In March 1864, a healthy-looking man, aged 27, with no acknowledged venereal antecedents, or any previous ailment, except rheumatic pains, came to the Western General Dispensary with a large ragged ulceration on the dorsum of the tongue, surrounded by extensive induration. It had begun three months previously as a lump, three weeks before had cracked, and for a fortnight had been a spreading ulcer. This could only be a syphilitic gumma, and it yielded to iodide of potassium in a fortnight.

In most of the following cases there are corroborative facts in the history which support the conclusion drawn from the character of the lesion, and facts of this kind are worthy of attention, since we have to rely greatly upon them to establish the character of syphilitic diseases of the nervous system.

Mary Ann L., aged 36, married, seen in February 1869, at St. Mary's Hospital, had a gummatous tumour of the tongue. She had had eight living children, of whom only two were alive, and she had had nine miscarriages.

Ann W., aged 32, a widow, had had eight children, two only of whom survived. She stated that she had had no illness till, five months previously, she had begun to suffer from sore throat. Old cicatrices and a deep ulceration in the soft palate were seen on examination; the uvula was quite gone.

Elizabeth A., aged 30, married, had suffered from sore throat after previous pregnancies and miscarriages, and presented indications of old destructive ulceration in the left half of the soft palate; and again, whilst suckling a four months' child, she had a deep ulcer behind the left fauces.

Emma R., aged 34, married, had had five children and four miscarriages. She had lost a great part of the soft palate, and was suffering from a deep ulceration low down in the pharynx.

But cases of this kind could be multiplied indefinitely; and the bearing of the whole matter is not so much upon the prevention of attacks on the nervous system, as upon the course to be taken in cases in which syphilis, from the nature and course of the symptoms, is suspected but not known to be the cause of the disease. As syphilitic affections are frequently curable, the patient should have the benefit of the doubt. This is so far recognised, that it has become a sort of rule among those who have given attention to the subject, when in doubt, to give iodide of potassium.

[To be continued.]

IODIDE OF POTASSIUM AND CARBONATE OF AMMONIA IN THE TREATMENT OF SYPHILIS, INTERNAL ANEURISM, AND CHRONIC RHEUMATISM.

SIR JAMES PAGET was the first to call the attention of the medical profession to the following interesting fact; viz., that carbonate of ammonia greatly increases the therapeutic action of iodide of potassium. I have had extensive experience in the treatment of syphilis, and have tried it with the best results, and find that five grains of iodide of potassium, combined with three grains of carbonate of ammonia, are equal to eight grains of the potassium salt administered in the ordinary way. The following case is a good example.

John —, aged 50, consulted me about a sore situated on his left arm. There was a profuse discharge from it, and the smell was intolerable. On asking him a few questions, I got the following history. He had been a married man, his wife having died a short time ago; he had no children. Some years ago he contracted syphilis, and was treated by mercury, pushed to excessive salivation. The secondary symptoms had been well marked, and the sore about which he consulted me was of eight months' standing. He consulted several surgeons, and could get no relief. I ordered him five-grain doses of iodide of potassium, combined with three grains of carbonate of ammonia. After taking a few tablespoonfuls of the bottle, the bad smell altogether disappeared, as a man told me who was sleeping in the same room; at first he could not bear the smell, but after taking a few tablespoonfuls of the bottle he could detect no smell. This man remained under my care for about a month, and in that short time was perfectly cured, and in very good health and spirits. I could publish five cases with almost similar results. I have also found it of the greatest service in the treatment of internal aneurism, by relieving the pain and helping to consolidate the tumour. Dr. Frerichs has recommended iodide of potassium in the treatment of the waxy liver occurring in syphilitic patients. I think that the preceding facts are well worth the notice of the profession; but I would caution medical men how they increase the dose of the iodide of potassium, for, if the carbonate of ammonia be good, it will greatly increase the therapeutic action of the iodide.

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LECTURES

ON

THE PATHOLOGY AND TREATMENT OF DIABETES MELLITUS.

BY

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LECTURE II.

