Friedreich's paralysis / by T. Duncan Greenlees and G. Carrington Purvis.

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Friedreich's ataxy is one of those forms of chronic spinal paralyses, standing midway between disseminated sclerosis and locomotor ataxy, and which is considered a comparatively rare disease.

The cases here described are, so far as we can ascertain, the first published in South Africa, and indicate, as has been previously pointed out, that the European inhabitants of this country are rather prone to degenerate nerve lesions.

The following cases occurred under our care at the Chronic Sick Hospital, Grahamstown, in a boy and girl—brother and sister. The girl died last May, and we were fortunate in securing a post-mortem examination. The boy still lives, and a careful clinical examination has been made of him. We are thus able to present a double picture—of the clinical symptoms, as found in the boy, and a microscopic description of the lesions, as found in the case of the girl. The symptoms, in both cases, were so nearly identical that we think the following description can be easily made to apply to both, and that, whereas we regret being unable to give the clinical picture history of the girl, we are at the same time in a similar position as regards the pathological details which may be found in the case of the boy.

Clinical Description.

Family history.—Careful enquiries were made to ascertain the family history of our patients, from their mother,

with the special object of ascertaining whether there existed a hereditary tendency to nerve troubles. The parents are not blood-related to each other, as so often occurs amongst the Dutch of this country; they are reported both to be healthy, and the father is, or was, fighting for the Transvaal. They had nine children, all of whom were in good health, except our patients, and one child who died from "convulsions" in infancy. The father is reported to be steady and temperate in his habits, is a poor farmer, and lives a healthy out-door life. The mother is in good health and of average intelligence. There are no known cases of paralysis in the family.

Onset of illness.—When Charlie was 9, and Nellie 12 years of age, they both had scarlatina, and while convalescing they got wet one day. It was noticed, shortly afterwards, that both children were weak in their ankles, and gradually the feet began to contract so as to make walking well nigh impossible. The disease progressed very slowly at first, but the parents noticed that both children were steadily getting worse. The contraction of the feet increased, and paralysis gradually affected both legs and arms so that the movements of the limbs became more and more limited in their range, and they became very helpless accordingly. They were admitted from Kimberley on March 11, 1896, being then 13 and 16 years of age respectively.

At that time the girl was very helpless indeed; she was unable to assist herself in anything, and had to be dressed and undressed and fed by the nurse. She sat on a chair all day with her head resting backwards on a pillow; gradually the general feebleness increased; she had several fainting attacks, and during the last few months of her life she had difficulty in swallowing and the respiratory functions became interfered with without pulmonary disease at all. The dysphagia was so distressing that, towards the end of her life, she was quite unable to take nourishment by the mouth.

That the disease, in her case, was one which ultimately implicated the higher nerve centres was evident from the symptoms which, in the end, proved fatal. The difficulty in

