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FUNCTIONAL DERANGEMENTS  
OF  
THE LIVER

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DR. MURCHISON



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Dr. Daniell  
with kind regards  
from the Author.

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CROONIAN LECTURES

FOR

1874

1875

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ON  
FUNCTIONAL DERANGEMENTS  
OF  
THE LIVER

BEING

*THE CROONIAN LECTURES*

DELIVERED AT THE

ROYAL COLLEGE OF PHYSICIANS

IN MARCH 1874

BY

CHARLES MURCHISON, M.D. LL.D. F.R.S.

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LONDON

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TO  
SIR WILLIAM JENNER, BART., M.D.

K.C.B., D.C.L. OXON., F.R.S.

PHYSICIAN IN ORDINARY TO HER MAJESTY THE QUEEN  
AND TO  
H.R.H. THE PRINCE OF WALES

IN ADMIRATION OF THOSE CONTRIBUTIONS TO MEDICAL SCIENCE  
WHICH HAVE PLACED HIM IN THE FIRST RANK OF  
BRITISH PHYSICIANS

These Lectures are Dedicated

BY

THE AUTHOR

THE UNIVERSITY OF CHICAGO

PHYSICS DEPARTMENT

CHICAGO, ILL.

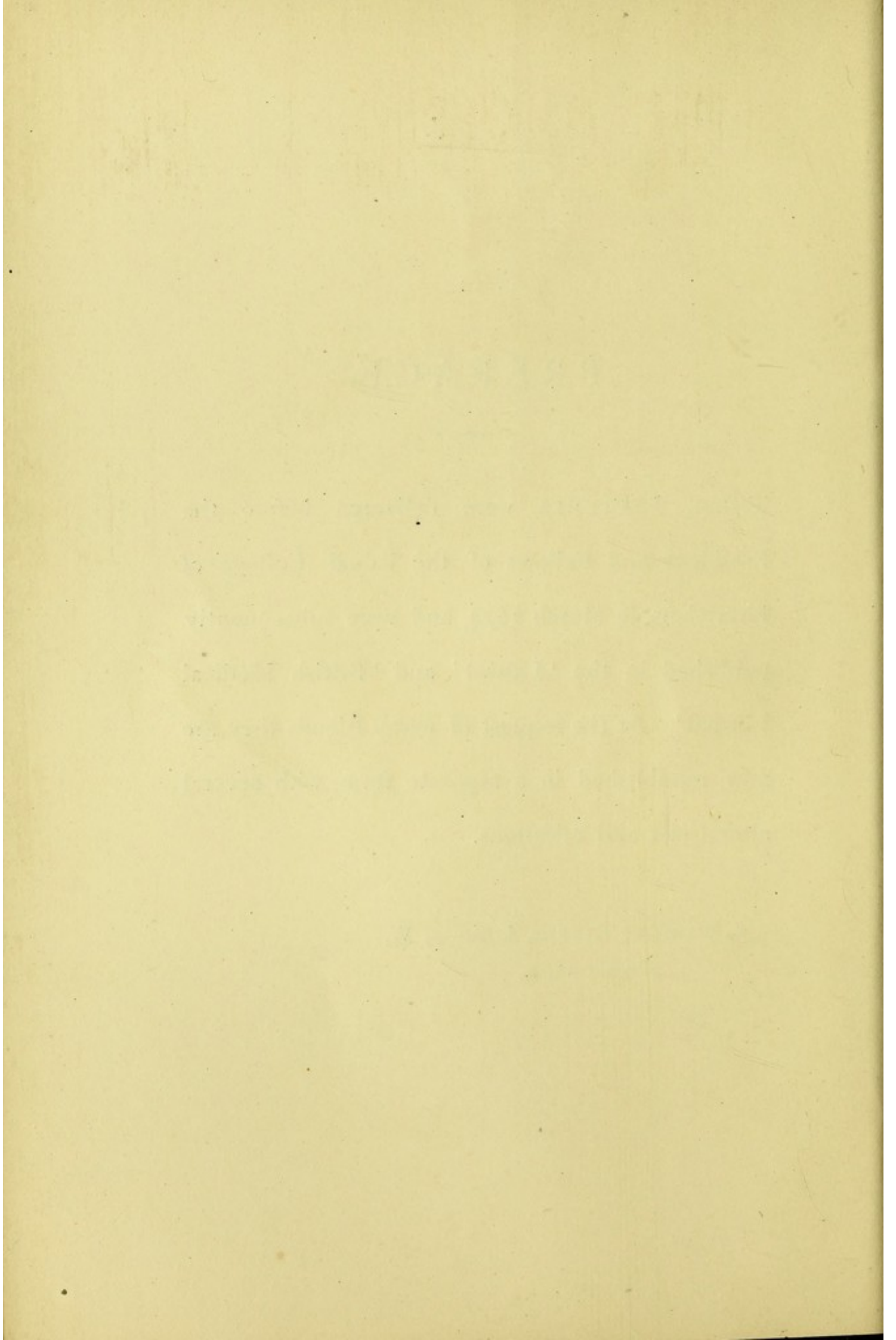
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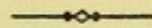
THESE LECTURES were delivered before the President and Fellows of the Royal College of Physicians, in March 1874, and were subsequently published in the 'Lancet' and 'British Medical Journal.' At the request of many friends they are now republished in a separate form, with several alterations and additions.

79 WIMPOLE STREET, LONDON, W.

*August 1874.*



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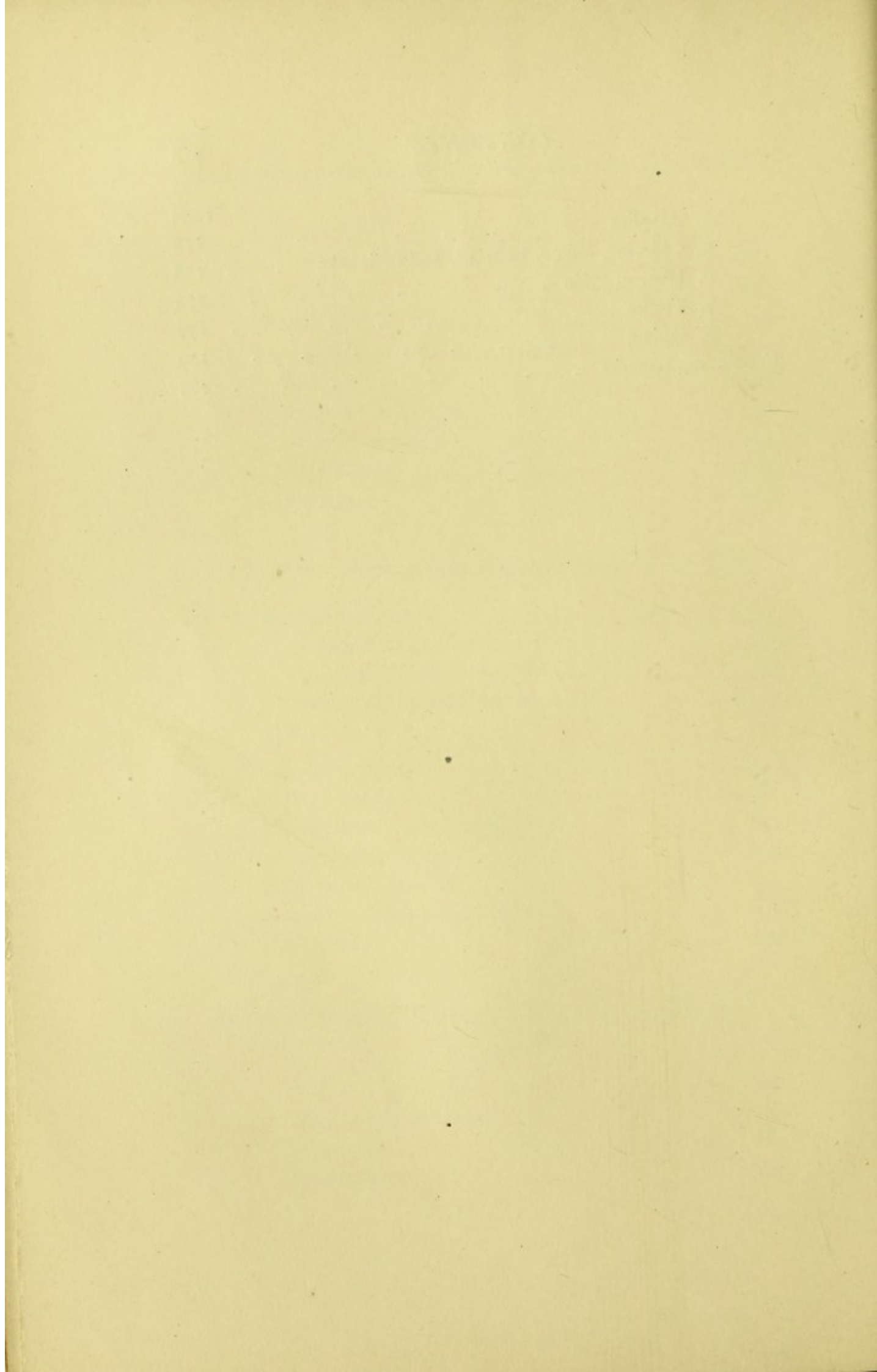
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# TABLE

OF

## CHEMICAL EQUIVALENTS.



Albuminoids (Lieberkühn)	. . . . .	$C_{72} H_{112} N_{18} SO_{23}$
Excretin	. . . . .	$C_{78} H_{156} SO_2$
Taurocholic acid	. . . . .	$C_{26} H_{45} NO_7 S$
Glyco-cholic acid	. . . . .	$C_{26} H_{43} NO_6$
Cholic acid	. . . . .	$C_{24} H_{40} O_5$
Taurin	. . . . .	$C_2 H_7 NO_3 S$
Glycocin	. . . . .	$C_2 H_5 NO_2$
Bilirubin	. . . . .	$C_{16} H_{18} N_2 O_3$
Biliverdin	. . . . .	$C_{16} H_{20} N_2 O_5$
Tyrosin	. . . . .	$C_9 H_{11} NO_3$
Leucin	. . . . .	$C_6 H_{13} NO_2$
Hippuric acid	. . . . .	$C_9 H_9 NO_3$
Xanthin	. . . . .	$C_5 H_4 N_4 O_2$
Cystin	. . . . .	$C_3 H_7 NSO_2$
Kreatin	. . . . .	$C_4 H_9 N_3 O_3$
Kreatinin	. . . . .	$C_4 H_7 N_3 O$
Uric or lithic acid	. . . . .	$C_5 H_4 N_4 O_3$
Urea	. . . . .	$CH_4 N_2 O$
Oxalic acid	. . . . .	$C_2 H_2 O_4$
Starch	. . . . .	$C_6 H_{10} O_5$

xvi *TABLE OF CHEMICAL EQUIVALENTS.*

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Dextrin . . . . .	$C_6 H_{10} O_5$
Glycogen, or animal starch . . . . .	$C_6 H_{10} O_5$
Cane-sugar . . . . .	$C_{12} H_{22} O_{11}$
Glucose, or grape-sugar . . . . .	$C_6 H_{12} O_6$
Lactose, or milk-sugar . . . . .	$C_6 H_{12} O_6$
Inosite, or muscle-sugar . . . . .	$C_6 H_{12} O_6$
Lævulose . . . . .	$C_6 H_{12} O_6$
Cholesterin . . . . .	$C_{26} H_{44} O$

# *Derangements of the Liver.*

---

## LECTURE I.

*Notice of Doctor Croone.—Present notions as to Functional Derangements of Liver unsatisfactory.—A. FUNCTIONS OF THE LIVER IN HEALTH. Historical Sketch; Galen's Views; Obsequies of Liver by Bartholin; Modern Views; Functions of Liver threefold. I. Sanguification and Nutrition. II. Disintegration of Albuminous Matter. III. Secretion of Bile; Composition, Origin, Quantity, and Uses of Bile.—B. FUNCTIONAL DERANGEMENTS OF LIVER. Objections to existing Classification; Proposed Classification. I. Abnormal Nutrition. 1. Corpulence; 2. Emaciation. a. Deficiency of Bile; b. Diabetes; c. Other Varieties of Emaciation. II. Abnormal Elimination; Symptoms of Retained Bile; Cholestearæmia.*

MR. PRESIDENT, FELLOWS OF THE COLLEGE, AND GENTLEMEN,—It may interest some of you if, by way of preface, I say a few words respecting the founder of the course of lectures which I am honoured by delivering before you. For the particulars I am indebted to the 'Roll' of the College, edited by our learned colleague Dr. Munk.

Dr. William Croone was born in London, and educated at Emanuel College, Cambridge. He became a Fellow of this College on July 29, 1675, and was Censor in 1679. In 1659 he was elected Professor of Rhetoric at Gresham College, and shortly afterwards he was made Secretary of the Royal Society, which then held its meetings in Gresham College. He resigned his professorship in 1670, on being appointed Lecturer on Anatomy at Surgeons' Hall. He died in 1684, and was buried in the churchyard of St. Mildred's, in the Poultry. He left behind him a plan for two lectureships, which he had designed to found—one course of lectures to be read before the College of Physicians, after a sermon to be preached in the church of St. Mary-le-Bow; the other to be delivered yearly before the Royal Society, upon the nature and laws of muscular motion. His will contained no provision for the endowment of these lectures; but his widow (a daughter of Alderman Lorimer, who subsequently married Sir Edwin Sadleir, Bart.) carried out his intention by devising in her will the King's Head Tavern, on Lambeth Hill, Knight Rider Street, in trust to her executors, to settle four parts out of five upon the College of Physicians, for the purpose of founding the annual lectures, now known as the Croonian Lectures, and the fifth part to found the Croonian Lecture of the Royal

Society. A fine portrait of Dr. Croone was presented to the College in 1738 by Dr. Woodford, Regius Professor of Physic at Oxford, and is now suspended in the Censors' room.

The founder of these lectures made no restriction as to their subject, as he did with regard to the lecture before the Royal Society; and it has been customary for each lecturer to select some subject in practical medicine which his experience has been most calculated to elucidate. The subject which I have chosen is one which it appears to me is well worthy of the attention of this College, and of medical men in general, viz., The Functional Derangements of the Liver. Professional opinion as to what constitutes functional disorder of the liver is vague and unsatisfactory. There is no expression more common among both patients and their doctors than that the 'liver is out of order,' or that certain symptoms are due to 'biliousness,' and yet few medical writers have undertaken to define with accuracy what symptoms are referable to a disordered liver. It is to be feared that symptoms are sometimes referred to the liver, with which it has little or no concern; while, on the other hand, there are grounds for suspecting that many symptoms, at first sight apparently referable to other organs, and even grave degenerations of tissue and organic disease, not



only of the liver itself, but throughout the body, may be traced back to functional derangements of the liver, although some of these may as yet be imperfectly understood. It is remarkable how systematic writers on Medicine and on Diseases of the Liver in particular entirely ignore the subject of functional disorders of the liver. The remarks which follow must be regarded as a feeble attempt to sketch with the light of recent investigation those symptoms and morbid conditions which may fairly be put down to a disordered liver. They do not pretend to place the subject upon a firm and lasting basis ; but, by calling attention to its importance and provoking discussion, it is hoped that they will prove a stepping-stone to a more certain knowledge of it, and in the meantime that they will help to supply what appears to be a deficiency in medical literature.

#### A.—FUNCTIONS OF THE LIVER IN HEALTH.

Before proceeding to discuss the results of derangement of the liver, it will be necessary for me to refer at some length to the functions of the organ in its healthy state. As in the case of the pathology of pyrexia and of inflammation, so with regard to the healthy functions of the liver, it is not a little remarkable that modern investigations have tended to reproduce in a scientific form

certain\*crude opinions entertained by the earliest writers on Medicine. From its large size, and from the extensive system of blood-vessels connected with it, the liver was believed to be the seat of many most important functions, and to be, in fact, the central organ of vegetative life. Galen, for example, taught that the liver was the centre of animal heat, that it was the seat of sanguification, and that it was the starting point of the venous system. He assigned to the veins distributed over the intestines the function of imbibing the fluid nutriment and of conveying it by the vena portæ to the liver, where he supposed that the processes of sanguification and of the generation of animal heat took place. He then traced the passage of the blood through the hepatic veins to the heart, and hence he regarded the liver as the starting point of the venous system. For upwards of sixteen centuries these views of Galen—more or less modified—were generally accepted by physiologists and physicians, and as late as the seventeenth century they were in the main upheld by our own Harvey. But the discovery in the first half of the seventeenth century of the lacteals and thoracic duct showed that chyle was conveyed to the blood independently of the portal vein and of the liver. The result was that this organ at once fell from its high estate, and ceased to be regarded as serving any purpose in sangui-

fication. Thomas Bartholin, in his 'Defence of the Lacteals and Lymphatics against Riolanus,' wrote for the liver an epitaph, in which the end of its dominion was announced, and its function was declared to be henceforth limited to the secretion of bile.

'Vivit, floretque pro bile separandâ, sed, si sanguinem conficiendum spectemus, funeratum creditur. Ivimus illi exsequias, nunquam redituro. Nam . . . .

. . . . . Facilis descensus Averni,  
Sed revocare gradum, superasque evadere ad auras,  
Hoc opus, hic labor.'<sup>1</sup>

Although it was *à priori* improbable that the largest gland in the body, deriving large supplies of blood from different sources, as well as holding peculiar relations to the blood returning from the placenta in the foetus and from the stomach and intestines in the adult, should have as its sole function the secretion of a fluid which is apparently of less importance in digestion than the gastric or pancreatic juice, yet for nearly two centuries the only object of the liver was believed to be the secretion of bile; and down to the present day its functional derangements are constantly spoken of as restricted to the secretion of bile abnormal in quantity or in quality.

<sup>1</sup> *Defensio vasorum lacteorum et lymphaticorum adversus J. Riolanum.* Hafniæ, 1655, p. 8.

For example, our late learned colleague Dr. Copland, one of the few modern medical authors who have discussed the functional disorders of the liver, describes them as coming under three heads, viz. : 1. Diminished secretion of bile ; 2. Increased secretion of bile ; and 3. Secretion of morbid or altered bile ;<sup>1</sup> and this classification probably represents with tolerable accuracy the views of the great majority of modern practitioners of medicine. It is the belief that the sole function of the liver is the secretion of bile, which has given rise to the expression in common use by professional men as well as laymen, that the 'liver will not act,' when all that is implied is a constipated state of the bowels. But the physiological investigations made within the last quarter of a century have in a great measure restored the liver to its former place of importance in the animal economy ; they have shown that the secretion and excretion of bile are far from being the most, if they be not the least, important of its functions ; and they have consequently added to the number of its functional derangements.

1. In the first place it is now known that the liver is one of the organs mainly concerned in the process of sanguification. So long ago as 1820, it was shown by

<sup>1</sup> *Medical Dictionary*, ii. 723.

Magendie and Tiedemann that the absorption of nutritive matters from the bowel was not limited to the lacteals, but that part was taken up into the blood through the portal vein;<sup>1</sup> and the researches of subsequent physiologists have clearly established that the liver exercises most important functions in assimilation and nutrition. The most valuable contributions towards our knowledge of this matter have been the researches of Claude Bernard and other observers, who have shown that the liver has the power of making and storing up for a time within its cells glycogen ( $C^6H^{10}O^5$ ), a substance resembling dextrin ( $C^6H^{10}O^5$ ) in its chemical composition and reactions, and like it capable of conversion into sugar by the action of albuminoid ferments. This substance always exists in the liver in larger amount during digestion than during fasting, attaining its maximum usually about four or five hours after a meal. It does not yet seem certain what the materials are from which it is mainly formed, but there can be no doubt that its amount is increased by the use of starchy or saccharine food. The starch ( $C^6H^{10}O^5$ ) of the food is believed to be converted into grape-sugar or glucose ( $C^6H^{12}O^6$ ) by

<sup>1</sup> *Versuche über die Wege auf welchen Substanzen aus dem Magen und Darm-Canal im Blut gelangen.* Heidelberg, 1820.

the saliva and pancreatic secretion, while the cane-sugar ( $C^{12}H^{22}O^{11}$ ) is transformed by the intestinal secretion into grape-sugar and another form of sugar called lævulose ( $C^6H^{12}O^6$ ). The glucose and lævulose are absorbed by the intestinal veins and carried by the portal vein to the liver, where they are converted partly perhaps into fat, but mainly into glycogen, which is stored up in the hepatic cells, and distributed for the nutrition of the tissues during the intervals of fasting. The circumstance, however, of glycogen being formed in considerable quantity in the livers of animals who have been fed for a month or more on flesh alone, and the fact that its quantity in the liver of a dog is always increased after a meal of flesh, show that it can also be produced from albuminous matter. The albumen of the food is converted by the gastric juice into peptone, which is also absorbed by the intestinal veins and carried to the liver, where it is believed to be decomposed into glycogen and nitrogenous products such as leucin ( $C^6H^{13}NO^2$ ) and tyrosin ( $C^9H^{11}NO^3$ ), which are ultimately resolved into urea ( $CH^4N^2O$ ).<sup>1</sup> The glycogen derived from these two sources does not remain long in the liver, for the large quantity formed after a meal is quickly diminished on

<sup>1</sup> See Fick in *Pflüger's Archiv*, vol. iv. p. 40; also Schultzen and Nencki, *Zeitschrift für Biologie*, vol. viii. p. 124.

fasting. It is not got rid of by the bile-ducts, for bile contains neither glycogen nor sugar. But either as glycogen, or more probably as sugar,<sup>1</sup> into which it is believed by Bernard and most other physiologists to be reconverted through the action of an albuminoid ferment

<sup>1</sup> In reference to the difference of opinion still existing on this matter, Dr. Brunton writes as follows, in Sanderson's *Handbook for the Physiological Laboratory*, 1873, p. 508: 'While Bernard considers that the formation of sugar goes on in the liver constantly during life, this has been denied by Pavy, Ritter, Meissner, and Schiff, who hold that it only occurs after death, or under pathological conditions, such as disturbance of the respiration or circulation during life. They base their opinions on the observations that the liver contains little or no sugar when examined immediately after death, and that the blood of the hepatic vein does not contain more sugar than that of the portal or jugular veins. It is quite true that sugar is found in very small amount in fresh livers; but the smallness of the quantity is in all probability due to the constant circulation through the liver during life washing the sugar out of it as soon as it is formed (Flint). The statement that the blood of the portal contains as much sugar as that of the hepatic vein rests on experiments vitiated by the omission to place a ligature on the former while removing the liver, so that, the hepatic vein having no valves, the blood from it flowed back into the portal system. When this fallacy is avoided, sugar is found in much larger proportion in the hepatic than in the portal vein. To meet the objection that sugar thus found has been formed after death, blood has been taken from the right side of the heart, or vena cava, and the quantity of sugar it contained compared with a similar specimen of blood from the jugular vein. Every precaution was taken to avoid disturbance of the circulation, yet the sugar in the former was found to exceed that in the latter considerably (Lusk).'

in the liver or in the blood, or transformed in some other way, it enters the blood by the hepatic vein.

One object of the glycogenic function of the liver is supposed to be that of continuously supplying an easily oxidisable material, such as sugar, which in the presence of oxygen and albuminous matter is readily converted in the lungs into carbonic acid and water, and thus contributes to the maintenance of animal heat. But although there is still some difference of opinion among those most competent to judge, the bulk of evidence goes to show that a portion only of the glycogen formed in the liver is transformed into sugar to be burnt in the lungs, and that the maintenance of animal heat is far from being its chief use. There are good grounds for believing that it assists in cell-growth; for, just as in plants the presence of sugar seems to be necessary for the most rapid development of cells, so in animals glycogen can be found wherever cell-growth is actively going on. Bernard and Rouget have found it in abundance in the cells of the placenta and amnion; and Rouget in many foetal tissues, such as cartilage, muscle, and the epithelial cells of the skin;<sup>1</sup> and it is also present in the inflammatory products of pneumonia, and in new growths

<sup>1</sup> *Journal de Physiologie*, 1859, tome ii.



whenever cell-formation is active. Hoppe Seyler has also shown that it is an ingredient of colourless blood-corpuscles, so long as they are active, but that when they lose their power of motion the glycogen disappears and is replaced by sugar.<sup>1</sup> In connection with these observations, it is important to note that the blood, on emerging from the liver, is much denser, and contains a far larger proportion of solid constituents (although less fibrin), and is also far richer in white blood-corpuscles, than the blood before it enters the liver. Bernard, Lehmann, and McDonnell ascertained that in blood drawn from the hepatic vein the colourless corpuscles are from five to ten times more numerous than in blood taken from the portal vein ;<sup>2</sup> while Hirt of Zittau estimated that the proportion of the colourless to the red corpuscles was in the portal venous blood as 1 to 524, but in the hepatic as 1 to 136.<sup>3</sup> The red corpuscles also from the hepatic vein are said to have a sharper outline and less tendency to aggregate into rolls, and to dissolve less readily in water than those from the portal vein. Again, we have the remarkable observations of Weber, confirmed by Kölliker,

<sup>1</sup> *Med. Chem. Untersuch.*, 1871, p. 486.

<sup>2</sup> See McDonnell's *Observations on the Functions of the Liver*. Dublin, 1865.

<sup>3</sup> Müller's *Archiv*, 1856, and Carpenter's *Principles of Human Physiology*, 7th edition, p. 228.

respecting the extensive generation of blood-corpuscles in the liver of the embryo. In the early stages of foetal life the blood-cells multiply throughout the entire mass of the blood ; but when the liver begins to be formed this process ceases, and a very active formation of colourless blood-cells is set up in the liver, these colourless cells undergoing a gradual change by the development of colouring matter in their interior into red corpuscles. According to Kölliker, this new formation of blood-corpuscles in the liver continues during the whole of the foetal life of mammalia.<sup>1</sup> The observations quoted above make it probable that the liver in the adult continues to perform the functions which pertain to many different tissues of the foetus ; the glycogen secreted in its cells combining with nitrogen, and forming an azotised protoplasm, which maintains the nutrition of the blood and tissues. Dr. R. McDonnell has suggested that part of the glycogen of the liver combines with nitrogen furnished by the fibrin of the blood, which is disintegrated in its passage through the liver, and that the result is a new protein substance which enters the cir-

<sup>1</sup> Todd and Bowman's *Physiology*, 1856, ii. 263 ; Carpenter's *Principles of Human Physiology*, 7th edition, 1869, p. 214 ; and Kölliker's *Manual of Human Histology*, Sydenham Society edition, 1854, vol. ii. p. 342.

ulation.<sup>1</sup> Our colleague Dr. Pavy is also of opinion that glycogen is capable of transformation into fat. As he contends, it is beyond dispute that starch and sugar introduced with the food lead in the animal system to the production of fat, while his experiments have shown that the ingestion of these principles is followed by a marked increase in the amount of glycogen in the liver.<sup>2</sup> The production of glycogen, then, may be regarded as the first step in the assimilation of the starchy and saccharine elements of our food ; and, as these elements are known to proceed on to fat, glycogen would seem to occupy a position intermediate between the two. The process of assimilation may go on to the production of fat in the liver, or it may stop short at the formation of another principle, which escapes from the liver and is elsewhere transformed into fat. Lastly, there are good grounds for thinking that both glycogen and sugar serve some purpose in muscular action ; at all events, it has been found that the quantity of sugar in blood becomes greatly diminished in passing through the vessels of contracting muscles.<sup>3</sup> According to Bernard, this de-

<sup>1</sup> *Op. Cit.*

<sup>2</sup> F. W. Pavy, *The Nature and Treatment of Diabetes*, 2nd ed., 1869, p. 113.

<sup>3</sup> Sanderson's *Handbook for the Physiological Laboratory*, 1873, p. 508.

struction of sugar in muscle is due to lactic fermentation.<sup>1</sup>

There may be other ways in which the liver contributes to assimilation and the nutrition of the body; but enough has been said to justify us, notwithstanding the prediction of Bartholin, in restoring to the organ the important function claimed for it by Galen and his successors, viz., that of sanguification.

II. But, in the second place, modern research has made it probable that the liver is endowed with a function not suspected by Galen, and which, from a pathological point of view, is even more important than that which we have been considering. Many observations, pathological as well as physiological, point to the conclusion that the liver is not only a blood-forming, but a blood-destroying or purifying organ, and that it contributes in a great degree to the destruction of albuminous matter derived from the food and textures, and the formation of urea and lithic acid, which are subsequently eliminated by the kidneys. First, there seems to be little doubt that the albumen and fibrin of the blood become largely disintegrated in the liver. Lehmann and Bernard have shown that, while portal blood

<sup>1</sup> Lectures delivered at the College of France, *London Medical Record*, October and November, 1873.

contains much fibrin, blood from the hepatic vein contains little or none.<sup>1</sup> Brown-Séquard has calculated that no less a quantity than 2,690 *grammes*, or about 86½ ounces, of fibrin is daily lost to the blood in its passage through the digestive organs and the liver.<sup>2</sup> If this be so, we can readily understand that, when anything occurs to interfere with this fibrin-destroying function, there should be a rapid increase of fibrin in the blood, as we know to occur in acute rheumatism and in other diseased states. Moreover, there are grounds for believing that, while white blood-corpuscles take their origin in the liver, the red corpuscles are destroyed there, and that the nitrogenous colouring matters of the urine are partly the result of this destructive process. Gréhaut has ascertained that there is a positive destruction of hæmoglobin in the passage of blood through the liver.<sup>3</sup> Red blood-corpuscles are known to be at once destroyed when brought in contact with a solution of bile-acids of a certain strength (12 per cent., Legg),<sup>4</sup> while the re-

<sup>1</sup> McDonnell, *op. cit.*, p. 29; G. Budd, *Diseases of the Liver*, 3rd ed., 1857, p. 47.

