single projection alluded to be conspicuous—in which case, there will always be a somewhat sharp, angular margin—it is, in my opinion, best to get rid of it at the time of the operation. In my own practice, I was at one time in the habit of cutting the projection away with sharp small bone-forceps, dividing gum and bone at the same time, and aiming chiefly at getting rid of the projection. This usually involved all the intermaxillary bone on that side, and implied, perhaps, little heed of what damage might be inflicted on the sound side, although, latterly, I always passed the blades into the mesial line between the intermaxillary bones, so as to secure this side from material injury. In the course of my experience, I fancy that I refined on this practice. I found that it was well to detach the portion as high up towards the nostril as could conveniently be reached, and here I discovered that, in all young subjects, there was only cartilage to be divided. This could easily be done with the knife or scissors, and so, for many years, I have used only one or other of these instruments. Usually, I have passed the scalpel through the mucous membrane, under the frænum, up between the bones, and divided the cartilage, periosteum, and gum, to sever the part; and thus the use of cutting bone-forceps has been dispensed with, for, to say the least, such an instrument is coarse-like and clumsy in an operation for hare-lip on an infant only a few weeks old.

Whilst I can offer little objection to this proceeding, I fancy that I have recently fallen on one equally efficacious and void of certain objections which, I think, might be urged against it. Instead of this sweeping wholesale abstraction, I content myself with making an incision, vertical, sloping, or horizontal, with a scalpel through the mucous membrane and periosteum, over the projecting piece of bone; with a few touches of the knife, or a little squeeze with finger and thumb, I so separate these tissues as to permit the entrance of a gouge of a quarter or three-eighths of an inch in breadth, with which I scoop out the body of the milk incisor-tooth in as far as it is formed, taking no heed of the cyst or of that of the permanent one, and even cut out such wall of bone as may be there; usually, at four or eight weeks, only small plates of bone. In this way, the hard projection is removed, and the tissues that remain offer no obstruction to the union of the junction of the lip in front, whilst the operation, as it appears to me, is less destructive, therefore more conservative, in character. There is thus left only the mucous membrane, with possibly some periosteum, which form a soft cushion behind the wound in the lip, and so the remaining intermaxillary bone is not divested of covering so thoroughly as when cutting instruments are passed in the mesial line to take all away on the offending side.

I have now adopted this plan in several cases, and have been much pleased with the effect and result. In one instance, I used a silk stitch to hold the edges of the wound in the mucous membrane together, but I doubt if it be needful, and I have not seen any spurt of blood from the deep part of the wound, such as that which I have often found, in other instances, has required the application of a pointed heated cautery. The wound has healed without attracting special notice. In the case where the stitch was used, the thread came away spontaneously, and, in the end, the gum appeared as if there had been no projection, and, therefore, no such operation.

[To be continued.]

CLINICAL MEMORANDA.

FRACTURE OF THE INDEX FINGER FROM MUSCULAR ACTION.

A SINGULAR accident occurred in the out-patient practice of Charing Cross Hospital to-day (March 16th), namely, fracture of the proximal extremity of the index finger of the left hand, as a result, presumably, of muscular action. A man, 55 years of age, in making a back-handed blow at his retreating son, as far as I can understand, just missed striking him, thereby expending the extreme radial extension of his wrist without meeting with the expected amount of resistance. He immediately experienced great pain and loss of power over the hand, and, on his coming for advice, it was evident what had occurred; the fragment, which was freely movable beneath the skin, was drawn upwards by the extensor carpi radialis major, and powerfully abducted by the lower fibres of the first dorsal interosseous muscle; and, when these muscles were put in action, the deformity was singularly apparent. The line of fracture being considerably beyond the reflection of the synovial membrane, it is not probable that further complication will follow. When one takes into consideration the mode of development of the bone, the accident appears the more remarkable. The treatment was sufficiently obvious.

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THE CROONIAN LECTURES ON FUNCTIONAL DERANGEMENTS OF THE LIVER.

Delivered at the Royal College of Physicians.

By CHARLES MURCHISON, M.D., LL.D., F.R.S.,
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LECTURE I.

Notice of Dr. 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; Cholestæramia.

