connective tissue of the mammary gland, are also of very unfrequent occurrence.

SECTION V.

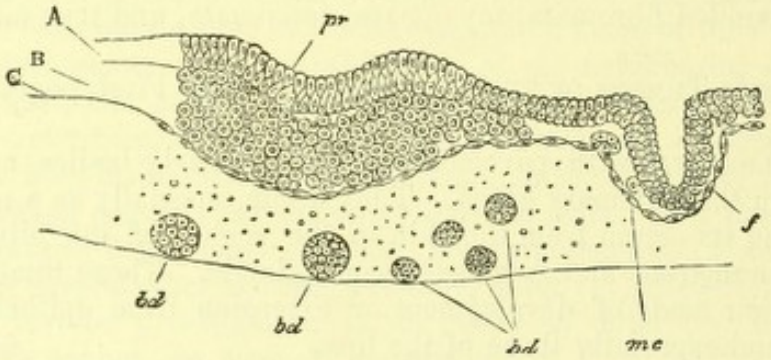
PATHOLOGICAL ANATOMY OF THE SKIN.

CHAPTER I.

Sect. 1.—Normal Histology of the Skin.

THE skin is formed of two layers, the *epidermis* and *derma*. The epidermis consists of cells united as in other epithelia by an intercellular cement, and arranged in layers covering the surface, and developed from the external or corneous layer of the blastoderm.

Fig. 345.



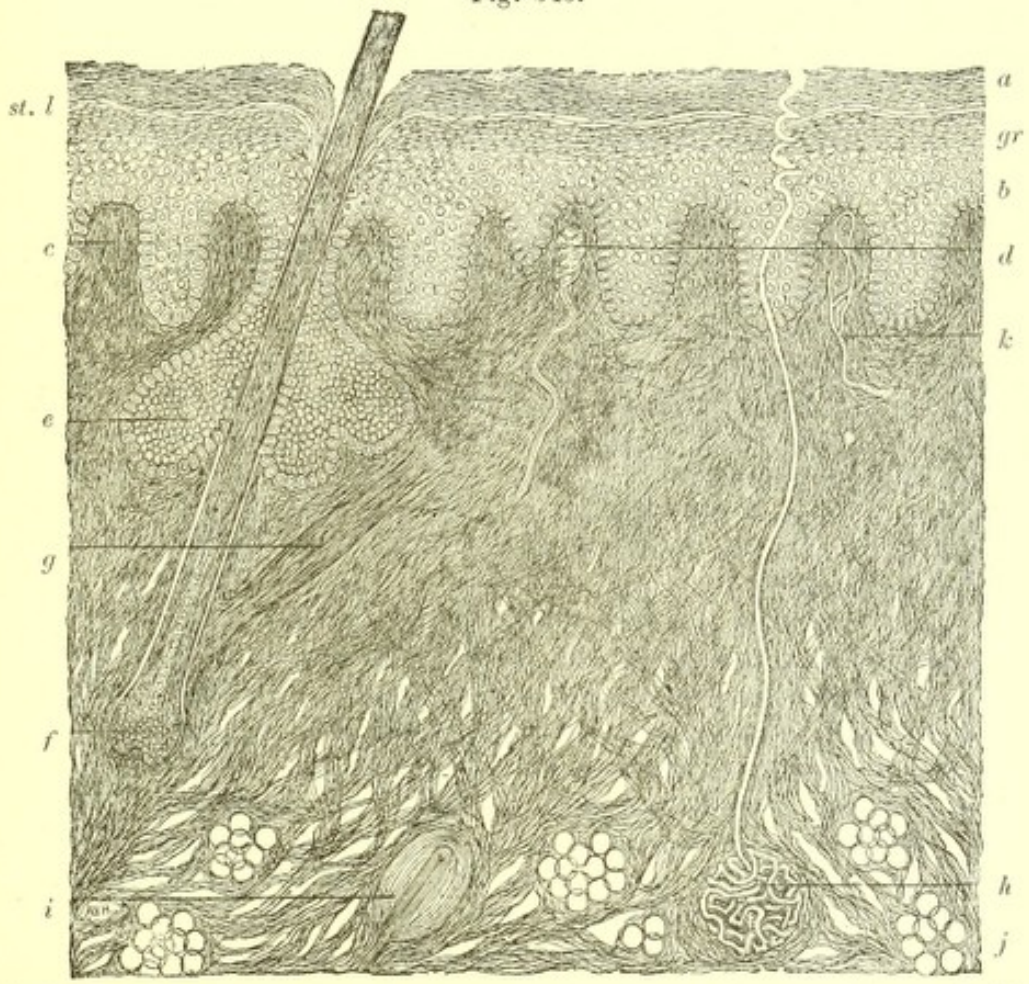
Section of the blastoderm of an embryo eight hours after incubation. *A*. Epiblast or external layer. *B*. Mesoblast or middle layer. *C*. Hypoblast or internal layer.

The derm developed from the middle layer consists of connective tissue. It contains the vessels and most of the nerve terminations of the skin In this membrane are to be studied the *Malpighian rete mucosum and corneous epidermis; the derma and papillæ; the vessels; the nerves and the glands.*

A. EPIDERMIS.—A vertical section of the skin shows the papillæ as irregular festoons covered with the cells of the Malpighian rete mucosum. The cells in the layer next to the papillæ are prismatic or cylindrical, and are implanted perpendicular to the wavy surface of the derm. These prismatic cells have at their base indentations or notches, into which are placed prolongations from the derm; upon the sides they are joined with the adjacent cells by extremely fine serrations, which fit in corresponding notches of the neighboring cells. In this deep layer is deposited around the nuclei the pigment which gives the color to the skin. Above the layer of prismatic cells is found the rete mucosum proper, consisting of several rows of polyhedral cells, with vesicular nuclei surrounded by a bright zone. At their periphery the cells are indentated, or have spinous processes which unite them to similar neighboring cells. In this manner

the dentate or spinous cells of the rete mucosum seem to be separated from one another by an interstitial cement (Kittsubstanz) formed of brilliant granules separated at intervals by the spinous processes which are united to each other in the middle of the intercellular space.

Fig. 346.



Vertical section of the human skin. *a*. Corneous layer of epithelium. *st. l*. Stratum lucidum. *gr*. Stratum granulosum. *b*. Rete mucosum and papillary layer of cylindrical cells. *c*. Papillæ of skin. *d*. Tactile corpuscle. *e*. Sebaceous gland. *f*. Hair-bulb. *g* Erector-pili. *h*. Convolution of sweat gland. *i*. Pacinian corpuscle. *j*. Panniculus adiposus. *k*. Vascular loop. Lower power. Partly diagrammatic. (*Duhring*.)[1]

Between the rete mucosum and the epidermis there exists a special layer; it is the *stratum granulosum*, and is formed of cloudy cells loaded with albuminous granules. Picro-carmine colors it deep red. The cells which form it are without spinous processes, their nucleus appears perceptibly atrophied, and the body of the cells is loaded with numerous granules which are deeply colored with carmine. They are feebly united to one another, and constitute a slightly resistant zone between the rete mucosum and the *stratum lucidum*, whose cells are firmly joined together. Immediately external to the thin granular zone is a transparent zone, the *stratum lucidum* of Schröa, consisting of several layers of very thin

[1] Our thanks are due to Dr. Duhring for his courtesy in permitting the use of this excellent cut, from a drawing of Dr. Van Harlingen, in advance of its appearance in the second edition of Dr. Duhring's work on the skin.

homogeneous transparent epithelial scales, in some of which traces of a staff-shaped nucleus can be seen. Therefore, when there is exaggerated pressure upon any part of the skin, acting from without inwards or within outwards, the epidermis is readily separated from the granular zone, and a vesicle is produced. Langerhans has recently considered the granular cells of this region as embryonic cells, from which are developed the cells of the epidermis, the deep portion of the rete mucosum having no part in the process. This hypothesis is wrong, because the progressive atrophy of the nuclei may be followed in the epidermic layer, and the corneous layer is re-formed, as will be shown, with great rapidity when the granular zone has been raised by a vesicle.

The most superficial layer is the corneous epidermis, differing in thickness according to the region. Upon the surface the protoplasm of the cells is dry, is transformed into keratin, and the cells are reduced to thin plates, which become gradually thinner, and form strata, the superimposed layers of which are intimately united together. When the corneous cells have been macerated by potassa or ammonia, they are seen to be polyhedral, extremely thin, frequently showing impressions of the adjacent cells, and often having at their centre only a rudimentary nucleus. This impression presents the form of rectilinear ridges, which project in different directions from the superior and inferior surfaces of the cells.

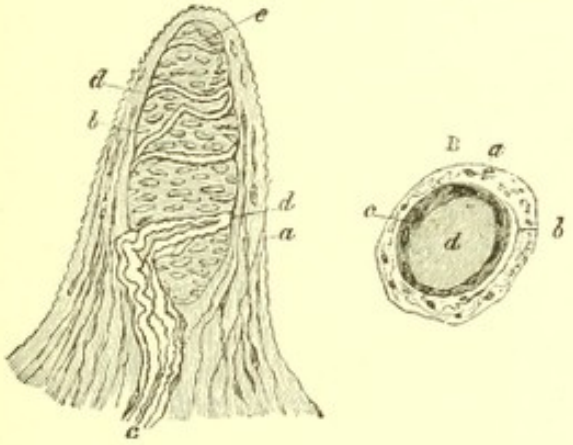
B. Derma; Papillæ.—The derm consists of connective tissue which has the appearance of a dense and resisting membrane. It supports the layers of the epidermis, and contains the glands and vessels of the skin, as well as the nerve terminations. It is formed of connective tissue fasciculi, analogous to those of tendon, which intersect each other in various directions, forming superimposed layers. There are in it numerous elastic fibres, anastomosing so as to form an elongated network, embracing the connective tissue fasciculi like the meshes of a net. In the papillæ, this elastic network is especially abundant, and in part constitutes the solid stroma of these eminences. The papillæ form under the rete mucosum a series of regular nipple-like projections, being more or less pointed. They contain loops of capillary bloodvessels, and a few nerve terminations.

C. Vessels and Nerves of the Papillæ and Derma.—Each papilla contains one or more loops of a capillary bloodvessel which ascend vertically in its substance in order to form a tuft. The afferent arteriole below the base of the papilla subdivides into capillary branches which anastomose, and forms immediately beneath the epidermis, without penetrating it, numerous loops. The efferent veinule arises from the capillary loops of the papilla and follows a course parallel with that of the arteriole. Beneath the papillary zone the superficial veins and arteries form a longitudinal network with elongated meshes, from which are vertically given off the vascular tufts of the papillæ and anastomosing branches which run through the derm and form a communication between the superficial network and the arterial and venous trunks of larger calibre which occupy the deep portions of the derm, and which supply the network with irregular meshes which surrounds the convolutions of the sudorific glands.

The *lymphatic vessels* of the derm are divided into *intra-dermic capillaries* and *small deep trunks*. The capillaries originate in the stellate clefts formed by the separations of the intersecting connective tissue fasciculi of the derma; they are limited by a fine elastic network, and are lined with endothelium.

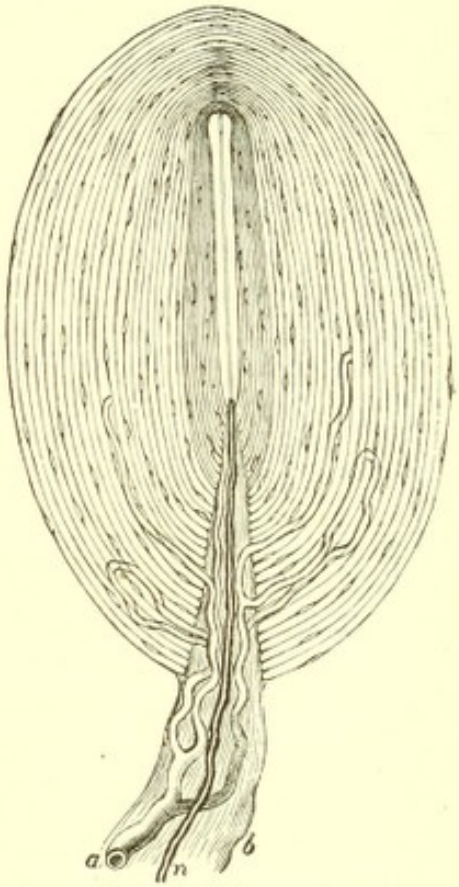
These capillaries appear to communicate freely with the meshes of the derm; they are nothing else than the stellated spaces of the connective tissue changed into clefts and channels to form the lymphatic passages. These passages have a distinctly canalicular form at the boundaries of the derm and subcutaneous adipose tissue. Here the small lymphatic trunks are seen passing obliquely into the deep portion of the derm, from

Fig. 347.



A side view of a papilla of the finger. *a*. Cortical layer. *b*. Tactile corpuscle with transverse nuclei. *c*. Small nerve of the papilla. *d*. Its two branches running in spiral coils around the corpuscle. *e*. Afferent termination of one of the fibres. B. A tactile papilla cut transversely. × 350. (*Gray*.)

Fig. 348.



A Pacinian corpuscle with its system of capsules and central cavity. *a*. Arterial twig. *b*. Fibrous tissue of the stem prolonged from the neurilemma. *n*. Dark bordered nerve fibre advancing to the central capsules, there losing its white substance, and extending along the axis to the opposite end where it is fixed by a tubercular enlargement. High power. (*Gray*.)

which they continue into the fat or follow the fasciculi of the connective tissue which separate the adipose lobules, or are insinuated between them. A transverse section of these passages is not now stellate in outline, but circular, and the lymphatic begins to form a true vessel provided with valves, not differing from other lymphatic vessels of small calibre.

Terminations of Nerves in the Skin.—The sensory nerves terminate in special bodies placed in the skin: the *tactile corpuscles* and *Pacinian corpuscles*. Langerhans has seen very fine nerve fibrillæ passing between the cells of the rete mucosum and communicating with stellate corpuscles scattered here and there between the spinous cells, forming a network similar to that described by Cohnheim as existing in the epithelium of the cornea; these investigations have been confirmed by Podcopaëw and Tomsa.

The tactile corpuscles are found in the papillæ where they are separated from the vessels only by bundles of connective tissue fasciculi. They are in immediate vicinity to the deepest layer of cells in the rete mucosum, and consist of an enlargement, shaped like a fir cone, formed of transparent cells (Langerhans) so united as to leave no cavity at the centre of the corpuscle. At the base of this small organ is seen a nerve fibre, the interannular segments of which gradually become shorter. By spiral turns this nerve passes around the cellular mass without penetrating it. Between the spiral turns of the nerve fibre provided with its medullary sheath, upon the surface of the corpuscle, fine filaments are seen, which pass around irregularly like threads upon a bobbin. These filaments are probably of a nervous nature, and give rise to the characteristic transversely striated appearance of the tactile corpuscles.

The tactile corpuscles may be formed of a single segment or superimposed segments; they are found frequently double or triple. Each segment is formed in the same manner as a simple corpuscle, and receives a special nerve fibre (Thin), frequently coming from a single nerve, which is bifurcated or trifurcated at the base of the corpuscle at the point of an annular enlargement (Ranvier).

D. Glands of the Skin.—Until towards the end of the third month after conception the surface of the skin has remained perfectly smooth. It then assumes a definite arrangement; the connective tissue of the derma forms numerous granulations which elevate the rete mucosum and develop into the papil'æ, while buds from the rete mucosum sink into the derma to form the *sebaceous glands*, the *sudorific glands*, and the *hairs*.

Sebaceous Glands.—Ordinarily these glands are, in pairs, attached to the hairs which they lubricate; they are wanting in places where the hair does not exist; they are inclosed by a basement membrane which represents the superficial layer of the derma. Within this first layer are seen one or two rows of cubical cells implanted upon the basement membrane. The cells of the central layers gradually undergo fatty transformation, so that in the centre of the gland there is seen free fat or epidermic cells in the process of granular fatty degeneration. The sebaceous glands are surrounded by a network of bloodvessels with narrow meshes which envelop them like the meshes of a net.

Sudorific Glands.—These glands are developed from epidermic buds or granulations which sink vertically into the derma, and roll themselves into a glomerulus or convoluted body. This latter is situated in the

deepest portion of the derma, in the midst of connective tissue surrounded by adipose vesicles and capillary bloodvessels. Later a cavity is formed in the tube, which in a section of the skin of a new-born child is seen as a narrow lumen surrounded by a row of distinct prismatic cells, implanted upon a thin wall. The excretory duct ascends vertically into the derma and reaches the epidermic layers through which it passes in a spiral manner. In its dermal portion it is lined with cells similar to those of the rete mucosum, and in the fœtus these cells, like those of the rete mucosum, are loaded with glycogen. In some regions the duct is provided with smooth muscular fibres longitudinally arranged. The sudorific glands seem to play an important part in the development of a number of cutaneous lesions.

Sect. II.—Œdematous Infiltrations of the Skin.

Œdematous infiltrations of the skin are of two kinds, and include: 1st. *Simple œdema*, which simply consists in the effusion of an albuminous serum between the connective tissue fasciculi of the derma. 2d. *Inflammatory œdema*, caused by the accumulation of lymph, containing coagulable fibrin in the interstices of the same fasciculi. We consider these two forms of œdema in one paragraph, although pathologically they correspond to two series of phenomena essentially different.

A. Simple Œdema, Serous Infiltration of the Skin.—It is known, that when the pressure in the capillaries exceeds a certain limit, diapedesis occurs and œdema is the result. The increase in pressure may take place from two causes: either because the passages which carry off the fluids are not free, in consequence of a venous obstruction; or because the contractile vessels are in a state of atony.

It is to the latter cause that primary œdema of the skin is due. The elevations of urticaria, and of papulous erythema, are nothing more than small points of circumscribed œdema. They are always accompanied by extravasation of blood. The fluid poured out at the time of the diapedesis, always contains a number of red blood corpuscles. Hence, in cutaneous œdema produced by the paralysis of a nerve, the skin at the location of the lesion sometimes has all the colors of an ecchymosis, and the papulæ of urticaria, for example, may have a hemorrhagic character. This variety is described by Willan and Rayer as *purpura urticans*.

The papulæ of urticaria are a type of local œdema of the skin. The white elevation corresponds to the infiltrated portion of the derma, the pink areola to the vascular congestion which surrounds it. The redness always precedes the appearance of the papulæ The white color is due to the interstitial distension of the derma by serum, as may be demonstrated by injecting water into the skin with a hypodermic syringe, when there is formed the pale pruriginous swelling of urticaria. The pruritus from hypodermic injection, comparable to that of urticaria, is in reality due to the action of the water upon the nerves.

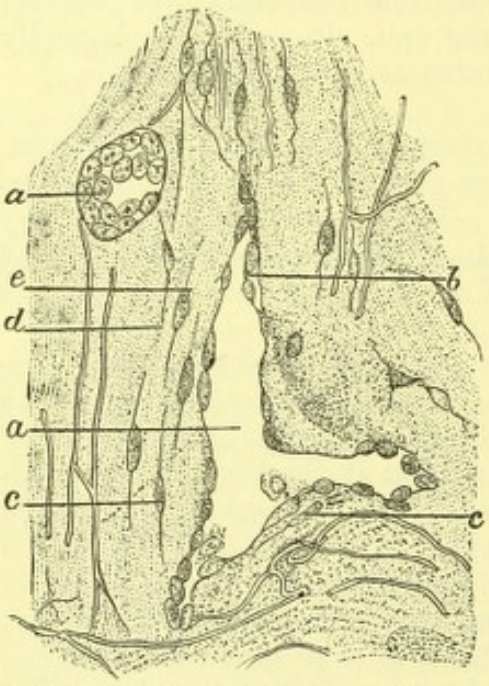
The white spots upon the surface of the skin in anasarca, isolated or running together so as to form networks, very similar to those of urticaria,

show that the derma is invaded by the subjacent œdema. As soon as this passive and diffuse cutaneous œdema occurs, the skin loses its smooth appearance, it becomes mammillated; frequently, over the elevations the epidermis is plicated; finally, the epidermis may excoriate, when a thin serum, which is not spontaneously coagulable in the air, flows out. This fluid contains the anatomical elements always met with in œdematous fluids, that is, white corpuscles and a few red disks.

A thin vertical section of the skin, when in this pathological state, shows the bloodvessels very distinct, engorged with blood and surrounded with white corpuscles. In the derma are seen, between the connective tissue fasciculi separated by serum, white corpuscles, in greater numbers than in normal skin. They frequently form collections or irregularly disseminated foci. The lymphatic capillaries are *very much dilated*, and instead of appearing as narrow clefts, as in normal skin, they are seen as large stellate, open spaces; their diameter frequently exceeding that of the largest bloodvessels of the derm.

This dilatation of the lymphatics is always present in œdema of the skin. At a time when the histological structure of connective tissue was not so well understood, Young described as *dilated lymphatics*, large spaces filled with fluid, circumscribed by thick fasciculi of connective tissue and partitioned by a delicate network of connective tissue fibres. These spaces, having no proper walls and communicating one with the other so as to form a true cavernous system, were correctly considered by Young as the seat of cutaneous œdema, but were incorrectly regarded as lymphatic vessels (fig. 349). These spaces accurately correspond to the description given by Ranvier of the connective tissue distended and separated by the serum of œdema; and they by no means resemble lymphatic capillaries, which are not spaces partitioned by intersecting connective tissue fibres. The lacunæ of Young are merely the connective tissue spaces of the derm swollen and distended by the fluid of œdema. Therefore Young had imagined rather than demonstrated the dilatation of the lymphatics in œdema. If, however, it is admitted that the connective tissue is nothing more than a partitioned lymphatic space, the conception of this histologist remains correct, and in œdema the transuded serum collects in the meshes of the connective tissue, that is, in the radicles of the lymphatic passages.

Fig. 349.



Dilated lymphatic capillary of the skin in a case of œdema. *a*. Cavity of the vessel. *b*. Its endothelium. *c*, *d*, *e*. Cells and fasciculi of the connective tissue in the midst of which the lymph lacuna is located.

Diffuse œdema frequently attacks the skin of limbs which have been

for a long time anasarcous. It is seldom primary; in new-born children it always commences with œdema of the subcutaneous cellular tissue, and constitutes a scleroderma.

We have seen that œdema is accompanied with serous exudation, with numerous white corpuscles and a few red blood corpuscles. If the definition that Cohnheim has given of inflammation is correct, there should not be any difference anatomically between inflammation and œdema; if, on the contrary it is admitted, that irritation and proliferation of the fixed cells of the tissue are also necessary in order to characterize the beginning of the inflammatory processes, œdema remains distinct from inflammation.

The phenomena so close to inflammation cannot continue for a long time in tissues without a chronic inflammation resulting. Therefore the history of a chronic œdema and chronic dermatitis are intimately connected, the former always by its long duration causing the latter.

To repeat, when the œdema of the skin is occasioned, either in consequence of local nerve paralysis, or by the extension of a subjacent œdema, there are seen: 1st. Serous transudations forming an interstitial injection of the derm; 2d. Migration of white blood corpuscles and a few red disks; 3d. Dilatation of the lymphatic passages, the enlargement of which is in correlation with the elimination of the œdematous products to such an extent, that in some cases the dilated lymphatic vessels are irritated along their course, and are seen as white cords. This always occurs in an intense œdema of the skin of an entire limb, as, for example, in *phlegmasia alba dolens*.

B. Œdema of the Lymph Passages.—This has been described by several writers, especially by Virchow as *leucophlegmasia*, and by Rindfleisch as *lymphangiectatic pachydermia*. At times also, when, in consequence of a prolonged œdema, the lymphatic canals and the corresponding lymph glands, for a long time irritated, contract in the same manner as a cicatrix, this variety of œdema is often seen to follow anasarca. The skin is hard mammillated, reddish-brown; upon puncture, there escapes a fluid spontaneously coagulable in the air; and in sections of the skin, after hardening in alcohol, the derm is seen filled with lymph which, after coagulation by the alcohol, remains in all the interstices of the fibrous tissue, distending the meshes like an injection of gelatine. The lymphatics are gaping and filled with lymph clots; very frequently this variety of œdema rapidly occasions in the skin a chronic dermatitis, which extends to the subcutaneous tissue and adds to the rigidity of the skin already engorged with fluid. The cellular infiltration is as intense as in simple œdema, only, instead of an albuminous serum, it is lymph which fills the lacunar spaces of the derm.

This stagnation of the lymph dependent upon the impermeability of the lymphatic glands which have usually become fibrous, frequently occasions the appearance of varicose lymphatics in the skin. The œdematous induration observed in these cases has been considered, by several dermatologists, as a variety of elephantiasis. This name may be retained, if it is applied to every chronic inflammation or induration of the skin as a generic term.

Sect. III.—Hemorrhages of the Skin.

In the skin, as in other tissues, hemorrhages may be occasioned by rupture of the capillaries, or by the passage of the blood corpuscles through their delicate walls; the latter phenomenon is termed diapedesis.

Hemorrhages caused by incisions of the skin or the division of large vessels will not be here considered; only interstitial hemorrhages and their evolution will be described.

When, as a consequence of a contusion, the small vessels of the skin are ruptured without tearing the derm, the red and white corpuscles of the blood infiltrate the connective tissue. There results a hemorrhagic focus of irregular outline. When the extravasation is large in amount in a circumscribed area, the blood separates the fasciculi of the derm, infiltrates the subcutaneous adipose tissue and forms a blood tumor (hæmatocele).

In other cases, under the influence of systemic diseases, of which scurvy is a type, the exanthemata and purpuræ being well-known examples, the hemorrhages spontaneously take place by diapedesis, and their distribution is probably determined by a special nerve paralysis.

The blood, once escaped into the tissue of the derm, undergoes retrograde changes. The blood plasma is first rapidly absorbed. The coloring matter of the red corpuscles is afterwards changed into hæmatin, the hemorrhagic spot having now a dark tint; the broken-down corpuscles are taken up and transported by the migrating cells and are deposited as pigment in the neighboring lymphatic glands, or in the protoplasm of the fixed cells of the derm. In this manner there results, in regions of the skin which have been the seat of hemorrhage, a brownish or yellow tint, which remains for a variable period, which does not disappear by pressure, and which serves as a diagnostic sign of previous hemorrhages.

With respect to that singular form of cutaneous hemorrhage called *hæmathydrosis* or blood sweat, but little is known anatomically. It forms in drops which seem to exude from the orifices of the sweat glands. It is supposed to come from the vascular network enveloping their glands.

When the blood breaks through the rete mucosum, elevating the epidermis into bullæ, or penetrates already-formed bullæ (hemorrhagic pemphigus, etc.), it experiences the same changes as if it were in contact with the air; it coagulates in a short time, and forms with the elevated epidermis a scab, which subsequently disappears by desquamation.

Sect. IV.—Diffuse Inflammations of the Skin.

