HEREDITARY APHASIA: A FAMILY DISEASE OF THE CENTRAL NERVOUS SYSTEM, DUE POSSIBLY TO CONGENITAL SYPHILIS.

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I.

UNDER the title of Hereditary Aphasia we have attempted to describe a disease that has been observed in eight members of a family; three cases occurring in one generation, and five in the generation following. There is a sufficiently close resemblance between each one of the series of cases and the rest to exclude the notion of an accidental similarity, and to justify the conclusion that we have to deal with one disease in all the cases, a disease due to the same cause throughout, and capable of recognition if it recurs by a limited group of well defined symptoms. The morbid anatomy and histology have been worked out in the latest of the cases, and the lesions observed suggest, though far from conclusively, a syphilitic origin for the disease. If this point can be proved, it will be of special interest, for the taint of the disease will have reached the grandchildren of the person originally affected.

The main features of the disease, which does not become manifest until the patient is attaining to adult life, are the following:—Incontinence of urine,¹ attacks of temporary aphasia with loss of power on the right side of the body, gradually increasing opacities in the vitreous humor of the eyes, loss or diminution of the senses by which pain and

¹ The term incontinence is here used, as the affection was so described in the earlier cases; but the symptom would be more correctly described as "retention of urine."

temperature are appreciated, muscular weakness, epileptiform convulsions, and sudden death preceded by complete unconsciousness. Wasting of the soft tissues is marked only during the later stages of the disease.

A family tree will briefly show the number of children in each generation, and how they were affected by the disease:—

It will be seen from this that there is no evidence of the disease in the great-grandparents on either side. Of the maternal grandparents, both furnish some suspicious points. The grandmother died suddenly, so suddenly as to require an inquest. The coroner's verdict, however, gives no details, only stating that "she died naturally and not from any "violence." The grandfather led an intemperate life, and died in the London Hospital when 40 years old of "gangrene of the lung." This was a chronic illness, lasting four months, but unfortunately no *post-mortem* examination was made, and no record of the case has been preserved to show whether the disease was syphilitic or not.

Of the second generation one male is now alive, and healthy, at the age of 67. He was younger than his three sisters. The only other male child died in his fifteenth

year, presumably too early to show symptoms of the disease. The three daughters all suffered from it. The mother of our patient was healthy as a girl and while a young woman. The only abnormal fact that is related of her previous to her marriage is that she suffered from time to time from a "curious reddish eruption on the fingertips." She was married at 27, and shortly afterwards began to suffer from attacks of aphasia, which came on at long intervals, "perhaps two or three times in the year." On these occasions she also "used to drop things." Seven years after her marriage, at the age of 34, her sight had become so much affected that she only retained a weak perception of light. Whether she suffered from urinary troubles cannot now be ascertained. She died at the age of 38, after four years' partial paralysis, the latter appearing to have taken the place of the occasional attacks at about the same time that the amblyopia became extreme. Her death occurred on December 29, 1878, and was ascribed to apoplexy.

Of her two sisters, the elder died on February 6, 1880, aged 40. Death was ascribed to an "aneurism of the heart," supervening upon "atrophic softening of the brain"; the latter had been of several years' duration. It is remembered of her that she had temporary attacks of aphasia, with loss of power in the right arm. She had no epileptiform attack, or at all events, none that caused unconsciousness. She does not seem to have suffered from any ocular trouble, and there is no evidence of "incontinence of urine."

The younger sister died July 14, 1869, aged 26. Her death was due to hæmorrhage from a gastric ulcer. She suffered from temporary attacks of aphasia and paralysis in the right arm; and also, like her married sister, from a gradual loss of vision. The following account of the eye symptoms in both of his patients has kindly been furnished to us by Mr. Brudenell Carter, whom they consulted twenty-seven years ago; it is especially interesting in conjunction with Mr. Lawford's report on our patient, which is given later. "(The married sister) had slight deep-seated cloudiness of the vitreous, when seen in 1875, with slight

impairment of vision; the right eye to about a $\frac{1}{2}$, the left to about $\frac{2}{3}$ of normal vision. Partly from the nature of the case and partly from the treatment by hyd. perchlor. and pot. iod., I have little doubt that I regarded the case as specific, but my notes do not say so. My last record is that the vision remained stationary, after slight improvement." This note was made three years before the patient's death, and, as has already been mentioned, blindness became almost complete before the end. Of the other sister Mr. Brudenell Carter writes: "I saw her on December 10, 1874, and on January 3, February 1, and March 23, 1875. My first note is, "Turbidity of R. vitreous, commencing ditto in L., probably hæmorrhagic in origin. Neurotic tendencies; occasional speechlessness with temporary paralysis of right arm. Under treatment the vision of R. rose from $\frac{5}{80}$ to $\frac{5}{18}$; the urine was normal."

