

FOUR CASES OF FRIEDREICH'S ATAXIA  
WITH A CRITICAL REVIEW  
OF RECENT LITERATURE ON THE SUBJECT.

*A Dissertation*  
*by*

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FOUR CASES OF FRIEDREICH'S ATAXIA  
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Amongst the diseases of the nervous system, just as amongst the diseases of other systems, it is found that some have a "family" character. By this is meant that they are prone to appear amongst various members of the same family, children of the same parents. Some of these "family" diseases have also a "hereditary" character; they appear in two or more generations. Again, the "family" character may be absent; the disease may appear in "isolated" form; either the family may be small, consisting of one or two members, or at least the mysterious causes of the affection may have singled out one. When the family consists of several members, it is usual to find that some have escaped the family disease.

The list of family diseases of the nervous system is now fairly lengthy. Higier (78) one of the most recent writers on the subject, makes out a list of thirteen groups, as containing the most important representatives, and some of these consist of several sub-groups. It is common to find, as Marie puts it, that each family even of fairly well-defined type such as Friedreich's disease, has its own special traits; consequently the grouping of affected families is more or less arbitrary, and in many cases as yet, premature. As we shall see farther on, the records of transition forms, connecting one class of disease with another, are multiplying. What is wanted is the continued careful recording of clinical cases of those rarer diseases with, if possible exhaustive autopsies; Friedreich's Ataxia is a well-marked clinical

type; many cases belonging to it have a "family" character, many are "isolated"; only a few are, properly speaking "hereditary".

This paper first gives a clinical account of four cases of Friedreich's Ataxia; then follows a discussion of a number of the more interesting points in connexion with the symptoms, diagnosis and pathology, along with a critical review of the recent literature.

(A) A group of three Cases of Friedreich's Ataxia in one family.

The parents of the first three cases of Friedreich's Ataxia about to be described were Irish. They lived in Ireland till after the birth of their fourth child. The father, a factory worker, was a heavy drinker, and died at fifty of liver disease. The mother was also alcoholic, and died of pneumonia. She suffered ~~also~~ from gastric ulcer, obstinate pruritus, and eczema of face and neck. The eldest son informs me that his father used to say he knew of no nervous affection previously in their family. No history of insanity, fits or any other nervous disease can be obtained. The circumstances seem generally to have been very poor, such as are common to many thousands of Irish in Dundee and Lochee. The patients belong to a family of nine accounted for as follows:-

1. First child, premature, died at two months.
2. Hugh - Ataxia.
3. Mary - Ataxic.
4. Nora, married, died, aged 25, in childbirth; shewed no Ataxic

symptoms; had three children, eldest alive and healthy; the other two died when a few days old.

5. Maggie, married, subject to headaches since her marriage; two premature children, dead; one alive and healthy.
6. John, died, aged 13, of typhoid; had shewn no ataxic Symptoms.
7. Agnes, healthy, recently married.
8. James, healthy. (aged 17).
9. Winifred, Ataxic.

Nos. 5 and 8 show nystagmoid jerkings; their knee-jerks are normal. All were suckled by the mother. Mary shared her mother's milk with another child.

Case 1. Winifred M'Anarney, aged 15, a mill worker.

Patient's history:- She seems to have had good health until March 1888, when she was sent into the Dundee Infirmary as suffering from typhoid fever. A brother, aged 13, had died at home of this disease. Her illness had begun with rigours and slight diarrhoea, and she had lain at home three weeks before admission to the Infirmary. She was there found to be underfed and to be suffering from slight diarrhoea, but beyond this there were no definite signs of illness, and she was soon discharged much improved.

A short time after this her father and eldest brother observed the first symptom of her present illness, namely, some difficulty in walking. Her mother also spoke of the way the girl kicked when asleep. Very gradually a change in her speech developed, so slight that it would probably have escaped notice, had not

her brother Hugh been on the outlook for symptoms of the disease from which he and his sister Mary had long suffered. On the sensory side there have been no complaints with the exception of some pains in the back of the thighs, occurring in the Spring of 1894.

In July of that year I sent her into one of my wards in the Dundee Infirmary, and since then she has been more or less constantly under my observation. During the past two years, the girl has frequently stumbled and fallen when running, and this seems to have been always in imperfect light, in the early morning or in the evening. Moreover, she says the staggering is worse when going to her work in the morning both in summer and winter, rest having, apparently, a greater influence than fatigue in increasing it.

Present condition. (February 21st. 1897).

Fairly well grown; expression of upper part of face bright and intelligent. The lower jaw usually droops and the mouth is partly open. Cheeks well coloured; nutrition rather below the average. (This is easily explained by her home conditions). Bones seem well formed; muscular development rather feeble, but not specially so in any locality.

Nervous system. The following conditions are to be noted on the motor side. When sitting, slight swaying movements of the upper part of the body occur; the hands can lie perfectly still. When standing, patient prefers to keep the feet some distance apart, and can then balance herself steadily enough if her eyes are open. She fixes them on some object in front of her. There is

swaying of the trunk and head, made much worse when the feet are brought close together. If the eyes are then shut, patient at once falls over to one or other side, or ~~for~~ forwards. The tendons on the dorsum of the foot are seen to contract (danse des tendons) and the toes grasp the floor; the great toe, however, is often over extended. Balancing on one leg is quite impossible. Her head is always bent forward a little, whether sitting, standing, or walking. Her gait is distinctly awkward and ungainly. The steps are of unvarying length, her feet are now wide apart, and again they knock against each other. She cannot keep to a straight line. Her feet are brought to the floor with a slight stamp, through a jerky movement with the character, not of spasm, but of inco-ordination. The staggering character is more marked when walking backwards, and still better if the eyes are closed. She can turn round fairly well, and can stop quickly when told to do so.

All voluntary movements can be carried out in a way, but the ataxia which is so marked in walking, is likewise manifest in other directions. For instance, when patient is told to pick up a small thread off a smooth wooden surface the hands and fingers oscillate a little, and she prefers to rest them on the surface before catching the object; there is an awkwardness about the act. When told not to touch the board the hovering movement described by Charcot is shown. Apart from this ataxia, however, she can carry out her intentions - can button her clothes behind her back, thread a needle &c. A full cup is slightly spilt when she carries it, but the oscillations are not increased when she puts it to her

mouth. When put through other tests for inco-ordination in the upper extremities with the eyes shut, there is a decided defect. When told to touch the tip of her nose, for instance, her forefinger first reached the upper lip at its lower border. My notes show a distinct increase in the ataxia of the upper extremities since 1894. When lying down she can touch objects with her heel or toes without very marked inco-ordination.

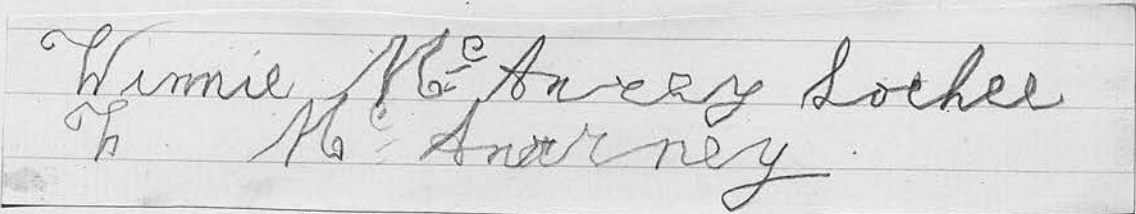
Involuntary movements, include some already mentioned -the swaying of the body, the oscillations in carrying out a voluntary movement. But there are also occasional ~~cho~~iform twitches in the face, especially drawing up the right side of the mouth, and some jerky movements of the same nature have been observed in the head and fingers. To this class belong also the evidently very marked jerkings that occur during sleep. Patient is quite <sup>un</sup>aware of them, but they must interfere considerably with the repose of her bed companions. They have been continuous since the onset of her illness.

Certain involuntary movements are seen in the eyes when they are strained by being directed to the extreme right or left, a slow nystagmus, about one oscillation per second. When the eyes are fixed on an object above or below the horizontal line, a very fine oscillatory movement can be detected.

When the lingua is protruded, constant slight movements are seen.

Disturbance of speech is to my ear decidedly more marked than it was in 1894. And yet it is not very bad, especially when patient is paying attention to it. Her voice is deep-toned, the

words are uttered slowly, there is rarely any slurring; long words or combinations as "post office savings bank", "articulation" can be uttered with a single effort. A stranger might find little difference between her speech and other girls of her class, but my own knowledge and her friends' statements shew some deterioration to have taken place. She can write legibly as shewn by the specimen annexed.



Winnie McAnaney Locher  
 To McAnaney

The writing is tremulous and uneducated; she holds the pen or pencil in a clumsy way, but one must remember that she has hardly written a line since leaving school three or four years ago. I do not think her writing has grown worse since I first knew her.

Sensory Functions. Patient used to have a giddy feeling at times, but she is now free from that. There are no abnormal sensations whatever, and the various forms of cutaneous sensibility are normal.

The muscular sense is affected; patient is a good deal astray in trying to localise the position of arm or leg when blindfolded. (In 1894 the sense of posture in the upper extremities was fairly correct). She constantly makes mistakes in trying to

distinguish between different weights with her legs, but with her arms is fairly correct. Hearing, sight and taste are normal; deglutition, defecation and micturition are normal. Patient has not yet menstruated.

The knee jerks are completely absent, and have been since I saw her first. Superficial reflexes normal.

Condition of Muscles and Deformities. There is no sign of flabbiness and no muscular atrophy can be detected. But there is an increasing deformity about the hands. When the right hand is extended, there is a very slight flexion of the wrist, a slight hyper-extension at the metacarpophalangeal joints of the fingers, especially the fourth and fifth, and a gentle flexion of the inter-phalangeal joints. The little finger shews a decided bend forward. The fingers can be well separated from one another, and the wrist moves freely in all directions when the fist is closed, but by no effort can patient extend the phalanges completely. The thumb is not affected in any way. The same description applies to the left hand, though here the deformities are rather less marked.

This condition of the hands is very distinctly worse since 1894.

The feet shew a very high instep and prominent dorsum when patient is resting, not so marked when standing. There is no talipes, and no hyper-extension of the great toe, beyond the occasional involuntary movement before mentioned.

A slight spinal curvature is present, convex to the left in the middle dorsal region, convex to the right in the upper dorsal

and cervical regions. The bend forwards of the head is due to a slight kyphosis.

Grasp is good on both sides, and the muscular power of the legs seems to be normal. Patient is easily tired, but works for the full day, earning seven shillings a week as a "shifter."

Electrical reactions are normal, both with Faradic and Galvanic currents.

Her psychical condition is normal; intelligence rather above the average.

Case 11. Hugh M'Anarney, aged 33, a mill worker, began to walk when 18 months old. Between his third and sixth year he suffered from some illness "like water in the head", and was for two years in bed. He went to school when six, and remained there until he was twelve, learning with normal facility.

At the age of nine he had a bad fall from a cart on the back of his head, and was rendered nearly unconscious, but there were no bad after effects. On leaving school he began to work in the mill, and shewed some nervous symptoms. Other workers were afraid he would fall among the machinery, and some suspected him of smoking. There do not seem to have been any ataxic symptoms sufficient to attract attention before this.

He soon got into the way of holding his head forwards, with his eyes bent on the ground that he might balance himself better; he preferred to keep his hands stretched out, <sup>the palms being</sup> ~~and rotated with~~ <sup>ducked forwards,</sup> ~~his arms outwards~~ when walking.

From the age of fourteen he found some difficulty in picking things up. There was not much change in his condition for the next four years, but he found that mill overseers were rather shy of engaging him in case of accidents. Between seventeen and nineteen he thinks he improved, but after that he became markedly worse and from the age of twenty walking has been impossible. About that time he had loss of sensation in his feet and got a burn on one of his soles through standing on a hot coal. For a long time he has suffered from numbness and feelings of creeping and prickling in his feet and legs, not in the arms. Often about two hours after going to bed he has a sensation of blood rushing up to his head, and his heart seems to stop. His legs sometimes start involuntarily at night. He has had no lightning pains, no girdle pains, no vomiting, no disturbance of bowels, no affection of vision. From about the time at which he lost the power of walking, he has had some difficulty in micturition.

On August 1st. 1894, he was admitted to the Dundee Royal Infirmary, and though the notes then taken are brief and evidently imperfect, it is worth while reproducing them for comparison with his present state:- "Head hydrocephalic in shape 22 inches in circumference. Dorsal spine shows right lateral scoliosis of very exaggerated character- sternum raised- left lower ribs touch crest of ilium.

Sensory Functions. Tendency to coldness in feet- formication in soles- tingling sensations in legs and feet- anaesthesia to touch and pain below level of iliac crests- pupils large, sight good, hearing good.

Motor Functions. Drop wrist well marked on right side when hand held out; muscles of fore arm and ball of thumb flabby; diminution of grasping power- no power in lower limbs except slight power of extension of hips and knees.

Visceral Reflexes. Normal except that patient sometimes takes half an hour before he can micturate. No skin or tendon reflexes in lower limbs.

Slight tendency to waste in muscles of legs. Sweats a good deal".

In July 1894 I examined him minutely and on comparing the notes taken then with those made now, I find very little alteration.

State on Examination February 1897 (see photograph<sup>1</sup>). An under sized, fairly nourished man, face somewhat flushed, expression intelligent, features thick, this being especially seen in lips, head large, brachy-cephalic, 59.4cm. in greatest horizontal circumference, held well forwards. His usual attitude is sitting in an arm chair, with his arms resting on a table in front of him. If he has no table before him he likes to twist his arms round the arms of the chair to keep himself from sliding off. When thus supported in a sitting position, his left shoulder is depressed, and if the spine is looked at (see photograph<sup>3</sup>) it is seen to be curved(convex aspect) to the right between the first and twelfth dorsal vertebrae. A slight compensatory curve the other way is seen in the lumbar region. The spine also shews a marked convexity backwards, in the upper dorsal regions, and a concavity (lordosis) in the dorsolumbar. The upper four dorsal, and the lower cervical

spines are nearly horizontal.

When lying as straight as possible on his back, the lower end of the sternum is very prominent, 7cm. higher than the upper end. The sternum is straight except the xiphoid, which is bent back. Intercostal spaces are narrow. No prominences at costochondral unions. The hand can be easily passed behind the back on account of the lordosis. The ribs on the left are depressed to the iliac level.

Extremities. (a) Upper. Muscles moderately well-developed and pretty firm. No marked atrophy, though the interossei seem thinner and softer than any other set. No contractures; no fibrillary twitches; no rigidity; passive movements possible in any direction.

(b) Lower. Muscles fairly firm but considerably wasted, apparently from disuse. Right calf 25.6cm., left 27cm. in circumference; legs lie helplessly in bed, generally flexed at knee; foot shows a permanent deformity, the shape closely resembling that of pes cavus, arch extremely well marked on both sides, less on right than left; dorsi-flexion of first phalanges of toes, clawing of other phalanges to some extent. The deformity is less marked when the feet rest on the floor (see photograph). On first exposing the right foot a fibrillary tremor was noticed in the muscle on the inner border close to arch - (short flexor of great toe) Limbs very cold, and red or blue below the knees.

Motor Functions. When in bed the patient prefers to lie on his right side, curled up. Cannot lie on left side longer than half an hour at a time. Has the greatest difficulty in raising him-

or turning round. In trying this he makes enormous efforts, painful to witness, and becomes very much flushed. The voluntary movements of the trunk are thus very jerky; he tosses himself round from one position to another.

Respiratory movements require a distinct effort; when sitting quietly with his table before him, both inspiration and expiration are audible through the room, a distinct pause separating them. The breathing is nasal, with each inspiration the head is jerked up a little. He is said to breathe more heartily and to snore at night. Power in the muscles of the neck seems well preserved; head can be moved in any direction. Occasionally there is a slight choreiform vibration of the head, especially on making a voluntary movement. Swaying movements of the head and body are constant, when sitting. No choreic twitchings of face or other disturbance of facial movements.

Voluntary movements in the arms moderately active, but not so powerful as one would expect from the appearance of the muscles. Grasping power much diminished; free movement at shoulders, elbows and wrist. When told to straighten the fingers, the hand resembles the main en griffe of progressive muscular atrophy. <sup>(see photograph 2)</sup> There is flexion at the wrist, over-extension at the metacarpo-phalangeal joints, and flexion at the first interphalangeal joints. There is dorsi-flexion of the second phalanx of the thumb, and also of the unguis phalanx of the right mid-finger. (This is the result of an accident). The index is less affected than the other fingers, and the condition is more exaggerated on the right side. In extension the fingers are

kept slightly apart, but they cannot voluntarily be completely adducted or abducted. The wrist and fingers can be quite easily straightened by an external force. The extensor tendons can be traced up the lower third of the fore-arm, and on the front the tendons of the palmaris longus and other flexors stand out. The palm is hollowed.

Movements of fingers and arms, in trying to pick up or touch objects, are badly co-ordinated. Patient likes to have the arms supported on the table etc; when this is done there is not much oscillation. Sense of posture in upper limbs defective.

As for the lower limbs, walking is quite impossible. Slight power of flexion and extension at hip. None at knee or ankle, very little at toes.

Sensory Functions. In the legs there is slight diminution of acuteness in sensibility to touch, but pain is felt normally. No lightning pains; some slight paraesthesiae in lower limbs are noted in the history.

Reflexes. No knee or Achilles jerks; plantar reflex well marked on right, slight on left. Cremasteric and abdominal reflexes marked. Visceral reflexes normal apart from delay in starting micturition.

Sight. Normal; pupils act readily to light and accommodation; a moderate degree of nystagmus, consisting of irregular jerkings on fixing eyes on an object to the side.

Hearing. Slightly dull, (this also the case in 1894).

R. h. d. 12" L. h. d. 3"

occasional sound of **rushing** water in his head.

Tongue. Flabby, marked by teeth, slightly furred on dorsum; when protruded a constant fine tremor pervades its whole extent.

Speech. is markedly disturbed. One requires to attend closely to make out all that he says, though if his attention is directed to words, he speaks much more clearly. The voice is monotonous, the words are somewhat slurred, not scanned.

"Remember" becomes "rememr", "Whether" becomes "wher". "British constitution" becomes "Brish constution". "A dainty dish" becomes "a den dish".

Psychical state is normal. Patient is said to be rather irritable, and to make what the others consider undue demands from his being the eldest of the family. His intelligence is quite unaffected.

Electrical reactions with galvanic current.

Extensors of left fore arm K C C 7, ACC 9, KOC 12, AOC 13.

Heart. Sounds normal; position altered, apex being in third left space external to nipple.

Case 111. Mary M'Anarney, aged 31, formerly millworker.

History. Patient had inflammation of the bowels, measles and whooping cough in infancy, but there was nothing indicating any ataxia or paralysis until she was fifteen. At this time in the month of July, she took ill one morning when on the way to work, feeling cold and suffering from bleeding at the nose and mouth. She became unconscious that night, and remained so for about six weeks. During the next eighteen months her mind was

enfeebled, and she could not walk steadily; she managed, however, to do some work in the mill, and in course of time her mind recovered its former clearness.

The staggering, however, increased to such an extent, that at the age of twenty-one she was refused further employment.

From the beginning of her illness she was subject to cramps and to jerkings in the legs at night.

At the age of nineteen, and again when she was twenty-one, she was a patient in the Dundee Royal Infirmary, on account of spinal curvature.

Until she was twenty-six she was able to get about on her legs, pushing a chair in front of her, but during the last few years she has been unable to walk at all. She says that her hands have both been weak, - the right more than the left, - ever since the acute illness which marked the beginning of her disease. Still she could sew, although her hands were shaky; she has never been able to read or write, her school education having been very imperfect and <sup>of</sup> short of duration.

Since July 1894, she has been almost constantly under my observation, in the Dundee Infirmary and the Parochial Hospital.

Present condition. A well nourished, fresh coloured woman, with cheerful expression, ruddy complexion and numerous freckles on face and neck. Her hair is light brown, strong and abundant; her nose is twisted from a fall four years ago, and on her right cheek is a scar, due to another accident. Through this

scar there is a puckering of the cheek below the inner part of the right eye, when the lids are firmly closed; there is also a slight drawing-up of the right angle of the mouth.

The head is well-shaped, and measures 55.4 cm in the greatest horizontal circumference; it is kept bent forwards through the spinal curvature, but patient says that she was accustomed to hold it so because she was ashamed of her staggering.

Her usual attitude is sitting up in bed, with the back well supported by pillows; the spine shows a marked dorsal curvature, with convexity to the left, extending from the sixth dorsal vertebra to the second lumbar; the deviation at its maximum amounts to  $1\frac{1}{2}$  inch; the ribs project backwards to a marked degree on the left side, and are well separated from one another. On the right they are crushed together, and the twelfth rib is on a level with the iliac crest. In the upper dorsal region, there is a slight curve with convexity to the right. Some kyphosis is present in the upper dorsal spine; this can be removed partially, and for a very short time, by an effort of the patient.

The dorsal curvature is somewhat less pronounced when she is raised up by the arm-pits.

She complains a little of soreness, on pressure over the spine in scapular region.

The mammae are well developed, and there is no striking asymmetry when the chest is examined from the front.