Fig 1

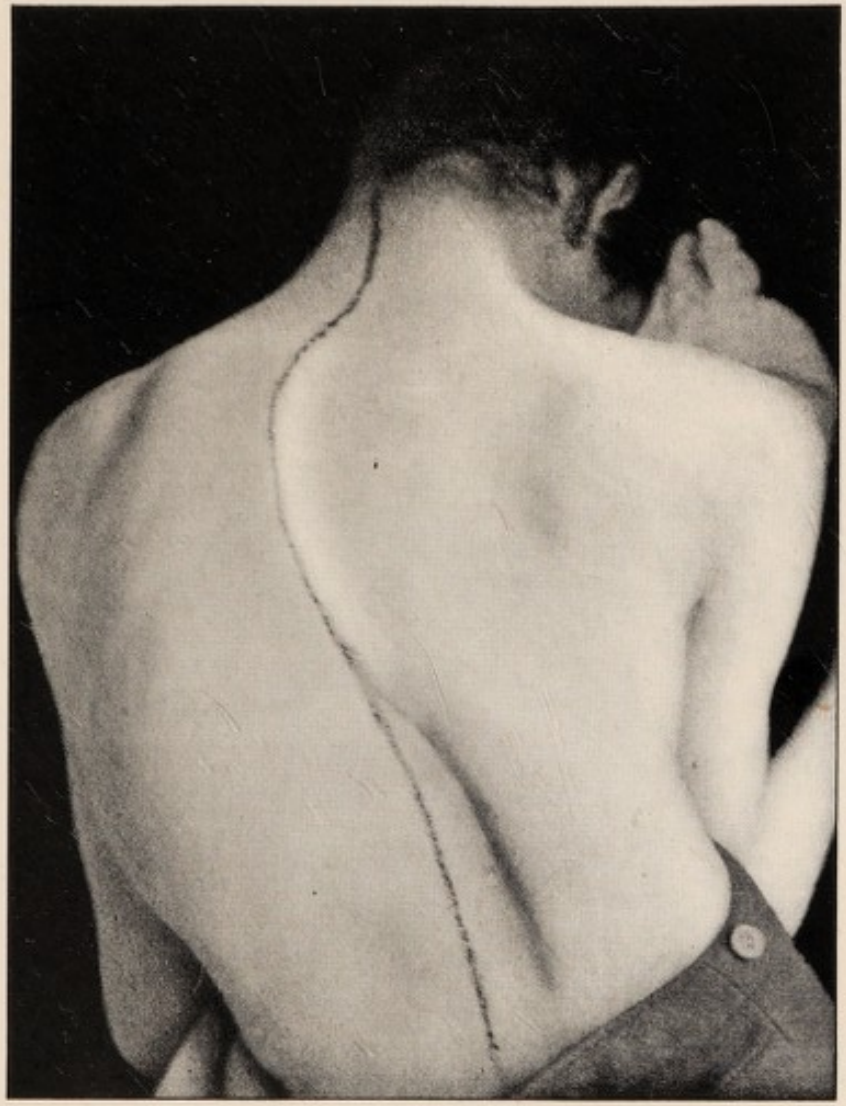

FIG. 2.

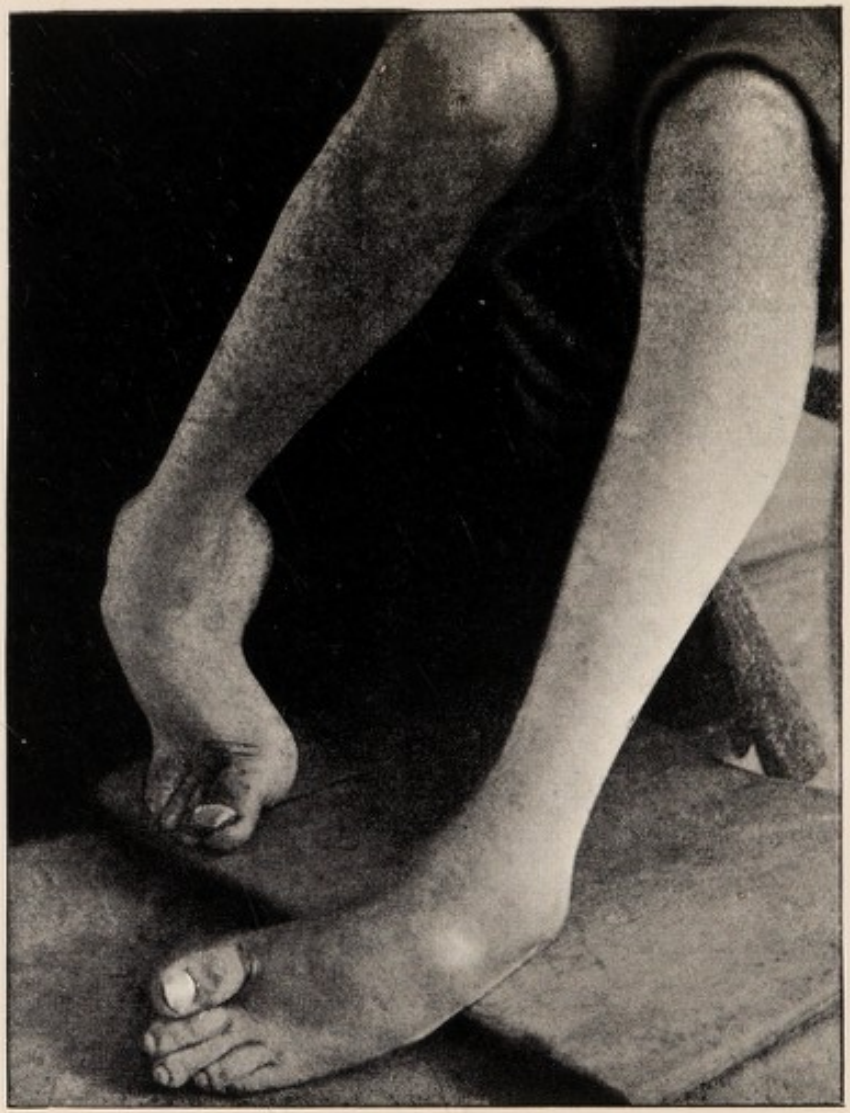

FIG. 3.