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 29th, 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 sanguification. 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 separanda, sed, si sanguinem conficiendum spectemus, funeratum creditur. Ivisus illi exsequias, nunquam redituro. Nam”

Facilis descensus Averni,
Sed revocare gradum, superasque evadere ad auras,
Hoc opus, hic labor.”*

Although it was *a 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 fœtus 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. For example, our late learned colleague Dr. Copland, one of the few modern medical authors who has 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 ;† 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 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 ;‡ 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 know-

ledge 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 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).§ 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 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,† into which it is believed by Bernard and most other physiologists to be reconverted through the action of an albuminoid ferment in the liver or in the blood, or transformed in some other way, it enters the blood by the hepatic veins.

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 fetal tissues, such as cartilage, muscle, and the epithelial cells of the skin ;‡ and it is also present in the inflammatory products of pneumonia, and in new growths 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.§ 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

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

† 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).”

‡ *Journal de Physiologie*, 1859, tome ii.

§ *Med. Chem. Untersuch.*, 1871, p. 486.

* *Defensio rasonum lacteorum et lymphaticorum adversus F. Riolanum*. Haf-nice, 1655, p. 8.

† *Medical Dictionary*, ii, 723.

‡ *Versuche über die Wege auf welchen Substanzen aus dem Magen und Darm Canal im Blut gelangen*. Heidelberg, 1820.

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;* 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.† 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, 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.‡ 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. McDowell 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 circulation.§ 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.|| 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.¶ According to Bernard, this destruction of sugar in muscle is due to lactic fermentation.**

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 contains much fibrin, blood from the hepatic vein contains little or none.†† 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.‡‡ 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.* 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)†, while the researches 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.‡ 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.§ Thirty years ago, our colleague Dr. Parkes examined the urine in a number of cases of hepatitis and 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.|| 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.¶ Lastly, there are grounds, to be referred to presently, for 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."*** 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,†† 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 .08 gramme of urea in 100 cubic centimètres; but, after passing through the liver once, it contained .14 gramme, and, after passing through the liver four times, 0.176 gramme. 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.‡‡ 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

* Sanderson, *op. cit.*, p. 498.

† 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, *St. Bartholomew's Hospital Reports*, vol. ix, 1873.

‡ G. Budd, *op. cit.*, p. 34; Sanderson, *op. cit.*, p. 499. "The very close resemblance of urine-pigment to bilifulin 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.)

§ Parkes, *On the Urine*, 1860, p. 330.

|| *On the Dysentery and Hepatitis of India*, by F. A. Parkes, 1846.

¶ Frerichs' *Klinik der Leberkrankheiten*, New Sydenham Society's Translation, vol. i, p. 221; Murchison, *Clinical Lectures on Diseases of the Liver*, 1863, p. 229.

** Henle's *Zeitsch. für rationelle Medicin*, Bd. xxxi, p. 246.

†† *Lancet*, 1871, vol. i, p. 460.

‡‡ *Centralblatt für die Med. Wissenschaften*, August 1870, p. 580.

* See McDonnell's *Observations on the Functions of the Liver*. Dublin, 1865.

† Müller's *Archiv*, 1856, and Carpenter's *Principles of Human Physiology*, 7th edition, p. 228.

‡ 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.

§ *Op. cit.*

¶ F. W. Pavy, *The Nature and Treatment of Diabetes*, 2nd ed., 1869, p. 113.

** Sanderson's *Handbook for the Physiological Laboratory*, 1873, p. 508.

†† Lectures delivered at the College of France, *London Medical Record*, October and November, 1873.

‡‡ McDonnell, *op. cit.*, p. 29; G. Budd, *Diseases of the Liver*, 3rd ed., 1857, p. 47.

§§ *Journal de Physiologie*, i, 304.

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,* 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 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.† 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, 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 } Taurocholate of soda }	91.4
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* ($C^{16}H^{13}N^2O^3$). On standing, it becomes greenish from oxydation, and is converted into *biliverdin* ($C^{16}H^{12}N^2O^3$), 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."‡ 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;§ by the discovery of Zenker and Frerichs of crystals of hæmatoidin in inspissated bile and in the bile of jaundiced urine;|| 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;¶ by the discovery of Frerichs, Kuhne, 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.* There are, on the other hand, grounds for believing that bile-pigment is in its turn converted into urinary pigment.† 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.‡ It is also a well known clinical fact, that nothing influences so much 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 conversion 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 ($C^{26}H^{45}NO^7S$). 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 that they are composed of cholic acid ($C^{24}H^{40}O^5$), which contains neither nitrogen nor sulphur, in combination with taurin ($C^2H^7NO^3S$), which contains both nitrogen and sulphur, and glycochin ($C^2H^3NO^2$), which contains nitrogen, but no sulphur.