Extremities. Upper extremities show, when at rest, no deformity,

the bones are well shaped, the muscles seem smaller than normal on the back of the fore-arm. The lower limbs on the other hand, shew a deformity about the foot, talipes equino-varus being present on both sides. The legs below the knee are more cylindrical than usual, from a want of development of the calf; the antero-lateral group of muscles is deficient in bulk; the heel is drawn up, some transverse wrinkles of the skin being present over the lower end of the tendo-Achillis. The hollow of the pedal arch is very much greater than usual, and this is so even when patient is made to stand. Most of the grooves on the sole run from within, outwards and forwards. The great toe, especially the right, is always over-extended. It can be brought voluntarily into line, but not flexed. The other toes show slight over-extension at the metacarpo-phalangeal joints; at the inter-phalangeal joints there is flexion. The dorsum of the foot is prominent. (see plethographs 4 and 6).

Motor Functions. Patient shows distinct weakness in the muscles that raise the trunk into a sitting posture. She can raise herself, but awkwardly and slowly. When sitting, there are constant swaying movements of the head and body; there are besides, frequent jerkings of the head, and also choreic twitchings of the face, especially in the right levator anguli oris. These are not by any means so marked as to cause any confusion with true chorea.

In the upper limbs, movements are free at the shoulder,

elbow and wrist joints (with hand closed). When told to extend the finger and hand, there is a marked imperfection: the wrist is somewhat flexed forwards, and to the ulnar side, the fingers are over-extended at the metacarpo-phalangeal joints, (especially the ring and little fingers) and flexed at the first interphalangeal joints. The terminal phalanges are in line with the middle. The deformity is in short the main en griffe. The thumbs are unaffected; the fingers can be separated, though less freely than normal. (See photo. 5)

Ataxia is present in the upper limbs, but patient can button her clothes, or thread a needle, if the elbows are supported. Her movement is like her sister's (Case 1) in picking up small objects, and in carrying out any movement oscillatory jerkings are very noticeable. The Ataxia is brought out by the usual tests of bringing the fore-fingers together, or by touching the point of her nose, with eyes shut. Hesitation and waving movement is more marked when she is near the point aimed at. The super-added movements are less marked if the eyes are open.

Power of grasping is still fair, though awkward from the extensor wasting. At elbow and shoulder, muscular power is well preserved.

Lower Limbs. Patient can flex and extend at hips and knees, but with lessened power. With legs extended she can raise the right foot two inches off the bed, the left twelve.

Even when supported on each side, she cannot walk; her feet are pushed too far forward, so that she is unable to get her balance. Her steps are very short, the right foot is cross-

ed over the dorsum of the left, and thrown two or three inches beyond the place where it ultimately touches the floor. She puts down her feet with a slight stamp, first the toes and then the heels. There is only very slight voluntary movement at the ankle, and that is mainly extension. The toes allow of somewhat freer voluntary movement. The ankle can be passively moved to a much greater extent, but dorsi-flexion of the foot is much interfered with, through contracture of the tendo-Achillis.

The heel can be placed on the opposite knee, but slowly.

Sensory Functions. occasional headaches, no giddiness; there is some slight delay in conduction of impressions from the lower extremities, but sensibility in its different modes is essentially normal. There is a small area on the front part of the dorsum of the left foot, which shews slight dulling of sensibility to touch, not to pain.

Reflexes. No elbow or knee jerk; abdominal reflexes well marked; plantar exaggerated; no disturbance of visceral reflexes.

Eyes. Reaction of pupils normal; when looking to either side, some nystagmus-like jerkings occur, about seven in five seconds, irregular in time; they are also seen when she looks up or down: sight is normal.

Hearing. The hearing distance varies, but is usually about three inches on each side.

The Tongue, when protruded, is constantly in a state of

movement, not the irregular jerks of chorea, but a fine oscillatory movement.

Speech. Her voice is low-pitched, not harsh, monotonous. She keeps her teeth rather close in speaking; some words are slurred - "Doer" for "Doctor". "I don't emember" for "remember". The speech is, consequently, somewhat slipshod; it is very like her brother Hugh's.

Vasomotor System. Feet tend to be cold.

Psychical condition normal.

Muscular sense normal.

Electrical Reactions. Faradic current much better borne on legs than normally; somewhat better on arms. Muscles of arms contract well under its influence, but the interossei act sluggishly.

Galvanic current. Inflexors of right fore-arm KCC 6, ACC 7; in extensors of right fore-arm KCC 6; ACC 7; KOC 8; AOC 8; in antero-lateral muscles of right leg, KCC 6; ACC 10.

The interossei, especially those of the third and fourth spaces, respond feebly to galvanism.

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(B) An "isolated" case of Friedreich's Ataxia. (Photographs 8).

Case IV. William Morgan, aged 13, admitted to Dundee Royal Infirmary, August 30th. 1894.

Family History, etc. Patient is third of a family of four, the youngest three by the same mother. His father died some years ago of inflammation of the lungs, after eight days' illness. His mother, sisters, younger brother, and nephew are all healthy. A slight nystagmus can be detected, on extreme lateral deviation of eyeballs in his brother and younger sister. There is no history of any nervous affection in any of the other members of the family, nor is there any evidence of syphilitic or tubercular taint. His home surroundings are good; he has not been overworked at school, and has shewn average intelligence.

Present Illness. About two years ago his mother noticed that he became easily fatigued, and did not care to join in the games of his companions. His gait was a little unsteady; if he ran or walked quickly, he was apt to stumble or fall. This was no worse in the dark, but if his feet were bare there was decided aggravation. There was no definite onset, no pain, shivering or feverish attack. His condition did not change much for some months, and then his upper extremities were seen to be slightly affected. He could not dress himself so quickly as usual, his hands were a little unsteady, and he was apt to spill the contents of a saucer in drinking.

His handwriting was rather shaky, there was a want of freedom in using his pen or pencil, and a difficulty in form-

-ing some letters. Both sides of his body seem equally affected. The only time he complained of pain, was a year ago, when his back ached at times, but this feeling passed off after the back was painted with iodine. He had no headache, or shooting pains in his limbs. During the past few months his arms and his legs have been getting thinner. No change has been noticed in his speech. There has been a steady deterioration from the beginning of the illness, <sup>increasing</sup> the difficulty in locomotion <sup>being</sup> ~~increasing~~ <sup>marked</sup> especially in trying to go downstairs.

State on Admission. A fairly well developed boy, with florid complexion, sad or pensive expression; brow transversely wrinkled, eyebrows often involuntarily drawn up while under observation. Weight 5st.

Nervous System. (The only system affected). The boy is quite intelligent, and has a keen sense of his unfortunate condition.

Motor Functions. Patient stands with his feet about twelve inches apart, but if his heels are brought together he sways from side to side, and would fall if unsupported. Head and upper part of body bent forward. Closure of eyes increases the unsteadiness; when sitting in bed he has difficulty in balancing himself. Various muscles are seen to be constantly working as he tries to steady himself when sitting or standing. When laid on his back he can raise himself up fairly easily, by means of the trunk muscles alone.

When standing he can stoop forwards, and pick any article off the floor.

Gait. He walks with head bent forwards, and eyes fixed on the ground, his legs widely straddling. He brings his foot down heavily with a slap, first the toes, then the heels, reeling from side to side as he goes, and swaying his arms irregularly. His eyes are a great help to him in walking, He walks backwards with great difficulty; it is impossible to get him to keep to a straight line. His gait has something of a festinant character; his steps are irregular in length, force, and direction.

Co-ordination, as tested by making him bring the tips of his fingers together, or touch other parts of his body, or place the heel of one foot on the opposite knee, is fairly good.

Writing is shaky; he presses his hands heavily on the paper. Nutrition of musclea, good, no hypertrophy or atrophy; no true fibrillar contractions, though muscular twitchings are noticed here and there even when he is lying at rest. No deformities about feet, but slight lateral curvature of spine, dorsal convexity and lumbar concavity to the left.

Speech is low-toned and somewhat slow, not jerky or scanning or monotonous. The muscles of his lips seem slightly weak in their action, but there is no paralysis of the facial muscles.

There is distinct nystagmus, (better marked on some days than others), brought out when the eyes are fixed on an object away from central line of vision.

Reflexes. Patellar reflexes gone; no ankle clonus; plantar reflexes present on both sides, rather better marked on left; epigastric and cremasteric reflexes present; visceral reflexes normal.

Sensory Functions. Has no abnormal sensations such as cold, heat, numbness or prickling. Sensibility to touch seems a little dull in lower limbs, the light touch of the head of a pin being frequently unfelt. Sensibility to pain, acute, can readily localise a pin prick, can easily distinguish heat and cold.

Sight, good; pupils equal, regular, reacting freely to light, but somewhat slightly to accommodation.

December 13, 1894. Tongue thick and flabby, constant tremors in it, especially on protrusion. Frequent involuntary jerkings occur in head and upper limbs. Complains of feeling weaker, and often lies in bed for a day. Has occasionally been troubled with cramp in muscles of calf. His walking and general power of balancing are much worse, and he often falls. In trying to touch an object he is more uncertain in his aim, from the irregular jerkings in his arms <sup>or</sup> ~~from~~ voluntary movement. There is a corresponding difficulty in carrying out the heel-on-knee manoeuvre.

Fundi of eyes show nothing abnormal. (Dr. Macgillivray).

February 19, 1897. Since last note patient has had fair general health. He has grown much taller, but there is no improvement as regards any of the symptoms described above. His speech is rather worse, the lips still seem somewhat at fault. The voice is more monotonous, and is low in pitch, distinct enough when speaking to me, but his mother says that when he is reading aloud to her, as he is fond of doing, she often has difficulty in understanding him. There is a thickness, a want of crispness about his utterance.

The ataxia of the hands is still as marked, if not more so. He can put in buttons, and write his name—always with the same awkward procedure. The super-added movements in using his hands, are much as before.

He can walk, but only with strong support. His soles feel the ground quite well; the feet are raised higher than normal and brought down with a stamp, paretic not spastic. Romberg's sign is present.

When in bed he lies on his back; he has often a painful cramp, which causes the left leg to draw up of itself. The pain is immediately above and below the knee. The limb has first to be rubbed over the knee and then pushed down. If it were simply pulled down, the pain would be severe.

In the morning he has some pain in the lumbar region, when bending to get on his clothes with his mother's help. This is probably due to some stiffness, developed through his position in sleep. His back is very weak, and shows still a

slight scoliosis; this is not of a permanent character. His favourite position is sitting on the floor, with his back against the wall.

A recent symptom is a difficulty in commencing the act of micturition; there is no dribbling afterwards.

A brief résumé of these cases will be useful, and will show the main diagnostic points in **Friedreich's ataxia**.

Case I.

1. Family character.
2. Onset soon after a fever, possibly typhoid, when seven years old.
3. First symptom, difficulty in walking.
4. Very slow advance of ataxia; cerebellar character slightly marked; worse in the dark (Romberg's symptom).
5. Slight change in speech, beginning somewhat early.
6. Slowly increasing ataxia of upper extremities.
7. Swaying of body; choreiform jerks.
8. Nystagmus.
9. Absence of knee jerks.
10. Slight weakness of interossei in hands.

Slight scoliosis.

No talipes, or hyperextension of great toe, but unusually high instep.

11. No marked paresis unless in hands.
12. Intelligence and sensory functions (general and special) normal.

Perhaps some impairment of muscular sense.

13. Visceral functions normal.

Pupil reflexes normal.

Case II.

1. Family character.

2. Severe cerebral affection in infancy.

3. Onset of present illness at twelve.

4. First symptom, - unsteadiness in walking.

5. Advance of ataxia, with remission, between seventeen and nineteen; again rapid advance, with paralysis of legs at twenty.

6. Marked articulatory defect.

7. Ataxia of hands at thirteen.

8. Choreiform jerks and swaying.

9. Nystagmus.

10. Absence of knee jerks.

11. Main en griffe, on extension of fingers.

Kypho-scoliosis, very marked.

Talipes equino-varus.

12. Great loss of power in arms, trunk, and especially in legs.

13. Intelligence normal. General and special sensory functions normal.

Muscular sense affected.

13. Delay in commencing act of micturition since age of twenty; visceral reflexes otherwise normal.  
Pupil reflexes normal.

Case III.

1. Family character.
2. Acute illness (? meningitis) at fifteen, immediately followed by symptoms.
3. First symptom doubtful.
4. Ataxia of gait, gradually increasing.  
Paraplegia nearly complete at twenty-six.
5. Articulatory defect.
6. Ataxia of hands since the age of fifteen.
7. Choreiform jerks and swaying.
8. Nystagmus.
9. Absence of knee jerks.
10. Main en griffe.  
Kypho-scoliosis.  
Talipes equino-varus.
11. Paretic condition in back and legs.
12. Intelligence normal.  
Sensory functions normal.  
Muscular sense normal.
13. Visceral functions and menstruation normal.  
Pupil reflexes unaffected.

Case IV.

1. No "family" character.
2. Onset, insidious at eleven.
3. First symptom, affection of gait.
4. Ataxia of legs, (tabeto-cerebellar) going on to complete inability to walk alone.  
Static ataxia.  
Romberg's symptom.
5. Speech only slightly affected, and that recently.
6. Ataxia of hands and fingers, noticed after some months affection of legs.
7. Constant swaying of body.  
Choreiform jerks.
8. Nystagmus.
9. Absence of knee jerks.
10. No deformity of hands or feet.  
No permanent scoliosis.
11. Weakness of muscles, especially in back and legs;  
no atrophies.
12. Intelligence normal.  
Sensory functions normal.
13. Visceral reflexes normal, till quite recently, when a difficulty in beginning the act of micturition came on. (as in case II.)  
Pupil reflexes unaffected.

Remarks on some of the more important  
symptoms.

Disturbances of the motor system are by far the most important in the symptomatology of Friedreich's ataxia. So much is implied by the name, and Friedreich himself pointed out that the ataxia appears in two forms; ataxia of voluntary movement, and static ataxia. Choreiform jerks, nystagmus, tremors of tongue, and possibly disturbances of speech, are further evidence of wide-reaching motor invasion, while in later stages of the disease, certain muscles are apt to become paretic or paralysed.

Ataxia of Voluntary Movement is well shown in the gait. It has often been described, and has a character which marks it off from that of tabes dorsalis. In two of my cases (Cases I and IV) alone, could it be examined. The patient in walking keeps his legs apart, and has difficulty in keeping to a line. He reels a little, sometimes a good deal, like a drunken person. The feet are brought down with a slight slap, first the toes and then the heels. The steps are short and vary in their length. The arms sway to some extent to aid in balancing, and for the same reason the eyes are fixed on the ground, a little in front; the head is bent forwards. In tabes the movements of the limbs are more disorderly, there is more excess of range, more exaggeration;

the foot is raised higher, and brought down with more noise. The patient can keep to a line, if not asked to put one foot directly in front of the other. The character of the gait in each case varies however, according to the stage of the disease, and, in tabes, according to the muscles worst affected. The point about the gait of Friedreich's ataxics, which is the most important from a diagnostic point of view, is its cerebellar character. This occurs also in Marie's disease, in multiple sclerosis ("rarely", Leyden.) and of course in cerebellar disease.

But, added to the cerebellar or tabeto-cerebellar character, are various movements of the limbs and trunk best studied when the patient stands. These movements come under Friedreich's designation of static ataxia.<sup>\*</sup> They are perhaps most strikingly shown when one looks through the camera at the patient. The inverted image is seen to be in a constant

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\* In one of Senator's cases (54) examined when the disease had made only very slight progress, the locomotor ataxia was very slightly marked, while the static ataxia was pronounced.

state of unrest, from swaying movements which are in inverse proportion to the amount of support afforded to the body. When patient lies in bed, they are absent; when sitting with the back well supported by pillows, the head and neck move; if sitting unsupported, the movements are more marked, as the trunk is now swaying; and when standing unsupported, they may be seen at their maximum. A rough examination then, shows the patient to be standing with legs apart, head and upper part of body bent forwards, tendons about ankle and on dorsum of feet in a state of perpetual motion (danse des tendons), toes often with an athetoid movement, grasping the floor.

A more careful examination may show the various muscles of thighs, hips, and back in a state of irregular contraction, in the endeavour to preserve equilibrium.

Ataxia of movement is shown in the lower limbs, when patient is lying, by such common proceedings as putting one heel on the other knee. This test is carried out by cases I and II very well, much better than one would expect.

Ataxia of upper limbs is easily brought out by writing, threading a needle, putting in buttons, picking up a small object.

The super-added oscillatory movements are present in carrying out any such attempt, and the movements are clumsy and awkward. The patient when lying, seems to have more control over the test movements of the feet, than of the hands, possibly because the latter are more delicate.

Senator (35) notes that in his first case, inco-ordination is less marked in the lower extremities when lying or walking than in the upper.

Case I illustrates the bad effect of rest, for she is always worse as regards the ataxia, in the morning, quite apart from the degree of light.

Tresidder (38) notes the same to a much greater degree in *his* case I. He says "when twenty-three years of age, the unsteadiness in walking was so pronounced that a London physician was consulted, who thought that the lateral curvature of the spine was producing paralysis, and the patient was ordered to lie down continuously. She did so for thirteen months. After this she began to walk again, and was at first very weak, but in the course of some months regained her strength until she could walk nearly as well as before the thirteen months' rest".

Besold's 2nd case, (54) a hawker, believed that his long walks (20 - 25 kilometers) were of great service to him.

These facts are of interest and importance, in view of the excellent results in the mechanical and gymnastic treatment of tabes, attained by Leyden, Frenkel and others.

Organic changes are not affected, but the function of the muscles is improved by this method of "compensation-therapeutics." (Leyden and Goldscheider Erkr. d. Ruckenm. page 589).

The test of making the patient close the eyes when standing or walking, (Romberg's sign) while of very great value in locomotor ataxia, is not so useful in Friedreich's disease. Increase of unsteadiness through this is often absent, as in three out of four of Friedreich's own cases, in Rosenbaum's (83) elder case, in Bramwell's (12) first case. In my own cases that could walk, (I and IV) there was no doubt about the existence of this sign. In Senator's first case, it was better marked on the second examination than on the first - a year and a half intervening between the two.

Where the patient can no longer walk, as in case III, the same test can be applied to the upper extremities; here there is increase in the super-added movements when the patient ~~is~~ is using her arms, with eyes shut.

The so-called nystagmus of Friedreich's disease, seems best classed with static ataxia. It is not a true rhythmical nystagmus, in the sense of the ophthalmologist, though this occurs in rare cases (noted in three of those analysed by Griffith). The symptom must be carefully looked for, and brought out by directing the patient's gaze to one or other side. When the muscles of the balls have their tension thus increased, distinct jerkings are seen, - slow they may be and irregular, as in case III, when the rate was seven in five seconds. Sometimes the movements can only be elicited by turning the patients three or four times round; as in

Geigel's (28) two cases, (brothers, aged twenty and eighteen). On turning the patients to the right, the eyeballs both turned to the right and the short jerking movements of nystagmus to the left followed, lasting a quarter of a minute.

In two of Mendel's (10) cases, the movements thus brought out were very marked, and lasted some minutes.

They are found in most cases of Friedreich's disease ("not in all", Gowers), but they are likewise often found in persons who have weak health, and even in the perfectly healthy.

This nystagmus I found in two quite healthy members in each of the families to which my cases belong, but no pathognomonic stress is to be attached to this.

On Schultze's instigation, Ausschlag (53) examined two hundred unselected cases, and of these only twenty-five showed no tremor though frequently there was only a single movement too far.

"Only a strikingly high degree, and special frequency of movements can be regarded as pathological." (Schultze (53))

Even modified nystagmus (nystagmoid jerkings) is very uncommon in locomotor ataxia, so this sign may in certain cases be a help in diagnosis.

The involuntary movements like an irregular tremor shown in the protruded tongue, may, without doubt be referred to the same category as those we have been considering, and some would similarly treat the speech disturbances.

Besides the swaying movements of static ataxia, there are frequent involuntary jerkings, choreiform in character, but not so constant or violent as in chorea.

Thus in case I, occasional twitchings are seen in the face, especially drawing up the right angle of the mouth. Very much the same facial movement is seen in her sister.

In case IV the brow is often raised involuntarily. The transverse wrinkles so marked in his brow may be associated with the bent position of his head, and may have been produced by his raising his eyebrows with his upper eyelids. A waggling or wobbling of the head is constantly to be seen in the two worst cases, and to a slighter degree in the others. Even when lying at rest occasional muscular twitchings, not fibrillar, are seen in case IV. He is subject to a cramp in the left leg at night.

The other three cases have all been subject to jerkings in the legs at night, as in the case of the eldest (case II), They seem to be more of the nature of cramps now, and another member of the family has often to get up to pull his legs straight.

The choreiform jerkings are an almost invariable part of the clinical picture of Friedreich's ataxia, and are of great diagnostic importance. They have sometimes led to a false diagnosis of chorea, as will be noted later on (v. diagnosis).

In one case (Zabludowski's (84) ) are noted " choreiform movements, especially when going to sleep", and also at that

time, twitchings in face and ears, and flexion of thighs on abdomen.

Painful cramplike contractions when in bed, have been noted by others (Bramwell (13) Atlas Vol.I p.46. Besold (54) case II). Nocturnal restlessness is noted in Bramwell's (12) case I.

Some of these exaggerated movements at night are probably analogous to the jerks which most people experience on dropping off to sleep.

