THE CROONIAN LECTURES ON FUNCTIONAL DERANGEMENTS OF THE LIVER.

Delivered at the Royal College of Physicians.

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LECTURE III.—*Concluded.*

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

2. *A Deficient Supply of Oxygen.*—Insufficient muscular exercise in the open air may derange the functions of the liver. It is well known that sedentary habits and confinement in badly ventilated rooms tend to induce derangements of the liver. It is also a common observation that persons who have eaten and drunk too freely have not suffered from their livers so long as they have led an active life in the open air; but that, as soon as from change of occupation, or other causes, they take to sedentary habits, without any corresponding change in diet, derangement of the liver ensues. Again, every sportsman who has suffered from hepatic derangement knows the effect of a single day's hunting or shooting in clearing his complexion and relieving his symptoms. A want of regular exercise in the open air leads to derangement of the liver in two ways; viz., *a*, by causing a deficient supply of oxygen to the system, as the result of which the oxydising processes which go on in the liver and elsewhere are imperfectly performed, and there is a tendency to the accumulation in the system of fat and of the imperfectly oxydised products of disintegrated albumen. Oxygen is, so to speak, the antidote necessary for the destruction of a *materies morbi* (lithic acid, etc.), produced by imperfectly oxydised albumen. *b*. By retarding the circulation of blood through the liver. Since the time of Haller,* physiologists have recognised the influence of the respiratory movements in promoting the circulation of blood through the liver; but, upwards of thirty years ago, Mr. Alexander Shaw, in a paper which has attracted too little notice,† showed more clearly than ever before, that the circulation of blood through the liver was greatly influenced by the alternate expansion and contraction of the thorax during respiration. Mr. Shaw called attention to the fact that the portal vein, without any provision for increasing its power, or any assistance beyond that *vis a tergo* which belongs to the veins generally, and being even destitute of valves to protect it from regurgitation of blood like the veins in other parts of the body, has to perform the duty usually fulfilled by an artery, which, besides receiving an impulse from the heart, is aided in distributing its blood by the contractility and elasticity of its coats. He suggested that this weak power by which the portal vein propelled its blood was compensated for by a suction-force communicated to the current of blood by the actions of respiration; the deeper the inspiration, the greater the force with which the blood rushed by the large veins to the right auricle. These reasonings have been confirmed by certain experiments of M. Bernard, who found that, when an incision is made into a lobe of the liver in a living animal, the blood may be seen to jet from the mouths of the hepatic veins during the movements of expiration, but

to return sucking in air with it at each deep inspiration, so that the animal soon dies from the passage of air into the heart.* In persons, then, who lead a sedentary life, this auxiliary force for promoting the circulation of blood through the liver is diminished, blood stagnates in the gland, and the functions of the organ are deranged, these results being all the more likely to arise if the liver be at the same time overstimulated by errors in diet.

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

4. *Nervous Influences.*—Many facts show the great influence of the nervous system upon the secreting organs. Sudden fear, or other severe mental emotion, has been known to arrest the secretion of milk and saliva, and we have already seen how injuries and diseases of nerve-tissue may produce diabetes by deranging the glycogenous function of the liver. But many other ailments of the liver besides diabetes have a nervous origin. Prolonged mental anxiety, worry, and incessant mental exertion not only interfere with the proper secretion of bile, but too often derange the processes of sanguification and blood-change, in which the liver is deeply concerned, and induce lithæmia, with many of the symptoms already described. These results are all the more likely to ensue if the diet have been such as favours hepatic derangement—if, for example, to drown grief, the patient have indulged in stimulants—and the habits have been sedentary. There is also good evidence that nervous agencies may not only cause functional derangement, but even structural disease, of the liver. Acute atrophy, in which the secreting cells are rapidly disintegrated and the functions of the organ arrested, appears in many instances to have a purely nervous origin; very often the first symptoms of the disease have occurred immediately after a severe fright, or an outburst of passion, in a person previously healthy. An impression made upon the brain appears to be reflected to the liver and to derange its nutrition. Many observations have satisfied me that the extrusion of gall-stones from the gall-bladder, as well as their formation, may be traced to nervous agency. Dr. Budd has also observed that mental anxiety or trouble has “great influence in the production of gall-stones”;‡ and I have repeatedly known attacks of biliary colic from gall-stones excited by some sudden emotion. Lastly, even cancer of the liver appears sometimes to result from the functional derangement induced in the first instance by mental trouble. I have been surprised at the frequency with which patients suffering from primary cancer of the liver have traced the commencement of their ill-health to indigestion following protracted grief or anxiety. The cases have been far too numerous to be accounted for on the supposition that the mental distress and the cancer have been mere coincidences. A similar observation has, I believe, been made by Sir Robert Christison and by other eminent authorities.

