PROGRESSIVE MUSCULAR DYSTROPHY

IN CHILDHOOD.

A THESIS

SUBMITTED FOR THE DEGREE OF

DOCTOR OF MEDICINE

IN THE UNIVERSITY OF CAPE TOWN

by

VICTOR DUBOWITZ, B.Sc.,MB.,Ch.B.,D.C.H.

August, 1960.

C O N T E N T S.

"The disease is one of the most interesting, and at the same time most sad, of all those with which we have to deal: interesting on account of its peculiar features and mysterious nature; sad on account of our powerlessness to influence its course.

It is a disease of early life and of early growth. Manifesting itself commonly at the transition from infancy to childhood it develops with the child's development, grows with his growth - so that every increase in stature means an increase in weakness, and each year takes him a step further on the road to a helpless infirmity, and in most cases to an early and inevitable death."

Gowers, 1879.

INTRODUCTION.

The words of Gowers are as true today as they were nearly a century ago. My interest in muscular dystrophy started in 1957 when, as Senior House Officer at Queen Mary's Hospital for Children, Carshalton, Surrey, I first observed a large number of children suffering from this tragic disease. The frustration of helplessly watching its inevitable course stimulated the present study.

After obtaining an initial impression of the condition from my clinical observations and a review of the hospital records between 1920 and 1950, I started a more systematic enquiry.

The present investigation comprises my personal observations on 65 cases ranging in age from 3 to 18 years. Of these, 57 were seen and followed up at Queen Mary's Hospital for Children, and 8 at the Southern Hospital, Dartford, Kent.

The scope of this enquiry was later widened from the initial clinical and genetic aspects to include a detailed study of some of the associated features and complications of the disease.

The histology of the affected muscles has been studied and correlated with the various clinical stages of the disease.

An attempt has been made to assess the incidence of cardiac involvement as shown by the electrocardiograms and pathological changes in the myocardium.

From my clinical impressions there appeared to be a high incidence of mental retardation in association with muscular dystrophy. Becuase of the implications this may have with regard to the aetiology of the disease, this feature has been investigated in greater detail.

In the hope of learning more about the fundamental defect responsible for muscular dystrophy, a histochemical study has been undertaken of the activity of various enzyme systems in affected muscle.

In this thesis electromyographic changes and the serum enzyme levels have been included, although these were not done personally. They have, however, contributed to the diagnosis, while the serum enzyme changes have made a therapeutic trial possible.

DEDICATED

TO

DAVID SMITH

He had the intellect to understand

and the courage to accept.

CHAPTER I.

HISTORICAL SURVEY AND CLASSIFICATION.

Progressive muscular dystrophy in childhood is usually associated with the name of Duchenne, the distinguished French neurologist.

Duchenne, however, was not the first to describe the disease. In 1838 Coste and Gioja (quoted by Schmidt, 1839) recorded two brothers suffering from progressive weakness in the lower limbs, which started at the age of ten years and later became generalised. It was associated with striking enlargement of several muscles. Meryon (1852) gave an account of 9 cases in his paper "On granular and fatty degeneration of the voluntary muscles." The autopsy findings in one of these cases had previously been reported by Partridge (1847). Both these authors commented on the marked enlargement of the calf muscles.

The literature prior to 1852 contained no other reference to the childhood form of progressive muscular dystrophy. Underwood's account (1797) "On the debility of the lower extremities" has been regarded by some recent authors (Bell, 1943; Levison, 1951) as an earlier description of muscular dystrophy. However, the reports of Underwood, as well as those of Badham (1835) and Kennedy (1841), do not resemble muscular dystrophy but are acute conditions more suggestive of poliomyelitis. Adolescent and adult forms of progressive muscular paralyses, on the other hand, were already recognised by Darwell (1830), Bell (1830) and Aran (1850). These early authors did not distinguish between those forms of muscular atrophy associated with diseases of the nervous system and those without neurological abnormality. It is interesting that "fibrillation" of muscle was noted in 22 of 59 cases reviewed by Wachsmuth (1855), indicating that nervous disease was responsible

for a high proportion of these cases.