We now come to the generation of the patient with whose case the present writers have been acquainted. There were six children, four sons and two daughters. The three elder sons died between the ages of 22 and 24. Of the two daughters one was older, one younger, than our patient. The elder of the two was healthy till her 30th year, but since then her eyesight has become defective, and the nature of the defect proves in this case also to consist in vitreous opacities. She is not known to have had any other symptoms of the disease. The younger daughter was neurotic, but showed none of the special symptoms characteristic of the disease. She died suddenly at the age of 24, from sudden heart failure during a severe attack of diarrhœa. There was no *post-mortem* examination.

The eldest son died at the age of 23, death being ascribed to "apoplexy." The first symptom of disease in his case is said to have been incontinence¹ of urine, which commenced in his twenty-second year. Previous to that time he had enjoyed good health, being educated at a public school where he played cricket and other games. After leaving school he

¹ Probably really retention.

"crammed" hard for the army. The "incontinence," at first intermittent, gradually became established; it was presently followed by attacks of aphasia, short in duration. Later on he had several epileptiform seizures, falling in the street and elsewhere; he never hurt himself seriously by these falls, but he became quite unconscious, and the tongue was bitten. He was not drowsy after the attacks. It is also reported that he occasionally became unconscious for a few minutes without other symptoms.

The second son was healthy as a boy, but did not go in for any form of athletics. He reached the age of 22 without misadventure; but then, one morning at breakfast, he suddenly lost the use of his right hand, while trying to lift the cover off a dish. The weakness lasted for two or three hours. There is some doubt as to whether aphasia was also observed at this time; but later on he did have one or two attacks of aphasia, and it was decided to send him for a long voyage to Australia on account of his "want of tone." He improved during the early part of the voyage; but one day, in rough weather, he was found insensible in his cabin, and he died without recovering consciousness. He does not seem to have suffered at any time from urinary troubles.

The third brother was also healthy for the first 22 years of his life. He played cricket and football at school, and went into his father's office when he grew up. He died at the age of 24, having been ill two years. He had suffered from "incontinence" for about twelve months before his death. He also suffered from attacks of temporary aphasia, and those who were with him related that the lips became full and the face congested before an attack. He suffered greatly from constipation, sometimes passing no motion for a week; he gradually grew weaker, heavier, and more drowsy; finally he became suddenly unconscious, and died. Towards the end, when very weak, he passed *fæces* as well as urine unconsciously.

The fourth son was the only one known to us, who saw him first in December, 1897. He was then 23 years of age, and had begun to show symptoms of the disease about nine months previously. His appearance was that of a strongly

built, rather tall young man. He had been healthy during boyhood and fond of all forms of athletics, including gymnastics, cricket and football. He had not suffered from incontinence as a child. There is no record of illnesses in childhood, except some unnamed illness at about the age of 14, a bilious attack followed by fever and delirium. At times he had been given to sleep-walking. As recently as 1895, when 20 or 21 years of age, he had been able to walk thirty-two miles in a day without more than ordinary fatigue.

In his case also the earliest symptom observed had been "incontinence of urine"; though an unusual degree of constipation had been present for two years before this occurred. It was preceded by pain in the tip of the penis, sufficiently severe to make him consult a doctor: the first escape of urine followed a week later. Since that time it had occurred only during the night; but, with three exceptions, it had occurred every night from March to December. The sexual functions seem to have been disturbed at the same time, the patient losing all sexual desire, and never having an erection of the penis. The account given by him in December, 1897, suggested overflow from a distended and atonic bladder rather than true incontinence. He said that, when he had passed water, more came on further effort; and that "coughing would then again cause the stream to flow out in jerks." The stream was at all times weak, and he passed water for about a quarter of an hour before going to bed, doing so while kneeling to say his prayers. It was at eight o'clock in the evening that he first came for advice, and a catheter was then passed. No stricture or other obstruction was found. A pint of urine was drawn off; it came fairly strongly at first, but for a long while at the end it merely trickled. The urine was acid, it contained albumen and pus, no casts were found. The albumen and pus disappeared later when the bladder had for some time been regularly emptied by the catheter and washed out at intervals.

Of other symptoms, the only one noticed at this time was some defect of vision. It caused him no serious in-

convenience; but he noticed that there were spots in groups, before the right eye. The pupils were at this time normal in size and shape, and re-acted both to light accommodation. The muscular strength was good everywhere. Knee-jerks were present, but perhaps a trifle sluggish. He had occasionally sudden and brief pains in the legs. The tongue was rather red and had a swollen appearance.

After this he was not seen for two months, re-appearing in February, 1898. The "incontinence" had become less troublesome, but there was again pus and albumen in the urine, and he did not seem to know by his sensations when the bladder was over-distended. He went away for several months to the Riviera, and was next seen in November, 1898, after an interval of nine months. He was suffering at the time from a febrile attack, with temperature 101-102° F., the fever lasting for four days. He had no headache, did not complain of pain in his back or limbs, was listless and heavy, and inclined to wander in his talk. On recovering, he gave some account of his experiences during the preceding nine months, and a fuller examination was made of the nervous system. He said that he had been better during the summer, but thought that he had lost some strength. He had come to use the catheter regularly, and could not pass water without it. The pus and albumen were no longer present, there was some slight improvement in the force with which the urine was expelled through the catheter.