<sup>2</sup> *Journal de Physiologie*, i. 304.

<sup>3</sup> Sanderson, *op. cit.*, p. 498.

<sup>4</sup> Kuhne, *Archiv für path. Anat.*, 1858, Bd. xiv. p. 324; Robin, *Mémoires lus à la Société de Biologie pendant l'Année 1857*; and Dr. J. W. Legg, *Bartholomew's Hospital Reports*, vol. ix., 1873.

searches of our late colleague Dr. Bence Jones make it very probable that the various shades of yellow, brown, and pink presented by the sediments of the urine are due to different degrees of oxydation of the pigment of the bile.<sup>1</sup> But, secondly, there is evidence that the liver is largely concerned in the formation of the nitrogenous matters which are eliminated by the kidneys. 1. First, there is the well-known fact, to which I shall have occasion to refer again in more detail, that among the most constant signs of functional derangement of the liver is an imperfect formation of urea, evidenced by the deposit of lithic acid or lithates, and of a dark colouring matter closely allied to lithic acid, in the urine. 2. Secondly, when a great part of the liver has been destroyed by disease, the urea discharged in the urine becomes greatly lessened, or it entirely disappears. For example, when a great part of the liver has been destroyed by cancer, there has been found to be a remarkable diminution of urea.<sup>2</sup> Thirty years ago, our colleague Dr. Parkes examined the urine in a number of cases of hepatitis and

<sup>1</sup> G. Budd, *op. cit.*, p. 34 ; Sanderson, *op. cit.*, p. 499. 'The very close resemblance of urine-pigment to bilifulvin is strongly suggestive of an hepatic origin. . . . An argument in favour of a liver origin may perhaps be drawn from the effect of liver-diseases on the urinary pigment.' (Parkes, *On the Urine*, 1860, p. 30.)

<sup>2</sup> Parkes, *On the Urine*, 1860, p. 330.

hepatic abscess in India, and found that in some instances there was abundance of urea, and in others scarcely any, while in some it was altogether wanting. The cause of the difference appeared to be the amount of suppuration. When this was excessive, so that the secreting substance of the liver was almost entirely destroyed, the amount of urea was greatly lessened, and in a degree proportioned to the extent to which the glandular tissue was destroyed by the abscess; and, on the contrary, when the liver was not suppurating, but was actively congested and enlarged, so that there was an increased activity of the secreting cells, the amount both of urea and lithic acid was increased.<sup>1</sup> Again, in that singular malady, acute atrophy of the liver, when every secreting cell of the liver becomes rapidly disintegrated, all trace of urea may disappear from the urine, its place being taken by albuminoid substances less oxydised, such as leucin and tyrosin, which are also found in large quantity in the hepatic tissue, as if they marked the arrest or modification of the transformation of albumen.<sup>2</sup> Lastly, there are grounds, to be referred to presently, for

<sup>1</sup> *On the Dysentery and Hepatitis of India*, by E. A. Parkes, 1846.

<sup>2</sup> Frerichs, *Klinik der Leberkrankheiten*, New Sydenham Society's translation, vol. i. p. 221; Murchison, *Clinical Lectures on Diseases of the Liver*, 1868, p. 229.

believing that, when cerebral symptoms supervene in any case of protracted jaundice with destruction of the liver, they are not due, as has been commonly thought, to saturation of the system with bile, but to non-elimination of urea. From these observations, it is clear, as Meissner has argued, that 'withering and destruction of the liver-tissue is connected with an important diminution in the formation of urea.'<sup>1</sup> 3. There is experimental evidence that urea exists in large quantity in the liver, and that it is formed there. Dr. Parkes, in the Croonian Lectures for 1871,<sup>2</sup> informed us that the experiments of Heynsius and Stokvis, followed up by those of Meissner, Bullard, Perls, and others, had placed on a certain experimental basis the fact, that urea can be largely found in the liver; while the more recent observations of Cyon seem to prove that there is an actual production of urea in the liver. Cyon ascertained, on analysing blood obtained by introducing tubes into the portal and hepatic veins of dogs, that the blood from the latter vessels always contained much more urea than that from the former. In one experiment, the blood from the portal vein contained only  $\cdot 08$  *gramme* of urea in 100 cubic *centimètres*; but, after passing through the liver once, it

<sup>1</sup> Henle's *Zeitsch. für rationelle Medicin*, Bd. xxxi, p. 246.

<sup>2</sup> *Lancet*, 1871, vol. i. p. 469.



contained  $\cdot 14$  gr.; and, after passing through the liver four times,  $0\cdot 176$  gr. He satisfied himself also that this increase was not due merely to washing out the liver, but that there was an actual formation of urea.<sup>1</sup> It is important to add, that the formation of urea in the liver is always greatly increased after food. Lithic acid has also been found repeatedly in the liver of man and mammalia, but always in small quantity; whereas, in birds, in which lithic acid takes the place of urea as the great eliminator of nitrogen, it also takes the place of urea in the liver, as it probably also does in the human liver under certain pathological conditions.

All these observations point to the liver as being largely concerned in the destructive metamorphosis of albuminoid matter, the products of which are eliminated by the kidneys, although it is not improbable that other glandular organs, and even the corpuscles in the circulating blood, as believed by H. Ludwig and Fuhrer,<sup>2</sup> may contribute to the process.

As might have been expected, these oxydising and disintegrative processes, as well as those connected with the formation of bile, are attended by a production of

<sup>1</sup> *Centralblatt für die Med. Wissenschaften*, August 1870, p. 580.

<sup>2</sup> Parkes, *Lancet*, 1871, vol. i. p. 470.

heat. The average temperature of the body generally being between 98 degs. and 99 degs. Fahr., the temperature of the healthy liver reaches 104 degs., or even, according to Bernard, sometimes 106 degs.<sup>1</sup> Bernard has also shown that, in dogs, the temperature of the blood in the hepatic veins is considerably higher than that of the blood of the portal vein. As heat is absorbed during organisation, and given off during disintegration, the high temperature generated in the liver makes it probable that the disintegrative processes taking place in the gland are in excess of the formative. It follows, therefore, that the precise observation of modern times has confirmed the statement enunciated centuries ago by Galen, that the liver is a great centre of animal heat.

III. The third function of the liver is the secretion of bile. The composition of this substance is complex, and its uses are not yet sufficiently known. Human bile, as found after death, is usually a dark brown fluid, of tenacious consistence, from the presence of mucin, which it derives from the gall-bladder and bile-ducts ; but, when fresh, as it flows from the liver, it is a thin transparent liquid, of a golden yellow colour like that of yolk of egg,

<sup>1</sup> On the Heat of the Body. The Gulstonian Lectures for 1871. By Dr. S. Gee, *British Medical Journal*, 1871, vol. i. p. 330.

of a very bitter taste, of alkaline reaction, and having a specific gravity of about 1018. It has an unctuous feel, and mixes freely with oil or fat. It contains from 9 to 17 per cent. of solid matters (the proportion being always greater soon after a meal), consisting for the most part of substances peculiar to bile. Excluding the mucin, its principal ingredients are—1. Bile-pigment; 2. Biliary acids combined with soda; 3. Cholesterin and fats; 4. Mineral matter, such as phosphates of soda, potash, lime, magnesia, and iron, chloride of sodium, and traces of copper.

The following analysis of bile obtained from a man aged 22, killed by an injury, was made by Frerichs:—

Water . . . . .	859.2
Solid residue . . . . .	140.8
	—
Glycocholate of soda } . . . . .	91.4
Taurocholate of soda }	
Fat . . . . .	9.2
Cholesterin . . . . .	2.6
Bile-pigment and mucus (of which, mucus about 1.4)	29.8
Salts . . . . .	7.7

The yellow pigment is now designated *bilirubin* ( $C^{16}H^{18}N^2O^3$ ). On standing, it becomes greenish from oxydation, and is converted into *biliverdin* ( $C^{16}H^{20}N^2O^5$ ), which accounts for the dark colour usually presented

by the bile in the gall-bladder after death and in the fæces. Biliverdin is also the principal colouring matter of the bile of the herbivora. Bilirubin is now known to be formed from blood-pigment or hæmoglobin by the hepatic cells, in the passage of the blood through the liver. That this was the source of the bile-pigment was suggested at the end of last century by a distinguished Fellow of this College, Dr. W. Saunders, who observed : ' Green and bitter bile, being in common to all animals with red blood, and found only in such, makes it probable that there is some relative connection between this fluid and the colouring matter of the blood, by the red particles contributing more especially to its formation.'<sup>1</sup> This view, revived in our own day by Virchow, is supported by the apparent identity of bile-pigment with the pigment hæmatoidin, found in old extravasations of blood, and by the fact that what appears to be bile-pigment can be produced from blood-pigment by the action of chemical reagents ;<sup>2</sup> by the discovery of Zenker and Frerichs of crystals of hæmotoidin in inspissated bile and in the bile

<sup>1</sup> *Treatise on Structure and Diseases of the Liver*, 3rd edition, 1803, p. 147.

<sup>2</sup> Virchow's *Cellular Pathology*, English translation, p. 144 ; Kühne, *Lehrbuch der Physiol. Chemie*, Leipzig, 1866, p. 89.

of jaundiced urine ;<sup>1</sup> by the observation of Gubler that bilirubin and hæmatin give the same play of colours with nitric acid, except that the green colour is most persistent in the former, and the violet in the latter;<sup>2</sup> by the discovery of Frerichs, Kühne, and others, that when any substance, such as bile-acids or even water, which has the property of dissolving blood-corpuscles and liberating hæmoglobin, is injected into the veins, bile-pigment (bilirubin) appears in the urine ; and by the statement of Gréhaut, that there is a positive destruction of hæmoglobin in the passage of blood through the liver.<sup>3</sup> There are, on the other hand, grounds for believing that bile-pigment is in its turn converted into urinary pigment.<sup>4</sup> A substance presenting spectroscopic characters similar to those of urinary pigment can be prepared by deoxidation from bilirubin ; and it is believed that, in the organism, bile-pigments are reduced by hydrogen or other reducing agents present in the intestines.<sup>5</sup> It is also a well-known clinical fact, that nothing influences so much

<sup>1</sup> *Jahresb. von der Gesellschaft für Natur-und Heil-kunde in Dresden*, 1858, p. 53.

<sup>2</sup> *Gaz. Méd. de Paris*, 1859, p. 469.

<sup>3</sup> Sanderson, *op. cit.*, p. 498.

<sup>4</sup> Bence Jones, referred to by G. Budd, *op. cit.*, p. 34 ; Parkes, *On the Urine*, 1860, p. 30.

<sup>5</sup> Sanderson, *op. cit.*, p. 499.

the characters of the urinary pigment as functional or structural disease of the liver. The liver, then, together with that osmotic circulation constantly going on between it, the blood, and the contents of the intestines, to be referred to presently, appears to be the medium of con-

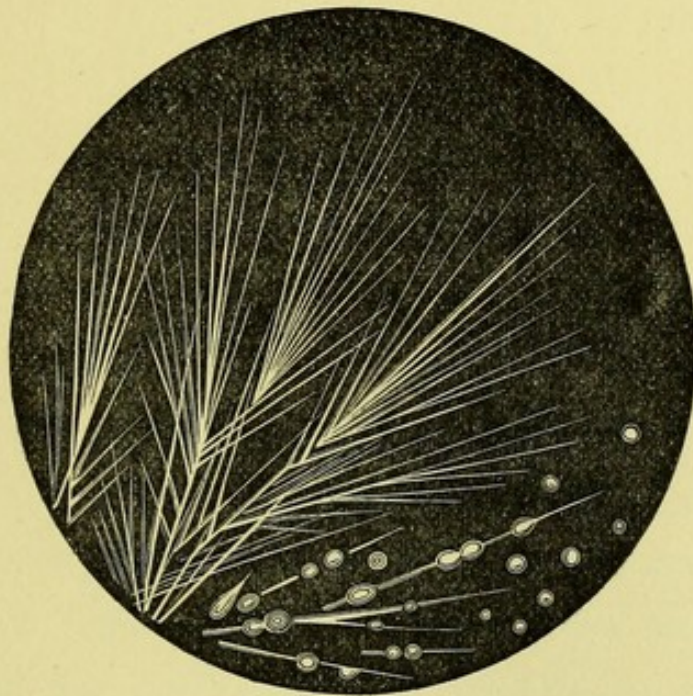


FIG. 1.—Glycocholate of soda from ox-bile after two days' crystallisation. At the lower part of the figure the crystals are melting into drops from the evaporation of the ether and absorption of moisture. After J. C. Dalton.

version of blood-pigment into bile-pigment, and of bile-pigment into urinary-pigment.

The bile-acids in human bile are two—glycocholic acid ( $C^{26} H^{43} NO^6$ ) and taurocholic acid ( $C^{26} H^{45} NO^7 S$ ). Both acids are derivatives of albumen, and contain

nitrogen; and taurocholic acid, to which the bitter taste of bile is due, contains all the sulphur of the bile. Both are in bile combined with soda, and both are what are called conjugate acids; that is to say, they are composed of cholic acid ( $C^{24} H^{40} O^5$ ), which contains neither

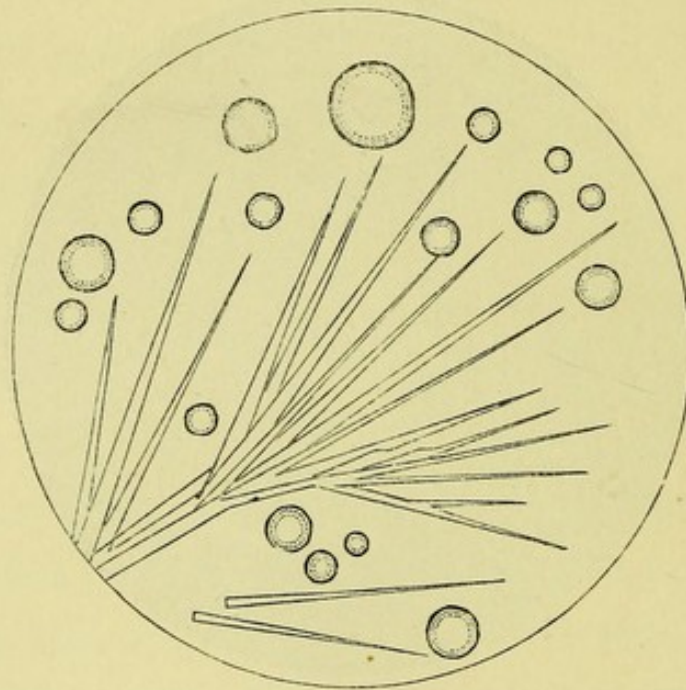


FIG. 2.—Glycocholate and taurocholate of soda from ox-bile after six days' crystallisation. The glycocholate is crystallised; the taurocholate is in fluid drops. After J. C. Dalton.

nitrogen nor sulphur, in combination with taurin ( $C^2 H^7 NO^3 S$ ), which contains both nitrogen and sulphur, and glycocin ( $C^2 H^5 NO^2$ ), which contains nitrogen, but no sulphur.

Cholesterin ( $C^{26} H^{44} O$ ) is a fatty substance, which

crystallises in colourless rhombic plates, one corner of which is often indented. It is met with in nerve-matter, in the spleen, in blood, and in certain morbid

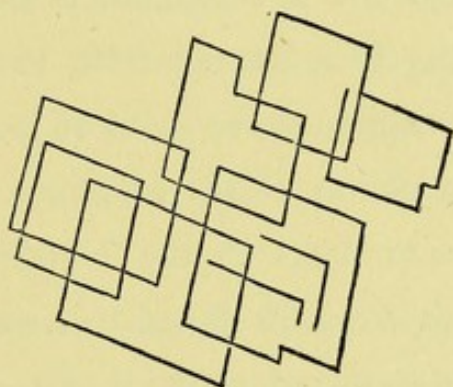


FIG. 3.—Crystalline Plates of Cholesterin.

exudations, as well as in bile. An American physician, Dr. Austin Flint, Jun., has endeavoured to show that cholesterin is formed for the most part, if not entirely, from nerve tissue, from which it is taken up by the blood; and that one of the chief functions of the liver is to eliminate this cholesterin, the accumulation of which in the blood, from the liver ceasing to act, is attended by cerebral and other symptoms of blood-poisoning.<sup>1</sup>

Bile thus constituted is being constantly secreted by the liver. There is still much difference of opinion as to

<sup>1</sup> *Recherches Expér. sur une nouvelle fonction du Foie.* Paris, 1868.



the part played by the liver in the formation of bile. It is generally admitted that the biliary acids are formed in and by the liver ; but many physiologists and physicians still maintain that the bile-pigment is preformed in the blood, and is merely separated from the blood by the liver ; and they explain those cases of jaundice in which there is no obstruction of the bile-duct, by saying that bile-pigment accumulates in the blood from the liver ceasing to act, or from its function being suppressed.<sup>1</sup> But it has long appeared to me that there are weighty objections to this view.

1. Although bile-pigment appears to be derived from the colouring matter of the blood, it has not yet been satisfactorily shown that bile-pigment, as such, exists ready-formed in the blood of persons who have not jaundice. Frerichs denies that it ever has. Lehmann, who has investigated with great care the changes which the blood undergoes in passing through the liver, has never been able to detect the colouring matter of bile in portal blood, and infers that this, as well as the bile-acids, must be formed in the liver itself.<sup>2</sup> The blood of the hepatic artery has been examined with a like result. It is

<sup>1</sup> Budd, *op. cit.* ; and G. Harley, *Jaundice, its Pathology and Treatment*. London, 1863.

<sup>2</sup> *Physiological Chemistry*, Dr. Day's translation, vol. ii. p. 87.

obvious that, if bile-pigment exist in healthy blood at all, its quantity must be very minute ; and, when we consider that the quantity of bile secreted by the human liver daily is about two pints, and yet that jaundice is not a normal condition, it seems impossible that all the bile-pigment secreted by the liver can be formed in the blood ; and it is not probable that part is formed in the blood and part in the liver.

2. The discovery by a few observers of a small quantity of bile-pigment in what appeared normal blood does not prove that it was formed in the blood. It is quite conceivable that it may have been formed in the liver, and been subsequently absorbed.

3. It often happens that, from various diseases, such as fatty and waxy degeneration, cancer, and cirrhosis, the secreting tissue of the liver is for the most part or entirely destroyed, bile is no longer secreted, and yet no jaundice results. Several cases of this sort are referred to by Haspel, where the gall-bladder and bile-ducts, after death, contained only a little white mucus.<sup>1</sup> Frerichs records a case of fatty liver, where the contents of the bowels were pale, the gall-bladder empty, and the biliary ducts coated with a greyish mucus, notwithstanding which the skin was of a chalky paleness, and the urine contained no bile-pig-

<sup>1</sup> *Maladies d'Algérie*, vol. i. p. 262.

ment.<sup>1</sup> Similar observations have been made by Budd in cases of waxy disease and cancer of the liver,<sup>2</sup> and several instances of a like nature have come under my own notice. If bile-pigment be formed in the circulating blood, it is difficult to account for what becomes of it in these cases.

4. If the constituents of bile are formed in the blood, intense jaundice ought at once to follow the extirpation of the liver in any of the lower animals, in like manner as urea accumulates in the blood after removal of the kidneys. But, so far from this being the case, Müller, Kunde, Lehmann, and Moleschott have repeatedly extirpated the liver of frogs, and have invariably failed to find a trace of the biliary acids, or of the colouring matter of the bile, in the blood, the urine, or the muscular tissue.<sup>3</sup>

The supposition that bile-pigment is formed in the blood appears to me for these reasons to be untenable.

The quantity of bile secreted by the liver has been shown experimentally to increase suddenly after a meal, reach its maximum in about two hours, and then gradu-

<sup>1</sup> *Op. cit.*, English edition, vol. i. p. 83.

<sup>2</sup> *Op. cit.*, pp. 329, 411.

<sup>3</sup> Carpenter's *Human Physiology*, 7th edition, p. 434.

ally decline, while by abstinence it is greatly lessened. In considering the functional derangements of the liver, it is very necessary to remember that the total quantity of bile secreted in twenty-four hours by a man eating an ordinary amount of food, is much larger than might be expected from that which is discharged from the bowel. The daily quantity of human bile has been usually calculated from what has been observed in dogs with artificial biliary fistulæ,<sup>1</sup> and the principal results have been as follow. According to Kölliker and Müller, a dog consuming daily about one-fifteenth of its own weight of meat secretes in twenty-four hours 36·1 parts of fluid bile in 1,000 parts of its own weight. According to Dr. George Scott, a dog consuming daily about one-fourteenth of its own weight of meat secretes in twenty-four hours 23·13 parts of fluid bile in 1,000 parts of its own weight. According to Bidder and Schmidt, a dog consuming daily about one-seventeenths of its own weight of meat secretes in twenty-four hours 19·19 parts of fluid bile in 1,000 parts of its own weight. Making allowance for the greater relative weight of the liver in the dog than

<sup>1</sup> On this subject, see Bidder and Schmidt, *Die Verdauungssäfte und der Stoffwechsel*, 1852, p. 186 ; Dr. G. Scott, *Beale's Archives of Medicine*, 1858, vol. i. p. 218 ; Carpenter's *Human Physiology*, 7th edition, p. 144.

in man,<sup>1</sup> it follows from these results that the amount of fluid bile secreted in twenty-four hours by a man weighing 160 pounds, and on full diet, is, according to

Kölliker and Müller . . . . .	66·742 ounces.
Scott . . . . .	42·763 „
Bidder and Schmidt . . . . .	35·476 „

Similar experiments have been made on dogs by Nasse, Platner, and Stackman, and from their data Carpenter has calculated that a man weighing 154 pounds should secrete daily about forty ounces of bile. It may be assumed, then, from experiments on the lower animals, that the quantity of bile secreted in twenty-four hours by the human liver is about forty ounces; and this inference is, on the whole, confirmed by what is observed in those rare cases where a biliary fistula discharging bile is produced in the human subject by ulcerative perforation of the fundus of the gall-bladder, the cystic duct remaining patent, while the common bile-duct is closed; although in some instances the quantity of bile has been less than in health, from the patient being greatly emaciated and taking little food. One case of the

<sup>1</sup> The weight of the liver of the dog is, from six observations of Bidder and Schmidt, as 1 to 26 of the whole body. According to Quain, the weight of the liver in man is as 1 to 36 of the whole body.

nature referred to has come under my own notice, the particulars of which are worth mentioning. The patient was a lady aged 40, whom I saw in October 1869, in consultation with Mr. Curling. Owing to an obstruction of the cystic duct by a gall-stone, the gall-bladder became inflamed and converted into a chronic abscess, which was opened externally. A fistulous opening resulted, which discharged a scanty colourless viscid fluid, and gave exit to several small gall-stones. But after four months, with a fresh attack of biliary colic and vomiting, the concretion in the cystic duct was dislodged and projected into the common bile-duct, which it obstructed, as was proved by the motions becoming white and by bile being poured in large quantity through the fistulous opening. This state of matters continued for forty-one days (the patient passing white stools, but having scarcely a trace of jaundice), when there occurred another attack of biliary colic and vomiting, during which the concretion escaped into the duodenum, and the flow of bile was restored to its proper channel. In this case, the quantity of bile secreted in twenty-four hours was fully two pints, although the patient did not weigh more than about 130 pounds, and was eating but a moderate diet.<sup>1</sup> I have collected several

<sup>1</sup> Further details of the case will be found in *Pathological Transactions*, vol. xxii. p. 152.

other cases<sup>1</sup> of a similar nature, in which the results more or less corresponded with that observed in my patient ;

<sup>1</sup> Dr. J. Hertz of Königsberg has recently recorded the case of a female aged 28, in whom the daily flow of bile from a biliary fistula was eighteen fluid ounces. It is doubtful, however, if all the bile secreted was really discharged from the fistula ; for, though the stools were of a pipe-clay colour, the fact that the flow of bile into the bowel was restored after closure of the external opening by needles (but not for six days, during which no jaundice appeared), seems to show that the obstruction of the common bile-duct was not complete. (*Berliner Klin. Wochenschrift*, April 7, 1873.)

In the twenty-seventh volume of the *Medico-Chirurgical Transactions*, Mr. W. R. Barlow records the case of a man aged 54, in whom, in consequence of a strain, the common bile-duct became temporarily obstructed, probably by a gall-stone. The result was, that in twelve days thirteen pints of fluid accumulated in the gall-bladder. Dr. Owen Rees found, on analysis, that four-fifths of this fluid was pure bile, so that nearly one pint of bile must have been secreted in the day, although the patient was under the antiphlogistic treatment of that time (1844), and had been repeatedly bled from the arm and leeches.

In the thirty-fifth volume of the *Medico-Chirurgical Transactions* the case is recorded of a female aged 64, in whom the daily discharge of bile from a fistula was only eight ounces. The fistula was the result of a large gall-stone obstructing the common bile-duct, and existed for six months, at the end of which time the woman died from exhaustion. The small quantity of bile in this case was accounted for by the circumstance of the patient being very poor and having insufficient food.

In the fourth volume of the *Transactions of the College of Physicians* Dr. Saunders recorded the case of a female, aged 66, who discharged a large gall-stone through the abdominal parietes. For three weeks afterwards 'a very profuse discharge of bile ran

but I will not occupy time in reading the details. I will merely mention that Fauconneau Dufresne, in his exhaustive memoir upon Biliary Calculi in the Human Subject, observes that from the external biliary fistulæ, to which they now and then give rise, enormous quantities of bile may be discharged, so as to inundate the patient. He mentions one case in which the daily amount was two pints.<sup>1</sup>

Although the amount of bile secreted daily must vary in different persons, and in the same person under different circumstances, being modified by the quantity and quality of the food, the activity of respiration, and other conditions, it is clear, from the facts now mentioned, that but a small proportion of what is ordinarily secreted is discharged from the bowel. Berzelius found in 1,000 parts of fresh human fæces only 9 parts of a substance similar to bile, which, on the calculation that the daily fæces of a man weigh  $5\frac{1}{2}$  ounces, would make a total of 24 grains

perpetually from the wound,' although the common bile-duct remained pervious.

Haller, in his *Physiology*, alludes to the case of a man with a biliary fistula, from which four ounces of bile escaped in six hours; but there is no mention as to whether or not the common bile-duct was closed. (*Physiologia*; Berne, 1764, tome vi. p. 605.)

<sup>1</sup> *Mém. de l'Acad. Royale de Méd.*, 1847, tome xiii.



of dried bile in the day.<sup>1</sup> Now, assuming that the liver secretes 40 ounces of bile in the day, containing only 5 per cent. of solid matter, which is considerably below the average proportion, the amount of dried bile secreted in one day would be 960 grains, or forty times the quantity discharged from the bowel. According to Bischoff, man discharges about 46 grains of the (altered) biliary acids by the fæces per diem; whilst Voit's estimates give 170 grains as the quantity daily formed by the liver; 124 grains must, therefore, be otherwise disposed of.<sup>2</sup> Bidder and Schmidt have also found that not more than one-eighth of the sulphur of the bile is normally excreted with the fæces.<sup>3</sup> The bile-pigment is generally believed to be all voided by the fæces; but this is clearly not the case, if there be any truth in the view already referred to, that urinary pigment is formed from bile-pigment; while the fact familiar to all clinical observers, that the bile-pigment discharged from the bowel is greatly increased by calomel and other aperients, without any corresponding increase of secretion by the liver, also seems to show that, under ordinary circumstances, much of the bile-pigment secreted by the liver is not discharged with the fæces. It

<sup>1</sup> Budd, *op. cit.*, p. 52.

<sup>2</sup> Carpenter's *Human Physiology*, 7th edition, p. 435.