Duchenne's initial description appeared in 1861 and was followed by numerous case reports in the German and French literature (Kaulich, 1862; Spielman, 1862; Eulenburg, 1865; Fritz, 1865; Griesenberg, 1865; Heller, 1866; Sigmundt, 1866; Bergenon, 1867; Lutz, 1867; Seidel, 1867; Wernich, 1867).

In 1868 Duchenne gave a comprehensive account of the disease based on a study of 13 cases. He defined it as a condition of childhood or adolescence, occurring more frequently in males, and characterised by 1) progressive weakness of movements, initially affecting the muscles of the lower limbs and lumbar spine, gradually getting worse and extending to the upper limbs; 2) enlargement of some of the paralysed muscles and in exceptional cases of almost all; and 3) hyperplasia of interstitial connective tissue in the paralysed muscle with production of abundant fibrous or adipose tissue in the final stages. He suggested the names "paralysie musculaire pseudohypertrophique" to describe the salient clinical features, or "paralysie myosclérosique" in view of the extreme fibrosis of muscle.

Contemporary English literature contained reports by Adams (1868), Hillier (1868), Russell (1869), Foster (1869) and Langdon-Down (1870). Cases were also recorded in America (Ingalls and Webber, 1870), Australia (Smith, 1871) and Denmark (Brünniche, 1874; Bay, 1877).

In 1879 Gowers gave 5 clinical lectures on "Pseudo-hypertrophic muscular paralysis." He described with masterly clarity the features of 21 cases and reviewed 139 cases of previous authors.

In the same year Möbius (1879) commented on the similarity

between the atrophic pelvic-girdle form of muscular weakness described by Leyden (1876) and the pseudo-hypertrophic muscular paralysis of Duchenne.

Landouzy and Déjerine (1884) drew attention to a progressive muscular atrophy affecting the scapulo-humeral muscles, and associated with weakness of the facial musculature. In some cases the facial weakness presented in early childhood as the first manifestation of the disease; whereas in others it only appeared later. (Duchenne had already described 9 cases of this facio-scapulo-humeral form of muscular paralysis in 1872). In 1885 these authors suggested that progressive muscular atrophy should be classified into myopathic atrophies and neuropathic atrophies.*

Erb (1884) described a 'juvenile' form of progressive muscular atrophy with onset in childhood or adolescence. Although the muscles of the back, shoulders and upper arms were usually more severely affected, some cases showed more marked involvement of the pelvic girdle and lower limbs. He commented on points of similarity between the various clinical types of progressive muscular atrophies without neurological involvement and proposed the name "dystrophia musculorum progressiva" to cover the whole group. He subsequently differentiated between childhood and juvenile forms (Erb, 1891).

A different form of progressive muscular atrophy which started in infancy and had a rapidly progressive course was described by Werdnig (1891) and Hoffmann(1892). In these cases autopsy showed degenerative changes in the anterior horn cells and the ventral roots of the spinal cord. This "hereditary progressive spinal muscular atrophy" is quite distinct from progressive muscular dystrophy.

* For details of classifications see Appendix I.

Batten (1910) published a critical review on the primary disorders of muscle and recognised 7 clinical types. Subsequent authors (Spiller, 1913; Hurwitz, 1936) accepted his classification.

In the meantime, advances in genetics stimulated other workers to correlate different modes of inheritance with various clinical patterns. (Weitz, 1921; Diehl, Hansen and v. Ubisch, 1927; Minkowski and Sidler, 1928; Dawidenkow, 1930; Sjövall, 1936; Bell, 1943). Efforts were also made to simplify the clinical classification (Milhorat and Wolff, 1943; Tyler and Wintrobe, 1950; Levison, 1951). Some of these papers brought more confusion than clarity.