Examination revealed the following facts:—

(1) In common sensation there was nowhere any change from the normal.

(2) The sense of pain and the temperature-sense were very markedly affected. While in bed he had allowed both his feet to remain in contact with an uncovered hot-water bottle; and while he felt no pain, large burns had resulted. These healed slowly but satisfactorily. The accompanying diagram shows fairly accurately the degree of analgesia, and the regions affected. It was most marked over both legs below the knee. On the right leg in front, it ascended also

FIG. 1.—Diagram of areas of analgesia.

to the groin. It was traceable over part of the abdomen and, in a slight degree, over areas of the forearms and upper arms. On the posterior surface of both legs it extended in varying degree to the buttocks. In several places there were small patches of acute sensation surrounded by analgesic regions, as, for example, in front of both knees, in the front of the left leg, and on the soles of both feet.

(3) The knee-jerks were, as before, present but sluggish.

(4) The muscular power was certainly not below the average in any part of the body, though the patient complained that his muscles felt weak. There were no tremors.

(5) The smell and taste were normal.

(6) The sight of the right eye had become less clear. He complained much of a sensation as of dust moving in front of it. The light-reflex in this eye was sluggish. The pupil was smaller (*sic*) than that on the left side. The optic discs appeared normal, and no disease of choroid was observed; but there were marked opacities in the right vitreous humor, and the left was not quite clear.

(7) Shooting pains in the limbs had become more frequent. They occurred usually in the feet or toes, coming on suddenly without warning and being momentary but severe. He had occasional twitchings in the lumbar muscles.

(8) Drowsiness had become a marked feature of the disease during the last few months. He slept twelve hours out of the twenty-four, from eleven to eleven.

(9) The hearing was imperfect. At first he could hear a watch at 4 inches only on the right side, and 1 inch on the left. Some cerumen was removed: but this only caused an improvement up to 10 inches on the right, and $3\frac{1}{2}$ inches on the left side. The membranes appeared normal.

Up to this time all the symptoms observed, with the exception of the drowsiness (and perhaps the eye and ear symptoms), were referable to the spinal cord; there were none of the brain-troubles—the aphasia and paralysis—that had been observed in the three elder brothers. The patient had also lived to a greater age than any of his brothers; and the disease had been observed in him for two years without making very rapid progress. But in March, 1899,

he went out to a dance, and came home at three o'clock in the morning. He was unable to get a cab, and had to walk for two or three miles. Having been warned to avoid fatigue, he stayed in bed till one o'clock the next day; but while dressing he dropped a glass from his right hand, and found that he was unable to express himself clearly in words. He was seen by one of us within three-quarters of an hour of the commencement of the attack; the aphasia was then still marked, and he failed to read when asked to do so, no less than to converse. The attack had subsided an hour later, and he felt and seemed quite well in the evening.

He was again away, staying at Weymouth, during the greater part of the summer. On the whole, he had fair health while there; but in August (1899) he had two more attacks of temporary aphasia. Once also, after having been out in a boat (but without exposure to cold or wet) he was seized with severe pains in the folds of the buttocks, lasting about four hours. The pains came on about once a minute. He also had the afore-mentioned shooting-pains about once a month throughout the year, usually in the legs, sometimes in the hands. At the same time he gradually became weaker, and when seen in November (1899) had lost a good deal of flesh, especially in the lower limbs. The areas of analgesia were again mapped out, and were found to show very little variation from those of a year earlier. At this time, too, the eyes were examined by Mr. Lawford, who has kindly given us the following report on their condition.

October 16, 1899. Pupils dilated by homatropin and cocain.

$$\text{V. R. } \frac{6}{36} + \frac{0.5}{2.0} \text{ sphl.} = \frac{6}{24}.$$

$$\text{L. } \frac{6}{18} \text{ vix } + \frac{0.5}{2.5} \text{ sphl. } 15 = \frac{6}{18} \times \frac{6}{12} \text{ tried.}$$

Fields of vision full. Ophthalmoscopically right and left no abnormal appearances detected in any part of fundus. Examination of right fundus much interfered with by vitreous opacity. Colour of O.D.'s healthy. Right cornea and lens clear. In vitreous there are numerous stringy, slowly moving opacities, chiefly about the middle of vitreous,

antero-posteriorly. They are all dark in appearance: no whitish bands seen. There is also much fine dust-like haze of vitreous. Left.—The changes in vitreous are very similar, but MUCH less obvious. The stringy opacities are about middle portion, but are few in number. Fundus can be easily and clearly seen.