Cholesterin ($C^{26}H^{41}O$) 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 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.§

Bile thus constituted is being constantly secreted by the liver. There is still much difference of opinion as to 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.|| 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.¶ The blood of the hepatic artery has been examined with a like result. It is 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.** Frerichs records a case of fatty liver, where

* Parkes, *Lancet*, 1871, vol. i, p. 470.

† On the Heat of the Body. The Goulstonian Lectures for 1871. By Dr. S. Gee, *BRITISH MEDICAL JOURNAL*, 1871, vol. i, p. 330.

‡ *Treatise on Structure and Diseases of the Liver*, 3rd edition, 1803, p. 147.

§ Virchow's *Cellular Pathology*, English Translation, p. 144; Kuhne, *Lehrbuch der Physiol. Chemie*, Leipzig, 1866, p. 80.

|| *Jahresh. von der Gesellschaft für Natur- und Heilkunde in Dresden*, 1858, p. 53.

¶ *Gaz. Méd. de Paris*, 1859, p. 460.

* Sanderson, *op. cit.*, p. 498.

† Bence Jones, referred to by G. Budd, *op. cit.*, p. 34; Parkes, *On the Urine*, 1860, p. 30.

‡ Sanderson, *op. cit.*, p. 499.

§ *Recherches Expér. sur une nouvelle fonction du Foie*. Paris, 1863.

¶ Budd, *op. cit.*; and G. Harley, *Jaundice, its Pathology and Treatment*. London, 1863.

|| *Physiological Chemistry*, Dr. Day's Translation, vol. ii, p. 87.

** *Maladies d'Algérie*, vol. i, p. 262.

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-pigment.* Similar observations have been made by Budd in cases of waxy disease and cancer of the liver,† 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 be 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.‡

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

[To be continued.]

ICHTHYOSIS LINGUÆ (SO-CALLED) FOLLOWED BY EPITHELIOMA.

By W. FAIRLIE CLARKE, M.A., F.R.C.S.,
Assistant-Surgeon to Charing Cross Hospital.

I AM sorry that Mr. Henry Morris had not an opportunity of speaking upon my paper, at the Royal Medical and Chirurgical Society, upon the so-called ichthyosis linguæ, for there were not many present who are better entitled to express an opinion upon the subject than he is. I will now endeavour briefly to reply to his comments.

1. Mr. Morris says truly, that I consider "the essential nature of ichthyosis linguæ to be a chronic inflammation, accompanied by an overgrowth of the papillæ"; but subsequently, when the disease has reached the stage of epithelioma, the rete mucosum, I add, "increases enormously at the expense of the papillæ, reducing them in many places to mere threads, and dipping down between them in the form of large club-shaped processes". In these statements he finds a contradiction and a *reductio ad absurdum*. "It would thus seem," he writes, "that, as the ichthyosis advances, the hypertrophied papillæ, which are its leading feature according to Mr. Clarke, must necessarily pass back to their normal life as they gradually dwindle down into a state of atrophy." The inference, then, is that there is a stage in the progress of the disease when part of its essential nature—viz., an overgrowth of the papillæ—no longer exists; or, in other words, that as the disease is growing worse and worse, it gradually recovers." But I do not see that there is any such inconsistency in my statements. The one refers to the ichthyosis, the other to the epithelioma. In ichthyosis linguæ, the papillæ are hypertrophied, but they retain their type; and in this condition they may remain for years. By and bye, however, the point is reached when the disease becomes epitheliomatous, and the rete develops in the manner I have described. The papillæ do not "gradually dwindle down into a state of atrophy", they do not "pass back to their normal size"; nor do I think that my language implies anything of the kind. They are actively invaded on all sides by the rete; their type is entirely lost; and they are very soon destroyed by the epithelial growth. The microscopical drawings and sections that I showed at the meeting demonstrated these points.

2. Mr. Morris criticises the features which I have said are distinctive of ichthyosis linguæ, and deprecates the name papilloma of the tongue, which I formerly suggested. I now readily admit that, though the disease often begins as a circumscribed wart, yet it has such a tendency to spread, that papilloma is not an appropriate name. As I said at the meeting, I think it would be best to adopt Dr. Ullmann's term, and to call it Tylosis Linguæ. From ichthyosis of the skin it differs, first, pathologically, because, in the former, the sweat-glands and the sebaceous follicles play an important part, while in the tongue there are no such glands or follicles; and, secondly, clinically, because ichthyosis of the skin, is (generally speaking) a congenital disease—a defect of development—and, moreover, has no proclivity to cancer; whereas the disease, which formed the subject of my paper, never occurs before puberty, and shows a strong tendency to become epitheliomatous. For these reasons, it appears to me to be undesirable to call it an ichthyosis.