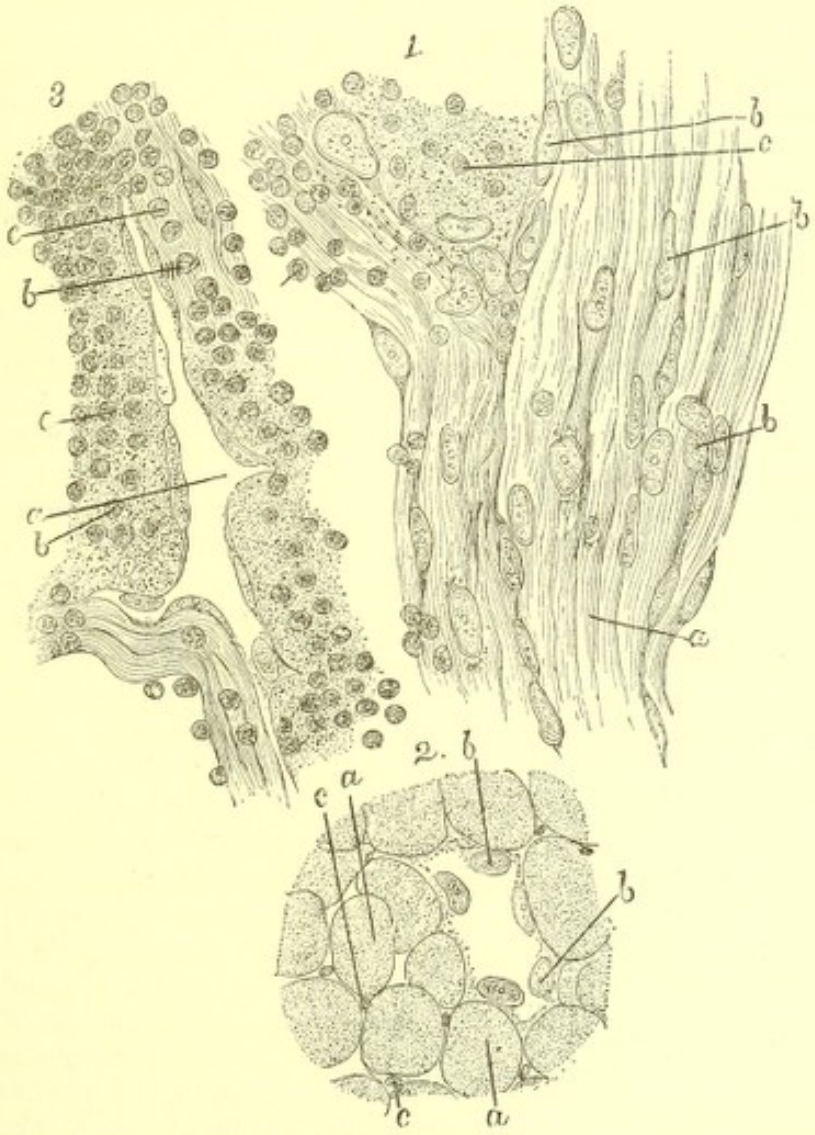
Diffuse inflammations of the skin are those which have spread over a large surface of this membrane. *Circumscribed inflammations* occupy only very limited parts, and their evolution throws a certain light upon the pathological anatomy of the principal elementary lesions of the skin.

A. Congestive Inflammation of the Skin, Acute Dermatitis.—As a type of dermatitis, we take one of the most frequent inflammations of the skin—*erysipelas*, which seldom passing to suppuration, permits us

to follow step by step, from its beginning to its complete recovery, the process of congestive dermatitis.

When the skin attacked by erysipelas is incised, it is found thickened, engorged with fluid, and lying upon a firm adipose tissue, which sometimes appears as compact as congealed fat; the serum which flows from

Fig. 350.



1. Proliferation of the fixed connective-tissue cells of the skin in erysipelas. *a*. Connective-tissue fibres. *b*. Connective-tissue corpuscles in process of division; they are much more numerous than normal; in some a large vesicular nucleus is hour-glass in shape, ready to divide; in others the nucleus has divided. *c*. White blood-corpuscles, in some places they are imbedded in the granular exudation. 2. Transverse section of a lymph capillary of the fibrous tissue. *a*. Transverse sections of connective-tissue fasciculi. *b*. Endothelium with large vesicular nucleus moulded upon the irregular surface of the lymph space. *c*. Connective-tissue corpuscles. 3. Lymph capillary (enlarged lymph space) of the derm in the beginning of erysipelas. *a*. Lumen. *b*. Endothelium. *c*. Leucocytes collected around the lymph spaces and imbedded in a granular exudation. High power.

the cut surface is very slightly fibrinous, contains numerous white corpuscles and a few red corpuscles, also some connective-tissue cells, the protoplasm of which has become active and granular.

Upon thin sections, it is seen that the derm is infiltrated with white

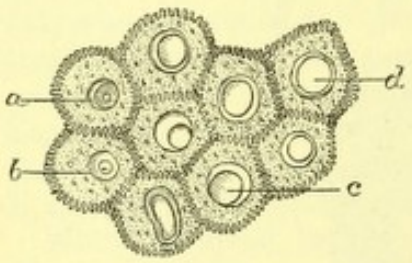
blood-corpuscles (Vulpian), which are usually placed along the course of the bloodvessels (Volkmann and Steudner). At points where the erysipelas is in course of development, that is, at the margin of the œdematous swelling, the transverse section of the vessels appears surrounded by a circle of white corpuscles, while in the meshes of the derm only a few are found.

Another locality for the collecting together of the infiltrating white corpuscles is the neighborhood of the lymphatic capillaries (lymphatic spaces of the derm). At the same time that the white corpuscles are accumulating around the connective-tissue spaces, the endothelia in some of the lymphatic clefts are seen swollen and granular, their nuclei divide, and the cells desquamate (fig. 350). In other points the lymphatics are filled with embryonic cells, resembling those which have infiltrated the derm, and they appear, in longitudinal section, as long tortuous cellular bands.

Later, the subcutaneous lymphatics in the adipose tissue are filled with migrating cells, which also are abundant around the vessels and even in their walls. Generally in intense congestive inflammation the cellular infiltration extends into the panniculus adiposus, and separates its vesicles. This infiltration is the principal cause of the induration of the skin.

The circuit of these changes is that the white blood-corpuscles escape out of the vessels by diapedesis, with a slight fibrinous transudation; they spread into the meshes of the derm; afterwards to pass to the lymphatic radicles, to be taken up by those vessels, which carry them to the veins. This is the process of œdematous inflammation, and it is probable that the evolutions of the wandering cells are but slightly different in acute œdema of the skin, of which papulous erythema furnishes a type. But besides, in congestive inflammation, there is seen a proliferation of the fixed conective-tissue cells; the nuclei divide, they are surrounded by a granular and active protoplasm, and contribute to the production of the embryonic elements which fill the derm. In congestive dermatitis this tendency to the proliferation of the fixed cells is much less marked than is the phenomenon of infiltration by diapedesis. From this circumstance, resolution usually may take place without leaving in the skin any appreciable trace of the inflammatory process. The red blood-corpuscles infiltrated into the derm at the same time as the white corpuscles, undergo the same changes as in ecchymoses, and cause the formation of a yellow spot, which disappears some time after the inflammation. From the effects of inflammatory congestion, the cells of the rete mucosum are also changed in their vitality, the nucleoli are enlarged (fig. 351), compressing and atrophying the substance of the nucleus, and the cells die in consequence of this atrophy; they do not secrete the cement-substance which in the normal skin joins them to the neighboring cells,

Fig. 351.



Epithelial cells, from the rete mucosum, during slight irritation. Spinous cells of the epidermis, the nuclei of which have become vesicular by a dilation of the nucleolus; *a*, normal nucleus and nucleolus; *b*, dilated nucleolus; *c*, *d*, a more advanced stage of the same alteration. High power.

and there is a desquamation of the epidermis. Phlyctenules and abscesses which may succeed congestive inflammation of the skin will be described further on.

In this variety of inflammation, the congestion plays an important part. It is accompanied with an exudation, which constitutes the inflammatory œdema and contains a varying amount of fibrogenic substance. But the exudation is not ordinarily deposited in the meshes of the derm, as occurs in the following variety of inflammations.

B. EXUDATIVE INFLAMMATIONS OF THE SKIN. *a. Suppurative Dermatitis, Simple Phlegmon of the Skin.*—This constitutes a rare termination of diffuse inflammations, and when it occurs the suppuration of the derm does not take place over large surfaces, but in foci more or less scattered. Each of the small dermic abscesses is similar to that produced in the skin around a foreign body—around a seton, for example.

In some inflammations, when suppuration occurs the cells are seen in places to accumulate in the meshes of the derm. The cells come either from a diapedesis of the white blood-corpuscles, or from a division of the fixed cells; they become fatty degenerated, and are but slightly colored with carmine. These cells are dead, and constitute small foreign bodies in the skin. Generally they are collected into foci at varying distances from the surface, while the surrounding fundamental substance (elastic fibres and connective-tissue fibres) of the derm is absorbed. Thus results a small cavity filled with pus, excavated in the derm. Surrounding it there exists a congestive inflammation of the connective tissue. The bloodvessels and especially the arteries of small calibre, are secondarily inflamed; endarteritis diminishes the calibre of the vessels, and in consequence the amount of blood to the part is lessened. The purulent focus is enlarged at the expense of the surrounding slightly vascular tissue, and when it reaches the surface ulceration occurs.

The method of formation of granulation tissue at the cutaneous surface, and the process of cicatrization have been considered (pages 69, 71). According to the investigations of Reverdin, the presence of transplanted epidermic cells upon a granulating wound of the skin occasions an active reproduction of the epithelium around the grafted cells. The epidermic cells appear to act, not by multiplying through division, but by their presence, which causes, as it were, an epidermic evolution of the surrounding embryonic cells, for the graft does not itself show any signs of activity, but is soon destroyed in the midst of the new epithelial tissue which it has caused to be developed.

b. Fibrinous Dermatitis; Diffused Phlegmon of the Skin.—This inflammation does not differ from that described under purulent inflammation of the connective tissue at page 253. At the same time there is an abundant cellular infiltration between the connective tissue fasciculi of the derm, a delicate fibrinous reticulum is seen which incloses in its meshes the wandering cells. Sometimes fibrin is exuded in abundance, and there is produced a very rapid necrosis of the derm. This is very marked in malignant pustule. Carbuncle is only a milder degree of this variety of gangrenous dermatitis. It occurs over large surfaces; is accompanied with a fibrinous exudation, which distinguishes it from simple

œdema; and it very soon terminates in mortification. When the latter takes place, the entire derm is infiltrated with granular fibrin and granulo-fatty embryonic cells. In the subcutaneous tissue, the fat of the adipose vesicles breaks up into small free fat drops, scattered in the interstices of the tissue; or there may be formed, during life, the characteristic crystals of fatty acids, similar to those generally found in the adipose tissue of the cadaver.

c. Pseudo-Membranous Dermatitis; Cutaneous Diphtheritis.—Cutaneous diphtheritis has not been studied as a special lesion; we will, therefore, refer for its consideration to page 65, where diphtheritic exudations have been studied generally. We have been able to demonstrate that the branching cells, having undergone the colloid transformation which has been described by Wagner, are found in the false cutaneous membranes. The nature of diphtheritis consists more in lesions of the epithelium than in changes in the connective tissues which support them; and if the mucous membrane of the pharynx can be compared with the skin, there is simply a diffused inflammation under the diphtheritic exudation.

C. Chronic Diffused Inflammations of the Skin.—When repeated inflammations occur in the skin, or, what is the same, there is a prolonged chronic œdema, the irritative process, maintained for a long time, occasions in this membrane chronic inflammations. Frequently a local inflammation, such as an ulcer, or an inflammation of a special nature, as eczema, after a time excites around it a zone of chronic inflammation of the derm, which progresses according to its special mode of origin and the morbid tendencies of the patient.

1. *Fibrous Hypertrophic Dermatitis.*—In this variety, which frequently follows prolonged irritations of the skin (especially varicose ulcers, chronic eczema of the legs, etc.), the derm is thickened, and the fibrous fasciculi composing it are more numerous and denser. The stellate lymph spaces form, in sections transverse to the direction of the fasciculi, large stellate spaces lined with endothelium. With this hypertrophy of the derm corresponds a relative atrophy of the papillæ. The epidermic layers are thin, and the nuclei of the cells are frequently atrophied by the dilatation of the nucleoli, whence there is an almost continual desquamation from the surface of the skin so inflamed. The subcutaneous adipose tissue, blended with the derm, is hard, because the adipose cells have proliferated in such a manner that each fat vesicle is diminished in size, and surrounded by a circle of embryonic cells. This change is termed lardaceous, and is especially evident around old ulcers.

2. *Papillary Variety; Diffused Papilloma of the Skin.*—This chronic inflammation of the skin is generally observed in localities which have been the seat of repeated œdemas, notably on the instep and around the ankle in persons with chronic heart disease. Some writers, particularly Virchow, have considered it a special variety of elephantiasis (*E. verrucosa*). It has been described by Hardy as hypertrophic lichen, in which the disease sometimes ascends as far as the knee, and is frequently accompanied by chronic varicose veins. The papillæ are at times enormous, and each is covered with a corneous layer, so that they

resemble the papillæ upon the tongue of a ruminating animal. Usually the skin is considerably thickened, wrinkled, and folded. In sections from the skin, in which the lymphatics have been injected, and colored with picro-carmine, the papillæ are seen enormously enlarged, formed of embryonic connective tissue (mucous tissue) analogous to that forming the Whartonian jelly, in which run delicate vessels and lymphatics, without special walls, as simple lacunæ lined with endothelium. In the derm the meshes are filled with embryonic elements, and the small cells at many points are undergoing division; generally an innumerable number of newly-formed capillaries are seen. These embryonic vessels are especially abundant in the deep parts of the skin around the sudorific glands.

This abundant formation of new vessels is especially seen after chronic œdemas. In the interior of the derm, the lymphatic capillaries are also much dilated, and gaping upon section.

The preceding form of diffusive dermatitis constitutes one of the varieties of elephantiasis Arabum. Very different chronic inflammations, however, have been classed under this name. The general law of development of elephantiasis is not yet determined; but it is known, that when congestive inflammations are repeated, or prolonged, or frequently return, as in erysipelas or œdema, the skin becomes hypertrophied, and an elephantiasic swelling is produced. In every case which we have seen during seven years, the only constant lesion has been dilatation of the lymphatic capillaries; the variety of chronic dermatitis has varied considerably.

3. *Elephantiasis Arabum.*—It is seen from the foregoing descriptions, that chronic diffuse dermatitis, whatever may be its cause, has a tendency to occasion hypertrophy of the skin.

a. If œdema has continued for a long time, there is produced, over a large extent of surface, an indurated engorgement, due to stasis of the lymph in the connective tissue spaces, in the dilated lymphatic capillaries, and in the afferent lymphatic trunks of the glands. The latter are transformed into impermeable fibrous tissue, and they exert considerable influence in the production and in the continuation of elephantiasic dematitis (lymphangiectatic pachydermia of Rindfleisch; lymphatic elephantiasic œdema). This variety is secondary to repeated œdemas, and is not unfrequent in the lower extremities of persons with chronic heart disease. Its most frequent seat is the skin of the scrotum, penis, and prepuce.

b. A second variety is characterized by a return to the embryonic state of the entire hypertrophied derm, with the formation of large lymphatic lacunæ in the granulation tissue into which the skin has been transformed. This variety has been briefly described under lymphangiomata (see p. 141, fig. 105). The seat is also, like the preceding variety, usually upon the genitals (skin of the penis, clitoris, labia majora).

c. A third variety has been described, and consists in an enormous increase in thickness of the derm, due to a multiplication of the connective tissue fasciculi and elastic network; frequently the smooth muscular fibres disseminated in small numbers through the derm, according to some pathologists, considerably increase in number and form in the deep parts of the skin superimposed layers of fibres running in different direc-

tions. As in the other varieties of elephantiasis, the lymphatic capillaries are dilated, engorged with lymph or stuffed with desquamated endothelium, and are widely gaping. Generally in these cases the skin is reddened, wrinkled, and projects in ridges, but presents no wart-like excrescences. Clinically this variety of elephantiasis is termed *smooth or glabrous elephantiasis*. But when the thickening of the skin is accompanied with papillary hypertrophy and new vascular formations (diffused papillary or vascular dermatitis), the elephantiasis is said to be warty (*E. papillaris seu verrucosa*). When the papillæ formed of embryonic tissue or of mucous tissue are enormously developed, as in *hypertrophic lichen*, the elephantiasis is named *E. tuberosa seu nodosa*. The ulceration upon the surface of the skin occurring in the different varieties of hypertrophy is termed *ulcerous elephantiasis*. [E. arabum is believed by some writers to be caused by the presence, in the lymphatics, of a species of filaria.]

Scleroderma.—Scleroderma has incorrectly been classed with elephantiasis. It is an atrophic disease of the skin, a true cirrhosis. The fundamental substance of the derm (connective-tissue fasciculi and elastic fibres) is greatly increased; the subcutaneous panniculus adiposus is chronically inflamed, and is finally transformed into fibrous tissue, and becomes hardened through the organization of the embryonic tissue interposed between the adipose vesicles, and through the absorption of the latter. According to Lagrange and Duret the vessels are contracted and compressed by the newly formed fibrous tissue. The epidermis, thin and transparent, is reduced to two or three layers of cells, and at the finger pulps, where they ordinarily attain considerable size, the projecting papillæ are much smaller or are completely effaced. This lesion begins in the skin; but the atrophy, extending to the bones, which it causes to disappear, and to the nerve trunks, which it alters in various ways (peri-neuritis—interstitial neuritis) is not without analogy with certain lesions of the integument, termed trophic. In paralysis, however, one of the varieties of elephantiasic œdema supervenes secondary to the nerve lesion, and not an atrophy, like that of scleroderma. The latter disease is often complicated with pemphigus-like bullæ, and ulcerations upon the altered surfaces, which may be due to the lesions of the nerves, and inflammatory changes of the vessels.

Sect. V.—Circumscribed Inflammations of the Skin.—Pathological Anatomy of the Principal Elementary Lesions recognized in Dermatology.

Inflammation, inflammatory œdema, and the phenomena of ulceration, instead of occurring over large surfaces, may be circumscribed. In this case, local lesions are produced, which macroscopically assume ordinarily one of the types usually described by dermatologists under the name of *elementary lesions of the skin*.

a. Congestive Localized Inflammation of the Skin, Papule.—When a congestive inflammation, instead of extending, is limited to a

small surface, it forms a red and circumscribed pimple termed a papule, of which the variolous papule preceding pustulation is a type. A vertical section of such a lesion shows the skin to be altered as in any congestive inflammation. The connective-tissue spaces are filled with young elements, and the vessels are surrounded with embryonic cells. The elevation is due to the local inflammatory œdema.

After some time the papule usually sinks, the epidermis upon its surface undergoes a slight desquamation, and, if examined histologically, the derma is found to be almost normal. This complete disappearance of the lesion occurs even in psoriasis, a papulo-squamous form of a cutaneous affection, in which the circumscribed inflammation causing the papule exists chronically, as it were, and from time to time has periods of exacerbation. In the papule of psoriasis, the cellular infiltration and œdema especially affect the papillæ, immediately beneath the rete mucosum: in the latter layer, evolution then becomes very active, and the dilatation of the nucleoli rapidly occasions atrophy of the nuclei; the epidermic lamellæ, which are continually renewed, desquamate in great numbers in the form of silvery scales. When psoriasis long continues in a portion of the integument, it occasions a hypertrophy of the papillæ and a dilatation of the vessels (Neumann). There is seen in this lesion a tendency to hypertrophy as in chronic dermatitis.

In *Prurigo* and *Lichen* where the papule has also a very prolonged existence, the papillæ are elongated and considerably enlarged; the inflammation is not so superficial as in psoriasis; the localized chronic dermatitis causes thickening of the derm, and, according to H. Derby, frequently also lesions of the hairs, increase in the number of smooth muscular fibres of the derm, as well as the accumulation of lymph in the interstices of the connective tissue. Hence, each papule of prurigo or lichen presents the structure of a small nodule of elephantiasis.

b. Lesions of the Epidermis in Circumscribed Inflammations of the Skin: Bullæ and Blisters.—When the inflammatory œdema at any point is of such intensity that the tension of the fluid is so great as to overcome the resistance of the epidermis, the latter yields and is elevated into the form of a blister or bulla. These two elementary lesions differ only in their size; the process of their formation is identical.

The point of least resistance of the epidermic layers is the granular layer, lying between the epidermic cells united by keratin and the spinous cells of the rete mucosum intimately united together. It is at the level of this granular layer that the epidermic layers yield and are separated. The fluid of inflammatory œdema is now collected into a bulla, and contains white blood corpuscles (wandering cells), a very few red disks, and a fibrinogenic substance which forms a fibrinous reticulum inclosing the cellular elements. The deeper layers of the rete mucosum are infiltrated with the migrating cells which subsequently penetrate into the bulla, and which are identical with those infiltrating the papillæ.

In some varieties of herpes (*hemorrhagic zoster*, *gangrenous zoster*), it is almost pure blood which fills the vesicles; in neuralgic zoster there are always found one or more vesicles having a sanguineous color (Lallier).

The evolution of a pemphigus bulla or of a blister is very simple. The

escaped fluid, containing living corpuscles, is at first clear and of a slightly yellow color. In a short time the white blood corpuscles die, and the contents of the blister become opalescent like diluted pus. Generally, the external part of the blister formed by the elevated epidermic cells is softened by imbibition of the subjacent fluid. The fluid escapes through a fissure, and the epiderm falls upon the surface of the rete mucosum; new epidermic layers are formed, and the lesion entirely disappears. This mode of repair, however, does not agree with that given by Langerhans, who considers the granular zone as the formative organ of the epidermis, for in the blister this granular zone is elevated and afterwards destroyed without there resulting any abatement in the formation of the epidermis. Neither does our description agree with that given by Neumann, who recognizes in the interior of the blister the existence of a reticulum formed by stellate and anastomosing cells—a modification of epidermic cells.

Vesicles.—The vesicles of eczema—those which form upon the surface of an erysipelatous skin, or those produced artificially by Croton oil—are formed by a process very different from the foregoing. They are formed in the substance of the rete mucosum. In the protoplasm of the spinous cells are developed highly refracting opalescent globules, not colored by carmine; as they increase, they push the nucleus to the periphery. The cells are transformed into enormous vesicles which open one into the other, forming a partitioned anfractuous cavity in the middle layer of the rete mucosum. In this cavity are found epidermic cells with several nuclei, besides wandering cells from the vessels having the characters of white blood corpuscles. In time, the cellular elements undergo fatty degeneration, and sometimes the fluid of the vesicle, which at first is clear, becomes yellow and opaque. This transformation is very distinct in rheumatic miliary eruptions, in sudamina, and in the vesicles of varicella, which are only different varieties of vesicles.

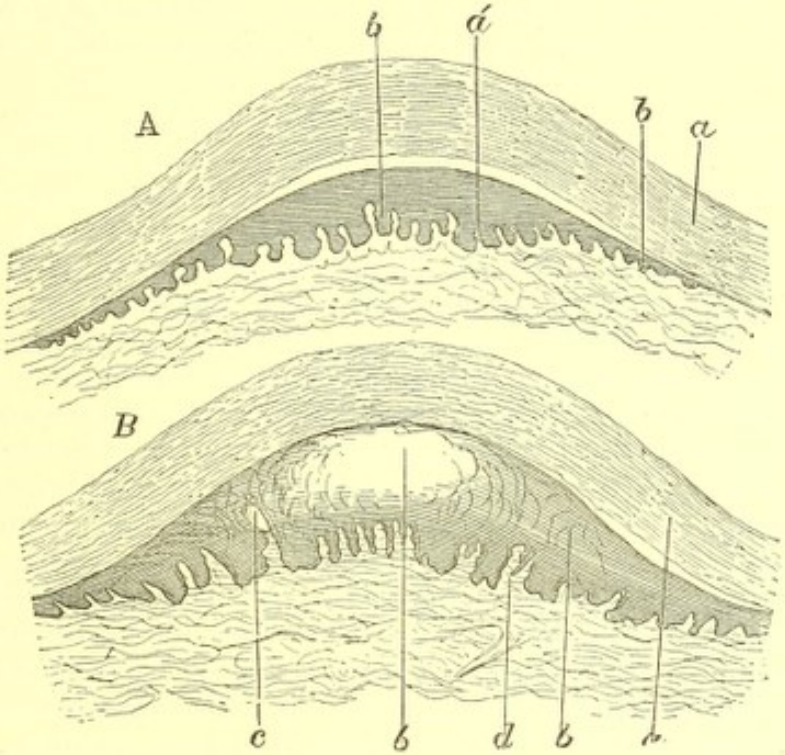
In eczema, this transformation of the very small and numerous vesicles does not take place before they break and discharge a serous fluid. But if the exuded fluid is kept in contact with the skin, by enveloping the latter in an impermeable cloth, in about twenty-four hours the fluid has all the characters of pus. The lesions produced in the derma by chronic eczema do not differ from those following chronic dermatitis.

Pustules.—The process of the formation of pustules has a very close analogy with the preceding. The evolution of the pustules of variola may be taken as a type. (Fig. 352.)

A papule of variola, examined on the fourth day, presents the characters of a congestive inflammation of the derma. Soon, in the middle of the epidermis, the spinous cells become distended by mucous masses forming in their protoplasm, transforming the cells into vesicles which open into each other, and forming an anfractuous cavity which contains white blood corpuscles and epidermic cells with several nuclei. If the vessels of the derma are injected with Prussian blue, soluble in water, the coloring substance is diffused to the neighborhood of the vesico-pustule. This formation is associated with a softening of the vessels, which very readily permits diapedesis. (Fig. 353.)

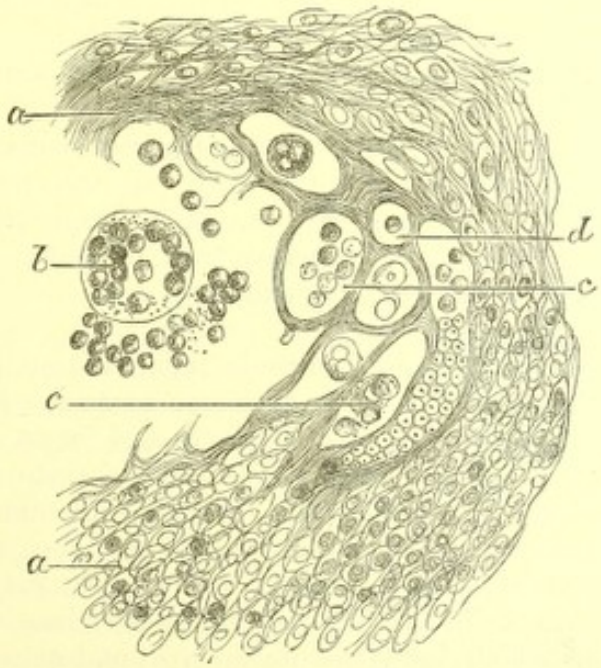
When suppuration occurs, the swollen epithelial cells are set free and enter in great numbers into the cavity of the pustule; the white corpuscles

Fig. 352.



A. Section of variolous vesicle. *a*. Layer of epidermis. *b*. Rete mucosum deepened at the location of the pustule. *d*. Papillary layer. *B*. Variolous pustule at a later stage; the letters have the same significance as in the preceding. Low power.

Fig. 353.



Vertical cut of the rete mucosum at the location of a variolous pustule. *d*, *c*. Cavities caused by the vesicular state of the cells, and, at the same time, filled with pus corpuscles. *a*, *a*. Epithelial cells. *b*. Mother cells containing pus corpuscles. × 200.

pass out of the bloodvessels and penetrate the altered epidermis. The vascular loops project from the floor of the pustule as far as the extreme limit of the derm. The papillæ are deprived of their epithelial covering, and the tissue of the derm attacked with diffused inflammation is changed into embryonic tissue. With the pustule there is a more or less complete destruction of the papillæ, which explains why in variola there is left a permanent mark, while a blister and vesicle leave no trace.

