ON
CERTAIN MORBID CHANGES IN THE
NERVOUS SYSTEM

ASSOCIATED WITH
DIABETES.

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DIABETES has hitherto been regarded as a functional disorder, and has been attributed to erroneous action rather than structural change. This view, however, must be looked upon as only provisional. Function is simply the expression of structure. Structure and function are inseparable as cause and effect. A temporary disturbance of function has its source in a transient alteration in the solids or fluids of the body. Where, as in diabetes, function is permanently altered, there must needs coexist equally abiding change in the mechanism of the organs concerned. In this belief, relying upon our improved means of research, I have, as opportunity offered, inquired into the state of the more important organs in diabetic subjects. Using the method of Dr. Lockhart Clarke, it was at once seen that the nervous system was the seat of important alterations, an observation which gained

significance from the discovery of Bernard that puncture of a certain part of the medulla oblongata rendered the urine saccharine. I have therefore had special regard to the condition of the nervous centres, though I have not neglected to examine the lungs, liver, stomach, spleen, and kidneys.

Since the discovery of Bernard attention has been directed to the state of the medulla in persons who have died of diabetes, and cases have been recorded in which softening and other morbid changes have been here found. The lesions, however, have been various in kind, and little pathological importance has been generally attached to them.

M. Abeille¹ quotes from M. Luys two instances of diabetes in which there was softening, discoloration, and injection of the medulla, which lesions he regards as consecutive upon the malady, not as antecedent to it. Dr. Lockhart Clarke² described a softened medulla from an epileptic patient who was also the subject of diabetes, and other instances might be given in which disease in this neighbourhood has been found to accompany a saccharine state of the urine.³

The changes which have been alluded to, however, have been found with such comparative infrequency in connection with diabetes, the brain in this disorder usually being, to

¹ Abeille's treatise 'On Albuminous and Saccharine Urine.'

² Beale's 'Archives.'

³ M. Lancereaux ('Bulletins de la Société Anatomique,' 1860, p. 221) describes the post-mortem examination of a diabetic subject in which the brain was softened, the ventricles dilated, and their walls discoloured, while there was much injection, with small extravasations about the calamus scriptorius, the nerve-cells being in this neighbourhood broken down and occupied by yellow granulations.

M. Luys, whose observations are alluded to above, describes the post-mortem appearances in two cases, one in the 'Bulletins de la Société Anatomique,' 1860, p. 247, the other in the 'Comptes Rendus de la Société de Biologie,' 1861, p. 24. The changes found in both were of the same kind—discoloration, vascularity, and loss of consistence in the neighbourhood of the fourth ventricle, with degeneration of the nerve-cells, which were occupied by yellow granulations.

M. Martineau ('Bulletins de la Société Anatomique,' 1861, p. 290) describes changes about the fourth ventricle similar to those previously described by M. Luys. The floor of the ventricle about the calamus scriptorius presented a greyish discoloration, with much injection of the blood-vessels.

ordinary examination, natural, that they have not been regarded as forming an essential part of the disease. In short, neither in the medulla oblongata nor elsewhere have such constant lesions been found, as to place the disease in question upon a pathological basis.

Dr. Pavy,¹ in his recent work upon the subject, thus expresses his own and the general view:—"Morbid anatomy has contributed nothing towards elucidating the pathology of diabetes. We have a manifestation of a disordered functional action without any discernible anatomical alteration to account for it."

As a contribution to the pathology of the disease I propose to describe, in somewhat minute but I trust not unnecessary detail, the post-mortem appearances in five cases, which are all I have been able to examine since my attention has been especially directed to the subject.

CASE 1.—Thomas Hatcher, 6 years of age, was brought to me as an out-patient at St. George's Hospital, on the 25th of January, 1868. He was haggard and emaciated; the skin was harsh and dry; the tongue red; he suffered much both from hunger and thirst. The urine, which was estimated by his friends at four quarts daily, was found to be highly saccharine and had a specific gravity of 1048. He had lived poorly, getting meat only once a week. The urine had been noticed as excessive for six weeks.

He was taken into the house and placed upon regulated diet. He had bran cakes, gluten bread, meat, eggs, beef-tea, green vegetables, and milk. He took glycerine in his tea instead of sugar, and was allowed a small quantity of gin. Bread was at first allowed in small quantities, but after a short time entirely prohibited.

He took by way of medicine cod-liver oil and tonics, and subsequently small quantities of opium. He remained in the hospital for a period of nearly four months, at the end of which time the general symptoms had so far improved as to suggest his removal to the convalescent establishment at Mitcham.

¹ 'Pavy on Diabetes,' edit. 2, 1869.

While in St. George's the urine varied in quantity from 24 ounces to 110 ounces in the twenty-four hours. In specific gravity it ranged from 1035 to 1056; it was always abundantly saccharine. The temperature taken in the axilla was always excessively low, varying from $93\cdot6^{\circ}$ to $94\cdot8^{\circ}$.

He returned from Mitcham, after a month's stay, much worse. He was thinner; the lips and tongue were dry; he lay in a lethargic state, as if half asleep, and resisted all attempts to give food or medicine. He had a frequent dry cough. The temperature had now risen to $97\cdot8^{\circ}$. He passed into a condition of restless delirium, in which he died on the 12th of June.

On post-mortem examination the body was extremely emaciated.

