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LECTURES

ON

THE PATHOLOGY AND TREATMENT OF DIABETES MELLITUS.

BY

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LECTURE I.

THERE are two diseases to which the generic term diabetes has been applied. They are distinguished by the specific names diabetes insipidus and diabetes mellitus. They resemble one another in the copious secretion of urine, which is the characteristic symptom of diabetes insipidus, and is generally present, though not always, in diabetes mellitus. In the former disease, the urine contains no abnormal ingredient; while the latter is characterised by the presence of grape-sugar in it. The term hydruria is employed by some writers to designate the copious secretion of urine, and glycosuria the presence of sugar. A large increase in the quantity of urine often occurs, and sugar may be occasionally found in it, in health.* It is, therefore, well to restrict the use of the terms diabetes insipidus or diabetes mellitus to the permanent continuance of these symptoms. As the former disease is comparatively rare, the simple name diabetes is always applied in ordinary language to the latter; indeed, it is now sometimes used instead of glycosuria to signify the mere presence of sugar in the urine, although it may be but temporary.

SYMPTOMS.—When patients suffering from diabetes come to a hospital, they usually complain that their mouth is dry, and they suffer from thirst. They pass a great quantity of urine, frequently having to rise during the night to micturate; and they have been losing flesh, although their appetite is undiminished or even greatly increased. Although these symptoms are generally present when patients apply for hospital relief, they are not, so far as my experience goes, the first indications of the disease. This fact was much impressed upon me by a circumstance which occurred while I was a medical student. I chanced one day to see a working man who was under treatment for diabetes by a medical friend of mine. Being anxious to display my newly acquired knowledge, I said to the patient, "I suppose that the first thing you noticed was, that you made water very often, and were very thirsty." His reply took me somewhat aback. "Oh no!" said he; "the first thing I noticed was, that I could not do my day's work as I used to do." My attention was thus directed for the first time to muscular weakness as one of the earliest symptoms of diabetes; and I find that it has been the very first to appear in a large number of the cases recorded by Seegen in his elaborate work on this subject.† I have noticed it in several cases where no complaint was made of thirst, increased appetite, or frequent micturition. Another frequent symptom of diabetes is dryness of the skin, or the presence of an obstinate cutaneous eruption. I have not observed any characteristic form of eruption, nor any particular situation, as either the face or the body may be affected; but itching of the vulva in women is common, probably on account of the irritation caused by the saccharine urine. For my own guidance in practice, I have laid down the two following rules. Always examine the urine for sugar—(1) whenever a patient, especially a male, complains of weakness without any obvious cause; (2) whenever an obstinate cutaneous eruption is met with. In his *Handbook of*

Medicine, Dr. F. T. Roberts gives the much more general and comprehensive rule to examine the urine in all cases of obstinate ill health; and this is, no doubt, better than the rules which I have just mentioned; yet, by following these, I have several times detected diabetes when most of the ordinary symptoms were absent.

PATHOLOGY.—The presence of sugar in the urine as an abnormal constituent has been long known; but the pathological processes which it indicates are only now, thanks to the labours of Bernard, Cyon, Eckhard, Flint, Lusk, Pavy, and others, beginning to be clearly understood. Even yet we generally find diabetes ranged in text-books with albuminuria and other diseases of the kidneys, although we now know that these organs are not at all in fault, but merely separate from the blood the excess of sugar present in it. The blood always contains more or less sugar;‡ but, unless it amount to more than about one-third per cent.,† it is not separated by the kidneys. Its appearance in the urine, therefore, indicates that an excessive quantity of it is present in the blood; and, if we can find out how this excess came to be there, we shall have discovered the pathology of diabetes. An analysis of blood from the crural or jugular veins, and from the femoral and carotid arteries, shows that less sugar is contained in the venous than in the arterial blood; and therefore destruction of sugar must go on somewhere in the organism.‡ Excess of sugar in the blood may thus be due to two causes—1, to increased introduction of sugar; or, 2, to diminished destruction of it; or to both of these together.

