

THE RELATIONSHIP BETWEEN PROGRESSIVE MUSCULAR
ATROPHY AND THE MUSCULAR DYSTROPHIES.

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My attention has recently been directed to the subject of progressive muscular atrophy by having had under my care, within a comparatively short time of one another, two cases showing marked degeneration of certain muscle groups.

These cases are illustrative of two types of muscular atrophy which, according to present day teaching, are separate and distinct from each other, viz: progressive muscular atrophy and muscular dystrophy.

It must be admitted however that the distinction between the two groups is not always so apparent clinically as might be inferred from a text-book study of the conditions. To quote no less an authority than the late Sir William Osler "The whole question is in a chaotic state, and it is at present better to keep to the old divisions. Even if it should turn out to be true, as Strumpell suggests, that all the forms depend upon a congenital tendency of the motor system to degenerate, they represent well-defined clinical types into which cases can, as a rule, be grouped without difficulty, while corresponding to each is a fairly well-determined anatomical basis." ¹

My own observations, though necessarily limited to/

to a small number of cases, have raised considerable doubt in my mind as to whether the distinction between progressive muscular atrophy and the myopathies is not too arbitrary. After all we are dealing with diseases the primary causal factor of which is unknown and it would not be difficult to point to parallel instances where erroneous distinctions between groups of symptoms, labelled as separate diseases, have been based on equally vague premises.

That the muscular dystrophies may owe their origin to degeneration of the sympathetic nerve supply to the affected muscles is a theory advanced by Edwin Bramwell in his Bradshaw Lecture of November 1925.² If this be so they can no longer be looked upon as primary or idiopathic diseases of muscle, but would appear to possess at least two features in common with progressive muscular atrophy, namely, impaired nerve supply or consequent degeneration of muscle fibres.

It is my purpose in what follows, to review the whole question of the relation of progressive muscular atrophy to the so-called muscular dystrophies. These two principal divisions of the muscular atrophies owe their existence to the fact that definite changes in the central nervous system are associated with the one, while no constant nervous changes have been demonstrated in the other.

The/

The names identified with each group are as vague as is our knowledge of the etiology of the diseases they indicate. For our purpose let us select the two which describe the main features of each without committing us to any theory as to their causation, namely, progressive muscular atrophy and muscular dystrophy. The analogy between the two conditions is sufficiently indicated by the similarity in the terms used to describe them.

HISTORICAL OUTLINE.

Our earliest records of progressive muscular atrophy as a definite disease we owe to two French physicians, Aran-Duchenne and Cruveilhier. Charcot subdivided the disease into two types, the one, as he believed, associated with degeneration confined to the anterior horn cells resulting in simple wasting; the other resulting from involvement of both upper and lower motor neurones and characterised by spasticity which frequently precedes the atrophy. To the former the name progressive muscular atrophy of the Aran-Duchenne type was given, while the latter was placed in a separate category under the heading of Amyotrophic lateral sclerosis. It must be admitted that the distinction seems unnecessary and Gowers among others believed the two conditions to be different manifestations of the same disease.

The names of Erb, Gowers and Marie are associated with much of the early work on this subject, particularly with the differentiation of progressive muscular atrophy from the muscular dystrophies.

C L A S S I F I C A T I O N .

The usual classification of progressive muscular atrophy which has been adopted is based upon the preponderance of certain symptoms in each case, three main subdivisions are thus formed:

- (a) Progressive muscular atrophy of spinal origin;
- (b) Amyotrophic lateral sclerosis; and (c) Progressive bulbar paralysis.

To my mind a better classification is one based on the anatomical distribution of the symptoms such as the following:-

(A) Involving trunk and limbs.

1. Atrophic type.

- (a) Local slowly progressing.
- (b) General rapidly progressing.

2. Spastic Atrophic type.

- (a) Spasticity and atrophy coincident in same muscles.
- (b) Atrophy affects upper limbs and spasticity lower.

3. Pure spastic type.

In this spasticity in the lower extremities precedes atrophy in the upper by months or years.

(B) Involving muscles supplied by the brain stem.(Bulbar form)

1. Pure atrophic bulbar paralysis.
2. Spastic atrophic bulbar paralysis.
3. Pure spastic bulbar paralysis.

There is no hard and fast line of demarcation between any of the foregoing varieties, for example, as the disease progresses practically all the voluntary muscles ultimately become involved, hence this classification can only be used to simplify description in the more typical cases.

Let us now glance for a moment at the dystrophies, these may be grouped clinically as follows:-

1. Pseudo-hypertrophic type.
2. Erb's juvenile type.
3. Facioscapulohumeral type.
(Landouzy-Déjérine)
4. Distal type.

The familial and hereditary muscular atrophies do not fit into either of the preceding classifications; they are (a) the peroneal muscular atrophy
of/

of Charcot, Marie and Tooth, and (b) the Werdnig-Hoffmann disease or progressive spinal muscular atrophy of children.

In order to define what is meant by the terms progressive muscular atrophy and muscular dystrophy, as at present used, we must rely upon the known nervous changes in the former, while our conception of the latter will be based largely upon negative findings where the nervous system is concerned. Both possess the common feature of a gradually progressing degeneration which may affect any of the skeletal muscles.

