FRIEDREICH'S ATAXIA.

A Report on Two Cases.

by

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THESIS PRESENTED
FOR THE DEGREE OF M.D.

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I. PRÉFATORY NOTE.

In an out-of-the-way part of the Country, such as the small group of islands constituting the County of Orkney, in which my practice lies, one does not readily light upon a subject suitable for a Thesis.

The majority of cases with which one is called upon to deal are commonplace, though they might furnish scope for investigation if one were in constant contact with Hospital, laboratory and Library.

All these aids to study are lacking in these islands and one has to depend for books and medical literature on the British Medical Association's Library in London.

It was therefore of great interest to me to find that in one of the islands under my medical charge there was a family in which were cases of Friedreich's Ataxia. My interest did not seem to be shared by any of the medical men whom I met from time to time in Orkney.

The condition is rare and unknown to most general practitioners except as a name recalling student days.

No case of Friedreich's Ataxia has hitherto been reported from Orkney and, at the suggestion of a medical friend to whom I mentioned the subject, I decided to study the cases more fully with a view to writing a Thesis.
A few remarks about these outlying islands; position, size, population and climate, may be appropriate.

The Orkney islands lie to the North of Caithness, from which they are separated by the Pentland Firth, only 6 miles across at the narrowest point.

Orkney is now an entirely agricultural county, fishing being no longer an important industry. There are 60 islands in the group, only 30 inhabited. To compare Orkney with "Midlothian, the metropolitan County of Scotland, may be of interest. Orkney is of very nearly the same size (only some 6,000 acres larger) but it has 7,000 acres less of mountain and moorland and 20,000 acres more of arable land, of which 5,000 more are under corn crops. It has twice as many cattle as Midlothian". (Orkney, The Magnetic North by J. Gunn, M.A., D.Sc.)

The population is 26,000. The prevailing stock is of Norse origin, though there is a considerable modern Scottish admixture drawn from Eastern and Lowland Scotland rather than from the nearer Highlands. The Norsemen who colonised Orkney also conquered Normandy and later England. (Gunn)

The climate is mild in spite of its northern position, and Orkney's average annual rainfall is from 30 to 35 inches. Winds are frequently of gale force in Autumn and Winter.

The/
The islands of which I have medical charge are Rousay, Egilshay and Wyre. The family to which I refer live on Egilshay. This island, shown on the accompanying map, is 3 miles in length from North to South and a mile across at its widest part. There are 14 farms or crofts. The population of the island is about 60, having decreased in recent years; many having gone to other parts of Orkney or elsewhere.

My introduction to the C. family took place in 1935 when there were only two children, a boy James and a girl Elsie: another boy was born subsequently (Alfred). Having been asked by the parents for a certificate of James' inability to attend school (a mile distant) in wintry weather, I decided to make a thorough examination of the boy. I had no difficulty in diagnosing Friedreich's Ataxia; not from previous experience of the disease, but from reading about this and kindred nervous diseases. I then proceeded to obtain a copy of Friedreich's original writing on the subject of this form of Ataxia (of which I give a brief extract); and also to enquire into the family history. I was able to obtain information both from my own observation and from relatives. The more distant ancestry was naturally more difficult to ascertain.

I have made some reference to associated congenital and other deformities or illnesses seen by me/
me in near relatives of the family, as well as to similar associated conditions referred to in the most recent literature obtainable on Friedreich's Ataxia from British, French and American sources.

I have discussed briefly the question of transmission and of marriage in families in which Friedreich's Ataxia occurs, basing my views on the current teaching of Genetics originated by Mendel.

Finally, I have made some remarks on treatment.
II. THE C. FAMILY AND THE QUESTION OF HEREDITY.

(GENEALOGICAL)

It has not been possible to discover any other case of Friedrich's Ataxia among the children's ancestry.

Their parents, Robert C. and Violet S. were very distantly related; their great grandfathers being cousins. I have not included the numerous members of Violet's family or of her father's, as they do not appear to have any bearing on the disease.

Robert's mother is well at the age of 74; his father is dead but his grandparents lived to a great age.

I/
I could not trace the origin of Mr Bs. who married Robina G. and had five children, cousins of Violet.

One of these M. is married and has four children— all healthy. She herself when nearly 40 in 1939 contracted Infantile paralysis. Her sister, Mary Ellen, died at the age of about 40. She was undersized and infantile in appearance and suffered from cataract but was not mentally defective. Hugh was also rather undersized, suffered from asthma and died soon after the age of 40. I have actually met about forty of the relatives of the two families.
III. PERSONAL OBSERVATIONS.

Egilshay is only about a mile from Rousay; but, in the winter, one is not able to visit the island so frequently because of sea and wind. Four years ago, 1940, the Father asked for a certificate of total exemption from School and I was told that James staggered about instead of walking. It was at this point, after having considered the possibility of Friedrich's Ataxia, suggested by my reading on this and kindred nervous diseases, that I made my first thorough examination.

The facts I observed were as follows:-
2. Divergent concomitant squint. Pupils react to light and accommodation.
3. Twitching of facial muscles - especially when about to speak.
4. Staccato speech.
5. Spinal column showed a definite scoliosis in the mid-dorsal region, the convexity being to the left.
7. Absence of ankle jerks.
8. Ataxia, affecting arms, hands, and especially legs.
9. Manus cava or Radio-ulnar-carpal flexion.
10./
12. Coldness of legs up to knees.
14. Mental condition very good.
15. Ataxic gait.

A little later in the year (Nov. 1940) I sent the boy to the Sick Children's Hospital, Aberdeen, where my diagnosis was confirmed and a further examination made. The Report stated:—

No signs of disease were found about heart, lungs, or abdomen.

Knee jerks and ankle jerks absent, nor could the arm jerks be elicited.

Wassermann reaction of the blood negative.

Lumbar puncture:

Spinal fluid was under normal pressure and was normal in its characters.

Postural and Vibrational Sensibility are impaired in the legs.

Pupils react to light. Slight pallor of both optic discs, the edges of which are well-defined and the laminae cribrosae exposed.

X-Ray examination showed no bony abnormality about the skull and X-ray of the spine was likewise negative, apart from a slight scoliosis and a spina-bifida of the Vth Lumbar vertebra.

The remainder of the Report merely confirmed my own observations and stated: "There is no doubt the case is one of Friedreich's Ataxia."
There are 3 children in the C. family - two boys and one girl. (1945).

James aged 14 years, Elsie 11 years, Alfred 5 years. There have been no deaths.

CASE I.

HISTORY:

Birth.

At the time of James' birth in June 1931, his Mother was aged 20. Neither Nurse nor Doctor was present, but the labour was easy and uneventful. The child weighed 8½ lbs. There was an umbilical hernia which has persisted.

Dentition.

This followed a normal course and the first lower incisor erupted at 6 months.

Speech.

There was no delay in learning to speak: he appears, indeed, to have been rather precocious.

Sitting and walking.