<sup>3</sup> *Die Verdauungssäfte und der Stoffwechsel*, 1852, p. 218.

may be added that, in carnivorous animals and in snakes, although bile-pigment is secreted in abundance by the liver, the quantity discharged with the fæces is even relatively less than in man.<sup>1</sup>

The question then arises as to what becomes of the bile which is not discharged from the bowel; and it is obviously one having an important bearing on the pathology of many cases of jaundice, as well as upon that of many functional derangements of the liver. The reply is to be found in the fact, that a large proportion of the bile secreted by the liver is again absorbed, either by the biliary passages, or by the mucous membrane of the bowel. From what is now known of the diffusibility of fluids through animal membranes, it is impossible to conceive bile long in contact with the lining membrane of the gall-bladder, bile-ducts, and intestine, without a large

<sup>1</sup> Liebig states that in the carnivora the whole of the bile is reabsorbed (Budd, *op. cit.*, p. 51). Todd and Bowman also state that in carnivorous animals 'little or no bile is found in the excrements;' and 'in the boa, although the liver is large, and no doubt secretes bile freely, the excrements contain no trace of bile' (*Physiology*, vol. ii. p. 259). Although the excrement of snakes, after feeding, does present a brownish colour, and differs from the white masses of uric acid voided at other times, Marcet, who is an authority on the subject, states that the excrement of the boa is 'nearly entirely composed of urates.' (*Philosophical Transactions*, 1854, p. 279.)

portion of it passing into the circulating blood. The constant secretion and reabsorption of bile is, in fact, merely part of that osmotic circulation constantly taking place between the fluid contents of the bowel and the blood, the existence of which is too little heeded in our pathological speculations<sup>1</sup> and in therapeutics, although attention was called to it eighteen years ago by Dr. Parkes, in the Gulstonian Lectures on Pyrexia delivered before this College. 'It is now known,' says Dr. Parkes,<sup>2</sup> 'that, in varying degrees, there is a constant transit of fluid from the blood into the alimentary canal, and as rapid reabsorption. The amount thus poured out and absorbed in twenty-four hours is almost incredible, and of itself constitutes a secondary or intermediate circulation never dreamt of by Harvey. The amount of gastric juice alone passing into the stomach in a day, and then reabsorbed, amounted in the case lately examined by Grünewald<sup>3</sup> to nearly twenty-three imperial pints. If we put it at twelve pints, we shall certainly be within

<sup>1</sup> The purging of cholera may result from a stoppage of this intestinal circulation—a diminished power of absorption, rather than an increased exhalation from the bowel. Many facts prove that in cholera the power of absorption by the bowel is greatly impaired or abolished.

<sup>2</sup> *Medical Times and Gazette*, 1855, vol. i. p. 333.

<sup>3</sup> An account of this case, abstracted by me from Grünewald's Latin memoir, will be found in Beale's *Archives of Medicine*, vol. i. p. 270.—C. M.

the mark. The pancreas, according to Kroeger, furnishes twelve pints and a half in twenty-four hours, while the salivary glands pour out at least three pints in the same time. The amount of the bile is probably over two pints. The amount given out by the intestinal mucous membrane cannot be guessed at, but must be enormous. Altogether the amount of fluid effused into the alimentary canal in twenty-four hours amounts to much more than the whole amount of blood in the body ; in other words, every portion of the blood may, and possibly does, pass several times into the alimentary canal in twenty-four hours. The effect of this continual outpouring is supposed to be to aid metamorphosis ; the same substance, more or less changed, seems to be thrown out and reabsorbed, until it be adapted for the repair of tissue or become effete.' How many times this cycle of movement is repeated, before the bile is extruded from the system, we have no means of knowing ; but, in the course of this osmotic circulation, much of the bile appears to become transformed into products which are eliminated by the lungs and kidneys, while at the same time this circulation assists in the assimilation of the nutritive materials derived from the food.<sup>1</sup>

<sup>1</sup> It may be thought improbable that the liver should secrete from the blood of the portal vein materials which are afterwards to be absorbed by the branches of the same vessel. But it has, per-

In the first place, it assists in the absorption of fat. It is a well-known clinical fact that, when the common bile-duct has been too readily assumed, from the comparatively large size of the vena portæ, that it furnishes the materials for bile. Although, when one vessel is diseased, its function may, in part, be performed by the other, it is probable that, under ordinary circumstances, the portal vein ministers chiefly to the assimilating functions of the liver, transporting to it the nutriment absorbed by its branches from the stomach and bowels; while the hepatic artery ministers to its secreting function, the biliary acids and bile-pigment being secreted from arterial blood, like urea and uric acid, which in the kidneys are secreted from the blood of the renal artery. This view is based on such facts as the following:—

1. In the *Philosophical Transactions* for 1793 a case is recorded where the portal vein passed direct to the vena cava inferior without entering the liver, and yet bile was found in the gall-bladder and intestines. Similar cases are referred to by Dr. Carpenter. (*Principles of Human Physiology*, 5th edition, p. 372.)

2. Many cases are on record where there has been complete obstruction of the portal vein from disease for some time before death, and yet bile has continued to be secreted. In 1856, Dr. Gintrac of Bordeaux collected thirty-four cases of obliteration of the portal vein in man, in not one of which was the biliary secretion interrupted. (*L'oblitération de la veine porte*, Bordeaux; see also Frerichs, *op. cit.*, vol. i. p. 274; and Dickinson, *Pathological Transactions*, vol. xiv. p. 63.)

3. In animals, the portal vein has been tied by Oré and other experimenters, and yet bile has been secreted. The reduction in the quantity may have been due to the febrile disturbance created by the operation, or to the absence of the fatty ingredients of the bile which may be contributed by the portal vein. (Oré, *Journ. de l'Anat. et Phys.*, 1864, p. 556; Carpenter's *Human Physiology*, 7th edition, p. 433; and *Comparative Physiology*, 4th edition, p. 424.)

duct becomes obstructed from any cause in man, the fat throughout the body wastes. Many years ago, also, it was shown by Drs. Bright and Owen Rees that, in cases of this sort, an unusual quantity of fat may often be detected in the stools.<sup>1</sup> Bidder and Schmidt likewise found that, after applying a ligature to the gall-duct of a dog, the animal absorbed less fat than before, and there was also a diminution of fatty matter in the chyle in the thoracic duct; the amount absorbed was calculated from a comparison of the fat eaten with the amount passed in the fæces.<sup>2</sup> There are also grounds for thinking that the entrance of bile into the bowel facilitates the absorption of the albuminous constituents of the food. The bile neutralises the acid that passes from the stomach into the duodenum, and in doing so causes a precipitate of peptones. It is difficult to say what purpose is served by this precipitation; but some experiments of Bernard led him to the conclusion that gastric juice, when mixed

4. Conversely, Kottmeier and Kütke found that no bile was secreted after ligature of the hepatic artery, although it is right to add that Schiff was unable to detect any diminution in a large dog, upon which he had performed the same operation; and Röhrig observed only a slight diminution in the flow of bile after obstruction of the hepatic artery. (Carpenter, *Human Physiology*, 7th edition, p. 433; and Röhrig, in Stricker's *Jahrb.*, 1873, part ii.

<sup>1</sup> *Guy's Hospital Reports*, series I. vol. i. p. 610.

<sup>2</sup> Sanderson, *op. cit.*, p. 505.

with pancreatic juice and bile, has a more solvent action on albuminous substances than the gastric juice alone.<sup>1</sup> The passage of bile into the bowel appears also to be in some way essential to the formation of glycogen by the liver. In a number of experiments recently made upon cats Dr. Wickham Legg found that the formation of glycogen was always arrested soon after ligature of the bile-duct ; in one cat, the diabetic puncture of the brain was made on the sixth day after ligature of the bile-ducts, but no sugar appeared in the urine.<sup>2</sup> The production of urea, however, in the liver appears to be quite independent of the passage of bile into the bowel, for in cases of permanent obstruction of the gall-duct the amount of urea voided in the urine may be quite normal.

But, lastly, there can be no doubt that bile is in part excrementitious, a portion of it being discharged from the bowel, and serving to rid the system of some of the products of waste of the blood and tissues. The biliary acid salts are decomposed, and, by their decomposition, they furnish the free alkali necessary for the precipitation of peptones and the saponification of the fatty matters ; they are believed also to become further split up, the taurin,

<sup>1</sup> Budd, *op. cit.*, p. 50. \*

<sup>2</sup> On the Changes in the Liver which follow Ligature of the Bile ducts. (*St. Bartholomew's Hospital Reports*, vol. ix. 1873.)

glycocin, and most of the cholic acid returning to the circulation, while a portion of the cholic acid is discharged with the fæces. The cholesterin is also decomposed in the bowels, and the products of its decomposition are discharged with the fæces. According to Dr. Austin Flint, Jun., the cholesterin is converted into a substance which he has discovered in the fæces and designated stercorin ; it appears also to be in some way related to another ingredient of the fæces discovered by Marcet and called excretin, although this contains sulphur. Marcet, at all events, made the observation that, in very young children, cholesterin may take the place of excretin in the stools.<sup>1</sup> The bile-pigment also becomes changed in its passage through the bowel ; the bilirubin becoming converted into biliverdin. Lastly, the bile, in its passage through the bowel, stimulates the peristaltic action of the gut ; and, in virtue of its antiseptic property, which can be demonstrated out of the body, it prevents putrefactive fermentation of the intestinal contents, and the excessive generation of gas.

From what has been stated, it follows that the functions of the liver may be summed up under three heads, viz. :—



1. The formation of glycogen, which contributes to the maintenance of animal heat and to the nutrition of the blood and tissues ; and the development of white blood-corpuscles.

2. The destructive metamorphosis of albuminoid matter, and the formation of urea and other nitrogenous products, which are subsequently eliminated by the kidneys, these chemical changes also contributing to the development of animal heat.

3. The secretion of bile, the greater part of which is reabsorbed, assisting in the assimilation of fat and peptones, and probably in those chemical changes which go on in the liver and portal circulation ; while part is excrementitious, and, in passing along the bowel, stimulates peristalsis and arrests decomposition.

#### B. FUNCTIONAL DERANGEMENTS OF THE LIVER.

Keeping in view the functions of the liver in health, which I have endeavoured thus briefly to sketch, we shall be the better able to discuss the symptoms resulting from derangements of these functions. The few medical writers who have described the functional derangements of the liver have, like the late Dr. Copland,<sup>1</sup> arranged

<sup>1</sup> *Medical Dictionary*, vol. ii. p. 723.

them under the three following heads: 1. Diminished secretion of bile; 2. Increased secretion of bile; 3. Secretion of morbid or altered bile. But this classification fails to recognise the most important functions of the liver; and, from what has been stated, it follows that the quantity and quality of the bile discharged from the bowel, upon which the classification is based, are no certain tests of the amount and quality of the bile secreted by the liver. The quantity secreted being the same, the quantity discharged from the bowel will vary with whatever stimulates or impedes absorption. Any substance like calomel or podophyllin, or certain articles of diet, which irritate the commencement of the small intestine, will sweep along the bile before there is time for its absorption, and thus cause an increased flow from the bowel, without the secretion by the liver being necessarily increased. Moreover, it must often be impossible to say whether the morbid or altered appearances of the bile in the fæces be due to a vitiated bile, or to changes which the bile has undergone in its passage through the bowel. For these reasons, I have ventured to suggest another classification of the functional derangements of the liver, based upon what are now believed to be the normal functions of the gland, and upon the symptoms

which a disordered liver may excite in the different physiological systems of the body.

*Classification of the Functional Derangements of the Liver.*

- I. Abnormal Nutrition.
- II. Abnormal Elimination.
- III. Abnormal Disintegration.
- IV. Derangements of the Organs of Digestion.
- V. Derangements of the Nervous System.
- VI. Derangements of the Organs of Circulation.
- VII. Derangements of the Organs of Respiration.
- VIII. Derangements of the Urinary Organs.
- IX. Abnormal Conditions of the Skin.

I. *Abnormal Nutrition.*

Functional derangement of the liver may lead directly to (1) an abnormal deposition of fat, or to (2) the opposite condition of emaciation. Indirectly, also, the nutrition of the body may become seriously impaired from derangements of the disintegrative functions of the liver.

1. *Corpulence*, by which so many persons are inconvenienced, owes its origin to different causes. We know that it is very liable to occur in persons who eat much fat and take little exercise. In this case, the lacteals

absorb more fat from the bowel than is sufficient to supply the carbon consumed in respiration, or there is a deficient consumption of fat in the system. Many facts, however, show clearly that the accumulation of fat is not due solely to an increased supply of fatty matter in the food, and its absorption by the lacteals. Thus, of two persons consuming the same amount of fat, and taking the same amount of exercise, one will accumulate fat and the other will not; and in many persons the accumulation of fat appears to be one of the characteristics of old age, just as other persons, in growing old, wither and dry up. Again: some persons, with every care as to diet, cannot avoid getting fat; while others, consuming much fat, as well as saccharine and starchy matter, remain permanently thin. And, thirdly, it is a fact established by many observations, both in man and in the lower animals, that fat is formed in large quantity from a diet containing much starch and sugar, and, from what has already been stated, it seems probable that the liver is mainly concerned in this transformation. Some of the fattest persons I have met with have been females, who have for a long time eaten little or no fat or oily matter, and who indeed have taken very little solid food, but who have contracted the habit of drinking frequently some mixture of alcohol and sugar, such as we find in

beer, champagne, and other wines, and who at the same time have taken little exercise, and have suffered from symptoms of deranged liver. M. Dancel relates the case of a young lady, who, finding herself getting stout, and with the object of preserving her symmetry, fasted, as she thought, four days in the week upon champagne and *marrons glacés*; but with this diet she accumulated fat with frightful rapidity, and it was only after returning to a more rational diet that she regained her normal figure.<sup>1</sup> The tendency to accumulate fat, or the reverse, appears to be due to some constitutional peculiarity transmissible by parents to their offspring; and, from what we know of the functions of the liver, it is highly probable that this is the organ mainly at fault. Possibly, there may be an abnormal proneness, or the reverse, to the conversion of glycogen into fat, in the manner suggested by Dr. Pavy; or, from some derangement of the liver, a larger proportion of the glucose derived from the food may be directly converted into fat than in health; or, in some instances, obesity may be due to a deficient oxydation of fatty matter. Although we can only as yet speculate as to the precise nature of

<sup>1</sup> Quoted by Dr. T. K. Chambers (*Clinical Lectures*, 1864, p. 547). I have failed to find the case in the *Traité Théorique et Pratique de l'Obésité*, par F. Dancel; Paris, 1863.

the morbid process, we know that, in animals eating much farinaceous, saccharine, or oleaginous food, the proportion of fatty particles in the secreting cells of the liver is much greater than in animals moderately fed and taking much exercise.

Persons of a corpulent tendency are very liable to flatulence, constipation, heaviness, and weariness after meals, and other symptoms of hepatic derangement. After a time, they lose all appetite for solid food ; they complain of great prostration and of sensations of sinking, which prevent their making much muscular exertion, and often encourage them in habits of tippling.

2. *Emaciation* may be induced by functional derangement of the liver in different ways.

*a.* In consequence of a deficient formation of bile, or of its impeded passage into the bowels, the assimilation of fatty and albuminous matters is interfered with. It is true that cases are occasionally met with in which the common gall-duct has been completely and permanently closed by a gall-stone, so that no bile could flow into the intestine, and yet the body has been tolerably well nourished after upwards of twelve months.<sup>1</sup> There are, however, few exceptions to the rule, that permanent closure of the common bile-duct destroys life in the end—usually in little

<sup>1</sup> Budd, *op. cit.*, p. 49.

more than twelve months, if not before—by causing a gradual impairment of nutrition. Most patients with obstruction of the bile-duct dislike fat, and cannot assimilate it, the fatty matters of the ingesta being, as already stated, discharged with the fæces. There are also reasons for thinking that the absence of bile from the bowel interferes with the absorption of peptones; while Dr. Legg's observation that ligature of the hepatic duct in animals arrests the glycogenous function of the liver, makes it probable that, when the flow of bile into the bowel is impeded, the nutrition of the body suffers in other ways than by the deficient absorption of fat and albumen. A deficient secretion or a morbid quality of bile may possibly lead to a similar result, though in a less degree.

*b.* But, secondly, emaciation may result from derangement of the glycogenetic function of the liver. *Diabetes*, in fact, may be said to be in most instances a functional derangement of the liver. It would be out of place here to consider in detail what are now believed to be the various causes of glycosuria;<sup>1</sup> but, briefly, they may be said to come under one of the three following heads.

1. *Imperfect glycogenesis* in the liver. One function of the liver in health appears to be to prevent the immediate

<sup>1</sup> These are well given by Dr. T. L. Brunton, in his Lectures in the *British Medical Journal* for January and February 1874.

passage into the blood of the glucose derived from the food, by converting it into glycogen. Thus, Bernard has shown that, if a ligature be applied to the portal vein in an animal, so that the intestinal blood, rich in glucose, reaches the systemic circulation without passing through the liver, sugar at once appears in large quantity in the urine; and, in man, diabetes has been known to occur when the portal vein has been obliterated.<sup>1</sup> Again, if sugar be injected into the crural vein or into the rectum, it appears in the urine; but, if it be injected slowly into the portal vein, the urine will contain none.<sup>2</sup> The capability of the liver to convert sugar into glycogen is not unlimited. When, therefore, sugar is swallowed in excess of a certain quantity, it appears in the urine; and the same thing happens when much sugar or starch is taken after long fasting, owing to the rapidity of intestinal absorption; or when, in consequence of disease, old age, injury of the liver, unsuitable food, or some other cause, the glyco-genetic function of the liver is impaired. Glycosuria, often temporary, from some of these causes is not un-

<sup>1</sup> See abstract of Lectures in *London Medical Record*, for October and November 1873.

<sup>2</sup> Pavy, *Nature and Treatment of Diabetes*, 2nd edition, 1869, pp. 142-43; and Bence Jones, *Lectures on Pathology and Therapeutics*, 1867, p. 42.



common. According to Bence Jones, in half of the cases of diabetes, the disease consists in an arrest of change in the food-sugar,

2. *An increased conversion of glycogen into sugar*, the destruction of the sugar remaining unaltered. In considering the functions of the liver, it was pointed out that the glycogen formed in it was partly converted into sugar, which disappeared in the lungs and muscles, but was probably mainly destined to support the nutrition of the blood and tissues throughout the body. Whatever, then, favours the reconversion of glycogen into sugar to an extent greater than can be consumed in the lungs and muscles, will lead to an excess of sugar in the blood and its appearance in the urine, and will to a corresponding extent interfere with the nutrition of the body. Now, whatever quickens the circulation of blood through the liver, particularly in the hepatic arteries, favours the conversion of glycogen into sugar, possibly by increasing the amount of albuminoid ferment already referred to ; and accordingly, whatever paralyses the vaso-motor nerves of the hepatic vessels, either directly or indirectly, dilates these vessels, produces an increased flow of blood through them, and so leads to diabetes. The tendency of glycogen to become converted into sugar appears to be moderated in health by some nervous influence, on the removal of which

the blood becomes surcharged with sugar, which enters the urine. Thus it is that diabetes is produced by irritation of the roots of the pneumogastric nerve in Bernard's 'diabetic puncture,' by certain injuries and diseases of the brain and spinal cord in man, by distress and anxiety of mind, by poisoning with woorari, and by injuries or lesions of the peripheral extremities of the pneumogastric nerve in the lungs, liver, stomach, or intestines.

3. *Diminished destruction of sugar.* If the sugar into which the glycogen formed in the liver is converted did not disappear from the blood, it would necessarily form one of the normal constituents of the urine. Hence it cannot be denied that the pathological presence of sugar in the urine may possibly depend in some cases upon a failure of the conditions under which the normal transformation of the sugar takes place. We are, however, in a great measure ignorant as to what these conditions are. A number of experiments make it probable that the sugar in the blood, under the influence of a ferment, is converted into lactic acid and glycerine, which undergo combustion, and so maintain the animal heat; and it is believed that, when this ferment is absent, the sugar is not decomposed, but is excreted in the urine. Whether this be the true explanation or not, many facts seem to show that diabetes may result from a morbid state of the

blood. Thus the introduction into the blood of ammonia, ether, chloroform, or phosphoric acid is followed by glycosuria ; while the introduction of carbonate of soda will prevent it. Prout long ago observed a saccharine condition of urine as not an uncommon result of gout ; and glycosuria has been repeatedly observed in cases of pneumonia, whooping-cough, and phthisis, which lead to deficient oxygenation of the blood.

c. It is not improbable that other wasting diseases are in their origin connected with some functional derangement of the liver. When there is derangement of the disintegrative functions of the liver, the blood and fluid effused from it become loaded with effete matter, as the result of which, the nutrition of the tissues is often impaired, and the body wastes. In *phthisis*, again, long before tubercle is deposited in the lungs, there is evidence of deficient assimilation of nutriment and imperfect sanguification—functions, in which we know that the liver is deeply concerned. Again, the protracted purulent discharge which usually precedes *waxy disease* may entail a hasty and imperfect sanguification, resulting in anæmia and the formation of an albuminous material little capable of organisation.

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## II. *Abnormal Elimination.*

In discussing the functions of the liver, I stated that bile is, in part, excrementitious, although this is probably far from being its chief use in the economy of digestion. In accordance with the belief, still held by many members of the profession engaged in practice, that the chief function of the liver is to excrete bile, the retention of bile in the blood and tissues is believed to give rise to serious symptoms. For example, when such symptoms as delirium, stupor, muscular tremors, subsultus, carphology, paralysis of the sphincters, coma, convulsions, a dry brown tongue, and other symptoms of the 'typhoid state' supervene in any case of jaundice, in acute atrophy of the liver, or in the advanced stage of cirrhosis, it is customary to attribute them to poisoning of the blood with retained bile. Experiments, also, have been performed on animals, with the object of showing that bile is a deadly poison. But that dogs should die, after injection into the cellular tissue of the bile of other dogs, admits of another explanation than that of the essential elements of bile being a poison. The injection of decomposing mucus would probably produce a like result. Pure bile, from which all

mucus has been removed, has been repeatedly injected into the large veins of dogs by Frerichs and other observers, without any cerebral symptoms or bad results ensuing, except that, in some instances, death has been caused by the entrance of air into the veins.<sup>1</sup> The operation has even been repeatedly performed on the same animal, without any lasting injury. But it is scarcely necessary to have recourse to experimental researches on the lower animals for evidence on the matter, and in all these experiments there are sources of fallacy. Every medical practitioner must be familiar with the fact, that the blood and tissues of man may be saturated with bile for months, without cerebral or any other symptoms of blood-poisoning resulting, so long as the glandular tissue of the liver is not destroyed, and the kidneys continue to perform their functions. Bearing such cases in mind, it is difficult to believe that bile is a deadly poison.

Reference has already been made to the views of an American physiologist, Dr. Austin Flint, Jun., who has written a work to show that the cerebral symptoms, which occasionally occur in jaundice and in structural diseases of the liver, are due to the retention in the blood of

<sup>1</sup> *Diseases of Liver*, Sydenham Society's translation, vol. i. p. 395.

cholesterin, or to what he has designated '*Cholestearæmia.*'<sup>1</sup> Dr. Flint regards cholesterin as an excrementitious product of nervous tissue, the elimination of which from the body he believes to be one of the functions of the liver. Having arrived in the bowel, the cholesterin, according to him, is converted into stercorin, and therefore it is not found in the fæces; but, when retained in the blood and tissues, he believes it to be a virulent poison like urea. But, if the non-excretion of all the elements of bile do not give rise to cerebral symptoms, it is difficult to understand how these symptoms can result from the retention of cholesterin alone. In cases, for instance, of permanent closure of the bile-duct, cholesterin is not discharged from the liver into the bowel; it does not accumulate in the biliary passages, nor, if it be present in the blood, does it necessarily give rise to cerebral symptoms.

From what has been stated, I think it must be clear that the cerebral symptoms, which occasionally supervene in certain morbid states of the liver, are independent of the non-excretion of bile, or of any of its component parts. The real cause of these cerebral symptoms will be referred to hereafter.

The symptoms usually associated with a deficient

<sup>1</sup> *Op. cit.*

excretion of bile are an irregular, usually costive, state of the bowels, the stools being insufficiently coloured with bile and of a pale yellow, drab, or whitish colour; loss of appetite; a white or yellowish furred tongue; a disagreeable, often bitter, taste in the mouth, especially in the morning; flatulence; a sallow or muddy tint of skin (indicating, unless there be concurrent hyperæmia of the liver, anæmia rather than jaundice); dingy conjunctivæ; languor and disinclination for exertion; frontal headache; dulness and heaviness, drowsiness after meals, great depression of spirits, and sometimes hypochondriasis; and frequent deposits of lithates in the urine on cooling. These symptoms are very apt to be induced, especially towards middle life, by sedentary or indolent habits, the habitual use of rich or indigestible food, neglect of the bowels, great or protracted anxiety of mind, or by a general want of vigour, consequent upon disease of the heart or of some other organ; and the tendency to them is in many cases inherited. They are commonly, and perhaps correctly, ascribed to what is called 'torpor of the liver;' but the non-excretion of bile may possibly be merely one of the symptoms, rather than the cause, of the morbid state, the real cause being the retention in the system, not of bile, but of those products of dis-

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integration, which it is the purpose of the kidneys to eliminate. At the same time, it is very probable that engorgement of the liver with bile interferes with the normal processes of disintegration of albumen which take place in the gland.



## LECTURE II.

III. *Abnormal Disintegration.* 1. *Lithæmia*; 2. *Gout*; 3. *Urinary Calculi*; 4. *Biliary Calculi*; 5. *Degenerations of the Kidneys*; 6. *Structural Diseases of the Liver*; 7. *Degenerations of Tissue throughout Body*; 8. *Local Inflammations*; 9. '*Constitutional Diseases.*'—IV. *Derangements of Organs of Digestion.* 1. *Tongue*; 2. *Appetite*; 3. *Taste*; 4. *Flatulence*; 5. *Constipation and Diarrhœa*; 6. *Vitiated Stools*; 7. *Intestinal Hæmorrhage*; 8. *Hæmorrhoids*; 9. *Hepatic Pain*; 10. *Jæundice, its pathology.*—V. *Derangements of the Nervous System.* 1. *Aching Pains in Limbs*; 2. *Pain in Shoulder*; 3. *Neuralgia*; 4. *Cramps*; 5. *Headache—megrin*; 6. *Vertigo*; 7. *Convulsions*; 8. *Paralysis*; 9. *Noises in Ears*; 10. *Sleeplessness*; 11. *Depression of Spirits*; 12. *Irritability*; 13. *The Typhoid State.*

MR. PRESIDENT, FELLOWS OF THE COLLEGE, AND GENTLEMEN,—In my first lecture I endeavoured to show that the secretion of bile was, perhaps, the least important of the functions of the liver; but that, in the first place, this organ contributed greatly to the processes of sanguification and of nutrition of the tissues; and, secondly, that it was probably the chief seat of the disintegration of albuminous matter; while even the secretion of bile,

although in part excrementitious, was mainly destined to assist the assimilation of the food. If these views were correct, I pointed out that the existing classification of the functional derangements of the liver, founded on the quantity or the quality of the bile in the stools, had become obsolete ; and I proposed to substitute another, founded on the more important functions of the liver, and on the derangements which the liver excites in other organs of the body. I then described some of the derangements of nutrition and elimination traceable to the liver ; and I now proceed to consider the more important disorders coming under the head of Abnormal Disintegration.

### III.—*Abnormal Disintegration.*

Modern investigations, pathological as well as physiological, go far to prove that one of the chief functional derangements of the liver, if it be not the foremost of all, is an imperfect disintegration of albuminous matter, or its non-conversion into a soluble product (urea), which can be readily excreted by the kidneys. A strong corroboration of the correctness of this view is furnished by the disease known as acute atrophy of the liver, to which I have already had occasion to refer. In this disease there

is a rapid destruction of the secreting tissue of the liver, and the result is a disappearance of urea from the urine, and the substitution for it of leucin ( $C^6 H^{13} NO^2$ ) and tyrosin ( $C^9 H^{11} NO^3$ ), products of the disintegration of albumen more complex and less oxydised than lithic acid ( $C^5 H^4 N^4 O^3$ ) and urea ( $CH^4 N^2 O$ ), and which are also found in abundance in the wasted tissue of the liver

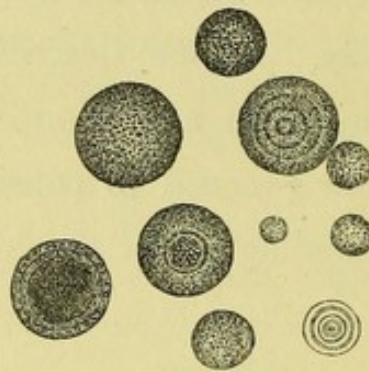


FIG. 4. Laminated crystalline masses of Leucin.

(Figs. 4, 5, and 6). The substitution of leucin and tyrosin for a portion of the urea of the urine takes place in other diseases of the liver, in which the destruction of the hepatic tissue is less rapid and less extensive than in acute atrophy, as, for example, in certain cases of cirrhosis and of obstruction of the common bile-duct. I have known it also to occur in certain febrile diseases, such as typhus and enteric fever, in which the hepatic tissue appears, in consequence of the increased work thrown

upon it, to undergo partial disintegration.<sup>1</sup> But these important changes in the urine, so far as we know, only occur in cases where there is structural change of the liver. The urine is liable to other changes indicating imperfect disintegration or oxydation of albuminous



FIG. 5. Needle-shaped crystals of Tyrosin, adhering in bundles and in stellate groups.