breathing, the fainting attacks, and the dysphagia, all indicated some lesion affecting the organic centre in the medulla, and this idea was borne out by the microscopic examination of this portion of the nervous system.

Clinical examination of Charlie.

Charlie is a boy now (October, 1900) aged 17 years. The expression of his face is that of happiness and simplicity combined—almost amounting to imbecility. His face is broad and flat, he always wears a childish smile, and he never loses his temper, nor looks cross. He is quite unable to articulate, but he knows what is said to him. His conduct generally is good, he is very patient, and a favourite with the other inmates of the hospital, who are always ready to assist the helpless boy. As is general with cases of slight mental defect, he is somewhat vain, and likes to wear cheap medals, brass chains, and rings on his fingers.

He is utterly helpless, is unable to walk, and, when moved or carried, his head falls limply from side to side as if the neck muscles were unable to support it. While there is a general wasting of the muscles there is no marked impoverishment of nutrition, and his appetite is very good.

His legs hang helplessly down, and when moved about he grips tight hold of the arms of the chair lest he should fall. When at rest both feet are slightly turned inwards, and there is well marked talipes equinus of both feet. This condition is more evident in the right foot, as also is a turning inwards of the foot so that the sole faces almost upwards—approaching to the condition of talipes varus. The great toes of both feet are hyper-extended, a condition likewise most marked in the right side (figs. 1 and 3).

The Spinal Column.—An examination of the back reveals marked lateral curvature, the convexity occurring in the upper dorsal region, and points towards the left side. The apex of the curvature approaches very closely to the posterior angle of the scapula (fig. 2).

Electric Reactions.

With galvanism:

(1) *Flexors of forearms.*

20 cells: Ma = 3.
KCC +; ACC +; AOC 0; KOC 0.
Note.—KCC slightly stronger than ACC.

27 cells: Ma = 4·3.
KCC +; ACC +; AOC 0; KOC 0.

27 cells: Ma = 4·75.
KCC + strongly marked; ACC + strongly marked;
AOC + very slightly marked; KOC 0.

32 cells; Ma = 10·5.
KCC + strongly marked; ACC + strongly marked;
AOC + slightly marked; KOC + very slightly marked.

(2) *Leg muscles* (posterior and outer aspects).

20 cells: Ma = 2.
KCC +; ACC 0; AOC 0; KOC 0.

25 cells: Ma = 3.
KCC +; ACC +; AOC 0; KOC 0.

30 cells: Ma = 6·5.
KCC +; ACC +; AOC 0; KOC 0;

35 cells: Ma = 10.
KCC +; ACC +; AOC 0; KOC 0.

It will be seen that the electrical examination—so far as it goes—presents reactions which are compatible, or nearly so, with health.

On applying the *Faradic current* it was noted that the muscles of both arms and legs were slow in responding to the interrupted current; as regards the legs a fairly strong current was required to make the muscles contract.

Reflexes.

(1) *Superficial.*—The plantar, cremasteric and abdominal superficial reflexes were tested and were only slightly