THE second great function of the liver is to give out, during fasting, the nutriment which it has stored up during digestion. This is effected by the glycogen, which has been stored up in the organ, becoming gradually transformed into sugar again, and, being washed out of the liver by the blood, is carried with it into the general circulation. The conversion of glycogen into sugar is effected by means of a diastatic ferment, of which a minute quantity only is present in the liver itself, but which is contained to a much larger amount in the blood. When the flow of blood through the liver is slow, the transformation of glycogen goes on gradually, but it is quickened whenever the current becomes more rapid. It seems probable that, although the blood of the portal vein may have something to do with the transformation of glycogen into sugar, this process is more closely connected with the circulation through the hepatic artery; for those lesions of the nervous system which increase the flow of blood through the liver and induce diabetes, have, according to Cyon,* little influence over the calibre of the vein, but cause the artery to dilate widely. As the blood from the artery flows into the portal vein, any increase in the circulation within it also quickens that in the vein to some extent. The circulation in the liver may be increased either by raising the pressure of blood in the arteries generally, so that the blood flows more quickly through the hepatic artery, although its size may remain the same as before, or by causing it to dilate, so that it receives a greater share of blood, while the pressure in the arteries generally remains the same.

The pressure of blood in the arteries generally may be raised by compressing any large artery, by violent muscular efforts, or by interference with respiration. The operation of these causes is followed by a greater production of sugar in the liver, and its increase in the blood of the vena cava, and even its appearance in the urine. Schiff was able to produce diabetes by ligaturing large vessels, and Pavy† found in his experiments that whenever an animal struggled either on account of discomfort or because its respiration was interfered with, the quantity of sugar in the blood of the vena cava and carotids was at once increased. According to Michea and Reynoso,‡ it appears temporarily in the urine after an epileptic or convulsive hysterical fit. This power of muscular action to increase the proportion of sugar in the blood is exceedingly interesting, for sugar is destroyed in the muscles during their contraction, and is in all probability to be looked upon as part at least of the fuel from which they derive their energy.§ The action of muscles, which causes the destruction of sugar within them, at the same time, leads to an additional supply being furnished to them, and thus the balance of waste and supply is properly sustained. The occurrence of sugar in the urine of persons suffering from cholera, or who have died from exposure to cold, is probably also to be attributed, at least in part, to the contraction of the blood-vessels near the surface of the body increasing the circulation in the liver. The intermittent glycosuria which has been observed to be present during or after a fit of ague, and absent during the interval, may also be ascribed to the rise in the general blood-pressure which occurs during the paroxysm.

Dilatation of the hepatic vessels, and increased flow of blood through them, may be produced by paralyzing their vaso-motor nerves either directly or reflexly. The vaso-motor centre (a), from which those constant stimuli proceed to all the vessels in the body by which their state

* Cyon and Aladoff. Reprint from the *Mélanges Biologiques* (which Professor Cyon was kind enough to send to me); and *Bulletin de l'Académie Impériale de Pétersbourg*, vol. viii, p. 91.

† Pavy, *On Diabetes*, pp. 62, 63, and 145.

‡ Troussseau, *Clinique Médicale*, ed. 2me., tome ii, p. 665.

§ Ludwig and Genersich, *Arbeiten aus dem Physiologischen Anstalt zu Leipzig*, 1871, p. 75.

of moderate contraction, or tone, as it is often termed, is maintained, is situated in the medulla oblongata. The vaso-motor nerves for the hepatic vessels, indicated in the figures by the dotted line which accompanies them, pass from it down the spinal cord for a certain distance, then proceed through some of the communicating branches to the sympathetic cord and through the splanchnic nerves to the liver. The point at which they leave the spinal cord and pass to the sympathetic is not quite certain. According to Cyon and Aladoff* they leave the cord by means of the fibres (c), which accompany the vertebral artery, passing in them to the lower cervical ganglia. Thence they proceed in two fibres (d), one of which passes on either side of the subclavian artery, forming the annulus of Vieussens, to the first dorsal ganglion (e), and thence through the gangliated cord of the sympathetic (f), the splanchnics (h), to the coeliac ganglion (i), and along the hepatic vessels to the liver. (Fig. 1.)