It was not until the last decade that more acceptable classifications were formulated. Stevenson (1953) made a study of progressive muscular dystrophy in Northern Ireland and based his classification on genetic and clinical grounds. He accepted Tyler and Wintrobe's concept of a specific childhood form of muscular dystrophy, but applied more rigid criteria, restricting this group to the classical Duchenne type with a sex-linked recessive mode of inheritance. This type was characterized by a) expression solely in the male, b) onset mainly in the first 2 years of life, c) high frequency of pseudo-hypertrophy of calves, d) universal affection of gluteal, thigh adductors, and later scapulo-humeral muscles, and e) rapid progression to inability to walk usually before the age of 12 and death in the teens, the subjects seldom surviving to the age of 20. All his remaining cases were classified as autosomal limb-girdle dystrophy, in which weakness might predominate in either the scapulo-humeral or the pelvi-femoral muscles. He sub-divided this group on the basis of whether facial weakness was present or not.

In the same year, Becker (1953) published a genetic

and clinical study of muscular dystrophy in Baden. He divided his cases on clinical grounds into either shoulder-girdle (descending) or pelvic-girdle (scending) forms. He found no overlap between these two broad groups in any of the families he studied. He further subdivided each clinical group on the basis of genetic differences (Becker 1955, 1957).

Walton and Nattrass (1954) made a detailed clinical study of various forms of progressive muscular dystrophy in North-East England. While retaining the "Duchenne type" as a separate entity, they disagreed with the rigid criteria of Stevenson. They included in this group some cases with the same basic clinical pattern and mode of inheritance but with later onset and relatively slower progression, as well as some female cases. On the other hand, they considered the "limb-girdle" group of Stevenson to be too heterogeneous and were in favour, both from a clinical and a genetic standpoint, of classifying separately those cases with facial involvement. Their classification thus contained three groups. The Duchenne type included the classical pseudo-hypertrophic muscular dystrophy but did not necessarily exclude cases not showing pseudo-hypertrophy. It also embraced some cases of the atrophic pelvi-femoral group starting in childhood. The facio-scapulo-humeral type was characterized by involvement of the facial and scapulo-humeral muscles and sometimes the pelvic girdle. The age of onset varied from early childhood to adult life and the course was essentially benign, often compatible with normal life expectancy. The third group was the limb girdle type in which weakness might predominate in either the shoulder or the pelvic girdle. The facial muscles were not affected. The age of onset varied from late in the first decade to middle age. The course was relatively slow but led to severe disablement and often shortened the life

expectancy.

In 1954 Nattrass reported 8 cases of muscular dystrophy in childhood resembling the Duchenne type but which had a complete or almost complete recovery. He thought that 2 of the cases probably had a form of benign congenital myopathy while the remainder were due to polymyositis. In their monograph on polymyositis, Walton and Adams (1958) also commented on the resemblance of this disease to progressive muscular dystrophy in some cases.

Blyth and Pugh (1959) made a genetic study of muscular dystrophy in childhood. They included patients in whom muscular weakness was apparent before the age of 12 years and subdivided their cases into a "severe group" who were unable to walk by the age of 11 years and a "mild group", still ambulant after that age.

In recent classifications the term pseudo-hypertrophic muscular dystrophy has been avoided as the title of a particular type of the disease. Although pseudo-hypertrophy is common in the classical muscular dystrophy in childhood, it is not invariably present; and it may also occur in other types of progressive muscular dystrophy as well as in polymyositis.

The eponymous title, "Duchenne type", for the rapidly progressive muscular dystrophy starting in the pelvic girdle, is preferable to "childhood type" because a similar pattern may occur in adults, while other forms of progressive muscular dystrophy such as the facio-scapulo-humeral type may also start in childhood.

It will be shown in the present investigation that it is impracticable to lay down rigid clinical or genetic criteria for the "Duchenne type". It is also impossible to obtain clear division of cases into groups based on the criterion of whether they are ambulant at the age of eleven years.

CHAPTER 2.

INHERITANCE.

A. HISTORICAL REVIEW.

The etiology of progressive muscular dystrophy is unknown. The many theories that have been put forward include primary degeneration of the muscle due to defective nutrition (Meryon, 1852); a chronic progressive myositis (Friedreich, 1873); trophic changes in the nerve cells (Erb, 1891) and a disease of the sympathetic nervous system. (Bramwell, 1925).