When the head was opened the brain appeared to be somewhat congested. The ventricles contained some excess of clear fluid, though not enough to distend their cavities. No further morbid appearances were as yet observed, but the medulla, pons, and adjoining parts, were preserved in chromic acid for further examination. When they had become hard enough to give clean and sharp sections it was evident to the naked eye that extensive morbid changes had taken place. There were in particular several remarkable excavations, evidently the result of disease, which will demand more minute description. Microscopic examination showed the existence of extensive excavations throughout the substance of the medulla and pons. I will proceed to describe the morbid appearances in their topographical order, tracing them forwards from the spinal cord.

In the spinal cord, immediately below the decussation of the pyramids (the only part of the cord which was kept), was a small hole in the immediate neighbourhood of the central canal, which to the naked eye looked like the prick of a needle. The microscope showed this to be a cavity of an irregularly oval shape, formed partly in the white and partly in the grey matter. Nearly isolated within this space were some large blood-vessels, one of which had the characters of an artery, which was imbedded in a mass of closely nucleated

fibroid tissue. The vessels and the tissue in immediate contact with them were, except at one point of attachment, separated from the surrounding nervous matter by an empty space. The blood-vessels in the neighbouring part of the cord were more than naturally conspicuous, and many of them, particularly in the grey matter, had small irregular spaces around them. The vessels in the anterior fissure were apparently dilated, and the bottom of the fissure was eroded so as to form an irregular cavity, from the walls of which broken nerve-tubes protruded. In one anterior horn the nervous structure had become partially broken down, taking the form of the large translucent globules which so often give evidence of the disintegration of nervous matter.

In the medulla oblongata marked changes were found. These were situated in the vicinity of the median plane, in and about the olivary bodies, and in the grey matter forming the floor of the fourth ventricle. Close on either side of the median plane of the medulla, reaching nearly its whole length, was a slit or elongated excavation which measured an eighth of an inch in length and was very visible to the naked eye. The two cavities, which closely resembled each other, in some places communicated across the septum. They each contained a dilated blood-vessel.

Within and about the olivary bodies extensive degeneration of nervous matter had occurred in immediate relation with the large vessels by which those parts of the medulla are supplied. In the white matter within and around both corpora dentata were many vessels (apparently arteries) which were more than naturally conspicuous, and some of which had been altered in shape by dilatation. In the neighbourhood of some of these exaggerated vessels the brain matter was intermixed with the translucent globules which result from disintegration. In other places, where the changes had reached a later stage, the vessels were surrounded by cavities of considerable size and irregular shape. Sometimes a material which, under a high power, was seen to consist mainly of large transparent globules, adhered in bulk to the vessel, leaving an empty space between itself and the wall of the

cavity. The drawing (Plate VII, fig. 2) shows a swollen artery, affected as described. It occupied a flask-shaped excavation in the centre of one of the olivary bodies. The material described, consisting largely of the products of nervous disintegration, was attached to its outside. Thus, several stages of the process of excavation could be here seen. First a dilatation of a vessel, then a degenerative change in the nervous matter in contact with it, then a breaking down of tissue; the products of the disintegration collecting upon the vessel from which the change had commenced.

In the white matter near the centre of the olivary body was an irregular cavity about $\frac{1}{8\frac{1}{4}}$ of an inch long, which contained no vascular structure but was irregularly occupied by the remains of nerve-fibres and globular *débris*.

Noteworthy changes were also found in the grey matter at the floor of the fourth ventricle. These were most numerous towards the upper end of the medulla, and resembled in character the alterations which have been described in the olivary bodies. Scattered through the grey matter were many small cavities of circular outline, one of the largest measuring $\frac{1}{70}$ by $\frac{1}{140}$ of an inch. Some were perfectly empty, others were traversed by blood-vessels and contained globular detritus.

In the pons Varolii morbid changes were found as striking as those in the medulla. At its posterior boundary, close to the root of one facial nerve, was a remarkable excavation, from the walls of which broken blood-vessels protruded. (See Plate VIII, figs. 3 and 4.) It had a somewhat oblong shape, was about an eighth of an inch long and half as wide, and lay a short distance beneath the surface of the pons in contact with, but not encroaching upon, the root of the facial nerve. This was evidently an enlargement of a fissure naturally existing in the pons which lodges a deep process of pia mater. This was seen on the other side of its natural size, quite inconspicuous compared with the large excavation described, and filled, as in health, with blood-vessels.

Near the front of the pons, in the median line, between the attachments of the anterior crura, was a cavity which

might have held a small pea. Its walls were irregular and broken, and from them several vessels protruded. Some comparatively trifling fragments of vascular structure lay in the cavity, which was for the most part empty. In the drawing (Plate VII, fig. 3) this excavation is represented of its actual size, and also slightly magnified.

Beside what have been described, many smaller cavities, mostly in connection with blood-vessels, were found in other parts of the pons. One, though narrow, measured a quarter of an inch in length. It had formed along the course of a large artery, which passed vertically into the pons in the median plane. It was traversed by the remains of nerve-fibres, and contained granular matter.

In the crura and optic thalami the blood-vessels were more than naturally conspicuous, and a few small cavities were seen such as were found elsewhere. Beyond this the examination of the brain did not extend.

The pneumogastric nerves were examined in section, and their structure ascertained to be perfectly natural. The semilunar ganglia were also examined without the detection of any abnormality.

The lungs were friable and loaded with serum. At the left apex was a small deposit of softened tubercle. The microscope showed many spots, apparently tubercular, where the air-vesicles were filled with a nuclear growth, and about which pigment had been deposited. In other parts the structure of the lung was natural.