When examined on a previous date without a mydriatic, the pupils were unequal and irregular. Right pupil oval, long axis horizontal: size 4 mm. Left pupil pyriform, size 6 mm. Actions of pupils to light very sluggish, and very small in amount; to accommodation fair, but less extensive than usual. Ocular movements and lid movements full. Tension normal.

The relatives were at this time anxious to try the effect of general massage, having seen the improvement produced in our patient's younger sister by Weir-Mitchell treatment; and a course was arranged for him, special care being taken to prevent his being over-tired. He was not seen again for a month. During that time he had become very distinctly worse. He had had about six attacks of aphasia, usually accompanied by temporary weakness in the right arm. In spite of this, however, he went out three consecutive evenings, and on the fourth day was so much worse that a doctor was again summoned. When seen he had not fully recovered from an attack of the preceding evening, his speech being imperfect, and the right grasp weaker than the left. His general weakness was now very great, and he could not be up for one hour without feeling fatigue. His memory and power of concentration were both feeble; the pulse usually rapid (90-100), the tongue absolutely dry. He complained of pain in his limbs of an aching character: the temperature was normal or subnormal. With rest, careful feeding, attention to the state of the bowels, and skilled nursing, he gradually recovered a certain amount of strength; and the attacks of aphasia, at first occurring every day, became less frequent. By February 20, 1900, he had been as much as ten days without an attack, and was able to be up for four or five hours without fatigue. During the spring and summer yet further improvement followed, and, while care-

fully avoiding all that tended towards over-exhaustion, he was able to move about freely out of doors, and to mix in society.

During the remainder of his life, the patient was under the care of Dr. R. Jocelyn Swan, to whom we are indebted for the following notes of that period. He lived for about nine months longer, and during that time had four convulsive attacks, in the last of which he died. "The first convulsive attack," Dr. Swan writes, "occurred on September 26, 1900, and lasted about twelve hours. A second similar seizure was on November 3, more violent and longer in duration, in all thirty-six hours. A third occurred on January 15, 1901, lasting nine hours, this was marked by a tonic contraction of the left arm, while the right moved aimlessly about, and the final attack was on May 24, commencing at 1 a.m., and lasting till he died at 9 a.m. of the same day." Dr. Swan adds that he continued to have "lightning-pains," especially at night; the two regions most affected being a spot on the outer side of the right foot below and in front of the external malleolus, and the folds of the buttocks. In the beginning of March he also had an attack of conjunctivitis of the right eye, which had become nearly blind; and there was some ulceration of the cornea leaving a nebula. It is not known whether the cornea had previously become anæsthetic; or whether the analgesia previously observed had extended over a larger area of the body.

II.

PATHOLOGICAL NOTE.

The *post-mortem* examination was made seventeen hours after death. The weather at the time was very warm. *Post-mortem* rigidity was well marked. There was considerable discoloration and lividity in the dependent parts. The head was opened first and on removal of the skull cap the dura was seen to be intensely congested. The venous sinuses were full and when the brain was removed blood oozed in considerable quantity from the spinal canal. In exposing

the spinal cord an abnormal density of bone in the vertebral laminae was observed, notably in the lumbar region, and there was some extra-meningeal hæmorrhage in front of the cauda equina.

Thorax.

The heart was normal. The right lung was adherent at the apex from some old pleurisy, and in both it and in the left there was some patchy hypostatic consolidation and the lungs were markedly congested throughout. There was no sign of tuberculous disease.

Abdomen.

The liver and the spleen were both in a state of venous congestion.

The kidneys had their capsules readily separable and had also the appearance of congestion, though microscopically they seemed absolutely normal. The bladder was normal.

For microscopic examination, most of the organs were hardened in 10 per cent. formalin. Some of the cord, however, was placed in Müller's fluid.

For the nervous system, the staining methods were those of Nissl, van Giesen, Marchi and Weigert-Pal, along with others.

Spinal Cord and its Coverings.

Macroscopic.—The dura showed marked congestion. On reflection of the dura a rusty-coloured substance was seen to be present between it and the cord. This was gelatinous, stringy and friable, and in consistence suggested a fibrinous exudate. It formed a more or less complete sheathing to the cord throughout its entire length. It was, however, most abundant in the lower parts of the cord and was less so as the higher levels were reached, being in the neck almost absent. It was found chiefly on the posterior aspect and in some regions it separated the dura from the cord to the extent of a sixth of an inch or more. Anteriorly it was seen mainly as stringy masses about the anterior nerve roots. It was moderately adherent to the dura, but more

so to the cord itself, so that the former could without difficulty be raised, leaving the cord surrounded by its shaggy covering (fig. 2).