The only aspect of the etiology that is established is the hereditary character of the disease. It was already recognised by many of the early writers. Meryon commented on the predilection of the disease for the male sex, but was unable to offer any explanation. Wachsmuth (1855) found evidence for an hereditary factor in 19 of the 59 cases he reviewed. It is surprising, on the other hand, that Duchenne's 13 cases of pseudohypertrophic paralysis (1868) were all isolated. A number of the German authors, however, reported multiple cases in the same family. (Heller, 1866, 1867; Seidel, 1867; Wernich, 1867.) Heller described 2 brothers and an illegitimate half-brother (with a mother in common) who had the typical disease, while a maternal uncle had also been affected. In one of the families described by Russell (1869) 3 brothers were affected and in addition 2 maternal uncles and a maternal great-uncle had suffered from the disease. Gowers (1879) described a number of similar family histories in his series. He painted the hereditary aspect in the following words: "In the vast majority of cases the disease appears to own no other causes than those which exist in, and are born with, the individual."

He commented on the fact that, while the disease seemed to affect predominantly males, it was inherited through the mother, who was apparently unaffected.

Attention was drawn to the hereditary factor in cases of facio-scapulo-humeral dystrophy by Duchenne (1872) and Landouzy and Dejerine (1884), and in the juvenile form by Erb. (1884).

It was not until the 1920's that serious attempts were made to define various modes of inheritance in this disease. Weitz (1921) suggested two hypothetical explanations: that there were either 3 separate mechanisms of inheritance (dominant, recessive and sex-linked recessive), or that it was due to a mutation affecting both males and females, after which it was inherited as a dominant with less manifestation in the female.

Diehl, Hansen and V. Ubisch (1927) put forward the hypothesis that two factors (C and D) were involved in the inheritance of the disease. (Their cases conform to the facio-scapulo-humeral type). Only individuals with both factors suffered from the disease, those with factor C were quite normal, while those with factor D had a particular diathesis which the authors were able to recognise. Subsequent workers have been unable to verify this hypothesis.

Minkowski and Sidler (1928) studied 13 cases of muscular dystrophy in 3 generations of a large kindred in an isolated Swiss valley. All the cases had consanguineous parents and the families could be traced back through 10 generations to a common ancestry. The age of onset of the disease varied from 3 to 40 years and the course was variable. Although pseudohypertrophy was a common feature the clinical pattern conformed to the limb-girdle rather than the classical Duchenne type. Minkoswki and Sidler concluded that inheritance was through a "double recessive mechanism."

(Hanhart (1949) made a further study of this kindred and suggested an autosomal recessive pattern of inheritance.)

Davidenkow (1930) postulated 2 forms of inheritance; a simple dominant in the facio-scapulo-humeral type and a dominant inheritance, limited mainly to the male sex, for the remaining forms of the disease.

In recent years there have been further efforts to correlate the various modes of inheritance with specific clinical types. The difficulty has invariably been the lack of accurate definition of the clinical categories and most authors have been aware of the inevitable overlap between the clinical groups.

Bell (1943) tried to correlate 3 clinical groups, ((a) pseudohypertrophic, (b) atrophic without facial involvement and (c) all cases with facial involvement), with the 3 main genetic mechanisms of inheritance (sex-linked recessive, autosomal recessive and autosomal dominant). In her analysis of 1341 cases from the literature and the records at the National Hospital, Queen Square, she concluded that each of the 3 main genetic mechanisms accounted for cases in each of her clinical groups. However, there was a preponderance of sex-linked recessive inheritance in category A, (due presumably to a large proportion of Duchenne-type dystrophy), while the majority of category C showed an autosomal dominant inheritance (in keeping with the experience of other authors for the facio-scapulo-humeral group). Category B had an almost equal distribution of the 3 genetic types. The lack of uniformity of inheritance in any particular group is due partly to the fact that she subdivided her cases on the basis of arbitrary symptoms rather than set clinical patterns, and partly to the occurrence of different modes of inheritance in individual types.