The liver weighed 22 ounces; it was very hard, but not obviously changed in any other particular. Translucent sections were compared with similar sections of the healthy organ. There was a remarkable accumulation and crowding of the epithelium, such as almost to destroy the reticulated appearance of the lobular network by closing the interspaces which naturally exist. Beyond this excessive formation and close packing of the epithelial cells nothing unnatural was observed. The cells were rather opaque, but not in other respects abnormal.

The kidneys were pale, their surfaces slightly mottled; the

tubes, both straight and convoluted, were stuffed with epithelium to an abnormal extent.

The spleen and stomach proved on microscopic examination to be natural.

CASE 2.—Edward Salisbury, aged 25 years, a plasterer, came under my care at St. George's Hospital, February 11th, 1869. His only complaints were of dryness of the throat and thirst. He had a ruddy complexion, rounded features, and the general appearance of health. It was learned, however, that the urine was excessive in quantity, and on examination it proved to be loaded with sugar.

His antecedents were as follows. From the age of seventeen he had been excessively given to promiscuous sexual indulgence, and furnished details of his performances in this particular which it is not necessary to repeat. A year later he began to drink ale and gin to the extent of becoming intoxicated on an average four times a week, sometimes going for a week without any interval of sobriety. At the age of twenty he unfortunately acquired a small inheritance, which gave him the means of indulging his vices without any interruption from the necessity of following his calling. Twelve months before he came to the hospital he began to pass water frequently during the night, but it was not until six months later that he noticed that the urine was increased in amount, the appetite at the same time being morbidly great. For the six weeks preceding his admission he had suffered from thirst, drinking water contrary to his previous habits.

When he came under observation the urine measured 188 oz. in the twenty-four hours, and had a specific gravity of 1033. The tongue was rather dry, and was evenly coated with a thin white fur. The pulse was small and numbered 68. The skin perspired freely.

He was first experimentally treated with peroxide of hydrogen, the diet being liberal, as suited to his appetite, but without restriction. Upon this he began to suffer from pain in the epigastrium and forehead, and the urine gradually increased, attaining on February 17th the maximum of 532 ounces, with a specific gravity of 1035.

Gluten bread was now substituted for the ordinary loaf, and grain doses of opium were given at intervals, instead of the peroxide of hydrogen. Under this treatment he improved in some respects. The urine diminished in quantity, but occasionally showed a trace of albumen. He more than once had attacks of vomiting, bringing up undigested food. He went on without any material change, but losing weight, slightly, until the 21st of April, when he expressed himself as feeling quite well, and could not be persuaded to remain longer in the hospital.

The quantity of sugar in the urine was determined eight times between February the 18th and March the 21st. The proportion ranged from 22 grains to 68 grains in the fluid ounce. The amount of sugar passed in the twenty-four hours varied from 24,378 grains (more than 50 ounces) to 3720 grains (not quite 8 ounces).¹

On the 15th of May I heard that he was worse and visited him at his own house. He was profoundly comatose, and died in this state on the following day.

With much difficulty permission was obtained to open the head, no other part of the body being disturbed. The brain to the naked eye appeared healthy; there was no marked injection of the vessels, nor any excess of fluid in the cavities.

The medulla, pons, and adjoining parts were removed, hardened in chromic acid, and examined with results which were almost identical with those obtained in the preceding case.

Beginning with the medulla there was on a level with the decussation a cavity in the same situation, and of the same kind as that described in the case of Hatcher. Close to the central canal, separated from it only by a thin layer of grey matter, was a circular cavity which, except that it was not empty, was like the prick of a needle. This contained an almost isolated core, consisting of a pair of dilated blood-vessels involved in a loose web of areolar tissue.

¹ For these observations, which may be relied upon as accurate, I am indebted to Mr. Noad.

Within and about the olivary bodies were some cavities in connection with blood-vessels, less striking, however, than those found in the preceding case.

Scattered about the grey matter forming the floor of the fourth ventricle, particularly towards its upper end, were many small cavities, some of which were empty, while others contained blood-vessels. The cavities were for the most part sharp excavations in the brain substance, looking as if a portion had been cut out. These frequently presented in transverse section, a more or less circular outline. Some were elongated, corresponding with the course of a vessel. The drawing (Plate VII, fig. 5) represents a cavity in this situation in which the vessel upon entering it was swollen into a bag; the space being traversed by nerve-fibres.

On reaching the pons a deep excavation was found at the root of one facial nerve, in the situation in which a similar cavity was found in the case of Hatcher. It communicated with the surface of the brain by a narrow neck, and was full of entangled arteries mixed with a small quantity of areolar tissue and broken-down nervous matter. This is represented (Plate VII, fig. 6) of the actual size.

Towards the front of the pons, in the median line, a vacuity was found, as in the preceding case, in connection with a process of pia mater. It was not, indeed, entirely empty, for it was partially occupied by something which to the naked eye had a gelatinous appearance. This proved to consist of a collection of vessels, mostly large and thick-walled, which lay sometimes in a parallel arrangement, sometimes tortuous and entangled, all imbedded in a translucent substance, which, from the delicate parallel lines it displayed was supposed to be an altered condition of the fibrous nerve-tissue. The vessels and all the surrounding tissues were sprinkled with minute yellow fragments. The edges of the space were fringed with broken vessels and nerve-fibres. The cavity, which, in its greatest extent, measured about $\frac{1}{16}$ of an inch, is represented of the size of nature. (Plate VII, fig. 7.) The contents of the space magnified 50 times are also displayed. The appearance was extremely striking.