Athetoid movements occur too, in a quite minor form as in one of Griffith's cases where there was no tremor but a slow ataxic movement resembling athetosis which appeared when the hands were lying passively in the lap.

Athetoid movements of the toes in walking are occasionally present (Ladame's case (1) p.477). In both of Wallace Anderson's (36) cases athetosis was distinctly marked in fingers and toes. These cases were peculiar in other ways; the eldest was twelve years old but looked seven, and his mental condition corresponded to this age. The knee-jerks were present though faint in both, and so was rigidity of legs with spastic gait. The onset in both was after measles two years previously.

The most remarkable movements of this class were observed in three cases reported from France. The first (Chauffard (33) ) was a boy of eight; symptoms since age of three; no heredity, sisters unaffected. No nystagmus, gait neither

cerebellar nor tabetic. One leg made to pass before the other with a jerky and exaggerated convergent movement. Among usual symptoms were the progress, absence of jerks, absence of ocular symptoms, comparative preservation of muscular force, slight equino-varus. Further there was marked lordosis (dorso-lumbar) with slight cervico-dorsal kypho-scoliosis. No choreiform instability in repose, but sudden involuntary flexions of lower extremities at hips, legs remaining extended. Intelligence good, no grimaces. "Hovering" inco-ordination in picking things up. Arms took up athetoid position in walking with support. Forearms in position of pronation, hands flexed, their backs being directed down, fingers extended or flexed in the palm. The movements were not the usual slow convulsive movements of double athetosis. They only appeared when other voluntary movements were made - a muscular synergy, an athetoid synkinesia.

Chauffard easily separates this case not only from athetosis, but from tabes, insular sclerosis, cerebral diplegias and chorea. But though there are several points of contact with Friedreich's ataxia it is difficult to get over the uncommon features. The other two cases (Londe and Lagrange) (72) are more like the ordinary type: Two sisters aged fifteen and sixteen; both took ill at six or seven. At first they were regarded as chorea. Absence of jerks, hollow-foot, marked inco-ordination, no nystagmus, internal strabismus in both; gait staggering; involuntary facial movement;

head continually moving in various directions; choreiform jerks in head and limbs; danse des tendons in standing; slight scoliosis. No sensory or sphincter troubles, no affection of pupils or fundi; mental dullness. Athetoid attitude exactly as in Chauffard's case.

It is curious that in no one of these three cases was nystagmus present; in the latter two the internal strabismus, the mental dullness, and the athetoid attitude confer a special family mark.

#### Deformities of extremities and spine:

Certain deformities affecting the feet and spine have been always regarded as characteristic of Friedreich's ataxia. To these must be added the affection of the hand shown in my first three cases. None of these conditions is essential; the talipes (equinus or equino-varus) was noted by Griffith in only twenty-seven cases out of a hundred and forty-three. In a number of instances besides these, there was dorsal flexion of all or some of the toes. The latter condition in itself might, as Besold suggests, be attributable to "Modernes Schuhwerk", unless commonly well marked. In Rüttimeyer's families Blattner and Kern, early prominence of the extensor propr. hallucis was regarded as a sign of very bad augury - it was one of the first symptoms (Ladame). Baskett's case (76), a girl thirteen and a half was treated at a hospital

for double talipes varus at the age of eight and a half. Her symptoms began when she was six, but usually deformity of the foot is of late occurrence. It is well marked in cases II and III, but not in the other two. In case I, however, there are indications in the high instep and occasional dorsi-flexion of the great toe, that the shape of her foot will become like that of her brother's and sister's. The general appearance in a marked case corresponds closely to pes cavus, "hollow claw foot". The claw position may or may not be assumed by the terminal phalanx of the great toe. In case II, (see photo) the right great toe is over-extended as regards both phalanges. This is so too in case III. In Plate X in Med. Annual for 1895, representing a case under the care of Mackay of Devizes, the great toes, like the others, have the second phalanges flexed, and this seems to have been the way in Ladame's patient.

Dreschfeld (50) describes a case which showed no talipes, but hyper-extension of great toes "resembling that seen in the early stages of peripheral neuritis".

Deformities of the hands have been rarely observed. Bramwell (25) gives a family of three showing main en griffe. Griffith (Amer. J. of Med. Sci. 1888 p.577) describes one of his own cases as having "grasp strong but claw-like," another as having claw-like hands, but he may be simply referring to the mode of prehension so common in Friedreich's ataxia.

In two of Rook's (7) cases, the hand was claw-like and one had wrist drop. One of Taylor's (55) cases had a little difficulty in extending the fingers.

In cases I, II and III, the attempt to extend fingers in line with the forearm, at once brings out a more or less pronounced main en griffe. (See photo of case II).

Let me recapitulate the description of the condition in this case: when the hand is lying passively, nothing wrong is noticed. When he is told to straighten his fingers, flexion is produced at the wrist, with some bending towards ulnar side. The near phalanges are over-extended in the four inner digits, more so in the fifth than the fourth, in the fourth than the third, and so on.

The middle phalanges are flexed and the terminals are nearly in line with these. In regard to these joints too, the deformity is more marked in the inner than in the outer digits. The fingers are separated a little from one another. The thumb is simply bent back. The more strongly patient tries to straighten the fingers, the more <sup>marked</sup> does the alteration in form become. The extensor com. dig.-tendons can be seen standing out on the back of the hand, and can be traced up the lower third of the forearm. The palmaris longus tendon too, stands out prominently. The fingers can be adducted and abducted, but to a much less degree than normal.

What is the mechanism of this condition? It has nothing to do with the proper flexors and extensors of the wrist, for when the hand is closed, movement may occur at the wrist in the normal four directions, - flexion, extension, ab- and adduction. It is not a paresis of the extensor com. digitorum: its tendons are inserted mainly into the near ends of the near phalanges, and Duchenne hence says they might be called extensors of the near phalanges. In our own case so far from there being any sign of their failure to act, the chief trouble would appear to be their over-action, (over-extension of proximal phalanges).

The cause is a paresis of the interossei, - not paralysis, though the condition seems to come nearer this the older the patient becomes, (compare condition in the three first cases).

The interossei flex the first phalanges, and extend the second and third, they also abduct and adduct the fingers. When they are weakened, and when the common extensor is thrown into action, the fingers assume the position above described. To keep the first phalanx in line with the metacarpals, antagonistic action of its extensor and flexor is needed. "When the interossei fail, the unopposed extensor causes an exaggerated extension of the near phalanges, and the extension of the middle and far phalanges does not only *not* occur, but they are on the contrary flexed in direct propor-

-tion to the degree of extension of the near phalanges".  
(Duchenne Syd. Soc. trans. p.265).

The flexion at the wrist may be thus explained; when the hand is extended, not only do the proper muscles of the wrist act together, but also the long extensors and flexors of the fingers. The combined effect of their synergic action is to place the metacarp in line with the forearm. If the interossei are weakened, and the near phalanges are over-extended, the balance is upset, the common extensor acts at a disadvantage as regards its extended action at the wrist and there is the appearance of a slight dropwrist. This can be imitated to some degree in a healthy limb.

The greater amount of distortion in the ring and ulnar fingers, corresponds to the condition in injury of ulnar nerve, and is accounted for in this case by the escape of the first two lumbricals, which are supplied by a branch of the median. That the whole terminal part of the ulnar is not affected is proved by the intact insensibility, among other points.

The simpler case here considered, leads to the consideration of the "Friedreich's foot", about which a good deal has been written. I believe it to be analogous to the condition just described, and that its formation can be referred to an

affection of the interossei of the foot, (including the short flexor and adductor of the great toe). There may also be a real weakening of the antero-lateral muscles of the leg; there is certainly some retraction of the calf muscles, and tightening of the tendo-Achillis.

Paretic condition of various muscles beside the interossei, is present in advanced cases. This is shown in the helplessness of cases II and III, especially as regards the whole of the lower extremities. The muscles that act on the spine may also be involved. In early cases, decided loss of power is usually absent.

Curvature of the spine is very common in Friedreich's ataxia. Soca, (quoted by Hallion (24) ), says it occurs in half the cases.

The photos of cases II and III, show the usual marked conditions. In the latter, the main convex curve is to the left, and is greatest about the ninth dorsal vertebra; in the former it is to the other side; it is both longer and more marked, and it is worst at the sixth or seventh dorsal vertebra. Perhaps the convexity to the left in the young woman, is associated causally with the greater weakness in her right arm from her acute illness. In the common lateral curvature of adolescents, the main dorsal convexity is usually an exaggeration of the natural curve to the right,

as in the brother (case II). In both there is kyphosis in the cervico-dorsal region, in the man this being so marked that the vertebral spines are nearly horizontal when he is sitting up. Observe how close the numbers on the spine appear to be, the effect of photographic distortion.

Hallion (24) has made a careful study of the spinal curvatures in nervous diseases, especially syringo-myelia, infantile paralysis, Friedreich's disease and locomotor ataxia. In all, the gray substance of the cord is affected in a different degree: in Friedreich's disease a pathological change is found in Clarke's columns, where some localize vaso-motor centres. Have we here, too, he asks, nervous lesions capable of causing an alteration of the bones, and specially of the vertebrae? He quotes Soca, to the effect that muscular weakness alone is sufficient to account for the condition. The want of tone may involve ligaments and bones too, as in the common scoliosis, but of this there is no proof. We do not require to postulate any marked paresis of the spinal muscles; adolescents who are subjects of the ordinary lateral curvature, are fairly muscular. A want of balance about the groups of muscles is more likely to start the scoliosis.

Remarks on the Condition of the Sensory System.

The sensibility of the skin is frequently quite normal as regards pain, touch, and temperature, but on the other hand, it is not uncommon to find a slight dulling. In cases I and IV, the condition is practically normal; in case III there is some delay in recognising touch in the lower extremities, but localization is correct. At one time there was absence of sensibility to touch on the dorsum of the left foot and the middle toes.

Case II shows slight diminution of acuteness in recognising touch in the legs, but pain is felt normally; in the upper extremities, sensibility to touch is normal. The curious thing about his condition is, that at one time, (1894 and earlier), there was decided anaesthesia to touch and pain below the level of the iliac crest, this being proved by the examination in the Infirmary (1884), and also by the fact that about the age of twenty, (1883) he burnt his foot by standing on a hot coal without feeling any pain.

It is interesting to compare this analgesia with the condition in the three cases recorded by Klippel and Durante (quoted in Londe's Thesis (61) ). These cases are amongst the most important selected by Marie, from which to build up his type hérédo-ataxie-cérébelleuse, but they are distinguished from the rest of this group, as well as from ordinary Friedreich's ataxics, by the disturbances of sensibility.

In Louis H. in 1892, tactile sensibility was abolished in legs and feet, much diminished in forearms and hands, and diminished in face: no plantar reflex; sensibility to heat recognised everywhere; retraction of field of vision. In 1894, Londe found analgesia in hands and legs; sensibility to touch present; sensibility to heat and cold weakened in the analgesic parts; retraction of field of vision hardly perceptible.

In François, sensibility to touch and cold, abolished below the knee in 1892; two years later no affection of sensibility.

In their sister, complete anaesthesia to all forms of sensibility of the internal aspect of the leg, in 1888; whereas a few years later, sensibility in her too, was normal. Londe gives various reasons for his opinion that these sensory disturbances were due to hysteria. Certainly one is justified in regarding the condition as functional, and it has to be remembered, that many of the symptoms in nervous diseases, which have a well marked organic foundation, are in all probability, purely functional.

One of Stintzing's cases (Munch. Med. Woch. no. 21, 1887) had complete anaesthesia in the lower extremities, and Senator's (35) second case felt on the feet, needle pricks and differences of temperature, only slightly or not at all.

Déjerine (4) describes a brother and sister who were

affected with marked sensory troubles of the extremities, diminishing towards the trunk; and also corresponding muscular atrophies: these he regards as true cases of Friedreich's ataxia, with very marked exaggeration of certain symptoms, sometimes met with in this disease, though only to a very slight degree. He refers them to lesions of the peripheral nerves, and sensory roots.

It is interesting to note, that Eisien Russell, by his recent experiments, (Trans. Phil. Soc) showed that anaesthesia and analgesia occur in the partially paralysed lower extremities, after removal of the cerebellum.

Subjective Sensations are also occasionally found; in case II these used to be, formication in the soles of the feet, and tingling sensations in the legs. Case I had for a short time pains in the back of the thighs.

Lightning pains occurred in one of Déjerine's cases, very much the same as in locomotor ataxia. Bramwell(13) reports a family group of three cases, all of whom suffered from lightning pains at one time or another, one from gastric crises and all from exaggerated sensibility. As he notes, one of Charot's showed lightning pains.

Other cases have involuntary spasms, associated with itching or other sensations. (Tresidder's).

Mental Condition.

A normal mental condition may still be looked upon as characteristic. Tresidder's (38) three cases showed remarkably high intelligence, one of them having taken an honours degree at Cambridge.

Ladame's (1) case had a very vigorous memory and intellect. Hector Mackenzie's (48) was bright and intelligent for his station in life.

My own cases are not affected mentally in the least degree. The expression of face is often intelligent, (as in case IV), and likely to mislead the observer. Cases that have normal mental power, may be easily excited to uncontrollable laughter, (Brock (41), Ladame, Bramwell).

Mental defect is noted in some cases. In one case, epileptic attacks and dementia (Hoffmann of Heidelberg (71) ); in another imbecility (Power, quoted by Gowers, St. Barts. Hosp. Reports 1882. p.505); in two sisters, marked mental defect (Londe and Lagrange (72) ); in one of Taylor's, (55) increased mental irritability, with pronounced feebleness of intellect; in the other, not related to the first, epileptic attacks; in Nolan's (63) three cases, congenital idiocy; in Vinaj's (89), mental degeneracy.

In some of these, however, the diagnosis is more <sup>than</sup> doubtful. In itself it would not be surprising, to find mental defect added to the usual symptoms; it would represent a

further stage of the neuropathic tendency.

An American professor, (Halbert (68) Hahnemann Hospl. Chicago) gives a report of two cases of inherited syphillis with spastic-paralytic symptoms, as cases of Friedreich's ataxia, and in regard to the elder, - eleven years of age, - makes the quaint observation that "his mental condition is not greatly impaired, except that it is infantile from the lack of development"

More will be found on this subject, under the heading of diagnosis.

### Reflexes.

The condition of the superficial reflexes in Friedreich's ataxia, may be regarded as normal.

In case II, plantar reflexes are well marked on the right, slightly on the left. The cremasteric and abdominal reflexes are well marked.

In case III, all are well marked, and the plantar exaggerated.

In cases I and IV, the superficial reflexes are normal.

In Berdez's (79) case, superficial reflexes were very lively.

In three of Besold's cases (54) they were normal, in the fourth, abdominal reflexes were absent.

Variations in degree of cutaneous reflexes are, of course, of constant occurrence in healthy persons, and the point under discussion is chiefly of importance as helping to distinguish Friedreich's ataxia from tabes. In the latter affection, the plantar reflexes especially, are often absent, this being due to the loss of cutaneous sensibility.

Much more important is the condition of the deep reflexes, of which the knee-jerk alone may be considered here, as it is easily tested, and its condition is typical of the state of the reflexes in the lower extremities.

In the four cases I have described, the knee-jerks are completely absent, and this is the case in the great majority of examples of Friedreich's ataxia.

Crozer Griffith (loc. cit.) in his analysis of a hundred and forty-three cases, describes the abolition of the knee reflexes, as very early and very constant. In ninety cases only, was their condition mentioned, and curiously enough, in as large a proportion as twenty-two of these they were present, in six being actually exaggerated. It is true that Griffith's statistics are compiled from an unsifted mass of cases, but one can certainly not go as far as Ladame, who holds that the abolition of patellar reflexes is an absolute rule in this disease, and that one would do right to mistrust the diagnosis of Friedreich's ataxia, whenever the knee reflexes are not lost, although all the other symptoms would

seem to confirm it. (Brain, Vol. 13. 1890. p. 492.)

When one comes across a typical family of Friedreich's ataxias, such as that described by Tresidder (38), and finds the knee-jerks completely absent in one, and present in the others, one is forced to the conclusion that this test is not infallible. Moreover it seems probable that the disappearance of the knee-jerks is, sometimes at least, not one of the earliest symptoms.

In Senator's (34 and 35) first case, these were found to be simply weakened, one year after the onset of the illness.

After the lapse of another period of eighteen months, the right was ~~soon~~ gone, the left could be obtained only by Jendrassik's method. A sister of this patient who had been ill for twenty years, had no patellar reflexes.

Brock's (41) second case, a man aged twenty seven, had knee-jerks, though they were absent in his ataxic brother and nephew.

Erb (9) and Mendel (10) both shewed undoubted cases in 1890 with tendon reflexes, Erb's being exaggerated.

In one of Mendel's the jerks were present in May, but absent in the following November.

Londe <sup>61</sup> (~~9~~) would class Erb's cases with Marie's hereditary cerebellar ataxia, simply on account of the exaggeration of the reflexes, though vision was normal and tabes present.

In the cases I have quoted, as in two of Bramwell's the presence of the jerks may not be sufficient to blur the picture of Friedreich's ataxia, but it is a different matter

When one finds, that, along with retention of knee-jerks, there are other important deviations from the type. Bouchaud (60) for instance, records a case which differs from Friedrich's ataxia, not only in retention of the jerks, but in the impaired mental condition, hallucinations, affection of vision, nature of gait, and too-pronounced nystagmus.

I might refer further to the cases reported by Wallace Anderson (36) Vinaj, (89) one of Nolan's (63) T.S. Wilson's (39) first and fourth, as examples that are open to the above criticism.

However, the pathological anatomy of the disease varies, as we shall see later on, to such a degree, that it is easy enough to suppose the knee reflexes might be free from interference in the minority of cases. Such cases might be comparatively free from sclerosis, in the lumbar portion of the cord.

Of the visceral disturbances, that ~~are~~ noted in cases <sup>II</sup> two and <sup>IV</sup> four, - viz. slow inception of the act of micturition, is not so very unfrequent (thirteen times in Griffith's analysis).

#### Order in which the symptoms appear.

This is not easy to fix, but usually the ataxia of the legs shows itself first. This seems to have been the way in all my cases; in case I, the speech was very soon involved, but so slightly that it would have remained unobserved, but for the brother's thorough knowledge of the symptoms that might

be expected.

In James' (40) and one of Brock's (41) cases, the spinal curvature seems to have been the first symptom noticed. Both cases were lads of eighteen. One of Besold's (54) shewed the ataxia first in the arms. In one of Mendel's (10), the ataxia of the arms was noticed in the thirteenth year (writing becoming worse and more illegible), while it was two years later before the gait was observed to be changed. Griffith in his analysis states that the lower extremities were first attacked in a hundred and fourteen, out of a hundred and forty-three cases, the ~~arms~~ legs in ten, and the arms and speech simultaneously with the legs, in eight.

#### Mode of Advance of Symptoms.

Some writers speak of the steady progress of the symptoms of the disease, and contrast this with the remissions of insular sclerosis. The mode of advance of the disease varies, however, to a great extent, in different cases, and one may often distinguish remissions, or at least periods in which the symptoms are quite stationary.

Case II showed slowly advancing symptoms till he was seventeen; then for two years there seems to have been a remission. At nineteen there was rapid deterioration; scoliosis and paralysis with unfitness for work developed. Then the disease passed into its present chronic and almost unchanging state.

In case III the periods are less distinct; for years there has been hardly any alteration, but at about the same age as

her brother, the extreme difficulty in walking developed rather rapidly.

The other cases (I and IV) show a steady advance, much more rapid in the latter case than the former. The age of nineteen or twenty will probably be critical in the history of case I.

#### Period of Onset.

The date of onset of Friedreich's ataxia is by no means easy to state. Friedreich himself, judging from his own cases considered that it was to be regarded as a disease of puberty. Most cases undoubtedly begin before this, the seventh and eighth years being most common (Gowers (88)) and it is rarely that one commences after sixteen. The onset is so gradual, unless precipitated by an acute illness, that it may be almost impossible to definitely mark it.

One of the latest cases seems to be Auscher's, - the woman being twenty-five when symptoms first appeared, but, as we shall see, the diagnosis of this case must be accepted with reserve.

Londe (Inèsè p.154) refers to two cases lectured on by Charcot in 1893, brothers, in whom the onset was at twenty-five and twenty-one respectively.

In my cases, the fourth took ill about the age of eleven, but the beginning was insidious.

Case 1 was seven when she had the illness which seems to

have been very soon followed by slight leg symptoms.

Case II had a prolonged illness, possibly hydrocephalus, between his third and sixth year; there was, however, a long interval of good health before the ataxia became noticeable at the age of twelve.

Case III, like her sister, took ill immediately after a severe illness, though in this patient it seems to have affected the brain. She was then fifteen years of age. The general statement holds good, that it is a disease of the developing period.

#### Diagnosis.

The diagnosis of Friedreich's ataxia seems to become more involved as time goes on, and cases accumulate. In typical family cases, such as the three first above recorded, there can be little difficulty if one is at all cognizant of the group of symptoms that are required to define the affection. But the symptoms are by no means few, and not infrequently some are wanting. Hence on the one hand there are close relationships with some other nervous disorders, and, on the other, more or less atypical cases occur, as to whose exact position there is disagreement amongst the highest authorities. And even in regard to some cases, where an autopsy has been made, and where very decided lesions have been found, there

are differences of opinion; the clinical symptoms may put a case into one category, and the pathological anatomy into another.