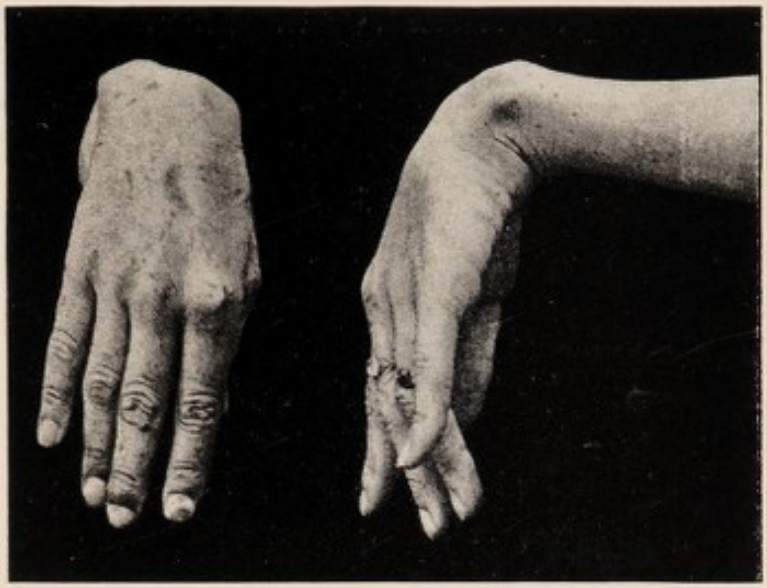

FIG. 4.

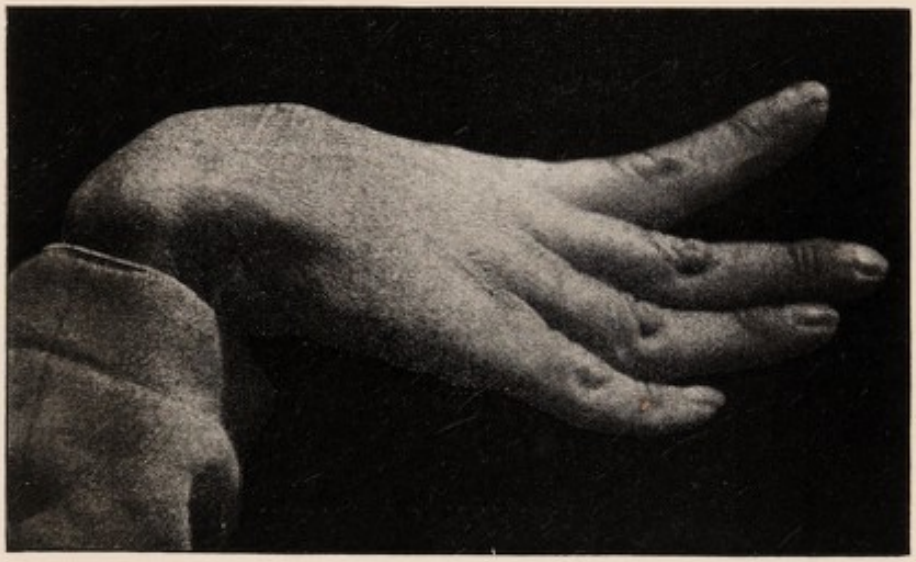

FIG. 5.

FIG. 6.

evident, while the epigastric, gluteal and interscapular reflexes could not be elicited.

(2) *Deep.*—Both the patellar tendon reflex and the ankle clonus were absent.

(3) *Organic.*—All the organic reflexes were normal except the act of micturition which was somewhat delayed.

The hot sponge test.—The patient felt it hot in the lumbar region as well as in the dorsal region, but only when first applied. The test failed on repetition.

Hot tube test.—Was not felt when applied to either the legs or the arms.

Pain sensation.—The patient felt a needle-prick in various parts of the body, but the needle had to be firmly pressed into the skin.

Muscular sense.—He was unable to differentiate between weights. When asked to touch the tip of his nose rapidly with his finger, he failed to do so, but when allowed to take his own time the act was slowly performed, his hand swaying from side to side while his finger approached his nose.

When told to hold out his hands he presented distinct drop wrist, but when he is asked to straighten them out the fingers are extended backwards to an extraordinary extent. This hyper-extension of the fingers is most marked in the right hand. There is wasting and probably some paresis of the interossei muscles of both hands (figs. 4, 5 and 6).

On being asked to put out his tongue he does so in the middle line; the tongue is large, flabby, and there are general tremulous movements of the organ.

His pupils react readily to light and accommodation, and there is slight nystagmus of both eyes.[1]

The other senses seem perfectly normal, and he complains of no objective symptoms such as pains in the head or sounds in his ears.

Pathology of Case of Friedreich's Disease.