The natural depression immediately in front of the pons was deepened, or rather undermined, by a large, irregular excavation which was in connection with a process of pia mater. This is represented of the actual size. (See Plate VII, fig. 4.)

The cavity was partly occupied by entangled arteries, belonging to the pia mater. The walls of the vessels were spotted with small yellow fragmentary or semicrystalline dots, as also was the adjacent nervous matter. Nerve threads and areolar tissue were entangled among the vessels.

In the optic thalami and corpora striata were many small rounded cavities, such as were found in the neighbourhood of the fourth ventricle.

CASE 3.—Oliver Passenger, a stone mason, died at the age of 23 years in St. George's Hospital, where he had been twice a patient. He attributed his disease, which was first manifested by excess of urine, to exposure to cold while working at a cemetery. Three months after the first symptoms, two years before his death, he was first admitted under the care of Dr. Barclay. The urine then contained 7 per cent. of sugar. He left the hospital and was again admitted two months before his death, when the urine, still saccharine, had attained the amount of 390 ounces in the twenty-four hours, and had a specific gravity of 1028. Under regulated diet, which included bran cakes and gluten bread, and treatment by opium, the quantity of urine gradually diminished to 170 ounces, the specific gravity remaining the same. He, however, lost flesh latterly at the rate of a pound a day. Towards the close he complained of pain at the pit of the stomach, which was succeeded by pain in the head, drowsiness and coma. He died in February, 1869.

At the post-mortem examination a single mass of old crude tubercle was found in the right lung. The kidneys were large, soft and fatty, weighing 19 ounces. Their pelves were dilated. All the other organs were thought to be natural, excepting the brain. The subarachnoid cavity, and the lateral ventricles contained a considerable excess of fluid. The large vessels and sinuses were full of dark blood. The

white substance was congested to a pink colour, the puncta being much increased in number.

Mr. Pick, who made the post-mortem, reserved for my examination the parts which are about to be more particularly described.

Examining the brain in successive sections from behind forwards, alterations were found which were almost identical with those described in the previous cases.

Several cavities which contained vessels were clustered about the central canal of the cord on a level with the decussation. In the largest of these, which lay in the grey matter close to the canal, the vessel was greatly dilated, contained coagulum, and was encased in a thick layer of loose areolar tissue, between which and the wall of the cavity was an interval. (Plate VIII, fig. 1.) The cavities in this region were found to involve both the grey and the white matter.

On the same level the vessel in the anterior fissure was surrounded by a considerable quantity of loose nucleo-fibrillated tissue, and the fissure itself was excoriated at its base.

Higher up, changes were found in the median plane of the medulla, in and about the olivary bodies, and in the grey matter bounding the fourth ventricle.

In the median plane was a long slit, distinctly visible to the naked eye, which had ragged edges of broken tissue, and contained a vessel of considerable size.

Within and around the corpora dentata of the olivary bodies were large hollows with broken walls, which contained vessels, some of which were partly disorganized. The cavities were edged with globular and fibrous debris of cerebral tissue. One of these which lay in the central white matter of the olive, is represented in the drawing. (Plate VIII, fig. 2.)

One of the smaller cavities in the same situation was filled with globular debris, which was dotted with small masses of intensely yellow translucent material, probably a modification of blood pigment.

The grey matter of the medulla, forming the floor of the

fourth ventricle, particularly about the origins of the pneumogastric nerves, contained cavities, such as have been described in the preceding cases. A section made opposite the deep roots of these nerves showed in a striking manner the number and size of the vacuities.

Towards the front of the pons, almost exactly in the same spot as in the preceding cases, was an empty hole $\frac{1}{12}$ of an inch in its longest or transverse diameter, which probably had been formed in connection with the filament of pia mater which penetrates the medulla in this situation. Many large vessels distended with blood, and spotted on their outsides with yellow pigment, lay in the surrounding tissue.

Small cavities also existed on both sides in connection with vessels immediately beneath the line which separates the corpora striata from the optic thalami.

The pneumogastric nerves were natural in their minute structure.

The kidneys presented a marked condition of epithelial accumulation within the convoluted tubes, such as belongs to tubal nephritis.

The other organs were not subjected to microscopic examination.

CASE 4.—Sarah Stewart, aged twenty-six years, married, came into St. George's Hospital under the care of Dr. Fuller, February 10th, 1869. She stated that for twelve months she had been out of health, and for eight months had been aware that the urine was excessive in amount. Five months before her admission she had miscarried.

When she came under observation the urine, which was highly saccharine and contained albumen, measured 200 ounces in twenty-four hours, and had a specific gravity of 1032.

She was dieted in the manner at present usual in diabetes, and was medicinally treated with peroxide of hydrogen. On the 17th of February she began to complain of pain below the epigastrium, and the peroxide was changed for a grain of opium twice a day.

On the 22nd she had pain in the head as well as in the epigastrium, and became languid and drowsy. The pupils then became closely contracted, she lapsed into a state of coma and expired on the 23rd.

Post-mortem examination.—The general aspect of the brain and spinal cord was natural; these organs, however, were not minutely examined in the fresh state, but were reserved for the microscope. After hardening in chromic acid the following changes were found.

The spinal cord presented throughout its whole length a striking dilatation and injection of the blood-vessels in the tissue and in the fissures; there was also an equally general disintegration of the nervous substance in their track, which was especially marked at the base of the anterior fissure and in the transverse commissure.