Senator (35) considers that Friedreich's disease is a clinical conception, which would exist without any anatomical substratum, just as the notion of diabetes mellitus is independent of anatomical ideas. The pathological anatomy of some forms of diffuse myelitis ("combined sclerosis") is very like that of some cases of Friedreich's disease, but the clinical appearances are so distinct that no one could confound them.

The following case, one would almost think, had been diagnosed as Friedreich's disease, after the post-mortem examination. It forms the basis of an elaborate paper by Tedeschi (85) entitled "Die Friedreich'sche Krankheit-kritische and pathologisch-anatomische Untersuchung."

The patient, an orphan boy, aged seventeen, was admitted into the asylum at Florence in May, 1893. Two cousins in an asylum with mania. First symptom, five years before, through a fright: tremor of right hand gradually involving arm, then left arm, next the legs. The tremor was like chorea. No pains; no remarkable affection of sight or hearing; no deformity. In asylum, increase of choreic movements, head involved.

Walking difficult through inco-ordination, like an advanced tabetic. Speech slow and distinct; irritable, quarrelsome; of limited intelligence; could hardly understand what was said. Died in February 1894, of tuberculosis.

One would like information about the knee-jerks, nystagmus, scoliosis, ataxia of upper extremities, and more about the sight and sensory system.

But even with the details given, - the mental affection, the uncommon onset, the asymmetry of onset, the absence of cerebellar type in the gait, - I would have no hesitation in saying one does not, from the description, get the clinical idea that is requisite for the diagnosis.

The autopsy showed, besides tuberculosis in various thoracic and abdominal organs, a degenerative process in the posterior ganglia, and posterior roots; marked sclerosis of the posterior columns and Lissauer's zones, (reminding one in extent and arrangement of the lesions in tabes dorsalis); marked atrophy of Clarke's columns and a slight change in the direct cerebellar tract in the cervical region. The cord was strikingly small, and there was chronic lepto-meningitis spinalis, specially posteriorly. The histological examination is most carefully described, but does not help the student of Friedreich's ataxia, if the above criticism is justified. This, like case IV, is a so called "isolated" case; that is, he is the only one of the family affected with the disease. We are thus deprived of one important element <sup>in diagnosis</sup>, namely the "family" character.

Isolated cases are found to be not uncommon, and a survey of a large number in the more recent literature makes it clear, that there are no outstanding characters which distinguish them from the true family cases occurring in collaterals. Divergences from the complete clinical type occur here and there, just as they do in the family form; and just as each family affected with Friedreich's disease shows its own special peculiarity, (Marie (26)) so one must make a certain allowance for individual differences in the isolated form. This much being granted, there is still room for the criticism that in some of the published cases the narrator has shewn a somewhat excessive desire to fit his irregularly shaped peg into the round hole of the "clinical picture". Take for instance the personally observed case given by Dana (17) in his Article on Friedreich's disease in Keetings Cyclopaedia of Children's Diseases.

A lad eighteen years old, got an injury to the back of his head five years ago. Soon he began to feel dull, heavy and drowsy, had pains about knees and ankles, severe pains in thighs, pains in lumbar region, constant and severe cephal<sup>l</sup>agia, formication in legs, back and shoulders. Stomach symptoms, vomiting occasionally, staggering gait, ankles unsteady. Felt as if ~~tongue~~ were tied back, consequently speech thick. Face became and remained flushed; much dizziness; persistent polyuria (180 -190 oz. daily. sg. 1005-1010 no sugar or albumen). Diplopia.

So much for the history.

Physical examination showed a vaso-motor paresis of face and hands; "drunken" gait; no choreic or tremulous movements, except that head oscillated to and fro when he stood; slight tendency to flat foot; no scoliosis; olecranon and patellar reflexes normal. Sometimes headaches, often vertigo; trunk ataxia; motor ataxia in using arms and legs; some nystagmus which disappeared. Intelligence good.

Whatever this case is, it is not a typical case of Friedreich's ataxia. The history gives unusually copious and varied abnormalities of sensation, and as the author himself says, the origin from a blow on the head, and the cerebellar ataxia are suggestive of tumour. The other symptoms all seem to point in the same direction (vomiting, polyuria, retention of knee-jerks, giddiness, etc.)

A case is reported by T. S. Wilson (39), (case III) as interesting from showing the symptom of glycosuria. The patient died at the age of ten, of diabetic coma, had been ill for five years, showed ataxia of gait, and slowness and hesitation in speech; a certain amount of clumsiness of hands; absence of knee-jerks; equino-varus; lateral curvature. There was no choreiform unsteadiness; no tremor on movement; great emaciation, (from the diabetes no doubt).

The case is certainly very interesting, and though the

details are meagre, I should be more inclined to class it with the peripheral neurites, than with Friedreich's ataxia. The sensibility was normal, but this may occur in a case of diabetic neuritis.

Case IV of the same physician, seems really to be what it was sent into the hospital as, - viz. St. Vitus' Dance. The unsteadiness became, in a fortnight from the onset, so marked that the least thing would knock him down. There was muscular weakness; lordosis; increased knee-jerks; spastic tendency; much improvement in hospital. Whole duration of illness to time of examination, only eight months.

Putting aside such cases as extremely doubtful, one finds considerable differences in those that remain.

Ladame's (1), M'Caw's (31), Baskett's (76), Mackenzie's (48), and Berdez' (79), (to name only a few) may be looked on as quite typical.

*My* Case IV shows the essential points, namely, onset in child-hood; first symptom (ataxia) in legs; progressive course involving legs and arms; affection of speech; swaying and choreiform jerks; absence of knee-jerks; Romberg's sign; nystagmoid movements; and amongst characteristic negative signs, absence of sensory defect; clearness of intellect; normal pupils; normal ocular fundi.

On the other hand there are some points of divergence. Though the disease is now far advanced, there is no clubfoot or extension of great toe and no marked scoliosis. Cases reported by Dreschfeld (50), D. Inglis (20), Besold (54), (cases III and IV) Zabłudowski (34), and many others quite undoubted, show no abnormality in this respect.

The hesitancy in beginning the act of micturition is not very uncommon, and is present in case II. The cramp, curiously enough, affects only the left leg. According to Griffith, spasmodic contraction of muscles occurred in twenty-one of his hundred and forty-three grouped cases, and was usually in the lower extremities.

Chorea is one of the diseases for which Friedreich's ataxia has several times been mistaken, (Ladame, Londe, and Lagrange, (72), Bramwell (12), (first case) one of Ormerod's (Med. Chir. Trans. Vol. LXVIII. p.149) etc.

It is to be distinguished by the slowly progressing character, the absence of knee-jerks, and the character of the involuntary movements. In marked cases of either disease there can be no difficulty. The tongue, for instance, in a choreic is jerked up and down, in and out, while in an ataxic it shows an irregular tremor with no rapid jerks.

The face is usually not affected in Friedreich's disease, though in cases I and II slightly marked exceptions may be noted.

Chorea does occur in families. "Though the proportion is not great, the family tendency in some cases is very marked". (Gower's).

"Huntingdon's chorea" is hereditary, begins in adult life, is accompanied by mental symptoms, and is always fatal.

Hereditary Cerebellar Ataxia.

It is by no means certain as yet, whether this is to be looked on as a definitely marked disease with independent pathology. So far it would appear that the symptoms may vary to an extraordinary extent, and the autopsies on which Marie (46) based his reasoning, amount to only two, amongst the sixteen cases that he reckoned up, as belonging to the new type.

Londe wrote a lengthy thesis on the subject, ("De l'hérod-ataxie cérébelleuse"), and added three new cases.

Marie recognises in all, the character of staggering and cerebellar inco-ordination, and connects this with the cerebellar atrophy found in the two autopsies; he is supported in this by the most recent observations on the function of the cerebellum.

Both Friedreich's disease and the new type are family diseases, the latter beginning more commonly in adult life, the former in child-hood. But as we have seen, Friedreich's disease may begin at twenty-five, and on the other hand, Fraser's patient (Glas. Med. J. 1880) showed signs in infancy.

This is one of the two cases of cerebellar hereditary ataxia in which an autopsy was made.

The various other points, when gone into, show a close parallelism in the two types. The symptoms of hereditary cerebellar ataxia may be summarised thus from Londe:-

1. Slow and gradual affection of legs, in standing or walking.
2. Usually in three years or so, uncertainty of hands and arms.
4. About the same time speech and vision involved. (In Londe's own cases, the eyes were not affected, if one excepts nystagmiform movements).
5. Reflexes remain or are increased. This is of course, very exceptional in Friedreich's disease.
6. Sometimes mental enfeeblement.
7. Death at advanced age, usually from intercurrent disease, frequently of the lung.

It is much easier to say that the cases collated by Marie and Londe, are not cases of Friedreich's ataxia, than it is to admit that they should be put together to form a homogeneous group. But the theory put forward by Marie is at least plausible, - that the same kind of degenerative process may be at work, involving the cerebellum only or mainly, in his cases, - the spinal cord in Friedreich's disease.

Relation of mental defect to Friedreich's ataxia.

In cerebellar hereditary ataxia mental enfeeblement is often present. This leads one to consider the question "What weight should be attached to this point in making a diagnosis of Friedreich's ataxia?"

The pure type of this affection involves no mental change unless occasional irritability and a tendency to uncontrollable laughter; even this is exceptional. In fact, if we exclude the nystagmus and the speech affection, in regard to the causation of which we are quite in the dark, we have no evidence of involvement of the cerebrum, one might almost say of the encephalon.

When the mind is affected, we may take it for granted, that the higher cerebral centres are diseased. We have seen that this condition is now and again present in cases that in other respects correspond to Friedreich's ataxia, but an examination of some cases recently reported, makes one disposed to think that they should be regarded, not as Friedreich's ataxics, but as transitional to other types, e.g. cerebral diplegia.

Amongst these I would reckon Nolan's (63) three cases of Friedreich's ataxia with congenital idiocy. These were a sister aged twenty-two, and two brothers aged fifteen and ten. Their mental condition was one of low intelligence; volition rarely manifested; memory defective; no delusions; speaking

only in answer to queries; anxious to please; good humoured; as a rule. All had nystagmus; internal strabismus; imperfect laboured articulation, many sounds not being uttered; ataxia in the arms and legs, with Romberg's sign.

The thyroid was enlarged in the two elder. "Universal partial analgesia," and "drop-ankle" were present in oldest and youngest, exaggerated and combined with ankle clonus in the other. No scoliosis or Friedreich's foot; a "suggestion" of main en griffe in two; no visceral disturbances, or ocular troubles other than those referable to the external muscles. The true jerky or choreoid movements do not seem to have been very marked. The disease was observed soon after birth.

There are indications here, of an extensive defect of development in the whole nervous system. The cases seem to be more closely allied to cerebral diplegia, than to Friedreich's ataxia.

Nearly related to these are the cases of a brother and sister, (Bouchaud (60)), who at the ages of six and seven, began to show mental enfeeblement, inco-ordination of the four extremities, and tabeto-cerebellar gait. No paralysis, nystagmus, or kypho-scoliosis. Speech slow but well articulated. The dementia steadily increased. Sight became lost; speech unintelligible; chewing and swallowing slow; rigidity of muscles increased, though knee-jerks were in one case absent, in the other diminished. The autopsy showed double sclerosis of lateral pyramidal tracts, diminution of sheathed

fibres in cortex, anterior and posterior columns healthy; ganglion cells of anterior and posterior horn diminished in number.

The same category ~~may be made~~ to include Vinaj's (89) family, about which he asks "Is this a hitherto unrecorded kind of case or a modification of Friedreich's ataxia?"

Father, mother and four children alive, second dead.  
Signs of nervous predisposition. *BirMs normal.*

(1) Eusebio, well till age of five, then difficulty in speaking and walking; intelligence affected, ending in idiocy; steady degeneration. When eleven, paralysis of legs; paresis of arms; physical degeneration; no control of bladder or bowel.

(2) Marietta, showed same symptoms at five; died of accident at nine; by that time had almost lost the power of speech.

(3) Iside, aged six; slight nystagmus; knee-jerks normal; gait uncertain; staggering; speech hesitating; scanning; memory weak.

(4) Egidio, aged five, large head; unequal pupils; nystagmus; hesitating speech, pronunciation like a child of three; normal jerks.

(5) Healthy child of fifteen months.

In these cases the evidence against a diagnosis of Friedreich's ataxia, consists in retention of knee-jerks, absence of talipes and scoliosis, and, most important of all, early and marked loss of intelligence. The family tendency, age of

onset, ataxia, affection of speech, nystagmus and preservation of sensibility bring it into relation with that disease.

The author rejects as diagnoses

- (1) Little's disease (origin; absence of special gait; absence of spastic rigidity; psychic phenomena).
- (2) Spastic tabes.
- (3) Primary progressive myopathy.
- (4) Chronic encephalitis; primary cerebral sclerosis of infancy, (time of onset; normal mode of birth; absence of convulsions; of contractures; of paresis or paralysis; the mental phenomena).

These cases are quite analogous to a number of others described by various authors, many of which are brought together by Higier (73) in his study of the rarer forms of paralysis of a hereditary and family character. After detailing four cases of his own in one family, he reviews the cases of "cerebral diplegia," reported by Sachs, Freud, Strümpell, Erb, Tooth, etc. The age of onset and the character of the affection are pretty constant in all, but each family has its distinctive characters. If one takes as the chief symptoms, onset in early childhood, spastic or flaccid paraplegia, idiocy, nystagmus, affection of speech and sight, one sees that Vinaj's and Nolan's cases are perhaps more nearly related to this group than to Friedreich's ataxia.

Higier's own cases are specially interesting in relation to the point now under discussion, from the fact that they

showed disturbances of co-ordination: weakness and awkwardness in upper extremities; intention-tremor; great difficulty in sewing, knitting, and writing; in lower extremities weakness and stiffness followed by spastic paresis in gait, in one spastic ataxia for a time. He draws attention to the "little known fact" that inco-ordination does now and then occur with increased tendon reflexes, quoting reports by Sachs, Haushalter, König, Dreschfeld. I may abridge the descriptions of Haushalter's cases: Parents near blood relations, father alcoholic. Four brothers and sisters, normal births. Two eldest affected, now eleven and ten years old. Symptoms first while at breast; rapid advance; inco-ordination of four extremities; fixed position of arms, hands and fingers; slight rigidity in extremities, more in tongue and face; choreiform jerks when at rest; increased knee-jerks; pes equinus; anomalies of speech; disturbances of swallowing; imbecility. Nystagmus only in eldest.

These cases differ from Friedreich's ataxia in the retention of knee-jerks, the imbecility, the rapid advance at an early age and some other minor points, but they are transition forms between this disease and cerebral diplegia.

Colling (75) reports a case quite allied to those transition forms:

A child, eleven years old, (whose brother died in his second year, defective mentally, and nystagmic), began to walk at end of first year. From third year gait stiffer, often falling; high myopia in fourth year; did not get on at school;

when seen at age of eleven, choreic movements of lower extremities; speech indistinct; old face; gait cerebellar ataxic, legs kept apart; ataxia of arms, especially left; increased knee-jerks; occasional ankle clonus; explosive ataxic speech; imbecile; sensibility and sphincters intact; no localized muscular atrophy; progressive paresis.

Here there is clearly a defective developmental condition of a nervous system in both cord and brain.

It is interesting to note how often in these cases which present a combination of the symptoms of Friedreich's ataxia with idiocy, the knee-jerks are retained. This tends to confirm the very high position of Westphal's sign as a diagnostic mark.

To the above list I might add the two cases of Londe and Lagrange (72) who showed imbecility with the exceptional athetoid attitude in walking, and Hoffmann's (71) case, where there were imbecility and epilepsy, a case he himself records as doubtful in regard to diagnosis.

One sees from this review that when the degenerative process has involved not only the spinal cord, but the higher cerebral functions, other symptoms besides simple imbecility or dementia, are almost invariably added to the symptoms of Friedreich's ataxia.

And in such cases there must be a doubt as to how far the cord changes, and symptoms are secondary to the cerebral affection, - a doubt which a post-mortem examination might not

clear away. Mental defect seems a much more important sign than the retention of the knee-jerk in making one doubt a diagnosis of Friedreich's ataxia.

#### Disseminated Sclerosis.

We pass now to consider the differentiation of Friedreich's ataxia from disseminated sclerosis. This disease is said never to occur in families, (Marie), but a difficulty may arise when <sup>one</sup> meets an isolated case of Friedreich's ataxia. A well marked case of insular sclerosis can present no difficulties: the intention tremor is coarse and jerky, much more so than in Friedreich's disease; the nystagmus is more pronounced; the course of the disease is liable to fluctuations in much greater degree; the tendon reflexes are exaggerated; ocular paralyses and affection of the optic nerve are frequent.

But the group of symptoms due to insular sclerosis varies much. The gait is at times cerebellar in type; knee-jerks are occasionally absent; scoliosis may be present; the speech may be similar to that in Friedreich's disease.

Brissaud (quoted in Londe's thesis) says it may be absolutely impossible to distinguish an isolated case of Hérédo-ataxie cérébelluse from a case of sclérose en plaques, and the following case may show the difficulty in diagnosing it from Friedreich's disease. Bouchaud (66) describes this one as "Maladie de Friedreich".

Boy aged eighteen, always rather delicate, fairly sharp at school. First symptoms at twelve, viz. awkwardness of

hands; tremor of upper extrimities; difficulty in walking. Apprenticed to saddler at fourteen but made no progress. On examination, asymmetry of face (left smaller); left arm and leg more awkward than right; intelligence much below normal; speech difficult to understand; does not speak much; no choreiform instability when at rest; static ataxia when trying to stand; inco-ordination; intention tremors; gait not tabetic, staggering, requires support; "tendency" to talipes equinus; exaggerated extension of great toe; knee-jerks both retained, left exaggerated; nystagmus marked; slight lateral curvature; acuteness of vision much diminished; hallucinations no evidence of loss of sensibility.

This case difers from Friedreich's disease, in quite a number of particulars, especially the mental condition, retention of knee-jerks, affection of Vision, gait, asymmetrical appearance of face, greater awkwardness on one side.

On all these points a diagnosis of disseminated sclerosis would be more adequate.

Ewart (11) gives a case of a female aged nineteen of "isolated" type. Symptoms began at sixteen. Menstruation first irregular, then ceased; slight affection of speech, only temporary, a year ago; knee-jerks exaggerated; slight tremor of hands on purposive movements; slight lateral nystagmus; marked ataxia of lower limbs; slight loss of sensation; functions of brain intact.

He thought disseminated sclerosis could be excluded by the insufficient degree of tremors and nystagmus and the normal cerebral condition. Friedreich's disease is however a doubtful diagnosis on account of the disappearance of speech affection, and the exaggeration of the jerks. These points would bring it nearer to disseminated sclerosis. An alternative diagnosis might be that of ataxic paraplegia (of Gowers). Friedreich's ataxia is regarded by Gowers as forming a transition between tabes and ataxic paraplegia.

Probably in a case like this, continued observation of the course would settle the question of diagnosis.

#### Locomotor ataxia.

The diagnosis from ordinary locomotor ataxia can present little difficulty. A comparative table of the symptoms is given in Ladame's paper. A difficulty comes up when cases of Friedreich's disease have to be distinguished from tabes commencing in childhood. In the latter there is usually a syphilitic heredity, but not in the former. In a summary of ten cases Hildebrandt of Berlin (27) found that six began before the tenth year, four before fourteenth. In some cases ataxia of extremities takes the leading place, lancinating pains in two, girdle sensation in four. Loss of patellar reflexes in all cases, eyes three times normal, nystagmus twice present, reflex paralysis of pupil twice, disturbances of sensibility in only half, disturbances of bladder six times. Moreover the speech often shows disturbances on

account of slight cerebral affection. Fortunately the symptoms are so grouped usually that there is not much difficulty in reaching a decision.

Again, tabes in the adult may take many forms. Auscher's (30) "case of Friedreich's ataxia" with autopsy presents several points of close correspondence to locomotor ataxia. The onset was not till the twenty-fifth year; there was mental degeneracy, and abolition of light reflex. The patient was a prostitute, and there were no other members of her family affected. She showed marked ataxia of limbs; choreiform movements of head and trunk; double **equino-varus**; loss of knee-jerks; nystagmus and affection of speech. Sensibility was retained, though in a case of marked mental defect it must be difficult to test it completely. Some lightning pains were present. The autopsy may be summarised thus:- meninges normal; cord much diminished in size, like that of a child seven years old; cerebrum and cerebellum much smaller than normal, but free from microscopic changes; posterior horns much atrophied in whole length, worst in dorsal region; atrophy of fibres of Clarke's columns, number of cells in them diminished; posterior columns sclerosed in whole length, worst in lower part, Goll's columns being more changed than Burdach's; only ~~in~~ a few medullated fibres; Lissauer's zone normal in lumbar and cervical portions, perhaps slightly degenerated in dorsal; posterior roots, and antero-lateral columns normal; motor nerves normal; sensory

nerves showed a great number of nonmedullated fibres, or fibres with an extremely thin sheath, perhaps embryonal.