With the aid of church records Tyler and Stephens (1950) were able to compile a pedigree of the 1249 descendants of an immigrant from England with progressive muscular dystrophy, who settled in Salt Lake City at the end of the 18th century. In the 159 affected cases of 6 generations the clinical pattern conformed to the facio-scapulo-humeral type and the inheritance was by an autosomal dominant character with complete penetrance.

In their study of 63 cases of childhood muscular dystrophy in 33 kindreds, Stephens and Tyler (1951) found that inheritance was consistent with a sex-linked recessive mechanism. They also postulated a high mutation rate to account for the large number of isolated cases.

In Levison's series (1951), the majority of his facio-scapulo-humeral cases had an autosomal dominant mode of inheritance, the scapulo-humeral group, an autosomal recessive, and the lower extremity type were either sex-linked (or possibly sex-limited) recessive, autosomal recessive or autosomal dominant. (The latter group included cases of the classical Duchenne as well as the atrophic pelvifemoral types).

Becker (1953, 1957) found that the pelvic-girdle (or ascending) type could be inherited by a sex-linked recessive or an autosomal recessive character. The autosomal recessive cases usually had a more benign course than the sex-linked recessive. In common with the experience of Walton and Nattrass (1954), he also observed cases of adults with typical Duchenne-type dystrophy (but a somewhat slower progression) which had a sex-linked recessive inheritance. On these genetic grounds he suggested a classification of muscular dystrophy with onset in the pelvic girdle or lower limbs into - 1) Malignant X-chromosomal type; 2) Benign X-chromosomal type and 3) Autosomal recessive type.

Category 1 corresponded to the classical pseudohypertrophic dystrophy of Duchenne but also included some cases occurring at a later age. Category 2 was similar in clinical pattern but with a slower progression and usually a later onset. He believed these two groups to be due to two distinct sex-linked recessive genes. Category 3 was similar in clinical pattern to 2, and also embraced the limb-girdle type (starting in the pelvic girdle) of other authors (Walton and Natrass, 1954, Stevenson, 1953).

Stevenson (1953), (1955) and (1958), who applied rigid criteria to his Duchenne group, concluded that they were always inherited through a sex-linked recessive mechanism and that there was a high mutation rate. In his limb-girdle group the inheritance was autosomal recessive with one exception.

Walton (1955), (1956), concluded from an assessment of 102 cases that the Duchenne type was transmitted through a sex-linked recessive gene, (although the disease in typical form might occasionally afflict females), the facio-scapulo-humeral type was inherited as an autosomal dominant character, and the limb-girdle group was usually due to an autosomal recessive trait, but possibly an autosomal dominant in some cases.

Blyth and Pugh (1959) found that their "severe" childhood group was always inherited through a sex-linked recessive (or possibly a sex-limited dominant) mechanism. The "mild" group (still ambulant at age of 11) was heterogenous and could be either sex-linked recessive, autosomal recessive or autosomal dominant.

The"severe" type of Blyth and Pugh conforms to the Duchenne type as defined by Stevenson. All the cases in both these series were males. Two sisters with typical "severe" Duchenne type dystrophy have been reported. (Dubowitz, 1960).

Various authors have commented on the high mutation rate associated with the inheritance of the Duchenne-type dystrophy.

By the use of Haldane's formula (1935) the following estimates have been made:

Stephens & Tyler	(1951)	:	95 per million.
Stevenson	(1953)	:	65 per million.
Walton	(1955)	:	43 per million.

This would indicate one of the highest mutation rates in human disease. The mutation on the X-chromosome may occur in either the male or the female.

B. MATERIAL AND METHODS.

The present series is composed of 65 cases occurring in 55 sibships. 63 are male and 2 (cases 56 and 57) female. Detailed information has been obtained from parents and available relatives. The pedigree charts, which have been condensed, are collectively presented on pages 20 to 38. The birth rank of all sibs of the propositus is given in correct sequence but the members of other generations are only given in sequence where a positive family history is present. The majority of sibs have been personally examined.