By dividing these nerves at any point between the medulla and the liver, the influence of the vaso-motor centre will be removed, and the hepatic vessels will dilate. Unless other circumstances should interfere, the flow of blood through the liver will be accelerated, and the production of sugar increased. Diabetes arising from division of the nerves is generally supposed to be permanent. In this it differs from diabetes induced reflexly by irritation of nerves, which ceases shortly after the irritation has passed off. This distinction is applied to that produced by operations; for, of course, permanent diabetes may depend on permanent irritation, and this is probably frequently the case where the disease occurs in man. Schiff† found that diabetes could be produced

Fig. 1.—Diagram showing the course of the vaso-motor nerves of the liver, according to Cyon and Aladoff. These nerves are indicated by the dotted line which accompanies them: a, vaso-motor centre; b, trunk of the vagus; c, passage of the hepatic vaso-motor nerves from the cord along the vertebral artery; d, fibres going on each side of the subclavian artery, and forming the annulus of Vieussens; e, first dorsal ganglion; f, gangliated cord of the sympathetic; g, the spinal cord; h, splanchnic nerves; i, coeliac ganglion, from which vaso-motor fibres pass to the hepatic and intestinal vessels; k, the lungs, to which fibres of the vagus are seen to be distributed; l, the liver; m, the intestine; n, the arch of the aorta.

Fig. 2.—Diagram, showing another course which the vaso-motor nerves of the liver may possibly take. The letters indicate the same parts as in fig. 1. The hepatic vaso-motor nerves are here represented as passing lower down the cord than in fig. 1, and leaving it by the communicating branches to the second dorsal ganglion. It is possible that they may sometimes leave by the branches to the first, and sometimes by those going to a lower ganglion. In such cases any irritation to the third or one of the other cervical ganglia may cause diabetes by being conveyed along the vertebral artery and up the cord, as indicated by the dark line, to the vaso-motor centre, where it may cause reflex inhibition, in the same way as any irritation to the vagus.

by division of the anterior columns of the spinal cord between the medulla and the fourth cervical vertebra. This lasted for days or weeks, in fact, till the animal died. Cyon and Aladoff have also observed diabetes which they attributed to paralysis of the vaso-motor nerves of the liver, after section of the fibres which accompany the vertebral artery, of the last cervical or first dorsal ganglion, or of the fibres forming the annulus of Vieussens. Eckhard has not succeeded in confirming their results;‡ and it is, therefore, by no means improbable that the vaso-motor nerves of the liver do not always leave the spinal cord to join the sympathetic, by the fibres accompanying the vertebral artery, but sometimes pass further down the spinal cord, and leave it by the communicating branches going to some of the dorsal ganglia. This is all the more probable, as we have an instance of a similar kind in the case of the cardiac nerves.† (Fig. 2.) As the vaso-motor nerves of the liver pass along the gangliated cord and the splanchnics, one would expect that section of these structures would produce diabetes. But this is not the case, for the sympathetic cord may be divided between the tenth and twelfth ribs, or the splanchnics may be cut, without sugar appearing in the urine. On the contrary, when other means, such as puncture of the fourth ventricle, have been employed to induce it, no sugar appears in the urine if these nerves have been previously cut. At first sight, this result is very perplexing; but Cyon has most ingeniously explained it, by reminding us that it is not mere dilatation of the hepatic vessels, but increased circulation through them, which accelerates the formation of sugar; and the width of the vessels is of little consequence if there be not sufficient blood to fill them. Now, the vessels of the intestine, especially when the digestive canal is long as it is in rabbits, are so capacious, that when dilated they can hold as much blood as all the rest of the vascular system put together, and their vaso-motor nerves are also contained in the lower part of the cord and in the splanchnics. Consequently, when these are divided, the vaso-motor nerves of the intestinal vessels become paralysed as well as the hepatic ones, the vessels themselves dilate and retain so much blood that there is not enough left to increase the flow of blood through the liver, even though its vessels may be standing wide open to receive it. But if the vessels of the liver be first dilated, and the cord or splanchnics be then cut, the formation of sugar is not arrested; for the liver, having once a brisk circulation established in it, keeps it up, although the intestinal vessels may become dilated.