In progressive muscular atrophy the following changes are constant:-

- (a) Atrophy of the motor cells in the ascending frontal convolution, accompanied by degeneration in the pyramidal tracts.
- (b) Atrophy of the anterior horn cells and their axons, resulting in trophic changes in the muscles.
- (c) Atrophy of the white matter of the cord which does not affect the posterior columns.

It is remarkable that in many cases no symptoms are/

are referable to the affection of the anterior and antero-lateral columns which is always present.

The muscles present a granular and fatty degeneration of their fibres which are ultimately replaced by connective tissue.

Turning now to the dystrophies we find that they have hitherto been excluded from the preceding category by the absence of demonstrable lesions of the nervous system. Here again muscular atrophy is the chief clinical feature of the condition. The exact nature of the changes in the affected muscles will be dealt with more fully later on, for the present suffice it to say that they may closely resemble those found in progressive muscular atrophy, though in most cases differences are to be noted.

E T I O L O G Y.

Little is at present known regarding the etiology of these conditions. Progressive muscular atrophy has its main incidence between the ages of 30 and 40, affecting males three times more frequently than females. Injury has been credited with the production of certain cases, while syphilis may be a factor in others..

Heredity as a rule has an unimportant influence if we except the progressive muscular atrophy of children and the peroneal type of muscular atrophy. These are absolutely separate and distinct types of progressive muscular atrophy arising in early life.

They help, however, to co-relate our two main groups in that they are familiar and hereditary, while at the same time they show definite nerve lesions.

The dystrophies usually set in before puberty but may occur at any age. The pseudo-hypertrophic form is exceedingly rare in its occurrence after childhood.

Of Erb's cases 56 per cent showed a hereditary predisposition to the disease.

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In this type of atrophy we again find males more frequently affected than females. Other etiological factors have been suggested from time to time but have not so far emerged from the realm of surmise into that of scientific fact.

CLINICAL FEATURES AND COURSE.

As a general rule the onset of progressive muscular atrophy is insidious though an acute onset is not unknown. There may be vague sensory manifestations such as pains in the limbs and partial anaesthesiae. Paralysis of a spastic or flaccid type appears in the affected muscles, which show the characteristic fibrillary tremors so long as the disease is actively progressing.

A partial reaction of degeneration is often present, A C C being greater than K C C. The reaction to both faradic and galvanic stimulation is diminished.

It is characteristic of the disease that the superficial, or skin reflexes, should be abnormally brisk. Other involvements of the pyramidal tract cause diminution in the reflex excitability of the skin.

Tendon reflexes, at least in the early stages, are as a rule exaggerated. Babinski's and Romberg's signs are frequently met with. Loss of sexual power is an early symptom.

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Though atrophy may begin in any group of muscles, we generally find it commencing in the short muscles of the hand, ultimately, when it has involved the forearm also, there is developed the "main en griffe" of Duchenne. Of the shoulder muscles the deltoid is usually the first to suffer.

Having spread to the trunk muscles the disease steadily progresses. It may show remissions from time to time, but there is no evidence that permanent arrest ever takes place.

It has been stated that the upper part of the trapezius survives longer than the other muscles of the shoulder girdle. ("Ultimum moriens" - Duchenne.) As a rule the sphincters are not affected, at least until a very late stage.

When the disease spreads to or commences in the muscles supplied by nerves arising in the motor nuclei of the medulla the first symptom noticed is defective speech. Later the muscles of mastication and deglutition atrophy and swallowing becomes difficult.

The prognosis is most hopeful in the slowly progressing/

progressing local cases which usually last for many years. The worst type is a generalised flaccid atrophy which may prove fatal within a few months of its onset. The bulbar type comes between these two in regard to rate of progress, having an average duration of about one year.

Death generally results from pulmonary complications or a sudden exacerbation of all the symptoms with involvement of the muscles of respiration. Mental changes are common in the later stages.

The only cases in which treatment has been shown to produce any amelioration are those in which there is a history of syphilis, and the appropriate treatment in such cases is by no means always followed by improvement.

As regards the muscular dystrophies, we again find that the varieties which have been described are but different manifestations of the same disease.

The pseudo-hypertrophic form is the most constant in its symptoms and course. It affects boys more frequently than girls, usually commencing before puberty. More than one member of the same family may suffer, and it is frequently hereditary, being transmitted/

transmitted through apparently healthy females to their offspring.

The muscles most often primarily involved are those of the pelvic girdle. Pseudo-hypertrophy first becomes apparent in the gluteal region, the calves of the legs and in the infraspinati.

Frequently the deltoids, triceps and supraspinati also show enlargement.

The child is easily tired, falls frequently and has difficulty in rising. The legs are widely separated in standing, and there is well marked lordosis.

A very characteristic feature is the way in which the child rises from the supine position. He first rolls over into the prone position, raises himself on knees and elbows, then on feet and hands. From this attitude he assumes the erect position by pushing his body up by means of hands and arms, climbing up his legs as it has been described.