We will first consider the ways in which an excess of sugar may be introduced into the blood; and this involves the question, How does sugar come to be present in it at all? The ultimate source of the sugar and of every other constituent of the body is, of course, the food we eat; and this, as we may easily see in a typical meal of beef-steak, bread, and pudding, consists of fat, albumen, starch, and cane-sugar. The fat takes no part in the production of sugar within the organism, but the other three do. After they have entered the intestinal canal, the starch is converted into grape-sugar by the saliva and pancreatic juice, and the cane-sugar into a mixture of glucose and another sugar called *lævulose*§ by the intestinal juice. The albumen is converted into peptone by the gastric and pancreatic juices. The sugar and peptones thus formed in the intestinal canal are absorbed by the intestinal veins, but they are not all at once poured into the general circulation and carried to the brain and muscles. If this were the case, these structures would get all their nutriment at once, and they would have to stow it away themselves for use during the intervals of fasting. Possibly the reserve-stores they would thus require to accumulate might clog their action; and, unless they could assimilate all the sugar at

* *Revue Scientifique*, 2nd ser., tome iv, p. 1023.

† Bernard, *Physiologie Expérimentale*, tome i, p. 302. (Several of these lectures of Claude Bernard have lately been reproduced in the *London Medical Record*, and are well worthy of perusal, both for their matter and as admirable examples of method in experiment and clearness in diction.)

‡ *Revue Scientifique*, 2nd ser., tome iv, p. 1022.

§ Sugars may be divided into two classes. Those of the first class are fermentable, yielding alcohol when acted on by yeast; and, when boiled with potash and sulphate of copper, give a deposit of oxide of copper. They have all the same formula, $C_6H_{12}O_6$, but are distinguished from each other by their action on polarised light. The chief members of the group are glucose, or ordinary grape-sugar, and *lævulose* or *lævoglucose*. Glucose turns the plane of polarisation to the right, and thus is sometimes called *dextrose* or *dextroglucose*, while *lævoglucose* turns it to the left, and hence its name. Glucose obtained from starch cannot be distinguished by chemical tests from that got from the liver; but it is quite possible that they are not the same, and that the one may be much more easily oxidised in the organism than the other. Indeed, Bernard states (*Physiologie Expérimentale*, tome i, p. 213) that sugar obtained from the liver is most easily destroyed in the body; next comes sugar from diabetic urine, then grape-sugar from starch, and, lastly, milk-sugar. The position of diabetic sugar between glucose from the liver and glucose from starch may be due to its being in many cases a mixture of the two—part of it consisting of sugar formed from starch in the intestine, and not altered by the liver, and part of it derived from the transformation of glycogen.

The second class of sugars has for its chief members cane-sugar or saccharose, and milk-sugar or lactose. They do not undergo alcoholic fermentation with yeast, nor do they reduce copper like those of the first group; but they can be transformed into the sugars of the first kind by boiling with acids, or by the action of certain ferments, and then they are capable of fermentation and reduce copper. They both have the same formula, $C_{12}H_{22}O_{11}$. They both turn the plane of polarisation to the right, though cane-sugar does so more than milk-sugar. They are distinguished by their different solubility and sweetness.

* Brücke, *Sitzungs-Bericht der Wiener Akad.*, vol. xxix, 1859, p. 346.

† Seegen, *Der Diabetes Mellitus*, p. 109.