FIG. 6. Globular masses composed of acicular crystals of Tyrosin.

matter, which are much more common, and which are also the result of functional derangement of the liver, but which are not necessarily associated with structural disease of that organ. The most common of these

<sup>1</sup> See Murchison, *On the Continued Fevers of Great Britain*, 2nd edition 1873, pp. 157, 210, 255, 533, 629.

changes in the urine are deposits on cooling of lithic acid, lithates, and pigmentary matters ; but there are probably others, less frequent and as yet but little studied, such as the presence of xanthin, cystin, kreatinin, etc. I need not remind an audience such as that which I have the honour to address, that deposits in the urine of lithic acid or lithates are not due to any morbid condition of the kidneys. What I wish to insist upon is, that the frequent occurrence of these deposits in the urine ought always to be regarded as a sign of functional derangement of the liver, arising from causes, sometimes temporary, at other times more or less permanent. Excluding those cases in which deposits of lithic acid or lithates are thrown down in the urine not until twelve or twenty hours after its emission, as the result of spontaneous changes, to which Scherer has given the name of acid urinary fermentation,<sup>1</sup> and those which are due to a marked deficiency of urinary water, deposits of lithic acid, lithates, and abnormal pigments, which appear in the urine as soon as it cools, are chiefly met with under the following conditions :—

1. In febrile diseases, in which we know that the

<sup>1</sup> *Ann. d. Chemie und Pharm.*, Bd. 42, s. 171. Dr. Bence Jones's experiments throw doubts upon the occurrence of the acid fermentation in the urine described by Scherer.—*Lect. on Path. and Therap.*, 1867, p. 216.

liver becomes enlarged and congested, and its gland-cells loaded with minute granules, and in which there always is an increased disintegration of albuminous matter. Everyone, for example, is familiar with the copious deposits of lithates which are so common during an attack of ordinary febrile catarrh.

2. In many structural diseases of the liver, and particularly in those which are characterised by an increased amount of blood in the organ, such as inflammation, cirrhosis, cancer, and simple hyperæmia, whether mechanical or active.

3. In functional derangements of the liver, either temporary or persistent.

To this third cause of an excess of lithic acid in the urine I wish now to restrict my remarks. What I desire to maintain is, that lithuria, like glycosuria, is very often due to a functional disease of the liver, although even glycosuria is still ranged in some text-books with albuminuria and diseases of the kidneys. In other words, abnormal disintegration of albuminous matter in the liver may lead to a morbid condition of the blood and of the entire system, which often manifests itself in lithuria. This morbid state of the blood I propose to designate *Lithæmia*.<sup>1</sup>

<sup>1</sup> It has been pointed out to me that Dr. Austin Flint has pro-

1. *Lithæmia*.—When oxydation is imperfectly performed in the liver, there is a production of insoluble lithic acid and lithates, instead of urea, which is the soluble product resulting from the last stage of oxydation of nitrogenous matter. Persons who habitually enjoy the best of health are liable to deposits of lithates in the urine after a surfeit of food, or even after partaking moderately of one of the fashionable dinners of the age. Under these circumstances, an excess of work is thrown upon the liver and the other glandular organs, and one result is that a quantity of albumen, instead of being converted into urea, is discharged by the kidneys in the less oxydised form of lithic acid or its salts. But what in most persons is an occasional result of an extraordinary cause is in some almost a daily occurrence, either from the food being always excessive in amount or unduly stimulating, or from some innate defect of power, often hereditary, in the liver, in virtue of which its healthy functions are liable to be deranged by the most ordinary articles of diet. Most persons appear to have more liver, just as they have more lung, than is absolutely necessary

posed the term 'uricæmia' to designate the excess of uric acid in gout and in cases of lead-poisoning (*Principles and Practice of Medicine*, 3rd edition, Philadelphia, 1868, p. 86). The term which I have employed appears to me to be preferable.

for the due performance of its functions. But in others, not unfrequently the offspring of gouty parents, the organ in its natural condition seems only just capable of performing its healthy functions under the most favourable circumstances, and functional derangement is at once induced by articles of diet which most persons digest with facility. This functional derangement may manifest itself by various symptoms of 'indigestion,' by disturbances of circulation and of other physiological systems, but especially by deposits of lithic acid, lithates, and pigments in the urine. These deposits, it is true, are often absent, and yet the urine may contain a great excess of lithic acid. Indeed, as Dr. Bence Jones<sup>1</sup> has shown, clear urine sometimes contains more lithic acid than that which thickens on cooling. But the frequent deposit of lithates shows that oxydation is less perfect than it ought to be. Very often, however, these urinary deposits exist for years, without the patient experiencing any general or local discomfort. But sooner or later, often about middle life, lithic acid and lithates are formed in such excess that they cannot be eliminated by the ordinary channels, and they accumulate and create disturbance in different parts of the organism, and then the urinary deposits begin to

<sup>1</sup> *Philosophical Transactions*, 1849, part ii. p. 249.



attract more attention than they had previously done, from their being accompanied by symptoms of indigestion, or from the evidence of some serious local mischief, the onset of which had been insidious. These symptoms are all the more likely to occur if the patient is what is commonly known as 'a generous liver,' if he take little exercise in the open air, or if he have much mental work. Of the symptoms referred to, the most common are the following :—

*a.* A feeling of weight and fulness at the epigastrium and in the region of the liver.

*b.* Flatulent distension of the stomach and bowels.

*c.* Heartburn and acid eructations.

*d.* A feeling of oppression and often of weariness and aching pains in the limbs, or of insurmountable sleepiness after meals.

*e.* A furred tongue, which is often large and indented at the edges, and a clammy, bitter, or metallic taste in the mouth, especially in the morning.

*f.* Appetite often good; at other times anorexia and nausea.

*g.* An excessive secretion of viscid mucus in the fauces and at the back of the nose.

*h.* Constipation, the motions being scybalous, sometimes too dark, at others too light, or even clay-coloured.

Occasionally attacks of diarrhoea alternating with constipation, especially if the patient be intemperate in the use of alcohol.

*i.* In some patients, attacks of palpitation of the heart, or irregularity or intermission of the pulse.

*k.* In many patients, occasional attacks of frontal headache.

*l.* In many patients, restlessness at night and bad dreams.

*m.* In some patients, attacks of vertigo or dimness of sight, often induced by particular articles of diet.

All these symptoms are liable to occasional aggravation from errors in diet. Gradually the patient is taught by experience to become more careful as to what he eats or drinks. One thing after another he is compelled to give up. First, he renounces malt liquors; then he discovers that Port-wine, Madeira, Champagne, and Burgundy disagree, and he betakes himself for a time to 'dry Sherry;' but at length this does not suit, and after an interval, during which a trial is made of Claret or Hock, the patient, probably under medical advice, finds temporary relief from the substitution for wines of brandy or whisky largely diluted with water. At last, unless he be misled by the fashionable, but to my mind erroneous, doctrine of the present day, that alcohol in one form or another is neces-

sary for digestion or to enable a man to get through his mental or bodily work, he finds that he enjoys best health when he abstains altogether from wine and spirits and drinks plain water. The patient goes through a like experience with regard to solid food; one dish after another, very often what he likes best, has to be given up, until at length, if he be well advised and have the sense to follow the advice, he restricts himself to the plainest food in moderate quantity. As a rule, those articles of diet are most apt to disagree which contain much saccharine or oleaginous matter, and not, as might perhaps have been expected, nitrogenous food, if plainly cooked. In most of these cases the digestion appears to be strongest in the morning, and the patient suffers from late dinners or suppers.

The picture which I have thus imperfectly drawn represents a morbid condition extremely common in this country, which is associated with a constant tendency to the deposit of lithic acid or lithates in the urine, and which, for the reasons already given, I believe to originate in functional derangement of the liver.

2. *Gout.* But, secondly, you cannot fail to recognise that this picture represents a train of symptoms very common in gouty people, and to which the terms 'gouty dyspepsia,' 'latent gout,' 'suppressed,' 'anomalous,' or

'irregular gout' have been applied ; although what I desire to maintain is, that they are also very common in persons, who neither inherit articular gout nor ever have it themselves. Gout itself, however, is merely one of the results of lithæmia. Thanks to the researches of our colleague Dr. Garrod, we now know that gouty inflammation of a joint is due to various exciting causes, which it is needless here to enumerate, determining a local deposit of lithate of soda, which has previously existed in abnormal quantity in the blood, as well as in the fluid that exudes from it into all the textures of the body. The accumulation of this substance in the blood will, no doubt, be favoured by non-elimination consequent upon disease of the kidneys ; but in most cases of gout the kidneys are in the first instance healthy, and the presence in the blood or tissues of lithic acid or its salts is the result of imperfect digestion, or more strictly of functional derangement of the liver. Articular gout is, so to speak, a local accident, which may occur at any time in persons in whom the normal process by which albuminous matter becomes disintegrated in the liver into urea, is persistently deranged. In other words, gout, like diabetes, is the result of a functional derangement of the liver ; and just as we found that in many persons in whom there is no evidence of articular gout, an innate defective power of

the liver, in virtue of which its functions are deranged with unusual facility, is often transmitted by parents to their offspring, so gout, which is one of the consequences of that condition, comes to be an hereditary disease. I hold, therefore, that what is called a 'gouty diathesis' always indicates, and is the result of, hepatic derangement, and that many symptoms commonly referred to gout would be more correctly ascribed to disorder of the liver.

3. *Urinary Calculi* are another consequence of lithæmia, and therefore of functional derangement of the liver. Of the concretions which form in the urinary passages the great majority consist, in the first instance, at all events, of lithic acid or its salts. According to Dr. William Roberts, lithic acid constitutes five-sixths of all renal concretions, and of vesical calculi which have only recently descended from the kidney.<sup>1</sup> The circumstances favourable to the precipitation of lithic acid are, catarrhal and other morbid states of the urinary passages and an acid condition of the urine, but mainly an excessive elimination by the kidneys of free lithic acid, which had previously existed (either free or combined) in excess in the blood, and which we have seen to be formed mainly, at

<sup>1</sup> *Urinary and Renal Diseases*, 2nd edition, 1872, p. 270.

all events, in the liver. There are also good reasons for believing that renal calculi composed of other substances than lithic acid have an hepatic origin. Cystin ( $C^3 H^7 NSO^2$ ), for example, which represents a different process of oxydation from that which produces lithic acid, closely resembles taurin, and, like it, contains a large proportion of sulphur;<sup>1</sup> and, moreover, it has been found by Scherer in the livers of patients suffering from enteric fever.<sup>2</sup> It would seem, therefore, that those rare renal calculi which are composed of cystin are due in the first instance to some functional derangement of the liver. Xanthin ( $C^5 H^4 N^4 O^2$ ), again, of which a few renal calculi, chiefly in young people, are composed, also appears to arise from imperfect oxydation of the products of albuminous matter. It differs from lithic acid only in containing one atom less of oxygen; so that it also is probably formed in the liver, in which organ it has been found by Scherer, as well as in the blood, spleen, and muscles.<sup>3</sup> Even oxalate of lime, which Dr. Bence Jones found, either alone or combined with other substances, in 163 out of 450 urinary calculi,<sup>4</sup> may in some way be connected with functional derangement of the liver, although the evidence on this point is

<sup>1</sup> Roberts, *op. cit.*, 2nd edition, 1872, p. 84.

<sup>2</sup> *Archiv. f. Path. Anat.*, Bd. x. p. 228.

<sup>3</sup> Roberts, *op. cit.*, p. 88.

<sup>4</sup> *Lectures on Pathology and Therapeutics*, 1867, p. 99.

less clear than in the case of other urinary concretions. I do not forget that it was maintained by so eminent an authority as our colleague Dr. Owen Rees, in the Croonian Lectures delivered before this College in 1856, that oxalic acid is never excreted from the blood, but is always formed in the urine after its secretion by decomposition of lithic acid; and that this opinion has more recently been advocated by another eminent Fellow of this College, Dr. Basham.<sup>1</sup> Facts, however, are now known which point strongly to an opposite conclusion. For example, oxalic acid and its compounds, when introduced into the stomach, will appear as oxalate of lime in the urine; while in one case, at least, oxalic acid has been found in the blood by Dr. Garrod.<sup>2</sup> It has also been found in saliva, in perspiration, and in mucus. The researches also of Beneke<sup>3</sup> make it probable that the chief, if not sole, source of oxalic acid is impeded metamorphosis of the nitrogenous constituents of the blood and food; while, from its composition ( $C^2 H^2 O^4$ ), it appears to be one of the penultimate stages in the oxydation of the more complex organic substances into carbonic acid and water. What part of the system is in these cases mainly at fault

<sup>1</sup> *Renal Diseases*, 1870, p. 187.

<sup>2</sup> *Medico-Chirurgical Transactions*, 1848.

<sup>3</sup> *Zur Entwicklungsgeschichte d. Oxaluria*, F. W. Beneke, 1852.

is not very clear, although we are quite certain that the liver contributes greatly to the disintegration of albuminous matter ; and it seems not improbable that, when an excess of lithic acid is formed in the liver, a portion of it may be subsequently converted into oxalic acid. Wöhler has succeeded in obtaining oxalic acid from lithic acid out of the body ; while Schunck <sup>1</sup> and other chemists distinctly state that, within the body, oxalic acid is formed by the oxydation of lithic acid. When lithic acid is imperfectly oxydised it is believed to break up into oxalic acid and urea. It may be added, that oxalate of lime usually coexists or alternates with lithic acid or its salts, both in the urine and in urinary calculi, and that the condition of oxaluria, as was long ago pointed out by Dr. Prout,<sup>2</sup> is often associated with symptoms similar to those which are common in lithæmia, such as irregularity of the heart's action, intermission of the pulse, palpitation, flatulence, and hypochondriasis. But whether the liver be concerned in the production of oxaluria or not, there can be no doubt that it is the organ fundamentally at fault in the great majority of cases of urinary calculi ; and that it is to it, and not to the kidneys, that we must mainly look for their prevention and treatment. This pathological inference is

<sup>1</sup> *Proceedings of the Royal Society*, No. 95.

<sup>2</sup> *Stomach and Renal Diseases*, p. 62.



confirmed by clinical experience. One of the greatest modern authorities on urinary calculi states, as the result of his observation, that patients with calculous disease are only temporarily benefited by the alkaline waters of Vichy and Vals, which dilute the urine and render it alkaline, but do not cure the disease ; whereas more permanent results are obtained by the use of the waters of Friederichshall, Carlsbad, and Püllna, which produce activity in all the digestive organs, and eliminate by other channels the waste matters previously thrown out as lithic acid by the kidneys, but which mainly act by relieving the overloaded liver and restoring its normal functions.

4. *Biliary Calculi*, which consist for the most part of cholesterin and bile-pigment, are another result of functional derangement of the liver. They are chiefly met with in persons of middle or advanced life who have led sedentary lives, and they are particularly common in those who have lived too well and eaten much saccharine food, and who are the subjects of lithæmia. It may be difficult to explain how the functional derangement of the liver which results in lithæmia should also lead to the formation of concretions composed of cholesterin and bile-pigment in the biliary passages ; but the frequent concurrence of the lithic acid dyscrasia with gall-stones is a clinical fact which I have had many opportunities of

verifying. This observation accounts for the frequent occurrence of biliary calculi in gouty people, and it also explains the frequent coincidence in the same individual of gall-stones and urinary calculi. I cannot agree with Frerichs in regarding this coincidence as purely accidental.<sup>1</sup> Many years ago, Morgagni insisted on the frequent coexistence of urinary and biliary calculi. The late Dr. Prout also remarked that the formation of gall-stones of cholesterin was frequently associated with a tendency to lithic acid deposits in the urine; and Dr. George Budd, in his classical work on *Diseases of the Liver*, states that 'the habit of drinking porter, which frequently leads to lithic acid deposits and to the most inveterate forms of gout in persons who inherit no disposition to them, may also frequently lead to the formation of gall-stones.'<sup>2</sup> Lastly, the intimate relation between urinary calculi, biliary calculi, and gout was in accordance with the great clinical experience of the late Professor Trousseau.<sup>3</sup> In connection with these remarks, it may be worth adding that, in a few instances, lithic acid has been found in biliary concretions.<sup>4</sup>

<sup>1</sup> *Klinik der Leberkrank.*, Sydenham Society's translation, vol. ii. p. 511.

<sup>2</sup> 3rd edition, p. 369.

<sup>3</sup> *Clinical Lectures*, Sydenham Society's edition, vol. iv. p. 231.

<sup>4</sup> Frerichs, *op. cit.*, vol. ii. p. 497.

5. *Degenerations of the Kidneys.*—From what has been already stated, it is clear that the kidneys and the liver are intimately connected in their functions, the main object of the kidneys being to eliminate certain products which are in great part secreted in the liver. Derangements of one organ are, therefore, very likely to lead to disorder of the other. In the first place, my experience has led me to regard lithæmia as one of the chief causes of ‘acute Bright’s disease’ or acute nephritis. Most cases of this disorder are traceable either to scarlatina or to a chill. In patients under twenty years of age few cases cannot be traced to scarlatina. In adults, when the attack follows a chill, and there has been no antecedent attack of scarlatina, it will almost invariably be found that the patients have previously suffered from derangements of the liver with lithæmia, while many have led intemperate lives. Again, we find that functional derangement of the liver resulting in lithæmia, with dyspeptic symptoms such as those which I have described, is a common cause of the contracted, granular, or gouty kidney. Our colleague Dr. George Johnson, one of the greatest living authorities on diseases of the kidneys, thus writes respecting the causes of this form of Bright’s disease :—‘It is often associated with the gouty diathesis, as one of its synonyms indicates ; and it is of common occurrence in

persons who eat and drink to excess, or who, not being intemperate in food or drink, suffer from certain forms of dyspepsia, without the complication of gouty paroxysms.' And further on, in the lecture from which I have just quoted, he observes:—'Dyspepsia is frequently associated with this form of disease, sometimes as a cause, sometimes as a consequence. You may often learn that a patient of strictly temperate habits has for months or years suffered from pain or uneasiness after food, flatulent distension of the stomach and bowels, habitual looseness or irregularity of the bowels, constipation and diarrhoea alternately. With this, there is often turbidity of the urine, which is high-coloured, excessively acid, and deposits urates abundantly. After a time, the urine, which had been scanty, becomes more copious, of pale colour, of low specific gravity, and is found to contain albumen and granular casts. In such a case probably *renal degeneration is a consequence of the long-continued elimination of products of faulty digestion through the kidneys*. I have seen this sequence of events so frequently, that I have no doubt as to their causative relationship. Dyspeptic symptoms, such as I have described, and consequent renal degeneration, are in some cases excited or greatly aggravated by habitual excess of alcohol.'<sup>1</sup>

<sup>1</sup> *British Medical Journal*, 1873, vol. i. pp. 161, 191.

Numerous cases which have come under my own observation, and which I have carefully watched, have satisfied me as to the strict accuracy of Dr. Johnson's description; but the dyspepsia which so commonly precedes the first symptoms of contracted kidney is that which I have already described as accompanying persistent lithæmia, and as consisting in derangement, not so much of the gastro-intestinal digestion, as of the disintegrative processes which go on in the liver.

Chronic degeneration of the kidneys with albuminuria is sometimes also a sequel of diabetes, the kidneys becoming diseased from the constant irritation of the saccharine urine. This is another way in which functional derangement of the liver may lead to structural disease of the kidneys.

6. *Structural Diseases of the Liver.*—It is highly probable that derangement of the disintegrative processes going on in the liver may lead to structural changes in the liver as well as in the kidneys. In the first place, fatty degeneration of the liver is well known to be a common lesion in persons who are large feeders or drink much alcohol and lead indolent lives, and in whose urine there are often copious deposits of lithates.<sup>1</sup> Under

<sup>1</sup> Fatty liver is also very common in a very different condition of the system, viz. in wasting diseases, such as phthisis and chronic dysentery. It is supposed that the blood in these cases becomes

these circumstances, the change in the liver is sometimes associated with a similar change in the structure of the heart or kidneys, or with general corpulence. Again, in a large proportion of the cases of catarrhal jaundice, occurring towards middle or in advanced life, the patients have either previously suffered from actual gout, or they have been the subjects of lithæmia, with some of the symptoms of dyspepsia already described as accompanying it. Thirdly, although cirrhosis is most commonly the result of the direct irritation of the liver by alcohol, there are certain cases in which it cannot be traced to such a source, but in which its symptoms have been preceded for years by the lithic acid dyscrasia and dyspepsia. Cases of this sort have come under my own notice, and have been described by Baglivi, Stoll, Scudamore, and Trousseau as a 'chronic gouty hepatitis.'<sup>1</sup> Lastly, if we carefully investigate the antecedent medical history of patients suffering from primary cancer of the liver, we often find that for many years they have been 'bilious,' or they have been liable to dyspeptic symptoms attended by copious deposits of lithic acid or lithates in the urine, charged with the oily matter which is rapidly absorbed from the patient's tissues, and that a portion of this becomes arrested in the liver.

<sup>1</sup> C. Scudamore, *Nature and Cure of Gout*, 4th edition, 1823, p. 43; Trousseau, *op. cit.*, vol. iv. p. 381.

either habitually or from the slightest error in diet. That protracted derangement of cell-function should ultimately lead to abnormal cell-formation, in persons predisposed to cancer, does not appear to be an unwarrantable assumption.

7. *Degeneration of Tissue throughout the Body.*—With the approach of old age, there is a tendency of the tissues throughout the body to undergo degeneration and decay, fatty, and sometimes calcareous matter, being substituted for the normal structures. More than twenty years ago, it was pointed out by Mr. Barlow,<sup>1</sup> that the ‘climacteric disease,’ described by a former President of this college, Sir Henry Hallford, and the ‘Decline of the Vital Powers in Old Age,’ described by Dr. Marshall Hall, were in great measure due to these degenerations, and the fact is now generally acknowledged. In no organs are these degenerations more marked, or the cause of greater danger to life, than in the heart and in the coats of the arteries, the degenerations of which lie at the foundation of apoplexy, paralysis, aortic incompetence, and other maladies of advanced life. The explanation of these degenerations of tissue is to be found in derangements of the nutritive and disintegrative processes in which the

<sup>1</sup> ‘General Observations on Fatty Degeneration,’ *Medical Times and Gazette*, May 15, 1852.

liver plays so important a part; and in many instances, I do not say in all, it is the liver which appears to be primarily at fault. The nutrition of the tissues becomes impaired, partly perhaps in consequence of the supply of faulty nutritive material, but mainly from the functional activity of the liver becoming weakened with advancing age, as the result of which the blood and juices of the body are impregnated with a quantity of disintegrated albuminous matter, not sufficiently oxydised to be eliminated by the kidneys. But what, in many persons, is merely a form of senile decay, may, under certain conditions, occur at a comparatively early period of life. Many observations have satisfied me that persons who habitually consume a large quantity of rich and stimulating food and of alcoholic drinks, who take little exercise, and whose urine is constantly loaded with an excess of lithic acid and lithates, are particularly prone to fatty degeneration. Andral and Lobstein long ago connected atheroma of the vessels with 'a particular taint of the fluids closely resembling gout,'<sup>1</sup> and it has been a common observation by physicians practising at spas resorted to by gouty patients, and borne out by my own experience, that atheroma of the arteries at an unusually early period

<sup>1</sup> C. E. Hasse, *Diseases of the Organs of Circulation and Respiration*, Sydenham Society's translation, 1846, p. 82.



of life, and diseases of the aortic valves which are not congenital and are independent of injury or rheumatism, are met with far oftener in persons who are the subjects of the lithic acid dyscrasia, or who have had gout, than in those who have no such tendencies.

8. *Local Inflammations.*—Lithæmia predisposes to local inflammations. Persons in good health, not apparently so, but in the strictest sense, are little liable to local inflammations. For example, when a given number of persons are exposed in common to an exciting cause of pneumonia, comparatively few are attacked with that disease; and, when the previous history of those attacked is investigated, it is usually found that, prior to the acute attack, they have been in an abnormal state of health. This was a point much insisted on by our late colleague Dr. Todd. In one of his remarkable clinical lectures, he writes as follows:—‘Simple pneumonia is very rare in another sense also, that is, in its freedom from complication with, or dependence on, some peculiarity of constitution. To make this clearer to you, let me take an illustration. If two men, A and B, both in good health, be exposed to some noxious influence—cold, for example—at the same time, and for the same period, A will get a severe attack of pneumonia and B will not. Now, at first sight, one can scarcely conceive

why the pneumonia should attack the one and not the other, for they were both apparently equally well at the time of exposure to cold ; but, if we carefully examine into the previous history of these individuals, we shall find that A is of a gouty or strumous constitution, or has some peculiarity of diathesis which B does not possess, and it is by reason of this that A is seized with pneumonia when subjected to the noxious influence which produces no such injurious effect upon B.'<sup>1</sup> One of the conditions predisposing to local inflammations is gout ; but the dyscrasia which I have designated lithæmia, and of which gout itself is only one of the local manifestations, acts in the same way. Having paid considerable attention to the matter, I am satisfied that persons with the lithic acid dyscrasia are much more prone than others to ordinary febrile colds, as well as to more severe local inflammations. They may appear robust and healthy up to the sudden occurrence of the inflammatory attack, but they have not really been in a normal state of health. I have also had occasion to observe that in certain persons who habitually pass an excess of lithates in the urine the lithates cease to be eliminated on the advent of a local inflammation or of an ordinary febrile catarrh, to be again dis-

<sup>1</sup> *Clinical Lectures on Acute Diseases*, 1860, p. 367.

charged in abundance on the subsidence of the pyrexia. In such cases the retention of lithates in the system has probably determined the local inflammation.

9. *Constitutional Diseases.*—When blood-poisons are taken into the system from without, the liver is one of the organs which first and mainly suffers ; but I trust that I have also made it clear that morbid states of the blood, or constitutional diseases, such as gout and diabetes, may be generated in the liver from derangements of the processes of disintegration and nutrition which normally take place in that organ. It is very probable, however, that other morbid states of the blood and constitutional diseases have their origin in the liver. In acute atrophy of the liver, the liver appears to be the starting-point of the pathological process, but all the subsequent phenomena show that the malady is essentially a blood-disease. In certain cases of erysipelas and pyæmia, I have long taught, in my lectures on medicine, that the *materies morbi* is engendered in the body ; and I think it might be shown that, as in acute atrophy, the liver is the organ at first mainly in fault.

Again, it is not improbable that the large quantity of fibrin found in the blood in acute rheumatism may result from fibrin not being destroyed in the liver to the proper extent. We know, also, that in certain states of the

body, as after surgical operations, childbirth, and acute febrile diseases, the blood is very prone to coagulate in the large vessels; and that, when these coagula form in the right side of the heart, sudden death may result. Our colleague Dr. Fayrer has shown that these phenomena are much more common in India than in this country;<sup>1</sup> and, since the commencement of these lectures, he has written to me to suggest that this may be due to the greater tendency to hepatic derangements in tropical countries.

On the other hand, the deficiency of red blood-corpuscles in anæmia, chlorosis, scrofula, and some other maladies, is also probably traceable, in the first instance, to functional derangement of the liver. There can be no doubt that patients with protracted functional derangement of the liver are often very anæmic. They present a pale, pasty appearance, and bear losses of blood or acute diseases badly. Many years ago, Messrs. Todd and Bowman observed that persons suffering from functional derangement of the liver are often pale, as if from loss of blood, although no such loss has been experienced; their nutrition is enfeebled, digestion impaired, and there is slight yellowness of the complexion, as in cases of

<sup>1</sup> *Clinical and Pathological Observations in India, 1873.*

hepatic disease, and yet after death no lesion is discernible, except perhaps slight enlargement of the liver.<sup>1</sup> In these cases, iron may disagree until the liver has been restored to its normal functions.

Indeed, it seems not improbable that most so-called constitutional diseases are due in the first instance to some defective action of the liver. The child of a gouty father is not born with the *materies morbi* or poison of gout either in his blood or in his tissues ; but he is born with a morbid tendency in his liver to produce that poison. The same may perhaps be said of cancer and of tubercle. Both are unquestionably, like gout, constitutional and hereditary diseases ; but the child of a cancerous parent is not born with the *materies morbi* of cancer in his blood or tissues, but only with a tendency to a certain form of abnormal nutrition, which results in a cancerous growth. This morbid tendency, resident at first, no doubt, in the entire ovum, is in the adult probably located in the blood-forming and blood-depurating organs, among which the liver holds the most important place. It is no argument against this view that the liver is not the part of the body most often affected with primary cancer, for neither is it the usual seat of the local explosions of gout.

<sup>1</sup> Todd and Bowman, *Physiology of Man*, 1856, vol. ii. p. 264.

The facts and arguments which I have now brought under your notice have led me to the conclusion that functional derangement of the liver, by interfering with the normal disintegration of albuminous matter, and by the production of peccant substances which are not readily eliminated, and which, therefore, accumulate in the system, may, in the long run, lead to many of the most serious maladies—both acute and chronic—to which our race is subject. I shall now proceed to consider certain symptoms, indicating derangement of the different physiological systems, but not constituting distinct diseases, which appear also to result from functional disorder of the liver.

