1. *The Albumose*.—This substance gave rise to no immediate results when injected in the proportion of less than 0.02 g. per kilo. of the body weight, but larger doses were usually followed by symptoms of local irritation, the animals violently scratching or biting the site of puncture for some considerable time.

In rats and guinea-pigs the injection was sometimes followed by evidence of a general constitutional disturbance, characterised by a slow and laboured respiration, bristling of the hair, and frequent efforts at micturition and defecation. These symptoms, however, rapidly subsided, and the animal usually regained its normal condition within an hour.

The subcutaneous administration of the albuminous extract in doses exceeding 0.02 g. per kilo. of the body weight was invariably followed by fever. In each variety of animal the first effect of the injection was to cause a slight fall in the temperature of the body, but this seldom exceeded 1.5° F., and did not persist for more than an hour. When this phase of shock had passed off the thermometer in the rectum failed to show any evidence of fever until after the lapse of from four to five hours, when the mercury commenced to rise, and continued to do so until it attained a maximum of 105° to 106.5° F. After remaining at this elevated point for a variable period of time, the temperature gradually but steadily declined, and finally regained its normal point from 18 to 32 hours after the commencement of the experiment.

Two-hour chart from a guinea-pig injected with 0.3 g. per kilo. of the albumose. The lower line indicates the temperature of the control animal.

During the pyrexial period the animal often exhibited a considerable amount of respiratory distress, and refused its food. The combined effect of the anorexia and fever was to cause a rapid diminution of the body weight, as much as 50 g. being sometimes lost in the course of the twenty-four hours. Occasionally the animal continued to eat sparingly, and to diminish in weight for some days after the deferrescence of the fever, but as a rule the normal state of health was speedily regained.

It was observed that as long as the dose of the albumose did not exceed 0.8 g. per kilo. of the body weight, the degree of fever bore a fairly definite relation to the strength of the injection; but when larger amounts than this were administered, the relation between the size of the dose and the resultant pyrexia was destroyed, and the maximum temperature never exceeded 107° F., even after a dosage equal to 2 g. per kilo. As a rule, rabbits were more susceptible to the action of the albumose than the smaller animals, and among the same species some individuals reacted more readily than others. It was never possible to produce any degree of toleration to the drug by the use of repeated injections. Occasionally after a large dose of the albumose had been given, the urine was found to contain a trace of albumen, but this symptom did not persist after the fall of the temperature. Injections of the albuminous extract on alternate days for a fortnight, in doses varying from 0.1 to 1 g. per kilo. gave rise to a continued form of pyrexia, during which the animal lost flesh and strength. But as soon as the injections were discontinued, the health was rapidly restored, and in no case did a fatal termination ensue. Intravenous administration

of the albumose to rabbits was also followed by pyrexia, but the fever was less severe and less abiding than in the former case. As a rule, the temperature rose within an hour of the injection, attained its maximum within four hours, and again fell to normal within the next three hours. *Post-mortem* examinations conducted upon the animals which were killed failed to demonstrate any macroscopic evidence of disease, even in those cases where large and repeated doses had been given. The gastro-intestinal tract appeared to be perfectly normal, and no enlargement of Peyer's patches, of the retro-peritoneal glands, or of the spleen could be detected. Under the microscope the various tissues of the body exhibited no deviation from the normal, except that, in a few cases, the renal epithelium gave evidence of cloudy swelling. But in these instances the glomeruli remained unaffected, and no indications of parenchymatous inflammation could be discovered.

2. *The Alkaloid*.—This extract was employed in doses varying from 0.05 g. to 0.5 gr. per kilo. of the body weight, and was administered both subcutaneously and by intravenous injection. No phenomena of interest followed the injection, and the temperature of the body remained unaffected. Death never occurred spontaneously, and the microscope failed to detect any morbid changes in the tissues in the animals which were killed.

3. *The Fatty Extract*.—This substance was liquefied by heat before its subcutaneous injection. Its only effect was to cause a temporary fall in the temperature, but neither fever nor visceral lesions followed its repeated injection.

CONCLUSIONS.

1. Three varieties of chemical substances can be extracted from the spleen after death from enteric fever during the third week of the disease—albumoses, alkaloids, and fatty bodies.

2. The injection of the albuminous extract into lower animals causes an elevation of the temperature of the body, which lasts for about thirty hours, and is associated with anorexia and emaciation. Under ordinary circumstances a fatal result is not observed, and no pathological changes of importance are to be detected in the tissues.

3. The administration of the alkaloidal and fatty extracts is unattended by any pathological results.

ON A CASE PRESENTING SYMPTOMS OF CEREBRAL TUMOUR, IN WHICH A LARGE AREA OF THE SKULL WAS REMOVED FOR RELIEF OF INTRACRANIAL PRESSURE.