The morbid changes in each region may be more particularly stated.

In the lumbar portion, to commence at the lower end of the cord, the vessels in the anterior fissure and in the anterior horns were dilated. In the latter situation the tissue in contact with their walls was uneven and tattered, the course of the vessel being fringed with detached and irregular ends of nerve-fibres.

In the dorsal region alterations of the same kind had attained a greater extent. In and about the grey matter were many vessels swollen with blood in a remarkable manner. The bottom of the anterior fissure was eroded and filled with the products of disintegration. The commissure contained one, and in some cases two perforations, through which vessels passed, a considerable interval existing between the vessel and the broken nervous matter which bounded the space.

A similar description applies to the cervical region, the enlargement having undergone most change. The vessels were in the same state of exaggeration as in other parts of the cord. The commissure, where traversed by vessels, was extensively eaten away, insomuch that in some places it was

nearly cut in two. There were generally two eroded perforations one on each side of the central canal. The vessels which passed through them were still in some instances enclosed in an investiture of areolar tissue, probably corresponding with what has been described as the perivascular sheath, there being an interval between this and the eroded nervous matter. In some cases the excavations beside vascular structure contained the remains of areolar and nervous tissue. In one place a cavity, empty, excepting for the remains of a small vessel, was found in the anterior horn. This is represented of the natural size, and also magnified 6 diameters. (Plate VIII, fig. 5.)

The medulla oblongata presented changes identical in nature, and similar in situation, to those observed in the previous cases.

About the median plane were some vessels which showed what seemed to be the first, or at least an early, departure from health. The vessel itself was unaltered, or altered only in capacity, but along its margin the brain tissue, which was as yet unbroken, was mingled with the globular matter suggestive of soap bubbles, which results from the decay of nervous structure. In the same neighbourhood were other vessels, around which the changes had proceeded to the formation of cavities, through which the vessel passed, enclosed in a thick irregular sheath of nucleated tissue, in which masses of pigment were scattered.

In the anterior fissure close to the pons, nearly in the spot where a similar change was found in the case of Salisbury, was an excavation at the root of a fold of pia mater. A group of arteries, swollen with blood and intermingled with a confused mass of extravasated corpuscles, passed into the fissure, and led to a broken cavity which lay among them, as if the tissue had been eaten away by its own vessels.

The lateral parts of the medulla, especially the olivary bodies, contained large vessels, external to the sheaths of which were traces of degeneration and erosion.

At the junction of the medulla and pons, the fissures,

into which the pia mater penetrates at the root of each facial nerve, were full of turgid vessels and extravasated blood. The vessels in the neighbouring tissue were similarly distended, and blood corpuscles were plentifully diffused into the surrounding nervous structure. It will be remembered that excavations were found in this situation in the cases of Hatcher and Salisbury.

In the pons varolii the vessels were generally injected, and were often edged with degenerate nervous structure. The changes here were not so far advanced as in the other cases.

In the septum of the ventricles the alterations were more striking. This was tunnelled more or less horizontally by channels, which when exposed by a transverse section, give an appearance of large porosity to the cut surface. Each canal held a vessel which, itself comparatively small, was surrounded by a sheath of loose translucent tissue, outside which was an empty zone bounded externally by the broken cerebral matter. Around and within the canals were many coloured grains, probably a form of blood pigment. In other parts of the septum were traces of degeneration around injected but otherwise natural vessels. (See Plate VIII, fig. 6).

Some of the convolutions presented a similar appearance. The white matter, exposed by a section perpendicular to the surface, was full of holes, of which the larger were one-twentieth of an inch across. These lay so close together as to give a cribriform aspect to the section; more than fifty were counted in a space less than half an inch square. Each was the section of a canal, which had an artery in its centre, the space around it being either empty, or occupied by a loose web of translucent tissue. The arteries were apparently enlarged; they were in most instances empty, but sometimes contained blood. Grains of a yellow colour were enclosed in the web around the vessels, and were abundantly sprinkled upon the walls of the canals. The grey matter of the convolutions remained perfectly natural; the nerve-cells were seen with typical distinctness. (See Plate VIII, figs. 7 and 8).

Passing to the other organs, the lungs were gorged with serous fluid, and contained two masses of grey hepatization, the larger of the size of an orange. The microscope showed that the smaller vessels were extensively occupied by coagulum evidently of some standing. The solidified parts showed the air-cells filled with a corpuscular semi-purulent product, among which were many small cavities caused by the breaking together of several adjoining cells.

The liver was fatty and loaded with blood, which was coagulated in many of the vessels. Under the microscope the coagulum was found to occupy many of the smaller veins both portal and hepatic. The epithelium was superabundant and densely packed, as in the case of Hatcher.

The kidneys, like the liver, were congested, and the smaller vessels occupied by coagulum. The epithelium of the convoluted tubes was excessive and crowded.

The organs which have not been mentioned were apparently natural; this statement includes the semi-lunar ganglia, which were minutely examined.

CASE 5.—The following case came under notice after the greater part of this paper had been written.

William Hudson, 32 years of age, came into St. George's Hospital under the care of Dr. Fuller, on the 16th of last December. He had had symptoms of diabetes for six months. He was much emaciated, had pain in the epigastrium, and was evidently near his end. The urine measured 96 ounces in the twenty-four hours. It had a specific gravity of 1026, and contained a considerable quantity of albumen as well as sugar. He died three days after admission, death being preceded by contraction of the pupils and coma.

