THE CROONIAN LECTURES ON FUNCTIONAL DERANGEMENTS OF THE LIVER.

Delivered at the Royal College of Physicians.

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LECTURE I.—*Concluded.*

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.* 1. 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; Cholestæremia.

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 gradually 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 fistulae,* 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 1000 parts of its own weight. According to Bidder and Schmidt, 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 1000 parts of its own weight. According to Bidder and Schmidt, a dog consuming daily about one-seventeenth of its own weight of meat secretes in twenty-four hours 19.19 parts of fluid bile in 1000 parts of its own weight. Making allowance for the greater relative weight of the liver in the dog than in man,† 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 the 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 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.* I have collected several other cases† of a similar nature, in which the results more or less corresponded with that observed in my patient; 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 fistulae, 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.‡

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 1000 parts of fresh human faeces only 9 parts of a substance similar to bile, which, on the calculation that the daily faeces of a man weigh $5\frac{1}{2}$ ounces, would make a total of 24 grains of dried bile in the day.§ 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 faeces *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.|| Bidder and Schmidt have also found that not more than one-eighth of the sulphur of the bile is normally excreted with the faeces.¶ The bile-pigment is generally believed to be all voided by the faeces; 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 faeces. It 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 faeces is even relatively less than in man.**

* Further details of the case will be found in *Pathological Transactions*, vol. xxii, p. 152.

† 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 7th, 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 the day (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 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.)

‡ *Mém. de l'Acad. Royale de Méd.*, 1847, tome xiii.

§ Budd, *op. cit.*, p. 52.

|| Carpenter's *Human Physiology*, 7th edition, p. 435.

¶ *Die Verdauungssäfte und der Stoffwechsel*, 1852, p. 218.

** 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 boæ, 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 boæ is "nearly entirely composed of urates". (*Philosophical Transactions*, 1854, p. 279.)

* On this subject, see Bidder and Schmidt, *Die Verdauungssäfte und der Stoffwechsel*, 1852, p. 186; Dr. G. Scott, Beale's *Archives of Medicine*, 1853, vol. i, p. 218; Carpenter's *Human Physiology*, 7th edition, p. 144.

† 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.

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 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* and in therapeutics, although attention was called to it eighteen years ago by Dr. Parkes, in the Goulstonian Lectures on Pyrexia delivered before this College. "It is now known," says Dr. Parkes,† "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 Grünwald‡ to nearly twenty-three imperial pints. If we put it at twelve pints, we shall certainly be within 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.§

In the first place, it assists in the absorption of fat. It is a well known clinical fact that, when the common bile-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.* 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 feces.† 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 with pancreatic juice and bile, has a more solvent action on albuminous substances than the gastric juice alone.‡ 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.§

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, glycerin, and most of the cholic acid returning to the circulation, while a portion of the cholic acid is discharged with the feces. The cholesterin is also decomposed in the bowels, and the products of its decomposition are discharged with the feces. According to Dr. Austin Flint, jun., the cholesterin is converted into a substance, which he has discovered in the feces and designated stercorin; it appears also to be in some way related to another ingredient of the feces 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.|| 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, arranged 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 the 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,

* 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.

† *Medical Times and Gazette*, 1855, vol. i, p. 333.

‡ An account of this case, abstracted by me from Grünwald's Latin memoir, will be found in Beale's *Archives of Medicine*, vol. i, p. 270.—C. M.

§ 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, perhaps, 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.)

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.

* *Guy's Hospital Reports*, series i, vol. 1, p. 610.

† Sanderson, *op. cit.*, p. 505.

‡ Budd, *op. cit.*, p. 50.

§ On the Changes in the Liver which follow Ligature of the Bile-ducts. (*St. Bartholomew's Hospital Reports*, vol. ix, 1873.)

|| *Journal of the Chemical Society*, October and November, 1862.

¶ *Medical Dictionary*, vol. ii, p. 723.

or certain articles of diet, which irritates 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 feces 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.* 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 it 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 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 tipping.

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

a. In consequence of a deficient formation of bile, or its impeded passage into the bowel, 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, yet the body has been tolerably well nourished after upwards of twelve months.* There are, however, few exceptions to the rule, that permanent closure of the common bile-duct destroys life in the end—usually in little 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 feces. 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 ligation 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;† 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 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.‡ 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.§ 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 glycogenetic function of the liver is impaired. Glycosuria, often temporary, from some of these causes is not uncommon. 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

* Budd, *op. cit.*, p. 49.

† These are well given by Dr. T. L. Brunton, in his Lectures in the BRITISH MEDICAL JOURNAL for January and February, 1874.

‡ See abstract of Lectures in *London Medical Record* for October and November, 1873.

§ Pavy, *Nature and Treatment of Diabetes*, 2nd edition, 1869, pp. 142-3; and Bence Jones, *Lectures on Pathology and Therapeutics*, 1867, p. 42.

* 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.

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.

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 state 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 was caused by the entrance of air into the veins.* 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 cholesterin, or to what he has designated "*Cholestæremia*".† 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 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 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 disintegration, 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.

REMARKS ON A CASE OF AMPUTATION.

By JAMES SEDGWICK, M.R.C.S., Boroughbridge.

I WAS hurriedly called on March 4th, 1874, to a farmer, aged 65, living four miles from me, who had just received such a severe injury to the wrist as to necessitate amputation. With the assistance of my friend Mr. Mitchell, when the patient was under chloroform, and after the application of Esmarch's plan of bandage, I amputated the forearm about three inches below the elbow-joint, and had the very great satisfaction of being able to make the skin-flaps, circularly divide the muscles, and saw through the bones, without the loss of a single drop of blood. But, after the arteries, six in number, were all secured, most troublesome venous and capillary oozing continued for between three and four hours, when it apparently ceased, and we were able to close the wound and apply steady and regular pressure.

The patient had influenza, with very frequent bronchial cough and expectoration. He was thin and very pale, and said that for many years no slight wound ever healed by first intention.

On March 6th, the oozing still continued to saturate the bandages; so much so, that in the evening I found it necessary, with the assistance of my partner, Mr. Leadman, to open and clear out the wound. We then applied styptic colloid freely, which at once stopped the bleeding without any further pressure.

Because a blush was visible along the course of the axillary vessels, tincture of iron was ordered every four hours, with frequent supplies of milk, beef-tea, eggs, etc., in small quantities.

As my object is to draw attention to the very troublesome oozing from the stump, after the adoption of Esmarch's plan for bloodless amputation, I will only add that now, March 21st, all risk of secondary hæmorrhage is past; for two days ago the last ligature separated, and the wound is closing rapidly, though for several early days it looked very unhealthy, and has made much slower progress than any other case that I have had in the country.

As Esmarch's plan is yet in its infancy, I thought it right to add my small quota of experience to the mass required to enable us to judge accurately of its perfection; and it certainly is perfect, as far as the comfort of the operator is concerned when he is using his knife and saw. I report my case especially because it was complicated, but trust that the extensive experience of many other surgeons may prove that the hæmorrhage was due to the condition of my patient, and not in any way to Esmarch's plan of bandage.

* *Diseases of Liver*, Sydenham Society's Translation, vol. i, p. 395.

† *Op. cit.*