The anfractuous cavity of the pustule is partitioned by anastomosing filaments, the arrangement of which at first sight appears similar to that of the delicate connective-tissue fasciculi of reticulated tissue. A number of the filaments are arranged in the form of arches; they are the remains of the ruptured cells of the rete mucosum, which have become vesicular and have opened one into the other. The trabeculæ thus formed by the remains of the cells exist only in the cavity of the pustule; but very fine filaments are seen reaching from the derma to the epidermic layer, which forms the roof of the pustule. From the top of each denuded papilla, projecting from the floor of the pustule, arise a number of these filaments, which at first seem to be continuous with the fibrils of the papillary connective tissue. This is, however, not the case, for it is known (Ranvier) that the fundamental substance of the connective tissue terminates beneath the rete mucosum by a series of serrations destined to receive the processes of the spinous cells, and the derm does not send into the epidermis any fibrillar prolongations. The network which has just been described as always existing, possibly represents the cement substance (Kittsubstanz) between the cells of the rete mucosum. It has, contrary to the opinion of some writers, no part in the umbilication of the pustule. When this umbilication exists, it is caused by the centre of the elevation being riddled by a partitioned cavity, while the pustule continues to increase at the periphery (Fœrster). The epidermic cells at the periphery being swollen, there results a comparative projection in the form of a circular elevation.

The hairs and glands take no part in the formation of pustules in variola (Charcot). Cicatrices exist only in the variety of pustules termed diphtheritic, and in which there is produced a true necrosis of the derm, consecutive to the infiltration of fibrin or of pus into the meshes of the latter. This occurs in confluent variola. The simple pustules, those of impetigo, for example, do not leave any trace of their existence, since the derm has not sphacelated beneath them.

Tubercules.—When a limited chronic inflammation extends into the deep portions of the derm, the latter first returns to the embryonic state, then elevates the superficial parts of the skin and forms a nodule, which to the touch has the feel of a *deep circumscribed induration*. In dermatology this is termed a tubercule. Its structure has been described under the affections in which it is developed—*syphilis*, *scrofula*, *glanders*, etc. A tubercule, whatever may be its nature, may ulcerate, may change into a fibrous nodule, or may become gangrenous, according to the systemic conditions which influence its growth, and cause a tendency to reparation, to new formations, or to gangrene.

Circumscribed Peri-glandular Inflammations. — Circumscribed peri-glandular inflammations frequently occur in the skin, as the result of an accumulation of the products of secretion in the interior of the gland or in its excretory canal. This is seen in *sudamina*, in the principal varieties of inflammatory acne, and in pustules which form around the hairs in inflammatory sycosis, or in the variety termed arthritic by Bazin.

Sudamina.—When the sweat is produced in excessive quantity, as occurs in acute articular rheumatism, or in some fevers, there appear upon the surface of the skin small blister-like elevations, at first containing transparent contents. The reaction of the fluid in these small elevations, is at the beginning distinctly acid (Lailler), which distinguishes it from all other morbid secretions. Neumann, on the contrary, asserts that its reaction is alkaline.

The contents of the sudamina consist of white corpuscles, identical with those of the blood, which are so numerous that in a drop of the fluid taken from the small blister they appear to touch one another. But in about twenty-four or forty-eight hours those sudamina which have not been emptied by spontaneous rupture, have become opaque or yellow. Their contents are alkaline, as all purulent fluids, and the suspended white corpuscles have become fatty granular; that is, they are transformed into pus corpuscles. A section of a recent sudamina through the orifice of the sudorific gland shows the epidermic cells accumulated in this opening, and slightly elevating the corneous layers. A section of a completely developed sudamina shows at the orifice of the glandular canal, and in the rete mucosum a very small blister, above which the layers of the epidermis form a roof, and in which closely packed white corpuscles are inclosed. It is probable that the fluid in which these corpuscles float is sweat, since it always has an acid reaction.

Acne Pustule; Phlegmonous Inflammation of the Sebaceous Gland.—This is secondary to the distension of the sebaceous gland, which becomes cystic, and is filled with epidermic cells united at the periphery and softened at the centre. Around the cystic gland, the contents of which constitute a foreign body in the skin, there is produced a slight congestive dermatitis, and, finally, the inflammatory induration of an acne pustule. Embryonic cells accumulate about the gland. At the same time around the obstructed glandular orifice, there are lesions of the rete mucosum similar to those which accompany the development of the variolous pustule; the epidermis finally ruptures, and the glandular contents (comedone), bathed in the pus of a small peri-follicular abscess, may be squeezed out by pressure. Termination by induration frequently occurs in this lesion; there is now produced around the gland a chronic inflammation, in every way identical with that which is seen around sebaceous cysts or wens. When the glands are close together, as upon the nose, there is frequently developed a *hypertrophic acne*. Each gland is surrounded at its periphery by a zone of embryonic tissue, which gradually is organized into fibrous tissue, while a new layer of indifferent cells is formed between the fibrous tissue, and the sac of the follicle. At the same time the vessels of the gland become varicose, and new ones are developed in the recently formed tissue separating the glands. These changes result in exuberant productions, termed in dermatology

molluscum sebaceum, and sometimes becoming very distinctly pedunculated.

The inflammation occurring around the hairs in *eczema* or *pityriasis pilaris* occasions the production of pustules (pustules of sycosis). The latter have for their origin the accumulation of the epidermic cells in the sheath of the hair, and the process of their formation does not differ from that of the acne pustule.

Inflammation localized around the sudorific glands has been considered as the cause of ecthyma, furuncle, and anthrax, but this is difficult to prove. In the skin spontaneously or artificially inflamed the epithelia of the gland proliferate, and inclose numerous embryonic cells. In the loose connective tissue surrounding the gland, there is also an infiltration of cells. Finally, the adjacent portions of the body of the gland open into each other and form a cavity. The disappearance of the sudorific glands is thus caused by a chronic inflammation of the skin.

Sect. VI.—General remarks upon the different tendencies and the various modes of Evolution of Cutaneous Inflammations.

It has been seen that inflammations of the skin have a great tendency, in many cases, to return to the *congestive variety*, of which erysipelas is the type. Diffuse suppuration of the skin almost never occurs. The type of *suppurative dermatitis* is the pustulous inflammation of variola, which occurs at more or less distant points. On the other hand, *hyperplastic* inflammations of the skin are frequent, as are also the *degenerative inflammations*, and they occur more frequently in the general diseases, of which they are the local manifestations, and from which they receive a peculiar impress.

1. Hyperplastic Inflammations; Formative Dermatitis.—It is known that prolonged irritation of the derma ends in the production of a hypertrophic dermatitis, and in new formations approximating tumors (diffused papillomata of the skin). This tendency to the formation of fibrous tissue is never more marked than in syphilitic inflammations of the skin, and the latter may be considered as the best types of formative dermatitis.

a. Syphilitic Papule.—At the beginning it cannot be distinguished from a simple inflammation. But very soon the papillæ of the skin are hypertrophied, the derma is thickened, and there is a new formation of connective-tissue fibres and elastic network beneath the papillary eminence. The subcutaneous adipose tissue becomes embryonic (Neumann), and the sudorific glands are inflamed. In very old syphilitic papules which are about disappearing, the congestive infiltration of the derma by white corpuscles no longer exists, and the lesion consists only in an enlargement of the papillæ and a greater thickness of fibrous tissue.

b. Syphilitic Tubercule.—In this lesion, frequently confounded with cutaneous gumma, the tendency of the syphilitic inflammation to produce fibrous tissue is still more evident. The syphilitic fibroma forms a nodule

in the derma; all around it there exist small collections of embryonic cells between the separated connective-tissue fasciculi. In the middle of the nodule the newly formed tissue is very similar to that of tendons, while at the periphery it resembles a sarcoma, except in containing numerous elastic fibres. The specific inflammation occasions, in the proximity of the tubercule, a very marked endarteritis, which causes the calibre of the vessels to be considerably narrowed. This narrowing probably has some influence in the production of ulcers. The tubercule deprived of vessels at its centre, and very poorly supplied at its periphery, rapidly undergoes a slow molecular softening, and opens externally as an abscess. The loss of substance is filled up with granulation tissue, and cicatrization takes place by the usual process.

c. False Keloid.—Sometimes localized pustular inflammations of the skin occasion a secondary chronic formative inflammation. Consecutively to variola, to the application of irritating ointments (Croton oil, tartar emetic), or to the existence of pustular syphilides, true fibromata of the skin, which have the homogeneous appearance of a tendon, may be developed. Surrounding the nodule formed of closely packed fasciculi, between which are numerous elastic fibres or elastic plates analogous to those developed so abundantly in fibrous carcinoma, there is a zone of embryonic tissue. This tissue is especially evident in the papillæ, which are enlarged, consist of embryonic tissue, and contain embryonic vessels. In the interior of false keloid the veins are frequently dilated into large irregular sinuses. The epidermic layers are thin, and desquamation is active upon the surface of the fibrous nodule. True or spontaneous keloids, which are true fibromata of the skin, do not essentially differ anatomically from false keloids.

2. Degenerative Inflammations; Specific Ulcers of the Skin.—In inflammations of the skin due to tuberculosis, to glanders, to leprosy, and to scrofula, the newly formed tissues die and degenerate in several ways; usually they undergo *caseous* (tuberculosis, scrofula) degeneration, or there is produced a true gangrene (glanders, etc.).

a. Tuberculous Ulcers of the Skin are a very unfrequent manifestation of tuberculosis. When they do occur, they are most frequently accompanied with tuberculous granulations in the skin, in the subcutaneous tissue, and between the primary fasciculi of the muscular layers immediately subjacent to the integument. The evolution of these granules is the same as tuberculous granulations in the tongue (see page 454). Around these granules the derma and subcutaneous tissue are ininvaded by a diffuse inflammation. The muscles near the skin (it is ordinarily upon the face or about the anus that these tumors are observed) are the seat of a destructive inflammation; the contractile substance disappears, while the nuclei divide, multiply, and fill the sarcolemma. In a short time the embryonic cells, which have accumulated in the different tissues, undergo fatty degeneration, and form caseous points. The vessels are obstructed by clots which become granular, and, as a consequence of the disintegration of the parts which they supply with blood, an ulcer is produced.

This ulcer does not granulate; it rests upon a thickened, degenerated

tissue, and extends by the molecular destruction of its base and edges. The granulations, and the inflammatory zone surrounding them, being completely degenerated, the recognition of the granules becomes impossible, and anatomically the ulcer is simply caseous. The process is comparable with the evolution of tuberculosis of the lung or of the mucous membrane.

b. Dermatitis of Glanders; Farcy Granules.—In man the cutaneous lesions of glanders are profusely suppurative; but in chronic farcy of the horse the farcy granule constitutes a degenerative variety of dermatitis. There is first produced a localized inflammation in the deep parts of the skin, and the formation of a nodule, consisting of embryonic cells. This focus, round or stellate, varying in size from a pin-head to a hemp-seed, is surrounded by a hemorrhagic areola, in which the blood separates the fasciculi of the derma. This primary lesion is surrounded by a secondary zone of very intense diffuse inflammation, so that in a short time the fundamental substance is absorbed, and the skin at the diseased point has the appearance of round-celled sarcoma. A nodule of glanders differs from a tuberculous granulation in being formed of very active cells which are not united together, and in not projecting above the cut surface. Besides, it is deeply colored by carmine in the central part, while tubercles are not. The cells which compose it have proliferating nuclei, and present none of the signs of the degeneration which is so early characteristic of the cells of gummata and tubercles. The cutaneous lesion of glanders may be considered as an inflammation of a special variety, and not as a tumor. Beside the hemorrhagic zone which surrounds the farcy granule, there are formed in the inflamed skin other blood foci due to the rupture of embryonic vessels. The arterioles of the granule are affected with endarteritis; their calibre is considerably narrowed, and ulceration is probably caused by the local anæmia and the presence of numerous interstitial hemorrhagic foci. The ulcer which results is atonic, and even gangrenous, on account of the intra-dermic hemorrhages. Surrounding the lesion are seen numerous lymphatic cords, which are somewhat characteristic of farcy granules.

c. Leprous Dermatitis; Cutaneous Tubercule of Leprosy. — By examining a recent tubercule of leprosy after teasing, it is found that the greater part is formed of flat connective-tissue cells having several nuclei, resembling giant cells. Upon section, it is seen that the fundamental substance of the connective tissue is destroyed, while the endothelial cells are multiplied. The appearance of the tubercule of leprosy is then very little different from a fascicular sarcoma. In a word, in this stage there is observed a formative irritation especially affecting the flat cells of the connective tissue.

At the same time, surrounding the tubercule of leprosy, there exists a diffuse inflammation of the derma, which extends in depth by rows of embryonic cells running towards the subcutaneous adipose tissue. The accumulation of embryonic cells, as in every chronic dermatitis, occurs at first around the vessels whose walls are thickened by endarteritis or endophlebitis. The vessels, however, ordinarily do not become embryonic as in the sarcomata.

As a consequence of the inflammation of the internal coat of the

vessels, there occurs in time an ischæmia of the leprous tubercule, the capillary network of which no longer communicates with that of the neighboring parts. The leprous neoplasm now undergoes granulo-fatty degeneration from the centre to the periphery, and may ulcerate like an atheromatous abscess. The hair follicles in the neighborhood of the lesion atrophy. The sebaceous glands, at first irritated by the chronic inflammation, are gradually destroyed. The sudorific glands also disappear, the destruction beginning in the excretory canals and extending downwards; this accounts for the dryness of the integument in a person affected with leprosy. Finally, the epidermis is very thin and smooth around the tubercule; it freely desquamates, even from the beginning, for leprosy commences in the skin as a macula. Beneath this spot the derma is inflamed and its vessels are dilated, causing permanent hyperæmia.

The nerves are primarily attacked by interstitial inflammation (Steudner). The tactile corpuscles disappear, or at least they cannot be found (Lamblin) in the finger pulps, where they are very numerous in the normal state. These changes connect leprosy with dystrophic affections of the skin which have their origin in nerve lesions, and account for the anæsthesia constantly present in this disease.

Sect. VII.—Dystrophies of the Skin.

A. Trophic Disturbances consecutive to Lesions of the Nervous System.—It is known that the nervous system exercises a direct influence over the nutrition of the anatomical elements. When the tissues are removed from this influence, their elements actively increase, as if from an individual impulse (see page 75, an experiment of Schroeder van der Kolk). There thus result aberrant formations, which generally have the type of inflammatory neoplasms of slow growth.

Cutaneous œdema very often is seen in the skin of paralyzed limbs, especially of the arms. The continuation of the œdema frequently excites a hypertrophic dermatitis, when the skin becomes warty. From time to time, there are also often seen upon the œdematous integument active congestions (erythema), which usually terminate by resolution, but sometimes are the origin of gangrenous spots.

The influence of nervous lesions upon the nutrition of the skin is well shown by the pathological histology of *perforating ulcer of the foot*. In this lesion it is found that the nerves of the skin in the proximity of the ulcer are the seat of a degeneration analogous to that met with in the inferior end of a divided nerve. The medullary substance breaks up into small drops, the nuclei of the interannular segments divide and cause a moniliform appearance of the nerve fibres. The axis cylinder has been destroyed, etc. Associated with the nerve lesions there is observed around the ulcer a zone of anæsthesia and of chronic inflammation. The cutaneous papillæ of the derma have become gigantic in size, resembling the subungual papillæ. They are long and slender, and contain vessels, and, if they are not entirely deprived of nerves, they at least contain but very few. The tactile corpuscles have generally disap-

peared. The bottom of the ulcer is formed of a disintegrating layer varying in depth, in which no detail of structure can be found. In the neighborhood of the ulcer the arteries show a chronic inflammation, and their calibre is contracted.

The changes in the epidermis covering the enlarged papillæ, consist in a thickening, at times enormous, frequently reaching several millimetres. The corneous cells are superimposed in thick layers, forming successive beds intimately united together. The nuclei of the cells in the rete mucosum, are not atrophied in the neighborhood of the ulcer; consequently desquamation does not occur.

As examples of cutaneous trophic disturbances, in which the influence of the nervous system has been evidently recognized, we cite the bullæ of zoster and pemphigus, in the neighborhood of which there is usually seen an inflammation of the nerves or rather an inflammation of the nerve sheath, or of the inter-fascicular connective tissue (Charcot, Bärengspung). Finally in some cutaneous lesions of leprosy Steudner has found lesions of the nerve fibres, more or less well determined.

B. Dystrophic Alterations of the Epidermis, and Analogous Epidermic Products.—The type of these alterations is found in the cachectic ichthyosis which occurs upon the surface of paralyzed limbs, and in congenital ichthyosis which is a true deformity of the skin.

In *pityriasic ichthyosis*, characterized by soft scales, there are found only the signs of rapid evolution of the cells of the rete mucosum. The nucleoli are enlarged, and the nuclei of many of the cells are atrophied; the cells are no longer closely united together, and they die before the epidermis acquires its normal firmness. From this process there results a constant desquamation.

Corneous ichthyosis is characterized by a superabundant formation of the epidermis, in spots. It presents a variety, *ichthyosis pilaris*, incorrectly termed pityriasis of the hairs. In this variety of ichthyosis the corneous epidermic layers are continually produced by the internal sheath of the hair follicle, and accumulate around its shaft in an imbricated manner. The hair follicle is soon stuffed with the corneous cone which surrounds the shaft, and the hair breaks off at the point of emergence. When the epidermis continues to accumulate, the small peri-pilar corneous mass excavates a cavity in the superficial portion of the derma; the skin now has a granular appearance. After a time, the hair and the corneous mass are thrown off, but the location of the intradermic cavity is marked upon the skin by a small variola-like cicatrix.

C. Abnormal Colorations of the Skin.—The abnormal colorations of the skin are numerous. The coloring matter of bile uniformly tinges all the histological elements of the tissues. In the skin it acts as an irritant, and usually occasions small congestive inflammatory points, and minute pruriginous papules. Frequently purpuric spots are also seen; they are due to the solvent action of the bile upon the corpuscles of the blood. Histologically, icteric purpura does not differ from any other interstitial hemorrhage of the skin.

The cause of the icteroid staining in cachexias (tuberculous, saturnine)

is not clearly understood. The coloration is sometimes bluish. The pigmentation of the rete mucosum is found to be more intense.

In Addison's disease the skin is not only pigmented in the deep layers of the rete mucosum, but frequently also in the derma. A transverse section of the skin in Addison's disease, shows not only the cylindrical cells of the rete mucosum which cover the papillæ loaded with pigment, as in the negro, but often dark pigment is also accumulated along the vessels of the papillæ, and in the fixed cells of the connective tissue. This is also observed in certain pigmentations from external causes.

Pigmentation produced by sulphate of lead is due to a metallic deposit, not in the cells of the rete mucosum, which are never colored, but in the fixed connective-tissue cells. The pigmentation is so abundant in the bands of connective tissue which accompany the vascular tufts of the papillæ, that it has been believed that the sulphate of lead is contained in the vessels. There is also found in the meshes of the derma a number of wandering cells loaded with dark granules of sulphate of lead (Renaut), and which probably play an important part in the process of pigmentation by transporting the colored granules.

Sect. VIII.—Parasitic Affections of the Skin.

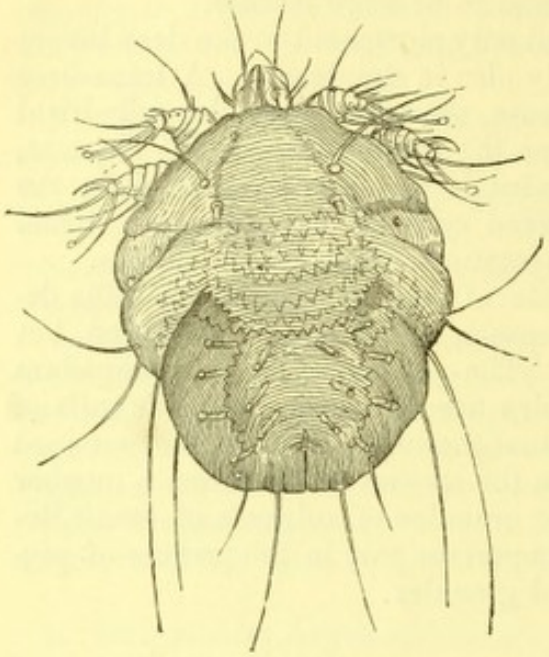
Parasites of the skin in man are of two orders, animal and vegetable.

A. Animal Parasites of the Skin of Man.—The true parasites of the skin are those which are born and developed, live and die upon the surface or in the substance of the cutaneous membrane. The most important are *acarus scabiei* and *acarus folliculorum*.

a. The *acarus scabiei* (*sarcoptes hominis*) occasions in the skin an eruption, with the characteristic burrows in which the eggs are deposited. The female acarus is most frequently found. It is visible to the unaided eye, measuring about 0.33 mm. in its greatest diameter. Under the microscope its integument appears striated by numerous parallel lines; the abdomen presents conical prominences, each terminating in long fine hairs. At each side of the head or rostrum there are found two pairs of limbs provided with suckers. At the posterior portion are seen two other pairs without suckers and terminating in long hairs. The insertions of the limbs are upon the ventral surface. The head consists of two cutting mandibles formed like scissors, behind which are two feelers ending in bristles. Posterior to the head is found the digestive canal whose terminal opening is in the posterior region of the animal. The ovary is distinct and generally distended with eggs. The respiratory apparatus appears to be rudimentary or absent. They live for a very long time without air, either in the substance of the skin, or submerged in petroleum (Burchard). According to Bourguignon they respire only by swallowing the air, the œsophagus carrying it into a number of sinuses. The male acarus is smaller and is about one-tenth as numerous. It is provided with an appendage (penis) situated between the two posterior pairs of limbs.

The female acarus impregnated and deposited upon the skin,

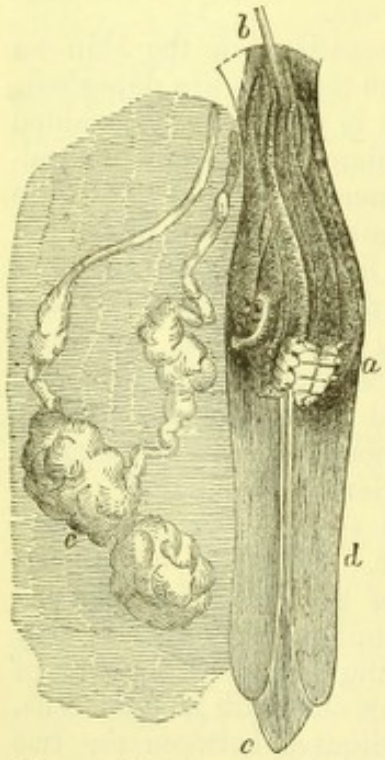
Fig. 354.



Acarus scabiei (female), dorsal surface.

pierces with its mandibles the superficial layers of the epidermis, and passes obliquely into the derma cutting its furrow as it goes. At intervals it deposits an egg in such a way that it cannot return by the same furrow, the egg obliterating the passage. It lays forty to fifty eggs and then dies. A number of these eggs are destroyed, generally only ten to fifteen are found in each furrow. By the fourteenth day after the laying, having undergone the first phases of their development, the young break the wall of the furrow formed by the epidermis, and appear upon the surface of the skin. They have now only six limbs, two anterior and one posterior pair; and are asexual. The itch does not reach its perfect development until after three successive moultings which are: first, the burrowing of the impregnated females into the substance of the epidermis; second, the presence of the young acari upon the surface of the skin; and third, the appearance of the characteristic polymorphous eruption of itch from the scratching.

Fig. 355.



Group of demodex folliculorum. *a*. Demodex. *b*. Hair. *c*. Its root. *d* Follicle. *e*. Glaud. Low power.

b. *Acarus Folliculorum* (demodex folliculorum).—This parasite lives in normal or cystic sebaceous follicles. Its body is long, measuring about 0.30 mm. Its head is provided on each side with a feeler formed by three articulations, and has a protuberance or proboscis provided with a peculiar three-forked organ, the points of which terminate by fine bristles. The head is blended with the thorax, which forms with it one-fourth the length of the animal. To the thoracic part are attached four pairs of very short limbs formed of three articulations, the last terminating in three small hook-shaped claws. The posterior or abdominal part of the body is long, and, according to some writers, contains an intestinal tube and a hepatic gland (fig. 355). According to Neumann, there exists another variety of acarus (demodex) folliculorum provided with only three pairs of limbs.

The acarus of the follicle lives in the comedon of acneous glands. Its presence

in the gland does not cause any local cutaneous lesion. The animal is met with in the sebaceous glands of the face, external auditory meatus and auricle which have become acneous.

B. Vegetable Parasites of the Skin of Man.—Upon examination of an uncolored section of normal skin, previously treated with ether and subsequently mounted in Canada balsam, there are seen in places where the epidermis is thick a number of vegetable spores contained in the corneous layers. These spores vary in size and shape. They do not correspond to any determined cutaneous affection; the probable multiple vegetable species to which they belong have not yet been accurately defined. When an inflammation occurs in the skin, and especially when the latter has been covered by a poultice, the number of microscopic plants is increased. If a vesicle or bulla is formed, the fluid in it frequently contains spores. A number of pathological anatomists, especially Orth (of Berne), believe that these organisms play an important part in the development of certain diseases of the skin, erysipelas, for example. But the true parasites of the skin, that is, those which accompany or occasion cutaneous affections, never exist primarily in the epidermis of the normal skin, and they cause in the diseased skin characteristic elementary lesions.

a. Vegetable Parasite of Tinea Favosa (*Achorion Schœnleinii*).—Discovered in 1839 by Schœnlein in the scabs of favus, afterwards by Gruby and Wedl, this parasite was first inoculated with success upon the skin of the arm by Remak.

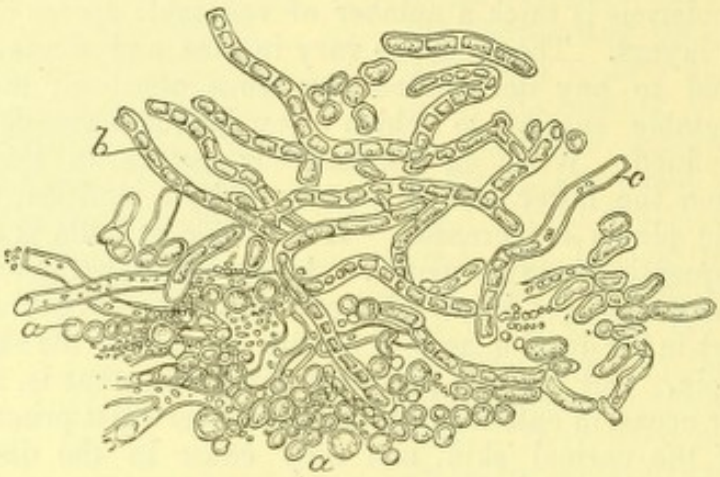
By removing a small piece of the yellow fungus of favus, and placing it in a solution of ammonia, it soon breaks up, when the parasite may be isolated. By the addition of a few drops of solution of iodine in water containing iodide of potassium, the fungus is colored red-brown, and its structure can be seen. It is composed of roundish spores, isolated or united in the form of chains. These chains of spores usually terminate the filaments of the mycelium (or thalus). At the free extremity of the latter they are at first spherical, afterwards becoming slightly elongated, so that the filament is formed by the union of short joints. The filaments of the mycelium are composed of elongated, distinct, dotted, dichotomously ramifying, firmly united joints. The spores forming chains are very frail, and are considered as a portion of the plant in the process of germination. (Fig. 356.)

Upon a vertical section of the skin through a spot covered by a favus fungus, at the surface formed by the fungus, the epidermic layers are seen filled with spores which are scattered between the corneous cells. With the spores are always seen micrococci and bacteria, besides small drops of fat. The accumulation of these foreign elements causes a prominence and a peripheral swelling of the fungus. The depressed centre is usually occupied by one or more diseased hairs; here is where the evolution of the fungus takes place and where recovery begins. The affection heals at the centre while at the periphery it extends in a circular manner.