The following remarks are founded upon the *post-mortem* examination of Nellie B., the sister of the above patient,

[1] Nystagmus was a marked symptom in patient's sister.

who died at the Chronic Sick Hospital on May 10, 1900, after a residence of four years, and in whom the disease had existed for nine years.

Autopsy (twelve hours after death).—Body of a European girl, much emaciated and muscles wasted. Rigor mortis present. Double talipes equino-varus marked. Small bedsore over sacrum. There was some wasting of the cerebral convolutions, with an excess of fluid in the cranial cavity. The veins of the pia were congested.

The heart and lungs were healthy except for some congestion of the lower lobe of the right lung, and the bronchial tubes contained frothy material.

With the exception of a small cyst in the centre of the left kidney, the abdominal organs presented nothing calling for special note.

A piece of the left frontal convolution, the crus cerebri, medulla oblongata, a portion of the great sciatic nerve, and portions of the cervical, dorsal, and lumbar regions of the spinal cord were placed in Müller's fluid, and forwarded to the Bacteriological Institute, Grahamstown. These were hardened and stained according to Weigert's method, and microscopic sections made.

Examination of the Spinal Cord.

An examination of sections from different portions of the spinal cord revealed the fact, which was even quite apparent to a naked-eye inspection, that the cord was much smaller than it should be. It was quite infantile in size, and it looked even smaller than a healthy cat's cord, with which it was compared.

Microscopical Examination.

Sections from various levels in the cervical, dorsal, and lumbar regions were examined microscopically, and revealed the following pathological changes :—

Cervical region at the level of the sixth cervical vertebra :—

(1) Sclerosis of the middle portion of the posterior internal tract (Goll's tract).

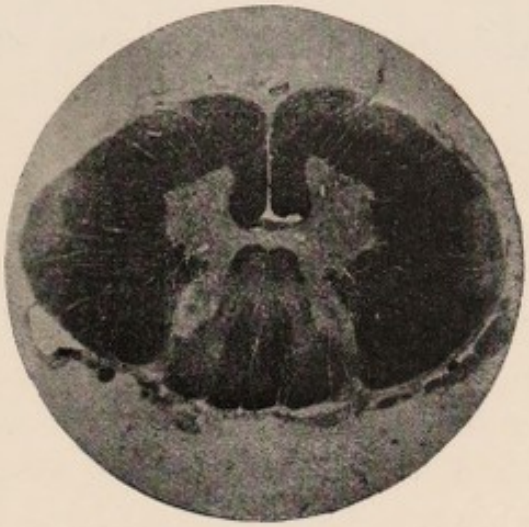

FIG. 7.

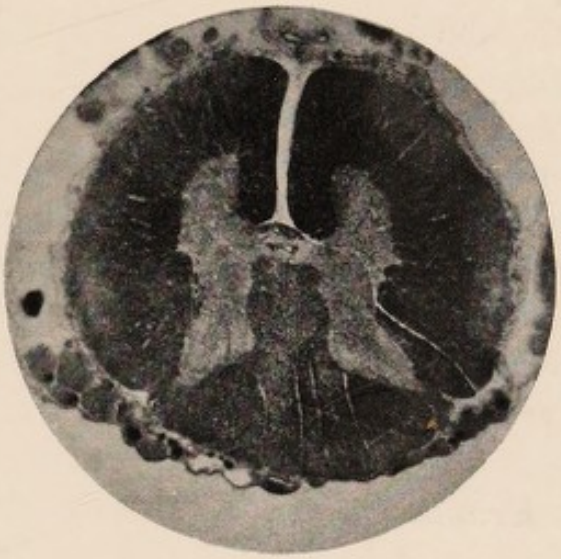

FIG. 8.

FIG. 9

(2) Sclerosis of the posterior external tract (Burdach's tract) external to the comma tract.

(3) Sclerosis of the ascending antero-lateral tract (Gowers' tract). This occurs as a small patch of sclerosis just where the anterior nerve-roots leave the cord.

(4) Sclerosis of the direct cerebellar (lateral) tract. This occurs on both sides of the cord to a marked extent, nearly all the nerve-fibres being replaced by fibrous tissue.

(5) In Clarke's column the cells were few in number, markedly atrophied, took the stain badly, and the intercellular tissue was much broken down.

(6) Lissauer's tract, with the exception of a small portion adjoining the direct cerebellar tract, was healthy, as also was the crossed pyramidal tract.