He is said by his parents to have been rather slow to acquire the habit of sitting up and always leaned forward in doing so.

It was two years before he learned to walk and he was "never able to walk properly", though I did not notice this myself at first.

Pain...
Pain.

He constantly complained of pain in his back. He indicated this at a very early age by putting his hand to his back; and then, on being asked if he had a pain there, nodded his head. He also had pain in the umbilical region, which may have been caused by the discomfort of the hernial protrusion. His Mother said: "There always seemed to be something wrong with him.

Weaning.

He was nursed by his Mother at the breast until he was 8 months old.

Subsequent History.

His Mother says that he was in the Hospital at Kirkwall at the age of 2½ years, for 5 days and to have "taken no food during that time." The nature of the illness is not known but was ascribed by the parents to "teething".

When James reached the age of five years, he began to attend school, which involved a walk of a mile each way over a very poor road, often in face of a strong wind.

After a time his parents wrote to me asking for certificates stating that he was unable to attend School. These were readily given from time to time in the winter; but it soon became necessary for his Father to carry him to and from School. It was clear that/
that this was due to something more than the severe weather and the rough road.

As already stated, he was sent to the Sick Children's Hospital, Aberdeen. He returned home and was confined to bed from that time. This was probably merely coincidence, though such patients often feel worse after having been confined to bed. James took a very intelligent interest in his journey by aeroplane and has never shown any mental deterioration. He is of a pleasant disposition and smiles readily though gradually his facial muscles have come to cause a contorted appearance. Thus the whole muscular system has degenerated, not only legs and arms but facial and abdominal muscles.

Quite recently he has had severe constipation, the bowel muscular effort being inefficient. He has required enemata and cathartics such as Calomel and Castor oil in large doses. One has had to resort to digital removal of the faeces and the boy has suffered prolonged and severe pain before the scyballous masses have been ejected.

His speech has grown steadily more indistinct, until now it is quite unintelligible. Even "yes" and "no" can hardly be distinguished.

In July of this year (1945) his Mother took him with the other 2 children Elsie and Alfred to Kirkwall for a holiday. She placed the two older ones in a pram
prambulator whilst Alfred walked. James knelt up as he was conveyed along and took great interest in all he saw.

He is quite unable to walk or even to stand, nor is he able to feed or dress himself. His mentality alone appears to remain unimpaired.

After I had written the foregoing, James had, for a time, severe constipation, loss of appetite and later tachycardia. The bowel musculature, in common with all the muscles of the body, was defective. He was unable to swallow, speech was by this time quite beyond the understanding, even of his mother; and on August 23rd 1945 he died. No post-mortem examination was made.
CASE II.

ELSIE C.

Born March 1934. Weight at birth, 6 lbs. Normal labour.

I first saw this child in 1935. She was awaiting admission to Hospital on account of a degree of hernial protrusion at the umbilicus. She was a weakly-looking child, often suffering from "colds". Her appearance was not at all that of a country child, but rather of one living in the slums of a city - pinched, pale, undersized. At the age of five years she went to School, and made fair progress with her schoolwork. When, however, she was 6½ years old, she began to show symptoms similar to those of her brother James, the foregoing case. She tended to fall when walking and, even in the house, clutched at any article of furniture to support herself as she moved about.

On examination, I found:-

1. Scoliosis.
2. Absent knee jerk.
3. Plantar reflex extensor.
4. Speech unaffected.
5. No nystagmus or squint.
7. Manus cava.
8. Ataxic gait.
It was impossible for her to continue going to School on account of the difficulty of walking; but, for at least two years, she walked to neighbouring houses, even further away. This she did under no constraint and at her own pace. She also continued to read school books at home. At length the home study fell into abeyance; and now, some 3\frac{1}{2} years after leaving school, she is hardly able to read. Moreover, a change for the worse has become evident in the symptoms previously noted.

**Walking.** She throws out her legs in a semicircular motion, raising them with a high-stepping gait. She cannot walk so far or so well.

**Speech.** This is very much affected and not easy to understand.

**Eyes.** She still has no nystagmus, but her Mother stated that she sometimes had a squint in her left eye. I found, on examination, that she seemed to be able to produce this momentarily, but it is not constant.

**Spine.** The scoliosis is more pronounced, the convexity being, as in her brother James' case, to the left in the dorsal region.

**Hands.** She is able to dress herself and use her hands quite nimbly. There is, however, abnormal flexibility of the wrist joint, enabling her hands to be flexed so that there is an acute angle between the palmar aspect of the fingers and the flexor surface of the forearm.

**Weight.**
Weight. Feb. 1943 at age nearly 9 (19th March) 2 stone 11 lbs. The normal weight for a girl of this age is about 61 lbs or 4 stone 5 lbs.

A possible Case III is the third child of the family, Alfred, now (1945) aged five years. The possibility of his becoming a victim of the same disease cannot yet be disregarded, though he is approaching the age at which his brother and sister showed manifest symptoms of Friedreich's Ataxia.

As Julia Bell says ("Treasury of Human Inheritance", Vol.IV, part III, p.146) "One can feel a considerable measure of confidence in assuring members of the family a few years older, who are still free from signs of the disease, that they are likely to remain so."

I have never been able to elicit tendon knee jerks in this boy, however, and therefore regard him as one who in all probability is not free from the inherited genetic defect.
16th July 1945.

<table>
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<th>Name</th>
<th>Height</th>
<th>Weight</th>
<th>Age</th>
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<tbody>
<tr>
<td>James</td>
<td>4' 0&quot;</td>
<td>3 st. 4 lbs.</td>
<td>14</td>
</tr>
<tr>
<td>Elsie</td>
<td>3' 10½&quot;</td>
<td>3 st. 5 lbs.</td>
<td>11</td>
</tr>
<tr>
<td>Alfred</td>
<td>3' 9⅛&quot;</td>
<td>3 st. 7 lbs.</td>
<td>5</td>
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29th Aug. 1944.

<table>
<thead>
<tr>
<th>Name</th>
<th>Weight</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>James</td>
<td>2 st. 12 lbs.</td>
<td>gained 6 lbs in 1 year.</td>
</tr>
<tr>
<td>Elsie</td>
<td>2 st. 12 lbs.</td>
<td>7 &quot; 1 year.</td>
</tr>
<tr>
<td>Alfred</td>
<td>2 st. 12 lbs.</td>
<td>9 &quot; 1 year.</td>
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III. FRIEDREICH'S ORIGINAL DESCRIPTION.

On coming to the decision that I had at least two cases of Friedrich's Ataxia in my charge, my first desire was to learn all I could, first about Friedrich whose name is now so indissolubly connected with the disease and then about his description of the condition.

FRIEDREICH.