#### IV.—*Derangements of the Organs of Digestion.*

1. *The Tongue.*—It is well to remember that there may be considerable functional derangement of the liver and yet the tongue may be perfectly clean and normal, or at most only slightly coated in the morning ; but in many cases, and particularly if the derangement be of old standing, the tongue presents the appearances commonly described as characteristic of ‘atonic dyspepsia.’ It is large, pale, and flabby, and indented by the teeth at the edge of the anterior third, while its surface is white, and

the papillæ often elongated, so as to produce a pilous appearance. If the liver be somewhat congested, with these appearances we may often observe the fungiform papillæ on the tip and edges larger and redder than natural. In other cases, and especially when there is at the same time more or less gastric catarrh, the whole surface of the tongue is uniformly covered with a thick fur, sometimes whitish, but occasionally of a yellowish or brownish tint.

2. *The Appetite* may be excellent, although there is great functional derangement of the liver with lithæmia, so that the patient is often tempted to eat what he knows from experience to disagree with him. But when the flow of bile into the bowel is deficient, the appetite is often bad, and there may be a loathing of fat and of greasy articles of diet. In cases, which are not uncommon, where there is much functional derangement of the liver in conjunction with hepatic congestion and chronic gastric catarrh, there may be a loathing of all food excepting alcoholic stimulants, which increase the existing mischief, but which, as I have already stated, may lead to the accumulation of large quantities of fat.

3. *A Bitter Taste* is not unfrequently complained of by persons who are the subjects of jaundice; but the symptom is not due to the presence in the blood of bile-

pigment, which is tasteless, but may be owing to its containing taurocholic acid, which is intensely bitter, or some abnormal product of disintegrated albumen. This may explain why many patients suffering from functional derangement of the liver, but who have not a trace of jaundice, often complain of a bitter, or sometimes a 'coppery,' taste in the mouth, especially in the morning.

4. *Flatulence* is a common symptom of functional derangement of the liver. It is one of the most frequent results of a deficient flow of bile into the bowel, and when the bile-duct is completely obstructed, it is rarely absent. It is also a common symptom in lithæmia, where there is often also a deficiency of bile in the bowel, and in all cases where the circulation through the liver is torpid. In all these cases, in consequence of a deficiency in the bowels of bile, which, as we have seen, is endowed with antiseptic properties, the intestinal contents undergo fermentation and gas is generated, which accumulates in the bowels, the distension being usually greatest from one to three hours after a meal.

5. *Constipation or Diarrhœa*.—In a large number of cases of functional derangement of the liver with lithæmia, the bowels are more or less constipated; there is, probably, a deficiency in the quantity of bile which passes down the bowel, and, therefore, a want of the normal



stimulus to peristaltic action. The motions are either unusually pale, or, from long detention in the bowel and the action upon them of the intestinal juices, they become black and lumpy. The latter condition is often associated with much depression of spirits, and hence the 'melancholia' of early writers on medicine.

But functional derangements of the liver may be attended by the opposite condition of diarrhoea, or constipation and diarrhoea may alternate. It is generally assumed that this diarrhoea is due to an increased secretion and discharge of bile; and, in fact, 'an excessive secretion of bile,' showing itself in 'copious, fluid, alvine evacuations, highly coloured with bile, often preceded by griping, by nausea, and sometimes by vomiting,' is one of the three functional derangements of the liver described by Dr. Copland<sup>1</sup> and other practical writers. Dr. Copland admitted that 'excessive biliary secretion is more frequently inferred from circumstances than proved by unequivocal evidence;' and, for my own part, without denying the possibility of the biliary secretion being sometimes excessive in quantity and unusually irritating, so as to excite diarrhoea, my experience has induced me to adopt a different explanation for most, at all events, of the cases of so-called 'excessive secretion of bile.' In

<sup>1</sup> *Medical Dictionary*, ii. 725.

most of these cases there is evidence of more or less congestion of the liver ; the circulation through the liver is impeded, and there is a general stagnation of blood in the coats of the stomach and bowels. This mechanical stagnation is very likely to become converted into an active congestion or a catarrhal inflammation under the stimulus of irritating ingesta, so that even a small quantity of such a stimulus as alcohol may excite diarrhoea and vomiting. In many of these cases of 'bilious diarrhoea' the stools contain much mucus as well as bile. From what has been stated in my first lecture, it is clear that the large quantity of bile discharged from the bowel in these cases is no certain sign of an increased secretion by the liver, but may be due to a diminished absorption, consequent on irritation of the mucous surface.

6. *Vitiated Stools*.—A 'vitiated biliary secretion' is one of the three functional derangements of the liver described by systematic writers. Although there can be no doubt that the appearances of the bile in the gall-bladder after death are subject to great variations, too much importance has, perhaps, been attached to the characters of the stools during life as an index of the state of the liver. It must be remembered that variations in the characters of the stools may be the result of functional derangements or structural disease of the long tract

of bowel between the entrance of the bile-duct and the anus, and may likewise depend on the rapidity or slowness with which this tract is traversed by the fæces. Bearing in mind these sources of fallacy, it may be said that when little bile is poured into the bowel, the stools are pale and unusually offensive, unless they be long delayed in the bowel, in which case they may be dark and lumpy; but when there is an excessive secretion or diminished absorption of bile, the motions are relaxed and liquid, and contain a much larger quantity of bile than in the normal state.

7. *Intestinal Hæmorrhage*.—Copious hæmorrhage from the bowels is well known to be an occasional result of cirrhosis and of other structural diseases of the liver which obstruct the portal circulation. I have frequently met with it, however, where there has been obvious derangement of the liver, but no reason to suspect structural disease. The patients have, for the most part, been beyond middle age; but I have known the attacks occur repeatedly in the same person at intervals of many years. The attack is usually preceded by a feeling of oppression and heaviness, or by creeping sensations and more rarely severe neuralgic pains suggesting gall-stones about the liver, by pain in the right shoulder, loss of appetite, nausea, and furred tongue. Great relief is usually

afforded by calomel or blue pill, with saline aperients. In the intervals of the attacks the patients may enjoy good health, except that they have to be careful as to diet. Not unfrequently they present the symptoms of the lithic acid dyscrasia, or they are subject to attacks of gout.

8. *Hæmorrhoids*.—In a large proportion of persons who suffer from hæmorrhoids the primary cause is in the liver. Hæmorrhoids are a common result of structural changes in the liver, such as cirrhosis; but they are also a frequent attendant of functional derangements, and especially of the loaded state of the liver so common in lithæmia.

9. *Hepatic Pain*.—With the exception just referred to, severe pain in the liver is not a common symptom of purely functional derangement of the organ. It may even be absent when there is advanced structural disease, unless there be inflammation of the peritoneal investment, or pressure upon a nerve by some morbid growth. But in cases of protracted lithæmia, a sensation of weight, fulness, or tightness in the hepatic region is not uncommon; and when the bowels are neglected, or the patient continues to eat rich food and drink alcoholic stimulants, the liver is apt to become enlarged and congested, and then it may be the seat of actual pain, which is

usually increased after meals, or by lying on the left side.

10. *Faundice*.—In considering whether jaundice may result from functional derangement of the liver, it will be necessary to enter somewhat in detail into its pathology. All cases of jaundice may be referred to one of two classes, viz. :—

I. Cases in which there is a mechanical impediment to the flow of bile into the duodenum, and where the bile is in consequence retained in the biliary passages, and thence absorbed into the blood.

II. Cases in which there is no impediment to the escape from the liver into the bowel.

The several causes of jaundice belonging to each of these classes are given in the annexed Table :—

#### TABULAR VIEW OF THE CAUSES OF JAUNDICE.<sup>1</sup>

##### A.—JAUNDICE FROM MECHANICAL OBSTRUCTION OF THE BILE-DUCT.

###### I. *Obstruction by Foreign Bodies within the Duct.*

1. Gall-stones and inspissated bile.
2. Hydatids and distomata.
3. Foreign bodies from the intestines.

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<sup>1</sup> For some account of the distinctive characters of the different forms of jaundice according to its cause, see my *Clinical Lectures on Diseases of the Liver*, Messrs. Longmans & Co., 1868.

II. *Obstruction by Inflammatory Tumefaction of the Duodenum, or of the Lining Membrane of the Duct, with exudation into its interior.*

III. *Obstruction by Stricture or Obliteration of the Duct.*

1. Congenital deficiency of the duct.
2. Stricture from perihepatitis.
3. Closure of orifice of duct in consequence of an ulcer in the duodenum.
4. Stricture from cicatrisation of ulcers in the bile-ducts.
5. Spasmodic stricture ?

IV. *Obstruction by Tumours closing the Orifice of the Duct or growing in its interior.*

V. *Obstruction by Pressure on the Duct from without, by—*

1. Tumours projecting from the liver itself.
2. Enlarged glands in the fissure of the liver.
3. Tumour of the stomach.
4. Tumour of the pancreas.
5. Tumour of the kidney.
6. Post-peritoneal or omental tumour.
7. An abdominal aneurism.
8. Accumulation of fæces in bowels.
9. A pregnant uterus.
10. Ovarian and uterine tumours.

B.—JAUNDICE INDEPENDENT OF MECHANICAL OBSTRUCTION  
OF THE BILE-DUCT.

I. *Poisons in the Blood interfering with the normal metamorphosis of Bile.*

1. The poisons of the various specific fevers :—
  - a. Yellow fever.
  - b. Remittent and intermittent fevers.
  - c. Relapsing fever.
  - d. Typhus.
  - e.

Enteric or pythogenic fever. *f.* Scarlatina. *g.*  
'Epidemic jaundice.'

2. Animal Poisons :—
  - a.* Pyæmia. *b.* Snake-poison.
3. Mineral Poisons :—
  - a.* Phosphorus. *b.* Mercury. *c.* Copper. *d.* Antimony, etc.
4. Chloroform and ether.
5. Acute atrophy of the liver?

II. *Impaired or Deranged Innervation interfering with the normal metamorphosis of Bile.*

1. Severe mental emotions, fright, anxiety, etc.
2. Concussion of the brain.

III. *Deficient Oxygenation of the Blood interfering with the normal metamorphosis of Bile.*

IV. *Excessive Secretion of Bile, more of which is absorbed than can undergo the normal metamorphosis.*

Congestion of the Liver :—

- a.* Mechanical. *b.* Active. *c.* Passive.

V. *Undue Absorption of Bile into the Blood from habitual or protracted Constipation.*

When any obstruction exists to the flow of bile through the hepatic or common bile-duct, the way in which jaundice arises is sufficiently clear. The bile-ducts and the gall-bladder become distended with bile, which is absorbed into the blood by the lymphatics and the veins. This was satisfactorily proved at the end of last

century by the experiments of Dr. Saunders,<sup>1</sup> which have been confirmed by many subsequent observers. If a ligature be applied to the hepatic duct of a dog, and the animal be killed after two hours, the lymphatics in the walls of the bile-ducts, which are very numerous, are seen to be distended with a yellow fluid; the fluid in the thoracic duct is also yellow, and so likewise are the intervening lymphatic glands. In patients, also, who die of obstruction of the bile-duct the lymphatics of the liver are often found to contain bile. On the other hand, the serum of blood taken from the hepatic vein two hours after ligature of the common bile-duct is found to contain much more bile-pigment than that of blood taken from the jugular vein,<sup>2</sup> which shows that, in obstruction of the gall-duct, bile is also directly absorbed by the veins.

But it is not so easy to account for jaundice when there is no mechanical impediment to the escape of bile from the liver. Boerhaave and Morgagni long ago suggested that the jaundice in these cases was the result of a suppressed secretion. They maintained that the

<sup>1</sup> *Structure and Diseases of the Liver, &c.*, 3rd edit., 1803.

<sup>2</sup> Dr. Legg states that he has recently repeated this experiment in the dog without success.—*St. Bartholomew's Hospital Reports*, vol. ix., 1873.



function of the liver was merely to separate the elements of bile which were already formed in the blood ; and that, when anything interfered with this function of the liver, the blood retained the ingredients of bile, and the result was jaundice. Although this view was strenuously opposed at the end of last century by Dr. Saunders, who contended that, 'in every case of jaundice bile must be secreted and carried into the blood-vessels,'<sup>1</sup> it is the view generally received at the present day. Our colleague Dr. George Budd, for instance, in his treatise on *Diseases of the Liver*, remarks respecting those cases of jaundice in which there is no obstruction of the bile-ducts, that 'the most obvious explanation of the facts is, that the biliary pigment exists in the blood, and that, in consequence of defective action of the secreting cells, it is not eliminated as it should be in the liver.'<sup>2</sup> It is right to add that he makes an exception with regard to the biliary acids, which he believes to be formed in and by the liver. This view—that the liver manufactures the bile-acids, while it merely eliminates the bile-pigment—has also been advocated by Dr. George Harley, in his essay on *Jaundice*.<sup>3</sup>

<sup>1</sup> *Op. cit.*, p. 107.

<sup>2</sup> *Op. cit.*, pp. 40, 467, 468.

<sup>3</sup> *Jaundice ; its Pathology and Treatment*, London, 1863.

In my first lecture, however, I gave reasons, which appeared to me to leave no doubt, that even bile-pigment does not exist already-formed in the blood; and, if the view which I then contended for be correct, it will be necessary to seek for some other explanation of those cases of jaundice in which there is no obstruction in the bile-duct, than that of suppressed secretion.

A solution of the difficulty has been proposed by Professor Frerichs of Berlin. According to this distinguished observer, a large proportion of the colourless bile-acids formed in the liver is either directly taken up by the blood in the hepatic vein, or is absorbed from the bowel. Under ordinary circumstances, these bile-acids become oxydised and assist in forming the large quantity of taurin found in healthy lung and the pigments voided in the urine; but these normal metamorphoses are liable to interruption by nervous agencies, or by poisons in the blood, and then the bile-acids, not being sufficiently oxydised, are converted into bile-pigment in the blood, and the result is jaundice.<sup>1</sup> This view has been supported by two experiments intended to show—1. That bile-pigment can be produced artificially from the bile-acids by the action of concentrated sulphuric acid; and

<sup>1</sup> *Klinik der Leberkrank.*, Sydenham Society's translation, vol. i. pp. 89, 394.

2. That colourless biliary acids, when injected into the veins of dogs, are converted in the blood of these animals into bile-pigment. These experimental results are still the subject of much discussion. They have been controverted by Kühne,<sup>1</sup> Hoppe, G. Harley,<sup>2</sup> etc., but confirmed by Stödeler,<sup>3</sup> Neukomm,<sup>3</sup> Folwarczny,<sup>3</sup> Röhrig,<sup>4</sup> etc. It has been contended, on the one hand, that the biliary acids in these experiments are decomposed in the blood; and on the other, that, in whatever manner they find their way into the blood, they are excreted unchanged by the kidneys. The majority of observers seem to concur with Frerichs; and his view is confirmed by the circumstance that, of the large quantity of bile-acids secreted by the human liver and subsequently absorbed, none appears in the urine. The decision of the question at issue, however, is not of material importance for explaining those cases of jaundice in which there is no obstruction of the bile-duct, provided there be any truth in the view set forth in my first lecture, that bile-pigment, as well as the bile-acids, is, under normal circumstances, reabsorbed

<sup>1</sup> Virchow's *Archives*, vol. xiv. pts. 3 and 4, Sept. 1858; and Beale's *Archives of Medicine*, vol. i. p. 342.

<sup>2</sup> *Op. cit.*

<sup>3</sup> See my Preface to the English edition of *Frerichs on the Liver*, pp. 15, 16.

<sup>4</sup> *Archiv für Heilkunde*, Aug. 1863, p. 385.

into the blood, becoming transformed, in the process of absorption, into products which are eliminated by the lungs and the kidneys. In the healthy state, the whole of the bile that is absorbed is at once transformed, so that neither bile-acids nor bile-pigment can be discovered in the blood or in the urine, and there is no jaundice. But, in certain morbid states, the absorbed bile does not undergo the normal metamorphoses; it circulates in the blood and stains the skin and other tissues, and in this way we have jaundice without any obstruction of the bile-duct. The morbid states which, so far as we know, conduce mainly to this result are, for the most part, precisely those in which we might expect abnormal blood-metamorphoses, viz. :—

1. Certain poisons, such as those of yellow fever, relapsing fever, pyæmia, and more rarely those of remittent fever, typhus, scarlatina, etc.; also snake-poison, chloroform, etc.

2. Nervous influences, such as a sudden fright, violent rage, great or protracted anxiety, and concussion of the brain.

3. A deficient supply of oxygen, as happens in certain cases of pneumonia, or in persons living in confined and crowded dwellings.

4. An excessive secretion of bile, especially when

conjoined with constipation, may also probably lead to jaundice. In this case, unless the bile be removed by purging, the quantity absorbed may be too great to undergo the normal metamorphoses, and the presence in the blood of the untransformed bile causes jaundice.

According to this view, the only pathological difference between jaundice from obstruction and jaundice independent of obstruction of the common bile-duct is that, in the former case, none of the bile secreted by the liver can escape from the body by the fæces, and consequently all that is secreted after the gall-bladder and biliary passages are fully distended is absorbed into the blood, the quantity thus absorbed being far too great to undergo the normal metamorphoses; while, in the latter case, bile passes into, and is discharged from, the bowel as usual, but that which is absorbed, which in quantity may not exceed that which is absorbed in health, remains unchanged in the blood. As might have been expected, the jaundice in the former case is much more intense than in the latter, although, when an obstruction of the bile-duct has lasted long, the jaundice often becomes paler, not from any diminution of the obstruction, but from the secreting tissue of the liver becoming destroyed and comparatively little bile being secreted; while, in cases where there is no obstruction of the bile-duct, the

intensity of the jaundice will vary according to the amount of bile which is absorbed and the degree of derangement of the blood-metamorphoses.

V.—*Derangements of the Nervous System.*

1. *Aching Pains in the Limbs and Lassitude*, coming on about an hour after a full meal, and sometimes associated with an irresistible tendency to drowsiness, are a very common symptom resulting from hepatic derangement with lithæmia. They are often attended by flatulence and other indications of atonic dyspepsia.

2. *Pain in the Shoulder*.—It is well known that, in organic disease of the liver, complaint is often made of a dull, heavy, or aching pain about the right, and more rarely about the left, shoulder-blade, which is accounted for by the connexion existing between the branches of the subclavius nerve and the phrenic. Patients with lithæmia often complain of a similar pain.

3. *Hepatic Neuralgia*.—In rare cases, a neuralgic pain seems to occur in the liver itself. Many, probably most, of the reported cases of 'neuralgia hepatis' have probably been examples of biliary colic, where the stone has never advanced beyond the neck of the gall-bladder or the cystic duct, so as to cause jaundice. My experience

would certainly lead me to doubt the purely neuralgic character of any such attack in which the pain is followed by jaundice, as has happened in some of the recorded cases. Other instances of supposed hepatic neuralgia have probably been examples of nephritic colic from renal calculi, where the pain, as I have known happen, radiates horizontally forwards, instead of taking the usual direction downwards towards the pubes. But, making allowance for such mistakes in diagnosis, a certain number of cases remain, which appear to be examples of true neuralgia of the liver. Cases of this sort have been described by Trousseau,<sup>1</sup> Anstie,<sup>2</sup> and other authors, and a few have come under my own notice. The patients in these cases have been liable to sudden attacks, often periodic, of severe pain in the right hypochondrium, and radiating thence to the right shoulder, with tenderness over one or more of the dorsal spinous processes. They have been for the most part of nervous temperament, and subject to neuralgic pains in other parts of the body; and in most instances the attacks have been attended with great depression of spirits. The cause of the attacks is to be sought for in a general neuralgic tendency rather than in any disorder of the

<sup>1</sup> *Clinical Lectures*, Sydenham Society's translation, iv. 236.

<sup>2</sup> Anstie, *On Neuralgia*, 1871, p. 61.

liver. Trousseau, however, has pointed out that hepatic colic from gall-stones may excite a true neuralgia. After showing how the peripheral irritation of a false tooth may excite facial neuralgia, he observes: 'The same thing obtains in hepatic colic. Fearful pain sets up suddenly in the pit of the stomach and in the region of the gall-bladder and of the ductus communis choledochus. So far, there is merely local pain, without neuralgia, and there is no tenderness on pressure of the dorsal spinous processes; but, after two or three days spent in acute pain, a sharp pain is frequently complained of in the seventh, eighth, and ninth intercostal spaces, in the shoulder, in the neck, and in the arm on the same side; from that time, neuralgia exists, and the vertebræ become very tender on pressure.'<sup>1</sup>

4. *Severe Cramps* in the legs and in different parts of the body are a common symptom in persons who are the subjects of lithæmia. They often come on during the night, and they are most common in cold and damp weather. The late Sir Chales Scudamore remarked that, in some gouty persons, they produced such intense suffering as to form the leading feature of the disease.<sup>2</sup> Sometimes they precede a paroxysm of articular gout. Two

<sup>1</sup> *Op. cit.*, Sydenham Society's edition, i. 482.

<sup>2</sup> *Nature and Cure of Gout*, 4th edit., 1823, p. 532.



remarkable instances of this result of lithæmia have been recorded by Dr. Bence Jones. The first was that of a gentleman aged 40, who for years had been liable to constant deposits of lithic acid and lithates in the urine. He then became the subject of attacks of violent pain in the stomach, coming on from one to five hours after a late dinner. The pain was intermittently spasmodic; the most intense pain was reached in half a minute; it then relaxed, and returned as badly as before in two minutes. His suffering lasted about an hour, when the pain gradually abated, leaving a tenderness on pressure and an irritability after food for two or three days. After the attack, the urine always deposited lithic acid crystals. These attacks had lasted for several months, but, under a careful diet and the use of alkalies, they entirely ceased. The second patient, who also was the subject of lithæmia, was seized with violent cramps in the rectum, coming on six or eight hours after food, and lasting from half an hour to an hour. The attacks entirely ceased under the same treatment as in the first case.<sup>1</sup>

5. *Headache* is a not unfrequent result of hepatic derangement. Most commonly it takes the form of a dull heavy pain in the forehead, more rarely in the occiput,

<sup>1</sup> *Lectures on Pathology and Therapeutics*, 1867, p. 85.

complained of as soon as the patient awakes in the morning, and either speedily ceasing or lasting the greater part of the day or for several days. Such headaches are common in the subjects of lithæmia after any indiscretion in diet, or when the bowels are constipated. Their immediate cause is probably the presence in the blood of some abnormal product of albumen-metamorphosis; the derangement of the liver is usually indicated by pain and fulness in the right hypochondrium, flatulence, and high-coloured urine loaded with lithates; and relief is usually afforded by mercurial and saline purgatives and alkaline diuretics.

From these headaches it is necessary to distinguish *Megrim*, which unfortunately is the form of headache to which the terms 'bilious' or 'sick' are still popularly applied. This is a neuralgia, which probably in most cases is in no way connected with hepatic derangement, the bilious symptoms being the result, and not the cause of the attack, and the presence of bile in the vomited matter being, as in sea-sickness, simply due to the urgency of the vomiting. Although this view was enunciated two centuries ago by Sydenham, and since his time has been clearly set forth in many medical writings, of which I would mention, in particular, the Gulstonian Lectures of the late Dr. Symonds, delivered in this college in 1858,

and the excellent work of Dr. Edward Liveing<sup>1</sup> recently published, it is still the fashion to attribute these attacks to 'biliousness,' or to 'an excess of bile in the system.'

But, while fully admitting that megrim is in no way connected with retained bile, I agree with those authors who believe that certain cases of megrim are toxic in their origin, being symptomatic of gout and of some other disorders. The late Sir Henry Holland, in his *Medical Notes and Reflections*, described hereditary periodic headaches associated with gout, and he added: 'In conformity with this view, there is reason to believe that the kidneys are the excretory organs most concerned in giving relief in these cases, and principally by an increased separation of lithic acid and its compounds.'<sup>2</sup> Megrim, as Dr. Liveing states, is sometimes the expression of what is called a latent gouty diathesis, or, in other words, of lithæmia. A father may have suffered from gout, and his son may become the victim of megrim. In some patients megrim terminates when they are attacked with gout. 'So evidently,' observes Trousseau, 'is it (megrim) a manifestation of the gouty diathesis, that articular gout and megrim are observed in the same person, the one subsiding on the appearance of the other; and that it is often also the

<sup>1</sup> *On Megrim and some Allied Disorders*, London, 1873.

<sup>2</sup> *Medical Notes and Reflections*, 1839, p. 288.

only expression of the hereditary tendency in subjects who are the children of decidedly gouty parents.'<sup>1</sup> In connection with these observations, I would call attention to certain cases which have come under my notice of severe neuralgic headache occurring in connection with contracted granular kidneys, and being sometimes the first symptom for which the patient has sought medical advice. The headache in these cases also was evidently toxic, and in one instance fatal coma followed the subcutaneous injection of a quarter of a grain of morphia. The headache has been so severe that more than once I have known the case diagnosed as one of cerebral tumour. I have met with these cases so frequently, that I believe it to be a good rule to investigate the condition of the kidneys in all cases of neuralgic headache occurring for the first time in persons of middle or advanced age, before having recourse to treatment.

In this way, then, megrim may sometimes be traced to hepatic derangement, this derangement consisting, not in the retention of bile, but in that condition of liver which we have found to produce lithæmia and often to lead to gout; and, in accordance with this view, I have often noticed that megrim has been produced by particu-

<sup>1</sup> *Op. cit.*, Sydenham Society's edition, iv. 378.

lar articles of diet, and relieved by mercury, podophyllin, and other remedies which unload the liver.

6. *Vertigo and Temporary Dimness of Sight.*—Sudden attacks of giddiness are in many instances similar in their pathology to megrim, and giddiness in certain patients replaces the neuralgia. But giddiness, according to my experience, is, in a much larger proportion of cases, connected with hepatic derangement, lithæmia, and gout, and follows the use of certain articles of diet, such as tea, champagne, citron, etc. Many years ago, Boerhaave's commentator related the case of a man who, during two years, was always seized with vertiginous symptoms when he attempted to stand up. In vain had the ablest practitioners endeavoured to cure him. Quite suddenly, he had an attack of gout, of which disease, up to that date, he had had no indication; and from that moment he found himself free from the vertigo to which he had formerly been liable.<sup>1</sup> A medical friend of my own who has long suffered from gout, as certainly as he drinks a cup of tea or a glass of champagne is seized, often while walking in the street, with sudden giddiness; his head feels empty, and neighbouring objects seem to whirl round him; he does not lose consciousness, but he

<sup>1</sup> Trousseau, *Op. cit.*, Sydenham Society's edition, iv. 379.

would fall did he not lay hold of the railing. After a few seconds or minutes, the attack passes off, but in some patients it is more persistent. Another friend, who never has had gout, but whose urine is frequently loaded with lithates, was seized with dimness of sight and giddiness every night while writing. He took iron, quinine, and other tonics, but he got worse instead of better. He was advised to give up his profession for a time and try the effect of change of air ; but, before taking so serious a step, he took a few doses of blue pill, and the symptoms at once and permanently disappeared. A third patient under my care, who for years had been subject to lithæmia, but never had gout, would be suddenly seized, while writing, with dimness of sight and specks floating before the eyes, or even with complete, but temporary, blindness of one eye. Here also iron and quinine disagreed, but the symptoms were removed by remedies directed against the liver. Many writers have referred attacks such as those which I have now described to derangements of the stomach. Trousseau, for example, who has described them under the designation of ‘*vertigo à stomacho læso*,’<sup>1</sup> speaks of them as associated with epigastric pain increased by food, flatulence, acid eructa-

<sup>1</sup> *Op. cit.*, Sydenham Society’s edition, iii. 537.

tions, and vomiting of glairy mucus ; but he admits that the gastric derangement in which the vertigo is supposed to originate may not show itself, and this admission certainly accords with my experience. On the other hand, the circumstance of the frequent association of the vertigo with gout or lithæmia, and the fact that alkalies and aperients, which are the best remedies for these conditions, are also the remedies most likely to prevent a recurrence of the attacks of vertigo, make it probable that this has a toxic origin, and that the liver is the organ mainly at fault.

7. *Convulsions.*—In January of the present year I saw a gentleman, about 58 years of age, suffering from cirrhosis of the liver. He had all his life been addicted to the pleasures of the table, and had suffered from hepatic derangements as long as he could remember. Six years ago, he became subject to severe spasmodic twitchings in his legs, followed on three occasions by several epileptiform seizures. Shortly after the last fit he had his first attack of gout, and since then he had suffered repeatedly from the gout, but there had been no return of the convulsions or of the muscular twitchings. There was no evidence of renal disease. Many similar cases are, I believe, on record. For example, Van Swieten mentions the case of a man who had violent abdominal

pains accompanied by delirium and general trembling, and subsequently a severe attack of epilepsy. From that date he had repeated attacks of gout, but no return of the nervous symptoms.<sup>1</sup>

8. *Paralysis*.—I have repeatedly met with patients who have complained of numbness, tingling and pricking sensations, and a feeling of coldness or creeping in the extremities on both sides, or only on one. These symptoms may be associated with headache, nausea, and depression of spirits, and often cause needless alarm by exciting the suspicion that paralysis is imminent; whereas, if associated, as they often are, with lithæmia, oxaluria, or other evidence of hepatic derangement, they may entirely and permanently disappear under the use of calomel, saline aperients, alkalies, and attention to diet.