Dorsal region at the level of the second dorsal vertebra :—

The lesions described as occurring in the cervical region were evident, but not to so marked an extent. The sclerosis of the posterior portion of the direct cerebellar (lateral) tract was, however, even more marked, and occurred as a distinct patch, under a low power, of lighter hue than the surrounding healthy nerve-fibres, and this condition was equally marked on both sides of the section (fig. 7).

Clarke's column was affected to a similar extent as existed in the cervical region ; its cells and fibres were both affected extensively.

Lumbar region at the level of the third lumbar vertebra :—

In this portion of the cord the sclerosis was very evident, and quite localised to a patch on either side of the posterior median fissure, embracing Bruce's and the comma tract, but leaving the free edge of the fissure healthy. A small patch of sclerosis likewise existed on either side of the posterior fissure more centrally situated and close to the commissure.

The degenerative changes in the lateral and anterior columns, although present, were not so evident as they were in the cervical region of the cord (figs. 8 and 9).

When a higher power was employed it was noted that, in some parts of the diseased portions of the cord, the nerve sheath appeared simply empty of its axis-cylinders. In other portions the axis was either shrivelled or else swollen.

As a result of the former condition, a honeycomb-like arrangement existed, consisting of empty nerve sheaths closely packed together, but where the disease appeared more advanced even the nerve sheaths became obliterated, and replaced by fibrous tissue, so broken down in places as to leave large, almost empty spaces.

The nerve-cells, for the most part, stand out prominently in all the sections; indeed, this prominence is unusually marked where it does exist. In the dorsal region, while the cells of one anterior horn were sharply defined and of a deep orange colour, those in the other horn were hardly evident at all and of a faint primrose colour, and were apparently atrophied, their dendrites and axons being shrivelled. Whereas in the former horn we counted, in one section, six large well-defined cells, the corresponding horn on the other side only showed two pale yellow cells.

The horn in which these faintly-stained cells were found was perceptibly smaller than the opposite anterior horn.

A further examination of these cells revealed several interesting points in cellular pathology. The faintly outlined cells appeared to be swollen, their nuclei indistinct and in some cells pushed out so as to form a prominence in the contour of the cell, and the nucleolus alone appeared sharply defined as a shining point. The contents of the cells were granular and there was an entire absence of Nissl-bodies or any attempt at an intracellular structure.

The cells, on the other hand, which presented a prominent appearance in the various sections, differed entirely in every respect from the others. They were sharply defined, of a darker orange colour, and in contour looked like orange-coloured black berries. They were more rounded than exists in health and their sharp edges had disappeared. In few examples were either axon or dendrite apparent. Nissl-bodies were absent, and chromatolysis in most of the cells was complete. Their contour was so peculiar and unusual that in no drawings illustrative of the pathological changes occurring in nerve-cells, given by Ford Robertson in BRAIN, 1899, and Ewing in *Archives of Neurology and Psycho-Pathology*, Vol. I., No. 3, have we discovered anything resembling the changes herein met with.

We can hardly consider this cellular change—mulberry-like alteration in its contour—to be due merely to "yellow globular degeneration," which, according to Colucci, is due to a morbid metabolism in the cell contents. The change is a change in the general shape of the cell whatever its cause may be, and is not altogether, at all events, the same pigmentary degeneration as that which is quite consistent with health.

Lugaro maintains, and perhaps rightly, that the displacement of the nucleus, as if it were pushed out from the body of the cell, bulging its contour in one place, is due to destruction of the chromatic reticulum which normally holds the nucleus in its central position, and Schäfer holds that the degeneration of nerve-cells in this, and similar spinal diseases, is due to degeneration of the posterior roots and consequent loss of the stimuli normally received therefrom. In fact, that loss of function first produces atrophy of the cell and ultimately degeneration of its contents.

The blood-vessels, as seen in the various sections, were full of blood, and their coats did not appear to be thickened to any extent.

The *Canalis centralis* was somewhat larger than normal, its lining epithelium appeared distinctly and was apparently quite normal.

The *Cerebral Cortex* (left frontal convolution) and the *Crus Cerebri* appeared quite healthy.

The *Medulla Oblongata* presented the following pathological changes:—

(1) The fasciculus gracilis (Goll's tract) was generally sclerosed.