Nikolaus Friedrich, son of Johann Baptist Friedrich (1796-1862) was born July 31, 1825. He became Professor at the University of his native city of Würzburg in Northern Bavaria in 1857 and in 1858 in the University of Heidelberg. His researches included a study of diseases of the heart, vessels and lungs and on croupous bronchitis. He wrote on these subjects but his outstanding work was that on "Degenerative Atrophy of the Spinal Cord" published in Virchow's Archives in 1863. His earliest work on the subject was in 1861; and, twelve years later, further studies on the same subject were published in contemporary journals: On Ataxia, with special reference to its hereditary form, and a monograph on Progressive muscular atrophy: on true and false muscular atrophy (Berlin 1873).

After suffering for 3 years from an aneurism of the thoracic aorta, he died at the age of 57 on July 6th 1882.
The first communication by Friedreich (1861) referred to a series of cases arising on an inherited diathesis in which a peculiar disorder of motility was associated with overgrowth of connective tissue in the posterior columns.

This description was amplified in 1863 when, under the title of Degenerative Atrophy of the Spinal (cord) posterior columns he gave an account of six cases in two families with three autopsies, discussed the clinical and pathological picture and declared it to be a new disease distinct from the usual type of Duchenne's locomotor ataxy (Kinnier Wilson, Neurology vol.ii. p.943).

Friedreich states that he had particularly favourable opportunities of studying chronic spinal diseases. He had "under continuous observation a relatively significant number of spinal diseases which, etiologically, symptomatologically and anatomically reveal conditions in such complete agreement that I think I am justified in separating them from the collective term 'Tabes Dorsalis' as a particularly clearly defined form of spinal degeneration".

SYMPTOMATOLOGY.

"The most important and characteristic symptoms that strike one are disorders of motor powers, which I found in a surprisingly similar form in all these patients."
The first symptom in every case was a feeling of weakness and continual tiredness in the lower extremities: sometimes first in one, then the other; sometimes in both.

In the course of several years, the condition generally increased to such an extent that walking and standing were greatly impaired, and eventually the sufferers were no longer able to stand upright.

Later, after three to eight years in some cases, to these symptoms were superadded sensations of weakness in the upper limbs also."

AETIOLOGY.

"It is noteworthy that the appearance of the first symptoms of the disease in all cases occurred at the beginning of puberty or shortly after its completion, and this circumstance seemed to show that those changes in the human organism which accompany the phases of sexual development must have exercised a decisive and preponderating influence on the origin of this illness.

While in general the aetiological relations of diseases of the spinal cord are still beyond the bounds of our knowledge, yet in the types of disease described there are examples of definite aetiological influence.

Firstly, it is noteworthy that the appearance of the/"
the first symptoms of the disease occurred at the age of puberty or soon after; and this circumstance seems to show that those changes in the human organism which accompany the phases of sexual development, and with which we are not yet sufficiently acquainted must have exercised a decisive and preponderating influence on the origin of this illness. Thus it will be noted that the age at which the disease began in the six foregoing cases ranged from 15 to 18.

In Case II an immediate and striking aggravation of the disease after childbirth seemed to indicate a certain connection between the degenerative process in the spinal cord and the events of sexual life. As to the sex of patients affected, it can be seen that 2 are male and 4 female; but the number of cases is obviously too small for us to conclude that women are more prone to the disease, and further observation is required on this point."

I may add, at this juncture, that Friedreich attributes to the drunkenness of the Father, even at the time of conception of the child, a part, at least, of the ensuing disease.

**THERAPEUTICS.**

"In none of the cases was this followed by any decided or permanent improvement; and when one considers the nature of the pathological changes that take place in the cord in this disease, one can hardly think seriously of successfully combatting the condition./
condition. The most that one could look for would be, perhaps, a restriction of the pathological process at the beginning of the illness or at least the achievement of longer periods of inactivity.

Although at the time the patients first came under observation, the symptoms were already developed to such a pronounced degree that every hope of successful treatment vanished at once, yet no method was left untried which might have been justified from a rational point of view or might have been indicated on empirical grounds. Cod liver oil, iodine iron (Jodeisen), preparations of Silver Nitrate etc, were administered continuously in individual cases and in gradually increasing doses, yet there was no trace of even a temporary success.

Just as little improvement in the symptoms was gained by the application of douches to the back, the use of baths, electric current or of hot irons on both sides of the vertebral column.

It was, indeed, discouraging to see how, in spite of all these methods, in individual cases the symptoms of the disease became steadily worse, visibly even though gradually. Now and then an obvious halt in the process was recognisable during a time when the patients had been treated purely dietetically, without any therapeutic interference.
Chiefly affecting the spinal cord, it begins in the lumbar region (Lendenabschnitt), spreads thence both upwards and downwards, and ends in the boundaries of the cord, having affected the roots and stems of the hypoglossal nerves.

**HISTOLOGICAL APPEARANCES.**

The affection is clinically marked by a very gradually developing disorder (ataxia) in the function of co-ordinated movement, spreading from the lower to the upper part of the body and finally always attacking the organs of speech whilst sensory powers are at the same time unaffected and complete integrity of the sense organs and cerebral functions is maintained.

There is no paralysis of sphincters and trophic disorders are absent.

Less constant symptoms are curvature of the spine, sensations of giddiness and nystagmus. From the clinical viewpoint, the illness could be designated as chronic progressive paralysis in co-ordination of movement and from the pathological-anatomical point of view/
view as chronic degenerative atrophy of the spinal cord. The point may be passed over, as the distinguishing features will readily reveal themselves to the experienced reader.

Twelve years later, he published further particulars of his well-known six cases, but referred to them then as "Ataxia with special reference to hereditary forms."

**TREATMENT.**

Under this heading, Friedreich notes that "in none of the cases was this followed by any decided or permanent improvement; and, owing to the nature of the changes in the spinal cord, as revealed by post-mortem examination, this could hardly be expected. At the time the patients came under observation, the symptoms were already developed to such a pronounced degree that every hope of successful therapy vanished at once. Yet no method was left untried; drugs, douches, baths, electric current."

Friedreich gives a very careful pathological account of those 3 cases which were examined post-mortem, though the introductory remarks are very general. "While great progress," he says, "has been made recently by scientific medicine in nearly every branch of pathology there is one branch in which less progress/
progress has been made, namely in the pathology of Spinal diseases." He then refers to the indispensability of histological examination and is confident that with increasing clinical and anatomical-pathological research the indefinite Tabes Dorsalis will be resolved into individual, and anatomically separable forms of disease.
The six cases to which Friedreich refers in the foregoing remarks are:-

1. Andreas Lotsch b. 1825, Illness began 18th year. Admitted to hospital age 33. d. age 34. Post-mortem examination.


5. Lisette Süss b. 1826, Illness began 15th year. Admitted to Hospital age 32. Returned home next year, symptoms having increased.

6. Friedrich Süss b. 1838, Illness began 15th year.

The patients were thus from two families: there were two males and four female patients. Three post-mortem examinations were made.

Friedreich's summary is as follows:-

"There is a chronic inflammatory degeneration leading to atrophy of the spinal cord, developing particularly at puberty in those with a hereditary predisposition/
predisposition to the illness. It begins in the lumbar region and spreads both upwards and downwards.