The facies is distinctive, it is dull and expressionless, the mouth being open and the lips protruding. It has been stated that the muscles of mastication and deglutition are never affected.

Three varieties of dystrophy remain to be studied, namely Erb's juvenile type, the facioscapulohumeral type of Landouzy-Déjérine and the distal type.

In these the sexes suffer equally and the common age of onset is later - 15 to 35 . Heredity has an important influence in most cases. The so-called juvenile type begins in the muscles of the shoulder and pelvic girdles. The facioscapulohumeral, as the name suggests, begins in the face, shoulders and upper arms, while the distal type commences in the legs and forearms.

The diagnosis of these conditions is based largely on their distribution as well as the absence of demonstrable nervous changes. A few observers such as Foix and Nicolosco have described phenomena referable to the nervous system as occurring in the myopathies.³ Erb considers that his juvenile form is not a pure myopathy but depends on structural and functional changes in the trophic cells of the anterior horn.⁴ These findings have not been confirmed by others, and this naturally raises a doubt as to whether the cases described were pure dystrophies or, as seems more probable, atypical forms of progressive muscular atrophy.

More particularly in those cases occurring in early adult life the progress of the disease is slow and usually confined to the groups of muscles primarily involved, so that a fatal termination is rare, the patient generally dying from some inter-current disease.

PATHOGENESIS AND MORBID ANATOMY.

In contrasting the two main forms of muscular atrophy now under discussion, it will be necessary to refer more fully to the pathological findings in each.

In progressive muscular atrophy very definite changes occur in the cerebrospinal nervous system. The primary lesion appears to be degeneration of the anterior horns of the cord, which, macroscopically, often appear shrunken and of a pinkish colour. At the same time the motor nuclei in the brain stem also show degenerative changes. Microscopically in these localities there is seen shrinkage of nerve cells accompanied by disappearance of Nissl's granules. The cells ultimately disappear entirely, being replaced by neuroglia. During the atrophic process there are deposited within the cells masses of yellow pigment which displace the nuclei.

"Pari passu" with these changes the motor fibres in the corresponding peripheral nerves degenerate. In exceptional cases however, though atrophy in the anterior horns and intermedullary roots may be well established, no corresponding change can be found in the/

the peripheral nerves. No explanation of this phenomenon has so far been forthcoming.

The cells of Betz in the precentral motor cortex also atrophy and disappear, but in their case the process commences in the distal ends of the axons and reaches the cortex by extending up the pyramidal fibres.

Degeneration is not confined to the motor system only, for some degree of atrophy in the afferent cerebrospinal tracts is constantly present.

The degeneration of nervous elements takes place cell by cell and fibre by fibre, healthy cells being mixed with dead and dying. It is therefore not surprising to find that the muscles atrophy in a similar manner, fibre by fibre. Hence the sluggish reaction to electrical stimulation and, at times, a partial reaction of degeneration.

What then are the histological changes which are commonly regarded as distinguishing the dystrophies from progressive muscular atrophy? Leaving aside for the moment the vexed question of the presence or absence of nerve lesions in the former, we find that a section from an affected muscle/

muscle in a case of muscular dystrophy shows the features about to be described.

In the early stages there is enlargement of some of the muscle fibres, variously described as swelling⁵ or hypertrophy.⁶ The enlarged muscle fibres may show simply the appearance of hypertrophy and may be well striated. Not infrequently they show signs of degeneration, their transverse striation being lost and their aspect being homogeneous and hyaline, with vacuolation in places. There is an increase in the number of sarcolemma nuclei in the affected fibres. At a later stage numerous small fibres make their appearance. These are accounted for by some as being simply atrophied fibres, others claim that they arise by longitudinal fission of hypertrophied fibres. These small fibres show much the same features as the large ones, some being well striated, while others have a homogeneous appearance.

As the disease progresses there is an increase in the connective tissue septa between the fibres and, especially in the pseudo-hypertrophic form, a tendency for fat to be deposited in this situation.

Thickening of the walls of the intra-muscular arterioles is usually present, and though no doubt

a contributory factor to the atrophy in certain cases, there is no evidence that is the cause of it.

The replacement of muscular by fibrous tissue is most marked in the neighbourhood of tendinous attachments.

Ultimately the picture presented is that of a few scattered fibres, some larger than normal, others small, atrophic and irregularly shrunken, separated by a large amount of fibrous and fatty tissue.

Buzzard and Greenfield sum up the changes occurring in muscle in progressive muscular atrophy as follows:-

"The changes in affected muscles are of an atrophic character, and they are characterised by the fact that different bundles show different degrees of shrinkage. Microscopical sections show that the fibres are diminished in calibre, although retaining a certain amount of transverse striation. Some bundles show a complete absence of muscular tissue, the fibres having been replaced by clumps of sarcolemma nuclei which undergo proliferation during the process of atrophy. Occasional swollen fibres are seen, and these may present other degenerative changes in the shape of fissures and vacuolation.