A similar explanation may be given of the results obtained by Pavy, in one of his experiments.‡ He isolated the hepatic artery, portal vein, and hepatic duct, and then carefully divided all the remaining structures in the lesser omentum, including therefore the nerves passing to the liver. Notwithstanding that the hepatic nerves had been thus divided, and the splanchnics left uninjured, no sugar appeared in the urine. At first sight, this seems rather extraordinary, but a little reflection will show that the conditions are similar to those in Cyon's experiment. It is almost impossible to divide all the nerves of the liver without irritating the intestines and causing a considerable amount of congestion in them. The dilatation of the vessels produced in this way, will have the same effect as the division of the splanchnics. While watching a distinguished German physiologist dividing some of the nerves in the mesentery, I have seen the intestine become greatly congested, and so much blood has gone to it that there was not sufficient circulation in the brain to sustain its activity, and the dog, which was being operated on, slept soundly, although it had received no narcotic.

The second way in which the hepatic vessels may be dilated is by reflex paralysis or inhibition, as it is generally termed, of their vaso-motor nerves. Every one knows that, when a sensory nerve is irritated, the impression is transmitted to the vaso-motor centre, and arrests its usual action over the vessels of the part to which the sensory nerve is distributed. Thus, when a grain of sand falls into the eye, the irritation which it occasions to the sensory nerves of the conjunctiva, is conveyed by them to the vaso-motor centre, and arrests the action of that part of it which regulates the contraction of the conjunctival vessels. In consequence of this, they become dilated and full of blood, and continue so while the irritation continues; but, so soon as it is removed, the vaso-motor centre again regains its wonted power, and the vessels return to their normal size. The same is the case with the liver; and its sensory nerve is the pneumogastric. If this nerve be cut across, and its lower end irritated, no effect on the liver can be noticed; but, if its upper end be stimulated, the vessels of the liver dilate, the circulation increases, and sugar appears in the urine. § Irritation of the roots of the pneumogastric, in Bernard's famous experiment of puncture of the fourth ventricle, has the same effect as stimulation of its trunk. This experiment is per-

* Eckhard, *Beiträge*, vol. vii. tome i, 1873, p. 19.

† Schmiedeberg, *Ludwig's Arbeiten*, vol. vi, p. 34.

‡ Pavy, *op. cit.*, p. 171.

§ Bernard, *Physiologie Experimentale*, tome i, p. 326.

* Cyon and Aladoff, *op. cit.*

† Schiff, *Untersuchungen ueber Zuckerbildung in der Leber*, 1859, p. 108.

formed by pushing an instrument like a bradawl through the skull and cerebellum till it reaches the olivary fasciculi in the medulla oblongata. The instrument is prevented from injuring the anterior motor fibres of the medulla by a needle-like point which projects about the eighth of an inch from the middle of its edge. This is too fine to injure them itself, and, by coming in contact with the occipital bone, it prevents the edge of the awl from going too far. The irritation thus occasioned to the vagus roots, inhibits the vaso-motor centre of the liver, and in half an hour or an hour, sugar appears in the urine. It does not remain more than a few hours, but disappears when the irritation has passed off; and in this it differs much from the diabetes produced by dividing the vaso-motor nerves of the liver. When this is done by cutting the anterior columns of the cord in the neck, sugar, as has been already mentioned, will persist for days or weeks.*

Irritation of the peripheral terminations of some branches of the pneumogastrics has a similar effect to one applied to their roots or trunks. These nerves are distributed to the liver, lungs, heart, stomach, intestines, etc., but these filaments do not all seem to have the same power of inducing dilatation of the vessels. Diabetes can be produced by irritating the liver by needles† or electrodes‡ placed in it; and irritation in the intestine seems occasionally to have the same effect; for there is a case on record of diabetes caused by the presence of a tapeworm in the intestines, and immediately cured by its removal. The influence of the cardiac, gastric, and other branches, has not been well ascertained. Eckhard has noticed the occurrence of diabetes after operations on the abdominal cavity without any definite lesion of nerves. The pulmonary branches seem to have a most important action, as the air inhaled during respiration appears to supply them with a constant stimulus, and thus continuously inhibits, to a certain extent, the vaso-motor nerves of the liver. When the pneumogastrics are cut across, this influence is, of course, removed, the hepatic vessels contract, and the production of sugar diminishes.