Friedreich refers to certain English writers on affections of the Nervous System, particularly Stanley, Topham, Gull (15 cases of paraplegia, Guy's Hospital Reports vol. IV, 1858), Brown Sequard. Searching through the literature indicated, one anticipated that there would be mention of cases similar to his own. This is not the case, the similarity consisting in the effects of disease or injury on tracts of the spinal cord. Finally, Friedreich refers to the differential diagnosis of the disease he describes – from Chorea, Paralysis Agitans, Senile and trophic tremors etc.– but adds that "although the assertion has been made here and there in individual works on diseases of the Central Nervous System, it is possible for separate tracts of the cord to become diseased. Yet the fact of such isolated affection has never been sufficiently accepted, nor has any attempt to diagnose such conditions clinically ever been made."

Twelve years later he published further particulars of his well-known six cases but now referred to them as "Ataxia, with special reference to Hereditary forms."
I have felt justified in making this rather long extract from the writings of Professor Friedreich; partly because it forms the most natural foundation for subsequent cases and comments, and partly because, though his famous cases are often quoted, I have not come across any other translation into English of this part of his writings.
IV. NATURE OF FRIEDREICH'S ATAXIA.

"Lesions of sclerosis of the posterior cords overlapping into neighbouring bundles are the classical attributes of this affection". (Pierre Klots).

In the spino-cerebellar class of degenerative disease the condition named after Friedreich stands practically alone. Sharp delineation from cognate forms is not always easy, for the atrophic process may extend beyond pathways, lesions of which stamp the affection as a combined sclerosis. Masked by heredo-familial incidence, the clinical syndrome is expressive of degeneration in the dorsal half of the cord and medulla oblongata, a degree of physical infantilism perhaps and occasional presence of developmental anomalies in the nervous system and elsewhere (Kinnier Wilson "Neurology," vol. II, chap. 49).

My Case I illustrates this developmental anomaly. He has, as noted, a spina-bifida of the Vth lumbar vertebra.

Onset is always insidious and the first symptom is invariably weakness in the lower limbs. The upper limbs then become affected and later, speech.

The age of onset is not the same in all affected families, but there appears to be:—

"Fairly close correspondence in this respect in any one family.

"Each/
"Each of the patients manifested gross signs of the disease at the same age."

(Giddings, Journal of American Medical Association 1927, Vol.89, p.1395 on "Friedreich's Ataxia in 10 members of a family.")

Two of the three members of the C. family first showed the earliest manifestations of the disease not long after they had reached school age.

There is thus a critical age in any affected family and if this age be passed unscathed by a year or two, such members of the family are unlikely to be affected.

It is pointed out that the age of onset must cause variation in type of case (Julia Bell). "If the process sets in early, when tissues are still developing and plastic, a maximum effect is more readily produced than at a later period when greater resistance of healthy tissue may be looked for".

Sex. The sexes are equally prone to the disease. Course and Duration. The disease is occasionally aborted or remains in abeyance for long periods. Usually, however, it progresses rapidly and patient becomes bedridden.

Members of an affected family may, on examination, show symptoms of the disease, such as absent knee-jerks, scoliosis, etc. indicating that they are potential sufferers, though the disease has been partially suppressed.

Eyes./
Eyes. Nystagmus is commonly but not always present; usually lateral in type and only to be observed when patient is at rest. It is indicative of morbid change in the region of the oculo-motor nuclei, thus being initiated from a source high up in the central nervous system. It is often a late symptom. Optic Atrophy is observed in some cases: also congenital cataract and strabismus. Muscular atrophy of hands only or of upper extremity, lower extremity or both upper and lower extremities.

Some patients suffering from Friedreich's Ataxia show a fine, titubant (staggering, restless) tremor; others gross choreiform twitches.

"Saunders, in 1913, made an investigation at the National Hospital, Queen Square, into the sensory changes in Friedreich's Ataxia, all presenting the usual skeletal deformities". He concludes that the sense of position and the recognition of passive movement are always more or less affected, especially in distal parts of the lower limbs. The frequency and consistency with which the elements of sensation are disturbed are indeed characteristic of the disease viz. 1. Sense of position and recognition of passive movement.

2. Appreciation of double contacts and of vibration."

(Bell & Carmichael; Treasury of Human Inheritance", Vol.IV, part 3.)
Inheritance is a most important factor in this disease. "The probability of two parents of unrelated stocks carrying the gene is very small... We have not met with a single case of Friedreich's Ataxia which was demonstrably of dominant, genetic type - i.e. they were markedly of Recessive genetic type."

55 cases examined by J. Bell and E.A. Carmichael include 7 individuals who were the offspring of first cousin marriages, a percentage of 12.7 and they conclude that the first cousin consanguinity rate among cases of hereditary ataxia of recessive type in this country (England and Wales) is not less than 9% and perhaps not higher than 13% though they think the number examined is too small to carry much conviction.

Our present understanding of the workings of inheritance we owe largely to the studies of an Austrian monk, Gregor Johann Mendel 1822-1884. Mendel's great contribution to the Study of Genetics slumbered on until in 1900 it was independently discovered and brought to light. To-day the literature of this subject has grown to be very large. Mendel's cross-breeding experiments with peas showed certain numerical relations among the progeny that gave rise to what has come to be rather indefinitely known as Mendelism, which is not a theory of hereditary origins, but a theory of the manner in which inheritance takes place.
When parents that are unlike in respect to any character are crossed, ordinarily the hybrid progeny of the first generation thus produced will be apparently like one of the parents with respect to the character in question, and not something intermediate between the two. Mendel termed the character that remains apparent the dominant, and the latent character that recedes from view the recessive, because it is covered up by the dominant. (Genetics, Herbert Eugene Walter, p. 54.)
CHARACTERISTIC FEATURES OF FRIEDREICH'S ATAXIA DESCRIBED SINCE FRIEDREICH'S DAY.

The 'classical' syndrome includes ataxia of skeletal musculature, nystagmus, kyphoscoliosis and foot deformity (pes cavus).

Of these, only nystagmus is lacking in my two cases, James and Elsie. This is, however, frequently a later development.

Ataxic gait is always prominent among motor symptoms. It was the first observed feature in my cases and steadily progressed from bad to worse.

Speech also is soon affected and in my first case has become incomprehensible.

With regard to sensory symptoms, one finds a- stereognosis and imperfect conduction from skin surface.

Reflexes. "Knee and ankle jerks vanish with such regularity that their presence has been thought to exclude the disease" (Ladame), but this view is untenable — as may be seen in Byrom Bramwell's cases (recorded in the Atlas of Clinical Medicine I. 1892)

"Oculomotor paralyses (ptosis, strabismus, external rectus palsy and other types) are very infrequent". (Kinnier Wilson, Neurology p.949). The accompanying photograph shows the strabismus in James' right eye.