While/

While there is considerable increase of fibrous tissue, it is noticeable that an excess of fat, such as is seen in myopathic diseases, is never laid down!"⁷

When we consider, therefore, the actual changes in the muscles themselves, we find a striking similarity between progressive muscular atrophy and the dystrophies. In each type the muscles are pale and flabby. Affected fibres show vacuolation and fissuring, they lose their striation and are eventually replaced by connective tissue. The nuclei increase and remain to mark the site of the fibres even when all other normal muscular tissue may have disappeared. That all the new fibrous tissue formed is not due to metaplasia of the muscle fibres is clearly shown by signs of active proliferation of the perimysium. Oppenheim in summing up the differences between the two diseases makes the following statement.

"Finally we must point out that not a few cases have been described which, from their clinical features, appear to be related as well to the spinal as to the myopathic and neuritic forms of progressive muscular atrophy, and can be completely included neither in the one nor the other group." (Observations of Strumpell, Pick, Abundo, Cassiree, Haushalter, Cohn, K. Mendel and others.)⁸

We are therefore forced to the conclusion that so far no really essential difference has been described between the muscle changes in the dystrophies and those found in progressive muscular atrophy. It is equally obvious that minor differences do exist. For example large muscle fibres preponderate in the early stages of the former, whereas they are scanty or absent in the latter. Fat is deposited in the interstitial connective tissue of the muscles in many cases of dystrophy, but this process is entirely absent in progressive muscular atrophy. Thickening of the walls of the intra-muscular blood vessels occurs in the dystrophies but not in the other variety of muscular atrophy.

It now remains for us to discover at least a working hypothesis which will explain the similarity as well as the differences between the two main groups of muscular atrophy with which we have been dealing.

Edwin Bramwell in his theory of the causation of the dystrophies points out that the muscles involved are those which develop early in foetal life, and were, in the process of evolution, originally concerned with the maintenance of posture. Even at the present time they are to a large extent used for/

for the fixation of limbs and trunk during the action of other muscles.

This, as will be seen later, is an important observation as it supports his assumption that, in all probability, a lesion of the sympathetic nerve fibres is a contributory factor to the degeneration.

Why should not this sympathetic derangement be common to certain of the atrophies as well as the dystrophies? If this should be so, we have the explanation of those mysterious cases of muscular atrophy in which there is degeneration of the anterior horn cells, the inter-medullary motor roots and the muscles without any discoverable histological change in the motor fibres of the peripheral nerves.

A perusal of the recent literature on the structure of muscle confirms the supposition that there are two separate neuro-muscular elements to be found in all voluntary muscle in man.

To quote from Sherrington:

"The existence in various invertebrates of muscles separately differentiated for the execution of movements and the maintenance of posture respectively seems without parallel in the skeletal muscles of vertebrates. In the latter one and the same muscle are used for the same purpose, though some muscles are predominantly concerned with the one, some with the other function."⁹

The researches of Hunter have thrown valuable light on how and by what mechanism these different functions are subserved.¹⁰ He points out that the same/

same muscle fibres do not undertake both functions. The evidence in support of this contention is found (a) in the structural differences in the two kinds of fibres in striated muscle; (b) in the different mode of innervation of thick and thin fibres; (c) in the different results produced by section of medullated (somatic) and unmedullated (sympathetic) nerves passing respectively to the thick and thin fibres; and (d) in the effects of stimulation of the sympathetic.

The anatomical distinction between the two varieties of striated muscle is summarised by Schafer as follows:-

"In the rabbit, as pointed out by Ranvier and Krause, certain voluntary muscles present differences in appearance and mode of action from the rest. Thus while most of the voluntary muscles have a pale aspect, and contract energetically when stimulated, some are at once distinguished by their deep red colour, as well as their slow and prolonged contraction when stimulated. When subjected to microscopical examination it is found that in the red muscles the fibres are more distinctly striated longitudinally and the transverse striae are more irregular than usual. The muscle fibres are generally/

generally finer (thinner) than those of ordinary muscle, and have a large amount of sarcoplasm. The nuclei are more numerous and are not confined to the inner surface of the sarcolemma, but occur scattered in the thickness of the fibre as well. There is also a difference in the blood supply to the two kinds of muscle a similar difference between red and pale muscles may also be seen in the rays among fishes. In other animals the distinction is not found as regards whole muscles. This is the case as shown by Klein, in the diaphragm in which in many of the fibres there are numerous nuclei, and these are inbedded in the protoplasm (sarcoplasm) which forms an almost continuous layer underneath the sarcolemma. The distribution of the two kinds of fibres in different muscles has been specially investigated by Grutzner.¹¹

According to Hunter there are in skeletal muscles two distinct sets of muscle fibres arranged in groups each with its own specific innervation and consequently its own specific function.

The fibres receiving somatic nerve endings are concerned in shortening as the result of voluntary and of reflex activity and in isometric contraction during continuation of the stimulation. During these movements the fibres innervated by the sympathetic/
etic/

sympathetic system are inhibited, then lengthened or shortened and remain in the new position passively imposed upon them. They are comparable to the "fixing muscles" of invertebrates.

The relative increase in large muscle fibres in the dystrophies and their partial or complete disappearance in many cases of progressive muscular atrophy lends colour to the theory that the trophic influences from the sympathetic are at fault in the former, while the influence of the somatic nerves is impaired in the latter. Less commonly other cases arise in which both sympathetic and somatic nerves are involved, these constitute the border-line types which have hitherto been so difficult to account for.