(2) Sclerosis affected the restiform body, and the cells were only faintly stained.

(3) Gowers' tract took on the stain badly and the axis cylinders appeared to be atrophied.

(4) The fillet fibres were normal anteriorly, but posteriorly there was general sclerosis with isolated patches of nerve-fibres which were undoubtedly degenerated.

The Sciatic nerve in cross sections presented changes which were markedly pathological. The nerve-fibres were

closely packed together and pressed into masses by an increased deposit of fibrous tissue, which in places was broken down into debris-like accumulations in which no nerve fibres were observed at all. Some fibres were devoid of axis cylinders altogether; in others the axis was swollen. The empty appearance presented by the sheaths in places was very characteristic and looked like a honeycomb arrangement.

There was no uniformity in the size of the nerve-fibres; some were large and some were small. Whether the latter were due to simple pressure or whether they are actually embryonal structures is doubtful.

In sections stained with hæmatoxylin (Weigert) there were patches of the section which failed to take on the stain at all, consisting of very small nerve-fibrils, much atrophied and evidently much compressed by replacing fibrous tissue. These patches of sclerosis were all the more evident for the other portions of the section took on the stain admirably.

Remarks.

In Brain (1898, page 72) there is an interesting clinical record of several cases of Friedreich's ataxy by Dr. Mackie Whyte, and in the same volume at page 438 there is a very thorough article on the pathology of this disease by Dr. H. Mackay—both papers being supplemented by an extensive bibliography.

It may here be of interest to review the symptoms presented by our case which justified our diagnosis.

(1) Two cases occurred in the same family. The occurrence of paralysis, of a progressive type, in more than one member of a family during childhood should make us suspect this disease, and lead us to further observation.

(2) The disease commenced in both our cases immediately after a post-scarlatinal chill, and most observers hold that, as an exciting factor, some acute disease, especially if accompanied by fever, is generally the direct cause of the paralysis, the predisposing cause, of course, being a tendency to degeneration of the neuron.

(3) The first symptom noticed in our cases was a difficulty in walking—the ataxia being progressive in character.

(4) There was a rapid change in the power of articulation, so that, early in the history of the disease, the power of speech became well nigh abolished.

(5) As a later symptom in the progress of the disease, ataxia of the hands occurred; and hyper-extension of the fingers and toes, especially of the right hand and foot, is a prominent symptom in the case of Charlie.

Main en griffe—claw-like hand—is a condition which all along has been absent in our cases, although it is described as occurring in several of Dr. Mackie Whyte's patients.

(6) Athetoid movements of the fingers and toes, especially when the attention is diverted, were well marked in the case of the girl, although they do not form so prominent a symptom in the boy.

(7) An utter helplessness of the body exists in the case of the boy, and was very marked in the girl. The patient has to be carried about from place to place; he is quite unable to support himself unless when he is seated, and then he lies back on the chair, or else when he is lying down in bed. His head falls from side to side as if the neck muscles were quite unable to support it.

(8) There is marked dorsal spinal curvature—lateral; the apex of the deformed spinal column reaching the posterior border of the scapula in the case of the boy, and scoliosis was just as marked and in the same position in the girl.

(9) Talipes equino-varus, especially of the right foot, occurs in the case of the boy. Double talipes equino-varus existed in the case of the girl.

(10) Nystagmus was a very marked symptom in the girl. It is only slightly evident in the boy.

(11) The visceral reflexes in micturition and deglutition were affected; the former slightly in the boy's case; the latter, to a marked degree, towards the end of the girl's life.

(12) There existed marked incoordination in both cases. They were unable to touch the point of the nose without

first some hovering and hesitation of the finger in its progress.

(13) Electrical reactions in the case of the boy, so far as they go, were practically normal.

(14) There was an entire absence of the knee-jerk, and most of the deep reflexes were either impaired or abolished altogether.

(15) Finally, the intellectual faculties in both cases were only slightly impaired; no more, indeed, than might be expected in any case of chronic paralysis.

One curious fact about one case is that although the motor symptoms are mostly bilateral, still the ataxia seems more marked on the right side than on the left, and it may be that the spinal curvature pointing to the left side is due to the more advanced paresis of the right arm as compared to the left. This explanation is given by Mackie Whyte.