9. *Noises in the Ears* are common symptoms in gout,<sup>2</sup> and also in lithæmia independent of gout. One patient has the feeling of a strong wind blowing into the ear; another compares the noise to that of flowing water, or of singing or buzzing; while in another the sounds have a pulsating character, the sounds corresponding to those of the heart.

10. *Sleeplessness* may, of course, arise from many

<sup>1</sup> Trousseau, *op. cit.*, iv. 379.

<sup>2</sup> Scudamore, *op. cit.*, p. 376.



different causes, but one of its causes is that derangement of the liver which produces lithæmia. When this is the case, the patient is often heavy and drowsy after a full meal, and he may fall asleep at once on retiring to rest; but, after one, two, three, or four hours, he awakes, and then he either lies awake for hours, or he is constantly falling asleep, dreaming, or having the nightmare and awaking—four or five times or even oftener in the course of one hour—until the morning comes, when he drops into a quiet sleep of an hour or more, or he is obliged to get up tired and irritable. This sleeplessness, like the vertigo we have already considered, is often induced by particular articles of diet, or by some unwholesome combination of them. What will excite headache, giddiness, or disorders of the circulation in some patients will in another cause sleeplessness. Sometimes, however, this symptom will occur when the patient is most careful as to diet. What is important also to note is, that, in most of these cases, there are no obvious symptoms of gastric dyspepsia; the appetite may be good—too good, in fact; the bowels may be regular; and there may be no pain, flatulence, or other discomfort after meals; but there will be found an unusual tendency to the deposit of lithates in the urine, and very often other phenomena of a so-called gouty diathesis. This form of sleeplessness was described a

century ago by Cullen, the distinguished nosologist, in these words : ' Persons who labour under a weakness of the stomach, as I have done for a great number of years past, know that certain foods, without their being conscious of it, prevent sleeping. So I have been awakened a hundred times at two o'clock in the morning, when I did not feel any particular impression; but I knew that I had been awakened by an irregular operation in that organ, and I have then recollected what I took at dinner, which was the cause of it. Dr. Haller is liable to the same complaint; and, in his larger work especially, he gives the particulars of his own case.'<sup>1</sup> The affection has also been well described by Dr. Dyce Duckworth in some excellent observations on different forms of sleeplessness recently published.<sup>2</sup> It is, however, a form of sleeplessness not generally understood, and harm is often done to patients suffering from it by the administration of opiates and other soporifics, from ignorance of its real cause. Very often the symptom will be greatly relieved, if not entirely removed, by careful attention to diet, and particularly by moderation in or abstinence from wine; and, in some cases, a dose of carbonate of soda when the patient goes to bed, or when he first awakes, is of service. Some

<sup>1</sup> *Institutions of Medicine*, 1770.

<sup>2</sup> *British Medical Journal*, December 27, 1873.

patients with this form of sleeplessness have told me that they never sleep so well as after a dose of calomel or blue pill.

11. *Depression of Spirits.*—The influence of the liver upon the animal spirits has been recognised by medical writers in all ages. To the belief in the existence of such an influence may be traced the origin of such terms as *Hypochondriasis* and *Melancholia*. Although it is not contended that the morbid states of mind, to which at the present day we apply these terms, have their origin in the liver, they are unquestionably, in many instances, accompanied and aggravated by derangements of this organ; and it is equally true that, independently of either hypochondriasis or melancholia, persons with functional derangement, or structural disease, of the liver are subject to fits of great depression of spirits and often groundless fears of impending danger, which cease when the liver is restored to its normal state.

12. *Irritability of Temper* is another common symptom of functional derangement of the liver, and is sometimes the first indication of anything wrong. A man who has previously borne the crosses of life with equanimity, and been amiable to those about him, gradually becomes disconcerted by trifles; his mind broods upon them; and he makes all around him unhappy, and himself the most

miserable of all. His relatives, perceiving no other sign of indisposition, and failing to recognise the true cause, too often put down the ebullitions of temper to something mentally or morally wrong, to moral depravity, or failure to make any mental effort; but remedial measures calculated to restore the liver to healthy action, if resorted to in time, will often remove the irritability, and either the patient's improvement under such treatment, or an attack of gout, reveals the cause of the patient's bad temper. In his 'Psychological Inquiries,' the late Sir Benjamin Brodie thus speaks of a patient with a superabundance of lithic acid in the blood: 'Uncomfortable thoughts are presented to his mind; he becomes fretful and peevish, a trouble to himself, and, if he be not trained to exercise a moral restraint over his thoughts and actions, a trouble to everyone about him. After a while, the poison, as it were, explodes: he has a severe attack of gout in his foot; he is placed on a more prudent diet; the system is relieved of the lithic acid by which it was poisoned. Then the gout subsides; happy and cheerful thoughts succeed those by which the patient was previously tormented, and these continue until he has had the opportunity of relapsing into his former habits, and thus earning a fresh attack of the disease.'<sup>1</sup>

<sup>1</sup> Second ed., 1855, p. 73.

13. *Cerebral Symptoms and the Typhoid State.*—It is well known that restlessness, delirium, stupor, coma, subsultus, tremors, convulsions, a dry, brown tongue, and other phenomena of the 'typhoid state,' are apt to supervene in certain cases of advanced disease of the liver, whether attended by jaundice or not. These symptoms have been usually attributed to a suppressed secretion of bile. But the assumption that the elements of the bile are preformed in the blood, and are merely separated from the blood by the liver, we have already found to be devoid of foundation; and we have also found that bile is far from being, as commonly supposed, a deadly poison, and that its presence in the blood, even to saturation, does not give rise to cerebral symptoms. The cerebral symptoms referred to are often most severe when the jaundice is slight, or when there is none; and they are readily accounted for by the knowledge of the disintegrating function which the liver is now known to perform. When this function of the liver is arrested or seriously impaired, urea is no longer eliminated in sufficient quantity by the kidneys; lithic acid and deleterious products of disintegrating albumen even less oxydised, such as leucin and tyrosin, and perhaps others with which we are as yet imperfectly acquainted, accumulate in the blood and tissues; and the result is the development of symptoms of

blood-poisoning similar to those which arise when the kidneys are unable to eliminate the products of albumen-disintegration, owing to disease of their own structure, or to an excessive formation of urea and other products, as happens in many febrile diseases. In acute atrophy, for example, the structure of the liver is destroyed and its functions arrested; leucin and tyrosin take the place of urea in the urine, and are also found in large quantity in the liver, spleen, and kidneys, while cerebral symptoms and the typhoid state are prominent features of the disease.

## LECTURE III.

VI. *Derangements of the Organs of Circulation.* 1. *Palpitations and Flutterings of the Heart*; 2. *Exaggerated Pulsation of the Large Arteries*; 3. *Irregularities and Intermissions of the Pulse*; 4. *Feeble Circulation*; 5. *Anæmia*; 6. *Angina Pectoris*; 7. *Venous Thrombosis*.—VII. *Derangements of the Organs of Respiration.* 1. *Chronic Catarrh of Fauces*; 2. *Bronchitis*; 3. *Spasmodic Asthma*.—VIII. *Derangements of the Urinary Organs.* 1. *Deposits of Lithic Acid and Lithates in Urine*; 2. *Renal Calculi*; 3. *Diseases of Kidneys*; 4. *Cystitis*.—IX. *Abnormal Conditions of the Skin.* 1. *Eczema, Lepra, Psoriasis, and Lichen*; 2. *Urticaria*; 3. *Boils and Carbuncles*; 4. *Pigment-spots*; 5. *Xanthelasma*; 6. *Pruritus*.—C. CAUSES OF FUNCTIONAL DERANGEMENTS OF THE LIVER.—I. SECONDARY. 1. *Structural Diseases of the Liver*; 2. *Disorders of Stomach and Bowels*; 3. *Diseases of the Heart and Lungs*; 4. *Pyrexia*.—II. PRIMARY. 1. *Errors in Diet*; 2. *Deficient Supply of Oxygen*; 3. *High Temperature*; 4. *Nervous Influences*; 5. *Constitutional Peculiarities*; 6. *Poisons*.—D. TREATMENT OF FUNCTIONAL DERANGEMENTS OF THE LIVER. 1. *Diet*; 2. *Free Supply of Oxygen*; 3. *Aperients—Cholagogues*; 4. *Alkalies*; 5. *Chlorine, Iodine, Bromine, and their Salts*; 6. *Mineral Acids*; 7. *Tonics*; 8. *Opium*. *Concluding Remarks.*

MR. PRESIDENT, FELLOWS OF THE COLLEGE, AND GENTLEMEN,—In my last lecture I considered some of the more important diseases and symptoms resulting from

abnormal disintegration of albuminous matter in the liver. I have still to refer to certain derangements of the organs of circulation and respiration, and abnormal states of the skin traceable to the same cause. I shall then mention some of the chief causes of functional derangements of the liver, and conclude the lecture by a brief sketch of the principal rules for treatment of these derangements.

VI.—*Derangements of the Organs of Circulation.*

1. *Palpitations and Flutterings of the Heart.*—Indigestion has long been regarded as one of the causes of palpitation independent of organic disease of the heart. Many patients with this functional derangement of the heart describe their sensations as that of a transient fluttering rather than a continuous palpitation; and when this feeling of fluttering comes to be investigated, it usually turns out to be produced by a strong thump of the apex of the heart following one or more weaker beats or a decided stop. In some of these cases of palpitation and fluttering a prominent symptom of the indigestion is flatulence; and then the common explanation of the cardiac symptoms is, that they are due to the pressure upon the heart of the distended stomach and bowels; and this explanation receives support from the fact that,



on the removal of the flatulence the cardiac symptoms are often relieved or cease. But in other of these cases the flatulence may be entirely removed, while the cardiac symptoms remain, while in others there is not the slightest evidence of flatulence, and still the cardiac symptoms are removed by remedies, such as alkalies and aperients, calculated to improve the condition of the liver. It seems probable, therefore, that in some, if not in many, cases, when flatulence and palpitations coexist, they do not stand in the relation of cause and effect, but are both the result of a common cause. Palpitations, and still more, flutterings of the heart, are particularly common in gouty people, whether they suffer from dyspeptic symptoms or not. Everyone present must have met with cases of the sort. Scudamore relates cases in which patients suffered from severe palpitations for six months without any relief from medicine; but, on the occurrence of a fit of gout, the palpitations suddenly and entirely ceased.<sup>1</sup> Dr. Garrod, in his work 'On Gout,' remarks: 'One of the most common symptoms produced by a gouty state of the system is palpitation of the heart, often accompanied by irregularity of its rhythm, and occasionally with pulsation of some of the larger arteries. In the

<sup>1</sup> *Op. cit.*, pp. 16, 98, 374.

majority of these cases, the condition is secondary to dyspepsia, but at times it may be directly excited by the impure condition of the blood ; and I have notes of some cases in which no organic mischief could be discovered in the heart, nor any signs of indigestion, and the symptoms ceased on the occurrence of gout in the joints.'<sup>1</sup> These cardiac symptoms are also very common in persons who are the subjects of lithæmia or oxaluria, but who never have gout. They are often the first symptoms to draw the patient's notice to the fact that his health is not what it ought to be ; they cause great depression of spirits ; and very often they are aggravated by injudicious treatment, and especially by the use of iron, which may seem to be indicated by the patient's anæmic aspect, but which is rarely tolerated until the liver has been brought into a healthy state by alkalies, aperients, and attention to diet. Although in the cases now referred to the cardiac symptoms result from pneumogastric irritation by a poison in the blood, the fact already referred to must not be lost sight of, that this same morbid state of blood may ultimately lead to degeneration of the muscular wall of the heart, or disease of the aortic valves. (See page 82.)

<sup>1</sup> *Nature and Treatment of Gout*, 1859, p. 510.

2. *Exaggerated Pulsation of the Large Arteries.*—Dr. Matthew Baillie, in a communication made to this College on December 2, 1812, was the first to call attention to cases of increased pulsation of the aorta in the epigastric region, simulating aneurism, but in some instances lasting twenty-five years or longer, and the result merely of ‘imperfect digestion with an irritable constitution.’<sup>1</sup> This exaggerated pulsation, not only of the aorta, but of other arteries, independent of either contracted kidney or aortic regurgitation, is now well known, and one cause of it appears to be a morbid state of blood resulting from derangement of the liver, and often associated with gout. Scudamore relates cases of palpitations in the head occurring in persons afflicted with bilious derangement and gout, and likewise the case of a gentleman who had gout and bilious derangement, and who suffered alternately from palpitation of the heart and pulsation of the aorta in the epigastric region.<sup>2</sup> Garrod also speaks of an irritable state of the aorta and pulsation of the larger arteries as occasionally resulting from gout.<sup>3</sup> The undue pulsation in these cases is often subdued by treatment directed against the liver.

<sup>1</sup> *Medical Transactions*, published by the College of Physicians, 1813, vol. iv. p. 274.

<sup>2</sup> *Op. cit.*, p. 98.

<sup>3</sup> *Op. cit.*, pp. 510, 511.

3. *Irregularities and Intermissions of the Pulse.*—An intermitting pulse, which may, or may not, be attended by the sensation of fluttering of the heart already referred to, may result from a variety of causes, of which the principal are these :—

*a.* Valvular and other diseases of the heart. In organic diseases of the heart, however, irregularity of the rhythm is more common than decided intermission.

*b.* A weakened or unduly irritable state of the nervous system, such as that which often occurs in old age, or sometimes appears to be constitutional, or those which are induced by fevers, delirium tremens, hysteria, protracted want of sleep, anxiety, etc.

*c.* Morbid states of the blood, associated with gout or lithæmia, or with other evidence of hepatic derangement. It has been the fashion to attribute the intermission in these last cases to pneumogastric irritation by gastric dyspepsia or flatulence ; but, just as we found in vertigo, there is very often neither flatulence nor other evidence of gastric derangement ; and my experience has led me to the conclusion that in most of these cases the pneumogastric irritation has a toxic origin, or is due to the presence in the blood of some morbid material resulting from derangement of the liver. What this material is we do not with certainty know. It is

not uncommon for the pulse to become very slow, or even to be irregular or to intermit, in jaundice. These symptoms do not appear to be due to the presence of bile-pigment in the blood, for in many cases of jaundice they are absent; but some experiments made a few years since by Röhrig showed that the bile-acids paralyse the heart and retard its action, while bile-pigment has no such effect.<sup>1</sup> It is possible, then, that slowness and intermission of the pulse may be caused by the presence in the blood of unchanged bile-acids, even in cases where there is no jaundice; but more probably the cause of the intermission is some other product of albuminous disintegration, inasmuch as it is so commonly met with in connection with lithæmia or gout, and as it is often entirely removed by blue pill, saline aperients, alkalies, and attention to diet. A notable fact in these cases is that the tendency of the pulse to intermit is usually greatest when the patient is at rest, and is diminished or ceases on his taking exercise. As in the case of vertigo or sleeplessness, the intermission may be excited by particular articles of diet. It may last for many years, during which the patient may enjoy very fair health and be capable of considerable exertion. I lately saw a

<sup>1</sup> *Archiv. für Heilkunde*, August 1863, p. 385.

gentleman, aged eighty, who had had an intermitting pulse for upwards of fifty years. He had suffered from gout and dyspepsia, but in his eightieth year he could walk long distances and up moderate ascents without difficulty. It is also worth noting that intermission of the pulse may last for years, and then entirely disappear. Dr. C. Lasègue of Paris, who has published an interesting memoir<sup>1</sup> upon intermitting pulse, thinks that it is chiefly met with under two conditions, viz.: firstly, as an accompaniment of some chronic general morbid state, which is the prelude of some more acute mischief, on the development of which the intermissions may cease; and secondly, as the accompaniment of a general morbid state consequent on the first establishment of some local disease, the general cachexia and the intermitting pulse after a time disappearing, although the primary local disease remains. The following case, communicated to me by Mr. Paul Jackson, is a remarkable illustration of the complete disappearance of the intermission after a duration of several years, and also of its toxic origin.

About the year 1838, Mr. J. T., then forty-two years of age, of nervous temperament, a generous liver, and subject to hepatic derangement, began to suffer from

<sup>1</sup> 'Des Intermittences Cardiaques,' par le Dr. C. Lasègue, *Arch. Gén. de Méd.*, December 1872.

intermission of the pulse, and a fluttering sensation at the heart. He had no dyspnoea or other symptom of cardiac disease, and there was no abnormal cardiac murmur. He saw a great many physicians, but got no relief; but, after upwards of three years, he had a severe attack of urticaria, whereupon the intermission and the fluttering entirely and for ever ceased. He lived for twenty years afterwards, and, with the exception of occasional attacks of gout and of sudden vertigo, he enjoyed good health. He died at last, however, suddenly, of rupture of the heart, at the age of sixty-five.

It may be well to add that, even when intermitting pulse coexists with valvular disease of the heart, it appears to be sometimes due to hepatic derangement rather than to the cardiac lesion. Take, for example, aortic incompetence. The rhythm of the pulse in this lesion is usually regular, but, in rare instances, it is irregular and intermitting. From the supervention of this symptom the patient's condition is often believed to have become more perilous, and yet there may be no aggravation of the other cardiac symptoms. The pulse may become regular, instead of more intermitting, after exercise, and the intermission may be entirely removed by the same remedies as are effectual when there is no cardiac disease. That the intermission of the pulse should be independent of the cardiac lesion is not sur-

prising, when we remember that atheroma of the arteries, which is the main cause of aortic incompetence occurring in middle or advanced life,<sup>1</sup> and intermitting pulse, may both result from the lithic acid dyscrasia. The following case is an illustration of what I have just stated.

A discharged soldier, aged 56, came under my care in July 1873 for what appeared to be muscular or neuralgic pains. He was found to have aortic incompetence, but he had never had any symptom of cardiac disease—pain, palpitation, or dyspnoea—and he had been employed as a porter in a public institution, one of his duties being to carry heavy coal-scuttles up long stairs, from which he had apparently suffered no inconvenience. His pulse was quite regular. He was treated with quinine, but he left the hospital after some weeks not much relieved, and returned to his work. In December he again came to me, complaining of pain in his right shoulder and constipation; his pulse was now very intermitting, and he had also a frequent feeling of fluttering about his heart. He had no other cardiac symptom, and, on walking, his pulse became regular. He was now treated with blue pill, colchicum, aperients, alkalies, and iodide of potassium, and in a short time the

<sup>1</sup> I do not remember to have met with intermitting pulse in cases of aortic incompetence of rheumatic origin.



pain in the shoulder, the fluttering, and the intermission disappeared.

4. *Feeble Circulation.*—In cases of protracted hepatic derangement, symptoms of feeble circulation, which may be independent of palpitations or irregularities of the pulse, are not uncommon. The patient complains of languor, debility, and coldness of the extremities. The heart is found to beat feebly, but to be free from organic disease; there is evidence of hepatic derangement, and the urine often deposits lithates. Iron, quinine, and alcoholic stimulants, which are frequently prescribed for this condition, may render the patient worse instead of better, and the surest way to increase the strength of the heart is to avoid alcohol and relieve the liver.

5. *Anæmia.*—(See page 87.)

6. *Angina Pectoris.*—The neuralgic affection known as angina pectoris probably arises in many different ways. One cause appears to be the lithic acid dyscrasia. It is now many years since an English physician, Dr. William Butter, described certain cases of this affection as diaphragmatic gout. The patients had been careless as to diet, and ‘particularly fond of the stronger malt liquors’; the urine deposited ‘a copious gross sediment’; and the attack might terminate in a fit of the gout.<sup>1</sup> Many

<sup>1</sup> *Treatise on Angina Pectoris*, second edition, London, 1806.

writers have since then described a 'gouty cardialgia'; and, more recently, Trousseau has pointed out that certain cases of angina pectoris are independent of any disease of the heart or great vessels, and are merely 'a manifestation of the gouty diathesis.'<sup>1</sup> Not long since, I saw a gentleman, aged 65, who complained of awaking in the night three or four times a week with violent pain in the cardiac region, extending up to the left shoulder and down the left arm. I could discover no sign of disease in his heart. He stated that, six years before, he had suffered for months from similar attacks, but had recovered under medical treatment. He had never had gout, but he was very careless as to his diet, and his brother I knew to be a martyr to gout.

7. *Venous Thrombosis*.—There are good reasons for believing that the morbid condition of blood resulting from functional derangement of the liver not unfrequently leads to the production of venous thrombosis. Cases of this sort have been described as 'gouty phlebitis' by Sir James Paget, who observes :—

'The use of this name is, I believe, justified by the number of cases in which phlebitis is associated with ordinary gouty inflammation in the foot or joints, and occurs, with little or no evident provocation, in persons of marked gouty constitution, or with gouty in-

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<sup>1</sup> *Op. cit.*, vol. iv. p. 379.

heritance. In such cases the phlebitis may have no intrinsic characters by which to distinguish it; yet, not rarely, it has peculiar marks, especially in its symmetry, apparent metastases, and frequent recurrences. Gouty phlebitis is far more frequent in the lower limbs than in any other part; but it is not limited to the limb that is, or has been, the seat of ordinary gout. It affects the superficial rather than the deep veins, and oftener occurs in patches, affecting (for example) on one day a short piece of a saphenous vein, and on the next day another separate piece of the same, or a corresponding piece of the opposite vein, or of a femoral vein. It shows herein an evident disposition towards being metastatic and symmetrical; characters which, I may remark, by the way, are strongly in favour of the belief that the essential and primary disease is not a coagulation of blood, but an inflammation of portions of the venous walls. The inflamed portions of vein usually feel hard, or very firm; they are painful, aching, and very tender to the touch; such pain, indeed, often precedes the clearer signs of the phlebitis, and not rarely begins suddenly. The integuments and the affected veins (where they are superficial) are slightly thickened and often marked with a dusky reddish flush. When superficial veins alone are affected there may be little oedema; but when venous trunks, as the femoral, the whole limb assumes the characteristics of complete venous obstruction. It becomes big, clumsy, featureless, heavy, and stiff; its skin is cool and may be pale, but more often it has a partial slight livid tint, with mottling from small cutaneous veins visibly distended. The limb thus enlarged feels œdematous all through, but firm and tight-skinned, not yielding easily to pressure, and not pitting very deeply. By this state alone the disease must sometimes be recognised, for it may be very marked when only a small portion of vein is affected, and that (as the lower part of the popliteal) so deeply seated as to be scarcely felt. The constitutional disturbance associated with this condition is that of slight feverishness, or of an ordinary gouty attack, more or less acute in different cases. The effects of the disease I have never had an opportunity of examining

by dissection, for in the only fatal case that I have seen no autopsy was allowed. So far as one may judge of them by after-events during life, the veins which may have been obstructed become in some cases pervious again ; for in some cases the clearing up of the œdema and the restoration of the healthy condition of the limb are complete, yet the veins remain apparently very susceptible ; they ache exceedingly during fatigue or trivial illness, or in changing weather ; and I have known phlebitis excited by trivial causes in the same veins three or four times. In other instances, however (but I think they are rarer than in other forms of phlebitis), the obstruction of the veins appears complete and permanent ; and then, if they be trunk-veins, the limb remains permanently enlarged, cumbrous, and heavy. Its superficial veins may after some time become varicose, and others may enlarge for collateral blood-streams ; and I believe that an increased growth may take place in some of the tissues, especially the muscles of the limb.<sup>1</sup>

As in other forms of thrombosis, so here the clot may become broken up and its fragments be dispersed, and in this way syncope, or even sudden death, may result from embolism of the pulmonary artery. Like gout, this form of thrombosis is often hereditary ; but it is well to remember that it may be induced by functional derangement of the liver in persons who neither inherit gout, nor have at any time had traces of it themselves.

<sup>1</sup> 'On Gouty and some other forms of Phlebitis,' *St. Bartholomew's Hospital Reports*, 1866, vol. ii. p. 83.

VII.—*Derangements of the Organs of Respiration.*

1. *Chronic Catarrh of the Fauces.*—The subjects of gout or lithæmia are very liable to an habitual excess of mucous secretion in the fauces and at the back of the nose, which usually accumulates during the night, and which may be associated with a troublesome cough. Errors in diet usually increase the amount of phlegm, and may cause an extension of the catarrh, with hoarseness of the voice, and this may account for Scudamore's statement, that a cough with much mucous secretion in the trachea sometimes precedes a fit of gout.<sup>1</sup>

2. *Chronic Bronchitis.*—The researches of Trousseau,<sup>2</sup> of our colleague Dr. Greenhow,<sup>3</sup> and of other observers, have clearly proved that chronic bronchitis has in many instances a similar pathology to that of gout, and, therefore, originates in functional derangement of the liver. Gout and bronchitis are very common in the same families; gout is disproportionately common among bronchitic patients, and the two diseases often alternate with one another in the same individual, gout subsiding on the development of bronchitis, and bronchitis being

<sup>1</sup> *Op. cit.*, pp. 17, 377.

<sup>2</sup> *Op. cit.*, vol. iv. p. 381.

<sup>3</sup> *On Chronic Bronchitis*, 1869, p. 55.

relieved on the appearance of gout ; while the bronchitis is benefited by the same remedies as are useful in gout. It may be added, that persons who have never had gout, and do not come of a gouty stock, but who are the subjects of lithæmia, are also very prone to bronchitis.

3. *Spasmodic Asthma*.—Although spasmodic asthma consists essentially in a morbid proclivity of the musculo-nervous system of the bronchial tubes to be thrown into a state of activity, the stimulus to contraction appears in some patients to be toxic, or to consist in the presence of some morbid material in the blood. ‘When,’ remarks Dr. Todd,<sup>1</sup> ‘the *materies morbi* of asthma has been generated, its effect is to irritate the nervous system, not generally, but certain parts of it, these parts being the nerves concerned in the function of respiration, viz. the pneumogastric and the nerves that supply the respiratory muscles, either at their peripheral extremities, or at their central termination in the medulla oblongata and spinal cord.’ The nature of this *materies morbi* appears to be very similar to that of gout, and, like that of gout, it appears to be due to derangement of the blood-changes of which the liver is the principal seat. Asthma, like gout, is an hereditary disease ; it is common among

<sup>1</sup> *Medical Gazette*, December 1850.

persons springing from a gouty stock ; it is not unfrequently associated with gout in the same individual ; and attacks of asthma have been known to alternate periodically with attacks of gout. Moreover, an asthmatic paroxysm, like an attack of gout, of vertigo, or of sleeplessness, is often excited by a fit of indigestion and by the use of particular articles of diet. Our late colleague Dr. Hyde Salter, who did so much to throw light upon the pathology of asthma, was of opinion that the asthmatic paroxysm in the cases now referred to was produced by ‘the actual presence in the vessels of the lungs of the materials taken up from the stomach and intestines ;’<sup>1</sup> but it seems to me that the *materies morbi* is far more likely to be a product of hepatic derangement consequent on the unwholesome ingesta, as in the analogous attacks of gout, vertigo, etc.

#### VIII.—*Derangements of the Urinary Organs.*

The remarks which I have already made render it unnecessary for me to insist further on the tendency of functional derangement of the liver to produce urinary symptoms. I will merely repeat that hepatic disorder is a common cause of—

<sup>1</sup> *On Asthma*, 1860, pp. 46, 117.

1. *Deposits of Lithic Acid and Lithates in the Urine* (p. 65).

2. *Renal Calculi* (p. 72).

3. *Diseases of the Kidneys* (p. 78).

I will now add that—

4. *Cystitis* is occasionally excited by the lithic acid diathesis.<sup>1</sup>

#### IX.—*Abnormal Conditions of the Skin.*

There is good evidence that many disorders of the skin originate in derangements of the processes of oxydation or disintegration which go on in the liver.

1. Almost all observers are agreed that *Eczema*, *Lepra*, *Psoriasis*, and *Lichen* may arise from lithæmia. Many years ago, the late Sir Henry Holland remarked that he had ‘so often seen psoriasis prevailing in gouty families—sometimes alternating with acute attacks of that disease, sometimes suspended by them, sometimes seeming to prevent them in individuals thus disposed—that it is difficult not to assign the same morbid cause to these results.’<sup>2</sup> Our late distinguished President, Sir Thomas Watson, in his *Practice of Medicine*, speaks of lepra and psoriasis as blood-diseases depending upon

<sup>1</sup> See Garrod, *op. cit.*, p. 512.