Increased respiration, on the other hand, seems to have the effect of increasing the formation of sugar; for Tieffenbach§ observed that artificial respiration, performed by blowing air into the lungs by means of bellows, sometimes produced glycosuria. The appearance of sugar in the urine of animals poisoned by woorara is probably due partly to the artificial respiration employed to keep the animal alive, as well as to the action of the poison on the muscles, which will be considered afterwards. This is all the more probable because, when respiration is kept up to allow the animal to recover the effects of woorara, sugar makes its appearance. The fact that it does not do so while the animal is completely paralysed, points to a reflex production of the phenomenon; for Schiff|| has found that large doses of woorara paralyse the sensory as well as the motor nerves; and, as this loss of sensibility will destroy reflex inhibition, it is sufficient to explain the non-occurrence of reflex dilatation of the hepatic vessels while much woorara is present in the system. He states also that, when the respiration is effected gently, and the cannula is not tied into the trachea, but only laid loosely in it, so that the lungs are not over-distended by the force of the bellows, diabetes is not produced.¶ When the nerve-centres are very deeply narcotised, as when an animal is thoroughly under the influence of ether, even puncture of the fourth ventricle will not cause diabetes;** and Pavy†† found no sugar in the urine of animals when he extirpated the superior cervical ganglion under the influence of chloroform, although it appeared when he narcotised the animals with the fumes of puff-ball, which, though it stupefied them, would probably not affect the vaso-motor centre through which the irritation of the operation would influence the hepatic nerves.

The glycosuria which is often observed after inhalation of carbonic oxide,‡‡ ether, and chloroform, may also be ascribed to irritation of the pulmonary branches of the vagus by these drugs before anaesthesia has become complete. If narcosis be quickly produced, sugar is not unfrequently absent; but it generally appears if narcosis be induced slowly, so that the irritant vapour acts long on the lungs, while the vaso-motor centre is yet unaffected by it. The glycosuria is not due to the struggles of the animal during the administration of the anaesthetic; for Schiff found it in a hedgehog which only succumbed to the influence of the anaesthetic after a long time, but did not make the slightest movement

during the whole time.* The beneficial effect of opium and codeia in diabetes is probably due in part to their lessening reflex inhibition in the liver, as opium most assuredly does in the case of some other glands, and thus diminishing the production of sugar. It seems probable also that reflex inhibition may follow irritation of other parts of the encephalon, and possibly also of sympathetic ganglia, as well as of the roots, trunks, and branches of cerebro-spinal nerves.