The relatively great size of some of the large fibres seen in muscular dystrophy may be accounted for by supposing that, as the fibres innervated by the sympathetic atrophy, the large fibres hypertrophy in order to take on to some extent the fixing function of the small fibres. As under other circumstances this compensatory hypertrophy of muscle is succeeded by atrophy and fibrosis, a change which is no doubt accelerated by vascular degeneration.

Referring to the not infrequent involvement of the pituitary body in these cases, as evidenced by/

by hypoglycaemia, excessive deposition of fat in the tissues and defective sexual development, Bramwell is of opinion that this is due to a common cause rather than that the muscular changes follow any endocrine deficiency.

Bearing in mind the close relationship between the nervous and endocrine systems, it is possible that any agent acting harmfully upon the one would also adversely affect the other.

ILLUSTRATIVE CASES.

My first illustrative case is one of muscular dystrophy of Erb's "Juvenile type" which, owing to its extremely local distribution and the deformity resulting therefrom, appears to be of unusual interest. Notes on this case have already been published.¹²

The patient, a soldier in an infantry regiment, age 25, service 6 years and 10 months, first came to my notice in February 1925 when he was in the British Station Hospital, Secunderabad for a fortnight on account of a contusion of the right shoulder resulting from a fall in the gymnasium. At that time it was noticed that owing to a pre-existing "malformation" of his shoulders he was unable to elevate his arms above the horizontal. In September of the same year he reappeared complaining that he found the disability due to his deformity increasing.

There was nothing in the family history indicating that the defect was hereditary or due to injury at birth. His father was alive and well at the age of 63. His mother died at the age of 53 from meningitis following erysipelas. He was one of a family/

family of thirteen. All his brothers and sisters were alive and, as far as he knew, normal, with the exception of one brother killed in France, and one who died at the age of 32 from "heart disease" said to have followed an attack of rheumatic fever at the age of 12. He himself was married and had two normal children aged 3 and 6 respectively.

He stated that he had always been healthy, the only illness he could recall was an attack of influenza at the age of 14 on account of which he attended a dispensary for three weeks.

On the 31st December, 1918, he enlisted in London and, according to his own statement there was then absolutely no limitation of the movements of the arms. There was no note at that date in his medical history sheet of the defect.

He stated that in the Summer of 1920, while acting as drill instructor at his regimental depot, he first noticed difficulty in elevating his outstretched arms, the difficulty had steadily increased since then, also his shoulders had become rounded and sloping.

On examination he was seen to be a well developed man of average height. A feature which struck the eye/

eye at once was the narrowness of his shoulders, an appearance which was enhanced by the fact that the outer extremity of the shoulder girdle on either side was thrown forward, and by the conical shape of the neck resulting from the tightly stretched elevators of the scapula and supra-scapular portions of the trapezii.

His chest fully expanded measured $34\frac{1}{2}$ inches, considerably below the average for a man of his height which was 5 ft. $9\frac{1}{2}$ inches. The range of expansion was only $2\frac{1}{2}$ inches. On enlistment his chest measurement was 34 inches and the expansion 3 inches.

On examining his back, with the arms hanging at rest by the sides, the scapulae were found to be raised and their superior angles carried forward so that they came to lie three quarters of an inch above, and one and a quarter inches behind the posterior borders of their respective clavicles. A line joining the superior and inferior angles instead of being almost vertical, with a slight lateral inclination at its lower end, sloped towards the spinal column. The vertebral borders were prominent. The inferior angles reached the level of the 5th intercostal space.

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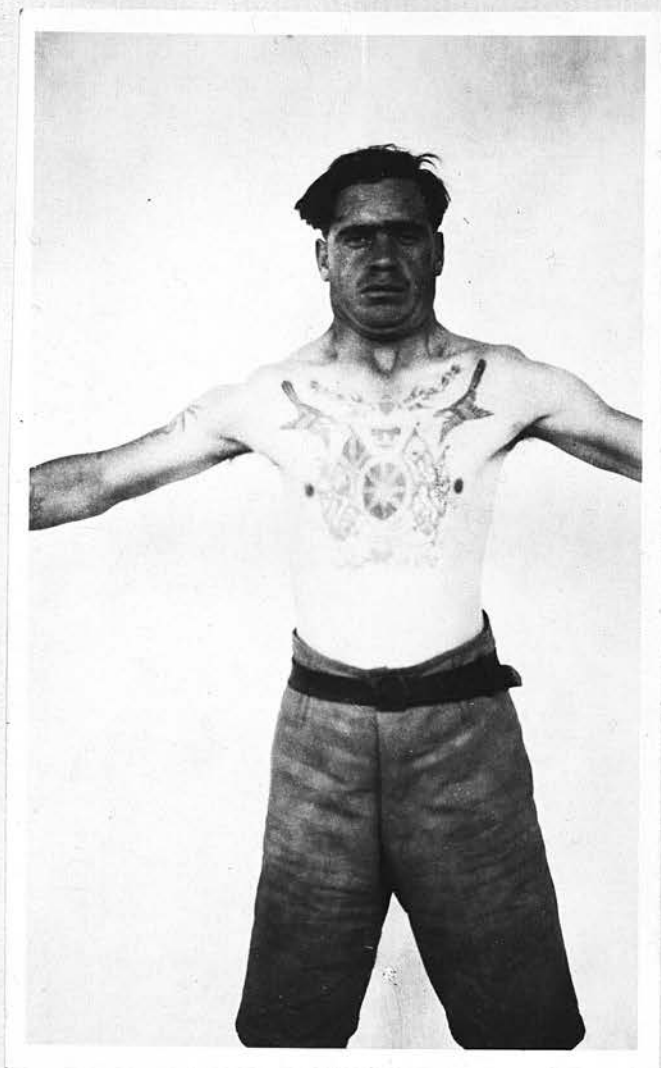