BY

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HISTORY OF CASE.

THE patient, J. W., an iron moulder, aged 38, was first admitted to the Bristol General Hospital on February 15th, 1894, after he had been attending as an out-patient for some time. He complained of very severe headache and of fits, and attributed his illness to injuries to the head when a boy, and to a shock received from the death of a sister during her confinement two years previously. The family history was good, except that seven brothers and sisters died at or under 12 months from fits or convulsions; he had four brothers and six sisters alive and well. When 12 years of age he fell off a wall 14 feet high on to his head, was unconscious two hours, and laid up for two weeks; he recovered perfectly, except for occasional headaches. He was a temperate man; had syphilis at the age of 19. With the exception of a mild attack of rheumatism, two to three years previously, he had had no other illness. Six weeks after his sister's death he was getting up from a chair, when he suddenly became unconscious and fell; he became rigid, and the rigidity was followed by general convulsions; the loss of consciousness

lasted for some time; according to his statement nearly half an hour. On recovering he "talked nonsense," and a splitting headache came on, which had been more or less constant ever since. He had eight similar fits during the following night; he did not pass water nor bite his tongue in any of them. Altogether he had had at least twelve fits. His memory since they came on had been gradually deteriorating; it was good before. His mental capacity had also decreased. The headache was often worse at night, preventing sleep. Appetite was bad; the tongue furred, and the bowels constipated. The pulse was 72, regular, small, compressible.

He was a small man, well nourished, but rather grey, and looking older than his years. There was a large reddish scar over the left malar bone. The thoracic and abdominal viscera presented nothing abnormal, and the urine contained no albumen or sugar. The head was of normal size and shape; there was a large depressed scar over the upper part of the occipital bone, and a smaller one posterior to it; there were also two small scars on the forehead. The face was symmetrical, and there was no oculo-motor or facial paralysis. He put out the tongue straight. The pupils were equal, and reacted well to light and accommodation. V R = $\frac{1}{2}$ Hm. +1, reads Jaeger 1 at 7", fields of vision slightly contracted below; L $\frac{1}{2}$ Hm. +0.75, reads Jaeger 1 at 8", double optic neuritis of moderate intensity; no hæmorrhages. No motor paralysis anywhere. Dynamometer registered right hand 35, left hand 33. There was no rigidity or wasting of muscles. Sensation to touch and pain was normal over the head and face, and all other parts of the body. The superficial reflexes were normal, the knee-jerks active, the right slightly more so than left. Touch, taste, smell, hearing, and speech were normal. The head pains appeared to start from the right temple.

He was given iodide of potassium, beginning with a dose of gr. x, rapidly increased to gr. xl, three times a day, and antipyrin to relieve the exacerbations of pain. For the first fortnight he improved considerably, the headache grew less, and Mr. Walker, the ophthalmic surgeon to the hospital, to whom I am indebted for the care and trouble he took in examining the eyes, considered the optic neuritis decidedly better. During the next week, however, he suffered from an increase of pain, but improved again and left the hospital decidedly better, though not altogether free from pain, on April 15th. During his stay he vomited about six times, most often at night; the vomiting took place at long intervals from a meal, and no cause could be traced for it. When the headache was worst and the vomiting most frequent the pulse-rate fell to 60 or 64; at other times it varied from 72 to 84. The temperature was persistently subnormal, from 97° to 98.4°.

On May 28th he was readmitted, and said that soon after leaving the hospital the headache came on again, and gradu-

Chart I.

ally increased in severity. It was constant, but worse at night. The pains were over the vertex and the forehead. He has been sick several times irrespective of taking food. On May 19th he had a series of seven fits during the night. The fits were thus described: He suddenly felt sick and giddy, lost consciousness, and fell down; he foamed at the mouth, became livid, and breathed rapidly. Violent convulsive movements then came on, affecting both sides of the body, but it was thought that on some occasions the right

side was most convulsed. The convulsions lasted 5 to 6 minutes; after which he recovered consciousness, feeling exhausted and sleepy. After about an hour the fits returned though each succeeding fit was less severe. Since this series of fits the sickness has occurred more often, and he has had a feeling of "giddiness" like that preceding the fit. On examination, the physical signs were much as above given: the knee-jerks were equal, the abdominal and cremasteric reflexes absent, and the power of grasp the same in each hand. Pulse-rate 72. The optic neuritis had increased in intensity, and was more marked in the left than in the right disc. A chart of the visual fields is given herewith (Chart 1). The visual acuity was: $R V' = \frac{3}{16}$ $v'' = \frac{1}{12}$ $v''' = \frac{1}{18}$ $L V' = \frac{1}{12}$ $v'' = \frac{1}{18}$ $v''' = \frac{1}{20}$ There was no affection of sensation and no paralysis of any muscle.