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

* *London Medical Record*, October 15th, 1873, p. 647.

† See *Pathological Transactions*, 1873, vol. xxiv, p. 266.

‡ *Diseases of the Liver*, third edition, 1857, p. 369.

§ *Op. cit.*, p. 55.

* “Vires quæ sanguinis per hepar motum accelerant.”—Haller's *Physiologia*, 1764, tome vi, p. 601.

† *Medical Gazette*, July 15th and September 30th, 1842.

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

6. *Poisons* of various sorts may derange the liver, the persistence of the derangement depending upon the length of exposure to the cause. One of the first effects of the poisons of the various specific fevers is upon the liver. Again, from protracted exposure to malaria, the liver often becomes deranged, anemia and lithæmia being the results. While some cases of acute atrophy of the liver have a nervous origin, there is good evidence that others are caused by a poison taken into the body from without, or sometimes, as suggested by Dr. Budd, "engendered in the body by faulty digestion and assimilation". Phosphorus also, in sufficient doses, is known to derange the functions of the liver; and one result of phosphorus-poisoning is the production of symptoms and structural changes in the liver closely resembling those of acute atrophy.* Various substances also taken as food, or by mistake along with food, may induce functional disturbance of the liver, the poisonous effect being often determined by some constitutional peculiarity of the individual.

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

D.—TREATMENT OF FUNCTIONAL DERANGEMENTS OF THE LIVER.

The time at my disposal only permits me to give a brief sketch of the general principles on which functional derangements of the liver ought to be treated; and my remarks will be for the most part restricted to the derangements resulting from abnormal disintegration and abnormal elimination.

1. *Diet*.—In functional derangements of the liver, much more permanent benefit is to be expected from careful regulation of the ingesta than from physic. It must not be forgotten that what may ultimately destroy the body too often enters by the same portal as that which is intended to nourish and maintain it. It is also well to remember that the hepatic derangement resulting in lithæmia may exist for years without any other symptom than the frequent deposit of lithates or lithic acid in the urine, and is then curable by attention to diet alone; but that, if neglected, it may ultimately develop gout, structural disease of the liver or kidneys, or some other serious result. Habitual lithæmia ought, therefore, to be always counteracted, and, from what has been already stated, it seems clear that the foods mainly to be avoided are saccharine and oleaginous articles, and especially cooked dishes containing both of these substances. Patients with lithæmia ought always to avoid made-up or highly seasoned dishes. In severe cases, potatoes, rice, sago, and fruits may have to be given up, and even bread must be taken in moderation. It will also always be well to ascertain if the lithæmia be due to any of those idiosyncrasies in virtue of which particular articles of diet are apt to derange the liver. In most cases of lithæmia, a diet consisting chiefly of stale bread, plainly cooked mutton, white fish, poultry, game, eggs, a moderate amount of vegetables, and weak tea or coffee, answers best. The quantity, as well as the quality, of the food must be attended to. Habitual lithæmia often results from the patient taking more food than can be converted into tissue or disintegrated in the liver. As Dr. Bence Jones has observed with regard to gout, so in habitual lithæmia, "a minimum of albuminous food should be taken, in order to produce the least uric acid; and a minimum of carbonaceous food, in order to allow the uric acid to be oxydised as much as possible".† In obstinate cases, the patient may be advised to take his principal meal in the morning, when the digestive powers are strongest. The free use of diluents, such as soda and seltzer waters, is also useful, as they help to eliminate from the system the morbid products of disintegration.

* Lead is known to cause an accumulation of lithic acid in the system, but apparently by impeding its excretion by the kidneys, rather than by increasing its formation in the liver. (See Garrod, *op. cit.*, p. 292.) Bence Jones, on the other hand, maintains that the accumulation of lithates in the system produced by lead is to be ascribed to diminished oxydation. (*Lecture on Pathology and Therapeutics*, p. 280.)

† *Op. cit.*, p. 142.