once, some of it would pass out in the urine, and thus be lost. It seems, at any rate, that such intermittent nutrition is not good for them, since a means of equalising it has been provided in the liver. This organ acts as a storehouse, in which the superfluous nutriment absorbed during digestion is laid up, and gradually given out again into the blood during fasting. The sugar which has been absorbed from the intestines is conveyed by the portal vein to the liver; and there it is converted into glycogen, and stored up in the hepatic cells. How the transformation is effected, we do not at present know; nor can we say whether the sugar is simply transformed into glycogen, or whether it splits up in some peculiar way so as to yield glycogen and fat. That glycogen is formed from sugar, and that sugar is stopped by the liver on its way from the intestine to the general circulation, is shown by several facts. In a starved animal, glycogen disappears entirely from the liver; but it quickly reappears if some sugar be injected into the stomach.* It is greatly diminished by fasting, and greatly increased by a full meal. When sugar is injected into the crural vein, it appears in large quantities in the urine; but when it is injected slowly into the portal vein, it is taken up by the liver, and not a trace of it is to be found in the urine. If the injection have been made too quickly, so that the liver cannot transform the sugar as rapidly as it is supplied, a portion of it passes into the general circulation and appears in the urine.† If the portal vein be ligatured, so that the blood finds its way from the intestines to the heart and body by means of the collateral circulation without passing through the liver, glycosuria occurs.‡ It would seem that it is only while sugar is being absorbed from the intestines that much of it is present in the portal blood, for generally there is less of it in the portal vein than of almost any other vessel in the body.§ From the power of the liver to use up sugar in this way, Tscherinow has proposed to call its function glycophthiric, or sugar-destroying. Peptones also form glycogen, for the liver of a dog always yields a much greater quantity of this substance after the animal has had a meal of flesh than when it is fasting. Fick has advanced the hypothesis that the peptones which result from the digestion of albuminous food in the stomach are not again built up into albuminous substances in the organism, as is usually supposed. Instead of this, they undergo further decomposition, and split up into non-nitrogenous and nitrogenous bodies. The non-nitrogenous products are stored up in the body, and serve it as fuel; while the nitrogenous ones are excreted in the form of urea.|| The urea is probably not formed directly from peptones; for, when they are injected into the blood, the urea is not increased till four or five hours after the injection; and, when meat is digested in the stomach, the increase of urea begins five or six hours after the meal.¶ It is probable, from Schultzen's researches,** that glycocine, leucine, and tyrosine, are first formed, and that these afterwards become converted into urea. Fick does not say where he supposes the decomposition of peptones to take place; but I think we are not far wrong in saying that it probably does so in the liver and muscles.

We may thus broadly say that albuminous food forms peptones in the stomach and intestines; and these are split up in the liver and muscles, so as to yield glycogen, a non-nitrogenous product, which is stored up in these organs, and urea which is excreted. This at once enables us to understand how it is that, in diabetic patients fed on animal food, the urea and sugar in the urine increase *pari passu*††; the sugar in them being in great part excreted with the urea, instead of being stored up as in the healthy body. The first great function of the liver, then, is to form glycogen from the sugar and peptones supplied to it from the intestines, and to store them up till wanted. This is termed by Bernard its glycogenetic function.‡‡ As the materials on which the liver acts are supplied to it by the *portal vein*, we may connect the formation of glycogen with this vessel; while, as I shall afterwards show, the *hepatic artery* is more closely related to its *destruction*; although, from the free anastomosis between them, neither vessel possesses any function exclusively. The portal vein in man has the power of contracting

very considerably;* but the source of its vaso-motor nervous supply is not so well ascertained as that of the hepatic artery. We shall, however, return to this subject in another part of this paper.

We can at once see that, if the glycogenetic function be imperfectly performed, too much sugar will pass into the general circulation, and be excreted by the kidneys. It will only do this, however, during the time that the sugar produced by the digestion of starchy or saccharine food is being absorbed from the intestines; and the glycosuria arising from this cause will be intermittent, coming on after meals, and disappearing during fasting.† It is evident that, if the meals be taken so frequently that the whole of the sugar obtained from one, cannot be excreted before absorption of the next one begins, the glycosuria will be remittent instead of intermittent. The sugar will be most abundant when digestion is at its height, and scantier when it is nearly finished; but it will never be entirely absent. This kind of glycosuria will be completely arrested by abstinence from farinaceous or saccharine articles of diet. According to Pavy, it is not uncommon among elderly people; and, so long as the urine is kept nearly free from sugar by attention to diet, it does not appear to injure their health.‡ Even in health, the power of the liver to use up sugar is limited; and, if it be absorbed too quickly from the intestine, it will pass through the liver and appear in the urine. This occurs when sugar is taken in large quantities by men or by animals, unless it be prevented by some circumstance or other from being too rapidly absorbed.§ Thus Bernard found that, when he injected a quantity of syrup into the stomach of a dog, sugar appeared in the urine. On repeating the experiment with a rabbit, no glycosuria was induced. The reason of this difference is, that the dog's stomach is generally empty, except immediately after a meal; and the syrup quickly passed into the intestine was altered by the intestinal juice, and was absorbed so rapidly that the liver could not convert it all into glycogen. The rabbit's stomach, on the contrary, always contains a large quantity of vegetable matter, even when the animal has been starved. This mass absorbs the syrup like a sponge, and only allows it to descend slowly into the intestine, so that digestion and absorption go on gradually, and the liver is able to convert all the sugar into glycogen.|| Bernard shows in a very ingenious manner that the sugar which appears in the urine of the dog is really the same sugar which has been absorbed from the intestine and passed unchanged through the liver, and is not sugar derived from glycogen. The latter consists entirely of glucose; but that obtained from the urine of the dog contains both glucose and *lævulose*, which are the ordinary products of the digestion of cane-sugar by the intestinal juice.