The sclerosis showed what Dejerine had a few months before described as a pure gliosis, great abundance of fine neuroglial fibres arranged in whorls; absence of granule cells, no thickening of vessel walls or of septa connected with the pia mater.

From the clinical account as well as from the autopsy, one would prefer a diagnosis of ~~the~~ locomotor ataxia, with an ill developed brain, the congenital mental defect being possibly aggravated by a progressive paralysis, as Schultze suggests (58).

Criticism of a case like this is most desirable, for from it the following conclusions have been drawn:

- (1) Friedreich's disease may start as late as twenty-five.
- (2) Cerebellar defect may account for the clinical signs of Friedreich's ataxia (Senator).
- (3) Mental degeneracy, abolition of light reflex and other exceptional conditions may occur in Friedreich's disease.
- (4) The motor nerves may be normal, and the sensory show certain changes in Friedreich's disease (Leyden and Goldscheider).
- (5) A full confirmation of Dejerine's views on the peculiar character of the histology in Friedreich's disease.

In making such inferences from a single case, the doubtful

nature of the diagnosis must be borne in mind.

Disease of Cerebellum may cause symptoms like those in Friedreich's disease: reeling gait with a zig-zag character; difficulty in standing; nystagmus; loss of knee-jerk (usually not constant); but there is no tabetic character in the gait; the choreiform movements are probably absent; "the arms are usually steady, rarely they present some jerky inco-ordination" (Gowers), and in the case of tumour, pressure symptoms are generally present. Some cases of simple atrophy or hypoplasia of cerebellum have been described, but the symptoms are variable. In König's (65) case, there was congenital cerebral diparesis, but no affection of inco-ordination at all, although the hypoplasia was very well marked.

"Oppenheim has observed cases of cerebellar sclerosis and has had one anatomically investigated by Arndt. He regards cerebellar sclerosis as associated with a clinical picture composed of vertigo, cerebellar gait, ataxiform disturbances of movement, weakness of bladder, difficulty of articulation, and motor weakness of the extremities" (Leyden and Goldscheider p.597).

Although there is undoubtedly a general resemblance here, to cases of Friedreich's ataxia, there would probably not be much difficulty in distinguishing actual cases.

Cardossi (19) publishes a case of "a rudimentary form of Friedreich's disease", which he admits is by no means typical:

Guiseppe P. aged forty, has a son aged eighteen who has

had tremor in right hand from age thirteen . He himself began to have tremor in writing at ten. Right arm and body affected; never so bad as to prevent him from attending to his usual occupation; gait, tabeto-cerebellar; has had phthisis for the last ten years, not much advanced; oscillation of body when standing, brief, ~~rhythmical~~, not well marked; intention-tremor in upper limbs, as in disseminated sclerosis; slight tremors of tongue; speech slow and hesitating; no nystagmus; pupils normal; sensory system normal; knee-jerks much diminished; no paresis or paralysis; no deformities of feet.

The symptoms are of too mild a type and too few for Friedreich's disease of thirty years' duration, and they can be resolved into tremor, but apparently not that of chronic chorea, nor of paralysis agitans. Possibly a functional disorder allied to one or other of those.

In this discussion of Diagnosis, I have not attempted to set forth exhaustively, the differences between Friedreich's disease, and the various affections likely to give rise to difficulty.

My desire has been rather, by giving groups of cases from recent medical literature to bring out the close relationships that bind one type to another. From a text-book stand-point, this would be most confusing, but one cannot be too often reminded of the somewhat arbitrary character of the boundaries.

The more numerous the doubtful cases that are published the better, though unfortunately there is sometimes a tendency to magnify this symptom or minimise that, so as to get the case included in a favourite type.

Pathological Anatomy.

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The following are the more important records of post-mortem examinations in Friedreich's disease -

- Nos. 1-5. Friedreich and Schultze. (*Ref. in Ladame. (1)*)
6. Everett Smith. Boston Med. and Surg. J. 1885.  
Vol. CXIII.
7. Newton Pitt. Guy's Hosp. Rev. Vol. XLIV.
- 8-9. Rutimeyer Virch. Arch. Vol. CX.
10. Letulle and Vaquez. (3)
11. Blocq and Marinescu (5a).
12. Dejerine and Letulle (2 and 6).
13. Guizzetti (49).
14. Mirto (37).
15. Michell Clarke (57).
16. Burr (74).
17. Dana (77).

Autopsies by Menzel, Brousse, Kahler and Pick, Erlicki and Rybalkin, Rossi and Auscher are rejected from the list as dealing with cases that can hardly be reckoned examples of Friedreich's ataxia.

For adequate reasons see Ladame (1), Tedeschi (35), and Schultze (53).

Most of the cases that have been fully described have shown extensive system lesions. They have been summarized by Ladame<sup>m</sup> 1889, and more recently Tedeschi has given an analysis of fifteen up to 1896. The most common conditions are diminution in bulk of the cord, sclerosis of posterior columns, (especially Goll's) and degeneration of Clarke's columns. Next in frequency is the degeneration of the direct cerebellar tract, and the antero-lateral ascending tract of Gowers. The crossed pyramidal tract may be partially involved but it is thought that the true motor fibres are unaffected unless in very advanced cases. In one of Friedrich's cases the direct pyramidal tracts were involved. Apparent involvement of motor tracts is explained by the presence in them to a greater or less degree of neurones with other than motor functions. The "system" arrangement of fibres is in short not an absolute one. Occasionally changes in the spinal ganglia have been observed. The posterior roots have sometimes been found atrophied. Changes in form of the central canal and sometimes peri-ependymal sclerosis have been seen (Dejerine and Letulle).

Ladame's opinion that the zone of Lissauer (fine fibres at outer side of posterior column stretching from the apex of the posterior horn to periphery) always remains intact can no longer be supported. He looked on this as a distinction from tabes. But in several cases (Letulle and Vaquez, Blocq and

Marinescu, Guizzetti, Mirto) it has been found more or less extensively altered.

The degeneration of Clarke's column, especially of its ganglion cells, seems associated with the sclerosis of the direct cerebellar tract. The view that these cells are trophic centres for the tract fibres is thus confirmed. In early tabes, Clarke's columns are affected. There is an absence of the fine fibrous network, while the coarse fibres, the ganglion cells and the fibres of the direct cerebellar tract arising from them are unchanged. In advanced tabes Clarke's columns are almost entirely degenerated and then the cerebellar tracts are said to be sclerosed. (See Leyden and Goldscheider (87) p.509).

There appears to be no constant anatomical character which would allow one to say from examination of a section of the cord that one had to do with Friedreich's disease and not with tabes or a combined sclerosis. Dejerine and Letulle (216) have endeavoured to find a distinctive character in the nature of the sclerosis. Those authors believe that the sclerosis in the posterior columns<sup>is</sup> purely neuroglial, a gliosis, consisting of fibrillae intercrossed in different directions and forming whorls like those described by Chaslin in the brains of epileptics. Further the pial prolongations into these columns are unaltered and not more evident than in a healthy cord. In tabes on the other hand, there is thick-

-ening of the pia mater and the prolongations which start from them, thickening of the neuroglial tissue between the nerve tubes, very pronounced changes in the vessels etc. A vascular sclerosis such as this they found in the lateral columns in their cases.

To meet the possible objection that they are making an extensive generalisation from two cases, they point out that similar changes have been seen by several authors but they have not interpreted them in their true sense. They quote to this effect from the histological descriptions of Friedrich himself, Newton Pitt, Rüttimeyer, and Blocq and Marinescu. Auscher in his doubtful case showed a similar condition at the Société de Biologie, July 26, 1890 and Dejerine after examining his specimens pronounced them examples of pure neuroglial sclerosis.

Schultze of Bonn re-examined by recent methods the cord of a case observed and described by Friedrich and himself in 1881, and he failed to find any justification for the distinction in the nature of sclerosis thus defined by Dejerine and Letulle. The whorls of fibrils were not present. The vascular thickenings were found in the posterior columns especially between the columns of Burdach and Goll. He sums up his re-examination thus: No proper chronic meningitis. The degenerations are essentially a degeneration of the posterior roots and their connections in the posterior

columns and posterior horns, disease of Clarke's columns, of the cerebellar fibres, and the pyramidal tracts - this so far as concerns the spinal cord.

Michell Clarke (57) describes the autopsy on a patient aged fourteen, a typical case except that the knee-jerks were normal, and that during the last few weeks of life ~~she~~ showed symptoms of cerebral tumour (cerebral vomiting, intense headache, optic neuritis, coma etc.). A round celled sarcoma was found growing from the under surface of the right half of the cerebellum, pressing on the pons and medulla. Apart from this no change in cerebellum. In cord no naked eye change except diminution in size. "No complete degeneration in any section, but a partial change chiefly in posterior columns, next most marked in lateral columns, with involvement especially of the margin of the cord, with thickening in the pia mater and the walls of the vessels, and probably with some excess of the neuroglia."

A brother and sister were affected with the same disease. Had it not been for this, in view of the presence of a tumour in the cerebellum, one would have been apt to ask could this not have accounted for the symptoms. Certainly the symptoms were very severe at the end, and the tumour was apparently growing rapidly then, but it might have been taken on an active character after a long comparatively latent course. The family had a strongly neuropathic tendency,

and it is of course quite possible that two members of such a family should have Friedreich's disease and a third a cerebellar tumour without Friedreich's disease. Clarke himself states that the changes in the cord were by no means so marked as he was led to expect from the symptoms.

Dana's (77) autopsy is briefly recorded. It is accompanied by some photographs of cord-sections. In addition to smallness of cord, thickening of pia, sclerosis of posterior columns, sclerosis of lateral columns (crossed pyramidal and direct cerebellar tracts) and marginal sclerosis, he observed vacuolization in the gray and white matter all through.

There is no note of the condition of Clarke's columns or Lissauer's tracts, nor could the author say whether the sclerosis was really a gliosis.

Burr's (74) autopsy was on a case that was eighteen years ill. He found (1) marked degeneration of Goll's columns, slighter of Burdach's, from top of cervical to lower lumbar cord; (2) degeneration of lateral and anterior pyramidal tracts; (3) degeneration of direct cerebellar tracts. The sclerosis of lateral columns was not systematic; (4) posterior roots much degenerated, anterior intact; (5) slight affection of posterior horns with degeneration of ganglion cells, while in anterior horns only a very few cells were atrophied; (6) degeneration of cells in Clarke's columns; (7) walls of

vessels slightly thickened.

The following are the chief points in Guizzetti's (49) case who died of heart disease at the age of twenty-eight, after the nervous affection had lasted eighteen years:

Small size of posterior roots, spinal ganglia and cord.

(1) Lumbar region- sclerosis of posterior columns except a portion immediately behind posterior commissure and inner border of posterior horn and also Westphal's posterior limiting zone. Numerous degenerated fibres in pyramidal tracts. (2) Dorsal region - posterior columns, (with exception of part as in the lumbar region), pyramidal tracts (numerous fibres), Clarke's columns, and Lissauer's band all involved (3) Cervical region - Goll's columns as seriously involved as lower down, Burdach's less so, more healthy fibres in pyramidal tracts. Longitudinal fibres degenerated even into the nuclei of Goll's and Burdach's columns in the bulb, the horizontal fibres remaining unaffected. Some altered fibres even in anterior pyramids of bulb, contrary to usual condition.

Posterior horns atrophic. Microscopic condition like that described by Dejerine and Letulle.

In peripheral nerves, diminution of coarse nerve fibres and presence of numerous fine fibres.

Mirto's (37) case (death after five years duration of illness at age of nineteen) had systemic degeneration of

posterior columns (Goll's, Burdach's, and Lissauer's) of lateral cerebellar tracts, of Gowers' tracts; slight degeneration in crossed pyr. tracts disappearing in cervical region, advanced sclerosis of Clarke's columns; rarefaction of reticulum nervosum in anterior and posterior gray columns with partial cell-atrophy, partial degenerative neuritis in motor nerves, (sensory not examined) - spinal ganglia affected as regards both cells and reticulum.

The latter two abstracts are taken from Tedeschi's critical digest and I have not seen the clinical reports of these cases. But supposing them to be typical, nothing of much importance has been added to what was known in 1889 to Ladame, or indeed to Friedreich himself. The posterior roots and ganglia have shown marked changes, and in this respect and the coincident or consecutive affection of the posterior columns the similarity to tabes is obvious. In two cases (Guizzetti's and Mirto's) the principal nerves showed embryonic characters. In Mirto's the sensory were not examined but the motor nerves were affected. Auscher's doubtful case presented similar appearances in the sensory nerves.

#### Pathology.

Various theories have been suggested to establish some causal relationship between the anatomical basis and the clinical symptoms. The general assertion that in a case of

typical Friedreich's ataxia the symptoms are mainly spinal is one which has been widely though not universally accepted. As for the nystagmus, the affection of articulation, the giddiness and certain choreiform movements, though their origin is in all likelihood intracranial they have as yet no morbid anatomy.

The strongest critic of the spinal origin of most of the symptoms is Senator (34 and 35). He has maintained the view that the disease is essentially cerebellar, that in its most outstanding features it depends on an arrest of development of the cerebellum or of single physiologically important parts of it, and that it is only in a somewhat advanced stage that other symptoms appear, referable to super-added degenerations in cord and cerebrum. The cord changes may be concomitant or consecutive. In confirmation he quotes Marchi's conclusion from experiments: "Destruction of cerebellum entails degeneration of lateral portions of anterolateral columns, of anterior part of direct cerebellar tracts and of a certain number of fibres in pyramidal bundles". He says we know nothing of the symptoms associated with disease of Goll's columns alone, that a separate or simultaneous affection of Burdach's would give a clinical picture like that of tabes dorsalis, more so as certain other peculiar changes in tabes (affection of Clarke's columns, of Lissauer's zone, atrophy of posterior roots and degeneration of peri-

-pheral nerves) are not wanting in hereditary ataxia. Moreover by reference to the autopsies he finds that the condition of the cerebellum was not mentioned in eight out of the fifteen analysed. In three cases out of the other seven there was a recognised atrophy (Menzel's, Rossi's, Auscher's,) In three cases nothing wrong was seen microscopically, and in one nothing either with the naked eye or microscope. This is the weakest point about the theory - the want of anatomical evidence, and this objection has not been removed by later post-mortem examinations, though Clarke's case given above is interesting in this relation. As regards the three cases he quotes, we have seen how unusual in some important respects Auscher's case was; as for Menzel's is generally regarded as not a case of Friedreich's disease, and Rossi's also seems to deviate considerably from the classical type.

The small size of the spinal cord in Friedreich's disease seems to have struck all observers and Friedreich and Schultze first advanced the view that the columnar degenerations were secondary to an arrest of development in cord and medulla. Shrinking of the cord no doubt occurs subsequent to the degeneration as connective tissue takes up less bulk than the nerve tubes but it is questionable if this would account for all the difference; it would hardly explain why the cord is so much less in this disease than in other scleroses, even if the points emphasised by Schultze are allowed their full weight. This author speaks of the general atrophy of the

cord in tabes in the dorsal and lumbar regions as due to long disuse of the lower extremities. So in Friedreich's ataxia one would, he says, still more look for such atrophy, on account of the inactivity enforced in childhood and the longer duration of the disease than in the case of locomotor ataxia.

The theory of developmental error is supported by other facts - the presence of numerous fibres without sheaths in peripheral nerves (Guizzetti, Mirto), anomalous development of central canal of cord (Dejerine, who quotes similar observations by Ohamerod, Pitt, Everett Smith), condition of syringomyelia (Friedreich's fourth case, quoted by Schultze).

No adequate explanation has yet been given as to why the cord should be able to perform its functions for a series of years varying from two to twenty or more, and then show signs of inadequacy. The demands made on the spinal cord of a young lad are great enough to test its capabilities most thoroughly. In certain families and certain isolated cases, parts of the central nervous system seem to be badly constructed. They may be looked upon as unfit to bear a long strain, and their decay and death gradually come about. Not that the change is analogous to a senile change; at least the differences are so great as almost to hide any analogy that may be supposed to exist. If the process of

disease or decay has once been started, it is likely to be aggravated by the struggle for existence among the cells that is taking place constantly at all ages, and so actively in youth. The neuroglia rapidly increases and not only fills the space formed by shrinking of the nerve tubes but compresses and destroys healthy nerve tissues. (Roux and Weigert, quoted by Edinger).

Edinger (90) a few years ago brought forward his repair theory to explain the condition found in several nerve affections. In any exertion there is waste of nerve cell and nerve fibre, compensated in health by repair. If nutrition is defective through any cause, as a toxin (syphilis, diphtheria) or injury, or hereditary nervous weakness, repair will be insufficient and degeneration will be the result. Some of the cord tracts seem more easily acted on than others viz. the posterior columns, pyramidal tracts and less frequently the cerebellar tracts. A greater strain may be put on certain nerve lines than on others. Thus, taking up tabes, he would explain the involvement of the nerve apparatus connected with the erect posture, the anaesthesia of soles (pressure on soles), affection of muscle sense, of eyes, &c.

In Friedreich's ataxia he thinks the progress of the disease may be explained as the legs and arms are used more with the progress of years. There is some abnormal weakness either hereditary or precipitated by an acute disease.

The posterior and lateral tracts which are more used are the weaker. "But the pupil, bladder and cerebral functions are intact through the whole course of the illness. The theory will not explain everything. We are still in great ignorance about all the sensory functions which do not reach the consciousness. Only a few of the nerves in the posterior columns reach the brain. The direct cerebellar tract we know little about, and yet it is often affected in similar circumstances with the pyramidal tract and posterior column."

Dr. C. Macalister (Brit. Med. J. April 8, 1895) suggests that the tendency to degenerate in certain diseases such as pseudo hypertrophic paralysis may be due to the diminution in the functional activity of some gland whose secretion exercises a controlling influence over the nerve elements. Stawell<sup>(67)</sup> would extend the theory to cover cases of Friedreich's ataxia.

It will be evident that the above theories, however suggestive, do not by any means suffice to explain the whole disease in any large and general way. We are thrown back on explanations of this symptom or that, through the aid of other affections perhaps more thoroughly understood. Atrophy of muscles for instance as of the interossei, may be referred to degenerations of their trophic cells in the anterior horns.

Atrophies in this disease are not so extensive or frequent as to lead one to expect any very striking evidence of wasting of ganglion cells, but such wasting as has been discovered.

The ataxia seems to be different from that of tabes both clinically and pathologically. The cerebellar character may be referred if not to the cerebellum, at least to the tracts conveying impulses to the cerebellum. The direct cerebellar and the antero-lateral ascending tracts are longitudinal Commissures between successive spinal segments and some part of the brain (Foster, Physiol. par. 580). Or, the theory may be true that the posterior columns are the main tracts for conveying motor impulses downwards. (Inglis, Journ. of nerv. and ment. dis. Jan. 1892). Hughlings Jackson's view that cerebellar ataxia is due to weakness of the back muscles, and to the consequent attempt of the legs to correct the weakness of the back, is strengthened by such cases as those we have been considering. (For valuable discussion of this subject see paper by Ormerod Brit. Med. J. Vol. II 1894. p.1291).

But the ataxia is not only cerebellar; it is tabetic also. The muscle-sense to whose impairment the most widely accepted theory refers the ataxia of tabes is usually, though as we have seen not invariably, well preserved in Friedrich's disease.

With a pathology so alike as regards the posterior columns one is tempted to think, that whatever explanation is adequate for the ataxia and absence of jerks in tabes is likely to be sufficient pro tanto in the case of Friedrich's disease.

Therapeutics.

Almost all writers on this part of the subject speak in the most hopeless tone. However, Zabłudowski in his patient, a little girl of nine, obtained decided improvement by a four weeks' course of massage. The case was an isolated one, and was exceptional in some minor points; for instance, regurgitation of fluids through the nose occurred in swallowing, formerly solids also had been thus returned. The "cure" so improved her that she seldom fell, walked straight and could feed herself without letting the spoon drop. Massage increases the functional capacity not only of healthy muscles but of those whose activity is impaired by direct or indirect causes. The nerves are better nourished through the improved circulation. Nerves and muscles only partially diseased may take up the work of those that are further gone. To this one might add Weigert's conception of the mode of action of a stimulus. "Neither cell nor organ is directly strengthened by the stimulus; the apparent strengthening is due to the fact that in action portions are used up and replaced by new fresh portions, a substitution which in many cases occurs in excess." (Edinger (90) ). Improvement thus obtained can hardly be anything but temporary. Case IV had a month's massage in hospital but without benefit. It is clear however that rest is the worst thing possible for such cases; they should be encouraged to take exercise, and to go through such actions as will best bring their co-ordinating faculty into

use, Touching definite points, picking up small objects and placing them on marked spots, writing, walking without or with aid - these and other exercises employed in the mechano-therapeusis of tabes should be useful in Friedreich's ataxia.

Literature.

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1. Ladame. "Friedreich's Disease."

Brain, Vol. XIII. 1890. p.467. A critical digest with full bibliography to 1889.

2. Dejerine and Letulle.- Etudes sur la maladie de Friedreich; sclérose nervroglie pure des cordons postérieurs. La méd. moderne Vol. I. No. 17. 1890.

3. Letulle et Vaquez. Un cas de maladie de Friedreich avec autopsie. Comptes rend. de la Soc. de Biol. 1890. p. 21.

Dejerine. Sur une forme particulière de mal. de Friedreich avec atrophie musculaire et troubles de la sensibilité. La Méd. Mod. 1890. No 25. Two excellent cases with paralysis of hands and feet.