Still greater caution is necessary in all forms of lithæmia, as to alcoholic stimulants. Malt liquors, port wine, champagne, and many other wines, ought to be strictly prohibited. Claret, or a small quantity of spirit largely diluted, as a rule, answers best; but even these should be taken sparingly, and many patients do best with no stimulants at all. This is not the occasion to discuss whether alcohol is necessary for the nutrition of the body in persons subjected to much mental or bodily toil, or whether, taking the masses in all walks of life, the standard of health would be better maintained by teetotal habits or by a moderate use of alcohol. What I desire now to insist upon is, that alcoholic drinks in quantities usually regarded as compatible with, if not conducive to, health, and far short of what are necessary to affect the brain, in many persons undermine the foundations of health by deranging the liver; and that, to some individuals, even very small quantities are injurious. In persons who have been indulging largely, the risk of a sudden withdrawal of stimulants is less, I believe, than is commonly imagined. Unless there be evidence of a very weak heart, which itself may be the result of alcohol, the only unpleasant effects of sudden and complete abstinence, in my experience, have been sensations of sinking at the epigastrium and craving for alcohol, which a repetition of the stimulus has only temporarily relieved and has rendered more persistent.

2. *A Free Supply of Oxygen*.—Next to careful regulation of diet, this is the most important object to be aimed at in the treatment of functional derangement of the liver, and especially in that which induces imperfect disintegration of albumen. An excess of fresh air, indeed, will often counteract the bad effects of too large a quantity of food. Although recent observations, more especially those of Parkes, have shown that the common impression that muscular exercise materially increases the elimination of nitrogen from the body, is erroneous, there can be no doubt that exercise in the open air quickens the circulation of blood through the liver, in the manner already explained, and promotes oxydation, and that, by thus preventing the accumulation in the system of the imperfectly oxydised products of albumen, it operates beneficially in the treatment of functional derangement of the liver attended by lithæmia. The observations of Beneke and other authorities have shown that *sea-air* is an oxydising agent of great power, and that nitrogenous and sulphur-holding tissues more rapidly disintegrate under its influence.* Accordingly, we find that many patients with hepatic derangement and lithæmia derive immense benefit from residence at the sea-side and sea-bathing, although unfortunately the good effects of sea-air are sometimes more than counterbalanced by unhealthy lodgings or improper and badly cooked food.

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

There are certain other aperients which have long enjoyed a great reputation for promoting the secretion and discharge of bile, and otherwise acting beneficially in derangements of the liver, and which have accordingly been designated *Chologogues*. Among these remedies, *mercury* and its preparations hold a pre-eminent place. At the present day, mercury has lost much of its former reputation as a chologogue and alterative, and there is much difference of opinion as to its power over the liver. The practical physician gives a dose of calomel, finds the quantity of bile in the motions greatly increased, and his patient's state much improved; and he argues that the liver has been stimulated

* Parkes *On Urine*, 1860, pp. 115, 129.

by the mercury to an increased secretion of bile, and that to this cause his patient's improvement must be ascribed. The physiologist, on the other hand, ties the common bile-duct in one of the lower animals, produces a fistulous opening into the gall-bladder, and then finds that calomel has no effect on, if it do not diminish, the amount of bile that drains away through the fistula. It may interest some who are present, if I refer briefly to the principal of these experiments.

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

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

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

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

The most recent experiments are those of Dr. Röhrig of Kreuznach, made in the Pathological Institute of Vienna. He found that, although large doses of calomel did seem to increase somewhat the secretion of bile, its power to do so was inferior to that of croton oil, colocynth, jalap, aloes, rhubarb, senna, and sulphate of magnesia, the cholagogue power of these drugs diminishing very much in the order in which they have now been enumerated, and calomel standing at the bottom of the scale.||