Cerebral and General Symptoms. It is said that patients/
patients suffering from Friedreich's Ataxia are frequently of a fair degree of intelligence. This is certainly the case with regard to my patients, who are both fully as alert mentally as most of their age.

"The characteristic foot deformity is not alluded to in Friedreich's original account; Charcot giving its first description". It was one of the first features observed by me in my first patient James C., helping me to make the diagnosis.

The term "ataxia", that is not-orderly (or disorderly) is said to have been in use before the days of Hippocrates: and Hippocrates, (in Precepts XIV) quoted by Julia Bell (preface to Treasury of Human Inheritance, Vol. IV, part III) says that Ataxia, that is irregularity, in a disease signifies that it will be a long one.

Although previously applied to various disorders, it is now restricted to those in which there is want of co-ordination of voluntary movements. This seems to be a very natural use of such a term. When associated with the name of Friedreich, it connotes a very definite disease with typical symptoms differentiating it from other diseases in which Ataxia is a leading symptom. The term Ataxia was evidently not in use in 1863 to describe this condition, for Friedreich in his paper used the title "On degenerative Atrophy of the Spinal Cord". Later, in 1876 he published another paper, with the title "On Ataxia, with special reference to the hereditary form".
Friedreich's Ataxia is a rare disorder in which a degeneration of the nervous system produces at first a loss of power in the lower extremities. The patient sways as he stands, and walks with difficulty.

Later, the Ataxis involves the trunk, arms, and head, speech becomes difficult and advanced cases may be unable to sit up. The condition is inherited as a simple recessive, and, consequently, it can hardly ever arise except from a mating between two heterozygotes. Their offspring will almost always be of the normal (dominant) type; for only when they marry a close relative is there any reasonable possibility of a back-cross result, which would show that the ostensibly healthy partner in the union is really a heterozygote. Still less is it likely that a marriage between two affected persons will ever be observed. Thus it is clear that those suffering from a rare disease inherited as a simple recessive will almost always have normal parents and, at first sight, the condition will appear merely sporadically in the history of affected families (Genetics for Medical Students", E.B. Ford, Oxford, Feb. 1942. p.16).

It is very well observed by Fraser Roberts ("An Introduction to Medical Genetics", Oxford University Press, 1940, p.253) that "The discovery that heredity is a factor in aetiology is not an indication that further/
further medical progress is impossible". He adds: "One peculiar feature about genetic observations is that they are so frequently made incidentally during the course of work primarily concerned with other departments of medicine. Thus, a physician comes across a family group displaying a rare, hereditary abnormality, and decides to place the facts on record. A further peculiarity of genetic observations is that they do not lose their usefulness with the passage of time. Unlike observations in most departments of medicine, which are comparatively rapidly replaced by the new results of newer methods, fresh genetic observations are simply added to the old. A careful family history may be more useful a hundred years later than on the day upon which it was written.

There is no need to be daunted because of the difficulty of seeing or obtaining information about remote relatives. The close relatives are much more important. Actually, records of parents, sibs and children only, with enquiry as to consanguineous marriages, would be thoroughly adequate for some of the most useful studies."

"An inherited abnormality is the primary cause of Friedreich's Ataxia, the disease being transmitted by persons affected or unaffected. The mode of inheritance says W.R. Brain, (Diseases of Nervous System 1940) cannot be satisfactorily explained on the assumption that/
that the disease behaves as a single Mendelian character whether dominant or recessive. The best interpretation is that it depends on the presence of two Mendelian characters, one dominant, the other recessive. It has long been held that parental alcoholism may cause the disease by damaging germinal material."

This was stated by Friedreich, among others, but it does not appear in any member of the family concerned in my cases: it does not seem to me to be justifiable as a suggested cause, "and the facts of heredity do not need any speculation of this kind". (Kinnier Wilson).

Apart from inheritance, aetiological factors are unknown, according to Kinnier Wilson (Neurology p. vol.II) who states that the disease is comparatively rare among nervous affections. At the National Hospital from 1909 to 1925 (17 years) there were 15,923 admissions: of these, 73 were Friedreich's Ataxia or about 0.4%.

No geographical, racial, or social peculiarities are discernible, except perhaps a higher rate of occurrence in England and America than in Germany.
VI. ASSOCIATED CONDITIONS.

LESIONS.

In recent and older contributions to the literature, I have found references to Diabetes Mellitus, Cardiac changes, haemolytic anaemia etc. associated with Friedreich's Ataxia.

Schlezinger and Goldstein, New York, (Archives of Neurology and Psychiatry 1939) (Chicago) report two cases of Friedreich's Ataxia, sisters.

CASE I. Aged 13. History of unsteady walking at age of 6 and steady development of typical symptoms until age of 15, when she developed, in addition, the symptoms of Diabetes Mellitus.

CASE II. Aged 22. Hospital. This girl showed symptoms of Friedreich's ataxia at the age of 15, with the onset of menstruation; the difficulty of walking being the first symptom. Diabetes began at age of 21.

These writers consider it is important that in all instances of this combination of diseases (Friedreich's Ataxia and Diabetes Mellitus) the onset of Friedreich's Ataxia preceded that of Diabetes. They also state that the combination has been reported in no less than 18 cases. Familial incidence has been reported four times, affecting a total of nine patients. Diabetes was present only in siblings affected by Friedreich's Ataxia. "Literature", (these authors add) "shows/
shows the association of Diabetes Mellitus in 18 cases", to which they add two.

W. Harris Best (Lancet, Feb. 1899) reported the case of a girl who began at age of seven to suffer from characteristic symptoms of Friedreich's Ataxia following the same course as that of a sister two years older. At the age of 14 (Aug. 23rd 1898) she suddenly developed polyuria and thirst typical of Diabetes Mellitus, of which she died nine days later.

Two sisters who had Friedreich's Ataxia together with Diabetes Mellitus are described by Störring and Schönberg in Zeitschrift für Neurologie and Psychiatrie 1935 (O L III).

Charlotte Lotsch, one of Friedreich's 6 cases already referred to, suffered from Diabetes Mellitus, in addition to her Ataxia.

THE HEART IN FRIEDREICH'S ATAXIA.

In my cases, no abnormality has been observed in the heart's action, either by myself or by the medical men under whose charge both James and Elsie have been, when in hospital for a short period.

M.M. Georges Guillain and Pierre Mollaret, (Societe de Biologie 17th Sept. 1932) however reported a case of a boy suffering from Friedreich's Ataxia, who entered the Salpétrière and on whom electrocardiographic observations were made "according to custom". Radioscopic/
Radioscopic examination showed a heart and aorta of normal measurements. The electrocardiogram, made the same day, was also normal, apart from the slight oscillation ("tremble du trace") "habitual in Friedreich's Ataxia". Subsequent tracings taken because of tachycardia, revealed for the first time some modifications.

Rhythm ranged between 110 and 120 and two extra-auricular systoles were noted.