On post-mortem examination the pleuræ were found to be adherent, the lungs congested, the bronchial glands occupied by cretaceous matter. The kidneys weighed jointly $11\frac{1}{4}$ ounces, they were slightly granular on their surfaces, and the tubes abnormally full. A small depression of old standing, which was attributed to caries, was found on the frontal bone. The encephalon weighed $49\frac{1}{4}$ ounces; it was

to the naked eye in all respects natural. The other organs were normal in appearance.

Dr. Whipham, who made the post-mortem, gave me an opportunity of subsequently examining the nervous centres. Without entering into minute detail, it will be seen that the results confirm the observations which relate to the preceding cases.

In the spinal cord the same excoriations existed in the fissures, and along the course of vessels in the commissure, and in the horns. There was also in the dorsal region a remarkable enlargement of the central canal, which occupied the greater part of the width of the commissure, and was a conspicuous object to the naked eye.

The central canal (of which an outline is given in the wood-cut) had an oblong shape; the transverse diameter, which was the larger, measured $\frac{1}{3}$ of an inch. The epithelial lining was still there, but had in places a somewhat irregular and frayed appearance. The canal contained a small quantity of granular matter, apparently derived from disintegration.

FIG. 1.—Outline showing the enlargement of the central canal of the cord in the case of Hudson.

In the medulla the olivary bodies were channelled along the beds of the vessels as already so often described. There were erosions in the central plane of the medulla which looked as if the tissue had been partially dissolved; and there

were large and numerous cavities about the vessels of the grey matter at the floor of the fourth ventricle.

The fissure on the inner side of the left facial nerve, which has, in the previous cases, been noticed as the seat of morbid change, contained traces of extravasated blood, while corpuscles had escaped into the tissue from some of the neighbouring vessels.

A large hole of the same character lay in the median plane near the front of the pons, exactly where found in those of the four cases already related, which was in connection with a process of pia mater which dips in between the anterior crura. It was an exaggeration of a natural cavity. The vessels within it were injected and blood was extravasated about them.

The corpora striata, optic thalami and the white matter of the cerebral convolutions also presented changes in connection with the vessels similar to those found elsewhere. A good example of extravasation and destruction of tissue existed about one of the vessels of the corpus striatum.

The right and left upper ganglia of the cervical sympathetic cord were examined in section without the observation of anything abnormal in their structure.

The results obtained in the five cases examined are briefly these; peculiar morbid changes were constantly found in the cerebro-spinal system. In all the alterations were of the same nature, and in similar situations. The earliest alteration recognised consisted in a dilatation of the blood-vessels, particularly of the arteries, with accumulation and frequent extravasation of their contents. The next was a degeneration of the nervous matter at certain points outside the swollen vessels, probably caused by the intrusion into it of blood-corpuscles. The degenerative process occasioned destruction and excavation of the tissue round the vessel. Cavities were thus produced, often large enough to be striking objects even without the microscope, which contained blood-vessels, extravasated blood, grains of pigment, and the products of nervous decay. Finally, the contents

appeared to become absorbed, so that simple vacuities were left. The perivascular sheath was variously stretched and altered in character and became loaded with pigment, but it seemed that these alterations were consequent upon the dilatation of the vessel, extravasation of blood, and excavation of nervous matter.

As to their situations the changes occurred in constant association with arteries. They were found in every part of the spinal cord and encephalon, attaining their greatest development in the medulla oblongata and pons Varolii. The excavations were generally the most marked where the blood-vessels piercing the brain were the largest and most numerous. They were frequently in connection with folds of the pia mater. The regions affected with the greatest frequency were the olivary bodies, the vicinity of the median plane of the medulla, the grey matter of the floor of the fourth ventricle, a fissure just internal to the origin of the facial nerve which lodges a process of pia mater, and a depression similarly occupied which penetrates from between the anterior crura towards the centre of the pons Varolii.

The optic thalami and corpora striata were involved, though to a comparatively slight extent. The septum of the ventricles and the white matter of the convolutions displayed the alterations in a remarkable manner. The changes especially affected the white matter, though the grey matter at the floor of the fourth ventricle and of the spinal cord are exceptions to this statement.

In the cord the most conspicuous change was the enlargement of the central canal probably connected with degeneration of tissue, of which many evidences were found there and elsewhere.

The nerve-cells of the brain and cord were generally perfect.

Such parts of the sympathetic system as were examined, namely, the upper cervical and semilunar ganglia, were apparently natural.

The only constant change found in the viscera was epithelial accumulation in the liver and kidneys.

So far as the foregoing observations extend it would seem that diabetes is associated with a substantial change, which follows the arteries of the brain and cord, and comprises injection, extravasation, and destruction of tissue. From the uniformity with which such alterations were found in the five cases examined, it may be presumed that there was a more than accidental connection between the symptoms of diabetes and the peculiar state of the nervous centres. The question at once presents itself whether the lesion is a result of the change of secretion or is antecedent to it; or have the lesion and the symptom no closer connection than as the effects of a common cause?

The last hypothesis may be dismissed as unsupported by our present knowledge. If such a common cause exists it has hitherto eluded our observation.