These results of experiments upon the lower animals have added greatly to the discredit previously thrown upon mercury by its failure, when brought to the test of accurate clinical observation, to absorb plastic lymph in most forms of inflammation; and some eminent physicians are even of opinion that mercury and its preparations ought to be erased from our Pharmacopœia.¶ On the other hand, it has been fairly objected that the results of experiments with mercury upon dogs do not warrant conclusions as to its effects upon man; and, even granting that in man mercury does not increase the quantity of bile secreted by the liver in health, it does not follow that in disease there may not be some condition adverse to the formation of bile, which mercury may have the power of removing. Much, however, of the difference of opinion between the physiologist and the practical physician may be reconciled by keeping in mind the osmotic circulation, to which I referred in my first lecture, as constantly going on between the intestinal contents and the blood. A large part of the bile secreted by the liver and thrown into the bowel is constantly being reabsorbed, to reach the liver again; and accordingly when the common bile-duct is tied and a fistulous opening into the gall-bladder established, the quantity of bile which escapes from the fistulous opening immediately after the operation is much greater than at any time subsequently (Schiff). Mercury and allied purgatives produce bilious stools, by irritating the upper part of the bowel and sweeping on the bile before there is time for its reabsorption. The fact of mercury standing at the bottom of the scale of cholagogues in Röhrig's experiments is accounted for by its surpassing other cholagogues in this property; for, of course, the larger the quantity of bile that is swept down the bowel, the less is reabsorbed and the less escapes from a biliary fistula. That mercury does act especially upon the duodenum, is proved not merely by the large flow of bile which follows its action, but by the fact discovered by Radziejewski, that leucin and tyrosin, which are products of pancreatic digestion, under ordinary circumstances decomposed in the bowel, appear in the feces after the administration of mercurials. It would appear, then, that mercury, by increasing the elimination of bile, and lessening the amount of bile and of other products of disintegrated albumen circulating with it in the portal blood, is after all a true cholagogue, relieving a loaded liver far more effectually than if it acted merely by stimulating the liver to increased secretion, as was formerly believed, and as some authorities still maintain; for in this case it might be expected to increase, instead of diminish, hepatic congestion. It is not impossible, also, that the irritation of the duodenum by calomel and other purgatives may be reflected to the gall-bladder, and cause it to contract and discharge its

contents, and thus account in part for the increased quantity of bile in the stools.

There are also, I think, grounds for believing that, apart from its increasing the discharge of bile from the bowel, mercury exerts a beneficial action in many functional derangements of the liver, in whatever way this is to be explained. Patients of the greatest intelligence suffering from hepatic disorders constantly declare that they derive benefit from occasional or repeated doses of mercurials, which no other medicine or treatment of any sort confers; and the scepticism of the most doubting physician would, I believe, be removed, should he unfortunately find it necessary to test the truth of their statements in his own person. It is not impossible that the good effects of mercury on the liver, and in some forms of inflammation, may be due to its property of promoting disintegration. Mercury appears to have the power of rendering effused fibrin less cohesive, and so more easily removed by absorption, than it otherwise would be.* Modern physicians of high standing, and little likely to be accused of credulity as to the beneficial action of drugs, have thought that mercury is useful in croup, by causing a degradation and disintegration of the plastic membrane. If this be so, it seems not improbable that mercury, which from experiments† we know to reach the liver, may under certain circumstances act beneficially by promoting, or in some way influencing, the disintegration of albumen. The remarkable effect of mercury on constitutional syphilis probably admits of a similar explanation. But in whatever way it is to be explained, the clinical proofs of the efficacy of mercury in certain derangements of the liver are to my mind overwhelming. I say so the more advisedly, because I was taught to regard mercury as a remedy worse than useless, not only in hepatic diseases, but in syphilis; it cannot, therefore, be said that the convictions forced upon me by experience are the result of preconceived opinions.

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

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

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

4. *Alkalies*.—Next to aperients, alkalies are the most useful drugs in the treatment of functional derangements of the liver. In lithæmia and in many of the symptoms which spring from this morbid state, the greatest benefit is often derived from a course of alkalies—such as the alkaline salts of potash, soda, or lithia, or some of the alkaline mineral waters, such as those of Vals, Vichy, or Ems. The comparative worth of the different alkalies for neutralising acids varies considerably. One grain of carbonate of lithia or of carbonate of ammonia is nearly equal to a grain and a half of carbonate of soda or two grains of carbonate of potash. The beneficial effects of alkalies in derangements of the liver are not due to their neutralising acidity, or to any direct action upon lithic acid. It is, in fact, in the form of lithate of soda that lithic acid is met with in gouty persons. Alkalies seem to do good by combating the pathological state, on which the formation of lithic acid depends. They are believed to promote oxydation, and thus increase the disintegration of albumen. Dr. Bence Jones tells us that in the body as well as out of it alkalies furnish the most marked evidence of assisting in oxydising actions.§ The experiments of Parkes with liquor potassæ seemed to show that it had the power of increasing the disintegration of the sulphur-holding materials of the body. The effect of its administration was to increase the amount of sulphuric acid and also of urea in the urine; although, with characteristic caution, Parkes adds that the increase of urea as the result of the potash was rendered probable,

* *Würzburg Verhandlungen*, Bd. v. 1855, s. 231.