5. Auscher. Anatomie path. de la mal. de Friedreich. Gén. Médicale No. 32 July 30, 1890. (with remarks at the Societe de Biologie by Dejerine).

5a. Blocq and Marinescu. Sur l'anatomie pathologique de la maladie de Friedreich. Archives de neurologie p. 118 and p. 331. 1890. Case of a girl, ill from age of nine, died at nineteen.

6. Dejerine and Letulle. Sur la nature de la sclérose dans la mal. de Friedreich. Semaine med. Mar.12. 1890.
7. Rook. Four cases of Friedreich's disease. Journal of new/ and ment. dis. 1890. p.173 (claw-like hands in two). Autopsy on one by Dana, 1896. see below.
8. Brown C. H. of New York. Two cases, not related. Journal of new/ and ment. dis. 1890. (abstract in neurol. Centralblatt. 1892 p.209). Both cases exceptional, doubtful.
9. Erb. Two cases of Friedreich's ataxia. Deutsche med. Woch. No.46. 1890. Short account, retained knee-jerks.
10. Mendel. Friedreich's ataxia, two brothers and male cousin. Dent. Med. Woch. No.47. 1890.
11. Ewart, Lancet. Vol.I. p.991. 1891. Case of Friedreich's disease with increased knee-jerks
12. Bramwell. Atlas. Vol.I. 1891-2. p.28. One case of Friedreich's disease with essay on whole subject.
13. Bramwell. ditto. p.45. Three cases of Friedreich's ataxia

14. Bramwell. ditto. p.178. Notes of three new cases of Friedreich's ataxia.
15. Lyman. Juvenile or hereditary ataxia. Intern. Clinics 1891. (knee-jerks increased).
16. Baumel. Considérations cliniques sur la maladie de Friedreich. Nouv. mercredi. med. Vol.II. 1891. p.49.
17. Dana. Keating's cyclop. of Dis. of children Vol.IV. pp.716-725. 1891. Article with one doubtful case.
18. Friedenreich. Et tilfalde af hereditär ataxi. Friedreich's sygdom. Hosp. Tid. 1891. (abst<sup>nach</sup>in Neurol. Centralblatt 1892. p.211). One case, second in family, from birth, never steady on legs. Optic atrophy. Intelligence defective.
19. Destrée. Un cas de maladie de Friedreich. Journal de méd. de Bruxelles. Nov. 5. 1891. One case with fulgurant pains, strabismus, and slight left ptosis.
20. Inglis. Friedreich's ataxia, its relation to conducting paths in cord. J. of Nerv. and Ment. dis. Vol.XIX. 1892 p.50. an isolated case, no nystagmus.

21. Sanger Brown. Brain, 1892. pp.250-282. Twenty-one cases in five generations of a hereditary ataxia, not Friedreich's Cerebellar gait, increased jerks, visual troubles, affection of deglutition, late onset.
22. Bramwell. Atlas Vol.II. 1892. p.22. Two cases of Friedreich's disease in which the knee-jerks were not lost.
23. Bramwell, ditto. p.70. Three cases of Friedreich's disease with main en griffe.
24. Hallion, des deviations vertebrales neuropathiques. Nouv. inconog. de la Salpêtrière. 1892.
25. Leegaard. Friedreich's sygdom (hereditär ataxi). Norsk. mag. f. Lagevidensk. 1892. s.444 (Ref. neurol. centr. 1893. p.618).  
Three cases, acute onset with fever and pains in limbs, spastic symptoms with pains in limbs supervening on the ataxia.
26. Marie. Leçons sur les maladies de la moelle. 1892.
27. Hildebrandt. Über tabes dors. in den Kinder-jahren. Berlin 1892. (abstr. in neurol. centr.)

28. Geigel. Über Friedreich's hered. ataxie. Sitzungsber.  
d. Würzb. phys. med. Gesellsch. 1892. (Neurol. Centr. 1892  
p.50. Two cases.
29. Burgess. Brit. med. J. Apr. 9, 1892.  
Two cases of Friedreich's disease.
30. Auscher. Sur un cas de maladie de Friedreich avec  
autopsie. Arch. de phys. norm. et path. 1893. Apr. p.340  
(See also No.4, same case).
31. M'Caw. Notes of a case of Friedreich's disease in a girl  
eight years old. Lancet 1893. Vol.II. p.484.  
An isolated case.
32. Krause. Et tilfælde af Friedreich's sygdom. Hosp. tid.  
1893. 4R. I. 30.  
Isolated case, classic sympt. (Neurol. Centr.)
33. Chauffard. Maladie de Friedreich avec attitude athe-  
toides. Sém. Med. 1893. Vol.XIII. p.409.  
Isolated case, marked jerky movements on exertion.
34. Senator. Über hered. ataxie. Berl. kl. Woch. 1893.  
Vol.XXX. p.489.

35. Senator. Second article. Berl. Klin. Woch. 1894.  
Vol. XXXI. No. 28.

Two cases in one family in those two papers.

36. Anderson, Wallace. Friedreich's ataxia. Glas. Med. J.  
1893. Vol. XL. No. 3.

Two cases, retained knee-jerks, mental impairment, slight  
athetosis.

37. Mirto. Atassia di Friedreich e atassia volgari. Giorn  
del ass. dei medici e naturalisti. Anno IV. Puntati  
3 e 4. 1893.

38. Tressader. Three cases of hereditary ataxia. Lancet  
1893. Vol. II. p. 304.

39. Wilson. Notes on Friedreich's disease. Birm. Med. Rev.  
1893. Vol. XXXI. Oct.

Four cases, two isolated, all somewhat typical.

40. James. Lecture on a case of Friedreich's ataxia.  
Edin. Med. J. 1893. Vol. XXXIV. p. 521.

An isolated case; spinal curvature first symptom.

41. Brock. Three cases of Friedreich's ataxia. Lancet 1893.  
Vol. I. p. 139.

42. Fry. Two cases of Friedreich's ataxia. Med. Fortnightly  
St. Louis, 1893. Dec. 15.  
Typical, sisters.
43. Benthall. A case of Friedreich's ataxia. Brit. Med. J.  
1893. Vol.I. p.1163.
44. Lunz. Ein Fall von Friedreich'scher Krankheit.  
Deut. Med. Woch. 1893. Aug. 17.  
A typical case with no nystagmus.
45. Rauzier. De la maladie de Friedreich, Nouv. Montpellier  
medical Vol.II. 1893. pp.725-748.
46. Marie. Sur l'héredo-ataxie cérébelleuse. Sémin. Med.  
1893. No.56.
47. Brissaud et Londe. Rev. neurol. 1894.  
One case of hereditary cerebellar ataxia.
48. Mackenzie H. W. G. A case of non-hereditary Friedreich's  
disease. Amer. J. of med. Sci. 1894. Vol.CVII. p.371.
49. Guizzetti. Contributo illa anatomia patologica della  
malattia di Friedreich. Il poliglino, 1894. p.433.

50. Dreschfeld. Lancet 1894. Vol. I. p. 1014.  
A short account of two isolated cases.
51. Nammack. Archiv. of pediater. New York. 1894. Vol. XI.  
p. 336.  
An isolated case.
52. Mackay. The isolated type of **Friedreich's** disease.  
Amer. J. of med. Sci. 1894. Vol. CVIII. p. 151.
53. Schultze. Fr. "über die **Fried. Krank.** und ähnliche  
Krankheits formen. Deut. Zeitschr. für Nervenhe. 1894 Vol.V.  
Heft 1-3, pp. 27 and 104.  
A criticism of Senator's case (No. 51 above), a re-examination of the cord of one of **Friedreich's** cases, with criticism of Dejerine and Letulle's observations, and a description of three new cases, which he calls a variety of **Friedreich's** disease (ähnlich).
54. Besold. Klinische Beiträge zur Kenntniss der **Friedreich-**  
schen **Krankheit.** Deut. Zeit. für Nerv. 1894. Vol.V. p.157.  
Four isolated cases.

55. Taylor, James. Pract. 1894. Nov.  
Two cases, one with marked family tendency; the other, isolated, with slight mental degeneration, and retained, though weak, knee-jerks.
56. Krafft-Ebing. Über Fried. Krankheit. Allg. Wiener Med. Z. 1894. No. 14.  
One case.
57. Michell Clarke. Case of Friedreich's disease with necropsy. Brit. Med. J. 1894. Dec. 8.
58. Schultze. Erwiderung auf den zweiten Artikel von Senator Berl. kl. Woch. 1894. No. 33.
59. Tirasek. Česopis lékařů českých. Praze. 1894  
One case of Friedreich's disease in a family with frequent inter-marriages.
60. Bouchaud. Rev. neurologique 1894. No. I. (Ref. Higier's article).  
Two cases allied to diplegia and Friedreich's disease.
61. Londe. De l'héredo-ataxie cérébelluse. Thèse de Paris 1895.

62. Guthrie. Case of early Friedreich's ataxia. Brit. Med. J. 1895. Vol. I. p. 813. (Also in Trans. Med. Soc. Lond. 1894-5. XVIII. p. 382).

A boy of nine; no family predisposition, no nystagmus, or speech defect.

63. Nolan. Three cases of Friedreich's ataxia, associated with genitous idiocy. Dublin J. of Med. Sci. 1895. XCIX. p. 369.

64. Small S. J. Friedreich's ataxia with cases. Med. Rec. New York. 1895. XLVIII. p. 85.

Four advanced typical cases in a family with strong neuropathic tendency. Onset at thirteen or fourteen.

65. König. Cerebrale diplegia der Kinder, Friedreich'sche Krankheit und multiple Sclerose. Berl. Klin. Woch. 1895. XXXII. p. 716.

A case like Friedreich's ataxia and disseminated sclerosis in some respects; also another case of hypoplasia of cerebellum and cord without inco-ordination.

66. Bouchaud. Maladie de Friedreich. Amblyopie. Persistence du reflexe rotulien. Jour. d. Sci. Med. de Lille. 1895. No.14. p.1313.

The parents were first cousins. An isolated case.

67. Stawell, R. K. Two cases of Friedreich's disease. Austral. Med. J. 1895. N. S. XVII. p.45.

Brothers, typical cases.

<sup>68</sup> Halbert. "Two cases of Friedreich's ataxia." Clinique, Chicago. 1895. No.XVI. p.636. Congenital syphilis, imbecility, spastic symptoms. Not examples of Friedreich's disease.

69. Cardosi, S. Contributo alla forme rudimentale del morbo di Friedreich. Gazz. d. osp. Milano. 1895. No.XVI. p.158.

70. Verhoogen. Journ. de Med., de chir. et de pharm. Bruxelles. 1895. Jan. 19, and Mar. 9. Two typical cases of Friedreich's disease.

71. Hoffmann. Münch. Med. Woch. 1895. Feb. 19.

Two cases, one typically Friedreich's disease, the other doubtful. Epilepsy and mental weakness in this. Both isolated.

72. Londe et Lagrange. *Annales de Méd. Paris.* 1895. Mar.7.  
Two cases of Friedreich's ataxia, sisters, athetoid  
attitude in walking, mental defect.
73. Collins. *New York Med. Rec.* 1895. Dec.21. A contribu-  
tion to the study of hereditary cerebellar and hereditary  
spinal ataxia, with the history of an atypical case of the  
first named disease. (*Ref. Neur. Centr.* 1896. p.372.
74. Burr. A contribution to the pathology of Friedreich's  
ataxia. *Univ. Med. Mag. Philad.* (neurolog. centr. 1895p.376
75. Mackenzie, H. W. G. Friedreich's disease. Article in  
*Med. Annual.* 1895. A short but valuable descriptive  
account with a list of references.
76. Baskett. A case of Friedreich's disease. *Brit. Med. J.*  
1896. Vol.II. p.749.  
No family affection.
77. Dana, C. L. A case of Friedreich's ataxia with autopsy.  
*Post-graduate.* New York. 1896. Vol.XI. p.328.
78. Higier. Über die Seltene Formen d. hered. u. fam. Hirn-  
und Rückenmarkskrankheiten. *Zeitschr. f Nervenheilkunde.*  
1896. Vol.IX. pp.1-61.

79. Berdez. Un cas isolé de mal. de Friedreich. Rev. Med. de la Suisse rom. Genève. 1896. Vol.XVI. p.304.
80. Fry, F. R. Additional cases of Friedreich's ataxia. Med. Rev. St. Louis. 1869. Vol.XXXIV. p.19.  
One isolated case; the <sup>two</sup> others sisters; of these one is very doubtful, the main feature being post-diphtheritic paralysis.
81. Ormerod. On Friedreich's ataxia. Clin. Journ. Lond. 1896-7. Vol.VIII. p.118.
82. Riggs, C. E. Two cases of Friedreich's ataxia. North-western Lancet, St. Paul. 1896. Vol.XVI.p.264.  
Cases not in same family, description very brief; one probably not correctly diagnosed (spastic gait, ankle and rectus clonus but no knee-jerks )
83. Rosenbaum. Friedreich'sche Krankheit. Deut. Med. Woch. 1896. Vol.XXII. p.433.  
Two cases of typical form, sisters.
84. Zabudowski. Ein Fall von Friedreich'scher Krankheit. Behandlung durch Massage. Berl. Kl. Woch. 1896. p.757.

85. Tedeschi. Die Friedreich'sche Krankheit, kritische und path-anat. Untersuchungen. Beitrage Z. path. anat. etc.  
Jena. 1896. Vol. XX. pp. 51-84.  
A useful summary of autopses. A careful pathological account of the case criticised above, and a bibliography.
86. Magnus-Levy. Deut. Med. Woch. 1896. No. 28. Ver. Beil. No. 19.  
Isolated case, doubtful. Details scanty.
87. Leyden und Goldscheider. Erkrankungen des Rückenmarkes. Wien. 1895-6.
88. Gowers. Diseases of the nerves and spinal cord. London 1892.
89. Vinaj. Malattia di Friedreich? Osservazione clinica. Estratto dalla Gazzetta Medica di Torino. No. 51 1894.
90. Edinger. Eine neue Theorie über die Ursachen einiger Nervenkrankheiten, insbesondere der Neuritis, und der Tabes. Samml. Klin. Vortr. No. 106.



Photograph 1. Case II. Hugh K. A.  
altitude shows general helplessness. He is  
partly supported by man behind curtain.



Photograph 2. Case II. Hugh McCall.  
Showing man en piffo + kyphosis.



Photograph 3. Case II. Hugh W. A.  
Showing Kypho-scoliosis.



Photograph 4. Case III. Mary M.A.  
showing wasting of legs, and foot deformity.



Photograph 5. Case III. Mary M'G.  
showing deformity of hands on extension.



Photograph 6. Case III. Mary M.A.  
showing foot deformity.



Photograph 7. Case III Mary M.A.  
showing scoliosis.



Photograph 8. Case IV - William M.

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## Original Articles.

### A CONTRIBUTION TO THE STUDY OF HEREDITARY CEREBELLAR AND HEREDITARY SPINAL ATAXIA, WITH THE HISTORY OF AN ATYPICAL CASE OF THE FIRST-NAMED DISEASE.

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DURING the past few years there have appeared many contributions to the literature of that constantly increasing class, the family and hereditary diseases of the nervous system. A class that now includes Friedreich's disease, Thomsen's disease, hereditary chorea, the various forms of familiar and hereditary spinal, myopathic, and neurotic muscular atrophy, hereditary spastic spinal paralysis and diplegias, a form of progressive bulbar palsy, diabetes mellitus, and perhaps other diseases. None of these contributions are of greater interest than those which have been grouped under the caption of hereditary cerebellar ataxia. Like a number of other diseases that have recently been raised to a separate entity, examples of this family disease, hereditary cerebellar ataxia, have been seen from time to time in the past, but they have been looked upon as non-conforming or atypical cases of hereditary spinal ataxia or Friedreich's disease, and as such have not been subjected to the careful scrutiny and examination which they deserved.

The first cases carefully observed were by Fraser, who recorded them in the *Glasgow Medical Journal*, page 90, 1880. On one of his cases a careful autopsy was made by the renowned pathologist, Joseph Coates. Fraser's cases are now considered among the fundamental observations of the disease.

It was Nonne's<sup>1</sup> great merit, that he, finding himself in the presence of three such cases, all of the same family, recognized the necessity of separating it from hereditary spinal ataxia, not only because of radical points of difference in its symptomatology, but of variance in time of development and in the mode of its occurrence. An autopsy of one of his cases showed that this autonomy was established by the pathological findings, which differed materially from those constantly found in cases of Friedreich's disease. A year later a paper by Sanger Brown,<sup>2</sup> containing a large number of observations of family ataxia, included a report of no less than six cases of this disease. To this paper of Brown were appended valuable remarks by Ormerod, of London, and Bernhardt, of Berlin. A point of great value in these commentaries was the emphasis both writers laid on the necessity of considering many of Brown's observations as cases entirely apart from Friedreich's disease. Since that time reports of cases have been made by Klippel and Durante,<sup>3</sup> by Brissaud and Londe<sup>4</sup> and by Londe<sup>5</sup> in which the symptomatology

has been so definite as to lead observers to place these cases unreservedly in the category of hereditary cerebellar ataxia.

In addition to these a number of cases have been reported which will be mentioned farther on in this article, in which the symptoms were intermediary between hereditary spinal and hereditary cerebellar ataxia, or which included symptoms outside of these two diseases. These latter cases furnish great opportunity for study, reflection, and investigation.

Two years after the publication of Nonne's paper, Marie, in discussing the former's cases in connection with the interesting series of cases reported by Sanger Brown, and the cases of Fraser, and of Klippel and Durante, suggested the name hereditary cerebellar ataxia in contra-distinction to hereditary ataxia, which is the name universally given to the disease first described by Friedreich<sup>1</sup> in 1863. A name which is associated anatomically and historically with lesion in the spinal cord. And this for two reasons: in the first place, because the constant attending lesions of this disease are spinal, and secondly, because Friedreich described, and for a long time considered, these cases as anomalous forms of tabes or locomotor ataxia. And although the anatomical investigations of Schultze,<sup>2</sup> Kahler and Pick, and others soon attested the incorrectness of Friedreich's view, they at the same time put the disease on a firm anatomical basis.

The name hereditary cerebellar ataxia, its sponsor considered, would not only indicate the important clinical manifestation, the ataxia, but would impress the kind of ataxia, viz., cerebellar, while it would also suggest the *sine qua non* of its genesis: heredity. Furthermore, it was suggested by the fact that in the cases of this disease that had come to autopsy the most manifest lesion was in the cerebellum. Although Marie's designation is a satisfactory one thus far, it should not necessarily be considered a permanent one, as there have already appeared observations to show that a strikingly similar condition (if not quite the same) may develop without any hereditary antecedents or consequences.

These cases will be referred to later. In fact it is probable that heredity, in the proper and literal interpretation of the term, is not an absolutely necessary antecedent. If it be granted that the case reported herewith is an example of this disease (an atypical example), the occurrence of the disease without defective heritage must likewise be admitted. That is, no such or analogous condition existed in the immediate antecedents extending back as far as the grandparents. That it is a family disease, however, is indicated by the occurrence of it in all the children of the family, viz., two.

It does not seem necessary to dwell on the distinction between familiar and hereditary diseases. That a disease may occur in a family without being in the strict sense hereditary, must be conceded. It is believed to have been proven that the germ plasm may be defective in its primary constituent, or during its development, without the source of its origin being diseased.

The name hereditary cerebellar ataxia is applied, therefore, to a class of diseases in which heredity is the

<sup>1</sup> Archiv. f. Psychiat. u. Nervenheilk., 1891, vol. xxii., p. 283

<sup>2</sup> Brain, Part lviii., 1892.

<sup>3</sup> Rev. de Méd., October, 1892, p. 745.

<sup>4</sup> Rev. Neurologique, 1894.

<sup>5</sup> Ibid., October 1, 1894.

<sup>1</sup> Virchow's Archiv, vol. xxvi., p. 408.

<sup>2</sup> Ibid., vol. lxviii., 1887.

genetic factor, ataxia the clinical, and the cerebellum the seat of the most important pathological change. The name is the same as that given to Friedreich's disease (hereditary ataxia) with the interposition of the word cerebellar. The latter, indeed, may be called hereditary spinal ataxia, the former hereditary cerebellar ataxia, while those cases which conform to neither type, the cases described by Nonne as transition forms, and with which the cases of Menzel, Erb, and my own may be reckoned, may be considered as cerebello-spinal hereditary ataxia, or hereditary cerebro-spinal ataxia. The latter name especially when psychical and other symptoms pointing to cerebral defect are prominent.

It is more than probable that such cases will be found to exist and Nonne's recent contribution,<sup>1</sup> in which he describes six cases, would seem to point in this direction. Hereditary cerebellar ataxia differs from hereditary spinal ataxia not only in its symptomatology, but in its etiology and course. The former seems to develop in the period extending from late youth up to maturity, although it may develop in earliest infancy.<sup>2</sup> In this it differs very materially from the spinal form in which the great majority of the cases develop during the cycle between childhood and adolescence. That the former may develop in infancy is shown by Fraser's cases, in which the disease began in the third or fourth year. As Fraser's cases were the first on record and with autopsy, this fact is important. So far as any conclusions may be drawn from the small number of cases published, it would seem that the former had been observed oftener in males than in females, the proportion being relatively similar to that of hereditary spinal ataxia. This is in keeping with a fact which is generally conceded, that in all of the family and hereditary diseases of the nervous system males are more frequently affected than the opposite sex. As in hereditary spinal ataxia the familiar or hereditary element is all that we can find bearing on the occurrence of the disease.