In favus fungi of considerable extent, the invasion of the parasite is not limited to the epidermic layers. The mycelium penetrates per-

pendicularly into the derma, and there ramifies. This penetration is not due to a simple pushing aside of the tissues, but to a true invasion (Malassez); the tubes of the mycelium arise from the bottom of the fungus, and pass in straight lines into the connective tissue between the

Fig. 356.



Achorion Schœnleinii after treatment with liquor potassæ. *a*. Spores. *b*. Chains of spores terminating the filaments of the thalus, which are there composed of short articulations. *c*. True filaments of the thalus composed of elongated and brilliant articulations. × 400.

fasciculi. The derm slightly reacts from this invasion, aud at the surface of the fungus there is a continual exudation or even suppuration. In every case the connective tissue invaded by the thalus of the *achorion Schœnleinii* is gradually absorbed, and it is probable that this absorbtion causes the cicatrices which are found beneath the fungi after recovery.

The beard and the hair are invaded. The fungus grows principally in the fibrous shaft of the hair between the longitudinal epidermic laminæ; here the filaments are found to consist mostly of spores; but the mycelium is found in the tunics of the hair bulb in the neighborhood of the root.

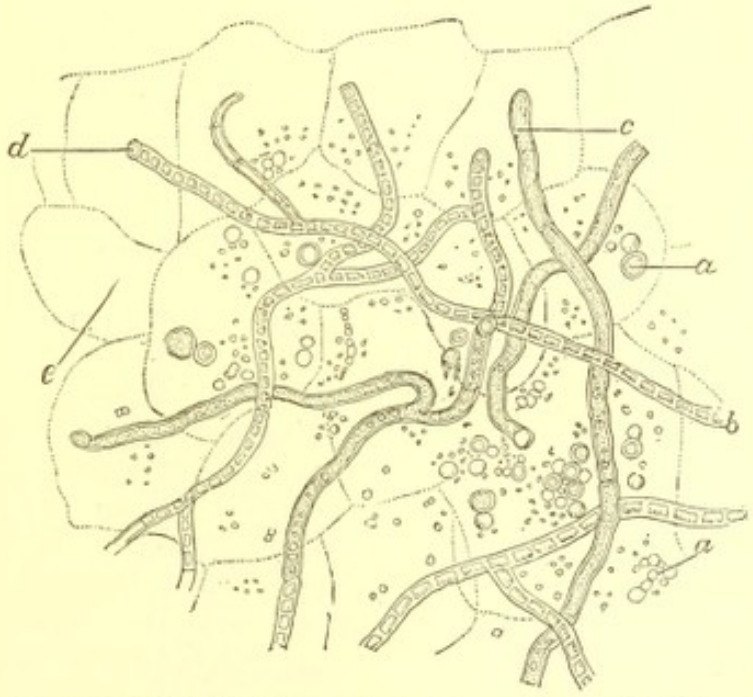
b. Tricophyton Tonsurans.—This parasite implanted upon the hair of the head causes the *tinea tonsurans;* upon the face where the beard grows the *tinea sycosa;* upon the smooth regions of the skin the *tinea circinata.* The reactions of the integument from the same parasite are different upon these several regions—a fact which is due simply to the varying structure which each part offers. The tricophyton implanted upon the smooth chin of an infant occasions the *tinea circinata.* If with the back of the hand one rubs a patch of tricophyton, *tinea circinata* is produced upon the hand by transplantation of the parasite. The fungus does not occur exclusively upon the integument of man, it may be transplanted to the cat, dog, or horse; thus these animals may become the agents of contagion.

Trichophyton tonsurans was discovered in 1840 by Malmsten. It is a growth formed of roundish spores, measuring about .005 mm. These spores are isolated or in groups, between the lamellæ of the epidermis.

A number are cylindrical in shape, and placed end to end. Neumann, in opposition to the assertion of Ch. Robin, has pointed out in this parasite the presence of a ramifying mycelium.

The parasite is ordinarily found in the lamellæ of the epidermis by scraping the surface of a tinea circinata and macerating it in a solution of potassa or ammonia. The growth of the parasite in the hair differs little from that of favus. The spores are usually abundant at the root of the hair, growing from below upwards between the longitudinal fibres of its cuticle. The epidermic laminæ of the shaft of the hair are somewhat separated, in consequence of which the hair becomes brittle and breaks. Around the hair in the inner epidermic sheath the parasite accumulates and causes an abundant formation of epidermic laminæ separated from one another by rows of spores. There thus is formed a kind of white collar around the hair, projecting above the point where it emerges from the skin. This ensheathing of the hair is of great diagnostic importance, but it is seen in other affections besides parasitic. Microscopic examination alone can fix the diagnosis in doubtful cases.

Fig. 357.



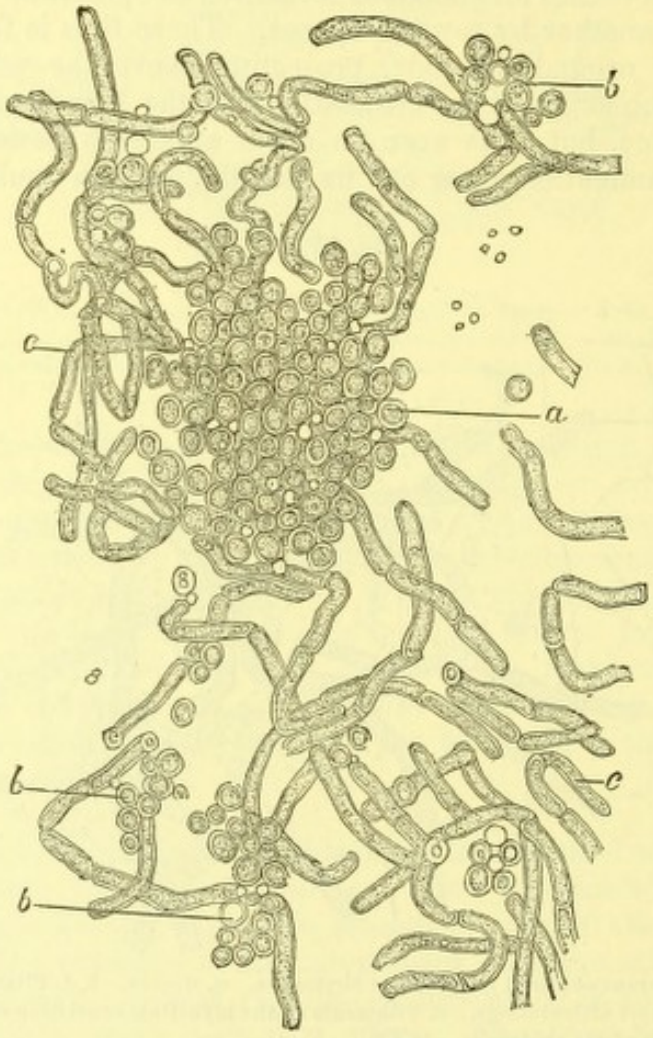
Trichophyton tonsurans obtained from herpes circinatus. *a*. Spores. *b*, *d*. Filaments of the mycelium, consisting of short articulations. *c*. Filaments of the mycelium consisting of long and shining articulations. *e*. Cell of the epidermis. × 400.

A number of dermatologists, and among them Hebra, consider the *Trictophyton tonsurans* as a simple variety of the *Achorion Schœnleinii*. But Kobner, in cultivating the parasite, has reproduced it indefinitely, with its specific characters. Hallier considers it identical with the *Penicillium*, and Neumann is lately of this opinion.

c. Vegetable Parasite of Pityriasis Versicolor.—The *Microsporon furfur* grows ordinarily in the layers of the epidermis. Its mode of implantation and the arrangement of its elements are characteristic. The

spores are roundish, collected into groups in the laminæ of the corneous epithelium. The groups are also roundish, and from their periphery proceed ramifying filaments of the mycelium, the joints of which are extremely long. The development of this fungus is extremely slow, but it is readily cultivated, and may be grown in neutral glycerine (Neumann). The spores have been seen to divide by segmentation, and as they elongate become the origin of mycelium filaments. Others become the source of new spores by endogenous generation. The *microsporon furfur* was discovered in 1846, by Eichstedt, and inoculated successfully in 1864, by Kobner upon the skin of man (fig. 358).

Fig. 358.



Microsporon furfur. *a*. Principal group of spores forming a rounded mass. *b*. Small groups of spores. *c*. Filaments of mycelium formed of long brilliant and curved articulations. × 400.

d. Vegetable Parasite of the Alopecia Circumscripta (Microsporon Audouini).—The existence of this parasite has been much disputed. Discovered in 1843, by Gruby, it was afterwards denied by many dermatologists, among whom were Hebra, E. Wilson, and Neumann. Bazin believed it to be always present in this form of alopecia, but his description differs from that given by Gruby.

Recently Malassez and afterwards Courrèges have give a good descrip-

tion of it. The seat of the parasite is in the corneous layer of the epidermis, upon the surface of the epidermic cells, and in their interstices. It does not penetrate into the hair follicle, and is only accidentally met with upon the hairs (fig. 359).

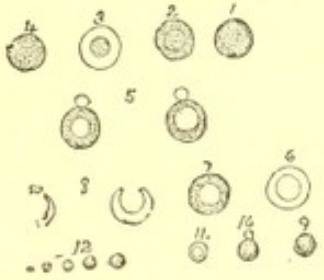
It consists solely of spherical spores without any trace of mycelium. The largest of the spores measure from .004 mm. to .005 mm. in diameter, and present a double contour; others are only .002 mm. in diameter, and have a single contour; and, finally, spores are seen less than .002 mm. in diameter. The parasite would then seem to multiply by budding (fig. 360).

Fig. 359.



A hair from a case of alopecia of rapid development: it is surrounded by epidermal cells filled with spores × 250.

Fig. 360.



Isolated spores of alopecia. 1, 2, 3, 4. Large spores seen at different focal points. 5. Budding spores. 6, 7, 8. Large empty spores. 9, 10, 11. Minute spores. 12. Sporules. × 1000.

Gruby affirmed that the *microsporon Audouini* is first developed upon the surface of the hair, at a distance of one to two millimetres from the surface of the skin, and that it sends ramifying filaments into the tissue of the hair. Malassez has not confirmed any of these assertions.

e. Vegetable Parasite of Pityriasis Capitis simplex.—This parasite was discovered in 1874, by Malassez, in the epidermic pellicles of the hair of the scalp.

Its seat is in the corneous layers of the epidermis, between the cells. It penetrates into the hair follicles, but only near the point of emergence and a little below it. It does not descend beyond the orifice of the sebaceous glands connected with the hair. It is frequently very abundant, although it has escaped the investigations of dermatologists until recently.

This parasite consists only of spores, generally elongated and budding; the largest have a length of .004 mm to .005 mm. and a width of .002 mm. to .0025 mm. The smallest are only .002 mm. long.

From the investigations of Malassez this parasite appears to play an important part in the production of the lamellæ of pityriasis. In this cutaneous disease the alopecia is caused by two processes: first, the me-

chanical action of the fungus separating the epithelial lamellæ; second, the parasite acting as a foreign body, irritating the epidermis and producing an increased activity in the evolution of the cells—the enlargement of the nucleolus, and the consequent atrophy of the nucleus. There is consequently a constant desquamation upon the surface of the integument. According to Malassez the alopecia of *Pityriasis simplex* is due to the obstruction of that portion of the hair follicle above the orifice of the sebaceous glands. This obstruction prevents the regular growth of the hair. It causes secondarily an irritation of the follicle, especially in the neighborhood of the bulb. Here the wall of the follicle undergoes an ascending hypertrophy causing at first a diminution in the calibre of the hair; and, finally, an obliteration of the follicle which is transformed into a fibrous cord.

The methods employed for the study of the vegetable parasites of the skin are very simple. The scales or hairs are removed and carefully washed in ether. In a few days all the fat is dissolved, and the possibility of mistaking fat granules for spores is then avoided. Afterwards the hairs or scales are dissociated upon a glass slide, in a drop of a solution of potash, 40 in 100, or ammonia. The latter is less rapid in its action, but is preferable. The dissociation being accomplished in the ammonia, the latter is allowed to evaporate. The parasite is then stained with iodine, and examined in glycerine, or is treated with oil of cloves and subsequently mounted in dammar.

APPENDIX.

PRESERVATION AND HARDENING OF TISSUES.

[For the benefit of those who are not practical microscopists, and who consequently are often obliged to refer interesting and valuable pathological specimens to some physician in whose skill and knowledge they have confidence, as well as in the interest of those who may be requested to examine and report upon diseased tissue, this appendix is added. Time and time again pathologists are called upon and expected to decipher the evidences and nature of morbid processes in tissues half rotten or so far decomposed that it is utterly impossible, even to the keenest and most practised eye, to recognize with certainty any but the grossest elementary lesions. Methods of preserving tissues and organs in the gross for naked eye inspection, with which the general practitioner of medicine has been so long familiar, are, as a rule, worse than useless, when employed in the preparation of tissues for examination under the microscope. Much of the destruction of the minute traces of disease, in specimens obtained from post-mortem examinations, is without remedy, for frequently the autopsy cannot be made within twenty-four hours after death, and after that lapse of time cadaverous decomposition has wrought considerable change in many of the most delicate tissues, particularly in the nervous system and the mucous membranes. It is obvious that no method of preparation can repair the damage already done by decomposition; hence the necessity of performing the autopsy at the earliest practicable moment, and the demand for the preservation of the specimens obtained without delay.

Those tissues which are secured during the life of the patient by the interference of the surgeon or otherwise, should be *at once* submitted to examination in the recent state or be *immediately* placed in a *proper* preservative agent for future study. The old custom of macerating or washing the tissue for the removal of blood, etc., should be avoided. In removing the piece great care should be exercised lest pressure of any kind be exerted. This caution is always important, but it should be especially regarded when handling any part of the nervous system or digestive apparatus. In histological examinations it is most important to study the relations of the elements as well as their individual conditions. For this, extremely thin sections must be made, and subsequently prepared for the microscope. Hence it is necessary that the tissues to be cut should be conveniently hard and cohesive. Soft parts must be hardened, and bony or calcareous substances must be softened. There are various methods of securing these essential conditions. It is not our purpose

here to discuss the many valuable methods of preparation of tissues employed at the present time by experienced histologists. Our object is solely to indicate, in the briefest manner, a very few of the most valuable and most generally applicable methods of preserving and hardening tissues for microscopic examination, for the guidance of the busy practitioner who has not the time or the inclination to study special works upon microscopical technology, but who often has the opportunity of securing for science most valuable pathological specimens, and of profiting by an inteligible interpretation of their nature. The following suggestions are important to observe:—

Size of the Piece to be Examined.—It is essential that every part of the tissue should be quickly reached and acted upon by the agent; this is the more essential the greater the delicacy of the tissue. Pieces submitted to the action of the hardening and preserving agent, as a rule, should not much exceed half a cubic inch. Nervous substance and other delicate tissues should have smaller dimensions. When the whole or a considerable part of an organ is to be examined, the relations of the different parts should not be entirely sacrificed to the demand for small isolated pieces, but the tissue should be incised in various directions in such a manner as to allow the fluid to quickly reach every cubic inch of it. The cutting instrument used for this purpose should have a keen edge, so that the slash can be made with a minimum of pressure. The spinal marrow should be cut across at intervals of half an inch.

Relative Proportions of the Tissue and the Fluid.—Five or six ounces of the fluid are usually requisite for every cubic inch of tissue to be prepared. Freshness of the fluid is also of great importance. As a rule the fluid should be changed every twenty-four hours during the first three or four days. The tissue should be suspended in the midst of the fluid by a thread instead of being allowed to rest upon the bottom of the vessel.

The choice of the fluids used for hardening and preserving should vary somewhat according to the nature and condition of the tissue and according to the methods to be followed by the histologist subsequent to the making of sections. Those fluids most generally efficient are named below.

Müller's Fluid.—Water, 100 parts; bichromate of potassa, 2 parts; sulphate of soda, 1 part.

Bichromate of Ammonia.—This agent may be used in the following strength: bichromate of ammonia, 2—5 parts; water, 100 parts.

Alcohol.—Alcohol, the oldest and one of the most generally useful hardening agents, should best be used in the following manner:—

The first solution should be 60 per cent. in strength.

The second solution should be 75 per cent. in strength.

The third should be the strongest alcohol.

The first solution should be used in the first 24 or 48 hours; the second for the next 48 hours, when the strong alcohol may be substituted.

Chromic Acid.—This reagent needs to be very carefully used. The solution should be made by weight and measurement, never by estimation from the depth of color, otherwise it becomes a very troublesome and often destructive fluid. The strength of this solution should be 2—5

parts of chromic acid to 1000 parts of water, commencing with the weaker and ending with a stronger proportion. This reagent makes the tissues too brittle if they are left too long exposed to its action. It is particularly valuable for the nervous system and extremely delicate tissues.

Picric Acid.—It should be used in saturated solutions. The crystals are not very soluble. Hence solutions should be made with warm water, or if made with cold water the sediment should be well stirred at intervals during two or three days. With this fluid the tissues are better placed at the bottom of the vessel.

Time Required for Hardening.—Most of the tissues are hardened in a few days when placed in alcohol or in picric acid. The latter frequently makes the tissue sufficiently firm for rough sections within twenty hours.

Nerve tissue, especially that of the centres, the brain, and spinal marrow, requires much longer exposure to the action of the reagent. The brain or spinal cord must be immersed in chromic acid, Müller's fluid, or bichromate of ammonia five or six weeks before it is sufficiently firm and tough.

Treatment of Tissues after Hardening.—When the specimen has become sufficiently firm, it should be removed from the hardening agent if chromic acid, picric acid, bichromate of ammonia, or Müller's has been used, should be thoroughly soaked in water until the tissue ceases to tinge the water, and finally placed in alcohol of 85 per cent. for indefinite keeping.

Decalcifying Agents.—Both saturated picric acid and chromic acid, in the strength of 2—5 parts to 1000, possess the property of dissolving the calcareous salts in bones or other tissues. Where the piece to be acted upon is very small and the fluid is in large amount, the acid should be often renewed.

The portion of tissue to be softened should not exceed a quarter of a cubic inch, and the fluid should not be less than five or six fluid ounces. These agents harden the elements at the same time that they dissolve the lime salts.]

BIBLIOGRAPHY.

Pathological histology of cells and tissues.—Rokitansky, Handb. der path. Anatomie, t. I. Vienne, 1841–1846, 3e édition, 1855–1861.—Lebert, Physiologie pathologique. Paris, 1845; Traité d'anatomie pathologique, in-folio, atlas, 1855–1861.—R. Virchow, Pathologie cellulaire.—A. Foerster, Handb. der path. Anatomie, 2e edition, t. I, 1864.—Billroth, Die allgemeine chirurgische Pathologie, 1863.—Pitha et Billroth, Handb. der allg. und spec. Chirurgie, 1864, t. I, par O. Weber.—Rindfleisch, Lehrbuch der path. Gewebelehre, 1867.

Atrophy and death of cells.—Paget, Lectures on surgical pathology. London, 1853, p. 93.—Wirchow, Handb. der spec. Path. und Therapie, t. I, p. 303. Sur un embryon momifié dans une grossesse abdominale, in Verh. d. Würzb. Ges., t. I, p. 105; t. III, p. 355.—Rokitansky, Lehrbuch, t. I, p. 114 et 319.—Robin, Note sur l'atrophie des éléments anatomiques, in Gazette médicale, 1854, p. 240—Demme, Ueber die Veränderungen der Gewebe durch Bränd, 1857.

Mucous and colloid degeneration.—Virchow, Arch., t. I, p. 105.—Wagner, Zur colloid Metamorphose der Zellen, in Archiv f. phys. Heilkunde, 1856, p. 106.—Eberth, Virchow's Archiv, t. XXI, p. 106.—Wagner, Archiv f. phys. Heilkunde, 1866.—Zenker, Ueber die Veränderungen der Muskeln, in-4, 1862.

Amyloid degeneration.—Virchow, Arch., t. VI, p. 135 et 416; t. VIII, p. 140 et 364.—Meckel, Speckkrankeit, in Charite Annalen, 1853, t. IV.—Friedreich, Archiv f. path. Anat., t. XI, 1857.—Bennet, Clinical Lectures. London, 1859.—Kekule, Verhandl. der naturhist. med. Vereins. Heidelberg, 1858.—Schmidt, Annalen der Chemie und Pharmacie, t. LX, p. 250, 1859.—Kuhne et Rudneff, Virchow's Archiv, t. XXIII, 1865.

Fatty degeneration.—Reinhardt, Ueber die Enstehung der Körnchenzellen, in Virchow's Archiv, 1847, t. I, p. 21.—Bardeleben, Jen. Annalen, 1851, t. II, p. 16.—O. Weber, Virchow's Archiv, t. XIII, p. 74; t. XV, p. 480.—Lewen, Virchow's Archiv, t. XXI, p. 506.—Buhl, Virchow's Archiv, t. XI, p. 275; Zeitschrift f. rat. Medecin, t. VIII.

Pigmentation.—Virchow, Die pathol. Pigmente, in Archiv, t. I, p. 379.—Traube, Deutsche Klinik, 1860.—Koschlakoff, Virchow's Archiv, t. XXXV, p. 178.

Calcareous infiltration.—O. Weber, Virchow's Archiv, t. VI, p. 561.—Virchow, Archiv, t. VIII, p. 103; t. IX, p. 618.

Uratic infiltration.—Virchow, Gesammte Abhandlungen, p. 833.—Garrod, De la goutte.

Tumors.—J. Müller, Ueber den feineren Bau der krankhaften Geschwülste. Berlin, 1838.—Vögel, Traité d'anatomie générale.—Hannover, Das Epithelioma. Leipzig, 1847.—Paget, Lectures on Tumors. London, 1851.—Robin (Charles), art. Tumeurs, Hétéroplasmes, Cancer, etc., du Dictionnaire de Nysten, éditions de 1858 et de 1863.—Follin, Traité de pathologie externe, 1er vol. Paris, 1861.—Virchow, Die krankhaften Geschwülste, 1er vol. Berlin, 1863; 2e vol. 1864; 3e vol. 1867.—Broca, Traité des tumeurs, 1er vol. 1866; 2e vol. 1869.

Sarcoma.—Lebert, Physiologie pathologique. Paris, 1845, t. II, p. 120.—Paget, Lectures on surgical path. London, 1853, vol. II, p. 151, 155, 212.—Robin, Comptes rendus de la Société de biologie, 1849, p. 119.—Eugène Nélaton, Tumeurs à myéloplaxes, thèse. Paris, 1860.—Virchow, Psammômes et gliômes (Pathologie des tumeurs), 18e leçon, t. II; Sarcômes, 19e leçon. Cornil et Trasbot, De la mélanose, in-4°. Paris, 1868.

Myxoma.—J. Müller, Müller's Archiv, 1836.—Virchow, Pathologie des tumeurs, 15e leçon, t. I.

Fibroma.—Verneuil, Quelques propositions sur les fibrômes ou tumeurs formées par du tissu cellulaire (Gaz. méd. de Paris, 1856, n° 5, p. 59; n° 7, p. 95).—Cruveilhier, Traité d'anat. path. génér., t. III, p. 63, 715.—Virchow, Pathologie des tumeurs, 13e leçon, t. I.

Lipoma.—Cruveilhier, Traité d'anat. path. gén., t. III, p. 302.—J. Müller, Ueber feineren Bau, etc., p. 50.—Verneuil, Gaz. méd. de Paris, 1854, n° 16, p. 242.—E. Godard, Recherches sur la substitution graisseuse du rein. Paris, 1859—Virchow, Pathologie des tumeurs, t. I, 14e leçon.—Broca, Traité des tumeurs, t. II, p. 375.

Carcinoma.—Cruveilhier, Anat. path., t. V.—Lebert, Phys. pathol., t. II.—Virchow, Virchow's Archiv, t. I, 1847.—Broca, Mém. de l'Acad. de méd., t. XVI, 1852.—E. Wagner, Archiv für phys. Heilkunde, p. 153, 1857; p. 306, 1858.—Billroth, Pathol. chirurg. gén., 1868, p. 757.—Cornil, Du cancer, in Mém. de l'Acad. de méd., t. XXVII.—Förster, Handbuch, t. I, 2e édit., 1865, p. 388.

Syphilis.—Clinique iconographique de l'hôpital des vénériens. Paris, 1851.—Baerensprung, Deutsche Klinik, 1858, n° 17; Annalen der Charité, Berlin, 1860, t. IX, p. 139.—Lorain et Robin, Gaz. méd. de Paris, 1855, n° 12.—Virchow, Syphilis constitutionnelle; Pathol. des tumeurs, t. II, 20e leçon.—Van Oordt, Des tumeurs gommeuses, thèse. Paris, 1859.—Ernst Wagner, Ueber das Syphilom (Archiv für Heilkunde), t. IV, p. 1, 161, 356, 430.—Lancereaux, Traité historique et pratique de la syphilis. Paris, 1866.

Tubercle.—Lebert, Comptes rendus Ac. sc., 4 mars 1844.—Reinhardt, Annalen der Charité, Berlin, 1850.—Virchow, Path. cellul., Tumeurs, 20e leçon.—Villemin, Du tubercule. Paris, 1862; Etudes sur la tuberculose. Paris, 1868, in-8.—Hérard et Cornil, De la phthisie pulmonaire, in-8. Paris, 1867.—Rindfleisch, Lehrbuch der Gewebelehre.—Niemeyer, Leçons cliniques sur la phthisie pulmonaire.—Lebert et Oscar Wyss, Ueber Cavernenbildung in den Lungen nach Impfung, etc. (Virchow's Archiv), t. XLI, p. 540.—Wilson Fox, On the artificial production of tubercle (British Med. Journal, 1868).

Glanders.—Virchow, Path. des tumeurs, 20e leçon.

Chondroma.—J. Müller, Rede zur Feier der 42 Stiftungstages des K. med. chir. Fried. Wilhelms Institutes. Berlin, 1836.—Dolbeau, Gaz. hebd., 1858, n° 42, p. 720; n° 44, p. 752; Bull. de la Soc. anat. 1859, p. 296–336, 1860.—Virchow, Tumeurs, 16e leçon.

Osteoma.—Henry Müller, Beiträge zur Kenntniss der Entwickel. d. Knochengewebes, in Zeitschr. f. wiss. Zool., IX, 3.—Rokitansky, Lehrbuch, t. I, p. 179; t. II, p. 96.—Soulier, Du parallelisme parfait, etc., thèse. Paris, 1864.—Virchow, Tumeurs, t. II, 20e leçon, 1864; Odontômes, p. 51.—Broca, Recherches sur un nouveau groupe de tumeurs (Acad. des sc., 30 décembre, 1867); Traité des tumeurs, t. II, 1869.

Myoma.—Zenker, Ueber die Veranderungen der willk. Muskeln in Typhus, etc. Leipzig, 1864.—Förster, Handbuch, t. I, p. 339.—Virchow, Die krankhaft. Geschw., t. III, p. 98.

Neuroma.—Odier, Manuel de médecine pratique. Genève, 1803, p. 278.—Dupuytren, Leçons de clinique chirurgicale, t. I.—Descot, Sur les affections des nerfs, in-8. Paris, 1825.—Valentin, Lehrbuch der Physiologie, t. I, p. 722.—Lebert, Traité d'anat. path., t. I, p. 160, pl. XXII, fig. 4–5.—Virchow, Gesam-

melte Abhandl., p. 999; Tumeurs, t. III.—Sangalli, Della ipertrofia parzialle del cervello. Milan, 1858.—Verneuil, Archives générales de médecine, 5e série, t. XVIII, p. 540.—Axmann, Beiträge zur mikr. Anat. der ganglion. Nervensystems. Berlin, 1853.