Fig. 1.

Case No. 1.

The arms are in the position of maximum active elevation. The muscular effort involved in maintaining this attitude is apparent from photograph.

The lower portion of the trapezius on either side was wasted, though the supra-clavicular portion was unaffected. The rhomboids were weak and the sternal portion of each pectoralis major was poorly developed. The muscle showing the greatest amount of atrophy was the serratus anterior, the outline of this muscle could not be traced on either side.

Owing to the displacement of the scapulae their articular surfaces were inclined downwards and forwards, thus limiting upward movement of the humerus. The upper arms could not be raised through more than an angle of 80° either in a lateral or anterior direction, the scapulae commenced to rotate when an angle of 45° was reached.

That there was also weakness of neck and back muscles was evidenced by scoliosis and the fact that when at rest the neck was bent forward, there was however no obvious atrophy of the muscles concerned.

The accompanying photographs and radiogram will serve to illustrate the exact nature of the deformity.

No signs of interference with the nerve supply to the affected muscles was discovered. There was no reaction of degeneration and the reflexes were unaltered. Fibrillation was not observed at any time.

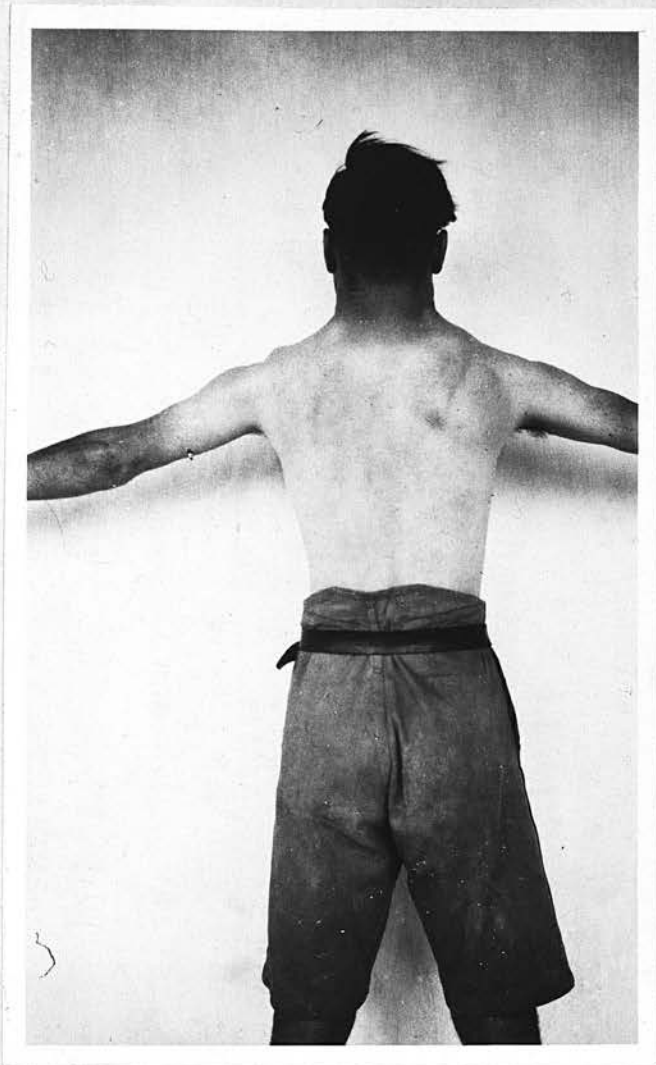


Fig. 2.

Case No. 1.

As in Fig. 1. Back view.

The diagnoses which suggested themselves were (a) interference with the nerve supply to the trapezius; (b) Sprengel's shoulder; (c) Progressive muscular atrophy; and (d) Muscular dystrophy.

A partial lesion of the nerve supply to the trapezii would have resulted in a similar displacement of the scapulae, as is sometimes seen after removal of diseased glands from the posterior triangle of the neck when the nerves have been divided accidentally. The absence of any sign of interruption of the motor nerve supply to the muscles at once disposes of this possibility.

The deformity is suggestive of that due to congenital elevation of the scapula, or Sprengel's Shoulder. A moment's consideration will convince us that this theory is untenable in face of the evidence of his medical history sheet that there was no disability on enlistment.