The association of the morbid change with the blood-vessels suggests that it may be a result of the state of the blood. We know that the blood in diabetes is altered by the presence of sugar; Is it to this that the deterioration is due? Several considerations militate against this, at first sight, probable explanation. The veins and capillaries appeared to take no share in the morbid process, though they must be equally permeated by diabetic blood, which, in the capillaries at least, is brought into more intimate relation with the tissues than in the arteries. If the changes in the tissue were directly due to the altered composition of the blood the capillaries could hardly fail to distribute its morbid influence. Beside this, the blood traverses the whole body without producing in any other organ an analogous failure of nutrition. We may probably abandon the view that the changes described are consequent upon the diabetic state of blood, and have recourse to the supposition that the nervous alterations are antecedent to, and productive of, the glycosuria.

The following considerations give likelihood to the belief that the nervous changes are primary. No organic alteration has been found elsewhere to which the saccharine state of the urine can be attributed. The changes in the brain are in their nature and situation such as physiology has shown to be

capable of producing that symptom. Further, we are the more disposed to regard the condition of the nervous centres as primary by the fact that alterations similar in kind, though differing in distribution, occur as belonging exclusively to the nervous system, quite independently of diabetes. This is the case particularly in the general paralysis of the insane. Dr. Lockhart Clarke¹ has, since most of the preceding descriptions were written, described the lesions observed in that disorder, and shown that, though differing somewhat in situation, they are of the same nature as those here described. In general paralysis the change chiefly effects the convolutions and pons varolii, leaving the lower part of the medulla and cord natural; there is also wasting of the nerve-cells. In diabetes, as has been seen, the medulla is affected throughout, the nerve-cells remaining perfectly natural.

The pathology of the nervous system is yet in its infancy. The minute anatomy of many disorders which are well known clinically has still to be unfolded. We cannot tell how far such alterations as are associated with diabetes and general paralysis are common to other cerebro-spinal disturbances. A loss of arterial tension in nerve-tissue appears to be the first recognisable step in tetanus as in diabetes, and it is not improbable that some such morbid process as has been described in this paper may prove to be a mode of nervous failure producing different symptoms, and known by different names according to its location in one part or another of the nervous structures.

The conclusion that diabetes is primarily and essentially a nervous disease accords with all that is known of its natural history; indeed, the opinion has of late years been gaining ground that the disorder is due to altered nervous action, though no structural change was known to account for it. The urine often becomes saccharine in consequence of injuries of the head, apoplectic seizures, intra-cranial tumours, and other sources of cerebral irritation. These traumatic and accidental forms of the disease are, as we may believe, not necessarily accompanied by the grave and general lesions

¹ 'Journal of Mental Science,' January, 1870.

which have been under consideration. Several kinds of irritation, if acting in the right situation, give rise to a similar change in the urine, though often temporary, and for the most part, though not always, unaccompanied by the serious symptoms which characterise what may be termed "idiopathic" diabetes.

Diabetes in its ordinary "idiopathic" form, though sometimes hereditary, and often taking its origin in causes which are not within our knowledge, continually results from circumstances which exert a depressing or otherwise injurious action upon the nervous functions; among them may be mentioned mental disturbances, rage, grief, anxiety, and intellectual toil, and the various forms of dissipation, among which sexual excess takes a prominent place.

Causes of this nature may readily give rise to modifications of circulation in the nervous centres, and it has been shown that, as far as could be learned from the microscope, a widening or distension of the arteries is the initial change in the pathological series.

The foregoing observations concur in leading to the belief that diabetes essentially belongs to the nervous system, a consideration which must have a practical issue in modifying the treatment of the disease.

Postscript.—Since the preceding paper was presented to the Society I have examined the nervous system in two other cases of diabetes with results which I will briefly state.

CASE 6.—The first was a man named William Rock, 39 years of age, who died February 5th, 1870, in St. Mary's Hospital, under the care of Dr. Handfield Jones, to whom, in conjunction with Dr. Payne, I am indebted for the opportunity of examining the nervous structures. The patient died somewhat unexpectedly of pneumonia, a considerable extent of grey hepatization being found after death. The liver and kidneys were somewhat enlarged but there was nothing to call for particular attention excepting in the nervous centres.

The spinal cord had a natural appearance externally, but on section there was found to be in the lumbar region an extraordinary enlargement of the central canal. This measured $\frac{1}{27}$ of an inch in width and was filled with granular material which seemed to have issued from two spots, one on each side of the canal, where the epithelium was absent, and the granular material was inseparable from the tissue around being superficially intermixed with it.

FIG. 2.—W. Rock. Lumbar region showing enlargement of the central canal.

This contained material was yellowish, granular, and nearly structureless. A few globules could be found in it suggestive of its origin in the degeneration of nervous tissue. It will be remembered that a similar enlargement of the central canal was found in the case of Hudson already related (page 250).

In the cervical region were such evidences of destruction of tissue as have been described in the previous cases. These were found particularly at the base of the anterior fissure, at one part of which was a deep excavation with broken edges, which nearly severed the commissure.

The brain weighed 2 lbs. 11 $\frac{1}{2}$ oz.; it was greatly hyperæmic; the subarachnoid and cerebro-spinal fluids were abundant, and were found to contain a large quantity of sugar.

The microscope brought into view changes of the same

kind as in the preceding cases. One of the most conspicuous was in the olivary body, where a large artery, with an irregular and thickened sheath, lay in an eroded channel in which was detritus of nerve-structure. This was much like what is represented as occurring in the case of Passenger (Plate VIII, fig. 2), but the destruction of tissue in the present instance was the more obvious.

The puncture for pia mater in front of the pons was exaggerated, as has been so often described before, and contained vessels which were distended with blood to considerably more than their normal diameter.