Angioma.—Plenck, Doctrina de morbis cutaneis. Wien, 1776.—Dupuytren, Clinique chirurgicale, t. II.—Alibert, Nosographie naturelle. Paris, 1838.—Breschet, Répertoire général d'anat. et phys. Paris, 1826, t. II.—Rayer, Maladies des reins, t. III, 1841, p. 612.—Schuh, Pathologie und Therapie der Pseudoplasmen. Wien, 1854.—Luschka, Virchow's Archiv, t. VI.—Esmarch, Virchow's Archiv, t. VI.—Broca, Tumeurs, t. II, chap. VII.—Virchow, Tumeurs, t. III, 25e leçon.

Lymphangioma.—Demarquay, Mém. Soc. chirurgie, t. III, p. 139.—Fetzer, Archiv f. physiol. Heilkunde, 1849, t. VIII, p. 128.—Michel, Gaz. méd. de Strasbourg, 1853.—Tilezen, Canstatt's Jahresb., 1856, t. III, p. 271.—Trélat.—Th. Anger, Thèse. Paris, 1867.—Virchow, Tumeurs, t. III, 25e leçon.

Lymphadenoma.—His, Zeitschrift. f. wiss. Zool. XI, p. 65; XII, p. 223; XIII, p. 445; XV, p. 127.—Hogdkin, Medic.-chir. Trans., t. XVII, p. 68, 1832.—Virchow, Froriep's Notizen, 1845.—Bennett, Edinb. med. and surg. Journal, 1845.—Trousseau, Clinique de l'Hôtel-Dieu. Paris, 1862, t. II, 1re édition.—Cornil, Archives de médecine, 1865, t. II.—Waldeyer, Virchow's Archiv, t. XXXV, 1865.—Böttcher, Virchow's Archiv, t. XXXVII, p. 163, 1866.—Bonfils, Société méd. d'obs., t. I, p. 157, 1857–58.—Ollivier et Ranvier, Obs. pour servir à l'histoire de la leucocythémie (Soc. de biol., 1866).

Epithelioma.—Max Schultze, Virchow's Archiv, XXX.—His, Die Haüte und Höhlen des menschl. Körpers. Bas., 1865.—Robin, Soc. biol., 1855, p. 210; id. p. 283. Gaz. méd., 1856.—Ordonez, Société de biologie, 1866.—Verneuil, Études sur les tumeurs de la peau (Archiv. de méd., série V, t. III, p. 555; t. IV, p. 447 et 693).—Thiersch, Das Epithelialkrebs. Leipzig. 1865.—Cornil et Ranvier, Développement hist. (Journal de l'anat., vol. II, p. 266 et 476).—Bidder, Müller's Archiv, 1852.—Gauwriloff, Würtzb. med. Zeitung, t. IV, 1863.—Demonchy, Épithéliôme pavimenteux, thèse. Paris, 1866.—Montfumat, Polypes de l'utérus, thèse. Paris, 1876.—Rindfleisch, Lehrbuch der path. Gewebelehre, 1867.—Billroth, Pathol. chirurg. générale, trad. française, 1868.

Adenoma.—Cruveilhier, Bulletin Acad. roy. de méd., t. IX, p. 360, 1844.—Velpeau, Dictionnaire en 30 vol., t. XIX, p. 59.—Lebert, Phys. path., 1845, Broca, art. Adénôme du Dict. encyclop., t. I.

Cysts.—Kohlrausch, Kystes dermoïdes (Müller's Archiv, 1843), p. 365.—Lebert, Anat. path.—Demoulin, Sur quelques productions hétérotopiques, etc., thèse, 1866.—Wilson Fox, Sur l'origine et la structure des kystes de l'ovaire (Journal de l'anat., 1865, p. 323).

Lesions of bone.—Troja, De novorum ossium in integris aut maximis, ob morbos, deperditionibus regeneratione experimenta. Paris, 1775, in-12.—Duhamel, Observations sur la réunion des fractures des os (Mém. de l'Acad. des sc., 1742–1743).—Tenon, Mémoire sur l'exfoliation des os (Mém. de l'Acad. des sc., 1758).—Cruveilhier, Essai sur l'anatomie pathologique, t. II, p. 426. Paris, 1816.—Gerdy, Recherches sur la carie (Gazette hebdomadaire, 1854, t. I, n° 27); Mémoire sur l'état matériel ou anatomique des os malades (Archives de médecine, février 1836, 2e série, t. X, p. 129); De la périostite et de la médullite (Archives générales de médecine, août 1853, 5e série, t. II, p. 130.—Ollier, Traité expérimental et clinique de la régénération des os, 2 vol. Paris, in-8, fig., 1867. V. Masson.—Ranvier, Considérations sur le développement du tissu osseux (Thèses de doctorat, Paris, 1865); Description et définition de l'ostéite, de la carie et des tubercules des os (Archives de physiologie, t. I, janvier 1868).—Chassaignac, Des abcès aigus sous-périostiques (Mém. de la Soc. de chirurg., vol. IV, p. 286); Mémoire sur l'ostéomylite (Gaz. méd., 1854, n° 33).—Verneuil, Note sur les cellules du tissu médullaire des os et sur leur état dans l'ostéomyélite (Gaz. méd. de Paris, 1852, n° 26).—Gosselin, Mémoire sur les ostéites épiphysaires des adolescents (Archives de méd., 1858, 5e série, t. XI, p. 513).—Giraldès, Gazette des hôpitaux, 1862.—

Louvet, De la périostite phlegmoneuse diffuse (Thèses de doctorat, Paris, 1867).—Nélaton, Recherches sur l'affection tuberculeuse des os (Thèses de doctorat, Paris, 1836).—Ranvier, Altérations histologiques des cartilages dans les tumeurs blanches (Société anatomique, 1865, p. 701).—Paquet, Étude sur les tumeurs blanches (Thèses de Paris, 1867) —R. Volkmann, Maladie des os, dans le Handbuch der Chirurgie de Pitha et Billroth ; Sur l'histologie de la carie et de l'ostéite in Langenbeck's Archiv, t. IV.—J. Guérin, Recherches sur le rachitisme chez les enfants (Gaz. méd., t. II, p. 6, 1834 et 1839, p. 433).—Baylard, Du rachitisme, de la fragilité des os et de l'ostéomalacie (Thèses de Paris, 1852).—Broca, Sur quelques points de l'anatomie pathologique du rachitisme (Bull. de la Soc. anat., 1852, p. 141).—Virchow, Das normale Knochenwachsthum und die rachitische Störungen desselben (Archiv für path. Anat., vol. V, p. 409).—Rindfleisch, Lehrbuch der pathologischen Gewebelehre, p. 486.—Ch. Robin, Sur l'existence de deux espèces nouvelles d'éléments anatomiques qui se trouvent dans le canal médullaire des os (Soc. de biol., 1845).—Eugène Nélaton, Mémoire sur les tumeurs à myéloplaxes (Thèses de Paris, 1860).

Lesions of cartilages and articulations.—Dupuytren, Dictionnaire des sciences médicales, t. XXII, p. 148.—Blandin, Dictionnaire de médecine et de chirurgie pratiques, t. X, p. 89.—Velpeau, Dictionnaire en 30 vol., art. *Maladies des articulations*.—Brodie, On Diseases of the Joints. London, 1818.—Bonnet, Traité des maladies des articulations. Paris, 1845.—Bouillaud, Traité du rheumatisme articulaire. Paris, 1840.—Redfern, Edinburgh Monthly Journal, October, 1849, January, 1854.—Virchow, Archiv für path. Anat., t. IV, 1852.—Broca, Bull. de la Soc. anat., t. XXIV, p. 438 (Bull. de l'Acad. de méd., 1855, t. XX).—O. Weber, Archiv für path. Anat., t. XIII, p. 74.—Richet, Mémoire sur les tumeurs blanches (Mem. de l'Acad. de méd., 1853).—Charcot, Rheumatisme articulaire chronique, Paris (Thèses de doctorat, 1853) ; Leçons faites à la Salpétrière, 1re série ; Arthropathies consécutives aux maladies du cerveau et de la moelle (Archiv. de physiol., 1868, p. 175 et 379).—Ollivier et Ranvier, Étude histologique sur l'arthropathie rheumatismale (Soc. de biol., 1865).—Vergely (Thèses de Paris), sur le Rhumatisme articulaire chronique, 1866.—Cabot, Thèses de Paris, 1865.—Volkmann, Archiv für klinische Chirurgie, t. II, p. 408.

Lesions of cellular and serous tissues.—J. Hunter, on Inflammation.—Bichat, Anatomie générale, t. I. Paris, 1812.—Hodgkin, Lectures on the Morbid Anatomy of Serous and Mucous Membranes. London, 1836–1840. Cohnheim, Entzündung und Eiterung (Archiv für path. Anat., t. XL, p. 1, 1867).—Recklinghausen, Die Lymphgefässe und ihre Beziehung zum Bindegewebe, 1862. Berlin.—Langerhans et F. A. Hoffmann, Uber den Verbleid des in Circulation eingeführten Zinnobers (Archiv für path. Anat., vol. XLVIII, p. 302).—A. Schmidt, Archives de Reichert et de du Bois-Reymond, 1861, p. 545 et 675, et 1862, p. 428 et 533.—L. Ranvier, Des éléments cellulaires des tendons et du tissu cellulaire (Archives de physiol.), 1869, p. 471 ; Lésions du tissu conjonctif dans l'œdème (Comptes-rendus de l'Acad. des sc., julliet 1871).—E. Wagner, Contributions à l'anatomie pathologique de la plèvre (Archiv der Heilkunde, vol. XI, 1re livraison).—Kœster, Développement du carcinôme, 1869 ; Sur l'inflammation fongueuse des articulations (Archiv für path. Anat., t. XLVIII, p. 95).

Lesions of muscles.—Zenker, Altérations des muscles dans la fièvre typhoïde, etc. Leipzig, 1864, in-4.—Waldeyer, Archiv für path. Anat., t. XXXIV, p. 473.—Duchenne (de Boulogne), Traité de l'électrisation localisée, 2e édit. ; Paralysie musculaire pseudo-hypertrophique (Archives gén. de méd., janvier 1868).—Hayem, Étude sur les myosites symtômatiques (Archives de physiol., 1870, p. 81, 269, 422, 478, 569).—C. O. Weber, Développement du carcinôme dans les muscles (Archiv für path. Anat., t. XXXIX).—Weismann, in Henle and Pfeufer's Zeitschrift, vol. XII, p. 126, et vol. XV, p. 60.—Virchow, Sur l'inflammation parenchymateuse (Archiv für path. Anat., t. IV, p. 261).

Lesions of blood, heart, and vessels.—Bouillaud, Traité clinique des maladies du cœur (Archives gén. de méd. 1839).—Legroux, Recherches sur les concrétions sanguines, Paris, 1827, et Gaz. hebd., 1856.—Bennett, Edinburgh Med. and Surg. Journal, 1845, vol. LXV.—Virchow, Sur la leucémie in Handbuch der spec. Pathologie und Therapie, 1854, t. I ; Mémoires sur la coagulation du sang, sur la

thrombose et l'embolie dans Gesammelte Abhandlungen, in-8, 1862.—Klebs, Archiv für path. Anat., vol. XXXVIII, p. 200.—Erb, Archiv für path. Anat., vol. XXXIV, p. 138.—Ranvier et Cornil, Contributions à l'histologie normale et pathologique de la tunique interne des artères et de l'endocarde (Archives de physiol., t. I. p. 551). —Thurnam, London Medical Gazet., 1838.—Foerster, Handbuch der speciellen pathologischen Anatomie, 1863.—Pelvet, Des anévrysmes du cœur (Thèses de Paris, 1867).—Lancereaux, article *Athérôme* du Dictionnaire des sciences médicales, t. VII.—Raynaud, article *Cœur* du Nouveau Dict. de med. et de chir. prat., t. VIII.—Peacok, Edinb. med. and surg. Journ., April, 1843; Monthly Journal, sept. 1849.—Charcot et Ball, art. *Aorte* du Dict. des sc. méd., t. V.—Bouchard et Charcot, Nouvelles recherches sur l'hémorrhagie cérébrale (Archiv. de physiol., t. I, p. 110, 643, 725).—Liouville, Anévrysmes miliaires (Thèses de doctorat, 1871).—O. Weber in Handbuch der Chirurgie von Pitha und Billroth.—Bubnoff, Sur l'organisation du thrombus (Centralblatt, 1867, nº 48)—Brücke (Archiv für path. Anat., vol. XII, p. 81 et 172).—Eberth, Wurtzburger Verhandlungen, t. VI, p. 27.—Durante, Sur l'organisation du caillot dans les vaisseaux (Archives de physiol., juillet 1872, p. 491).—Robin, Structure des capillaires de l'encéphale (Journ. de la physiol., t. II, 1859, p. 537).—Billroth, Histol. path. et Archiv für path. Anatomie, vol. XXI, p. 423.—Rebsamen, Sur la mélanose des ganglions lymphatiques (Archiv für path. Anat., vol. XXIV, p. 92).—His, Zeitschrift für wiss. Zoolog., vol. X, p. 333; vol. XI, p. 65.—Shakespeare, E. O., Reparatory Inflammation of Arteries after Ligature, Acupressure, and Torsion. Toner Lectures, No. VII. Smithsonian Institution, 1879.

Lesions of nervous system.—Rokitanski, Lehrbuch der path. Anat., t. II, p. 498.—Curling, A Treatise on Tetanus. London, 1836.—Lepelletier, Rev. méd., 1827, t. IV, p. 183.—Descot, Sur les affections locales des nerfs. Paris, 1825.—Philippeaux et Vulpian, Sur la régénération des nerfs (Mém. de la Soc. de biol., 1859, p. 343).—Arloing et Tripier, Recherches expérimentales sur la pathogénie du tétanos (Arch. de physiol., 1870, p. 235), Physiol. des nerfs vagues (même recueil, juillet 1872).—Ranvier, Recherches sur l'histol. et la physiol. des nerfs (Archives de physiol., mars et juillet 1872).—Schiff, Comptes-rendus de l'Acad. des sc., 1854.—Waller, Nouvelle méthode anatomique pour l'investigation du système nerveux. Bonn, 1852.—Lent, Zeitschrift für wiss. Zoologie, t. VII, p. 145, 1855.—Remak, Archiv für path. Anat., t. XXIII, p. 411, 1862.—Cornil, Lésions des nerfs dans les hémiplégies anciennes (Soc. de biol., 1863); Tumeurs épithéliales des nerfs (Journ. de l'anat., 1864, p. 183); Du tubercule dans ses rapports avec les vaisseaux (Arch. de physiol., 1868, p. 99).—Liouville. Méningite cérébro-spinale tuberculeuse (Archives de physiol., 1870, p. 490).—Brown-Séquard, Leçons sur les paraplégies.—Magnan, De la lésion anatomique de la paralysie générale (Thèses de Paris, 1866). Voyez aussi Archives de physiol., 1868, t. I, p. 322 et 1869, t. II, p. 250.—Frerisch, Clinique des malad. du foie, traduction française, p. 268.—Bouchard, Des dégénérescences secondaires de la moelle épinière (Archives génér. de méd., 1866); Pathogénie des hémorrhagies, thèse d'agrégation, 1869.—Charcot et Vulpian, Sur l'anat. pathol. de l'ataxie locomotrice (Gaz. hebd., 1862).—Prevost et Cotard, Études physiologiques et pathologiques sur le ramollissement cérébral (Mém. de la Soc. de biol., 1866, p. 49).—Rostan, Rech. sur le ramollissement du cerveaux. Paris, 1820.—Andral, Clinique méd., 4e édit., t. V, p. 373; Anat. pathol., t. II, p. 302.—Hayem, Études sur les différentes formes d'encéphalite (Thèses de Paris, 1868).—Virchow, Congenitale encephalis (Archiv für path. Anat., 1867, vol. XXXVIII).—Duguet, Faits de sclérose du cervelet (Soc. anatomique, 1863, p. 37).—Parrot, Étude sur la stéatose de l'encéphale (Archives de physiol., 1868, p. 530, 622, 706).—Turk, Dégénérescences secondaires de la moelle (Acad. des sc., de Vienne, 1851, 1853, 1855). —Gubler, Du ramollissement atrophique envisagé comme lésion consécutive à d'autres affections encéphaliques (Archives gén. de méd., 1859, t. II, p. 31).—Charcot et Joffroy, Cas de paralysie infantile spinale (Archives de physiol., 1869, p. 134).—Vulpian, Méningite spinale avec sclérose corticale annulaire de la moelle (Archives de physiol., 1869, p. 279).—Beaumetz, De la myélite aiguë, thèse d'agrégation, 1872.—Damaschino et Roger, Recherches sur la paralysie spinale de l'enfance (Soc. de biol., 1872).—Laborde, Paralysie essentielle de l'enfance. Paris, 1864. —Lockhart Clarke, On the pathology of tetanus (Medico-chirurgical Transactions,

1865, vol. XLVIII); On the morbid anatomy of nervous centres (Lancet, Sept. 1866).—Joffroy et Parrot, Un cas de paralysie infantile (Archives de physiol., 1869, p. 310).—Joffroy et Duchenne, Atrophie des cellules nerveuses, etc. Même recueil, 1869, p. 499.—Duchenne (de Boulogne), Paralysie atrophique graisseuse de l'enfance (Archives gén. de méd., juillet 1864); Paralysie musculaire pseudo-hypertrophique (Archives gén. de méd., janvier 1868); De l'ataxie locomotrice (Arch. de méd., decembre 1858, janvier, février, avril 1860).—Bourdon et Luys, Études cliniques at histologiques sur l'ataxie locomotrice (Archives gén. de méd., novembre 1861).—Fromman, Untersuchungen über die normale and pathol. Anatomie des Rückenmarkes. Jena, 1867.—Demme, Beiträge zur pathol. Anat. der Tetanus. Leipzig, 1852.—Lancereaux, Mém. Soc. biol., 1861, p. 223.—Michaud, Lésions du système nerveux dans le tétanos (Archives de physiol., 1872, p. 59).—Pierret, Note sur la sclérose des cordons postérieurs (Archives de physiol., 1872, p. 364).—Benjamin (Archiv für path. Anat., t. XIV, p. 552).

Respiratory apparatus — Nasal fossæ.— Schultze, Unters. über den Bau der Nasenschleimhaut, 1862.—Kolliker, Histologie.—Giraldès, Mémoires de la Société de chirurgie, 1853.—Muron, Structure des polypes naso-pharyngiens (Société de biologie, 1870, p. 223).

Larynx.—Coyne, Thèse de doctorat, 1874.—Éberth, in Rindfleisch, Traité d'histologie pathologique, translated by M. Gross, 1873, p. 348.—Fœrster, loc. cit.—Louis, Recherches anatomiques, pathologiques et thérapeutiques sur la fièvre typhoïde. Paris, 1840, 2 vol. in-8.—Maurin, Des accidents laryngés de la fièvre typhoïde (Thèse, Paris, 1865).—Krishaber et Peter, article *Larynx* du Dictionnaire encyclopédique des sciences médicales.—Causit, Études sur les polypes du larynx chez les enfants et en particulier sur les polypes congénitaux. Thèse, Paris, 1867.

Bronchi and lung.—Laennec, Traité d'auscultation médiate.—Andral, Clinique médicale, 4e édit., et Traité d'anat. path.—Barth, Recherches sur la dilatation des bronches, Paris, 1856.—Gombault, Études sur l'anatomie pathologique de la dilatation des bronches. Paris, 1858.—Rilliet et Barthez, Traité des maladies des enfants, 1843.—Fauvel, Recherches sur la bronchite capillaire. Paris, 1840.—Rossignol, Recherches antomiques, etc., sur l'emphysème pulmonaire, avec planches. Bruxelles, 1849.—Bouillaud, Dictionnaire en 15 vol., vol. VII, p. 121.—C.-H. Ehrmann, Histoire des polypes du larynx. Strasbourg, 1844 et 1850.—Trousseau et Belloc, De la phthisie laryngée (Mémoires de l'Académie royale de méd., t. VI, 1837).—Bretonneau, Des inflammations spéciales du tissu muqueux. Paris, 1826.—Schrader, Deutsche Klinik, n° 18, 1854.—Leroy, Des concrétions bronchiques, Thèse de doctorat, Paris, 1868.—Duguet, De l'apoplexie pulmonaire. Thèse d'agrégation, 1872.—Gairdner, Monthly Journ. of Med Sc., vol. XIII, 1851, On the patholog. anat. of bronchitis. Edinburgh, 1850.—Corrigan, Dublin Journal, 1838, n° 38, et Archives génér. de méd., 1838, t. II; 1854, t. II. Dublin Hospital Gazet., n° 24, 1857.—Cornil, Leçons sur l'anat. patholog. et sur les signes fournis par l'auscultation dans les maladies du poumon, in-8, 1874, G. Baillière.—Cruveilhier, Atlas d'anatomie pathologique, 20e livr.—Raymond, Thèse de Paris, 1842.—Chomel, Nosographie de la pneumonie chronique, fondée sur huit faits, 1845.—Charcot, De la pneumonie chronique. Thèse de concours pour l'agrégation, 1860.—Traube, Deutsche Klinik, 48, 49, 1849.—Schroeder van der Kolk, Obs. anat. path., 1826.—Gavarret, De l'emphysème pulm. Thèse, Paris, 1843.—Villemin, Recherches sur la vésicule pulmonaire et l'emphysème (Archives génér. de méd., 1866, t. II).—Maurice Raynaud, Mémoire sur l'angioleucite généralisée des poumons (Société médicale des hôpitaux, 13 mars 1874).—Ferréol et Thaon, Société médicale des hôpitaux, 1874.—Troisier, Recherches sur les lymphangites pulmonaires. Thèse de doctorat, 1874.

Tuberculosis.—Kuss, Gazette médicale de Strasbourg, 1847 et 1855.—Virchow, Wiener med. Wochenschrift, 1856. Pathologie cellulaire.—Martel, Thèse de Paris, 1865.—Villemin, Du tubercule (Gazette médicale de Strasbourg, 1864.—Villemin, Etudes sur la tuberculose, Paris, 1867. De la virulence et de la spécificité de la tuberculose (Bulletin de l'Académie de médecine, t. XXX, p. 76). Discussion sur la tuberculose à l'Académie de méd. (Bulletin de l'Académie, 1867 et 1868).—Empis, De la granulie, Paris, 1865.—Hérard et Cornil, De la phthisie

pulmonaire, Paris, 1867.—Lebert, Physiologie pathologique 1856. De l'anatomie pathologique, et de la pathogénie de la pneumonie disséminée et chronique et des tubercules (Gazette méd. de Paris, 1867, p. 350).—Lépine, De la pneumonie caséeuse (Thèse d'agrégation, 1872).—Thaon, Recherches sur l'anatomie pathologique de la tuberculose (1873).—Grancher, De l'unité de la phthisie. Thèse, 1873.—Niemeyer, Leçons cliniques sur la phthisie pulmonaire.—Schuppel, Observations sur la tuberculose des ganglions lymphatiques. Tubingue, 1871.—Sanderson, Report on the inoculability and development of tubercle, also Transact Path. Society of London, vol. XXIV, pl. XII, XIII, XIV et XV).—Carl Friedlaender, Bemerkungen über Riesenzellen und ihr Verhältniss zur Tuberculose (Berliner Wochenschrift, 1874, nº 37).—Minteguyaga, Essai sur la séméiologie des crachats considérés surtout au point de vue microscopique. Thèse, Paris, 1868.—Rasmussen, Continued observation on hæmoptysis. Edinburgh, 1870.—Ferréol, Ulcération tuberculeuse de la langue (Notes lues à la Société médicale des hôpitaux, le 12 juillet et le 25 octobre 1872).—Julliard, Des ulcérations de la bouche et du pharynx dans la phthisie pulmonaire. Thèse, Paris, 1855 (Note sur l'ulcère tuberculeux de la bouche, Lausanne, 1870).—Gosselin, Gazette des hôpitaux, 1869.—U. Trélat, Note sur l'ulcère tuberculeux de la bouche et en particulier de la langue (Acad. de méd., 27 nov. 1869), et Archives gén. de méd., 1870, t. I, p. 35.—Landrieux, Des pneumopathies syphilitiques. Thèse, 1872.—E. Metzquer, Prophylaxie de la phthisie pulmonaire. Strasbourg, 1869.—Putégnat, Maladie des tailleurs de cristal de Baccarat (Bulletin Acad. de méd., 1859).—Feltz, Maladie des tailleurs de pierre (Gazette méd. de Strasbourg, 1865, nº 2 et 3).—Grainger Stewart, On dilatation of the bronchi or bronchiectasis. Edinburgh, 1867.—Woodward, J. J., Prt. 2d, Med. Vol. of Med. and Surg. Hist. of the War of the Rebellion.

Stomach.—Billard, De la membrane muqueuse gastro-intestinale, 1825.—Cruveilhier, Ramollissement de l'estomac, mémoire lu à l'Institut en 1821; Médecine pratique éclairée par l'anatomie et la physiologie pathologiques; Anat. path. générale, p. 392 et suiv.—Louis, Archives générales de médecine, vol. V.—Raynaud, Sur en cas de gastrite phlegmoneuse (Société anat., 1860).—Cruveilhier, Anat. path., livraison 20, pl. V, VI, liv. 20, pl. V, VI. Mémoire sur l'ulcère simple de l'estomac (Académie des sciences, 21 janvier 1856 et Archives générales de médecine, 1856, t. I, p. 149 et 442).—Ebstein, Archiv. v. Virchow, t. XL.—Krauss, Das perforirende Geschwür im Duodenum.—Cornil, Note sur les lymphangites pulmonaires à propos d'un cas de syphilis viscérale (Soc. méd des hôpitaux, 22 mai 1874).

Intestine.—Vulpian, Leçons sur l'appareil vaso-moteur, 13e et 14e leçon, t. I, 1875.—His, in Zeitschrift für wiss. Zoologie. XI, p. 65; XII, p. 223; XIII, p. 455; XV. p. 127.—Teichmann, Das Saugadersystem, von anat. Standpunkt beobach. Leipsig, 1861.—Debove, Archives de physiologie, 1870.—Thiry, Sur une nouvelle méthode d'isoler l'intestin grêle (Comptes rendus de l'Acad. des sciences de Vienne, 1864).—Radziejewsky, Zur physiologischen Wirkung der Abfürmittel. Reichert's und Dubois-Reymond's Archiv, 1870, 1-67.—A. Moreau, Expériences sur l'intestin (Note communiquée à l'Acad. de médecine, 5 juillet 1870).

Digestive apparatus.—Gianuzzi, in Sitzungsbericht der sachs. Akademie, nov. 1865.—Debove, Du psoriasis buccal (Thèse de Paris, 1874).—Davaine, Recherches sur les infusoires du sang dans la maladie connue sous le nom de sang de rate (Comptes rendus de l'Académie des sciences, t. LVII, p. 220, 351, 386, 1863, t. LIX, p. 393, 429, 1864 et t. LX, p. 1296, 1865, t. LXI, p. 3349.—Charcot et Vulpian, Sur les lésions des nerfs dans la paralysie diphthéritique du voile du palais (Gazette hebdomadaire, t. IX, 1862, p. 368). Dolbeau et Grancher, Sur en cas d'eléphantiasis de la lèvre (Bulletin de thérapeutique, 1875).—Guyon et Thierry, Note sur l'existence temporaire de kystes épidermiques dans la cavité buccale chez le fœtus et le nouveau-né (Archives de physiologie, 1869, p. 368 et 530).—Quinquaud, Nouvelles recherches sur le muguet (Archives de physiologie, t. I, 1868, p. 308).—Gueneau de Mussy, Traité de l'angine glanduleuse, Paris, 1857, in-8.