<sup>2</sup> *Medical Notes and Reflections.*



some poison bred within the body.<sup>1</sup> Dr. Garrod also bears testimony to the frequent connexion of eczema and psoriasis with gout. My own experience fully bears out the correctness of these observations; but, in many cases, these cutaneous diseases appear to arise from the functional derangement of the liver which often precedes gout, although neither the patient nor any member of his family has ever suffered from this disease. On this point Dr. Tilbury Fox, in his recent work on cutaneous diseases, makes the following pertinent remarks: 'All disorders which are connected with retention of excreta in the system, and their circulation throughout the blood-current, may furnish the exciting cause of eczema. This is a clinical fact of very great importance. Given the tendency to eczema, then the transmission of uric acid through the capillaries of the skin will so far derange as to aggravate certainly, and now and again excite, an eczematous eruption. This is what is meant by gouty eczema; and, by securing the absence of uric acid from the circulation, the eczema will often disappear, and always be more amenable to treatment. . . . Such cases as I now refer to sometimes exist off and on for years, and are saturated with arsenic and mercurials, but are

<sup>1</sup> *Lectures on the Principles and Practice of Medicine*, fifth edition, 1871, vol. ii. p. 1023.

only relieved by recognising the complicating item of the free production and circulation of uric acid, and by instituting a *régime* calculated to arrest the continuance of those conditions.’<sup>1</sup> Dr. Fox also calls attention to the fact that children with eczema have often white stools.<sup>2</sup>

2. *Urticaria* I have not unfrequently met with in connexion with jaundice and other derangements of the liver. The late Dr. Graves observed eight or nine instances of persons suffering from acute rheumatism who became suddenly jaundiced from the supervention of hepatitis (congestion of liver?), and in whom the jaundice was followed by urticaria.<sup>3</sup> Among the causes of urticaria, Dr. Tilbury Fox mentions ‘the circulation of acrid or effete products, for example, uric acid, bile, etc., which, coming to the surface, become oxydised and more active.’<sup>4</sup> He also mentions that ‘asthma has been observed to be associated with urticaria in a peculiar manner’<sup>5</sup>—an association which is readily explained by the foregoing remarks. Scudamore refers to violent

<sup>1</sup> *Skin Diseases*, third edition, 1873, p. 175.

<sup>2</sup> *Ib.*, p. 11.

<sup>3</sup> *Clinical Lectures on the Practice of Medicine*, second edition, vol. i. p. 446.

<sup>4</sup> *Op. cit.*, p. 120.

<sup>5</sup> *Ib.*, p. 121.

urticaria as existing for two days before a gouty paroxysm;<sup>1</sup> and I have myself known patients in whom champagne or certain articles of diet have almost invariably produced either gout or urticaria. Recently, I have had under my care a boy, aged 9, with *urticaria tuberosa* and *purpura urticans*, complicated with hæmorrhages from the bowels, kidneys, and urinary passages, and with the discharge of much lithic acid in the urine, which there was good reason for suspecting to be due, in the first instance, to functional derangement of the liver.

3. *Boils and Carbuncles* are occasionally observed in connexion with jaundice, and are also excited by the presence in the blood of urea and other effete products. In the connexion also between phlegmonous or carbuncular inflammation and diabetes, it is possible again to trace the influence of a disordered liver in the production of skin-diseases.

4. *Pigment-spots* of various sorts on the face, hands, and other parts of the body are not uncommon in functional derangements of the liver. They are sometimes designated 'liver spots' by non-professional persons, who, perhaps, attach too much importance to them as indicative of hepatic derangement. They may, as Dr.

<sup>1</sup> *Op. cit.*, p. 103.

Laycock observes, be induced by imperfect oxydation, or excessive production of carbon, in derangements of the liver,<sup>1</sup> but they may also arise in other ways.

5. *Xanthelasma or Vitiligoidea*, which consists in a fatty degeneration of the subcutaneous or submucous tissue analogous to atheroma,<sup>2</sup> is a remarkable affection of the skin, which was first described in a joint memoir by the late Dr. Addison and Sir William Gull.<sup>3</sup> It occurs in two forms, either as tubercles varying from the size of a pin's head to that of a large pea, isolated or confluent; or more commonly as yellowish patches of irregular outline, slightly elevated, and not at all indurated. The tubercles are most numerous on the face and ears, on the outside and back of the forearms, and especially about the elbows and knees. The yellow patches are always first observed on the eyelids, usually near the inner canthus; but they may subsequently appear on the neck, the palms and flexures of the fingers, and even the gums. The more severe forms are almost always associated with persistent jaundice and great en-

<sup>1</sup> Fox, *op. cit.*, p. 404.

<sup>2</sup> See *Pathological Transactions*, vol. xx. p. 187, and vol. xxiv. p. 242.

<sup>3</sup> *Guy's Hospital Reports*, second series, 1851, vol. vii. p. 265.

largement of the liver,<sup>1</sup> which may subside under treatment ; and, in most cases where there has been no jaundice, the patients have been of middle or advanced age, and there has been a history of frequent and severe attacks of functional disturbance of the liver.<sup>2</sup> It may be added that several cases of xanthelasma have been observed where there has been diabetes, but no jaundice.<sup>3</sup> In some instances the disease appears to be hereditary.

6. *Pruritus* is a troublesome symptom which often results from hepatic derangement. It is known to be a frequent accompaniment of jaundice ; but it is not due to the presence of bile in the blood, for in many cases of jaundice it is absent, and I have repeatedly known it precede the appearance of jaundice by several weeks, or cease while the jaundice persisted. Moreover, I have frequently known itchininess of the skin a source of extreme distress to patients with hepatic derangement unaccompanied by jaundice. It may attack various parts of the body in succession, or it may be universal. It is unat-

<sup>1</sup> See a fatal case recorded by me in *Pathological Transactions* for 1868, vol. xx. p. 187.

<sup>2</sup> See 'Clinical Report on Xanthelasma Palpebrarum,' by Jonathan Hutchinson, F.R.C.S., *Medico-Chirurgical Transactions*, 1871, vol. liv. p. 171.

<sup>3</sup> *Guy's Hospital Reports*, second series, vol. vii. p. 268 ; and Bristowe, in *Pathological Transactions*, vol. xvii. p. 414.

tended by any eruption. It is always worse in heated rooms and after stimulating food, and it is greatly aggravated by scratching. This symptom is not uncommon in gouty people<sup>1</sup> and in subjects of the lithic acid diathesis, and it is often removed by attention to diet and a few doses of blue pill and alkalies. As Dr. Bence Jones has observed, 'itching, nettle-rash, eczema, and herpes are the outbursts of an over-acid state.'<sup>2</sup>

C.—CAUSES OF FUNCTIONAL DERANGEMENTS OF THE  
LIVER.

The remarks which I shall make under this head will be restricted to abnormal disintegration in the liver. The causes of diabetes and of certain other functional derangements of the liver have been already referred to. The disorder of the liver which induces lithæmia may be primary, or secondary to other morbid states of the body. It is with the former that we are now chiefly concerned; but the main causes of secondary derangement of the liver may be briefly referred to. They are as follows:—

<sup>1</sup> Scudamore, *op. cit.*, p. 103.

<sup>2</sup> *Lectures on Pathology and Therapeutics*, 1867, p. 84.

1. *All structural diseases of the liver* derange more or less the functions of the organ. These derangements are usually judged of solely by the characters, of the alvine evacuations, and the far more important functions of sanguification and depuration of the blood performed by the liver are lost sight of. But it is well to remember that in structural diseases of the liver these functions may be seriously deranged, without any obvious change in the characters of the stools. In all structural diseases of the liver unattended by fever, and involving a considerable destruction of the glandular tissue, there is a tendency to a diminished excretion of urea, and an increase of lithates in the urine, and before long the patient becomes anæmic. At last, symptoms of blood-poisoning may supervene, although there may be no jaundice and plenty of bile in the motions. These results are well seen in acute atrophy of the liver ; but are also notable, though in a less degree, in abscess, cirrhosis, cancer, etc.

2. *Disorders of the Gastric and Intestinal Digestion* often lead to secondary derangement of the liver. For example, the liver may become deranged as the result of gastric dyspepsia, or of protracted constipation from atony of the bowels or from deficient intestinal secretion ; and sometimes it may be difficult to say whether the hepatic derangement is primary or secondary.

3. *Diseases of the Heart and Lungs*, by obstructing the circulation and impeding oxydation, are a common cause of functional, and ultimately indeed of structural, disease of the liver. It is unnecessary for me here to insist on the frequency with which the symptoms of valvular disease of the heart are aggravated by those of functional derangement of the liver, and on the necessity of attending to these in the treatment of the primary disease.

4. *Pyrexia*.—In all diseases attended by pyrexia, whether arising from some general cause, such as a specific poison, or from a local inflammation, there is more or less functional derangement of the liver. The liver, indeed, plays a prominent part in the pathology of the febrile process. It is one of the few parts of the body which do not waste during the fever. On the contrary, it becomes enlarged and congested, while its gland-cells are swollen out with minute albuminous granules; and it is well known that these changes are attended by an increased disintegration of albuminous matter and an increased production of urea and less oxydised products. On the cessation of the febrile process the liver resumes its normal functions; but now and then it happens that, after a severe attack of fever, these functions are permanently impaired. I have repeatedly known a permanent tendency to hepatic derangement induced by a severe



attack of typhus, enteric, malarious, or scarlet fever, in persons who had exhibited no such tendency previously.

\*Functional derangements of the liver, when primary, may be due to a variety of causes. Of these the principal are—

1. *Errors in Diet.*—There can be no doubt that the present system of living, and especially the consumption of even what are regarded as average quantities of rich food and stimulating drinks, contribute largely to derange the liver. It will be generally admitted, nor would it be difficult to prove, that most persons are in the habit of eating a quantity of food far greater than suffices to maintain the nutrition of the body. Much of this excess is fortunately never assimilated and is got rid of in the fæces; but very often much more is taken into the blood than can be converted into tissue or pass through the ordinary processes of oxydation preparatory to elimination. The result is that the excess of food is thrown out in an imperfectly oxydised form by the kidneys, lungs, etc., or accumulates in the system; while more work is thrown upon the liver than it can readily perform, and functional derangement of the organ ultimately ensues. With regard to individual elements of food, speaking generally, it may be said that the liver is most apt to be deranged by saccharine and fatty substances. The de-

rangement of the liver which leads to lithæmia or gout is more likely to be induced by even small quantities of these substances than by a moderate excess of purely nitrogenous food, such as meat. Cooked articles of diet containing a large proportion of both sugar and fatty matter are in many persons certain to derange the liver. The excess of carbon in these substances must either be deposited as fat or must take away the oxygen, so as to leave little free to act on the nitrogenous matter passing out from the tissues or derived from the food; and hence, as Dr. Bence Jones has observed in speaking of gout, 'with carbonaceous diet in excess, the whole of the uric acid from the tissues might pass off through the blood unoxydised.'<sup>1</sup> There are also constitutional peculiarities with regard to many articles of food, which always derange the liver in certain individuals, though they are comparatively harmless in others.

But of all ingesta the various alcoholic drinks are most apt to derange the liver. They do so in two ways. *a.* They may cause persistent congestion of the liver. Even small quantities of alcohol in healthy persons produce a temporary hepatic congestion; but if alcohol be taken in excess, or too frequently, the congestion of the liver

<sup>1</sup> *Op. cit.*, p. 142.

becomes permanent, and the functions of the organ are deranged. Like results may ensue from comparatively small quantities in certain persons, who may be said to have a constitutional intolerance of alcohol. Of course, if the congestion be long maintained, structural disease may follow. *b.* But wines and other alcoholic drinks often cause derangement of the liver, which a corresponding quantity of pure alcohol would not produce, and which, in fact, cannot be accounted for by any one ingredient of the offending liquid—neither by the free acid, the ether, the salts, gum, sugar, or extractive matter. This general rule, however, I believe holds good, that the injurious effect of alcoholic beverages upon the liver increases in a direct ratio with the amount of sugar plus alcohol which they contain. It would seem, indeed, that a mixture of alcohol and sugar produces injurious results, which would not be caused by the admixture of a much larger quantity of sugar, or of alcohol alone, with the food. In accordance with this view, the alcoholic drinks which are found from experience to be most apt to disagree with the liver are malt liquors of all sorts, but especially porter and the stronger forms of mild ale, port wine, madeira, tokay, malaga, sweet champagne, dark sherries, liqueurs, and brandy; whilst those which are least likely to derange the functions of the organs are

claret, hock, moselle, dry sherry, and gin or whisky largely diluted.

Derangement of the liver from excessive eating or from other errors in diet usually first shows itself in middle life—from thirty-five to forty-five. Young people, who take much exercise, and whose bodies are still undergoing development, require more food, and can often with impunity eat more than they require. But by the age of forty the body is fully developed, and most persons take less exercise than before, while at the same time they often indulge more freely at table. At any age, errors in diet will be all the more likely to tell upon the liver, if there be any constitutional weakness in the functional power of the organ.

2. *A Deficient Supply of Oxygen.*—Insufficient muscular exercise in the open air may derange the functions of the liver. It is well known that sedentary habits and confinement in badly ventilated rooms tend to induce derangements of the liver. It is also a common observation that persons who have eaten and drunk too freely have not suffered from their livers so long as they have led an active life in the open air ; but that, as soon as from change of occupation, or other causes, they take to sedentary habits, without any corresponding change in diet, derangement of the liver ensues. Again, every

sportsman who has suffered from hepatic derangement knows the effect of a single day's hunting or shooting in clearing his complexion and relieving his symptoms. A want of regular exercise in the open air leads to derangement of the liver in two ways; viz., *a*, by causing a deficient supply of oxygen to the system, as the result of which the oxydising processes which go on in the liver and elsewhere are imperfectly performed, and there is a tendency to the accumulation in the system of fat and of the imperfectly oxydised products of disintegrated albumen. Oxygen is, so to speak, the antidote necessary for the destruction of a *materies morbi* (lithic acid, etc.), produced by imperfectly oxydised albumen. *b*. By retarding the circulation of blood through the liver. Since the time of Haller,<sup>1</sup> physiologists have recognised the influence of the respiratory movements in promoting the circulation of blood through the liver; but, upwards of thirty years ago, Mr. Alexander Shaw, in a paper which has attracted too little notice,<sup>2</sup> showed more clearly than ever before that the circulation of blood through the liver was greatly influenced by the alternate expansion and contraction of the thorax during respiration. Mr. Shaw

<sup>1</sup> 'Vires quæ sanguinis per hepar motum accelerant.'—Haller's *Physiologia*, 1764, tome vi. p. 601.

<sup>2</sup> *Medical Gazette*, July 15 and September 30, 1842.

called attention to the fact that the portal vein, without any provision for increasing its power, or any assistance beyond that *vis a tergo* which belongs to the veins generally, and being even destitute of valves to protect it from regurgitation of blood like the veins in other parts of the body, has to perform the duty usually fulfilled by an artery, which, besides receiving an impulse from the heart, is aided in distributing its blood by the contractility and elasticity of its coats. He suggested that this weak power by which the portal vein propelled its blood was compensated for by a suction-force communicated to the current of blood by the actions of respiration : the deeper the inspiration, the greater the force with which the blood rushes by the large veins to the right auricle. These reasonings have been confirmed by certain experiments of M. Bernard, who has found that, when an incision is made into a lobe of the liver in a living animal, the blood may be seen to jet from the mouths of the hepatic veins during the movements of expiration, but to return sucking in air with it at each deep inspiration, so that the animal soon dies from the passage of air into the heart.<sup>1</sup> In persons, then, who lead a sedentary life this auxiliary force for promoting the circulation of blood through the liver is

<sup>1</sup> *London Medical Record*, October 15, 1873, p. 647.

diminished, blood stagnates in the gland, and the functions of the organ are deranged, these results being all the more likely to arise if the liver be at the same time overstimulated by errors in diet.

3. *A high temperature* favours certain functional derangements of the liver, and particularly those relating to sanguification and disintegration of albumen. Functional derangements, as well as congestion and inflammation of the liver, are more apt to occur in tropical than in temperate climates, and in our own country the liver more often becomes disordered in summer and autumn than in winter. The diet which is suitable in a cold or temperate climate in the tropics produces hepatic derangement. These results of a heated atmosphere are, no doubt, due in part to the rarefaction of the air and a corresponding diminution in the supply of oxygen to the system; the hotter the air, the less will be the amount of oxygen in a given volume inhaled by the lungs. But this is, perhaps, not the sole, if the chief, explanation. Experiment has shown that one of the effects of a high temperature upon the lower animals is to produce a degeneration of the parenchyma of the liver, its secreting cells becoming filled with minute granules and presenting appearances similar to those found after death from

febrile diseases.<sup>1</sup> It is possible, then, that some of the functional derangements of the liver from which persons suffer in tropical climates may be owing to similar degenerations, not necessarily permanent, of the secreting cells.

4. *Nervous Influences.*—Many facts show the great influence of the nervous system upon the secreting organs. Sudden fear, or other severe mental emotion, has been known to arrest the secretion of milk and saliva, and we have already seen how injuries and diseases of nerve-tissue may produce diabetes by deranging the glycogenous function of the liver. But many other ailments of the liver besides diabetes have a nervous origin. Prolonged mental anxiety, worry, and incessant mental exertion not only interfere with the proper secretion of bile, but too often derange the processes of sanguification and blood-change, in which the liver is so deeply concerned, and induce lithæmia, with many of the symptoms already described. These results are all the more likely to ensue if the diet has been such as favours hepatic derangement—if, for example, to drown grief, the patient has indulged in stimulants—and the habits have been sedentary. There is also good evidence that nervous

<sup>1</sup> See *Pathological Transactions*, 1873, vol. xxiv. p. 266.



agencies may not only cause functional derangement, but even structural disease, of the liver. Acute atrophy, in which the secreting cells are rapidly disintegrated and the functions of the organ arrested, appears in many instances to have a purely nervous origin; very often the first symptoms of the disease have occurred immediately after a severe fright, or an outburst of passion, in a person previously healthy. An impression made upon the brain appears to be reflected to the liver and to derange its nutrition. Many observations have satisfied me that the extrusion of gall-stones from the gall-bladder, as well as their formation, may be traced to nervous agency. Dr. Budd has also observed that mental anxiety or trouble has 'great influence in the production of gall-stones;'<sup>1</sup> and I have repeatedly known attacks of biliary colic from gall-stones excited by some sudden emotion. Lastly, even cancer of the liver appears sometimes to result from the functional derangement induced in the first instance by mental trouble. I have been surprised at the frequency with which patients suffering from primary cancer of the liver have traced the commencement of their ill-health to indigestion following protracted grief or anxiety. The cases have been far too numerous to be accounted

<sup>1</sup> *Diseases of the Liver*, third edition, 1857, p. 369.

for on the supposition that the mental distress and the cancer have been mere coincidences. A similar observation has, I believe, been made by Sir Robert Christison and by other eminent authorities.

5. *Constitutional Peculiarities.*—In considering the causes of functional derangement of the liver it must not be forgotten that there are constitutional peculiarities—inherited or acquired—in virtue of which the liver is deranged from causes which under ordinary circumstances would be harmless. Most persons, as Dr. Budd observes, have more liver, just as they have more lung, than is absolutely necessary.<sup>1</sup> A portion of their liver may be destroyed by disease, or become less active, without any derangement of the general health. In others, the liver seems only just capable of performing its functions under the most favourable conditions, and it at once breaks down under adverse circumstances of diet, habits, or climate. This innate weakness of the liver is often inherited. The person is born with a tendency to biliary derangements. Gout and diabetes, which we have found to originate in hepatic derangement, are hereditary diseases; and the liver is always very readily disordered in persons who inherit a tendency to gout. This con-

<sup>1</sup> *Op. cit.* p. 55.

stitutional tendency to hepatic derangement is too often lost sight of by patients, and perhaps sometimes by their medical advisers. The habitual use of alcohol is often recommended for various ailments by the medical attendant, without due regard to the tendency of the individual to hepatic derangement, and thus serious consequences may ultimately arise from alcohol taken with a medicinal object. Again, a patient often argues that his liver-troubles cannot be due to what he eats or drinks, because he is most careful as compared with friends who indulge largely and suffer nothing, forgetting the adage: 'One man's food is another man's poison.' One man, for instance, may drink a bottle of wine and be none the worse, whereas another has his liver deranged by a single glass.

6. *Poisons* of various sorts may derange the liver, the persistence of the derangement depending upon the length of exposure to the cause. One of the first effects of the poisons of the various specific fevers is upon the liver. Again, from protracted exposure to malaria, the liver often becomes deranged, anæmia and lithæmia being the results. While some cases of acute atrophy of the liver have a nervous origin, there is good evidence that others are caused by a poison taken into the body from without, or sometimes, as suggested by Dr. Budd, 'engendered in

the body by faulty digestion and assimilation.' Phosphorus also, in sufficient doses, is known to derange the functions of the liver; and one result of phosphorus-poisoning is the production of symptoms and structural changes in the liver closely resembling those of acute atrophy.<sup>1</sup> Various substances also taken as food, or by mistake along with food, may induce functional disturbance of the liver, the poisonous effect being often determined by some constitutional peculiarity of the individual.

These causes of functional derangement of the liver will, of course, act more injuriously if the functions of the liver be already disordered by structural disease, by disease of the heart or lungs, or by derangements of the stomach and bowels.

#### D.—TREATMENT OF FUNCTIONAL DERANGEMENTS OF THE LIVER.

The time at my disposal only permits me to give a brief sketch of the general principles on which functional

<sup>1</sup> Lead is known to cause an accumulation of lithic acid in the system, but apparently by impeding its excretion by the kidneys, rather than by increasing its formation in the liver. (See Garrod, *op. cit.*, p. 292.) Bence Jones, on the other hand, maintains that the accumulation of lithates in the system produced by lead is to be ascribed to diminished oxydation. (*Lectures on Pathology and Therapeutics*, p. 289.)

derangements of the liver ought to be treated ; and my remarks will be for the most part restricted to the derangements resulting from abnormal disintegration and abnormal elimination.

1. *Diet.*—In functional derangements of the liver, much more permanent benefit is to be expected from careful regulation of the ingesta than from physic. It must not be forgotten that what may ultimately destroy the body too often enters by the some portal as that which is intended to nourish and maintain it, and that for the maintenance of health it is necessary for most persons to put a curb upon their appetites. To use the words of the late Sir Benjamin Brodie, ‘We are all anxious to obtain rank, reputation, and wealth ; but that for which we have most reason to be anxious, not only for our own sake, but also for that of others, is such a state of our bodily functions as will enable us to make use of our higher faculties, and promote in us happy and contented feelings. . . . The agricultural labourer who has enough of wholesome food and warm clothing for himself and his family, and who has the advantage of living in the open air, has more actual enjoyment of life than the inheritor of wealth living in a splendid mansion, who has too much of lithic acid in his blood.’<sup>1</sup> It is also

<sup>1</sup> *Psychological Inquiries*, second edition, 1855, p. 76.

well to remember that the hepatic derangement resulting in lithæmia may exist for years without any other symptom than the frequent deposit of lithates or lithic acid in the urine, and is then curable by attention to diet alone ; but that, if neglected, it may ultimately develope gout, structural disease of the liver or kidneys, or some other serious malady. Habitual lithæmia ought, therefore, to be always counteracted, and, from what has been already stated, it seems clear that the foods mainly to be avoided are saccharine and oleaginous articles, and especially cooked dishes containing both of these substances. Patients with lithæmia ought always to avoid made-up or highly seasoned dishes. In severe cases, potatoes, rice, sago, and fruits may have to be given up, and even bread must be taken in moderation. It will also always be well to ascertain if the lithæmia be due to any of those idiosyncrasies in virtue of which particular articles of diet are apt to derange the liver. In most cases of lithæmia, a diet consisting chiefly of stale bread, plainly cooked mutton, white fish, poultry, game, eggs, a moderate amount of vegetables, and weak tea, coco, or coffee answers best ; while in others the patient enjoys best health on a diet composed of milk, farinacea, vegetables, eggs, and occasionally fish. The quantity, as well as the quality, of the food must be attended to. Habitual lithæmia often results from the

patient taking more food than can be converted into tissue or disintegrated in the liver. As Dr. Bence Jones has observed with regard to gout, so in habitual lithæmia, 'a minimum of albuminous food should be taken, in order to produce the least uric acid; and a minimum of carbonaceous food, in order to allow the uric acid to be oxydised as much as possible.'<sup>1</sup> In obstinate cases, the patient may be advised to take his principal meal in the morning, when the digestive powers are strongest. The free use of diluents, such as soda and seltzer waters, is also useful, as they help to eliminate from the system the morbid products of disintegration.

Still greater caution is necessary in all forms of lithæmia as to alcoholic stimulants. Malt liquors, port wine, champagne, and many other wines, ought to be strictly prohibited. Claret, or a small quantity of spirit largely diluted, as a rule, answers best; but even these should be taken sparingly, and many patients do best with no stimulants at all. This is not the occasion to discuss whether alcohol is necessary for the nutrition of the body in persons subjected to much mental or bodily toil, or whether, taking the masses in all walks of life, the standard of health would be better maintained by teetotal

<sup>1</sup> *Op. cit.*, p. 142.

habits or by a moderate use of alcohol. What I desire now to insist upon is, that alcoholic drinks in quantities usually regarded as compatible with, if not conducive to, health, and far short of what are necessary to affect the brain, in many persons undermine the foundations of health by deranging the liver; and that, to some individuals, even very small quantities are injurious. In persons who have been indulging largely, the risk of a sudden withdrawal of stimulants is less, I believe, than is commonly imagined. Unless there be evidence of a very weak heart, which itself may be the result of alcohol, the only unpleasant effects of sudden and complete abstinence, in my experience, have been sensations of sinking at the epigastrium and craving for alcohol, which a repetition of the stimulus has only temporarily relieved and has rendered more persistent.

2. *A Free Supply of Oxygen.*—Next to careful regulation of diet, this is the most important object to be aimed at in the treatment of functional derangement of the liver, and especially in that which induces imperfect disintegration of albumen. An excess of fresh air, indeed, will often counteract the bad effects of too large a quantity of food. Although recent observations, more especially those of Parkes, have shown that the common impression that muscular exercise materially increases the elimination



of nitrogen from the body, is erroneous, there can be no doubt that exercise in the open air quickens the circulation of blood through the liver, in the manner already explained, and promotes oxydation, and that, by thus preventing the accumulation in the system of the imperfectly oxydised products of albumen, it operates beneficially in the treatment of functional derangement of the liver attended by lithæmia. The observations of Beneke and other authorities have shown that *sea-air* is an oxydising agent of great power, and that nitrogenous and sulphur-holding tissues more rapidly disintegrate under its influence.<sup>1</sup> Accordingly we find that many patients with hepatic derangement and lithæmia derive immense benefit from residence at the sea-side and sea-bathing, although unfortunately the good effects of sea-air are sometimes more than counterbalanced by unhealthy lodgings or improper and badly cooked food.

3 *Aperients; Cholagogues.*—In a large number of cases of functional derangement of the liver, great advantage is derived from the frequent use of aperient medicines, whether there be a tendency to constipation or not. Aperients bring away not merely bile, but the products of disintegration contained in the fluid circulating between

<sup>1</sup> Parkes *On Urine*, 1860, pp. 115, 129.

the liver and bowel prior to their further elaboration and elimination by the lungs and kidneys. Saline aperients, from the promptness of their action and the large quantity of watery exhalation from the bowel which they bring away, are among the best for the purpose now mentioned. Recourse is usually had to the sulphate of magnesia (Epsom salt), the sulphate of soda (Glauber salt), or the tartrate of potash and soda (Rochelle salt), or to various combinations of these salts with chloride of sodium, carbonate of soda, and other alkaline salts, such as are found in the mineral waters of Carlsbad, Friederichshall, Püllna, Harrogate, or Cheltenham, or in the recently discovered Hungarian spring, Hunjadi János. Daily experience shows the great benefit derived by patients with lithæmia from a course of one or other of these mineral springs, or from some artificial imitation of them, all of which are best taken with warm water, and in the morning fasting. All of these salts have little or no affinity for animal textures, so that they excite few changes in them; they cause very little irritation of the mucous membrane of the bowel, and do not excite peristalsis, so that they purge without producing griping or pain. They act apparently by preventing the re-absorption of the fluid which is constantly being exhaled from the blood-vessels into the bowel.

There are certain other aperients which have long enjoyed a great reputation for promoting the secretion and discharge of bile, and otherwise acting beneficially in derangements of the liver, and which have accordingly been designated *Cholagogues*. Among these remedies, *mercury* and its preparations hold a pre-eminent place. At the present day mercury has lost much of its former reputation as a cholagogue and alterative, and there is much difference of opinion as to its power over the liver. The practical physician gives a dose of calomel, finds the quantity of bile in the motions greatly increased, and his patient's state much improved; and he argues that the liver has been stimulated by the mercury to an increased secretion of bile, and that to this cause his patient's improvement must be ascribed. The physiologist, on the other hand, ties the common bile-duct in one of the lower animals, produces a fistulous opening into the gall-bladder, and then finds that calomel has no effect on, if it do not diminish, the amount of bile that drains away through the fistula. It may interest some who are present if I refer briefly to the principal of these experiments.