*Microscopic.*¹—Examined under a low power. Sections taken from the level of the third cervical segment to the cauda equina all showed undue vascularity. This was not so striking in the cervical region, but got greater in lower levels, and became intense in lumbar and sacral regions. This vascularity affected chiefly the pial layer of the pia-arachnoid and the contents of the arachnoid space, viz., the nerve roots and the arachnoid tissue. But the vessels of the dura and the cord itself were also distended. The vessels seemed increased both in size and number. In the arachnoid space was a relatively large quantity of a fibrous material probably a hyperplasia of the normal fibrous trabeculæ. In general appearance it was similar to the fibres of the arachnoid tissue, but the cellular elements were fewer. It had the form of nodulated rods or fibres with a maximum diameter of about thirty times that of a red blood cell. There were also spheroidal bodies, though these probably were cross sections of the fibres. This tissue was found in different situations in the arachnoid space, among the nerve roots—sometimes actually among the nerve bundles of the roots—and more plentifully posteriorly.

There were usually aggregations of it in the following situations where normally a collection of arachnoid tissue might be expected :

¹ The terminology is that used by Ford Robertson by which *pia-arachnoid* is taken to mean the whole membrane, "pia," "arachnoid," and intervening tissue: and *arachnoid* is taken to mean the trabecular tissue which extends from the outer to the inner aspect of the membrane, thus, arachnoid trabeculæ, arachnoid spaces, arachnoid fluid.

FIG. 2.—Portion of dorsal cord; posterior aspect, dura reflected.

FIG. 3.—Photomicrograph. Mid-dorsal cord, transverse section, between posterior dura and cord (region about septum posticum). Hæmalum, $\times 105$. *a.* Dura. *b.* Red blood cells. *c.* Arachnoid tissue.

FIG. 4.—Photomicrograph. Lumbar cord, transverse section, mass of arachnoid tissue, opposite one of the posterior roots. Hæmalum, $\times 60$. *a.* Engorged blood-vessel. *b.* Hæmorrhage. *c.* Dura. *d.* Arachnoid tissue.

An aggregation at 1, presumably the septum posticum, was found chiefly in the higher regions: an aggregation at 2, chiefly in the lower regions. At 3, the position of the ligamentum denticulatum, there was an aggregation in all regions. The material was also present in the neighbourhood of the anterior fissure.

The fibres of this tissue had no definite arrangement, except in the above-mentioned groupings, but were disposed in all directions forming in places a loose network (figs. 3 and 4).

Under a high power they were seen to be fibrillar and with Weigert's fibrin stain they gave negative results. In the cauda equina it was present chiefly near the dura, but it was also to be seen among the nerve roots. In the interstices of this tissue collections of red blood cells were everywhere abundant, especially in the lower levels of the cord.

Stratified bodies (*geschichtete Körperchen*) were found in considerable numbers near the dura. The pial layer of the pia-arachnoid was much thickened. Its vessels were engorged, and in places there were hæmorrhages. There was in it an extensive round cell infiltration which invaded also the periphery of the cord itself, especially along the lines of the connective tissue septa and was marked in the neighbourhood of the posterior roots (fig. 5). The nerve roots presented the same appearance of intense congestion and round cell infiltration, and these conditions, though to a less extent, were also evident in the dura. In several of the smaller arteries there was distinct thickening of the intima presumably endarteritis. This was evident throughout the whole length of the anterior median artery. Thrombosis seemed to have taken place in several of the vessels in the more highly congested areas, and some of the thrombi were apparently undergoing organisation. The endarteritis did not affect the whole intima equally, being usually seen in transverse sections as an encroachment on one side of the lumen of the vessel (fig. 6).

Treated with the Weigert-Pal and Marchi staining methods the cord showed a degeneration in the posterior columns.

In the lower lumbar region the degenerated fibres were found mainly in the postero-external columns, but gradually as one passed up the cord they became more and more strictly limited to the postero-median columns. The degenerated fibres extended anteriorly in the postero-median columns as far as the gray commissure, except in the cervical region, where they only reached about one half of that distance. It was in fact exactly such a degeneration as would be occasioned by damage to the lower lumbar and sacral roots. In addition to this there was a marginal degeneration all round the cord, and extending to the parts bounding the anterior fissure (fig. 7).

Sections through the upper part of the cauda equina treated with the Weigert-Pal method showed many of the roots much degenerated.

The nerve cells in sections taken at many levels of the cord treated by Nissl's method, appeared absolutely normal. There was no evidence of chromatolysis or other degenerative change. The chromophile substance, as represented by the "Nissl-bodies" seemed normal in quantity, arrangement and staining reaction. This applies to cells in all situations—in anterior and lateral horns and Clarke's column. In a few cells there was a deeply staining nucleus, but this was taken to be a *post-mortem* change. Beyond engorgement, the vessels of the cord itself were not affected. There was no perivascular round cell infiltration. Concentric bodies, giving "amyloid reaction," were present in the white matter in moderate numbers.

Brain and its Coverings.

Macroscopic: The dura showed great congestion. It being reflected, the surface of the brain was seen to be intensely congested, especially over its convexity, while covering the medulla and base of brain, was found what appeared to be the same gelatinous, friable substance already described as surrounding the cord. The pia-arachnoid was cloudy and thickened over Sylvian fissures, and on opening up the latter, the same substance was found filling them up and causing the two sides to be adherent.