The starch and cane-sugar contained in food are not usually converted into grape-sugar by the saliva, pancreatic and intestinal juices, so quickly as to supply sugar to the liver more rapidly than it can convert it into glycogen. An increase in the amount of any of these secretions, such as might be expected to occur in hypertrophy of the pancreas, for example, by leading to more rapid conversion of the food into sugar, might cause diabetes, presenting similar characters to that produced by incomplete glycogenesis in the liver. Almost the only distinction between them would be that, digestion being completed more rapidly in the latter sort, the secretion of saccharine urine would begin sooner after meals and last for a shorter time than in the former. To ascertain this, an examination of the urine would require to be made very frequently; and I am not aware that any observations of this sort are on record. Several cases of glycosuria apparently depending on such alterations in the liver or digestion as have just been described, and arrested by abstinence from starch and sugar, have been recorded by Camplin,¶ Parkes, Traube,** Rayer, Bence Jones, and others. In some of these cases, the failure of the liver to perform its glycogenetic function seems to have been the sole cause of diabetes; in them, it could be warded off for many years by abstinence from farinaceous food. In others, the failure of this function seems to have been quickly followed by other changes; and then abstinence from starch failed to prevent the appearance of sugar in the urine, although it had done so at the commencement of the disease. It is possible that another imperfect kind of glycogenesis sometimes occurs when the liver forms glycogen rapidly enough, but of such a kind as to be too readily broken up again. The glycogen obtained from the livers of animals is by no means always of the same quality; for, according to Kühne,

* Tscherinow, *Wiener Acad. Sitzber. Math.-Naturwiss.*, vol. li, Abth. 2.

† Schöffer, *Archiv für Exper. Pathologie und Pharmacologie*, vol. i, p. 71.

‡ Bernard, *Revue Scientifique*, 2nd series, tome iv, p. 1066. Compare also the analysis (*Revue Scientif.*, tome iv, p. 1108), and *Observations* (p. 1023); also Schiff, *Untersuchungen über Zuckerbildung*, 1859, p. 3.

§ Kühne, *Lehrbuch der Physiologischen Chemie*, p. 65. It is difficult to understand the conflicting statements of different observers on this point, except by supposing that their experiments were made on animals in different stages of digestion or fasting.

|| Fick, *Pflüger's Archiv*, vol. iv, p. 40; also Rabuteau, *L'Union Médicale*, 1873, No. 107.

¶ Fick, *Verhandlungen der Physikal.-Medicin. Gesellschaft zu Würzburg*, new series, vol. ii, p. 53.

** Schultzen and Nencki, *Zeitschrift für Biologie*, vol. viii, p. 124.

†† Ringer, *Medico-Chirurgical Transactions*, vol. xliii, p. 323.

‡‡ *Revue Scientifique*, 2nd ser., tome iv, p. 1155.

* *Verhandlungen der Physikal.-Medicin. Gesellschaft zu Würzburg*, 1854, p. 1.

† See Traube, *Ueber die Gesetze der Zuckerausscheidung im Diabetes Mellitus*, *Virchow's Archiv*, vol. iv, p. 118.

‡ Pavy on *Diabetes*, second edition, p. 144.