Kölliker and Müller, in 1855, tried the effects of calomel upon the secretion of bile in a dog with a biliary fistula. The results were somewhat contradictory. Once the bile seemed to be increased, and twice

it seemed to be diminished, by the administration of calomel.<sup>1</sup>

Of four experiments made in 1858 on a dog with a biliary fistula, Dr. George Scott found that in all the administration of large doses of calomel was followed by a diminution of fluid bile and of bile-solids.<sup>2</sup>

In the same year (1858), Dr. Mosler made similar experiments upon two dogs with biliary fistulæ. The administration of calomel was not followed by any increase of bile, nor could mercury be detected in the biliary secretion.<sup>3</sup>

Ten years later (1868), a committee of the British Medical Association, with Professor Hughes Bennett of Edinburgh as chairman, made a number of similar experiments on dogs, and came to the conclusion that 'mercury did not increase the flow of bile, but rather diminished it.'<sup>4</sup>

The most recent experiments are those of Dr. Röhrig of Kreuznach, made in the Pathological Institute of Vienna. He found that, although large doses of calomel did seem to increase somewhat the secretion of

<sup>1</sup> *Wurzburg Verhandlungen*, Bd. v., 1855, s. 231.

<sup>2</sup> Beale's *Archives of Medicine*, 1858, vol. i. p. 209.

<sup>3</sup> *Virchow's Archiv.*, 1858, Bd. xiii. s. 29.

<sup>4</sup> *British Medical Journal*, 1868, vol. ii. pp. 78, 176, 191.

bile, its power to do so was inferior to that of croton oil, colocynth, jalap, aloes, rhubarb, senna, and sulphate of magnesia, the cholagogue power of these drugs diminishing very much in the order in which they have now been enumerated, and calomel standing at the bottom of the scale.<sup>1</sup>

These results of experiments upon the lower animals have added greatly to the discredit previously thrown upon mercury by its failure, when brought to the test of accurate clinical observation, to absorb plastic lymph in most forms of inflammation ; and some eminent physicians are even of opinion that mercury and its preparations ought to be erased from our Pharmacopœia.<sup>2</sup> On the other hand, it has been fairly objected that the results of experiments with mercury upon dogs do not warrant conclusions as to its effects upon man ; and, even granting that in man mercury does not increase the quantity of bile secreted by the liver in health, it does not follow that in disease there may not be some condition adverse to the formation of bile, which mercury may have the power of removing. Much, however, of the difference of opinion between the physiologist and the practical physician may be reconciled by keeping in mind the

<sup>1</sup> Stricker's *Jahrbuch*, 1873, part 2.

<sup>2</sup> See Bennett, *British Medical Journal*, 1868, vol. ii. p. 176.

osmotic circulation, to which I referred in my first lecture, as constantly going on between the intestinal contents and the blood. A large part of the bile secreted by the liver and thrown into the bowel is constantly being re-absorbed, to reach the liver again; and accordingly, when the common bile-duct is tied and a fistulous opening into the gall-bladder established, the quantity of bile which escapes from the fistulous opening immediately after the operation is much greater than at any time subsequently (Schiff). Mercury and allied purgatives produce bilious stools by irritating the upper part of the bowel and sweeping on the bile before there is time for its re-absorption. The fact of mercury standing at the bottom of the scale of cholagogues in Röhrig's experiments is accounted for by its surpassing other cholagogues in this property; for of course the larger the quantity of bile that is swept down the bowel, the less is re-absorbed and the less escapes from a biliary fistula. That mercury does act especially upon the duodenum, is proved not merely by the large flow of bile which follows its action, but by the fact discovered by Radziejewski, that leucin and tyrosin, which are products of pancreatic digestion, under ordinary circumstances decomposed in the bowel, appear in the fæces after the administration of mercurials. It would appear, then, that mercury, by

increasing the elimination of bile, and lessening the amount of bile and of other products of disintegrated albumen circulating with it in the portal blood, is after all a true cholagogue, relieving a loaded liver far more effectually than if it acted merely by stimulating the liver to increased secretion, as was formerly believed, and as some authorities still maintain; for in this case it might be expected to increase, instead of diminish, hepatic congestion.<sup>1</sup> It is not impossible, also, that the irritation of the duodenum by calomel and other purgatives may be reflected to the gall-bladder, and cause it to contract and discharge its contents, and thus account in part for the increased quantity of bile in the stools.

There are likewise, I believe, grounds for believing that, apart from its increasing the discharge of bile from the bowel, mercury exerts a beneficial action in many functional derangements of the liver, in whatever way this is to be explained. Patients of the greatest intelligence suffering from hepatic disorders constantly declare that they derive benefit from occasional or repeated doses of

<sup>1</sup> This view as to the action of mercury upon the liver has been taught by me in my lectures for many years, and was enunciated in my *Clinical Lectures on Diseases of the Liver*, published in 1868, pp. 126, 309, 404.

mercurials, which no other medicine or treatment confers; and the scepticism of the most doubting physician would, I believe, be removed, should he unfortunately find it necessary to test the truth of their statements in his own person. It is not impossible that the good effects of mercury on the liver, and in some forms of inflammation, may be due to its property of promoting disintegration. Mercury appears to have the power of rendering effused fibrin less cohesive, and so more easily removed by absorption, than it otherwise would be.<sup>1</sup> Modern physicians of high standing, and little likely to be accused of credulity as to the beneficial action of drugs, have thought that mercury is useful in croup, by causing a degradation and disintegration of the plastic membrane. If this be so, it seems not improbable that mercury, which from experiments<sup>2</sup> we know to reach the liver, may under certain circumstances act beneficially by promoting, or in some way influencing, the disintegration of albumen. The remarkable effect of mercury on constitutional syphilis probably admits of a similar explanation. But in whatever way it is to be explained, the clinical

<sup>1</sup> Bence Jones, *op. cit.*, p. 283.

<sup>2</sup> Authenrieth and Zeller found mercury in the bile of animals treated with mercurial frictions. (*Budd, op. cit.*, p. 57.)



proofs of the efficacy of mercury in certain derangements of the liver are to my mind overwhelming. I say so the more advisedly, because I was taught to regard mercury as a remedy worse than useless, not only in hepatic diseases, but in syphilis ; it cannot, therefore, be said that the convictions forced upon me by experience are the result of preconceived opinions.

*Podophyllin* is a remedy which seems to act in a very similar manner to mercury. Dr. Anstie's experiments with it on dogs and cats show that it has a special affinity for the small intestines, and especially for the duodenum. So far as my experience goes, it is less certain in its action, and even in moderate doses more likely to cause griping and mucous stools, than the preparations of mercury. It is a good substitute however, for mercury, when from any cause this is contraindicated.

*Colocynth, Aloes, Rhubarb, Senna, and Jalap* are also useful aperients in functional derangements of the liver resulting in lithæmia, constipation, or deficient excretion of bile. The experiments of Röhrig seem to show that they actually increase the amount of bile secreted by the liver. *Colchicum* also is a useful adjunct to other aperients, in cases of liver derangement with lithæmia. According to Dr. Garrod, it 'may often be given with advantage to gouty subjects as a cholagogue in lieu of

the preparations of mercury,'<sup>1</sup> which, I may add, are often contraindicated in chronic gout with renal disease.

With these remedies we may include *Taraxacum*, which has long been thought to exercise a specific action upon the liver, but which probably acts mainly as a mild aperient. When there is a tendency to constipation, it may be advantageously combined with either alkalies or mineral acids.

4. *Alkalies*.—Next to aperients, alkalies are the most useful drugs in the treatment of functional derangements of the liver. In lithæmia and in many of the symptoms which spring from this morbid state, the greatest benefit is often derived from a course of alkalies—such as the alkaline salts of potash, soda, or lithia, or some of the alkaline mineral waters, such as those of Vals, Vichy, or Ems. The comparative worth of the different alkalies for neutralising acids varies considerably. One grain of carbonate of lithia or of carbonate of ammonia is nearly equal to a grain and a half of carbonate of soda or two grains of carbonate of potash. The beneficial effects of alkalies in derangements of the liver are not due to their neutralising acidity, or to any direct action upon lithic acid. It is, in fact, in the form of lithate of soda that

<sup>1</sup> *Op. cit.*, p. 410.

lithic acid is met with in gouty persons. Alkalies seem to do good by combating the pathological state, on which the formation of lithic acid depends. They are believed to promote oxydation, and thus increase the disintegration of albumen. Dr. Bence Jones tells us that in the body as well as out of it alkalies furnish the most marked evidence of assisting in oxydising actions.<sup>1</sup> The experiments of Parkes with liquor potassæ seemed to show that it had the power of increasing the disintegration of the sulphur-holding materials of the body. The effect of its administration was to increase the amount of sulphuric acid and also of urea in the urine; although, with characteristic caution, Parkes adds that the increase of urea as the result of the potash was rendered probable, rather than proved, by his experiments.<sup>2</sup> From experiments on dogs with biliary fistulæ, Nasse was led to the conclusion that carbonate of soda taken with the food diminished greatly the secretion of bile;<sup>3</sup> and a similar result has been observed by Röhrig to follow the introduction of the same salt into the intestine or the veins; the diminution affected the solids as well as the water of the bile, and especially the biliary salts. Nasse also found that after taking two drachms of carbonate of soda

<sup>1</sup> *Op. cit.*, p. 280.

<sup>2</sup> *On the Urine*, 1860, p. 151.

<sup>3</sup> *Archiv. für Wissensch. Heilkunde*, 1864, Bd. vi. p. 508.

the urine (human) was very rich in hippuric acid. The only inference at present to be drawn from these experiments is, that alkalies exert a powerful influence over the chemical changes going on in the liver. When alkalies are employed in lithæmia, it is well to suspend their use occasionally, as they are apt, when long continued, to derange the gastric digestion ; but in cases where they are strongly indicated they are better tolerated than is usually thought. In the fifth volume of the *Medico-Chirurgical Transactions*, Dr. Bostock has recorded the case of a young lady who for months took carbonate of soda to the amount of two ounces and a half daily. The appetite and strength were much improved ; and her blood, instead of being thin, coagulated firmly, the coagulum being strongly buffed and cupped.

5. *Chlorine, Iodine, and Bromine* are closely related in their chemical properties, and are believed to promote oxydation in the body by taking hydrogen from water and liberating oxygen. An aqueous solution of chlorine is of service in certain cases of lithæmia associated with general debility ; and we know that the various salts of chlorine enter largely into the composition of the mineral waters which are most useful in hepatic derangements. Bromide of potassium will reduce certain enlargements of the liver and spleen, and may be given with advantage in cases of

lithæmia associated with congestion of the liver and want of sleep. But among the remedies of this class the chloride of ammonium holds a pre-eminent place. It has obtained a great and well-deserved reputation in India and other tropical countries for the treatment of hepatic congestion ; and I have found it of great service in the functional derangement of the liver attended by lithæmia. Given in scruple doses three times a day, it acts as a diaphoretic and diuretic, and exercises a powerful influence in relieving the portal circulation. It is not oxydised, but passes out of the system unchanged in the urine. According to Böcker's experiments,<sup>1</sup> it increases the nitrogenous solids of the urine ; the mean daily increase of urea under its use he found to be not less than seventy-four grains—a quantity indicating a vast augmentation either of metamorphosis or of elimination, but from its beneficial effect on the liver, most probably of the former. Chloride of ammonium has this advantage, that it may be combined with either alkalies or mineral acids.

6. *Mineral Acids* are employed by many physicians in the treatment of functional derangements of the liver. Nitric acid especially has long been thought to have the

<sup>1</sup> Parkes, *op. cit.*, p. 165.

power of augmenting the flow of bile ; but there is no good evidence of this, either clinical or experimental. According to my experience, the action of mineral acids upon the liver is much less direct than that of alkalies. In all morbid states of the liver attended by congestion, and in most cases of lithæmia, I have found that they either did no good or they aggravated the symptoms. They may, however, be of service when there is debility and want of tone ; but the chief good which they effect is probably that of improving the gastric digestion. In some cases, both acids and alkalies may be given advantageously—the alkalies before, and the acids after, a meal.

7. *Tonics*.—Clinical experience shows that, notwithstanding the existence of debility and anæmia, tonic remedies are apt to disagree in many cases of functional derangement of the liver. This remark applies especially to the functional derangement resulting in lithæmia. I have repeatedly known patients in this state improve at once on substituting abstinence from alcohol, with aperients, blue pill, alkalies, and careful regulation of diet, for quinine, iron, the mineral acids, and stimulants ; the strength, flesh, and colour returning under what at first sight might have appeared a lowering treatment. Different opinions have been expressed with regard to the utility

of iron in chronic gout. According to Dr. Bence Jones, iron is one of the two most potent remedies we possess for indirectly promoting oxydation in gout as well as in other maladies ;<sup>1</sup> whereas, in Dr. Garrod's opinion, the preparations of iron are very likely, when indiscriminately given to gouty subjects, to excite a paroxysm of the disease, and for the most part are contraindicated.<sup>2</sup> My experience coincides with that of Dr. Garrod ; and in simple lithæmia I have constantly known iron to increase the tendency to deposits of lithates in the urine, constipate the bowels, and aggravate any symptoms from which the patient may have previously suffered. As a rule, also, I have found that patients with chronic gout or with lithæmia do not tolerate even small doses of quinine. From some careful experiments made by Dr. Ranke of Munich, quinine appears to have the power of diminishing the amount of lithic acid in the urine.<sup>3</sup> The experiments were made on three persons, and the results were uniform. The effect continued for about two days after a single dose of twenty grains ; and there was no evidence of any increased excretion after the effect of the quinine had passed off, so that probably the quinine acted by lessening the formation of lithic acid in the liver, or by

<sup>1</sup> *Op. cit.*, pp. 143 and 279.

<sup>2</sup> *Op. cit.*, p. 453.

<sup>3</sup> Parkes, *op. cit.*, p. 167.

substituting some other substance for it. From these experiments it might be inferred that quinine and bark should be of essential service in chronic gout and in lithæmia, but this inference is opposed to clinical experience.<sup>1</sup>

When tonics are given in lithæmia, gentian, chiretta, cascarilla, and serpentaria are preferable to quinine and other preparations of bark. The best preparations of iron are the reduced iron, the citrate of iron, or the tartrate of iron and potash; these preparations are sometimes advantageously combined with alkalies and saline aperients. In many cases, whether attended by flatulence or not, I have seen great relief follow the use of small doses of nux vomica or strychnia. In cases of lithæmia attended by great nervous prostration I have also seen advantage follow the use of phosphorus in doses of one-thirtieth of a grain three times a day. The lithates have disappeared from the urine, and all the symptoms have improved. In some of these cases the circumstances seemed to leave no doubt that the improvement was due to the phosphorus. Many patients also with lithæmia who cannot take iron derive benefit

<sup>1</sup> Ranke's experiments have been repeated by Dr. Garrod, who found that quinine did not materially influence the excretion of lithic acid.—*Garrod, op. cit.*, p. 451.



from arsenic, which has long been known to be of service in some of the complications of gout.

8. *Opium* and its preparations are contraindicated in most functional derangements of the liver, and particularly when there is evidence of lithæmia. Opium impedes elimination both by the bowels and kidneys, and also appears to check the disintegrative processes which go on in the liver. It is generally believed to diminish the amount of bile secreted by the liver; and this view is favoured by the light-coloured stools which often follow its use. The result, however, of Röhrig's experiments on animals with biliary fistulæ was to show that opium increased the secretion of bile instead of diminishing it, so that probably the discharge of bile from the liver is only temporarily suspended by a similar influence on the coats of the bile-ducts to that which opium exerts on the coats of the bowel. Be this as it may, there can be no doubt that opium constipates the bowels, favours portal congestion, and checks the elimination, not only of bile, but of the products of disintegration which go on in the liver. The experiments of Böcker<sup>1</sup> and clinical experience alike show that opium impedes the elimination of the nitrogenous solids of the

<sup>1</sup> Parkes, *op. cit.*, p. 167.

urine, and that dangerous and even fatal consequences ensue from its employment in structural diseases of the kidneys. These considerations explain why in hepatic derangement, attended by lithæmia, opium is contraindicated for the relief of pain, sleeplessness, or other symptoms for which it is commonly prescribed.

On the other hand, in the functional derangement of the liver which exists in diabetes opium is tolerated in large doses, and is often of signal service in checking the formation of sugar.<sup>1</sup> Its good effect is probably in great measure due to some influence on the vaso-motor nerves of the hepatic vessels, a reflex paralysis of which we have found to be one of the causes of diabetes.

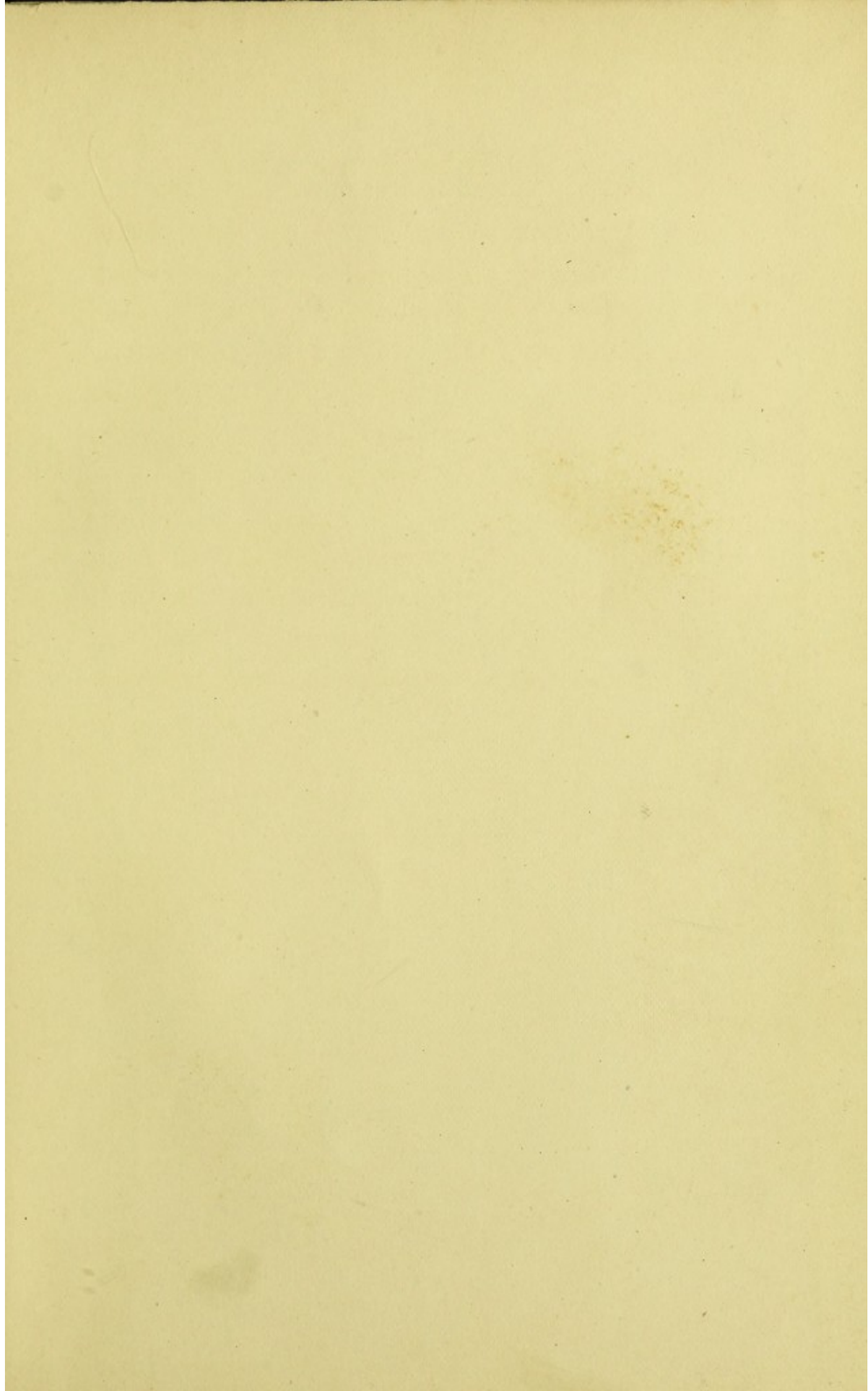
In bringing these lectures to a close, I beg to tender to you, Mr. President, and to the Censors' Board my thanks for the honour you have done me in appointing me to deliver them. I am very sensible of their manifold imperfections, and in apology can only plead a multiplicity of other engagements during the brief period

<sup>1</sup> This is no new discovery. Sixty years ago, Sir Benjamin Brodie communicated to the Royal Medical and Chirurgical Society a case of diabetes treated with opium. Twenty-four grains of opium were taken in the day with the effect of reducing the urine from twenty-five to seven pints, but without any of the usual effects of opium.—*Medico-Chirurgical Transactions*, vol. v. p. 236.

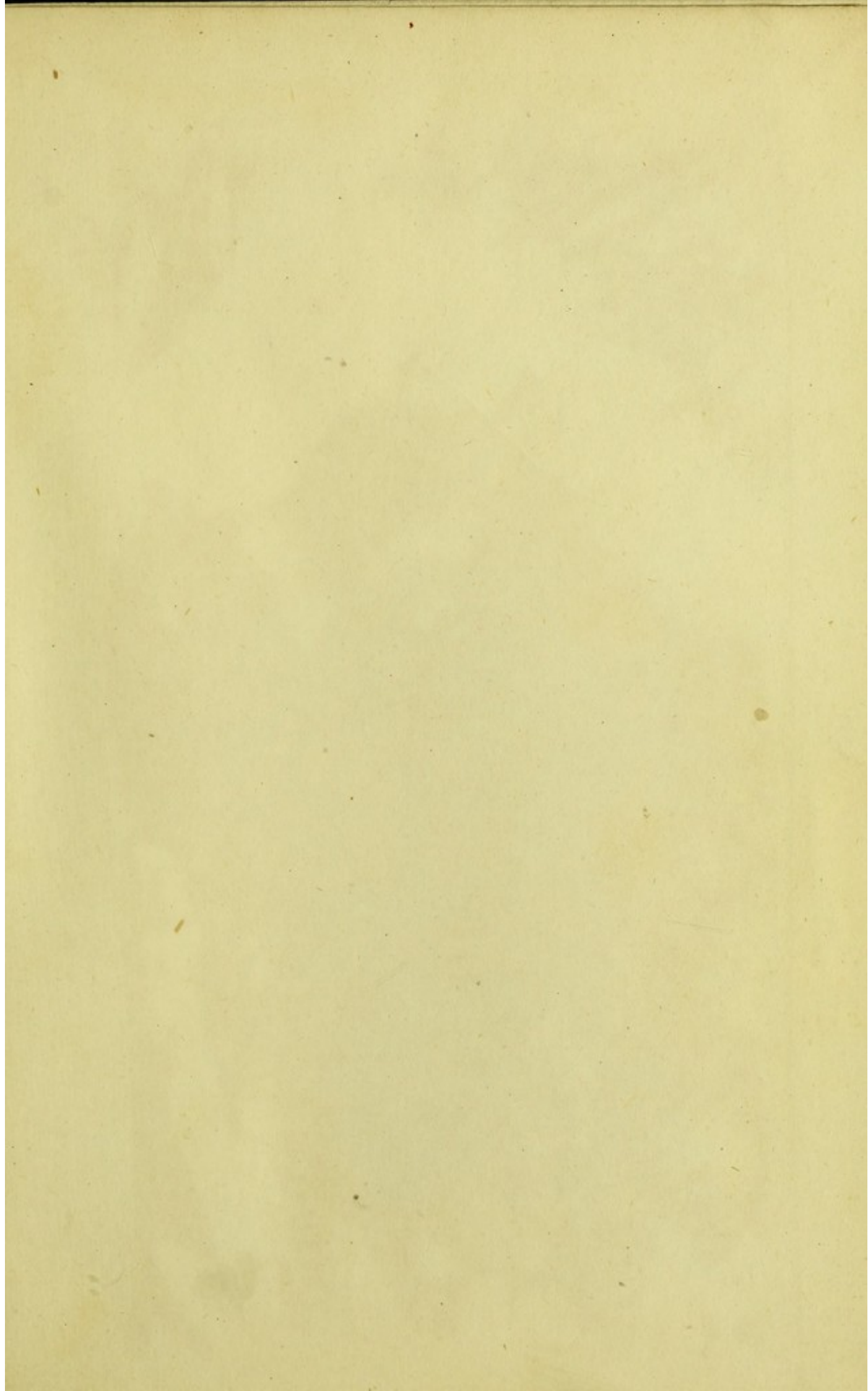
allotted to their preparation. I am well satisfied, however, as to the great importance of the subject which I have brought before your notice, and that it is one worthy of more attention from the Fellows and Members of this College, and from the profession generally, than it has yet received. The day, I believe, will come when, with a more perfect knowledge than we now possess of the healthy functions and of the signs of functional derangement of the liver, we shall be enabled to prevent, or to arrest at their commencement, many of the most serious ailments to which mankind are liable, and thereby to add another chapter to the volume of Preventive Medicine.

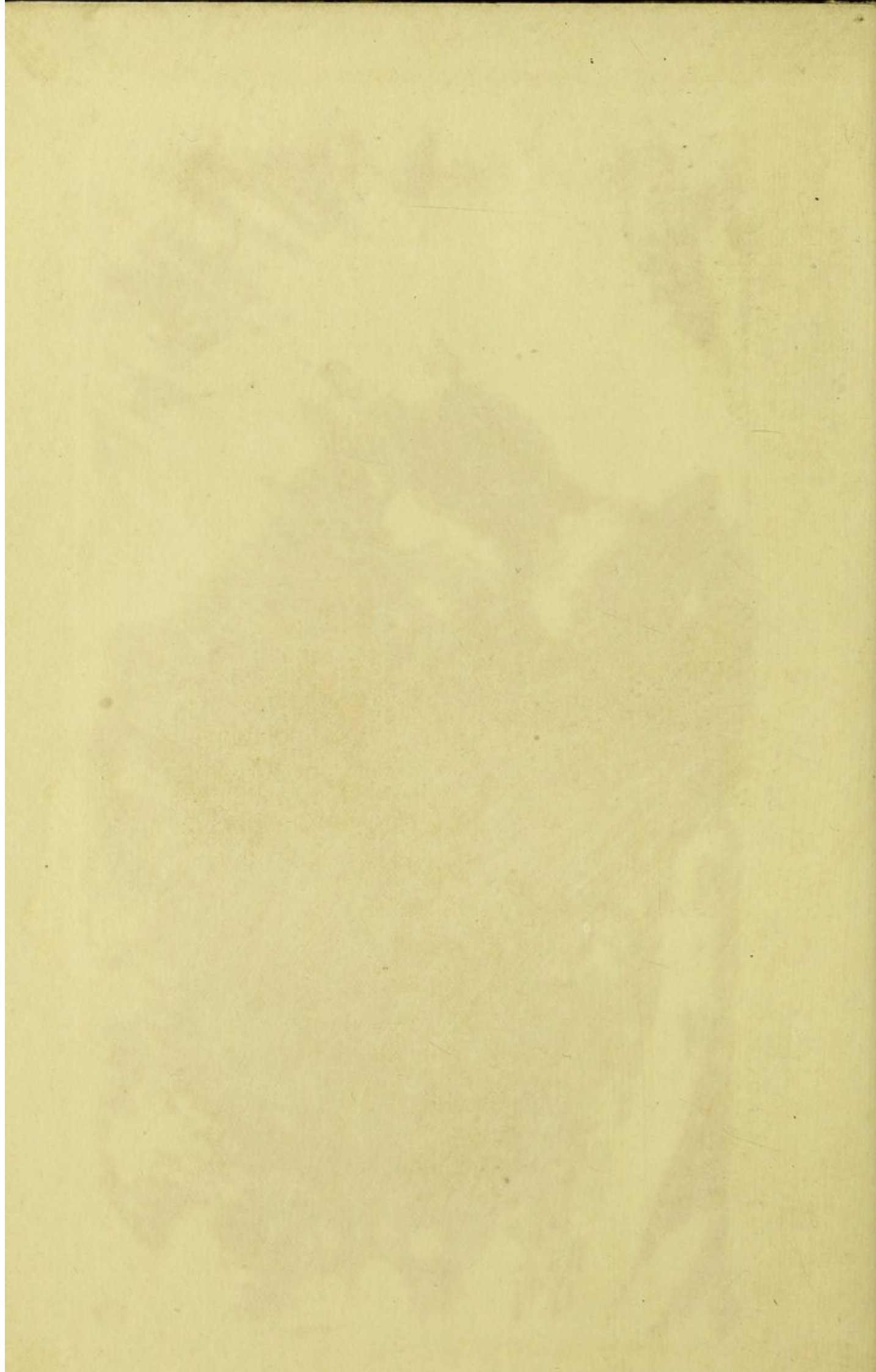
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