FIG. 5.—Photomicrograph. Sacral cord, region about anterior fissure. Hæmalum, $\times 300$. *a.* Artery with thickened intima. *b.* Dilated blood-vessels, possibly hæmorrhage. *c.* Artery with thickened intima. *d.* Artery with thickened intima. *e.* Thickened pial layer of pia-arachnoid. *f.* White matter of cord. *g.* Dilated blood-vessels. *h.* Arachnoid tissue.

FIG. 6.—Photomicrograph. Lumbar cord, transverse section of anterior median artery. Hæmalum, $\times 270$. *a.* Lumen of vessel. *b.* Thickened intima. *c.* Media. *d.* Adventitia. N.B.—This appearance is due to obliquity of section.

FIG. 8.—Photomicrograph. Floor of fourth ventricle in pons, showing "hyaline" bodies of Van Gieson, high power.

FIG. 7.—Drawing from sections prepared by the Weigert-Pal method to show cord degeneration.

It was also present between the two frontal lobes below the corpus callosum, making them adherent, and surrounding the anterior cerebral arteries and their branches. The pia-arachnoid did not separate easily from the cortex. In all other respects, the brain appeared quite normal. The left Sylvian artery with its main branches contained clot, but this was red and non-adherent, and probably *post mortem*. Recent clot was present also in several other branches of the circle of Willis.

Microscopic.—Sections were made through Basilar artery, both Sylvians, both anterior cerebrals and posterior communicatings. All were found perfectly normal with the exception of the first, which showed very slight endarteritis.

Sections of the third left frontal convolution, and of many other parts of the cortex were examined. There were practically the same appearances in all. There was a fibrous hyperplasia of the arachnoid tissue, with increased vascularity. The cortical arterioles were normal. The cortical nerve-cells were likewise normal, examined by Nissl's method. Many however, had the deeply staining nucleus and indistinct chromophile substance, described by Ford Robertson as *post-mortem* change.

Sections of the left internal capsule and of the corpora striata were also examined with portions of the white matter from various other regions, and all seemed quite normal.

Sections through the medulla and pons showed the nerve-cells at the floor of the fourth ventricle normal, and the same appearance of the pia-arachnoid, as was seen on the cord.

In the medulla and pons, immediately subjacent to the ependyma lining the fourth ventricle, were numerous, roundish, homogeneous, hyaline-looking bodies with concentric markings, not staining very deeply with methylene blue, and about ten or fifteen times the diameter of a red blood cell. These bodies did not blacken with osmic acid, nor did they give the "amyloid reaction" with iodine, or iodine and sulphuric acid (figs. 8, 9, 10).

These bodies were not present under the ependyma of the lateral ventricle. The cerebellum was normal.

FIG. 9.—The same, low power.

FIG. 10.—Photomicrograph. Floor of the fourth ventricle in medulla, at level hypoglossal nucleus, showing "hyaline bodies, Van Giesen, $\times 370$.

FIG. 11.—Photomicrograph. Artery from great sciatic nerve, showing thickened intima. Hæmalum, $\times 270$.

Peripheral Nerves.

The peripheral nerves as represented by the ulnar and great sciatic were examined by the Marchi and Weigert-Pal methods, and were found to be normal, showing no sign of either neuritis or degeneration. Some of the arteries, however, in the great sciatic had the same thickened intima already described in the vessels of the cord (fig. 11).

The Eye.

The right eye was embedded in celloidin, and it was examined in antero-posterior sections. There was no direct evidence of choroiditis, but in the posterior chamber there was a considerable quantity of filmy, fibrinous looking material. The eye in other respects appeared normal.

The condition thus seems to have been primarily a spinal lepto-meningitis extending from below upward until the cerebral meninges were affected in a like manner, chronic in its course, but intense enough to implicate the cord superficially, and many of the nerve-roots in the inflammatory process.

The great vascularity and numerous hæmorrhages in the inflamed area suggest an inflammation hæmorrhagic in type, and the excess of arachnoid tissue suggests that this constituent of the pia-arachnoid was especially involved.

The tract degeneration in the cord is manifestly the result of damage to the lower posterior roots. The bodies in the floor of the fourth ventricle are not fatty, and not amyloid as is seen by their staining reaction. They seem to belong to the group of hyaline bodies.

Our best thanks are due to Dr. Lazarus-Barlow for many kind suggestions, and for allowing us to make use of the pathological laboratory of Westminster Hospital during the preparation of this part of our paper.

We have found among other works the following of particular service :—

- KEY AND RETZIUS. "Studien in der Anatomie des Nervensystems, &c."
OBERSTEINER AND HILL. "Anatomy of Central Nervous System."
FORD ROBERTSON. "Pathology of Mental Diseases, 1900"; and "Normal and Pathological Histology of Nerve-Cell," BRAIN, 1899.