On May 29th pain was, as usual, worse over the right temporal region. Since coming in he had been unable to pass urine. This day, whilst being examined, he complained of pain in the head and giddiness, and passed for a few minutes into a semiconscious condition, not entirely losing consciousness; the respirations became hurried and shallow, reaching 52 to the minute at the end of the attack. The pulse remained unaltered; there was no rigidity, and no muscular twitching. The pulse-rate throughout the day was 54, regular and weak. The next day it was 66. He was given iodide of potash and phenacetin for the paroxysms of pain. On June 8th the left pupil was larger than the right. At this time he seemed dull and heavy, and was slow in answering questions. He became dissatisfied and left the hospital, but returned worse after a fortnight.

On July 17th he was decidedly worse as regards headache, and had had several attacks of vomiting and frequent fits of giddiness. He said he had felt some numbness and twitching in the left hand and the calf of the left leg, but no affection of sensation could be made out. The right knee-jerk was very slightly more active than the left. He felt very weak, but could stand and walk well with eyes open or shut. There was no superficial tenderness over scalp, but he was tender to forcible percussion over the temporal and occipital regions. As the man was steadily getting worse, he was, after consultation, transferred to Mr. Morton's ward with the view of trephining him.

ACCOUNT OF THE OPERATION BY MR. MORTON.

Although the classical symptoms of cerebral tumour were present, there were no definite localising ones, hence the operation was not exploratory, but was simply undertaken to relieve these symptoms by reduction of the intracranial pressure. It was performed on July 20th. In order to avoid the superior longitudinal sinus, the lateral sinus, and the branches of the middle meningeal artery, the bone was removed from the parietal eminence and portion of skull immediately below and behind it. An area, almost a circle, with a diameter of $2\frac{1}{2}$ inches, was removed, in three portions, by means of a $1\frac{1}{2}$ -inch trephine, the three trephine discs overlapping slightly, the angles being cut away with Hoffman's forceps. The bulging dura mater had to be depressed with the finger and flat copper spatulae whilst the last disc was being removed, and then it projected slightly beyond the surface of the bone forming the margin of the large opening. It pulsed distinctly. The large flap which had been turned down was then replaced and sutured, a small drainage tube being inserted at each lower angle. There was no shock from the operation.

The second night after the operation was, he said, the best he had had for a long time, as he was quite free from headache. On the third night and day he had a good deal of pain in the neighbourhood of the wound, and on the morning of the third day his temperature rose to 102°, but there was no sign of suppuration about the wound. The pain did not continue, and the temperature was never again raised. Ten days after the operation the wound had healed, and he was up and going about the ward. He said "he felt as if he had a new head." The headache had entirely gone, and he thought his sight better. The optic neuritis seemed much the same. There was slight recurrence of headache during the first week in August, but after that only a very slight pain about the right temple and back of the right orbit. For this he took 5 grains of antipyrin at night, with complete relief. He was

discharged on August 14th, and after that we lost sight of him for a time. The optic neuritis, when he left the hospital, seemed stationary.

I was much encouraged to perform this operation, not only by the recommendation of Professor V. Horsley¹ and the record of his case of cerebellar tumour² so greatly relieved by it, but also by the marked relief of symptoms in a case of tumour of the pituitary body recorded by Dr. Caton and Mr. Paul,³ and I was careful in our case to remove nearly as large an area of bone. Dr. Beevor and Mr. Ballance consider⁴ that removal of the bone alone without incision of the dura mater is not likely to relieve the intracranial pressure much; but the actual increase in the bulk of the cranial contents may not be considerable if the tumour is small, and the bulging of the dura mater even to a very limited extent may be sufficient to relieve the increase of intracranial pressure caused thereby. Clinical evidence, both in Dr. Caton and Mr. Paul's case and in our own, distinctly shows that removal of an area of bone alone is sometimes sufficient; and in connection with this point I must refer to some interesting cases reported by Dr. Kammerer and Dr. Wyeth to the New York Surgical Society.⁵

AFTER-HISTORY.

The subsequent history of the case is as follows. He attended at irregular intervals as an out-patient, and remained quite free from headache and sickness, and in much better health than before the operation. His sight improved, and the optic neuritis subsided, leaving the discs white and partially atrophied, the left disc being the worse.

On November 27th, 1894, V. R=§, reads J. 1 well; L=§ badly, reads J. 6 slowly at 10 inches. Right field of vision contracted somewhat; left field markedly contracted all round, most below. At one of these visits I took a tracing with the cardiograph of the pulsation at the trephine hole.

Left Eye

Right Eye.

Chart II.