Syphilis of the œsophagus.—West, Dublin Quarterly Journal, Feb. 1860, et Archives de méd., t. I, p. 714, 1860, Rétrécissement syphilitique de l'œsophage (The Lancet, 9 August, 1872).—Follin, Traité élémentaire de pathol. externe, t. I, p. 696, 1861.—Lancereaux, Traité historique et pratique de la syphilis, 2e edit., 1874.

Dysentery.—Charcot, Recherches anatomo pathologiques sur la dysenterie (Thèse de Sacher, V, Section III, n° 3).—Cornil, Sur l'anatomie pathologique des ulcérations intestinales dans la dysenterie (Archives de physiologie, 1873, 311–318). —Kelsch, Contribution à l'anatomie path. de la dysenterie chronique (Archives de physiologie, 1873, p. 406 et 573).—Contribution à l'anatomie path. de la dysenterie aiguë (Archives de physiologie, 1873, p. 734).—Woodward, J. J., Prt. 2d, Med. Vol. of Med. and Surg. Hist. of the War of the Rebellion, 1879.

Cholera.—Hayem et Raynaud, Société médicale des hôpitaux, 1873, p. 262 et 267.—Pacini, Sur la cause speciale du choléra asiatique, Florence, 1865.—Davaine, article *Bactérie* du Dict. encyclopédique des sc. médicales.—Pouchet, Infusoires microscopiques dans les dejections des cholériques (Acad. des sciences, 23 avril 1849). —Kelsch et J. Renaut, Progrès médical, 1873, et Journal des Connaissances médicales, 1873, p. 274.—Treitz, Des affections urémiques de l'intestin (Prager Vierteljahrschrift, t. IV, et Archives gén. de méd., 1860, t. I).—Louis, Recherches sur la fièvre typhoïde, 1829.—Gosselin, De l'étranglement dans les hernies (Thèse d'agrégation, Paris, 1844).—Nicaise, Des lésions de l'intestin dans les hernies, Thèse, 1866.—Malgaigne, Mémoire sur les pseudo-étranglements et sur l'influence des hernies (Archives gén. de méd., 1841, et Journal de chirurgie, 1843, t. I, p. 129). —Gosselin et Labbé, Leçons sur les hernies abdominales, 1865.—Jobert, Maladies du canal intestinal, t. II.—Broca, De l'étranglement dans les hernies (Thèse d'agrégation, 1853).—Labbé, Expériences rapportées dans la thèse de M. Nicaise. —Pozzi, Etudes sur les fistules de l'espace pelvi-rectal supérieur (Thèse de doctorat, 1873).

Syphilis of the intestine.—Cullerier (Union médicale, 1854).—Fœrster, Handbuch der speciellen pathol. Anatomie, p. 148. — Meschede (Archiv. v. Virchow, t. XXXVII, p. 565).—Eberth (Archiv. v. Virchow, t. XL, p. 326).— Klebs, Syphilitic ulcerations of the intestine, in Handbuch der pathologischen Anatomie, p. 261.

Lymphadenoma.—Demange, Etude sur la lymphadénie, etc. (Thèse de doctorat, Paris, 1874).—Picot et Rendu, Paris, 1878.—Kelsch, Société anatomique, 1873.—Landouzy, Société anatomique, 1871.—Debove, Société anatomique, 1872.

Liver.—Budge, Ueber der Verlauf der Gallengänge in Müller's arch., 1850, p. 642.—Andrejevié, Ueber den feineren Bau der Leber, in Wien, Sitzungsber., t. LIII, p. 379.—Mac-Gillavry, In Wien Sitzungsber., t. LII, p. 207.—Eberth, in med. Centralblatt, 1866, n° 57 et in Virchow's Archiv, t. XXXIX, p. 70.—Köliker, Eléments d'histologie humaine.—Dutrouleau, Traité des maladies des Européens dans les pays chauds, Paris, 1861. Archives générales, 1853.—Griesinger, Traité des maladies infectieuses.—Frerichs, Die Melanæmie (Zeitschrift f. klinische Medicin. Breslau, 1855).—Traité pratique des maladies du foie. 2e edit. Paris, 1866.—Murchison, Treatise on Continued Fevers, London, 1862.—Garrod, Traité de la goutte.—Haspel, Maladies de l'Algérie, 2 vols. 1852.—Cruveilhier, Anat. path., liv. XVI, pl. 3; liv. XL, pl. 30.—Sinety, De l'état du foie chez les femelles en lactation (Thèse, Paris, 1873).—Dance, Archives gén. de médecine, t. XVIII, 1828, t. XIX, 1829.—Louis, Recherch. anat.-path. sur diverses maladies (Mém. de la Société médicale d'observ., t. II).—Rouis, Recherches sur les suppurations endémiques du foie, 1860.—Bichat, Dernier cours sur l'anatomie pathologique, publié d'après un ms. par P.-A. Béclard, avec notes par Boisseau. Paris, 1826, p. 188–190; J.-B. Baillière.—Laennec, Auscultation médiate, 1re éd., obs. 25, 29, 35, 36; 2e édit., obs. 35 et note annexée à cette observation.—Boulland, Mém. 1819, de la Société médicale d'émulation, t. IX, p. 170.—Cruveilhier, Anatomie pathologique, atlas, livraison 12, pl. 1; Traité d'anatomie pathologique générale, t. III, p. 210 et suivantes, 1856.—Andral, Précis d'anatomie pathologique, t. II, 2e partie, p. 583 et suivantes. Paris, 1829.—Bouillaud, Dictionnaire de médecine et de chirurgie pratique, art. *Cirrhose*.—Becquerel, Recherches anatomo-pathologiques sur la cirrhose du foie. In Archives générales de médecine, avril 1840.—Gubler, Bulletin de la Société anatomique, juillet et août 1848, mars 1849.—Thèse d'agrégation sur la théorie la plus rationnelle de la cirrhose, 1853. Gazette médicale de Paris, 1852 et 1854.—Kiernan, Philosophical Transactions, 1833.—Rokitansky, Lehrbuch der Path. Anatomie.—Requin, Pathologie médicale, t. II, p. 774, et Supplément au Dictionnaire des dictionnaires de médecine, art.

Cirrhose, 1851.—Sappey, Bulletins de l'Academie de médecine de Paris, t. XXIV, 1859.—Frerichs, Traité pratique des maladies du foie, trad. fr. par Duménil et Pallagot.—Duperray, Thèse de Paris, 1867.—Forster, Handbuch der pathol. Anatomie, 2e édit., 1872.—Rindfleisch, Lehrbuch der path. Anatomie.—Klebs, Handbuch der pathol. Anatomie, 1868–1873.—Cornil, Note pour servir à l'histoire de la cirrhose hépatique. In Archives de physiologie, n° de mars 1874, et Académie de médecine, séance du 4 nov. 1873.—Hayem, Contribution à l'étude de l'hépatite interstitielle chronique avec hypertrophie. In Archives de physiol., 1874.—Olivier (P.). Sur la cirrhose hypertrophique. In Union médicale, p. 61, 71, 75; 1871.—Hanot, Etude sur une forme de cirrhose hypertrophique du foie. Thèse, Paris, 1876.—Bertrand, Etude sur le cancer da la vésicule biliaire. Thèse de Paris, 1870.

Pancreas.—Verneuil, Mémoire sur l'anatomie du pancréas (Gazette médicale, 1851).—Cl. Bernard, Mémoire sur le pancréas. Paris, 1856 et Cours de physiologie professé au Collége de France, t. II, 1846.—Sappey, Traité d'anatomie.—Eberle, Physiologie der Verdaung. Wurzburg, 1834.—Bouchardat et Sandras, Annuaire de thérapeutique, 1843 et 1846.—L. Corvisart, Sur une fonction peu connue du pancréas, 1857, et Comptes rendus de l'Acad. des sc., 1859.—Klob, Wiener, Zeitschrift, 1859.—Aran, Archives génér. de médecine, 1846.—Willigk, Prag. Vierteljahrsschrift, 1856.—Cornil et Lépine. Société de biologie, 1874.—Recklinghausen, Archiv. v. Virchow, t. XXX.—Lucke et Klebs, Archiv. v. Virchow, t. XLI.—Virchow, Pathologie des tumeurs, t. I.

Spleen.—Frey, Histologie.—Gerlach, Zeitschrift für rationale Medicin, t. VII, 1848.—Billroth, Virchow's Archiv, t. XX et XXIII.—Sweigger-Seidel, Disquisitiones de liene. Halis, 1861, Virchow's Archiv, XXIII et XXVII.—Axel Kéy, Virchow's Archiv, XXI.—Müller, Ueber feineren Bau der Milz.—Peltier, Pathologie de la rate (Thèse de Paris, 1872).—Leon Colin, Rapports qui existent entre la pigmentation splénique et celle des autres tissus dans la mélanémie (Société med. des hôpitaux, 1873).—Carswel (Illustrat. fasicul. 8, pl. 3, fig. 6). Abcès de la rate.—Besnier, art. Rate du Dictionnaire encyclopédique des sciences médicales.—Ponfik, Etudes sur le typhus récurrent (Archiv von Virchow, mai 1874).—Lefeuvre (Charles), Etudes sur les infarctus viscéraux (Thèse de Paris, 1867).—Billroth, Arch. von Virchow, t. XVIII.—Virchow, Pathologie des tumeurs.—Gée, Augmentation de la rate dans la syphilis héréditaire in Roy. Med. and Chirurgic. Society, 1867, et Arch. de méd., 1867.—Parrot, Société de biologie, nov. 1872.—Sée, Leçons de pathologie expérimentale, 1866.—Andral, Kystes de la rate (Anatomie path., t. II, p. 93).—Leudet, Clinique méd. de l'Hôtel-Dieu de Rouen, 1874.—Magdelain in Péan, Ovariotomie et Splenotomie. Paris, 2e édit., G. Baillière, 1869.—Ernest Wagner, Archiv der Heilkunde, 1852, 5e liv.

Supra-renal capsule.—Ogle, Archives of Medicine, t. I.—Kusmaull, Würzburg. med. Zeitschrift, 1863.—Dæderlein, Inaugural Dissertation, Erlangen, 1860.—Addison, On the constitutional and local effects of Disease of the Supra-renal Capsules. London, 1855.—Bærensprung, Die hereditäre syphilis. Berlin, 1864.—Béhier, Leçons cliniques.—Martineau, Thèse de doctorat sur la maladie bronzée d'Addison, 1864.—Jaccoud, art. *Maladie d'Addison* du nouveau Dictionnaire de méd. et de chirurgie pratiques.—Ball, art. *Maladie bronzée* du Dictionnaire encyclopédique des sciences médicales.—Lancereaux, Traité historique et pratique de la syphilis. Paris, 1874, 2e édit. et. art. *Rein et Capsules surrénales* du Dictionnaire encyclopédique des sciences médicales.

Kidney.—Kolliker (*loc. cit.*). Henle, Zur Anatomie des Nieren Göttingen, 1862.—Ludwig, Structure du rein. In Stricker's Handbuch der Lehre von den Geweben, 1870.—Charcot, Leçons professées en 1874 à l'Ecole de médecine sur les maladies du rein. In Progrès médical, 1867.—Kelsch, Revue critique et recherches anatomo-pathologiques sur la maladie de Bright. In Archives de physiologie, n° de septembre 1874.—Reinhardt, Annalen der Charité zu Berlin, 1851.—Frerichs, Die Brightsche Nierenkrankheit.—Virchow, Ueber parenchymatöse Entzündung. In Arch. für path. Anatomie, t. IV, p. 260; 1852.—Johnson (G.), British and Foreign Medico-Chirurgical Review, 1855; Med. Soc. of London in Lancet, July, 1858; Medico-Chirurg. Transactions, t. XLII, p. 154; t. LI, p. 57, 1868; Medical Times and Gazette, April, 1869; Medical Journal, April, 1870.—Gull et Suton,

On the Pathology of the Morbid State commonly called Chronic Bright's Disease with contracted Kidney (arterio-capillary-fibrosis). In Medico-Chirurgical Transactions, t. LV, p. 273; 1872.—Grainger-Stewart, British Med. Journal, July, 1872, and Brit. Rev., January 1867.—Hood, Lancet, August, 1872.—Traube, Gesammte Abhandlungen, t. II.—Wilks (Samuel), Cases of Bright's Disease. In Guy's Hosp. Reports, 2d Series, vol. VIII, 1854.—Handfield Jones, On the Curative Treatment of Chronic Morbus Brighti. In Medic. Times and Gaz., 1855.—Todd, Clinical Lectures on certain Diseases of the Urinary Organs and on Dropsies. Lond., 1857.—Charcot et Cornil, Contribution à l'étude des altérations anatomiques du rein chez les goutteux. In Société de biologie, 1863.—Garrod, Traité de la goutte, trad. franç. par M. A. Ollivier, notes de M. Charcot, 1867.—Lecorche, Traité des maladies des reins, in-8. Masson, 1875.—Cornil, Des différentes espèces de néphrites, Thèse d'agrégation, 1869.—Cornil, Note sur la dégénérescence amyloïde des organes étudiée au moyen de réactifs nouveaux (Archives de physiologie, 1875).

INDEX.

ABNORMAL colorations of skin, 740
Abscess, biliary, 540
embolic, 330
large, of liver, 541
metastatic, of kidneys, 644
of liver, 536
of bone, 203
of brain, 376
of connective tissue, 255
of epiphysis, 245
of heart, 297
of kidney, 643
of liver, large, 541
of lung, 419
of pancreas, 579
of prostate, 670
of spleen, 589
of urethra, 654
retro-pharyngeal, 458
Absorption of bone, 197
Acarus folliculorum, 742
scabici, 742
Acephalocysts, 193
Acetic acid, action on pus corpuscles, 67
Achorion Schœnleinii, 743
Acinous adenoma, 160
glands, 38
Acne pustule, 735
Acute phlegmon, 253
Adænia, 142
Addison's disease, 602
Adenitis, acute, 352
chronic, 353
Adeno-chondroma, 128
Adenoid tissue, 24
Adeno-lymphocele, 141
Adenoma, 160
acinous, 160
diagnosis of, 162
of intestine, 514
of larynx, 403
of mammary gland, 715
prognosis of, 164
tubular, diagnosis of, 164
with cylindrical cells, 162
Adeno-myoma of prostate, 671
Adeno-sarcoma, 355
Adhesive inflammation of serous membranes, 265
Adipo-fibroma, 95
Adipoma, 95
Adipose tissue, 24
in inflammation, 60
in œdema, 251
Albuminous interstitial nephritis, 631
nephritis, 619
Albuminuria, 619
from cold, 624
of alcoholism, 624
of arthritis, 626
of cardiac diseases, 626
of gout, 626
of phthisis, 624
Alcoholism, albuminuria of, 624
liver in, 522, 544
Alopecia circumscripta, parasite of, 746
Alterations of cells and tissues, 39
Alveolar carcinoma, 104
sarcoma, 84
Alveoli of carcinoma, 98
Amœboid movements, 19
Amyelinic neuroma, 138
Amyloid degeneration of arteries, 332
of capillaries, 337
of cartilage cells, 26
of hepatic cells, 525
of kidney, 627
of liver, 557
of pancreas, 580
of spleen, 591
of stomach, 465
of supra-renal capsule, 600
infiltration, 46
Anæmia, 287
of brain, 368
of kidney, 617
of lung, 408
of stomach, 464
Anatomy of miliary tubercle, 116
Aneurisms, 314
arterio-venous, 318
clot in, 315
cystogenic, 315
dissecting, 315
false, 317
fusiform, 315
irritation from, 317
laminæ in, 316
miliary, of brain, 371
of heart, 295
sac of, 316
spontaneous, 315

Aneurisms—
valvular, of heart, 302
Angeioleucites, 345
Angiolithic sarcoma, 85
Angioma, 139
anatomical diagnosis of, 140
cavernous, 139
development of, 140
nutritive alterations of, 140
of kidney, 651
of liver, 559
of muscle, 282
prognosis of, 141
seat of, 140
simple, 139
species of, 139
trabeculæ of, 139
Angioses, 139
Animal parasites of skin, 741
Antero-lateral sclerosis of spinal cord, 387
Anthracosis, 426
Aorta, degenerations of, 313
Apoplexy, capillary, of brain, 369
of lung, 409
Appendix, 749
to tumors, 189
Argyria, 450
Arteritis, 307
acute, 307
chronic, 311
deformans, 312
syphilitic, 331
Artery, amyloid metamorphosis of, 332
atheroma of, 311
calcification of, 312
fatty degeneration of, 310
healing of, after acupressure, 325
after ligature, 318
after torsion, 325
histology of, 306
lesions of, 306
obliteration of by endarteritis, 326
by ligature, 318
by thrombosis, 326
obstruction of by embolism, 326
spontaneous obliteration of, 325
syphilitic lesions of, 331
thrombus in, from ligature, 318
tubercles of, 333
tumors of, 332
Arthritis, 228
acute, lesions of cartilage in, 230
synovia in, 228
synovial membrane in, 229
albuminuria of, 626
chronic, 233
by continuity, 233
lesions of cartilage in, 233
rheumatic, 234
ecchondroses in, 235
deformans, 234
dry, 234
gouty, 241
perforating, 235
purulent, 231
Arthritis—
rheumatic, 228
scrofulous, 238
simple, 228
traumatic, 228
Articular foreign bodies, 238
Articulations, inflammation of, 228
lipoma of, 244
normal histology of, 227
pathological anatomy of, 227
tumors of, 244
Atelectasis, 411
Atheroma of arteries, 311
Atrophic scirrhus, 103
of mammary gland, 710
Atrophy, acute yellow, of liver, 532
from compression, 42
from insufficient nutrition, 41
of heart, 292
of liver from cirrhosis, 547
of lung, 411
of muscle, 270
of pancreas, 580
of skin, 730
of spleen, 584
physiological, 41
red, of liver, 531
without degeneration, 42
Authors' preface, v
Axillary glands in carcinoma of mammary gland, 175, 712
Axis cylinder of nerves, 33

BACTERIA, in bladder, 653
in blood, 289
in feces, 485
in mouth, 455
Balbiani, investigations of, upon ovule, 19
Bibliography, 753
Biliary abscesses, 540
calculus, 568
passages in cirrhosis of liver, 550
vessels, cysts of, 565
inflammation of, 567
Bladder, carcinoma of, 655
catarrhal inflammation of, 653
enchondroma of, 655
histology of, 652
hyperæmia of, 652
hypertrophy of, 653
tuberculosis of, 654
tumors of, 655
varicose veins of, 652
Blastoderm, 18, 716
Blenorrhagia, 654
Blister of skin, 731
Blood-clot, in heart, 304
organization of, in arteries, 319
Blood, coloring material of, 285
histology of, 20, 59, 284
of cholera, 500
parasites in, 289
pathological histology of, 287
pigment in, 288

Blood—
red corpuscles of, 284
white corpuscles of, 286
Bloodvessels in granulation tissue, 69
in sclerosis of spinal cord, 386
of kidney, changes of, 615
tumors formed of, 139
Bone, absorption of, 197
callus, 209
carcinoma of, 214
caries of, 207
cells in caries, 208
chondroma of, 218
congestion and hemorrhage of, 196
corpuscles, 26
cysts in, 218
development of, 28, 195
eburnation of, 202
encephaloid sarcoma of, 213
epithelioma of, 218
fascicular sarcoma of, 213
fracture of, in carcinoma, 214
in rachitis, 224
in sarcoma, 214
gumma of, 111, 217
hemorrhage of, 196
histology of, 28–30, 195
inflammation of, 197
lesions of, 195
lipoma of, 214
lobulated epithelioma of, 150
lymphadenoma of, 218
marrow of, 27
medullary cavity of, 27
myeloid sarcoma of, 214
myxomatous tumors of, 214
necrosis of, 204
ossifying sarcoma of, 214
osteoma of, 218
round-celled sarcoma of, 213
sclerosis of, 202
sequestrum of, 205
softening of, 219
spindle-celled sarcoma of, 213
structure of, 26
tuberculosis of, 215
tumors of, 212
Bowman, sarcous elements of, 31
Brain, abscess of, 376
capillary apoplexy of, 369
congestion of, 368
cysts of, 380
embolic softening of, 372
fibroma of, 378
hemorrhage of, 369
hemorrhagic foci of, 370
histology of, 31
infarctus of, 372
inflammation of, 375
inflammatory softening of, 375
lipoma of, 378
melanæmia of, 369
miliary aneurism of, 371
neuroma of, 380
œdema of, 368
Brain—
papilloma of, 378
red softening of, 375
sclerosis of, 377
softening of, 372
syphilis of, 378
thrombosis of, 374
tubercle of, 378
tumors of, 378
yellow softening of, 375
Bright's disease of kidney, 621
Bronchi, calcification of, 407
congestion of, 404
dilatation of, 405
hemorrhage of, 404
histology of, 390
inflammation of, 404
lipoma of, 407
ossification of, 407
tubercle of, 407
tumors of, 407
ulceration of, 407
Bronchiectasis, 405
Bronchitis, 404
chronic, 405
diphtheritic, 404
Buccal cavity, tumors of, 453
mucous membrane, histology of, 446
parasites of, 455
pathology of, 448
psoriasis of, 451
tumors of, 453
Bulla of skin, 731
Bursa, mucous, 248

CALCAREOUS infiltration, 51
transformation of pus corpuscles, 68
Calcification of arteries, 312
of bronchi, 407
of capillaries, 337
of cartilage, 26, 225
of lymph glands, 354
of stomach, 472
of veins, 342
Calcified cartilage, 26
Calculi of bladder, 653
of kidney, 645
of liver, 568
of prostate, 671
of veins, 52, 342
Calculous pyelitis, 645
Calculus, biliary, 568
of pancreas, 582
Callus, cartilaginous, 210
formation of, 209
peripheral, 212
provisional, 212
Cancroid, labial, 454
Capillaries, amyloid degeneration of, 337
calcareous infiltration of, 337
embolism of, 369
endothelium of, 37
fatty degeneration of, 336
histology of, 334

Capillaries—
inflammation of, 335
nutritive lesions of, 336
Capillary apoplexy of brain, 369
Capsule of Glisson in cirrhosis, 548
Carapaces of serous membranes, 265
Carcinoma, 96
anatomical diagnosis of, 106
calcareous infiltration of, 106
caseous metamorphosis of, 105
cells of, 97
colloid, 104
definition of, 96
development of, 99
encephaloid, 103
fatty degeneration of, 105
fibrous, 103
general description of, 97
generalization of, 101
growth of, 101
hard, 103
inflammation of, 106
juice of, 97
lipomatous, 103
lymph glands in, 102
lymphatics of, 98, 347
medullary, 103
melanotic, 105
of bladder, 655
of bone, 214
of Fallopian tube, 688
of gall-bladder, 569
of intestine, 515
of kidney, 650
of larynx, 402
of liver, 561
of lung, 428
of lymph glands, 356
of mammary gland, 710
of muscle, 281
of nerves, 363
of ovary, 678
of pancreas, 581
of pericardium, 292
of peritoneum, 576
of pleura, 445
of prostate, 672
of rectum, 515
of serous membranes, 267
of spleen, 594
of stomach, 475
of supra-renal capsule, 601
of testicle, 668
of thyroid gland, 597
of trachea, 403
of uterus, 694
prognosis of, 106
seat of, 107
species and varieties of, 102
stroma of, 98
ulceration of, 106
villous, 106, 713
Cardiac liver, 530
Caries, 207
caseous transformation in, 209
Cartilage, amyloid degeneration of cells, 26
calcification of, 26
development of, 25
embryonal, 25
fatty degeneration of, 225
fibrous, 26
fœtal, 26
irritative lesions of, 225
lesions of, 225
in acute arthritis, 230
in chronic arthritis, 233
in chronic rheumatic arthritis, 235
in gouty arthritis, 241
in scrofulous arthritis, 239
in white swelling, 239
mucous, 26
nutritive lesions of, 225
ossification of, 133
reticular, 26
structure of, 25
tumors of, 126
Cartilaginous callus, 210
Caseous metamorphosis of carcinoma, 105
pneumonia, 433
transformation, in caries, 209
of pus corpuscles, 68
Casts, formed in uriniferous tubules, 611
of uterus, 685
Catarrh, gastric, 465
uterine, 690
Catarrhal nephritis, 620
pneumonia, 414
pyelo-nephritis, 645
salpingitis, 687
Cavernous angioma, 139
Cells, amœboid movements of, 19
and tissues, alterations of, 39
cloudy swelling of, 43
definition of, 19, 20, 21
embryonic, 19
epithelial, 34
fibrinous degeneration of, 46
in fibrinous exudation of serous membranes, 261
lesions in formation of, 53
membrane of, 19, 22
mucous and colloid degeneration of, 44
multinucleated, 21
nerve, 31
nucleolus of, 19
nucleus of, 19
of carcinoma, 97
of gangrene, 41
of sarcolemma, multiplication of, 278
of sarcoma, 77
of tubercle, 114
origin of, 18
pigmentation of, 49
spontaneous generation of, 17
structure of, 17
Cell theory, 17
Cerebral abscess, 376
anæmia, 368
capillary apoplexy, 369

Cerebral—
congestion, 368
cysts, 380
hemorrhage, 369
infarctus, 372
inflammation, 375
melanæmia, 369
œdema, 368
rheumatism, 364
sclerosis, 377
softening, 372
syphilis, 378
thrombosis, 374
tubercle, 378
tumors, 378
Cerebro-spinal meningitis, 364
Chalk-stones, 242
Chancre, induration of, 107
Cholera, 499
blood of, 500
Cholesterin crystals, 41
Chondroma (*see* Enchondroma)
Chondroma of bone, 218
Choroid plexus, cysts of, 367
Cicatrization of nerves, 361
of wounds, 71
Circulation in cirrhosis of liver, 549
Cirrhosis, capsule of Glisson in, 548
hepatic cells in, 553
of liver, 543
biliary passages in, 550
circulation in, 549
vessels in, 549
with atrophy, 547
with granular surface, 547
with smooth surface, 545
Classification of tumors, 75, 172
Clinical forms of inflammation, 73
Cloudy swelling of cells, 43
of hepatic cells, 524
of muscle, 271
Cohnheim's theory of inflammation, 61
Colitis, 486
Colloid carcinoma, 104
cysts of kidney, 637
infiltration, 44
matter, 44
pneumonia, 436
Colostrum corpuscles, 38, 705
Comedones, 165
Compact osteoma, 132
Concentric cell-nest of epithelioma, 151
Concretions in contracted kidney, 638
in prostate, 671
Condensing osteitis, 202
Congenital hydrocele, 662
Congestion and hemorrhage of bone, 196
cerebral, 368
inflammatory, 63
of Fallopian tube, 686
of intestine, 483
of kidney, 618
of liver, 528, 532
of lung, 408
of meninges, 364
Congestion—
of nerves, 360
of ovary, 676
of pleura, 438
of spinal cord, 380
of spleen, 585
of stomach, 464
of uterus, 689
Connective tissue, 23
abscess of, 255
and serous cavities, lesions of, 247
chronic phlegmon of, 256
congestions and hemorrhage of, 248
diffused phlegmon of, 255
gangrene of, 256
histology of, 247
hydatids of, 258
induration of, 255
inflammation of, 252
œdema of, 250
of kidney, lesions of, 614
purulent inflammation of, 253
serous cysts of, 257
tumors of, 257
type of tumors, 89
Contents, table of, vii
Contraction of œsophagus, 459
Cordée, 654
Corneal fibroma, 93
Corneous ichthyosis, 740
papilloma, 158
Corns, 158
Corpus luteum, 675
Corpuscle, Pacinian, 720
tactile, 720
Coryza, 394
Croup, 397
Croupous exudations, 65
gastritis, 468
nephritis, 623
pneumonia, 416
Cryptococcus cerevisiæ, 455
Crystals found in gangrene, 41
Cutaneous diphtheritis, 728
parasites, 741
Cylindrical-celled epithelioma, 154
Cylindroma, 156
Cysticercus cellulosæ, 191
Cysticercus of muscle, 282
Cystic hydrocele, 662
myxoma, 90
Cystitis, 653
ulcerating, 654
Cysto-chondroma, 129
Cysts, 164
colloid of kidney, 637
dermoid, 166
developed from glands, 168
development of, 170
hydatid, 191
mucous, 168
multilocular, 169
of bone, 218