The diabetes which has been observed after injuries of the cerebral lobes in man, of the cerebellum in animals by Eckhard,† of the superior cervical ganglion by Pavy, of the optic thalami, cerebral peduncles, pons Varolii, middle peduncles of the cerebellum, and of the cervical sympathetic cord and sciatic nerve by Schiff,‡ is probably due to this cause, as in all these cases it is only temporary, and not permanent. Irritation of the sciatic nerve in man seems to have the same effect as in animals, for temporary diabetes has been observed during an attack of sciatica. There is another possible cause of increased formation of sugar in the liver; and that is, a greater proportion of diastatic ferment in it or in the blood which flows through it. The quantity of ferment in the liver of animals varies, and it is sometimes absent altogether. The same is probably the case with the blood. We do not know whether this ferment is peculiar to the blood, or whether it is ptialin or pancreatic ferment absorbed from the intestines. Tiegel,§ indeed, states that it differs from pancreatic ferment in being insoluble in glycerine; but Von Wittich has obtained a diastatic ferment from the liver by glycerine, and I have done the same. It is possible that there may be two ferments having a similar action. Pepsin seems to be absorbed from the stomach, for it has been found in the muscles and even in the urine by Brücke; and pancreatic ferment seems also to be absorbed, for Hüfner found a ferment possessing like it the properties of converting starch into sugar and of digesting fibrine in the salivary glands and lungs. The increased secretion of a hypertrophied pancreas, which Niemeyer asserts to be common in diabetes, may thus not only act by quickening the conversion of starch into sugar in the intestines, but by increasing the transformation of glycogen after its absorption into the blood. But atrophy of the pancreas is quite as common a lesion in diabetes as hypertrophy; and, if we suppose, as is usually done, that the only function of the pancreas is that of forming ferment, it is difficult to explain the occurrence of diabetes under these conditions, except on the supposition that in both of them the nerves of the organ are irritated, and cause reflex dilatation of the vessels of the liver in the same way that irritation of the liver itself does. But, if we suppose that the pancreas not only forms ferment, but also excretes ferment already circulating in the blood, in much the same way as the liver both forms and excretes bile, we at once see that the diastatic ferment which Hüfner supposes to be found in many parts of the body may accumulate in the blood because the pancreas can no longer excrete it, and thus lead to diabetes; for both bile and pancreatic juice can only be partially absorbed in the normal condition; another part will be evacuated with the faeces. I apprehend, however, that this explanation will seem to many persons to be too hypothetical, and that of irritation of the pancreatic nerves and reflex dilatation of the hepatic vessels will appear more probable. Plosz and Tiegel|| have found that the ferment is contained in the blood-corpuscles alone, and not in the serum. When the blood-corpuscles are destroyed, the ferment acts vigorously,¶ as it is then set free. The diabetes observed by Harley after the injection of ether into the portal vein is probably due to the blood-corpuscles being dissolved by the ether.

I have already mentioned that the muscles contain glycogen, and, during their action, sugar is actually formed in them. The possibility of changes similar to those in the liver occurring in them must be borne in mind as a possible factor in diabetes. Having now considered the effect of increased formation of sugar, we must look at its diminished combustion as a cause of diabetes.

TESTIMONIAL.—On New Year's Day, Dr. Haining, who, on relinquishing for private practice the office of House-Surgeon to the Chester General Infirmary, which he has held for upwards of four years, was presented with a set of gold studs and a handsome claret jug by the visiting surgeon, matron, dispenser, nurses, and servants of the institution, as a token of their regard and esteem for him.

* Senff, Inaugural Dissertation, Dorpat, 1869; Henle und Meissner's *Jahresbericht*, 1869, p. 173.

† Eckhard, *Pester Medicin-Chirurgische Presse*, No. 7, 1873, p. 98; and Hülz, *Beiträge zur Hydrurie und Melliturie*; Marburg, 1872.

‡ Schiff, *Journal de l'Anatomie et de la Physiologie*, 1866, p. 376; and *Untersuchungen über Zuckerbildung*, p. 114.

§ Tiegel, *Pflüger's Archiv*, vol. vi, p. 249; Von Wittich, *Pflüger's Archiv*, vol. iii, p. 339; Hüfner, *Journal für Praktische Chemie*, vol. v, p. 372.

¶ Pflüger's *Archiv*, 1873, vol. vii, p. 391.

¶ Tiegel, *Pflüger's Archiv*, vol. vi, p. 249.

* Schiff, *Untersuchungen über Zuckerbildung in der Leber*, 1859, p. 108.

† Schiff, *op. cit.*, p. 106.

‡ Pavy, *op. cit.*, p. 137.

§ Tieffenbach, Inaugural Dissertation; Königsberg, 1869. Abstracted in *Centralblatt für die Medicinischen Wissenschaften*, 1869, p. 179.

|| I am uncertain where this is published. Schiff himself informed me verbally several months ago of his discovery.

¶ Schiff, *Journal de l'Anatomie et de la Physiologie*, 1866.

** Schiff, *Untersuchungen über Zuckerbildung*, p. 10.

†† Pavy, *On Diabetes*.

‡‡ Schiff, *Untersuchungen über Zuckerbildung*, p. 124.