§ Pavy, *op. cit.*, p. 141; and Vogel, in *Virchow's Handbuch speciellen Pathologie und Therapie*, vol. vi, Abth. 2, p. 49.

|| *Revue Scientifique*, second series, tome iv, p. 1066.

¶ Camplin on *Diabetes*; and *Medico-Chirurgical Trans.*, vol. xxxviii, p. 69; also other cases quoted by Parkes in his work on *Urine*, p. 317.

** Traube, *Virchow's Archiv*, vol. iv.

some specimens are converted by ferments into sugar with great rapidity, while others are only changed by them after the lapse of hours, although these very specimens may be at once changed into sugar by boiling them with acids.*

It is to be observed that the liver is not the only organ in the body which contains glycogen, although it is the chief one. The muscles also contain this substance;† and it is found in considerable quantities wherever cell-growth is actively going on, as, for example, in foetal structures, or in the inflamed parts of the lungs in pneumonia. It is possible that it is first formed in the liver, and is merely carried to these other parts; but as it is readily changed into sugar in the blood, it seems much more likely that muscles and young cells possess also, to some extent, glycogenetic powers, and that the glycogen they contain is actually formed by them from sugar, or peptones supplied to them by the blood. The sugar they receive may either be derived from glycogen in the liver, or directly from intestinal digestion, for it is almost certain that, although a great part of the sugar and peptones is stopped by the liver, the whole of them is not.

Diabetes, from imperfect glycogenesis, then, is to be ascribed chiefly to the liver; but the possible participation of the muscles is to be borne in mind.

A LECTURE

ON

THE PROPER METHOD OF TREATING TAPEWORM.

Delivered at the Middlesex Hospital, Wednesday, December 10th, 1873.

By T. SPENCER COBBOLD, M.D., F.R.S., F.L.S.,

Lecturer on Parasitic Diseases at the Hospital.

GENTLEMEN,—The treatment of that common form of helminthiasis technically called "tapeworm" unfortunately constitutes one of those departments of the healing art, about which people generally suppose that little or nothing need be said. Excellent practitioners will tell you that the administration of turpentine and castor oil, or the giving of half a drachm of the ethereal extract of male fern, suffices to dislodge the parasite; and, should the worm unhappily return—which is usually the case under such a rough-and-ready mode of treatment—all that you have to do is to repeat the remedy until the entozoon is finally destroyed. This kind of advice has the merit of being delightfully simple; but I have no hesitation in saying that, in the majority of cases, the practical results following its adoption are eminently unsatisfactory. I am not stating that the particular drugs in question are inefficient; on the contrary, viewed as tæniacides, I believe them to be superior to koussou, areca-nut, and other more or less well-known vermifuges. What I contend for is that, although in a small proportion of cases thus treated you may have the good fortune to be successful, yet, in by far the greater number of instances, the parasite will return, because neither the head nor even the neck of the worm will have been dislodged.

If I read the moral of professional conduct correctly, it should be our endeavour to effect cures as speedily as possible, thereby preventing the recurrence of the disease. The ordinary mode of prescribing is, to say the least, slovenly, and it fully accounts for the very incomplete results that are obtained. If it be urged that I ought to produce evidence of the truth of what has just been stated, I can only point to my own experiences in this connection, and assure you that nine out of every ten cases in which my opinion has been solicited have been cast-off or rejected ones, so to speak. I mean that they have been cases where the patients have long previously undergone treatment, experiencing only partial relief.

As observed in one of my former lectures delivered at this hospital, some persons think it fair and honest to record all cases as successful where the body of the parasite is eliminated from the bearer. Thus, one practitioner, desirous of extolling the merits of turpentine, had the politeness to inform me that this drug, with its appropriate aperient combination, "never failed to bring away the worm where it had been known to have been present." This statement was based on experiences obtained by the treatment of thirty or forty dispensary cases. The inadequacy, however, of conclusions drawn from such a source must, I think, be obvious, for in no single instance does it appear that

the head of the parasite was obtained, or even that it was so much as sought for by the medical attendant. On grounds, therefore, of this order, I maintain that it is unfair to speak of such cases as cures, and it is, further, an entire mistake to characterise the results thus obtained as successful.