On January 5th, 1895, his wife woke up at 12.50 A.M. to find him struggling and in a fit. The convulsions were general, and not of a unilateral type. He passed out of one fit into another, having twenty-four in all before the following night; the intervals of consciousness between the fits lasted from twenty to thirty minutes. They were all of the same character, and commenced quite suddenly. He remained on his back, not turning to either side, and neither the head nor eyes, which were turned upwards, showed any lateral deviation. He passed water and bit his tongue in some of them. After the eleventh fit he vomited two chamber-vessels full of dark brown grumous fluid. He had been strange in his head for several days before the fits came on. He got up and dressed in the middle of the night on January 4th, and went out into the street shouting. After the fits the scalp over the trephine opening became more bulging, and showed marked increase of pulsation.

After admission on January 9th he was quiet and gave no trouble, but did not seem very clear in his head, thought that the other men in the ward were smoking, and wanted to smoke too. He was given a mixture containing iodide and bromide of potassium. On examination the right pupil was

a little larger than the left; both reacted well to light and accommodation. No paralysis of any cranial nerve. No paralysis of the limbs. No disorder of sensation anywhere detected. Dynamometer registered 40 on right and 39 on left side. Special senses normal (for sight see below). Reflexes knee-jerks equal. Right plantar reflex obtained with difficulty; others normal. No headache or sickness. Urine normal. Pulse 80, regular; good wave. Both optic discs white and atrophic, and vessels small; the left much more than the right, and there are white lines on the vessels in this disc. Vision: R=§ well, Jaeger 1, at 10" to 15"; L=§ well, Jaeger 2 slowly, at 12".

January 24th.—Since he entered the hospital he has had no return of fits, nor any other bad symptom. The bulging and pulsation over the trephine hole, so marked on admission, have both much lessened. He seems quite clear in his head, with unimpaired memory and intelligence, and is free from headache and vomiting. His only complaint is now of bad sight, and to the ordinary tests this defect is not great as regards central vision, though there is certainly contraction of the visual fields, especially on the left side (Chart II.) The temperature is normal instead of subnormal as formerly, and the pulse-rate 74 to 80.

REMARKS.—On the patient's first appearance the cardinal symptoms of intracranial tumour: optic neuritis, headache of very intense (often agonising) character, vomiting of cerebral type were present, together with the occurrence of epileptiform convulsions. These symptoms had come on and gradually grown worse during two years. Secondary or localising symptoms were entirely absent, but it is well known that a cerebral tumour may attain a considerable size without giving rise to local destruction, whilst at the same time causing a general increase of pressure within the skull, and thus no focal symptoms are observed. Such a course is especially favoured by slow growth of the neoplasm. In our patient the symptoms slowly increased during two years. Failure of memory and impairment of mental faculties were the only other important symptoms. The man had had syphilis nineteen years before. It was therefore possible that a syphilitic neoplasm was present, and this was rendered more likely by the fact that his first stay of two months in the hospital under treatment with mercury and full doses of iodide of potassium brought about temporary amelioration of symptoms.

No other cause of optic neuritis, vomiting, headache, and convulsions could be discovered. The improvement mentioned above lasted but a short time, and during a second course of the same treatment in the hospital the symptoms grew progressively worse. There were still only the primary symptoms to go upon, as no focal symptoms of any value appeared. To the subjective feelings of transient stiffness in the right arm and leg after one or two of the fits, and of numbness in the left hand after another, no importance for localising purposes could be attached. The pressure symptoms were increasing, and it seemed time—two fair trials of antisyphilitic remedies having been tried without effect—to make some further effort to relieve the intense headache and the optic neuritis. The slow progress of the case seemed to indicate no immediate danger to life, and we were anxious to save the man from becoming blind. The case appeared, therefore, to be a suitable one for the removal of a large area of the skull with the object of relieving pressure, in the way that has been recommended and carried out by Professor Victor Horsley and others, and it was thought that such an operation, if done at all, should not be further delayed. The patient himself was anxious for the operation.

Mr. Morton, therefore, trephined merely to relieve pressure and not with any idea of seeking for the growth. If, later on, localising signs appeared, something more might still be attempted. So far, except for the recurrence of the fits five months afterwards, the operation has completely fulfilled the object for which it was undertaken. The optic neuritis has subsided, leaving, it is true, a certain amount of consecutive atrophy; but the patient has good vision, has been entirely free from headache ever since, and from vomiting, except once during the last series of fits; has recovered his mental powers, and been enabled to lead a comfortable existence.

¹ BRITISH MEDICAL JOURNAL, 1890, vol. ii, p. 1290; and 1893, vol. ii, p. 1365.

² BRITISH MEDICAL JOURNAL, 1893, vol. ii, p. 1366.

³ BRITISH MEDICAL JOURNAL, 1893, vol. ii, p. 1421.

⁴ BRITISH MEDICAL JOURNAL, 1895, vol. i, p. 8.

⁵ *Annals of Surgery*, 1894, vol. xix, p. 685.