Cysts—
of brain, 380
of choroid plexus, 367
of dysentery, 496
of Fallopian tube, 688
of kidney, 650
of liver, 565
of mammary gland, 715
of mouth, 453
of œsophagus, 460
of ovary, 679
of pancreas, 581
of spleen, 595
of stomach, 467
of testicle, 669
proliferous, 169
of ovary, 680
sebaceous, 165
serous, 167
of connective tissue, 257
spermatic, 662
unilocular, of ovary, 680

DEATH of the elements, cause of, 39
Degeneration, amyloid, of capillaries, 337
of hepatic cells, 525
of kidney, 627
of lymph glands, 355
of pancreas, 580
of spleen, 591
calcareous, of lymph glands, 354
caseous, of lymph glands, 354
of supra-renal capsule, 602
of tubercle, 122
colloid, of lymph glands, 355
consecutive to inflammation, 72
fatty, 48
in inflammation, 72
of arteries, 310
of capillaries, 336
of carcinoma, 105
of cartilage, 225
of heart, 293
of kidney, 629
of liver, 557
of pancreas, 579
of pus corpuscles, 68
fibrinous, of cells, 65
pigmentary, of heart, 294
of muscle, 274
secondary, of spinal cord, 381
waxy, of lymph glands, 354
of muscle, 274
vitreous, of muscle, 274
Demodex folliculorum, 742
Dermatitis, acute, 724
fibrinous, 727
fibrous hypertrophic, 728
formative, 736
leprous, 738
of glanders, 738
pseudo-membranous, 728
suppurative, 727
Dermoid cysts, 166
of ovary, 682
tumor, 91
Destruction of tissue in gangrene, 40
Development of angioma, 140
of carcinoma, 99
of cartilage, 25
of concentric cell-nest epithelioma, 152
of cylindrical-celled epithelioma, 156
of cysts, 170
of enchondroma, 129
of fibroma, 94
of fibrous tissue, 23
of gumma, 110
of lipoma, 96
of lobulated epithelioma, 149
of lymphadenoma, 145
of mucous papilloma, 159
of myxoma, 136
of nerve cells, 32
of nerve fibres, 33
of osseous tissue, 27
of osteoma, 132
of sarcoma, 87
of tubercle, 122
of tubulated epithelioma, 153
Diagnosis, anatomical, of angioma, 140
of carcinoma, 106
of fibroma, 94
of gumma, 112
of myoma, 136
of myxoma, 91
of neuroma, 138
of tubercle, 125
differential, of sarcoma and chronic phlegmon, 257
of acinous adenoma, 162
of cylindrical-celled epithelioma, 156
of lymphadenoma, 145
of papilloma, 160
of tubular adenoma, 164
Diarrhœa, 483
Diffused abscess of connective tissue, 255
congenital encephalitis, 375
meningo-cephalitis, 376
nephritis, 621
phlegmon of connective tissue, 255
Digestive apparatus, 446
Dilatation of bronchi, 405
Diphtheritic bronchitis, 404
exudations, 65
laryngitis, 397
pharyngitis, 457
stomatitis, 452
Diphtheritis, cutaneous, 728
Distoma of kidney, 651
Division of epithelial tissues, 36
of nerves, lesions following, 361
of normal tissues, 22
Dry arthritis, 234
gangrene, 41
Duhring, L., 717
Dujardin, definition of cells, 18
Duodenitis, 486

Duodenum, ulcer of, 471
Dura mater, hæmatoma of, 367
inflammation of, 367
Dysentery, 489
chronic, 493
cysts of, 496
stools of, 492
Dysmenorrhœa, pseudo-membranous, 685
Dystrophies of skin, 739

EBURNATED osteoma, 132
Eburnation of bone, 202
Ecchondroses, 244
in chronic rheumatic arthritis, 235
Ecchymoma, 139
Ecchymosis of heart, 294
of pericardium, 290
of stomach, 464
Echinococcus, 192
Eggs of Naboth, 163, 684
Elastic tissue, 25
Elements, hypertrophy of, 53
of milk, 705
Elephantiasis Arabum, 141, 720
glabrous, 730
tuberosa, 730
verrucosa, 728
Embolic abscess, 330
infarction of muscle, 277
softening of brain, 372
Embolism, 326
of liver, 536
Embryonic cells, multiplication of, 21
Emigration of white blood-corpuscles, 62
Emphysema of lung, 412
Encephalitis, 375
chronic, 377
diffused congenital, 375
Encephaloid carcinoma, 103
of mammary gland, 713
of stomach, 476
pultaceous, 103
sarcoma, 79
Enchondroma, 126
development of, 129
hyaline, 128
modifications of, 129
of bladder, 655
of lung, 428
of lymph gland, 357
of mammary gland, 714
of muscle, 281
of ovary, 678
of testicle, 663
ossifying, 128
osteoid, 131
prognosis of, 131
seat of, 129
varieties of, 128
with ramifying cells, 129
Endocarditis, acute, 300
chronic, 302
Endocardium, histology of, 298
Endothelial coverings, 35
Endothelium of serous membrane, 38
of vascular system, 37
of vessels in inflammation, 58
Enostoses, 133
Epiphyseal exostoses, 132
osteitis, 203
Epiphysis, abscess of, 245
Epistaxis, 394
Epithelia, inflammation of, 56
Epithelial cells, 34
nests, 147
pearls, 147
pegs, 147
tissue, 34
division of, 36
Epithelioma, 146
concentric cell-nest, development of, 152
cylindrical-celled, 154
development of, 156
diagnosis of, 156
lobulated, 146
development of, 149
generalization of, 150
of muscle, 150
of sebaceous gland, 150
prognosis of, 151
of bone, 218
of gall-bladder, 570
of intestine, 516
of larynx, 402
of lip, 454
of liver, 564
of lymph gland, 358
of mammary gland, 715
of mouth, 454
of muscle, 281
of nasal fossæ, 396
of nerves, 363
of œsophagus, 460
of ovary, 678
of rectum, 516
of serous membranes, 268
of stomach, 476
of supra-renal capsule, 601
of thyroid gland, 598
of tongue, 454
of uterus, 696
pavement-celled, 146
tubulated, 152
development of, 153
prognosis of, 154
varieties of, 146
with concentric cell-nests, 151
Epithelium, formation of, on ulcers, 72
glandular, 38
Epulis, 83, 214
Erectile lipoma, 96
tumors, 139
Erysipelas, 724
Erysipelatous laryngitis, 398
Exostoses, 132
epiphyseal, 132
parenchymatous, 133
subungual, 83, 214
Extension of sarcoma, 87

Exudation, croupous, 65
diphtheritic, 65
fibrinous, 64
of serous membranes, 260
hemorrhagic, 65
inclosing cellular elements, 65
inflammatory, 64
mucous, 64
of serous membranes in inflammation, 259
pseudo-membranous, 65
serous, 64

FALLOPIAN TUBE, carcinoma of, 688
congestion of, 686
cysts of, 688
hemorrhage of, 686
histology of, 683
inflammation of, 687
tubercle of, 688
tumors of, 688
Farcy granule, 738
Fasciculated fibroma, 93
neuroma, 137
sarcoma, 80
Fatty degeneration, 48
in inflammation, 72
of fibroma, 93
of lipoma, 96
of muscle, 272
infiltration, 47
osteoporosis, 220
Favus fungus, 743
Feces, bacteria in, 485
Fibres of fibrous tissue, development of, 23
of Remak, 33
Fibrin, 286
coagulation of, 64
Fibrinogenic substance, 64, 286
Fibrinoplastic substance, 64, 286
Fibrinous dermatitis, 727
exudations, 64
of serous membrane, 260
pleurisy, 440
pneumonia, 416
Fibro-cartilage, 26
Fibro-chondroma, 128
Fibroid polypi of uterus, 693
tumors, 91
Fibroma, 91
anatomical diagnosis of, 94
calcareous infiltration of, 94
corneal, 93
definition of, 92
description of, 92
development of, 94
fasciculated, 93
fatty degeneration of, 93
flat-celled, 92
molluscum, 93
mucoid, 93
of brain, 378
of intestine, 513
of larynx, 401
Fibroma—
of lung, 428
of mammary gland, 710
of meninges, 367
of mouth, 453
of muscle, 281
of pleura, 445
of testicle, 664
prognosis of, 95
seat of, 94
species of, 92
Fibro-myoma of intestine, 513
of œsophagus, 460
of ovary, 678
Fibrous carcinoma, 103
hypertrophic dermatitis, 728
lipoma, 96
polypi of nasal fossæ, 396
tissue, lymph spaces of, 23
structure of, 23
Fistula, rectal, 507
Flat-celled fibroma, 92
Fœtal cartilage, 26
Foot, perforating ulcer of, 739
Foreign bodies, articular, 238
Formation of callus, 209
of cells, 17
of osseous trabeculæ, 199
of pus, theory of, 67
Formative arthritis, 234
dermatitis, 736
osteitis, 202
Fracture of bone, compound, 210
division of, 210
in carcinoma, 214
in osteomalacia, 220
in rachitis, 224
phenomena in, 211
simple, 210

GALACTOCELE, 707
Gall-bladder, carcinoma of, 569
epithelioma of, 570
inflammation of, 567
tumors of, 569
Ganglionic neuroma, 137
Ganglions, 68
Gangrene, cells in, 41
crystals in, 41
dry, 41
humid or moist, 40
in inflammation, 72
of lipoma, 96
of lung, 421
of mouth, 453
phenomena of, 40
senile, 41
Gangrenous connective tissue, 256
gastritis, 469
Gases in pericardium, 290
Gastric catarrh, 465
Gastritis, 465
chronic, 466
croupous, 468

Gastritis—
gangrenous, 469
phlegmonous, 468
Gastro-intestinal mucous glands, hypertrophy of, 163
Gelatinous cysts of ovary, 680
General description of carcinoma, 97
Generalization of carcinoma, 101
of lobulated epithelioma, 150
of sarcoma, 87
Gestation, changes of uterus during, 686
Giant cells, 20
in sarcoma, 81
in tubercle, 118
Glanders, 126
dermatitis of, 738
laryngitis of, 399
Glands, acinous, 38
cysts of, 168
of skin, 720
of stomach, lesions of, 465
tubular, 38
varieties of, 38
Glandular epithelium, 38
Glioma, 83
Glio-sarcoma, 83
Glottis, œdema of, 399
Goitre, 596
aneurismal, 597
calcified, 597
cystic, 597
fibrous, 597
soft, 597
Gonorrhœa, 654
Gout, albuminuria of, 626
Gouty arthritis, 241
urate of soda in, 241
Graafian follicle, 674
dropsy of, 679
Granular kidney, 626
liver, 547
os uteri, 691
pharyngitis, 458
Granulation tissue, 69
Gross, S. W., 78, 82, 84
Growth of carcinoma, 101
Gumma, 107
absorption of, 112
anatomical diagnosis of, 112
description of, 109
development of, 110
metamorphoses of, 111
of bone, 111, 217
of intestine, 512
of kidney, 647
of liver, 111, 560
of muscles, 281
of ovary, 678
of pancreas, 580
of spleen, 594
of supra-renal capsule, 601
of testicle, 667
prognosis of, 112
seat of, 112
Gum, lead line on, 450
silver line on, 450

HÆMATIN, 285
Hæmatocele, 663
of skin, 724
peri-uterine, 688
Hæmatoidin, 50, 286
Hæmatoma of dura mater, 367
Hæmin, 285
Hæmoglobin, 285
Hæmorrhoids, 513
Hard scirrhus, 103
Haversian canals, 27
Healing of arteries after ligature, 318
of wounds, 71
Heart, abscesses of, 297
aneurisms of, 295
atrophy of, 292
blood-clots in, 304
congestion of, 294
diseases, albuminuria of, 626
ecchymosis in, 294
fatty degeneration of, 293
fatty infiltration of, 292
fibroid induration of, 297
hemorrhages of, 294
hypertrophy of, 293
inflammation of, 296
muscular fasciculi of, 30
pigmentary degeneration of, 294
ruptures of, 295
tumors of, 298
valvular aneurisms of, 302
vegetations on, 300, 303
Hemorrhage, nasal, 394
of bones, 196
of brain, 369
of bronchi, 404
of connective tissue, 248
of Fallopian tube, 686
of heart, 294
of kidney, 618
of muscle, 276
of nerves, 360
of ovary, 676
of pericardium, 290
of serous membranes, 258
of skin, 724
of spinal cord, 380
of supra-renal capsule, 600
of uterus, 689
Hemorrhagic exudations, 65
infarction, 330
of lung, 410
inflammation of serous membranes, 262
foci of brain, 370
myxoma, 90
pericarditis, 291
peritonitis, 574
pleurisy, 443
Hepatic cells, amyloid degeneration of, 525
changes in, 522
clouding swelling of, 524
fatty infiltration of, 525
in cirrhosis, 553
Hepatitis, 532
Hepatitis glabra, 544
interstitial, 543

Hepatitis, interstitial—
syphilitic, 111
miliary interstitial, 545
parenchymatous, 532
purulent, 536
Hernia, lesions of intestine in, 506
strangulated, 506
Hernial sac, dropsy of, 662
Herpes circinatus, 744
Heteroplasia, 53
Histology, normal, 17
of arteries, 306
of articulations, 227
of bladder, 652
of blood, 284
pathological, 287
of bronchi, 390
of buccal mucous membrane, 446
of capillary bloodvessels, 334
of connective tissue, 247
of endocardium, 298
of Fallopian tubes, 683
of intestine, 479
of kidney, 604
of larynx, 389
of liver, 517
of lung, 390
of lymphatic glands, 348
of lymphatic vessels, 345
of mammary gland, 701
of muscles, 269
of nasal fossæ, 389
of nerve tissue, 359
of œsophagus, 456
of ovaries, 673
of pancreas, 578
of pharynx, 456
of prostate, 670
of respiratory apparatus, 389
of serous cavities, 247
of skin, 716
of spleen, 583
of stomach, 461
of supra-renal capsule, 599
of synovial membrane, 227
of testicles, 657
of thyroid gland, 596
of trachea, 390
of ureter, 652
of urethra, 652
of uterus, 683
of veins, 338
Hobnail liver, 547
Horns, 158
Hyaline enchondroma, 128
Hydrarthrosis, 233
Hydatid cysts, 191
of connective tissue, 258
of liver, 565
of mammary glands, 715
of muscle, 282
of peritoneum, 577
tumor, multilocular, 193
Hydræmia, 287
Hydrocele, 661
Hydrocele—
congenital, 662
cystic, 662
of cord, 662
spermatic, 662
Hydro-pericardium, 290
Hygroma, 168
Hyperæmia, 63
of bladder, 652
of lung, 408
of ovary, 676
of spleen, 585
of supra-renal capsule, 600
Hyperplasia, simple, 53
Hyperplastic inflammation of serous membranes, 265
Hypertrophy of elements, 53
of gastro-intestinal mucous glands, 163
of heart, 293
of lips, 453
of mammary gland, 707
of muscle, 271
of muscular tissue of stomach, 477
of prostate, 671
of thyroid gland, 596
of tongue, 453
of uterus, 697

ICHTHYOSIS, corneous, 740
Ichthyosis pilaris, 740
Ichthyosis pityriasis, 740
Icterus, 535
Ileitis, 487
Illustrations, list of, xxv
Induration, fibroid, of heart, 297
of lymphatic glands, 353
of chancre, 107
of connective tissue, 255
of pancreas, 579
Infarction, 40
embolic, of muscle, 277
hemorrhagic, 330
of brain, 372
of kidney, 619
of spleen, 589
Infiltration, amyloid, 46
calcareous, 51
of capillaries, 337
of carcinoma, 106
of fibroma, 94
of lipoma, 96
of myoma, 135
of pericardium, 291
of veins, 342
fatty, 47
of heart, 292
of hepatic cells, 525
of liver, 555
of myoma, 136
of pancreas, 579
mucous and colloid, 44
of urates, 52
serous and albuminous, 42
serous, of skin, 721

Inflammation, catarrhal, of bladder, 653
of uterus, 690
chronic differential, from sarcoma, 257
diffused, of skin, 724
of connective tissue, 256
of liver, 543
of lymph glands, 353
of muscle, 279
of supra-renal capsule, 602
circumscribed, of skin, 730
clinical forms of, 73
Cohnheim's theory of, 61
congestive, of skin, 724
definition of, 55
degenerative, of skin, 737
diffused, of skin, 724
exudative, of skin, 727
hemorrhagic, of serous membranes, 262
hyperplastic, of serous membranes, 265
of skin, 736
in non-vascular tissues, 55
new formation of vessels in, 68
of arteries, 307
of articulations, 228
of biliary vessels, 567
of bone, 197
of brain, 375
of bronchi, 404
of capillaries, 335
of carcinoma, 106
of colon, 486
of connective tissue, 252
of duodenum, 486
of epithelia, 56
of Fallopian tube, 687
of gall-bladder, 567
of heart, 296
of ileum, 487
of intestine, 483
of kidney, 619
of laryngeal cartilages, 401
of larynx, 396
of lipoma, 96
of liver, 532
of lung, 414
of lymph glands, 352
of lymphatics of lung, 420
of lymphatic vessels, 345
of mammary gland, 706
of mucous membrane of mouth, 448
of muscle, 278
of nasal mucous membrane, 394
of nerves, 360
of œsophagus, 459
of osseous tissue, 59
of ovary, 677
of pancreas, 578
of pericardium, 290
of peritoneum, 571
of pharynx, 457
of pleura, 440
of prostate, 670
of rectum, 488
of sebaceous glands, 735
of serous membranes, 259
Inflammation—
of spinal cord, 383
of spleen, 587
of stomach, 465
of subcutaneous tissue, 60
of supra-renal capsule, 601
of testicle, 659
of tonsil, 452
of trachea, 403
of tunica vaginalis, 661
of urethra, 654
of vascular tissues, 59
of veins, 339
of vermiform appendix, 488
peri-glandular of skin, 735
puerperal, of uterus, 692
purulent, of connective tissue, 253
of serous membranes, 263
scrofulous, of lymph glands, 354
suppurative, of portal vein, 537
ulcerative, of large intestines, 489
Inflammatory congestion, 63
exudations, 64
new formations, 66
softening of brain, 375
Innoma, 92
Intermittent fever, spleen in, 585
Interstitial hepatitis, 543
myelitis, 384
nephritis, 631
pneumonia, 423
Intestinal catarrh, 483
lesions of typhoid fever, 501
ulcers of tuberculosis, 510
Intestine, adenoma of, 514
carcinoma of, 515
congestion of, 483
epithelioma of, 516
fibro-myoma of, 513
fibroma of, 513
gumma of, 512
histology of, 479
inflammation of, 483
large, ulcerative inflammation of, 489
lesions of in hernia, 506
lipoma of, 513
lymphadenoma of, 514
polypus of, 514
post-mortem changes of, 483
syphilitic tumors of, 512
syphilitic ulcers of, 512
tuberculosis of, 508
uræmic ulcerations of, 501
vascular tumors of, 513

JAUNDICE, 535
Juice of carcinoma, 97

KELOIDS, 737
Kidney, abscess of, 643
amyloid degeneration of, 627
anæmia of, 617
angioma of, 651

Kidney—
Bright's disease of, 621
calculi of, 645
carcinoma of, 650
changes in bloodvessels of, 615
changes in epithelial cells of, 609
colloid cysts of, 637
concretions in contracted, 638
congestion of, 618
cysts of, 650
fatty degeneration of, 629
granular, 626
gumma of, 647
hemorrhage of, 618
histology of, 604
infarction of, 619
inflammation of, 619
in phosphorous poisoning, 629
large white, 621
lesions of connective tissue of, 614
lymphadenoma of, 648
metastatic abscess of, 644
parasites of, 651
sarcoma of, 648
suppuration of, 642
surgical, 643
tuberculosis of, 646
vessels in contracted, 638
waxy, 621

LABIAL cancroid, 454
Lactation, fatty infiltration of liver, during, 555
Lænnec's theory of tuberculosis, 112
Laminated epithelium, 36
Large white kidney, 621
Laryngitis, catarrhal, 391
chronic, 397
diphtheritic, 397
erysipelatous, 398
œdematous, 399
of glanders, 399
of typhoid fever, 399
ulcerous, 400
variolous, 398
Larynx, adenoma of, 403
carcinoma of, 402
epithelioma of, 402
fibroma of, 401
histology of, 389
inflammation of cartilages of, 401
lymphadenoma of, 403
papilloma of, 402
parasites of, 403
syphilis of, 399
tubercle of, 402
tumors of, 401
Leio-myoma, 135
Leprosy, cutaneous tubercule of, 738
Leprous dermatitis, 738
Leptothrix buccalis, 455
Lesions caused by death of the elements, 39
by excess of nutrition of cells, 53
Lesions caused—
by insufficient nutrition, 41
following division of nerves, 361
in formation of cells, 53
irritative, of cartilage, 225
nutritive, of capillaries, 336
of cartilage, 225
of muscle, 270
of arteries, 306
of bone, 195
of cartilage, 225
of corrosive irritants in stomach, 469
of myelitis, 334
of nutrition of elements and of tissues, 39
Leucin and tyrosin in gangrene, 41
Leucocythæmia, 142, 288
splenic, 593
Leucocytosis, 287
Leucophlegmasia, 723
Leukæmia, 288
Leukæmic tumors of liver, 561
Lip, epithelioma of, 454
hypertrophy of, 453
Lipoma, description of, 95
development of, 96
erectile, 96
fatty degeneration of, 96
fibrous, 96
gangrene of, 96
inflammation of, 96
myxomatous, 96
of articulations, 244
of bone, 214
of brain, 378
of bronchi, 407
of intestine, 513
of mouth, 453
of muscle, 281
of œsophagus, 460
of peritoneum, 577
of stomach, 472
prognosis of, 96
seat of, 95
species and varieties of, 96
Lipomatous carcinoma, 103
myxoma, 90
sarcoma, 86
List of illustrations, xxv
Liver, abscesses, large, of, 541
metastatic, of, 536
acute yellow atrophy of, 532
amyloid degeneration of, 557
angioma of, 559
atrophy of, from cirrhosis, 547
biliary passages in cirrhosis, 550
carcinoma of, 561
chronic inflammation of, 543
circulation of, in cirrhosis, 549
cirrhosis of, 543
cirrhotic, with granular surface, 547
with smooth surface, 545
congestion of, 528
cysts of, 565
degeneration of, 555

Liver—
embolism of, 536
epithelioma of, 564
fatty degeneration of, 557
fatty infiltration of, 555
during lactation, 555
general cirrhosis of, 544
granular, 547
gumma of, 111, 560
histology of, 517
hobnail, 547
hydatid of, 565
in cardiac disease, 530
inflammation of, 532
in typhoid fever, 535
lesions of cellulo-vascular system, 526
lesions of vessels of, 527
lukæmic tumors of, 561
metastatic abscesses of, 536
nutmeg, 530
partial cirrhosis of, 543
post-mortem changes of, 527
pulsation of, 532
red atrophy of, 531
thrombosis of, 537
tubercle of, 559
tumors of, 559
vegetations on, 548
vessels of, in cirrhosis, 549
Lobar pneumonia, 416
Lobular pneumonia, 414
Lobulated epithelioma, 146
of bone, 150
myoma, 135
Lung, abscess of, 419
anæmia of, 408
apoplexy of, 408
atrophy of, 411
carcinoma of, 428
congestion of, 408
emphysema of, 412
enchondroma of, 428
fibroma of, 428
gangrene of, 421
hemorrhagic infarction of, 410
histology of, 390
hyperæmia of, 408
inflammation of, 414
of lymphatics of, 420
metastatic abscess of, 420
œdema of, 408
osteoma of, 428
pigmentation of, 424
sarcoma of, 427
tuberculosis of, 429
tumors of, 427
Lymph glands, amyloid degeneration of, 355
calcification of, 354
carcinoma of, 356
caseous degeneration of, 354
colloid transformation of, 355
enchondroma of, 357
epithelioma of, 358
fibrous induration of, 353
Lymph glands—
in carcinoma, 102
inflammation of, 352
pigmentation of, 351
scrofulous, inflammation of, 354
suppuration of, 353
syphilis of, 357
tuberculosis of, 356
tumors of, 355
waxy degeneration of, 354
Lymph lacuna of fibrous tissue, 23
plastic, 252
Lymphadenoma, 142
changes in, 145
development of, 145
diagnosis of, 145
of bone, 218
of intestine, 514
of kidney, 648
of larynx, 403
of ovary, 678
of pancreas, 580
of stomach, 472
of testicle, 667
prognosis of, 145
seat of, 143
Lymphangiectasis, 346
Lymphangiectatic pachydermia, 723
Lymphangioma, 141
Lymphangitis, 345
Lymphatic glands, histology of, 348
vessels, dilatation of, 346
histology of, 345
in carcinoma, 98, 347
inflammation of, 345
tuberculosis of, 346
Lymphatics of lung, inflammation of, 420
of skin, dilatation of, 722
in œdema, 723

MACRO-GLOSSIA, 453
Malarial fever, spleen in, 585
Malpighian glomeruli, changes of, 616
Mammary gland, adenoma of, 715
atrophying scirrhus of, 710
axillary glands in carcinoma of, 712
carcinoma of, 710
cysts of, 715
encephaloid of, 713
enchondroma of, 714
epithelioma of, 715
fibroma of, 710
histology of, 701
hydatid of, 715
hypertrophy of, 707
inflammation of, 706
melanotic tumors of, 190
myxoma of, 709
sarcoma of, 81, 708
scirrhus of, 710
syphilis of, 710
tumors of, 707
villous carcinoma of, 713