Two cases were reported in "Bulletin et Mémoires de la Société Medicale des hopitaux de Paris" (18th May 1936.)

1st Case: Boy, aged 16 when Friedreich's ataxia first observed. Examination of circulatory apparatus showed no abnormality. At age of 19, various rhythmic disturbances appeared, chiefly tachycardia; and very marked electrocardiac modification, though auscultation revealed only extra systoles and muffled bruits. Pulse rate 100.

2nd Case: Affected by Friedreich's ataxia from age of thirteen.

When aged 30, suddenly seized by dyspnoea and palpitation: tachycardia (120) and cardiac bruits developed. Shortly after several paroxysmal tachycardial crises occurred, alternating with complete arrhythmia and Cheyne-Stokes respiration. Cardiac insufficiency followed, with oedema of lower limbs and fall in pulse tension/
tension. Electrocardiograms showed many alterations. Dyspnoea, rhythmic disturbances, oliguria and oedema increased and patient died suddenly.

Post-mortem the coronary arteries were found intact, contrary to the hypothesis of some French collaborators, and the writers conclude with the observation that the nervous origin of the original disease (Friedreich's Ataxia) is likewise responsible for the heart condition.

In this connection there is a further report by Evans and Wright (of the Cardiac Department, London Hospital, 1942).

They remark that it has been the custom to regard Friedreich's Ataxia as affecting only the Central Nervous System, but "an examination of 38 cases has convinced us that the heart also is often affected." In their opinion the investigation of the subject of Friedreich's Ataxia is incomplete without electrocardiography and cardioscopy.

Their first patient was a young woman who, in addition to being a sufferer from Friedreich's Ataxia, had Stokes-Adams attacks. The point of particular interest was that her brother, similarly affected, had died at the age of 18 during an attack.

SUMMARY AND CONCLUSIONS by Evans and Wright.

The Electrocardiogram was specially studied in 38 cases and they were convinced that the condition may sometimes be as much an affection of the heart as of/
of the nervous system". In only one patient, with Stokes-Adams disease, did clinical examination of the heart show any abnormality, the pulse being slow from complete heart-block and irregular from extra systoles. Cardioscopy showed slight enlargement of the left ventricle in 8 and 5 of these had prominent cardiographic changes. The cardiogram showed significant or conspicuous changes in 13 of the 38 patients. They found that nerve signs were "more widespread in patients with the more conspicuous cardiographic changes."

Haemolytic Disease accompanying Friedreich's Ataxia is described by M.M. Lemaire, Dumolard & Portier.

Two brothers, North African (Berber) tribesmen, mendicants, aged 23 and 25 respectively. Both were suffering from Friedreich's Ataxis of several years duration.

On admission to hospital (23rd Oct. 1936), both were suffering from marked anaemia and splenomegaly.

Case I. Red blood corpuscle count 2,240,000
White corpuscles 4,400
Pulse Rate 78.

Case II. Red blood corpuscle count 1,940,000
White corpuscles 10,400
Pulse Rate 84.

Both patients left hospital on 12th Feb. 1937, "whilst laboratory evidence of haemolytic condition were still present."
IDIocy ASSOCIATED WITH FRIEDREICH'S ATAXIA.

M.J. Nolan (Dublin Journal of Medical Science XCIX 369–382 Dublin 1895) gives an account of three cases of "genetous" idiocy associated with Friedreich's Ataxia.

It is, however, generally agreed that the mental condition of patients suffering from Friedreich's Ataxia is not affected and that their intellectual capacity is sometimes of a high standard. My own cases bear this out, though lack of education has greatly thwarted progress.

SPINA BIFIDA.

This condition, due to failure of union of the cartilaginous bars to form the vertebral arch during the fourth month of foetal life most commonly occurs in the lumbosacral region. Usually associated with anomalies of the spinal medulla and its membranes, it may occur alone - spina bifida occulta.

This, as shown in the accompanying X-ray photograph, is present in the case of James. Spina bifida is comparatively common. It is said to be met with, in about one out of every thousand births, (Thomson & Miles Surgery vol.II, p.454) though Kinnier Wilson's figures do not support this (Neurology p.1418). With regard to this anomaly and its association with Friedreich's Ataxia, Bell & Carmichael say that though it/
it is one of the most frequent of anomalies so associated yet information regarding Spina Bifida Occulta is manifestly very incomplete. It is only recognisable when looked for by X-ray examination and is believed to be no rarity in the general population. (Treasury of Human Inheritance Vol.IV, part 3, p.165). The Vth lumbar vertebra is the one affected in the case illustrated though in the position of the IVth lumbar vertebra spine there is a very distinct gap into which the finger sinks as one runs it down the vertebral column.

Eye defects occasionally noted in association with Ataxia of all clinical or genetic types include congenital cataract and strabismus. In perhaps the large majority of cases the eyes show no abnormality except nystagmus. (Treasury of Human Inheritance Vol.IV, part III. Bell & Carmichael).

In the boy James C. there is, thus far, no nystagmus; but there is strabismus affecting the right eye, as will be seen from the photograph.

Moreover, in a cousin (lately deceased) of Mrs C. there was cataract either congenital or at a very early age. This is referred to in Genealogy, p.6a.

There is no optic atrophy, a condition sometimes associated with Friedrech's Ataxia.

Two/
Two first cousins of Mrs C., the children's mother, (a son and daughter of Mrs Bs.) were definitely defective. Hugh was below the average physically: he suffered from asthma and died about the age of 40 from some chest affection, not tubercular. Mary was much below the average in size and looked like a girl of twelve when she was twenty-eight. She was an albino and had cataract and an epibulbar dermoid in one eye. She did not marry, and died recently at the age of about forty, but her death took place on the Mainland and the cause is unknown to me.

Another daughter of Mrs Bs., happily married and with four apparently healthy children, lives in Egilshay. In her thirties, in 1939, she was suddenly affected with "Infantile paralysis." I did not recognise this at first but as development took place it became obvious. She was in the Astley-Ainslie Institute for some time, but, when war broke out, she preferred to return home. Her condition is stationary and she remains cheerful and contented.
VII. PROGNOSIS.

The prognosis, in cases of Friedreich's Ataxia, cannot, I think even at the best be very sanguine. Bell & Carmichael (p.153 Treasury of Human Inheritance Vol.IV, part III) do not appear to think that we have sufficient information regarding the expectation of life. In some cases there is a "stationary phase" and it may be that the distinguished writer on the subject, M. Pierre Mollaret, had such a patient under his care when he ascribed improvement to treatment. Julia Bell, however, states that the disease tends to limit the life of its victim to something approaching sixteen years ...."moreover the average short life of patients after the age of onset, must tend very mercifully to control and limit the reproduction of affected families as a whole." Another writer states that the duration of life, after commencement of the disease, is twenty years. This is applicable to my two definitely affected patients, who will not be able to marry, however long they may live. I have observed these two children for over ten years and have seen them steadily becoming worse. Even if the advance of the disease should be halted, their condition would still be deplorable. Friedreich's well-known cases lived to the early thirties; and many cases have been recorded of patients living to middle age.
Though it is now more than 30 years since Professor Friedreich wrote his famous treatise, treatment of this condition has made no advance.