As regards the differential diagnosis of Friedreich's paralysis it is to be noted that there is a close similarity between it and hereditary cerebellar ataxia. Marie's theory, as pointed out by Whyte, may be correct, that the same degenerative process affects the spinal cord in the one case and the cerebellum in the other.

From disseminated sclerosis and locomotor ataxy, Friedreich's disease may be distinguished clinically by its family character, its occurrence in childhood, and an absence of many of the symptoms characteristic of these diseases, such as jerky "intention" tremors and ocular affections in disseminated sclerosis, and the "girdle" pain, and various crises—gastric and otherwise—of locomotor ataxy.

It should not be forgotten that cases have been described, among other observers by Friedreich himself, in which the symptoms indicated disease of a hybrid nature. Such cases are, however, the exception, and do not disprove the fact there is a group of symptoms, affecting the motor nervous system and characterised by distinct lesions in the spinal cord, medulla and nerves, forming a distinct entity and to which Friedreich gave his name.

A consideration of the pathogenesis of Friedreich's disease is both interesting and instructive. Dr. Pitt (*Guy's Hospital*

Report, 1886-7) puts forward the theory that this disease, with its imperfect development of the spinal cord, is vascular in its origin, because—

(1) The posterior columns of the cord are the most vascular, and here the sclerosis is most marked.

(2) Vascular lesions have been described in some cases, and the disease is always aggravated by acute affections.

(3) Development of the cord begins in the most vascular regions, so that degeneration attacks, by preference, the latest developed parts.

(4) The sclerosed regions correspond to tracts, the filaments of which are covered by myeline after the fifth month of fœtal life.

(5) The symptoms become more marked at puberty, which is accompanied, as we know, by great vascular modifications in the organism.

And, again, Guizetti (*Reforma Medica*, June, 1893) maintains that Friedreich's disease "depends upon a congenital predisposition, in consequence of which, in the early years of life, certain systems of fibres and nerve-cells undergo a process of progressive atrophy, and that the process is independent of any contributory effect from vascular alterations."

Mackay describes these "certain systems of fibres and cells" quoted by Guizetti, as those which are latent to undergo medullation and those which are functionally related to the postero-internal tract.

The entire absence of disease of the coats of vessels in our case, although they were mostly full of blood, disproves somewhat Pitt's theory as to a vascular origin. On the other hand, while there may be a predisposing factor in developmental arrest and congenital malformation of the spinal cord, it is interesting to note that, in the majority of cases recorded, the first symptoms of the disease observed have followed upon some acute febrile state of the system, in which it is reasonable to suppose a congested condition of the spinal cord vessels existed.

We are disposed to favour both theories, in part. That the disease is due to an arrest in the development of certain strands of nerve-fibres and cells in the cord, the results of

which are not evident until some intercurrent acute affection occurs, sums up briefly our present ideas of the pathogenesis of Friedreich's paralysis.

It remains for us briefly to discuss the prognosis and treatment. As regards the former, Friedreich's ataxia is progressive and chronic, many cases living, according to Ladame (BRAIN, 1890, p. 525), to upwards of 40 years of age.

Although intermissions are said to have occurred, yet in no case has a recovery been reported. The disease either kills by itself or some intercurrent affection may cause a fatal termination.

As in all spinal cord affections, the duration of life depends, to a marked extent, upon the character of the nursing, and it is interesting to note here the almost entire absence of any tendency to bedsores occurring. Our patient sits day after day on the same chair, and yet his skin remains unbroken, and the girl's slight bedsore was due more to emaciation than to any trophic affection.

With such a prognosis little need be said as to the treatment of Friedreich's ataxy. Charcot recommended "suspension" with apparent benefit; Zalludowski gave temporary relief to a little girl by means of massage to the limbs, and Mackie Whyte recommends exercise and an education of the functions of those muscles which tend to become affected. Our patient says that he feels very much better after the use of the continuous current. Drugs seem to have little influence in the arrest of symptoms, and the most we can do for cases is to nurse them carefully and attempt to combat the graver symptoms as they occur.

In conclusion, we would express our thanks to Dr. le Doux, of the Bacteriological Institute, for his kindness in making sections and photomicrographs of various parts of the nervous system which illustrate this paper.