Marrow of bone, 27
Masses, melanic, 189
Mastitis, 706
Medullary carcinoma, 103
cavity of bone, 27
neuroma, 137
Melanæmia, 288
of brain, 369
Melanic masses, 189
tumors of lung, 427
Melano-carcinoma, 105
Melano-sarcoma, 86
Melanotic tumors of mammary gland, 190
Melicerous wens, 165
Membrane of Schwann, 32
Meninges, colloid degeneration of, 367
congestion of, 364
fibroma of, 367
tumors of, 367
Meningitis, cerebral, acute, 364
cerebro-spinal, 364
chronic, 366
tuberculous, 365
Meningo-encephalitis, diffused, 376
Metamorphoses of gumma, 111
Metastasis of sarcoma, 88
Metastatic abscess of liver, 536
of lung, 420
Metritis, internal, 690
Microsporon Audouini, 746
Microsporon furfur, 745
Miliary aneurism of brain, 371
interstitial hepatitis, 545
tubercle, anatomy of, 116
cells of, 114
Milk, elements of, 705
Milky patches of pericardium, 292
Miners, pneumonia of, 426
Mixed tumors, 170
Modifications of enchondroma, 129
Moist gangrene, 40
Molluscoid fibroma, 93
Molluscum sebaceum, 737
Morbus coxæ senilis, 234
Mortification, 40
Mouth, cysts of, 453
epithelioma of, 454
fibroma of, 453
gangrene of, 453
lipoma of, 453
parasites of, 455
tubercle of, 454
tumors of, 453
Mucin, 44
Mucoid fibroma, 93
Mucous and colloid infiltrations, 44
bursa, 248
cartilage, 26
cysts, 168
of uterus, 693
exudations, 64
metamorphosis of myoma, 136
papilloma, 159
patches of mouth, 451
polypi of nasal fossæ, 395
Mucous polypi—
of uterus, 691
tissue, 23
Multilocular cysts, 169
of ovary, 680
hydatid tumor, 193
Multinucleated cells, 21
Muscle, angioma of, 282
atrophy of, 270
carcinoma of, 281
chronic inflammation of, 279
cloudy swelling of, 271
cysticercus of, 282
embolic infarction of, 277
enchondroma of, 281
epithelioma of, 281
fatty degeneration of, 272
fibres in frog, destruction of, 39
fibroma of, 281
gumma of, 281
hemorrhage of, 276
histology of, 269
hydatid of, 282
hypertrophy of, 271
inflammation of, 278
lipoma of, 281
lobulated epithelioma of, 150
myxoma of, 281
nutritive lesions of, 270
osteoma of, 281
parasites of, 282
pigmentary degeneration of, 274
rupture of, 280
sarcoma of, 280
suppuration of, 279
trichniæ of, 282
tumors of, 280
vitreous degeneration of, 274
waxy degeneration of, 43, 274
Muscular fasciculi of heart, 30
fibres, striated, 31
hypertrophy of stomach, 477
tissue, 30
tumors of, 134
Myelin, 32
Myelinic neuroma, 138
Myelitis, 383
interstitial, 384
lesions in, 384
suppurative, 383
Myeloid sarcoma, 81
Myocarditis, 296
Myocardium, 292
tumors of, 298
Myo-fibroma of stomach, 473
Myoma, 134
anatomical diagnosis of, 136
calcareous infiltration of, 135
development of, 136
fatty infiltration of, 136
lobulated, 135
mucous metamorphosis of, 136
of prostate, 671
of uterus, 699
prognosis of, 136

Myoma—
seat of, 136
strio-cellulare, 134
varieties of, 135
with smooth fibres, 135
Myositis, 278
Myxoid epithelioma of ovary, 680
of testicle, 665
Myxoma, anatomical diagnosis of, 91
cystic, 90
definition of, 89
description of, 89
hemorrhagic, 90
lipomatous, 90
of mammary gland, 709
of muscle, 281
papillary, 91
polypoid, 91
prognosis of, 91
seat of, 91
Myxomatous lipoma, 96
tumors of bone, 214
Myxo-sarcoma, 86

NÆVUS, 139
Nasal fossæ, epithelioma of, 396
fibrous polypi of, 396
histology of, 389
papilloma of, 396
tumors of, 395
hemorrhage, 394
mucous membrane, inflammation of, 394
mucous polypi, 395
Necrobiosis, 40
Necrosis of bone, 204
phosphorus, of bone, 206
syphilitic, of bone, 206
Nephritis, albuminous, 619
catarrhal, 620
croupous, 623
diffused, 621
interstitial, 631
albuminoid, 631
non-albuminous, 641
parasitic, 644
parenchymatous, 621
partial, interstitial, 641
scarlatinous, 623
superficial, 620
suppurative, 642
Nerve, axis cylinder of, 33
carcinoma of, 363
cells, 31
in spinal sclerosis, 387
longevity of, 39
congestion of, 360
epithelioma of, 363
fibres, development of, 33
varieties of, 32
hemorrhage of, 360
inflammation of, 360
lesions following division of, 361
tissue, 31
Nerve tissue—
histology of, 359
tumors of, 137
tumors of, 362
Nervous system, central, 364
Neurilemma, 32
Neuritis, 360
Neuroma, 137
amyelinic, 138
anatomical diagnosis of, 138
fasciculated, 137
ganglionic, 137
medullary, 137
myelinic, 138
of brain, 380
painful, 137
plexiform cylindrical, 137
prognosis of, 138
seat of, 138
New formations, inflammatory, 66
Nodular rheumatism, 234
Noma, 453.
Non-albuminous nephritis, 641.
Non-laminated epithelium, 36
Normal histology, 17
Normal tissues, 22
Norris, W. F., 63
Nucleolus of cells, 19
Nucleus of cells, 19
Nutmeg liver, 530
Nutrition, excess of, 53
lesions of, 39
Nutritive alterations of angioma, 140
modifications of tubercle, 121

OBLITERATION of arteries by endarteritis, 326
spontaneous, 325
Odontoma, 134
Œdema, lymphatic, of skin, 723
of adipose tissue, 251
of brain, 368
of connective tissue, 250
of glottis, 399
of lung, 408
of skin, 721
theory of, 251
Œdematous laryngitis, 399
Œsophagitis, 459
Œsophagus, cysts of, 460
epithelioma of, 460
fibro-myoma of, 460
histology of, 456
lipoma of, 460
stricture of, 459
tumors of, 460
Oidium albicans, 455
Orchitis, 659
chronic, 660
syphilitic, 661
Organic muscle, elements of, 30
Organs and tissues, diseases of, 195
Osseous tissue, 26
development of, 27

Osseous tissue—
inflammation of, 59
tumors of, 132
trabeculæ, formation of, 199
tumors, 212
Ossification from cartilage, 28
from fibrous tissue, 29
from periosteum, 29
of bronchi, 407
of cartilages, 133
Ossiform tissue, 28
Ossifying enchondroma, 128
sarcoma, 83
Osteitis, 197
condensing, 202
epiphyseal, 203
formative, 202
rarefying, 200
simple, 200
suppurative, diffused, 203
Osteoid enchondroma, 131
tumors, 131
Osteoma, 132
compact, 132
development of, 132
eburnated, 132
of bone, 218
of lung, 428
of muscle, 281
seat of, 132
spongy, 132
varieties of, 132
Osteomalacia, 219
fractures in, 220
senile, 220
Osteo-myelitis, 203
Osteophytes, 202
Osteoporosis, fatty, 220
senile, 220
Ovarian cysts, 679
Ovaritis, 677
Ovary, carcinoma of, 678
dermoid cysts of, 682
enchondroma of, 678
epithelioma of, 679
fibro-myoma of, 678
gelatinous cysts of, 680
gumma of, 678
hemorrhage of, 676
histology of, 673
hyperæmia of, 676
inflammation of, 677
lymphadenoma of, 678
multilocular cysts of, 680
myxoid-epithelioma of, 680
proliferous cysts of, 680
sarcoma of, 678
tubercle of, 678
tumors of, 678
unilocular cysts of, 680
Oviducts, histology of, 683
Ovisacs, 675
Ovula Nabothi, 684
Ovule, Balbiani's investigations of, 19
segmentation of, 18
Ozæna, 394

PACCHIONIAN BODIES, 367
Pachydermia, lymphangiectatic, 723
Pachymeningitis, 367
Pacinian corpuscle, 720
Painful neuroma, 137
Pancreas, abscess of, 579
amyloid degeneration of, 580
atrophy of, 580
calculus of, 582
carcinoma of, 581
cysts of, 581
fatty degeneration of, 579
fatty infiltration of, 579
gumma of, 580
histology of, 578
induration of, 579
inflammation of, 578
lymphoma, 580
tuberculosis of, 580
tumors of, 580
Papillæ of derm, 718
Papillary myxoma, 91
sarcoma, 87
Papilloma, 157
corneous, 158
diagnosis of, 160
diffused, of skin, 728
mucous, 159
of bladder, 655
of brain, 378
of larynx, 402
of nasal fossæ, 396
of stomach, 468
prognosis of, 160
seat of, 160
varieties of, 158
Papule of skin, 730
Parasite of alopecia circumscripta, 746
of ptyriasis capitis simplex, 747
versicolor, 745
Parasites, animal, of skin, 741
cutaneous, 741
of blood, 289
of kidney, 651
of larynx, 403
of mouth, 455
of muscle, 282
of spleen, 595
vegetable, examination of, 748
of skin, 743
Parasitic affections of skin, 741
nephritis, 644
Parenchymatous exostosis, 133
hepatitis, 532
nephritis, 621
Pathological pigmentation, 50
Pavement-celled epithelioma, 146
Pearly bodies, 147
Pemphigus of stomach, 468
Pepper, Wm., 450
Perforating ulcer of foot, 739
Perforation of trachea, 403
Periarteritis, acute, 309
chronic, 313
Pericarditis, 290
hemorrhagic, 291

Pericarditis—
purulent, 291
tuberculous, 291
Pericardium, 290
adhesions of, 291
calcareous infiltration of, 291
carcinoma of, 292
dropsy of, 290
ecchymoses of, 290
gases in, 290
hemorrhages of, 290
inflammation of, 290
milky patches of, 292
pneumatosis of, 290
Perichondritis of larynx, 401
Periosteum, structure of, 27
Periostitis, phlegmonous, 203
Peripheral callus, 212
Perisplenitis, 588
Peritoneum, carcinoma of, 576
hydatid of, 577
lipoma of, 577
tubercles of, 574
Peritonitis, 571
carcinomatous, 576
chronic, 573
hemorrhagic, 574
tuberculous, 574
Perityphlitis, 488
Peri-uterine hæmatocele, 688
Peyer's patches in typhoid fever, 501
Phagedenic ulcer of uterus, 693
Pharyngitis, 457
diphtheritic, 457
granular, 458
of scarlatina, 457
of typhoid fever, 457
Pharynx, histology of, 456
syphilis of, 458
tumors of, 460
Phlebitis, 339
Phleboliths, 52, 342
Phlegmasia alba dolens, 723
Phlegmon, acute, 253
chronic, diagnosis from sarcoma, 257
of connective tissue, 256
of skin, 727
Phlegmonous gastritis, 468
periostitis, 203
Phthisis, 433
albuminuria of, 624
Phosphorus necrosis of bone, 206
poisoning, kidney in, 629
Physiological pigmentation, 50
Pigment of blood, 288
Pigmentary degeneration of muscle, 274
infiltration of pus corpuscles, 68
Pigmentation of elements and tissues, 49
of gum, 450
of lung, 424
of lymph glands, 351
of serous membranes, 258
of spleen, 588
Pilaris ichthyosis, 740
Pityriasis capitis simplex, parasite of, 747
Pityriasis—
ichthyosis, 740
versicolor, parasite of, 745
Pleura, carcinoma of, 445
congestion of, 438
fibroma of, 445
inflammation of, 440
tumors of, 445
Pleurisy, chronic, 444
fibrinous, 440
hemorrhagic, 443
idiopathic, 141
purulent, 443
Pleuritis, 440
Plexiform cylindrical neuroma, 137
Pneumatosis of pericardium, 290
Pneumonia, 414
caseous, 433
catarrhal, 414
colloid, 436
croupous, 416
fibrinous, 416
interstitial, 423
syphilitic, 108
lobar, 416
lobular, 414
of miners, 426
syphilitic, 425
tuberculous, 433
catarrhal, 433
croupous, 437
interstitial, 437
Polypoid myxoma, 91
Polypus of intestine, 514
of nasal fossæ, 395
of stomach, 468
Portal vein, suppurative inflammation of, 537
Posterior spinal sclerosis, 385
Post-mortem changes of intestine, 483
of liver, 527
of stomach, 465
Preface, authors', v
translators', iii
Proctitis, 488
Prognosis of adenoma, 164
of anginoma, 141
of carcinoma, 106
of enchondroma, 131
of fibroma, 95
of gumma, 112
of lipoma, 96
of lobulated epithelioma, 151
of lymphadenoma, 145
of myoma, 136
of myxoma, 91
of neuroma, 138
of papilloma, 160
of sarcoma, 88
of tubercle, 125
of tubulated epithelioma, 154
Proliferating rheumatism, 234
Proliferous cysts, 169
Prostate, abscess of, 670
adeno-myoma of, 671

Prostate—
carcinoma of, 672
concretions of, 671
histology of, 670
hypertrophy of, 671
inflammation of, 670
myoma of, 671
tubercle of, 672
tumors of, 671
Protoplasm of cells, 18
Provisional callus, 210
Psammoma, 85
Pseudo-membranous dermatitis, 728
dysmenorrhœa, 685
exudations, 65
pyelitis, 645
Psoriasis, buccal, 451
Pulmonary anæmia, 408
apoplexy, 408
gangrene, 421
Pulsation of liver, 532
Pultaceous encephaloid, 103
Purpura urticans, 721
Purulent arthritis, 231
hepatitis, 536
inflammation of connective tissue, 253
of serous membranes, 263
pericarditis, 291
pleurisy, 443
pyelitis, 645
Pus corpuscles, 66
calcareous transformation of, 68
caseous transformation of, 68
fatty degeneration of, 68
pigmentary infiltration of, 68
serous acid transformation of, 68
Pustule of skin, 732
Putrefaction, 40
Pyelitis, calculous, 645
pseudo-membranous, 645
purulent, 645
Pyelo-nephritis, 645
Pylephlebitis, suppurative, 538
Pyo-pneumothorax, 444

RACHITIS, 220
Ranula, 168, 453
Rarefying osteitis, 200
Rectal fistula, 507
Rectum, carcinoma of, 515
inflammation of, 488
Red atrophy of liver, 531
blood disks, 284
softening of brain, 375
Remak, fibres of, 33
origin of cells, 18
Resection of nerves, union of, 361
Respiratory apparatus, histology of, 389
Reticular cartilage, 26
Reticulated tissue, 24
Reticulum of blood corpuscles, 20, 285
Retro-pharyngeal abscess, 458
Rhabdo-myoma, 134
Rheumatic arthritis, 228
Rheumatism, cerebral, 364
formative, 234
nodular, 234
proliferating, 234
Round-celled sarcoma, 79
Rupture of heart, 295
of muscle, 280
of spleen, 591

SAGO SPLEEN, 591
Salivary glands, 447
Salpingitis, catarrhal, 687
Sarcode, 18
Sarcodic movements, 18
Sarcolemma, 31
multiplication of cells of, 278
Sarcoma, 76
alveolar, 84
angiolithic, 85
carcinomatodes, 84
cells in, 77
development of, 87
diagnosis, from chronic phlegmon, 257
encephaloid, 79
of bone, 213
extension of, 87
fasciculated, 80
fascicular, of bone, 213
general description of, 77
generalization of, 87
lipomatous, 86
melanotic, 86
metastasis of, 88
myeloid, 81
of bone, 214
myxomatous, 86
of kidney, 648
of lung, 427
of lymph glands, 355
of mammary gland, 81, 708
of muscle, 280
of ovary, 678
of supra-renal capsule, 601
of testicle, 664
ossifying, 83
of bone, 214
papillary, 87
prognosis of, 88
round-celled, 79
of bone, 213
species and varieties of, 78
spindle-celled, 80
of bone, 213
synonyms of, 76
Sarcoptes hominis, 741
Scarlatina, nephritis of, 623
pharyngitis of, 457
Schmidt, theory of formation of fibrin, 286
Schneiderian membrane, 389
Schwann, formation of cells, 17
membrane of, 32
Scirrhus, 103
atrophic, 103
of mammary gland, 710

Scleroderma, 730
Sclerosis of bone, 202
of brain, 377
of lateral spinal columns, 387
of posterior spinal columns, 385
of spinal cord, 384
nerve cells in, 387
Scorbutic stomatitis, 451
Scrofula and tuberculosis, 114, 125
Scrofulous arthritis, 238
Sebaceous cysts, 165
gland, inflammation of, 735
lobulated epithelioma of, 150
Segmentation of ovule, 18
Senile gangrene, 41
osteomalacia, 220
Sequestrum of bone, 205
of caries, 208
Serous acid transformation of pus, 68
and albuminous infiltrations, 42
cavities, histology of, 247
stomata of, 248
cysts, 167
exudation, 64
membranes, carapaces of, 265
carcinoma of, 267
endothelium of, 38
epithelioma of, 268
exudation of, in inflammation, 259
fibrinous exudation of, 260
hemorrhage of, 258
hemorrhagic inflammation of, 262
hyperplastic inflammation of, 265
inflammation of, 259
pigmentation of, 258
purulent inflammation of, 263
tubercles of, 266
tumors of, 265
Shakespeare, origin of white cells in blood of inflammation, 58
reparatory inflammation in arteries, 321
Sharpey's fibres, 30
Siderosis, 426
Simple angioma, 139
Skin, abnormal colorations of, 740
animal parasites of, 741
blister of, 731
bulla of, 731
chronic diffused inflammation, 728
circumscribed inflammation of, 730
congestive inflammation of, 724
degenerative inflammation of, 737
diffused inflammation of, 724
papilloma of, 728
phlegmon of, 727
dilatation of lymphatics, 722
dystrophies of, 739
exudative inflammation of, 727
glands of, 720
hæmatocele of, 724
hemorrhage of, 724
histology of, 716
hyperplastic inflammation of, 736
lymphatic œdema of, 723
Skin—
nerves of, 718
œdema of, 721
papillæ of, 718
papule of, 730
parasitic affections of, 741
peri-glandular inflammation of, 735
phlegmon of, 727
pustule of, 732
serous infiltration of, 721
specific ulcers of, 737
tubercule of, 734
tuberculous ulcers of, 737
vegetable parasites of, 743
vesicle of, 732
Softening of bone, 219
of spinal cord, 380
Spermatic hydrocele, 662
Spermatozoids, 658
Spinal cord, congestion of, 380
hemorrhage of, 380
in tetanus, 388
inflammation of, 383
sclerosis of, 384
secondary degeneration of, 381
softening of, 380
tumors of, 388
Spindle-celled sarcoma, 80
Spleen, abscess of, 589
amyloid degeneration of, 591
atrophy of, 584
carcinoma of, 594
cysts of, 595
gumma of, 594
histology of, 583
hyperæmia of, 585
infarction of, 589
inflammation of, 587
of heart disease, 586
of infectious fevers, 585
of intermittent fever, 585
of typhoid fever, 585
parasites of, 595
pigmentation of, 588
rupture of, 591
tubercle of, 594
tumors of, 593
Splenic leucocythæmia, 593
Splenitis, interstitial, 587
suppurative, 589
Spongy osteoma, 132
Steatoma, 91, 95
Steatomatous wens, 165
Stomach, anæmia of, 464
calcification of, 472
carcinoma of, 475
catarrh of, 465
congestion of, 464
cysts of, 467
ecchymoses of, 464
encephaloid of, 476
epithelioma of, 476
histology of, 461
hypertrophy of muscular tissue of, 477

Stomach—
inflammation of mucous membrane, 465
lesions of corrosive irritants in, 469
glands of, 465
of vessels of, 465
lipoma of, 472
lymphadenoma of, 472
myo-fibroma of, 473
papilloma of, 468
pemphigus of, 468
polypus of, 468
post-mortem change of, 465
scirrhus of, 476
syphilis of, 473
tubercles of, 472
tumors of, 472
ulcer of, 469
Stomata of serous cavities, 248
Stomatitis, 448
diphtheritic, 452
of typhoid fever, 449
scorbutic, 451
ulcerative, 452
Stools of cholera, 499
Strangulated hernia, 506
Striated muscular fibres, 31
Stricture of urethra, 654
Stroma of carcinoma, 98
Structure of cells, 17
Subcutaneous tissue, inflammation of, 60
Subungual exostosis, 83
Sudamina, 735
Suppuration, 66
of connective tissue, 253
of kidney, 642
of lymph glands, 353
of muscle, 279
Suppurative dermatitis, 727
myelitis, 383
nephritis, 642
osteitis, diffused, 203
Supra-renal capsule, amyloid degeneration of, 600
carcinoma of, 601
caseous degeneration of, 602
congestion of, 600
epithelioma of, 601
gumma of, 601
hemorrhage of, 600
histology of, 599
inflammation of, 601
chronic, 602
sarcoma of, 601
thrombosis of, 600
tuberculosis of, 602
tumors of, 601
Surgical kidney, 643
Synovia in acute arthritis, 228
Synovial membrane, histology of, 227
in acute arthritis, 229
tubercles of, 244
Syphilis of brain, 378
of larynx, 399
of lymph gland, 357
Syphilis—
of mammary gland, 710
of pharynx, 458
of stomach, 473
of uterus, 694
periods of, 107
Syphilitic hepatitis, interstitial, 111
lesions of arteries, 331
of buccal mucous membrane, 451
necrosis of bone, 206
orchitis, 661
papule of skin, 736
pneumonia, 108, 425
tubercule of skin, 736
tumors of intestine, 512
ulcers of intestine, 512

TABLE of contents, vii
Tactile corpuscle, 720
Tænia echinococcus, 192
solium, 191
Telangiectases, 139
Teratoma, 171
Testicle, carcinoma of, 668
cysts of, 669
enchondroma of, 663
fibroma of, 664
gumma of, 667
histology of, 657
inflammation of, 659
lymphadenoma of, 667
myxoid epithelioma of, 665
sarcoma of, 664
syphilitic inflammation of, 661
tubercles of, 665
tumors of, 663
Tetanus, spinal cord in, 388
Theory of cells, 17
of formation of pus, 67
Thrombosis, 326
of brain, 374
of liver, 537
of supra-renal capsule, 600
venous, 340
Thrush, 455
Thyroid gland, carcinoma of, 597
epithelioma of, 598
histology of, 596
hypertrophy of, 596
tubercle of, 597
Tinea carcinata, 744
favosa, 743
sycosa, 744
tonsurans, 744
Tissue, adipose, 24
cartilaginous, 25
connective, 23
elastic, 25
epithelial, 34
fibrous, structure of, 23
granulation, 69
mucous, 23
muscular, 30
nerve, 31

Tissue—
normal, 22
osseous, 26
ossiform, 28
pigmentation of, 49
reticulated, 24
Tongue, epithelioma of, 454
hypertrophy of, 453
papillæ of, 447
Tonsillitis, 452
Tophus, 242
Trachea, carcinoma of, 403
histology of, 390
perforation of, 403
ulcers of, 403
Tracheitis, 403
Translators' preface, iii
Traumatic arthritis, 228
congestion of liver, 532
Trichina spiralis in muscle, 282
Tricophyton tonsurans, 744
Trophic cutaneous disturbances, 739
Tubercle, anatomical diagnosis of, 125
caseous degeneration of, 121
development of, 122
elements of, 114
intestinal ulcers of, 510
miliary, anatomy of, 116
nutritive modifications of, 121
of bladder, 654
of bone, 215
of brain, 378
of bronchi, 407
of Fallopian tube, 688
of intestine, 508
of kidney, 546
of larynx, 402
of liver, 559
of lung, 429
of lymph glands, 356
of lymphatic vessels, 346
of mouth, 454
of ovary, 678
of pancreas, 580
of peritoneum, 574
of prostate, 672
of serous membranes, 266
of spleen, 594
of stomach, 472
of supra-renal capsule, 602
of synovial membrane, 244
of testicle, 665
of thyroid gland, 597
of urethra, 654
of uterus, 693
prognosis of, 125
seat of, 124
varieties of, 121
Tubercule, cutaneous, of leprosy, 738
of skin, 734
syphilitic, of skin, 736
Tuberculosis, 112
Tuberculous catarrhal pneumonia, 433
croupous pneumonia, 435
interstitial pneumonia, 437
Tuberculous—
meningitis, 365
pericarditis, 291
peritonitis, 574
pneumonia, 433
Tubular adenoma with cylindrical cells, 162
glands, 38
Tubulated epithelioma, 152
Tumors, appendix to, 189
classification and description of, 75, 172
definition of, 74
dermoid, 91
fatty, 95
fibrous, 91
formed of bloodvessels, 139
of embryonal tissue, 76
of muscular tissue, 134
of nerve tissue, 137
of osseous tissue, 132
melanic, of lung, 427
mixed, 170
of arteries, 332
of articulations, 244
of bone, 212
of brain, 378
of bronchi, 407
of buccal cavity, 453
of cartilaginous-tissue type, 126
of connective tissue, 257
of connective-tissue type, 89
of epithelial-tissue type, 145
of Fallopian tube, 688
of gall-bladder, 569
of heart, 298
of larynx, 401
of liver, 559
of lung, 427
of lymph glands, 355
of lymphatic system type, 141
of mammary gland, 707
of meninges, 367
of muscle, 280
of nasal fossæ, 395
of nerves, 362
of œsophagus, 460
of ovary, 678
of pancreas, 580
of pharynx, 460
of pleura, 445
of prostate, 672
of serous membranes, 265
of spinal cord, 388
of spleen, 593
of stomach, 472
of supra-renal capsule, 601
of testicle, 663
of uterus, 693
of veins, 344
osseous, 212
osteoid, 131
Tunica vaginalis, inflammation of, 661
Typhlitis, 488
Typhoid fever, intestinal lesions of, 501
laryngitis of, 399
liver in, 535

Typhoid fever—
pharyngitis of, 457
spleen in, 585
stomatitis of, 449

ULCER of duodenum, 471
Ulcer of stomach, 469
Ulcer of trachea, 403
perforating, of foot, 739
skipping of, 72
specific, of skin, 737
tuberculous, of skin, 737
Ulcerating cystitis, 654
Ulceration of bronchi, 407
of carcinoma, 106
of intestine, uræmic, 501
Ulcerative stomatitis, 452
Ulcerous laryngitis, 400
Umbilical cord, structure of, 23
Uræmic ulcerations of intestine, 501
Urate of soda in gouty arthritis, 241
Urates, infiltration of, 52
Ureter, histology of, 652
Urethra, abscess of, 654
histology of, 652
stricture of, 654
tuberculosis of, 654
Urethritis, 654
Urine, casts in, 611
Urticaria, 721
Uterus, carcinoma of, 694
casts of, 685
catarrhal inflammation of, 690
changes during gestation, 686
congestion of, 689
epithelioma of, 696
fibroid polypi of, 693
hemorrhage of, 689
histology of, 683
hypertrophy of, 697
mucous cysts of, 693
polypi of, 691
myoma of, 699
phagedenic ulcer of, 693
puerperal inflammation of, 692
syphilis of, 694
tubercle of, 693
tumors of, 693

VARICOSE veins, 342
Varicose veins of bladder, 652
Variolous laryngitis, 328
Vascular system, endothelium of, 37
tissues, inflammation of, 59
tumors of intestine, 513
Vegetable parasites, examination of, 748
of skin, 743
Vegetations on heart, 300, 303
on liver, 548
Veins, calcareous infiltration of, 342
histology of, 338
inflammation of, 339
tumors of, 344
varicose, 342
Venous thrombosis, 340
Vermiform appendix, inflammation of, 488
Vesical fungus, 655
Vesicle of skin, 732
Vessels, new formation of, in inflammation, 68
of contracted kidney, 638
of granulation tissue, 69
of liver in cirrhosis, 549
lesions of, 527
of stomach, lesions of, 465
Villous carcinoma, 106
of mammary gland, 713
Vitreous degeneration of muscle, 45, 274
humor, structure of, 23
Voluntary muscular fibres, 31

WAGNER, fibrous degeneration of cells, 46, 65
Warts, 158
Waxy degeneration of muscle, 43, 45
kidney, 622
Wens, 165
White blood-corpuscles, 19, 286
emigration of, 62
reticulum of, 20, 285
swelling, 238
Woodward, J. J., theory of tuberculosis, 119
Wounds, cicatrization of, 71

ZENKER, waxy degeneration of, 43

WELLCOME LIBRARY INSTITUTE



Dunn & Wilson Ltd