Though powerless to influence the course of the disease, we should not hesitate to treat symptoms with a view to temporary improvement. Notwithstanding spinal degeneration, tenotomy should be practised e.g. in a talipes equino-varus, if thereby walking is helped be it only for a time (Kinnier Wilson).

In my two cases I would not advise even this, for it would merely be an addition to the sum of physical suffering already borne.

Electrical treatment has been tried by various investigators, beginning with Friedreich, only to be abandoned.

M. Pierre Mollaret presented a case before the Paris Neurological Society on May 4th 1939 - a youth suffering from Friedreich's Ataxia, to whom he had given Vitamin C. for nearly 3 years. 3 tablets of 5 centigrammes of Ascorbic acid were given daily, each corresponding to 1000 international units and 20 tablets were given at the beginning of each month. The boy returned for examination every 6 months; and, on each occasion he was presented before the Neurological Clinique of the Salpêtrière. M. Mollaret affirmed that 6 months from the beginning of treatment there was/
was improvement. This led me to adopt the same treatment in my cases, following so illustrious a writer. I cannot, however, say that there is any evidence of improvement, though their mother thinks that Elsie is better than she was. One can only conclude that treatment in M. Mollaret's case merely coincided with a temporary retardation of symptoms which is sometimes seen in Friedreich's Ataxia. M. Mollaret adds that he has tried the same treatment in other cases but sufficient time had not elapsed to enable him to judge of the result.

Since then the War has prevented our obtaining any further guidance from this source.

Recently I wrote to Professor Mollaret at the Salpêtrière Hospital for Nervous Diseases in Paris asking him if he still found improvement in his Friedreich's Ataxia cases.

He replied that he would have liked to report progress but during the German occupation there had been no opportunity for laboratory investigations and he was unable to do so, but promised to send me his publications on the subject.
IX. RISKS OF TRANSMISSION IN A FAMILY IN WHICH THERE ARE CASES OF FRIEDREICH'S ATAXIA.

"It is particularly important that those who belong to a family in which a dangerous recessive disease has appeared should not marry a near relation". (Genetics for Medical Students, p.138)

My patient's parents cannot be said to have been nearly related, being the children of second cousins. Yet there is hardly a family on the island of Egilshay to which they are not more or less connected as well as many in Westray and Rousay.

The question of marriage will certainly not arise in the case of James or Elsie; but it might, in some fifteen years, in the case of Alfred, who, at present, has no indication of disease except the significant absence of knee-jerks or patellar reflexes. It would be important that he should not marry in the Orkney islands around his home, otherwise the serious recessive defect which he inherits might be doubled. No doubt, "an extensive programme of positive eugenics is one for the distant future and the question of eugenic reform encroaches upon one of the special preserves of the fanatic, the problem of Race" (Ford). The tragedy of such diseases as Friedreich's Ataxia compels one to think that marriage is often too lightly undertaken. Sir Thomas More is, I believe, the earliest English writer to draw attention to the subject. In his imaginary island of Utopia, he describes/
describes the measures taken to prevent the transmission of disease in those who contemplate marriage. These measures consist merely of an examination for any external blemishes in man and woman. Nevertheless, Sir Thomas More* continues to emphasise the wisdom of the inhabitants of the Island in this matter, showing that he had this idea of preventive medicine very much at heart. It is to be regretted that subsequent generations have not built upon this foundation.

Sir Thomas More (in the reign of Henry VIIIth of England) in "Utopia" (1516) expresses views which I think have a definite bearing on the possible avoidance of tragedies such as the continuance of Friedreich's Ataxia and similar inherited diseases.

If a combination of Sir Thomas More's wisdom together with the doctrines of Mendel (or Eugenics) were to be part of our medical training, it would, in due time, permeate society, greatly to its benefit.

Premarital Examination Laws exist in thirty of the United States of America - the requirements varying in the different States. Seventeen require examination only for syphilis: others demand absence of tuberculosis, mental defectiveness, chronic alcoholism. In commenting on the action of the laws dealing with premarital examinations, Foster and Shaughnessy point out that the differences in the various States would have been eliminated if there had been some central authority to co-ordinate them (Journal of American Medical Association 1942 118, 790.)

* Utopia, Every man series. p.85.
"This American experience should be of value to this country if it should ever decide to make the issue of a marriage licence depend upon medical evidence of a clean bill of health for the contracting parties. Were we living in Erehwon a certificate of psychological fitness would also be a stipulation" (British Medical Journal, Sept. 5th 1942, p. 285). In similar vein, a well-known Metropolitan magistrate remarks: "Perhaps, in some more enlightened and utopian age, we may see the establishment of a Ministry of Marriage and, before any couple are permitted to marry they will have to obtain a licence certifying a clean bill of health.

If a knowledge of the Highway Code is considered essential for the purpose of saving lives upon the roads, some similar instruction might well be worth while if we could thereby do something to minimise the countless tragedies of the marriage state". "What is really needed is more difficult marriage". (G.K. Chesterton).

Henderson and Gillespie ("A Text Book of Psychology" p. 45) express their views thus:-- There are people who ask for help and advice in regard to marriage, but the advice given is usually acted upon only when it coincides with the applicant's own ideas. It is not wise to dogmatise ...... it is a matter that can only be approached/
approached when the public are so enlightened as to realise for themselves the difficulties, the trials and the sorrow which the propagation of defective stock means, both to the parents and the offspring. An attempt should be made to mould public opinion to the appreciation of its vast importance." These remarks have a direct bearing on Friedreich's Ataxia for we do not know how it originates, its "causa causans"; and, in some States of America, Sterilisation is demanded in those so afflicted. (Journal of American Medical Association 1927 vol.89, p.1395).

"Sterilisation has been strongly advocated as a certain and permanent method for preventing the birth of unhealthy children" (Henderson and Gillespie p.42). There are, no doubt, cases in which this drastic step may be advised, though it does not commend itself as desirable in my cases. As already stated, marriage cannot be considered in the case of the two actively affected, James and Elsie; and Alfred, if he reaches marriage age unaffected outwardly might marry with no more than ordinary risk, provided he married outside Orkney.

"In/
"In choosing wives and husbands, they observe earnestly and straytelye a custom which seemed to us very fond and foolish. For a sad (i.e. sedate) and an honest matron showeth the woman, be she maid or widow, naked to the wooer.

And likewise a sage and discreet man exhibiteth the wooer naked to the woman.

At this custom we laughed and disallowed it as foolish. But they, on the other part, do greatly wonder at the folly of all other nations, which in buying a colt, whereas a little money is in hazard, be so chary and circumspect that, though he be almost bare, yet they will not buy him, unless the saddle and all the harness be taken off, lest under those coverings be hid some gall or sore.