POLLACK (JACK). "Methods of Staining the Central Nervous System," 1899.

MOTT. "Tabes dorsalis"; Clifford Allbutt, "System of Medicine," vol. vii.

III.

Before considering the nature of the disease we may here review shortly some of the more prominent symptoms, and consider in what degree they may be accounted for by the lesions above described.

(1) *The Bladder Symptoms* occurred in three out of the four males who suffered from the disease. With regard to the three females of the earlier generation no mention is made of this symptom, but the records concerning them are not full enough to justify us in concluding from this that the bladder was unaffected. Usually the nocturnal escape of urine was the first symptom in the disease to attract the attention of the patient himself, and in the earlier stages of the male cases it was regarded as an isolated symptom, like the incontinence of children, and treated with belladonna, &c. Later, however, the bladder becomes undoubtedly atonic, urine is retained in the bladder, and cystitis is set up, and in the light of the fuller knowledge of the last case that we now possess there can be little doubt that the primary defect is *retention* due to some fault in the nervous mechanism of micturition.¹ When we first saw our patient the bladder walls had already become very considerably weakened. He could expel very little urine with any force, the remainder trickling slowly away; the catheter showed several ounces of residual urine, after the first free flow of urine had ceased; pus and albumen were present, and disappeared when the bladder was regularly washed out. At this time he was having what he called "incontinence of urine" every night, and the most probable cause for this is that the bladder was only half empty when he went to bed, in a few hours it became full to its utmost capacity, and then discharged a certain portion of its contents, either by

¹ J. RISIEN RUSSELL (Clifford Allbutt "System of Medicine," vi., 877), says that in affections of the spinal meninges retention is common, incontinence also occurs, though more rarely.

reflex stimulation of the lumbar centre or by simple overflow. Later in the disease all power of voluntary micturition was lost, and the bladder was emptied at regular intervals by the catheter, this prevented over-distension from occurring, and the so-called incontinence now disappeared. Three nervous lesions suggest themselves as possible causes for this retention :

- (1) Disturbance of the lumbar centre for micturition.
- (2) Disease of the white fibres in the lumbar or dorsal region, carrying impulses from the brain to the centre.
- (3) Analgesia of the bladder, similar to that existing in the legs, allowing distension to occur frequently without discomfort, and in time to weaken the muscular fibres of the bladder wall.

(1) *Disturbance of the Lumbar Centre.*

The cord has suffered considerable damage in the region of the lumbar enlargement, enough possibly to account for imperfect action of the centre, and this explanation of the symptom is tempting, inasmuch as similar damage to neighbouring centres would account both for the constipation and for the loss of sexual power. But the early symptoms suggest that the centre is cut off from the usual stimuli rather than that it fails to act in response to them, and the later stages of disease of the centre should cause paralysis of the sphincter, with continuous overflow, rather than retention.

(2) *Disease of the Descending Tracts above the Lumbar Centre.*

A lesion of this nature would cause retention of urine, and a series of symptoms not unlike those observed ; but no such lesion has been discovered on examination of the cord ; and the absence of discomfort when the bladder was distended is hard to explain. It is possible, however, that this might be attributable to further damage elsewhere, *e.g.*, in the posterior roots.

(3) *Analgesia of the Bladder Wall.*

A failure to perceive the pain and discomfort normally felt when the bladder is over-distended might lead to a condition such as has been described; and it is known that retention sometimes occurs in syringomyelia.¹ If, however, the cause lies here, it will, no doubt, have been at work long before the first escape of urine; indeed, dissociated anæsthesia will be the first symptom of the disease. The sequence of events would be as follows:—The patient allows his bladder to be over-distended on many occasions without feeling the discomfort that would trouble a healthy man;² the bladder becomes distended, weakened, atonic; then it is incompletely emptied, and cystitis occurs. Finally, it loses all muscular power, and no longer responds even to the reflex stimulus of great distension.³

It does not seem impossible that more than one of these agencies may have been effective in producing the symptoms described.

Opacity of the Vitreous Tumour of the Eye.

This was present in two out of the three patients in the earlier generation, and in two out of the five in the later generation; while in the others we have no record as to the presence or absence of the trouble. The constant lesion consists in vitreous opacities, the appearance of which has been carefully described for us by Mr. Lawford; almost complete blindness may follow, as occurred in the mother of patient. A variation in the size and shape of the pupils has also been observed in the latest of the cases. No hæmorrhages within the eyeball have at any time been seen, and no choroiditis was observed in that part of the choroid that

¹ Ref. WALTER VOUGHT, "Syringo-myelia and Allied Diseases." *N.Y.M.J.*, November 21, 1891.

² It is possible that the penile pain felt a week before the first voluntary escape of urine was caused by great pressure on the neck of the bladder, which still retained some pain sense.