† *Beale's Archives of Medicine*, 1858, vol. i, p. 209.

‡ *Virchow's Archiv*, 1858, Bd. xiii, s. 29.

§ *BRITISH MEDICAL JOURNAL*, 1868, vol. ii, pp. 78, 176, 191.

¶ *Stricker's Jahrbuch*, 1873, part 2.

¶ See Bennett, *BRITISH MEDICAL JOURNAL*, 1868, vol. ii, p. 176.

* Bence Jones, *op. cit.*, p. 283.

† Autenrieth and Zeller found mercury in the bile of animals treated with mercurial frictions. (Budd, *op. cit.*, p. 57.)

‡ *Op. cit.*, p. 410.

§ *Op. cit.*, p. 280.

rather than proved, by his experiments.* From experiments on dogs with biliary fistulæ, Nasse was led to the conclusion that carbonate of soda taken with the food diminished greatly the secretion of bile;† and a similar result has been observed by Röhrig to follow the introduction of the same salt into the intestine or the veins. The diminution affected the solids as well as the water of the bile, and especially the biliary salts. Nasse also found that after taking two drachms of carbonate of soda the urine (human) was very rich in hippuric acid. The only inference at present to be drawn from these experiments is, that alkalis exert a powerful influence over the chemical changes going on in the liver. When alkalis are employed in lithæmia, it is well to suspend their use occasionally, as they are apt, when long continued, to derange the gastric digestion; but in cases where they are strongly indicated they are better tolerated than is usually thought. In the fifth volume of the *Medico-Chirurgical Transactions*, Dr. Bostock has recorded the case of a young lady who for months took carbonate of soda to the amount of two ounces and a half daily. The appetite and strength were much improved; and her blood, instead of being thin, coagulated firmly, the coagulum being strongly buffed and cupped.

5. *Chlorine, Iodine, and Bromine* are closely related in their chemical properties, and are believed to promote oxydation in the body by taking hydrogen from water and liberating oxygen. An aqueous solution of chlorine is of service in certain cases of lithæmia associated with general debility; and we know that the various salts of chlorine enter largely into the composition of the mineral waters which are most useful in hepatic derangements. Bromide of potassium will reduce certain enlargements of the liver and spleen, and may be given with advantage in cases of lithæmia associated with congestion of the liver and want of sleep. But among the remedies of this class the chloride of ammonium holds a pre-eminent place. It has obtained a great and well deserved reputation in India and other tropical countries for the treatment of hepatic congestion; and I have found it of great service in the functional derangement of the liver attended by lithæmia. Given in scruple doses three times a day, it acts as a diaphoretic and diuretic, and exercises a powerful influence in relieving the portal circulation. It is not oxydised, but passes out of the system unchanged in the urine. According to Böcker's experiments,‡ it increases the nitrogenous solids of the urine; the mean daily increase of urea under its use he found to be not less than seventy-four grains—a quantity indicating a vast augmentation either of metamorphosis or of elimination, but from its beneficial effect on the liver, most probably of the former. Chloride of ammonium has this advantage, that it may be combined with either alkalis or mineral acids.

6. *Mineral Acids* are employed by many physicians in the treatment of functional derangements of the liver. Nitric acid especially has long been thought to have the power of augmenting the flow of bile; but there is no good evidence of this, either clinical or experimental. According to my experience, the action of mineral acids upon the liver is much less direct than that of alkalis. In all morbid states of the liver attended by congestion, and in most cases of lithæmia, I have found that they either did no good or they aggravated the symptoms. They may, however, be of service when there is debility and want of tone; but the chief good which they effect is probably that of improving the gastric digestion. In some cases, both acids and alkalis may be given advantageously—the alkalis before, and the acids after, a meal.