Our choice therefore must lie between progressive muscular atrophy and muscular dystrophy. In favour of the latter diagnosis we have the distribution in the muscles of the shoulder girdle and the absence of nervous phenomena, especially fibrillation in the affected muscles, though it is true that progressive muscular atrophy may commence in any situation/

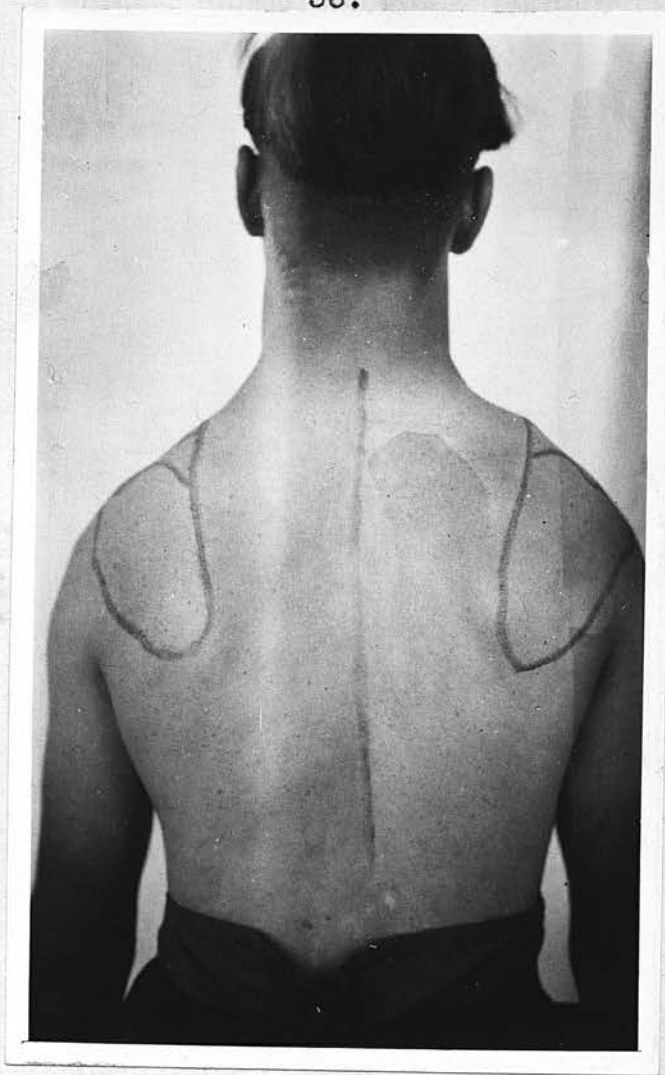


Fig 3.

Case No.1.

Back view, scapula and spinous processes have been outlined on skin.

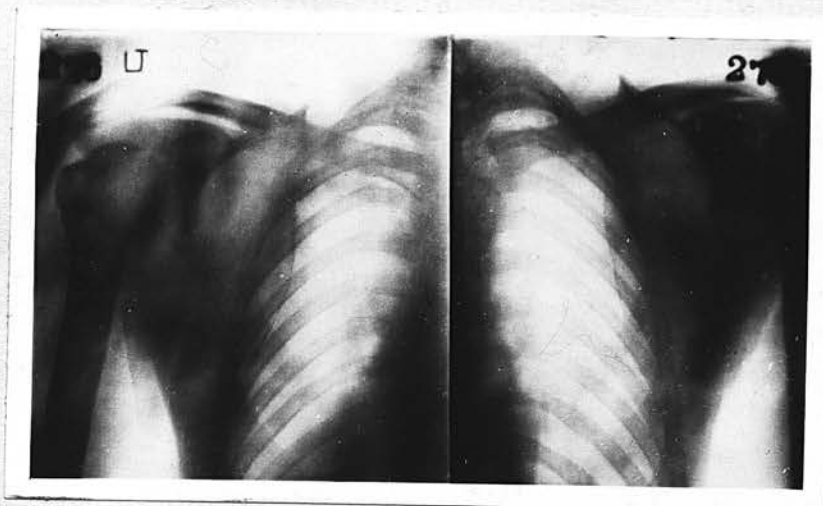


Fig. 4.

Case No. 1.

Radiogram showing displacement of scapulae.

situation and that fibrillation may be absent when the disease is not actively progressing. The age of onset, which must have been in the neighbourhood of 20, favours the diagnosis of muscular dystrophy. Dystrophies of this type, though often hereditary, are not necessarily always so.

On the whole, therefore, it would appear that clinically our patient's case fits best into the category to which it has been assigned, namely, muscular dystrophy.

My second case may be taken to represent a progressive muscular atrophy of the localised type. The patient, an artillery driver, age 23, service $5\frac{1}{2}$ years, gave the following history: In July 1924 he first noticed weakness and stiffness in the left leg. The calf muscles wasted rapidly at first, this was particularly noticeable owing to the alteration in the adjustment of his puttees which became necessary from time to time as a consequence. Slight wasting of the thenar and hypothenar eminences of the left hand was also noticed.

The atrophy progressed rapidly for a month and then came to a sudden standstill, when I saw him in October 1925 it had remained stationary for over a year.