Like in a great many other protal or teratological diseases, an antecedent or coincident history of tubercle may be discovered in the family. This can have no other significance than a general one, viz., the prevalence of this infectious disease and the greater vulnerability of those handicapped by inheritancy or by acquisition. The fact that a tubercular history has been found relatively more frequently in the antecedents of hereditary cerebellar ataxia than in hereditary spinal, is in keeping with the universal knowledge that tuberculosis is much more common during the epoch when the former occurs than it is with the latter.

Factors which may be considered incidental have been remarked by some reporters, such as psychical trauma (Nonne), the occurrence of infectious disease (Londe, Marie), etc. Naturally, such conditions may precipitate or aggravate incipient symptoms so as to render those previously unnoticed quite perceptible.

In none of the cases reported thus far has parental syphilis played any part. The entailment of neurotic inebriety has, however, been noticed as it has in hereditary spinal ataxia.

The etiology of hereditary spinal ataxia is practically similar to this, with the exception that direct inheritance has been traced only in a few instances, while the familiar occurrence of the disease is rarely, if ever, absent. Moreover, it is supposed by many to be not only familiar, but congenital. Nevertheless, Friedreich himself, and recently Schultze,<sup>3</sup> have stated that the familiar character may be absent.

The difference in the symptomatology of the two diseases is set forth in the following parallel columns:

#### HEREDITARY CEREBELLAR ATAXIA.

1. Gait: Uncertain, reeling; gait of one inebriated. Patient frequently walks with body bent forward and the head thrown backward, and the feet wide apart.

Does not have to watch the feet. Feet wide apart.

2. Station: Romberg symptom absent.

3. Titubation and inco-ordination and loss of dexterity in the upper extremities. Choreiform movements exaggerated on voluntary effort; "intentional."

4. Not infrequently oscillations or jerky movements of the head, less often of the trunk.

5. Exaggerated contraction of the mimetic muscles on speaking.

6. Ataxia is very much less, or disappears when the patient is lying, but the inco-ordination persists.

7. Speech: Hesitating, abrupt, explosive, ataxic, defective.

8. Eyes: Twitching of the eyeballs very common, but not nystagmus. Optic atrophy, progressive choroiditis, paralysis or paresis of the external recti sometimes.

9. Myotatic irritability increased; reflexes exaggerated, such as knee-jerks; often ankle clonus.

10. Mental shortcomings varying from slight psychical disturbances up to a considerable degree of dementia.

11. Deformities of the extremities and spine, such as pied bot or scoliosis, do not occur or are most rare.

#### HEREDITARY SPINAL ATAXIA.

1. Gradual impairment of co-ordination, first in legs, afterward in arms. Later in the disease the patient may reel as if under the influence of alcohol.

A quick backward and forward balancing movement.

2. Station: Closure of eyes, as a rule, increases the unsteadiness; this may be absent.

3. Titubation of upper extremities very uncommon. Irregularity in voluntary movements of arms and fingers.

4. Frequently jerky, irregular movements of head and neck. Sometimes like an irregular tremor.

5. Mimetic muscles do not show ordinarily over-contraction.

6. Ataxia is not so great when the patient is lying.

7. Affection of speech may be absent; when it does occur is a late symptom, and consists of an eliding of syllables and an occasional hesitation.

8. Nystagmus is a very common symptom, but it may be lacking.

9. Myotatic irritability is lost. Knee-jerks may be present in the beginning of the disease, but they soon disappear. Ankle clonus is never present.

10. Mentally, normal. Very rarely any defect.

11. Deformities of the extremities, such as pied bot and spinal curvature, very common.

These are the principal symptoms of these two familiar diseases. There are additional symptoms, but they do not occur with sufficient regularity to justify considering them a part of the clinical picture. It will be seen that, even in parallel columns, the symptomatology of the two diseases does not appear to be so radically different. This will convey some idea of how similar some of the cases seem in reality. They are both family and progressive diseases. There is practically the same titubation in the gait, the same instability, and the same loss of co-ordination and choreic movements of the hands, and perhaps, also, of the face. The appearance of the face both when in repose and on speaking furnished a minor point of difference: in hereditary cerebellar ataxia there is a look of astonishment habitual to the features, and over-action of the mimetic muscles when the patient speaks or betrays emotion. This has not been considered a phenomenon of Friedreich's disease.

It is in the condition of the deep reflexes that these two diseases differ materially. In the former they are always present and frequently exaggerated; in the latter they are often absent, at least after the disease is developed, and no typical case has been recorded in which they were found increased. The presence of even the slightest clonus of the foot indicates a spastic condition to which the anatomical conditions existing in Friedreich's disease are inimical. To show the great importance that is attached to the state of the tendon reflexes as a diagnostic factor, it may be permitted to quote from Brissaud, who, lecturing on a patient with hereditary cerebellar ataxia (in whom there

<sup>1</sup> Archiv. f. Psychiat., etc., vol. xxvii., part 2, p. 479.

<sup>2</sup> Besold: Zeitschr. f. Nervenheilk., vol. v., pp. 2 and 3.

<sup>3</sup> Zeitschr. f. Nervenheilk., vol. v., parts 1 and 2.

were no visual troubles and the presence of scoliosis), said, "En somme, si j'ai éliminé la Maladie de Friedreich, c'est pour la seule raison que les reflexes rotuliers sont exagérés."

The remaining symptomatology in which they differ materially are the ocular and the mental conditions. Whereas such ocular symptoms as diplopia, dischromatopsia, achromatopsia, contraction of the visual field, and loss of light and accommodative reaction, all pointing to optic nerve lesion, have been found in several cases of hereditary cerebellar ataxia, these are most uncommon manifestations in hereditary spinal ataxia. In fact, it must be said that, whereas cases of the latter disease have been reported in which there has been diplopia and loss of light reflex, optic atrophy never occurs.

Cases of hereditary cerebellar ataxia in which there has been no real involvement of the optic nerve have been reported, so that, although it constitutes a very important line of demarcation between cerebellar and spinal ataxia, its absence should not convey the non-existence of the former disease. Marie, and following him Brissaud,<sup>1</sup> have both laid undue stress on the eye-symptoms in hereditary cerebellar ataxia, the former going so far as to say that if the eye-symptoms are lacking the diagnosis cannot be made with certainty.

Londe, whose monograph on the subject aims to encompass all that has been written on the subject of hereditary cerebellar ataxia up to the date of its publication, emphasizes the belief that visual disturbances, ocular, motor, or sensory, which Marie considers pathognomonic, do not constitute an essential feature of the disease, and that in typical cases the symptom picture may be reduced to its simplest expression: general inco-ordination, with conservation or exaggeration of the tendon reflexes.

A careful examination of the records of the reported cases shows that in some there were no ocular symptoms, and in others very slight departures from the normal.<sup>2</sup> Brissaud proposes to call these cases in which ocular symptoms are wanting, *variétés frustes* of hereditary cerebellar ataxia. We do not admit the necessity or propriety of such subdivision.

The history of the case which I wish to communicate is as follows: A boy eleven years of age, of mixed English and Irish parentage. The parents are living and in good health. There is no history or manifestation of syphilis in either parent. No disease like the one from which the child is suffering, nor any symptom complex resembling it, can be traced in any of the ancestry. His paternal grandfather and grandmother both died of consumption. Five paternal aunts died in childhood, all with some tubercular manifestations, and his only paternal uncle has hip (tubercular?) disease. Thus it will be seen that there is a most pronounced tendency to the transmission of a constitutional condition favorable to tuberculosis. There is no history of defective mental or physical development, or the possession of morbid atavistic traits in any of the patient's immediate family. He is the second of two children. The fact that the mother has not conceived in the past eleven years, although she and her husband are apparently normal and vigorous, indicates relative unfecondity which bespeaks degeneration. The child born previous to the patient was a girl, who died at the end of her second year. The parents say that she had a "sort of a paralysis," that her eyes "danced" continually, that she was very "backward," never having learned to say words, to walk, or to use her hands. She had two or three attacks of convulsions, and finally died during an attack. The child did not look natural, the back of the head was flat and the forehead was bulging. This is quoted practically verbatim from the account given by the mother, and can be taken, I believe, to mean that the first child was defective in a way similar to the patient here described,

only that the defect was greater and showed itself earlier. The "sort of a paralysis" spoken of by the mother was in all probability extreme inco-ordination of the extremities, which prevented it from learning to creep, to walk, or to use its hands. The fact that the child could move all four extremities speaks in favor of this view and against the supposition of any real paralysis. The "dancing" of the eyes indicates that nystagmus was very marked, just as the "backwardness" implies defective mentality.

Between the first and second pregnancies there was a space of two years. The pregnancy with the present patient terminated with a normal delivery. The child never had spasms; the teeth began to appear at the proper time, and when he was a year old he began to walk. The mother says that he began to walk and talk at about the customary time. Since his third or fourth year it has been remarked that he was "stiff in his joints," that he took "short steps" and was "continually tumbling;" "but he was always a great runner and walker," but was not able to climb like other boys. When he was four years of age it was noticed that he was short-sighted, a condition which was on the increase, and since then he has worn glasses. He has had measles, pertussis, and scarlatina, all in a very temperate form and without the slightest after-effect from any of them. When he was five years of age he began going to school, but in the following six years he has not been able to progress beyond the grade in which he started, except after the first two years he was once promoted, but later he had to be put back, and now at eleven years he is still in the baby class, or was until a short time ago, when he was returned with the advice that it was impossible to make any progress with him.

In April, 1894, in his tenth year, the mother says he had an attack in which he was unable to use the left side of the body. Although he could move the extremities, the left arm and leg were very clumsy and the hand lost all its dexterity. At this time speech was very indistinct. This seeming exacerbation of inco-ordination has recurred a few times since then, two or three times under my own observation; sometimes on one side, sometimes on the other, but more frequently on the left. And more than once has it been diagnosed as St. Vitus's dance. The hands and fingers are often blue and extremely cold, and slight depressions of temperature make him very cold. It is quite impossible to keep him warm in winter. He complains of general fatigue, and of numbness and occasional cramps in legs; but not of pain. About a year ago, after having returned from a walk with his father, he felt ill and vomited a great amount of clotted blood. The hæmatemesis continued for three or four days. Some months ago he had a fall from a flight of steps and since then they think he is worse.

**Examination.**—A, moderately tall, anæmic boy. Face has an aged, astonished, or frowning appearance which is heightened by the powerful convex lenses which he wears. Face looks somewhat asymmetrical, the right side being slightly more innervated than the left. Under the influence of the emotions, particularly those of depression, there is over-activity of the mimetic muscles, the face becomes a mass of wrinkles and takes on an elf-like expression.

He stands with the body bent forward and the chin pushed out, and with the feet wide apart. Station is quite as well preserved with the eyes closed as open. No Romberg. The gait is shambling, uncertain, titubating. This is most conspicuous when he endeavors to walk within a narrow space or to avoid successive obstacles. He falls with the greatest readiness. Lack of co-ordination is very manifest on attempts at purposive movements with the hands, worse with the left; while with the right hand there is a great deal of titubation. When he attempts movements requiring some dexterity, such as picking up successively a number of

<sup>1</sup> Leçons, Salpêtrière, 1893-94.

<sup>2</sup> Oulmont: Mercredi Méd., No. 9, 1895.

coins and retaining them in the hand, grasping and holding a pencil to write, etc., clumsiness and inco-ordination are particularly manifest, while the ataxia of the upper extremities is seen distinctly when he puts the tip of the finger on the apex of the nose. This is more marked with the left hand than the right. Defective co-ordination of the lower extremities is seen



FIG. 1.—Facial Expression.

best when he attempts to go upstairs, to run, and to step over anything. When he lies on his back purposive movements with the lower extremities are much more accurate. The tendon reflexes are all more active than normal. The knee-jerks are exaggerated and there is varying ankle clonus on both sides; sometimes this latter is well marked, while at other times it cannot be brought out. The triceps reflex is lively, and muscular contraction to mechanical stimulus is pronounced, such as is obtained by tapping the extensors of the forearm. The lower extremities resist somewhat passive motion. There seems to be an inability on the part of the patient to relax the contraction of the muscles, which gives an impression of passive rigidity. Then the contraction will disappear. So it cannot be said that there is real spasticity. The muscular strength of the upper extremities is very considerably diminished, especially the extensors, and the grip of the hands is very slight, he being scarcely able to make the dynamometer register. The muscles of the back and thighs are also weak, and this is strikingly manifest when he attempts to rise from the completely prone posture. He gets up very like a patient with dystrophy of the pseudo-hypertrophic type, except that the crawling up the thighs and trunk is not so pronounced. The muscles feel flabby and pultaceous; when the tissues on the back of the forearm are pinched up there is none of that characteristic muscular resistance, and the mass lifted up is perfectly translucent, yet the contour of the extremities is well rounded, and there is no atrophy of individual parts of the body.

Careful examination of the sensory sphere fails to reveal any constant deviation from normal. The mother says that sometimes in the morning he complains of headache, and is excessively sensitive to touch on being handled or rubbed, but it has been impossible for me to corroborate this. There is no vesical weakness, and aside from slight constipation the bowels are normal. Muscle sense intact. The disturbance of speech is most striking, but a somewhat difficult one to describe. The sound is abrupt and the articulation defective. The linguals and labials are often not

sufficiently constructed to be recognizable. When he attempts long words or tries to say several words, one after the other, they get jumbled up and it is quite impossible to recognize the words. There is none of the scanning of multiple sclerosis, but rather abrupt, forcible ejaculation attended by very perceptible effort of the muscles of expression. "Explosiveness," "abruptness," and ataxia are the three prominent characteristics.

Examination of the eyes reveals a paleness of the disk which Dr. W. A. Holden, who examined the eyes, considers to be within physiological conditions, and slowly progressing choroiditis. It is difficult to speak positively as to whether there is dyschromatopsia or not, but it is certain that there is no achromatopsia. The pupils are wide, alike on both sides, and respond slowly to light and accommodation. There is a progressive myopia. Forcible side to side movements of the eyeballs are accompanied by slight jerky movements which are not sufficiently rhythmical to be designated nystagmus. The movements of the eyeballs are free in every direction, but outward rotation is much less vigorous and complete than it is normally. There would seem to be no defect in the function of the other cranial nerves except the asymmetry of the face, which has already been mentioned, the exaggerated condition on display of the emotions, and the fact that he cannot whistle. This last does not seem to be due to inability to pucker the lips, for that he can do, but to the lack of reciprocal action between the muscles of the lips, the cheeks, and the respiratory muscles. It is also worthy of remark that until a year or two ago he could whistle. There is an irregular tremor of the tongue. Senses of smell, taste, and hearing are apparently intact.

As has been said before, he is deficient mentally, but he is not demented nor idiotic by any means. He would seem to have receptive faculties and a considerable capacity for memory; but in power or process of association he would seem to be entirely lacking. He has rational likes and dislikes, and has, apparently, ideas of right, of wrong, of possession, etc. He answers questions rationally, and also asks questions becoming a child of much fewer years. Yet, withal, he has never been able to put letters together so as to form words, nor to develop sufficient faculties to write simple sentences, although he could write his name. He has a bad temper, is easily provoked, does not like to be contradicted, and can be led more easily than dominated. He has no capacity for attention. One may try in the most forcible and praiseworthy manner to hold his attention, but after holding it for a moment it flits. There are no objective sensory troubles.

The genital organs are extremely undeveloped, the penis like an infant's, and only one testicle can be felt. The skin is dry, the hair falls out more than normally, and it is said that he does not perspire. He becomes fatigued rather easily, and oftentimes he is very drowsy and will sleep in the day. There is a deformity of the right foot, a typical so-called pied-bot, which is shown in the accompanying illustration. This deformity has not yet been noticed by the parents, nor is it to be remarked in the patient's gait. The shoes that he wears are of a pair.

The course of the disease has been a progressive one even since the patient has been under my observation. The fact that when the parents first brought him for treatment it was stated that symptoms dated from the fall already mentioned, may be taken as evidence that the disease has made a considerable progress in that time. It is unnecessary, probably, to add that fall was incidental to the disease, and not *vice versa*. The defective formation of bodily heat; the consequent depressed vitality; the increasing inco-ordination of gait, of movements, of speech; the retrogression of mental acquisition; the increasing loss of muscular strength, all go to show that the anatomical conditions at the

bottom of his disease are not only preventing anything like normal somatic and mental development as had gone on up until three or four years ago, but that there is an actual retrograde process at work. The muscles respond to the galvanic and faradic current, sluggishly of course, considering the pronounced lack of development, especially of the extensors, and there is normal

conditions which are found so frequently in hereditary spinal ataxia as to be considered of considerable diagnostic importance. Such is the pied-bot, a form of talipes dependent upon defective action, paresis, and subsequent contracture in the peroneal group of muscles. It is more than probable, however, that a history of this deformity will be found in subsequent reports of

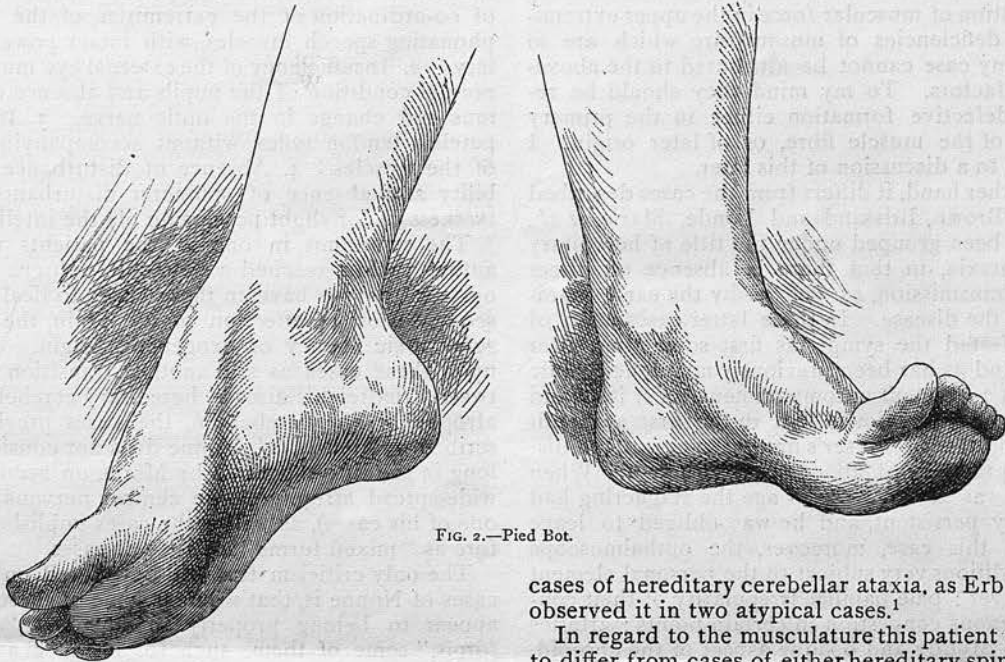


FIG. 2.—Pied Bot.

cases of hereditary cerebellar ataxia, as Erb has already observed it in two atypical cases.<sup>1</sup>

In regard to the musculature this patient would seem to differ from cases of either hereditary spinal ataxia or hereditary cerebellar ataxia. In the former muscular power is usually normal, even after the ataxia has be-

polar relationships. Faradic irritability of some of the nerves, notably the musculo-spiral, is diminished.

To recapitulate briefly the salient points of this case: 1. Absence of direct hereditary transmission. Evidence of its being familial, a sister, in all probability, suffered from the same disease. 2. Onset in early childhood. The accompanying photograph is evidence that in infancy the child was free from the manifestations of the disease. 3. Disturbance of co-ordination manifested in all four extremities. Titubation of the hands and feet. 4. Gait: feet wide apart, reeling, inco-ordinate. 5. Increased tendon reflexes; exaggerated knee-jerks and ankle clonus. 6. Marked disturbance of speech, explosive, inco-ordinate; articulation very defective. 7. Profound deviation of intellect; associative faculties lacking; defective in attention. 8. Absence of sensory disturbance and intactness of the sphincters. 9. Progressive loss of muscular strength and tonus. 10. Shrivelled appearance of skin, lack of perspiration, senile, position of body and staring expression of countenance.

Thus it will be seen that in some points it differs very radically from hereditary spinal ataxia or Friedreich's disease, combined lateral and posterior sclerosis; while other of its symptoms point in no uncertain way to this disease. But the fact is that the case presents characteristics directly inimical to the postulated pathological condition of this disease. In brief these contradictory symptoms are: 1. The exaggerated tendon reflexes, knee-jerks, and ankle clonus. In Friedreich's disease the tendon reflexes are diminished or absent, particularly after the disease has been absent for some time. A case in which ankle clonus was an accompaniment has never been described. 2. The absence of nystagmus. 3. The striking defect of the mind.

The extremely early onset (Friedreich's disease comes on generally between the tenth and fifteenth years), the absence of sensory symptoms, the intensity of inco-ordination in the upper extremities, and the titubation are likewise uncommon concomitants of Friedreich's disease.