³ J. RISSEN RUSSELL (Clifford Allbutt "System of Medicine," vol. vi., p. 877) has described residual anæsthesia as being especially common in the bladder and rectum in affections of the Spinal Meninges.

can be examined with the ophthalmoscope; but it is most probable that the primary cause of the opacities is hæmorrhagic, and it is possible that disease may have been present in the anterior portion of the choroid, or other parts of the uveal tract, though, as has been pointed out, no evidence of this was found microscopically.

The disturbance of the sense of heat and pain, along with unimpaired tactile sensation, seems to point to the probability suggested by Gowers¹ that the paths of conduction of heat and pain sensation are close together, but are widely separated from the path conducting tactile impressions.

It has been suggested by Starr² that on their way from the surface of the body the sensations of heat and pain traverse the gray matter and then go on in the centripetal fibres of the antero-lateral-ascending tract of Gowers. If this is so it might well be that the disturbance of heat and pain sense was due to the implication of this tract in the marginal myelitis which we have seen to be present, the gray matter being to all appearance normal.

With regard to the cerebral symptoms, drowsiness, impaired hearing, aphasia, right-sided hemiplegia, loss of memory and power of concentration, convulsive attacks and coma, we would suggest that they were due to a condition of cerebral anæmia caused, in the first place by venous congestion associated with the inflamed meninges interfering with the normal arterial blood supply; and in the second place by actual compression of the arteries by the new inflammatory material.

The latter might account for any local increase of the anæmia, such as that capable of causing aphasia or hemiplegia, and indeed the quantity of new material found in the Sylvian fissures and elsewhere at the base of the brain, matting everything together, makes this hypothesis not very improbable.

This does not, however, explain the transitory nature of the attacks of aphasia and paralysis.

¹ "Diseases of the Nervous System," vol. i., pp. 235, 237.

² Clifford Allbutt, "System of Medicine," vol. vii.

Finally, a few suggestions may be made with regard to the nature of the disease, which we have described. We think that it will be admitted that the consistent grouping of symptoms is sufficiently marked to constitute the disease a definite entity; and that in character it corresponds to no form of hereditary nervous disease that has hitherto been described.

There is, however, a superficial resemblance to some of the known diseases. Thus, it resembles syringomyelia in the one symptom of dissociated anæsthesia; and it is also like this disease (as well as certain other hereditary affections, *e.g.*, hereditary chorea, hereditary cerebellar ataxy, and hereditary ataxic paraplegia) in the late onset of the symptoms, after a healthy childhood and youth. There is a closer resemblance to locomotor ataxia in the lightning-pains, the diminution of knee-jerks and of light-reflex, and in one actual lesion found *i.e.*, the posterior sclerosis (though this symptom in our case was presumably secondary to the pia-arachnitis): while both locomotor ataxia¹ and Friedreich's ataxia² may be accompanied by dissociated anæsthesia and impairment of the sexual and bladder functions.

Now there is strong reason to believe that there is a close connection between locomotor ataxia and syphilis and the pathological evidence that has arisen in the investigation of the last case suggests the possibility of the disease being caused by the action of the virus of hereditary syphilis on the structures surrounding the spinal cord. The likelihood of this factor was considered during the lifetime of the patient; but was put aside because no satisfactory evidence existed that syphilis could involve three successive generations;³ but that this objection is not final must be admitted in consideration of the following facts:—

¹ Clifford Allbutt, "System of Medicine," vii., 116.

² "Gowers," 1892, 1st Edit., 464.

³ J. HUTCHINSON (Clifford Allbutt, "System of Medicine," ii., 263) says that no facts have yet been published on this subject. Out of eight families investigated in which the parents had suffered from hereditary syphilis, there were no syphilitic offspring "with one doubtful exception." He adds, however, that "several surgeons have expressed the belief that the influence of syphilis once acquired may be felt through several subsequent generations."

(1) The vascular pia-arachnitis, closely resembling that found in syphilitic meningo-myelitis.¹

(2) The thickening of the tunica intima in some arteries similar to that found in syphilis.

(3) The ocular lesions, which suggest former hæmorrhages like those of syphilitic choroiditis.

(4) The thickening of the neural arches in the lumbar region, found at the *post-mortem* examination.

(5) The character and duration of the disease from which the grandfather died ("gangrene" of lung lasting four months), and his dissipated life.

(6) The frequent occurrence of temporary attacks of aphasia in cerebral syphilis.

(7) The diminution of pain-sense and temperature-sense,² common in syphilitic meningo-myelitis.

We therefore suggest that this may be yet another manifestation of this polymorphic disease; though it is impossible to say why the virus should have selected these special regions, while producing none of the better-known symptoms that accompany the hereditary form of the disease.

¹ *Vide* OPPENHEIM (Mayer) "Text-book of Nervous Diseases"; RISIEN RUSSELL, Clifford Allbutt, "System of Medicine," vi.; ZIEGLER, "Special Path. Anat.," &c.

² Clifford Allbutt, "System of Medicine," vi., 895.