His/

His family history was as follows:-

Father alive and well, aged 62; mother died at the age of 20, cause unknown. He had one sister aged 30, who was said to be healthy.

As regards his previous health, he had suffered from scarlet fever and measles in childhood. While in India he had had several attacks of Malaria for which he was treated with quinine both orally and by injection, the last attack was three years previously.

On examination, with the exception of the affected muscles, he was well developed. The atrophy was most evident in the left lower extremity, left thenar and hypothenar eminences, and to a lesser extent in the short muscles of the right thumb.

The following were the comparative measurements of the lower extremities:-

	<u>Right.</u>	<u>Left.</u>
Calf	14 in.	11½ in.
Thigh	20 in.	17½ in.

Both feet were highly arched, on the left side this amounted to a condition of pes cavus. The intrinsic muscles of the left foot were extremely atrophic.

Fibrillation/

Fibrillation was to be seen from time to time in the affected muscles. The patellar reflex was exaggerated on both sides. The Achilles jerk was active on the right but absent on the left side. The abdominal reflex was easily elicited. Babinski's sign was present on the left but not on the right side. Sensation was unimpaired. Excitability to stimulation with the faradic and galvanic currents was diminished in the left calf muscles, but there was no reaction of degeneration.

This case then is typical of one of those slowly progressing forms of muscular atrophy which long remains localised to the muscles in which it commences.

The differential diagnosis from the distal type of muscular dystrophy depends mainly upon the alterations in the reflexes, though their absence in extreme wasting is common to both diseases. Fibrillation, which was present in this case, is strong confirmatory evidence in favour of our diagnosis.

The age of onset, 22, is below the average for progressive muscular atrophy, but cases have been recorded which occurred even as early as the 12th year. The condition may be distinguished from/

from peroneal muscular atrophy, which generally commences in young subjects, by the absence of a family history of this complaint and by the distribution which in the peroneal type is strictly distal in the muscles themselves, that is affecting the lower ends of the muscles of the thigh and calf while their upper portions remain more or less normal. The presence of an extensor response to the plantar reflex on the left side is strongly in favour of our diagnosis.

The accompanying photograph gives a good idea of the stage to which this case had progressed.



Fig. 5.

Case No. 2.

Showing localised muscular atrophy.

SUMMARY AND CONCLUSIONS.

It has been my endeavour in the foregoing to indicate the essential similarity between the muscular dystrophies and progressive muscular atrophy.

It must be admitted that much histological work still remains to be done before absolute proof of this is attained. Given the material and a proper conception of the neuro-muscular changes involved, it may be confidently expected that ere long an important part of the mystery surrounding the pathogenesis of these diseases will be cleared up. Having attained this stage it would appear that an underlying cause, common to both, might not be beyond the reach of discovery by following up the clues thus provided.

As is well known, progressive muscular atrophy is a disease associated with well-marked changes in the brain and spinal cord, the motor neurons more particularly being affected. Certain cases arise in which central degeneration of the brain and cord is present without what have so far been regarded as the ordinary nerves of supply to the affected muscles being appreciably involved. It would appear not unlikely that in such cases the peripheral lesion will be found in the sympathetic nerves.

This brings us to the consideration of the muscular dystrophies in which, so far, no constant nerve changes have been found. The absence of alteration in the muscle reflexes and electrical reactions, except in so far as they become weak and sluggish, is strongly suggestive of the probability that the "thick" motor fibres are not primarily involved, but that the "thin" fixing fibres innervated by the sympathetic nerves may be the principal sufferers.

Though I am not aware of any work having been done with a view to substantiating this theory, yet it is significant that the dystrophies should, in the early stages, invariably show an increase in the number of large muscle fibres present in the affected muscles.

Until some definite proof to the contrary is adduced there seems little reason to doubt that progressive muscular atrophy and muscular dystrophy are different manifestations of the same disease affecting the neuro-muscular mechanism at different points and in varying degree.

B I B L I O G R A P H Y.

1. Osler, Sir Wm. Principles and Practice of
Medicine. 1905. Edn. V. 936.
2. Bramwell, Edwin. Lancet, 1925. II., 1103 et seq.
3. Foix, C. & Nicolesco, I. Compt. Rendu. Societé
de Biologie, Feb. 15th, 1924, 90. 354-356.
4. Erb. Handbuch der Electrotherapii 1882.
389. - 21 idem.
5. Buzzard, E.F. and Greenfield, J.G., Pathology of
the Nervous System, 1921. 274.
6. Muir, R. Text-Book of Pathology, 1925. 675.
7. Buzzard and Greenfield. Path. of Nerv. Syst.
1921. 67.
8. Oppenheim, H. Text-Book of Nervous Diseases.
Authorised translation by A. Bruce, 1911.
Vol. I. 236.
9. Sherrington, Sir Chas. Brain, 1915. 205.
10. Hunter, J.I. Br. Med. Jour. Jan. 1925, 197 et seq.
11. Schafer, Sir E.S. Quain's Elements of Anatomy,
1912. Vol. II, pt. I. 190.
12. Graham, W.T. Jour. R.A.M.C. 1926. Vol. XLVI, 305.