And yet, in choosing a wife, which shall be either pleasure or displeasure to them all their life after, they be so reckless that, all the residue of the woman's body being covered with clothes they esteem (i.e. estimate) her scarcely by one handbreadth, (for they can see no more but her face) and so to join her to them not without great jeopardy of evil-agreeing together, if anything in her body afterward should chance to offend and mislike them.

For all men be not so wise as to have respect to the virtuous conditions of the party. And the endowments of the body cause the virtues of the mind more to/
to be esteemed and regarded; yea, even in the marriages of wise men. Verily so foul deformity may be hid under those coverings that it may quite alienate and take away the man's mind from his wife, when it shall not be lawful for their bodies to be separate again.

If such deformity happen by any chance after the marriage is consummated and finished, well, there is no remedy but patience. Every man must take his fortune "well a worth". But it were well done that a law were made whereby all such deceits might be eschewed and avoided beforehand."

The principle involved in the foregoing pre-marital examination as described by the author of "Utopia", is that marriage, whilst losing none of its romantic, aesthetic and mysterious attraction, should nevertheless be regarded, at least in the abstract, as being fraught with very great responsibility.

No doubt it is so regarded by the vast majority of people; but the responsibility has reference rather to the ability to support wife and perhaps a family on the available income and very seldom to the much more serious responsibility of passing on one's inherited or acquired characteristics.

We now know, moreover, that the child inherits, not merely from its parents, but from grandparents and more remote ancestors. Hence the importance of a good family tree.

It/
It is not to be supposed that such facts will have any weight with young people on the verge of marriage. But it is to be hoped that, as time goes on, emphasis will be laid rather on a good health inheritance than on wealth and social position.

It is, I think, desirable that this should be impressed on the minds of medical students who are to be the future guides to the Nation in matters relating to health. Both Sir Thomas More and Gregor Mendel have given us wise counsel, to which we would do well to take heed.
In the foregoing pages I have given some particulars about the islands in which my practice lies, before introducing the subject of Friedreich's Ataxia. I have then related the history of the C. family and described the symptoms as I have seen them in these cases. Following this I have given a brief resumé of Friedreich's original description in 1863 and some characteristic features of Friedreich's Ataxia described since Friedreich's day, mentioning the congenital deformities associated with this disease.

I have then referred to the Prognosis in cases of Friedreich's Ataxia and made some comments on Treatment.

I have given some genealogical notes and discussed the risks of transmission of the disease in a family in which there are cases of Friedreich's Ataxia. Subsequently I have discussed the question of marriage, sterilisation, etc, and laid emphasis on the value of Public Health Measures and of the Study of Eugenics.

Finally I have given a list of some of the books consulted.
Woo Ter (A.C.) & Parks (B.S.), Friedrich's ataxia.

Ross (A.T.), Combination of Friedrich's ataxia and Charcot-Marie-Tooth atrophy in each of 2 brothers.

van Bogaert (L.) & Moreau (M.), Combination de l'amyotrophie de Charcot-Marie-Tooth et de la maladie de Friedrich chez plusieurs membres d'une même famille.

Schlezinger (N.S.) & Goldstein (K.), Freidreich's ataxia associated with diabetes mellitus.

Mollaré (P.), Maladie de Friedrich n'atteignant qu'un jumeau.
Amélioration régulière depuis 3 ans après vitaminothérapie.

Bøtt (E.), Un caso de asociación de enfermedad de Friedrich con cardiopatía.

Yang (C.S.) et al., Hereditary ataxia; familial occurrence in 5 generations.

Turner (E.V.) & Roberts (E.), Family with sex-linked hereditary ataxia.

Hassin (G.B.), Freidreich's ataxia; histopathologic study.

Klotz (H.P.), Notions recentes sur la parenté de diverses amyotrophies et ataxies familiales.

Lauber (C.) & Hier de Balsac (R.), A propos des troubles cardiaques de la maladie de Friedrich.

Dubre(r) et al, Modification electrocardiographiques chez un enfant atteint de maladie de Friedreich, et chez son père. Type coronarien du tracé électrique chez l'enfant.

van Bogaert (A.) & Bogaert (L.), A propos des altérations de l'électrocardiogramme dans la maladie de Friedreich.

Schachter (H.), Maladie de Friedreich avec troubles endocriniens (nanosomie, vitiligo et leucotryptie).
Rev.belge sc.méd. 9: 341-345, May, 1937.

Guillain (G.) & Mollaret (P.), Maladie de Friedreich avec altérations electrocardiographiques progressives et solitaires.
BABONNEIX (M.L.), Maladie de Friedreich et Spécificité congénitale.

GUILLEMIN (G.) & MOLLARET (P.), Considérations cliniques et physiologiques sur la maladie de Friedreich: l'héredo-dégénération spino-cérébelleuse.
La Presse medicale No.73. 1417-1420; 13 Sept. 1933.

WHYTE (J. Mackie), Four cases of Friedreich's ataxia with a critical digest of recent literature on the subject.
Brain. 21: 72-137; 1898.

ORMED (J.A.), On the so-called hereditary ataxia, first described by Friedreich.
Brain 7: 105-116; 1884-1885.

GULL(W.), Cases of Paraplegia: second series.
Guy's Hospital Reports. 4: 3rd Series. 169-208; 1853.

BELL (J.) & CARMICHAEL (E.A.), On Hereditary ataxia & spastic paraplegia.

NORMAN (R.M.), Primary degeneration of the granular layer of the cerebellum: an unusual form of familial cerebellar atrophy occurring in early life.
Brain. 63: 365-379; 1940.

GUILLEMIN (G.) ET AL: Les lésions sus-médullaires dans la maladie de Friedreich.
Comptes rendus Société de Biologie, 111: 965-967; 1932.

MOLLARET (P.), Maladie de Friedreich n'atteignant qu'un jumeau.
Amélioration régulière depuis 3 ans après vitaminothérapie.
C. Revue neurologique 71: 603-607; May, 1939.

Reports of Societies:
CATON (R.), Dr. R. Caton read a report on 3 cases of Friedreich's ataxia in one family.

FRIEDREICH (N.), Ueber degenerative Atrophie der spinalen Hinterstränge.

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XI. BIBLIOGRAPHY.

Archives of Neurology & Psychiatry 1939 (Chicago).
Bramwell, Byrom. Atlas I & II.
Four cases of Friedreich's Ataxia, Mackie Whyte.
Genetics, H.E. Walter.
do. for Medical Students. E.B. Ford.
London Hospital Report 1942.
do. Purves Stewart.
N.Y. Medical Record, Kellogg 1914.
Sometimes I think. Sir Gervais Rentoul.
Text Book of Nervous Diseases, Oppenheim (trans. Bruce)
Treasury of Human Inheritance, J. Bell & Carmichael.
(Ualton Lab., London Univ.)
Utopia, Sir Thos. More (Everyman Library).