In the corpora striata were corroded channels which contained large, irregular, and apparently dilated, vessels, with much bright yellow pigment upon their outsides, while their cavities were often crammed with blood-corpuscles.

In the white matter of the cerebellum was an irregularly ovoid channel, $\frac{1}{16}$ th of an inch in diameter, the sides of which were encrusted and the interior partly filled with the globular debris of nerve-structure. An irregularly swollen artery, which contained altered coagulum, and a small vein lay within: about them were many grains of yellow pigment. The cavity, as seen in section, was very striking; from its irregularity and discoloration it was evident to the naked eye as the result of disease.

The upper cervical ganglia of the sympathetic were also examined. Dr. Payne, in taking them out, observed that the right ganglion was somewhat larger than the left, and was of a pink colour. With the microscope I could not detect anything abnormal further than that the vessels of the right were injected, those of the left empty.

CASE 7.—Dr. Sturges sent me the central parts of the brain of a woman who, while suffering from diabetes, died in the Westminster Hospital of an illness apparently unconnected with that disorder.

Without describing the brain in detail, I may say that the morbid appearances in the medulla were of the same kind as has been described in the preceding cases, though less extensive.

In the white matter of the cerebellum were large vessels, packed with corpuscles, which lay in eroded channels. The appearances were most conspicuous in the central part of the dentate body; the numerous and naturally large vessels in

FIG. 3.—Corpus dentatum of cerebellum.

this situation were irregularly crammed with blood, and the tissue around them was eroded and discoloured.

In front of the pons were striking and instructive changes. These consisted of scattered extravasations which had to the naked eye the appearance of large black dots and streaks disposed with some regularity about the divergence of the anterior crura. The dark masses consisted of blood-corpuscles in irregular or elongated heaps, through the midst of which a vessel could often be traced. In some places the corpuscles were not accumulated, but were disposed as a narrow fringe along the course of the vessel. Here and

there cracks and fissures had occurred between the vessel and the extravasated blood; on the side removed from the vessel the corpuscles were intermixed with the tissue without any abrupt separation. It was clear that these hæmorrhages had taken place as the result of transudation or migration, not of rupture.

The two additional cases coincide closely in the nature of the post-mortem appearances with the five previously related, and support the views which have been expressed.

The last instance is of especial interest from the fact that the patient died while apparently the diabetic changes were in a comparatively early stage. Extravasation of blood was found where in the more advanced examples was destruction of tissue. Blood and blood-pigment were frequently noticed in the preceding cases in and about the perivascular excavations, but the nature of the connection between the hæmorrhage and the erosion was a matter only of conjecture. The last case places the two processes in their natural relationship, and shows that interstitial hæmorrhage is an active agent in the destructive operation.

DESCRIPTION OF PLATE VII.

Figs. 1—3 illustrate the post-mortem changes in the case of
Hatcher (Case 1, page 235).

Fig. 1.—An oval cavity at the lowest part of the medulla close to the central canal. Shown of the natural size, and also magnified 150 diameters.

Fig. 2.—An excavation around an artery in the central part of the olivary body. The artery is covered with the products of nervous degeneration. Magnified 150 diameters.

Fig. 3.—A large excavation in the anterior part of the pons Varolii. Shown of the natural size, and also magnified 4 diameters.

(Further illustrations of this case are given in Plate VIII.)

Figs. 4—7 represent the post-mortem appearances in the brain of
Salisbury (Case 2, page 240).

Fig. 4.—An excavation in front of the pons. Natural size.

Fig. 5.—A cavity around a dilated blood-vessel in the grey matter near the floor of the fourth ventricle. Of the natural size, and magnified 50 diameters.

Fig. 6.—Cavity at the root of the facial nerve. Natural size.

Fig. 7.—Cavity in the median line near the front of the pons containing arteries and nervous detritus. Natural size, and magnified 50 diameters.

DESCRIPTION OF PLATE VIII.

Figs. 1, 2, represent the post-mortem appearances in the brain of Passenger (Case 3, page 243).

Fig. 1.—A cavity around an artery opposite the decussation in the lowest part of the medulla. Of the natural size, and magnified 50 diameters.

Fig. 2.—Cavity around an artery, in the white matter of the olivary body, edged with broken-down tissue. Of the natural size, and magnified 50 diameters.

Figs. 3 and 4 represent the post-mortem appearances in the pons Varolii of Hatcher (Case 1, page 238).

Fig. 3.—A section of the posterior part of the pons Varolii of the natural size. It shows the excavation at the root of the facial nerve.

Fig. 4.—The cavity at the root of the facial nerve magnified 20 diameters. The broken vessels are seen protruding from the wall. The root of the nerve is seen close to the end of the cavity.

Figs. 5—8 represent the post-mortem appearances in the brain and cord of Stewart (Case 4, page 245).

Fig. 5.—The grey matter of the spinal cord in the cervical region, showing considerable excavations in the commissure and the lateral grey matter. Of the natural size, and magnified 4 diameters.

Fig. 6.—A transverse section of the septum of the ventricles, showing large excavations about its blood-vessels. Of the natural size, and magnified 6 diameters.

Fig. 7.—The white matter of a cerebral convolution, showing numerous cavities, some containing blood-vessels. Of the natural size, and magnified 20 diameters.

Fig. 8.—One of the cavities in fig. 7 magnified 50 diameters, showing a loose web containing grains of pigment around the vessel, presumed to be an altered condition of the perivascular sheath.