Undoubtedly, now and then, cures have been effected without finding, or without any endeavour on the part of the practitioner to find, the head of the parasite; but I hold that no medical man is entitled to pronounce his patient as absolutely cured, unless he has dislodged and produced the head from the matters discharged, after and in consequence of the advice and remedies offered and administered. It may be, indeed, that the head, though expelled, escapes observation, however diligently sought for; and it is quite certain that much practical experience is often necessary to enable the searcher to find the small isolated and detached head in the midst of dark-coloured faecal matters. Repeatedly, I have obtained it after hours of search.

Again, in proof of the statement which I have advanced, respecting the comparative unfrequency of cure by the ordinary methods, I may mention that not a few of the numerous cast-off cases to which I have adverted have been those of patients who had undergone more or less severe drugging at intervals extending over a period of several years; moreover, as bearing on the question of diagnosis, it is also my duty to observe that patients have come to me for advice about their tapeworm disorders under far graver circumstances. I mean, that they have been subjected to the trying discipline of taking nauseous and drastic vermifuges for the expulsion of tapeworm and other parasites which, to my certain knowledge, never had any existence, excepting either in their own imaginations or in those of their medical advisers. This is a painful statement to have to make, but it is nevertheless strictly true. One of the most remarkable cases of this description is already recorded in my published *Lectures on Practical Helminthology*, case xxiv, p. 44. Others of a similar kind are given in the volume referred to, where it will be seen that the majority of such purely imaginary cases of tapeworm occur either in overworked men or in hysterical women. Certainly, they are amongst the most painful cases that we have to deal with; but, taken in connection with the phenomena of true parasitism, they have served to convince me that special knowledge on this subject is not without its practical value.

To return to the particular point previously urged, I have further to remark that, with more care in the exhibition of the ordinary remedies backed by a more thorough appreciation of the general economy and modes of development of the human tapeworms, a much larger professional success will be obtained. Lengthened experience justifies me in making this statement. I can say, indeed, that, during the year now closing, it has been my good fortune to obtain unusual success in the treatment of tapeworm. Some of these helminthiasis were regarded by the patients not merely as obstinate, but as incurable cases. However, to cut the matter short, let me say that, in all instances, without exception, where I have this year had an opportunity of actually examining the faeces and other matters passed by stool, as a consequence of remedies prescribed by myself, I have succeeded in procuring the head of the worm. In every instance, therefore, I have been enabled to assure my private patients that they were permanently and absolutely cured. This success, unique, perhaps, of its kind, of course only holds good in the case of those persons who have properly placed themselves under my personal care. In the more numerous instances where my opinion has merely been sought, I cannot tell what results may have followed the advice given.

Here, it is only just that I should likewise remark that, in all the cases above referred to, I have had to deal with the very prevalent beef-tapeworm. Had it been otherwise, a similar degree of success could not possibly have followed. It seems to me that the pork-tapeworm (*Tenia solium*) becomes rarer and rarer, whilst that derived from beef (*T. mediocanellata*) is extremely common. I am, indeed, informed by a practitioner of great experience that, of late years, the tapeworm disorder has very sensibly increased in Somersetshire, and it would not surprise me to learn that such was the case in other counties. Be that as it may, I can now only find time further to observe that, in the diagnosis and treatment of tapeworm, there are many other practical points which I should have been glad to have brought under your notice. For these, however, it must suffice me to refer you to the work already quoted.

By way of bringing the subject to an appropriate conclusion, I will mention one interesting case which came under my care last July. It was that of a gentleman who had carried the cestode entozoon about with him for a period of sixteen years. Previously to my seeing him, he had been repeatedly dosed with male fern, as much as one drachm and a half of the extract being taken by him at a single dose. The body of the tapeworm had several times come away; nevertheless, the

* Kühne, *Lehrbuch der Physiologischen Chemie*, p. 63.

† Bernard, Kühne, and McDonnell; Kühne's *Lehrbuch der Physiologischen Chemie*, p. 307; Nasse, *Pflüger's Archiv*, vol. ii, p. 97.