3. Mr. Morris cannot agree with me in regarding the change in the

mucous membrane as one which is due to chronic inflammation, excited by irritation. Whether it ought to be classed among chronic inflammations is a point which is fairly open to a question. But I think I adduced enough evidence to warrant me in the opinion that the disease (whether a chronic inflammation or not) is due to local irritation. That cases occur in which we cannot trace the irritation, is not wonderful. When we consider how subtle are the nutritive processes, and how easily their balance may be disturbed, the wonder is, not that in many cases the cause escapes our observation, but that in a few we are able to assign it with a high degree of probability. Some warts in other parts of the body spring up from a recognisable irritation; others we know not how. Some cancers arise in consequence of a recognisable irritation; others we know not how. So with the disease in question. Some warty spots on the tongue are due to a recognisable irritation; others arise we know not how, but it is reasonable to suppose that there is some subtle irritation which has excited them.

Mansfield Street, Cavendish Square, March 18th, 1874.

THE COOLING OF THE BODY AFTER DEATH.

By J. WILKIE BURMAN, M.D.,
Resident Medical Officer and Superintendent of the Wiltshire County Asylum,
Devizes.

THE subject of the cooling of the body after death, as indicated by the thermometer, though it has already been investigated by such careful observers and high authorities as Drs. Wilks, Taylor, and Goodhart, has not, it appears to me, been as yet sufficiently made the object of inductive research for its proper and full elucidation. It is a subject that has for some little time past engaged my attention, seeming to me to be of considerable interest from a practical point of view. The cases in which I have so far made observation have neither been sufficiently numerous nor varied to warrant my speaking at present authoritatively on the subject; but I think I may safely venture to corroborate those who affirm that the cooling of the body after death, as indicated by the thermometer, is a much more gradual process than the experience of our unaided tactile senses has hitherto led us to suppose it to be.

It is not an uncommon occurrence for medical officers of asylums to be called up at night to see a patient found dead by the night-watch at one of his visits; and the question as to how long the patient has been dead is of considerable medico-legal importance in such cases. I think I am right in asserting that the decision on this point of the medical officer has generally been, and continues for the most part to be, based on the feeling or degree of warmth or coldness as experienced by the mere application of the living hand to the corpse—a process which, as compared with thermometric observation, I have found to be more or less fallacious and productive of uncertain results.

I was induced to make *post mortem* thermometric observations in the hope that, by carefully studying thus accurately the cooling of the body after death, as it occurs in the various forms of disease and under the usual varying conditions in which the corpse may be found, I might with greater certainty and precision be able to fix the time at which death had taken place; and I intend continuing my observations, with this object in view. I have had a special thermometer made for the purpose, which indicates the temperature as low as 50 deg. Fahr.—the average surrounding temperature; and it will no doubt be necessary, for the thorough investigation of the subject, to have another made that will register the descending temperature down as far as zero. My method of procedure is to take the temperature of moribund persons, and then carefully note the temperature of the body and of the room at stated intervals (shorter at first, and longer later on), until it descends as low as that of the surrounding atmosphere; the thermometer being fixed from the first, and kept fixed, in the left axilla. In this way, having ascertained, in a sufficiently numerous and varied body of cases, the actual and usual rate of cooling of the *corpus* after death, it appears to me that all we should require to do in ordinary cases, on being called to inspect a dead body and determine as to the length of time that has elapsed since death took place, would be to take the temperature of the body as indicated by the careful application of a good thermometer; and, after estimating to its proper extent—as shown by previous experimental research and observation—the influence which the form of death and condition in which the body is found may be fairly considered to have had over the rate of cooling, be thus enabled to give a tolerably precise opinion in the matter, instead of making the usual vague statement. I am simply desirous, for the present, of indicating the scope of my humble researches with regard to this subject, and of drawing attention to a field for observation which, it appears to me, may be more extensively worked, with good practical results of very considerable medico-legal importance.

* *Op. cit.*, English Edition, vol. i, p. 83.

† *Op. cit.*, pp. 329, 411.

‡ Carpenter's *Human Physiology*, 7th edition, p. 434.