On the other hand, this patient shows symptoms and

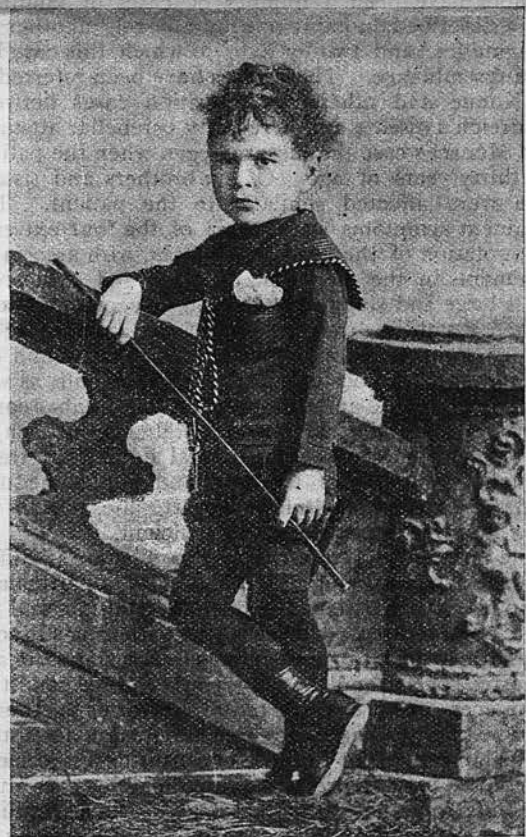


FIG. 3.

comes well pronounced, and although it sometimes becomes impaired in the course of the disease, the flexors suffer more than the extensors. Wasting of the mus-

<sup>1</sup> Neurologisches Centralb., 1890, p. 378.

cles is very slight.<sup>1</sup> In the latter disease Londe,<sup>2</sup> in his analysis of all the cases on record, reached the conclusion that the subjective sensation of fatigue and feebleness of muscular force is but slightly diminished; and when it is diminished it is but the consequence of hospitalization and prolonged inability to give the muscles their proper stimulation. Nevertheless, in Menzel's case (a so-called intermediary case) there was remarkable diminution of muscular force in the upper extremities. The deficiencies of musculature which are so striking in my case cannot be attributed to the above-mentioned factors. To my mind they should be referred to defective formation either in the primary constituent of the muscle fibre, or of later origin. I shall return to a discussion of this later.

On the other hand, it differs from the cases described by Nonne, Brown, Brissaud and Londe, Marie, *et al.*, which have been grouped under the title of hereditary cerebellar ataxia, in that there is absence of direct hereditary transmission, as well as by the early manifestation of the disease. In these latter cases many of them manifested the symptoms first some time after puberty. And as has been previously mentioned, optic atrophy was a frequent accompaniment. Yet it should be conspicuously mentioned that in the first authenticated case on record, Fraser's first observation, the disease began gradually at about the fourth year. When the patient was seven years of age the staggering had become very persistent, and he was obliged to leave school. In this case, moreover, the ophthalmoscope showed conditions very subject to the personal element of the observer: pale papillæ, irregularity of their contour with venous congestion in certain points; arteries contracted. Muddy and opaque aspect of the choroid. Except in the absence of oscillations of the head and the mental defect, the case herewith reported resembles very closely the case of Fraser.

There have been a number of cases of familiar ataxia described, notably one by Menzel,<sup>3</sup> another by Seeligmüller,<sup>4</sup> and two by Erb,<sup>5</sup> to which this case has some resemblance. These cases have been referred to by Nonne and others as transition cases between Friedreich's disease and hereditary cerebellar ataxia.

In Menzel's case the disease began when the patient was thirty years of age. Of six brothers and sisters, three were affected similarly to the patient. The prominent symptoms were ataxia of the four extremities; rotation of the head to the right, with associated movements in the face; speech slow and explosive; pupils large and sluggish to light and accommodation; marked Romberg; exaggeration of the knee-jerks; no sensory troubles. Anatomically, there was found degeneration of the posterior columns and roots, as well as atrophy of the anterior roots in the lumbar cord; degeneration of the columns of Goll and Burdach, of the direct pyramidal and lateral cerebellar tracts throughout the rest of the cord and in the medulla. The pons and cerebellum were atrophic, and in the latter Purkinje's cells were very deficient.

The recitation of this case shows wherein it differs from the accompanying observation. It is particularly in the age of the patient, the mental condition, and the severe contractures. Otherwise my patient has in common with it the exaggerated knee-jerks, the slow and explosive speech, and the very nearly normal condition of the eyes. The case, therefore, conforms neither to the type of cases described under the name hereditary cerebellar ataxia, nor to those constituting Friedreich's disease. Furthermore, its symptomatology is quite different from the symptomatology of such familiar diseases as cerebral diplegia, as described by Sachs, by Freud, and by others; from paraplegia ataxo-spasmodic of Gowers, and familiar spasmodic paraplegia which has been described by many writers.

It is advisable also to contrast it with the symptomatology of six cases recently described by Nonne.<sup>6</sup> He sums up his conclusions in these cases as follows: "The disease developed in patients without any hereditary condition existing in the family. It may follow a disease of the brain, as we have seen it after a sunstroke. The most important symptoms are: 1. A static and locomotoric, not purely ataxic, disturbance of co-ordination of the extremities, of the trunk and phonating speech muscles, with intact power of mimicry. 2. Insufficiency of the external eye muscles, with normal condition of the pupils and absence of nystagmus and change in the optic nerve. 3. Increase of patellar tendon reflex without accompanying rigidity of the muscles. 4. Absence of disturbance of sensibility and absence of sphincter disturbance. 5. Intactness of (or slight perversion of) the intelligence."

The symptoms in one of the patients which the author details reached a standstill. Nonne is of the opinion that we have in these cases to deal with the sequences of an affection of the brain, the result of some toxic agency of exogenetic origin. He looks upon these cases as still another transition form between Friedreich's disease, hereditary cerebellar ataxia, atrophy of the cerebellum, the cases previously described by him (which Nonne does not consider to belong in the title suggested by Marie, on account of the wide-spread atrophy of the central nervous found in one of his cases), as well as the cases published heretofore as "mixed forms" of these diseases.

The only criticism that will be offered on these last cases of Nonne is, that whereas some of these six cases appear to belong properly to so-called "transition forms," some of them, such for instance as the one coming on after sunstroke, can be explained by the previous existence of an encephalitis. They differ essentially in some points from the case herewith reported. Particularly in the intactness of intelligence, the absence of any familiar history. In common with it they have the early beginning, the abnormal liveliness of the tendon reflexes, the absence of eye-symptoms, the absence of sensory and sphincter disturbance, etc.

The symptoms of the patient herein described can be most rationally and logically explained, when more extensive defect of the nervous system is postulated than exists in either hereditary spinal or hereditary cerebellar ataxia. In the former disease there is sclerosis and shrinking of the posterior columns of the spinal cord, and of the columns of Goll and Burdach, analogous to that found in tabes. In addition a similar pathological process goes on in the crossed pyramidal tracts, in Gower's tract, in the direct cerebellar tract, in the medullary bridge of Lissauer; and with these there is a diminution of the cells of Clarke's columns. The lesions in the latter disease are pronouncedly in the cerebellum, and consist of a reduction in weight and volume which is associated with a thinning of the gray layer and a lessening in number of the cells of Purkinje. Naturally, with such a lesion there are others of such fibres or bundles of fibres the neurons of which are situated in the degenerated areas of the cerebellum. The projection fibres of the cerebellum are, happily, now very much better known than they were a few years ago, even although we are still in the dark as to their connections and functions. Therefore, just what these outlying lesions are, or what they will be found to be, cannot yet be said.

The patient, R. L.—, has symptoms which cannot be explained by either set of lesions or by both combined. The retrocession of slight mental attainment at the sixth or seventh year, and the lack of mental development in the five years following on that age—years in which children make more radical mental progress than at any other period of their existence; a period when they acquire ideas of spoken and written

<sup>1</sup> Gowers: Diseases of the Nervous System, vol. i., p. 464.

<sup>2</sup> Loc. cit.

<sup>3</sup> Archiv f. Psychiat., vol. xxii., 1891, p. 162.

<sup>4</sup> Ibid., vol. x.

<sup>5</sup> Ibid., vol. xxvii., p. 749.

<sup>6</sup> Archiv f. Psychiat., vol. xxvii., 1895.

language, of moral and social relationships, when there is an enormous awakening as to their being and function—point unmistakably to lack of cerebral development which we believe could be called a lesion if it were possible to examine it.

The psychical condition of the child at the present time forms an interesting subject for study. His possessions and lackings in this line have before been commented on in some detail, but it may be well to repeat that it is the neural processes underlying attention, association, and complex memories that he is strikingly deficient in. These qualities of the mind we believe to be subserved principally by the great system of association fibres or tracts. And the fact that these mental attributes are deficient and undevelopable is in evidence that the neural processes on which they are dependent are lacking. Other symptoms, such as the decided exaggeration of myotatic irritability, the lack of readiness in the relaxation of muscular contraction, are explained most naturally by defect in the system of long projection fibres, which interrupts in part the inhibitory activity of the cerebrum on the former and interferes with the conductivity of impulses necessary to the latter.

Taking the symptoms which this patient presents in their entirety, it seems to me that they bespeak a defective formation of the nervous system, not of any individual portion such as certain parts of the cord or the cerebellum, but of the entire cerebro-spinal and sympathetic nervous system. In fact, if we take our perspective from the broad view-point of the development of the nervous system, it is not difficult to conceive how some perversion of the germ plasm destined for the portion of that part of the epiblast from which the nervous system is to develop, may cause a deficiency in the proper development of the nervous system. Such a defect, by very virtue of its protal origin, would not be limited to any individual part of the nervous system, but would be manifested throughout it. That is, it would not be alone in the central neuron, in the projection and association fibres which are built from them, but in the peripheral neuron as well.

The condition of the musculature of the patient R. L.—I consider of no small importance in bearing on the process underlying his disease. As has been said, the contours of the extremities are quite normal in appearance. There is neither apparent atrophy nor hypertrophy. The fact that the musculature is deficient is conveyed by what has been said concerning the way in which he rises from a lying posture. Then, when it comes to an examination of the muscles, it is seen that in some parts of the body, such as on the back of the forearms, they are strikingly deficient, as is shown by the translucency of the parts when the tissues are pinched up, by the extremely small amount of muscular tissue which can be recognized by the touch in these parts and by the rapidity with which the upper extremities become fatigued.

That the muscles exist, and that there is no degeneration in the muscles, is shown by their behavior to the electrical tests. That is, it would seem that some groups of muscles are represented in miniature. This is not the result of disuse, or of disease of the muscles themselves, but is, I believe, the result of defective formation consecutive to deficient protal distribution of peripheral neurons. I am aware that this theory leaves unexplained the integrity of the sensory system, but the fact that it is intact should not prevent an attempt at furnishing a rational explanation of existing defects.

The absence of sensible perspiration, the condition of the skin and appendages, to which attention has been called, bespeak shortcomings in the performance of its duties by the sympathetic nervous system. We have, therefore, in this case symptoms which, although partaking of the symptomatology of both hereditary cerebellar and hereditary spinal ataxia, has in addition

certain conditions which are dependent upon a more extensive defect in the nervous system than either of these two diseases has been found associated with. The purpose of this report is to show that cases such as this cannot be encompassed by unvarying boundaries.

It also, I think, goes to show, as Nonne has pointed out, that there exist clinically cases which vary in their clinical manifestations from the picture produced by cerebellar ataxia, through the category of his original cases, through the cases described under hereditary cerebellar ataxia, to the many transition forms that have been described, and that these cases can be differentiated clinically from hereditary spinal ataxia.

I deem it a privilege to thank Professor C. L. Dana, in whose clinic at the Post-graduate Medical School this patient was found, not alone for the consent given to study the case, but for valuable suggestions made while studying it.

43 WEST THIRTY-NINTH STREET.

#### A CHEMICAL AND EXPERIMENTAL RESEARCH ON "ANTIPHTHISIN" (KLEBS'S).

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AND

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IN spite of the ill repute into which Koch's tuberculin so quickly fell, many investigators, struck with the specific and selective influence which it exercises on the lesions of experimental tuberculosis, as well as with some favorable clinical observations noted in certain types of the pulmonary disease treated by tuberculin, have persevered in its further study and have attempted to analyze its constituents, to do away with the manifestly dangerous products contained in liquid cultures of the tubercle bacillus, and if possible to separate some pure substance which might favorably influence the tuberculous process, or produce in men and animals a certain degree of immunity.

Koch,<sup>1</sup> shortly after his announcement of the discovery of tuberculin, published the result of his attempts to purify this substance, claiming, however, for the product he obtained no therapeutical advantage over crude tuberculin. Kühne<sup>2</sup> made a chemical analysis of its component parts, and found that the active substances present in it are of the nature of albumoses.

Baumgarten<sup>3</sup> obtained temporary cures of eye tuberculosis in the rabbit by treatment with tuberculin. Trudeau<sup>4</sup> demonstrated, by the treatment of the experimental disease in the rabbit's eye, that the substances which bring about reaction and, under certain experimental conditions, even temporary cure, are to be found in the filtrate of liquid cultures, and not in a solution or suspension of the washed bodies of dead bacilli, and that the heat used in making Koch's tuberculin precipitates some of the proteids present in the cold filtrate. The studies of Hunter<sup>5</sup> and Klebs<sup>6</sup> were directed more particularly toward the separation by chemical methods of the injurious from the possibly curative elements of tuberculin.

In a communication made in 1892,<sup>7</sup> and in an exhaustive and more recent publication on this subject, Klebs claims, by chemical methods which he describes, to have separated from tuberculin, and later from the filtrate of over-ripe liquid cultures, a product which, owing to its specific germicidal action, is capable of killing the tubercle bacillus even when entrenched in

<sup>1</sup> Koch: *Deutsch. Med. Woch.*, October 22, 1891.

<sup>2</sup> Kühne: *Zeitsch. f. Biologie*, 1892, xii., No. 2.

<sup>3</sup> Baumgarten: *Deutsch. Klin. Woch.*, 1891, No. 19.

<sup>4</sup> Trudeau: *Transactions of the Association of American Physicians*, May 24, 1892.

<sup>5</sup> Hunter: *British Medical Journal*, July 25, 1891.

<sup>6</sup> E. Klebs: *Deutsch. Med. Wochenschrift*, April 14, 1892.

<sup>7</sup> E. Klebs: *Die Causale Behandlung der Tuberculose*, 1894, pp. 578-81.

the living tissues of infected men and animals, and thus curing the disease.

According to Klebs's observations, the cure is brought about, not, as Koch thought, by the power of the specific product to incite a reactionary effort on the part of the body cells, but directly and solely through its germicidal influence on the tubercle bacillus. Klebs, having observed that tubercle bacilli in cultures die when a certain period in their cultivation is reached, holds that they perish because they produce toward the end of their existence in the culture medium a peculiar germicidal substance which destroys them; that, by the chemical processes he describes, he has obtained this specific substance freed from the poisonous alkaloids and albumoses also produced by the microbes during their growth, and present in tuberculin; that he has succeeded in separating from over-ripe cultures this germicidal substance, which he calls "sozalbumose," and that it is the natural specific for this dreaded disease.

Such deductions, if proved correct, would have so important a bearing, not only upon our existing knowledge of the tubercle bacillus and of the treatment of tuberculosis, but upon the etiology and treatment of many other bacterial diseases as well, that a study of the claims made for "antiphthisin," both from the chemical and experimental stand-points, and of the theory upon which these claims are based, was undertaken by us at the Saranac Laboratory for the Study of Tuberculosis, and an answer to the following questions sought:

1st. *Can a specific substance, differing chemically from the albumoses already known to be contained in the filtrate of liquid cultures of tubercle bacilli, be separated from such cultures in a state of purity by the chemical methods proposed and described by Dr. Klebs?*

As the directions given by Dr. Klebs for the preparation of "antiphthisin" were evidently intended to be sufficient for the guidance of others who might desire to prepare this substance, we preferred not to limit our chemical study to an analysis of his own product, but to include in our research a test of the chemical problems involved in the process of manufacture as laid down by him.

In order to ascertain the nature of "antiphthisin" we prepared large quantities of it according to the directions given, which were closely followed.

"Antiphthisin" is stated by Klebs to resemble "tuberculocidin" (the name given to a former preparation), but is made directly from the fluid filtered from the over-ripe bouillon cultures without heat, instead of from crude tuberculin, as is the latter. The same method is used in both, but the "antiphthisin" presumably contains more of the active albuminoid substances, because some are removed by heat in the manufacture of tuberculin, from which "tuberculocidin" is made.

Kühne<sup>1</sup> examined 100 c.c. of Klebs's "tuberculocidin" and found a small amount of deuterio-albumose and traces of peptone as the ingredients, excepting the phenol used to preserve it and inorganic salts. The albumoses, etc., resembled those contained in the peptone of the culture medium, though possibly derived from the bacilli. The important step in making these modifications of tuberculin is said by Klebs to be the removal of harmful, fever-producing substances by precipitation with sodium-bismuth-iodide (a reagent used to separate alkaloids) in acetic acid solution. The useful germicidal substances are assumed to be retained in the filtrate, which is then treated with NaOH to remove the bismuth. This being filtered off, absolute alcohol is added to the filtrate. The resulting precipitate collected and dissolved in water is called "antiphthisin." This is preserved in 0.2 per cent. trikresol, and is made of  $\frac{1}{2}$ ,  $\frac{1}{3}$ , or  $\frac{1}{10}$  bulk of the original culture fluid.

We first procured some potassium-bismuth-iodide through the kindness of Professor C. E. Colby (Columbia College, School of Mines), and with this made several samples of "antiphthisin." Later, with sodium-bismuth-iodide prepared by ourselves, we made larger quantities.

Seven flasks containing 900 c.c., covered with thick pellicles beginning to sink, and all showing a rich growth of ripe, pure cultures grown from December 20, 1894, to February 18, 1895—eight and a half weeks—on peptone-bouillon, were filtered free of bacilli, and 12 c.c. of trikresol, twenty per cent. solution in glycerine, added as a preservative. After standing twenty-four hours sodium-bismuth-iodide was added until no further precipitation occurred, the reagent being first treated with sodium acetate and acetic acid. To avoid great excess, the quantity of the precipitant needed was first closely determined by titration three times with 5 c.c. of the culture fluid. The bulky, red precipitate was settled and filtered; the filtrate tested gave no further precipitate with  $\text{NaBiI}_2$ ; NaOH (norm.) added until reaction just alkaline; warmed, settled, and filtered, free of  $\text{Bi(OH)}_3$ ; to the clear filtrate absolute alcohol added until no further opalescence produced. The final precipitate, washed with absolute alcohol and dried, was readily dissolved in 70 c.c. distilled water.

#### EXAMINATION.

Color—light straw (resembled "tuberculocidin" obtained in market).

Odor—none (without trikresol).

Reaction—slightly alkaline.

+ heat = O + acetic acid = O (absence of albumin).

+ NaOH +  $\text{CuSO}_4$  = rose color distinct (indicative of albumoses or peptones).

+  $(\text{NH}_4)_2\text{SO}_4$  (saturated) = opalescence (albumoses?).

+ NaCl (saturated) = O + acetic acid = opalescence (deuterio-albumoses?).

+  $\text{PtCl}_4$  (excess) = opalescence (not found by Klebs).

+  $\text{NaBiI}_2$  + acetic acid = precipitate (the first was evidently incomplete—not found by Klebs).

+ HCl +  $\text{H}_2\text{S}$  (warmed) = O—(absence of Bi).

+  $\text{HNO}_3$  (conc.) + starch paste = O (absence of I).

The above reactions and others indicated that we were dealing with an albumose, or peptone-like body, which was incompletely precipitated by the first treatment with sodium-bismuth-iodide. The whole quantity remaining was therefore again treated with sodium-bismuth-iodide in acetic acid. This time there was much less "antiphthisin," and by a third treatment it was possible to completely remove all of it—no proteid being left.

These results show the absence of any substance different from the albumoses already described by Kühne as deuterio-albumose, produced by the bacilli in very small quantities.

Klebs thinks this substance to be elaborated by the bacilli in growing. To test this point we treated some unimplanted bouillon by the same method above described.

Two hundred and fifty cubic centimetres gave a residue identical in appearance and reactions with that obtained from the cultures. It was, however, less in quantity than that obtained from cultures of same bulk.

As it was evident that some of the albumoses, etc., in the original culture—*i.e.*, contained in the peptone or meat extract—might be in the product called "antiphthisin," we prepared some from peptone-free cultures, grown on the asparagine fluid suggested by Schweinitz.<sup>1</sup> 475 c.c. of this gave a trace of antiphthisin," which from its reactions resembled a deuterio-albumose. Obviously this must have been derived from the bacilli, because a control experiment with the culture fluid gave nothing. A second treatment of the presumably pure "antiphthisin" with sodium-bismuth-iodide completely precipitated the proteid substances.

Some experiments with deuterio-albumose were next made to determine whether this is incompletely precipitated by sodium-bismuth-iodide. This substance

<sup>1</sup> Kühne: Loc. cit., p. 252.

<sup>1</sup> Schweinitz: New York Medical Journal, February 3, 1894.