7. *Tonics*.—Clinical experience shows that, notwithstanding the existence of debility and anæmia, tonic remedies are apt to disagree in many cases of functional derangement of the liver. This remark applies especially to the functional derangement resulting in lithæmia. I have repeatedly known patients in this state improve at once on substituting for quinine, iron, the mineral acids, and stimulants, abstinence from alcohol, with aperients, blue pill, and alkalis, and careful regulation of diet; the strength, flesh, and colour returning under what at first sight might have appeared a lowering treatment. Different opinions have been expressed with regard to the utility of iron in chronic gout. According to Dr. Bence Jones, iron is one of the two potent remedies we possess for indirectly promoting oxydation in gout as well as in other maladies;§ whereas, in Dr. Garrod's opinion, the preparations of iron are very likely, when indiscriminately given to gouty subjects, to excite a paroxysm of the disease, and for the most part are contraindicated.|| My experience coincides with that of Dr. Garrod; and in simple lithæmia I have constantly known iron to increase the tendency to deposits of lithates in the urine, constipate the bowels, and aggravate any symptoms from which the patient may have previously suffered. As a

rule, also, I have found that patients with chronic gout or with lithæmia do not tolerate even small doses of quinine. From some careful experiments made by Dr. Ranke of Munich, quinine appears to have the power of diminishing the amount of lithic acid in the urine.* The experiments were made on three persons, and the results were uniform. The effect continued for about two days after a single dose of twenty grains; and there was no evidence of any increased excretion after the effect of the quinine had passed off, so that probably the quinine acted by lessening the formation of lithic acid in the liver, or by substituting some other substance for it. From these experiments it might be inferred that quinine and bark should be of essential service in chronic gout and in lithæmia, but this inference is opposed to clinical experience.†

When tonics are given in lithæmia, gentian, chiretta, cascarrilla, and serpentaria are preferable to quinine and other preparations of bark. The best preparations of iron are the reduced iron, the citrate of iron, or the tartrate of iron and potash; these preparations are sometimes advantageously combined with alkalis and saline aperients. In cases of lithæmia attended by great nervous prostration, I have seen advantage follow the use of phosphorus in doses of one-thirtieth of a grain three times a day. The lithates have disappeared from the urine, and all the symptoms have improved. In some of these cases the circumstances seemed to leave no doubt that the improvement was due to the phosphorus.

8. *Opium* and its preparations are contraindicated in most functional derangements of the liver, and particularly when there is evidence of lithæmia. Opium impedes elimination both by the bowels and kidneys, and also appears to check the disintegrative processes which go on in the liver. It is generally believed to diminish the amount of bile secreted by the liver; and this view is favoured by the light-coloured stools which often follow its use. The result, however, of Röhrig's experiments on animals with biliary fistulæ was to show that opium increased the secretion of bile instead of diminishing it, so that probably the discharge of bile from the liver is only temporarily suspended by a similar influence on the coats of the bile-ducts to that which opium exerts on the coats of the bowel. Be this as it may, there can be no doubt that opium constipates the bowels, favours portal congestion, and checks the elimination, not only of bile, but of the products of disintegration which go on in the liver. The experiments of Böcker‡ and clinical experience alike show that opium impedes the elimination of the nitrogenous solids of the urine, and that dangerous and even fatal consequences ensue from its employment in structural diseases of the kidneys. These considerations explain why, in hepatic derangement attended by lithæmia, opium is contraindicated for the relief of pain, sleeplessness, or other symptoms for which it is commonly prescribed.

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

In bringing these lectures to a close, I beg to tender to you, Mr. President, and to the Censors' Board, my thanks for the honour you have done me in appointing me to deliver them. I am very sensible of their manifold imperfections, and in apology can only plead a multiplicity of other engagements during the brief period allotted to their preparation. I am well satisfied, however, as to the great importance of the subject which I have brought before your notice, and that it is one worthy of more attention from the Fellows and Members of this College, and from the profession generally, than it has yet received. The day, I believe, will come, when, with a more perfect knowledge than we now possess of the healthy functions and of the signs of functional derangement of the liver, we shall be enabled to prevent, or to arrest at their commencement, many of the most serious ailments to which mankind are liable, and thereby to add another chapter to the volume of Preventive Medicine.

ERRATA.—In Lecture II, BRITISH MEDICAL JOURNAL, April 11th, p. 471, last word of first paragraph, for "Elimination", read "Disintegration".—In Lecture III, p. 536, last paragraph of first column, for "Dr. William Butler", read "Dr. William Butler".

* Parkes, *op. cit.*, p. 167.

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

‡ Parkes, *op. cit.*, p. 167.

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

* *On the Urine*, 1860, p. 151.

† *Archiv für Wissenssch. Heilkunde*, 1864, Bd. vi, p. 508.

‡ Parkes, *op. cit.*, p. 165.

§ *Op. cit.*, pp. 143 and 279. || *Op. cit.*, p. 453.