C. RESULTS:

Of the 65 cases 41 were isolated. Of the remainder, inheritance was by a definite sex-linked recessive pattern of inheritance in 8 cases and an autosomal recessive pattern in 2.

1. Isolated Cases. Consanguineous marriages occurred in 3 instances, (cases 7, 10 and 36). This is of significance only in case 36 where the parents are related, the father's (II. 9 and III. 27) grandfather (I. 5) being the brother of the propositus' maternal grandmother (I.4). This might increase the possibility of an autosomal recessive gene occurring in both

parents and thus account for the disease in the propositus. In the other two cases the consanguineous marriage occurred prior to the preceding generation and would thus not increase the chances of an autosomal recessive mode of inheritance in the propositus.

2. Definite Sex-linked Recessive Inheritance. This is indicated by the presence of affected maternal uncles or great uncles, the mother herself been unaffected. In addition, where an unaffected woman has affected sons by different unrelated normal fathers, a sex-linked recessive inheritance is responsible.

Case 5 had an affected elder brother who died at the age of 16. His mother had 2 affected brothers (II. 11 and II. 14) who both died aged 14.

Cases 14 and 15 are brothers with the same mother but unrelated fathers. The most likely mode of inheritance is sex-linked recessive.

Case 21 has an unaffected brother of 4. Three previous generations on the maternal side have been affected by the disease. The occurrence of muscular dystrophy in a female (IV. 7) in this family is of particular interest. Her mother (III, 11), who had 2 affected brothers and an affected maternal uncle, was a carrier. Her father was normal. (This patient was reported by Walton (1956, case D1, IV, 1)).

Case 35 has no brothers and 2 normal sisters. His mother had a brother with the same disease who died at the age of 14 (III, 5).

Case 58 has two unaffected brothers aged 21 and 15 and an unaffected sister aged 12. Two miscarriages occurred in this sibship. The mother had 2 brothers with the disease (II. 19 and II. 20) who died at the ages of 15 and 19. The maternal

grandmother had an affected brother (I.5) who died at the age of 19.

Case 60. This patient has an unaffected sister of 14. His mother had a brother (I. 7) affected by the disease.

Case 64. A younger sib aged 13 (III. 6) has a similar pattern of disease to the propositus. A maternal uncle (II. 5), suffering from muscular dystrophy, died at the age of 19. The inheritance is sex-linked recessive.

3. Autosomal Recessive Inheritance. This is indicated by the presence of consanguineous marriages in the parents of the propositus, both of whom are unaffected.

Cases 56 and 57 have 3 unaffected female sibs aged 14, 9 and 4. The parents (III. 10 and III. 11) are first cousins. There is no previous history of the disease. Clawed toes were present in case 57 and also in a sib (IV. 16) not affected by muscular dystrophy. This additional abnormality is probably due to a separate autosomal recessive factor.

4. Mode of Inheritance doubtful. This group contains those families with multiple cases in one generation only and no history of the disease previously.

Case 8. An older brother (III. 24) was affected by the disease and died of pneumonia at the age of 12. 3 brothers aged 23, 22 and 6, and 3 sisters aged 20, 19 and 13 are normal. The one maternal uncle is normal and the 6 maternal aunts have 9 unaffected sons between them.

Cases 26, 27 and 28 are brothers. They have a normal sister aged 3 and there was one miscarriage. The family history on both sides is negative.

Cases 32 and 33 are brothers who have one normal male sib of 17. The mother's two brothers were normal but her sister

(II. 11) had 3 miscarriages and lost 4 sons (III. 35-38). One died aged 11 of poliomyelitis. A second son, who died at 9, had retarded speech and was unable to walk. The exact nature of his illness is not known. The cause of death in the other two sons was also unknown but they did not have any muscular weakness.

Cases 40, 41 and 42 are brothers. Case 40 is the only child of the mother's first marriage. After the death of her husband she married his brother and had two more affected sons.

Cases 48 and 49 are brothers. They have 3 unaffected brothers aged 20, 12 and 11, and 2 unaffected sisters. The family history is negative.

Cases 50, 51 and 52 are brothers and have 2 unaffected female sibs. Apart from a maternal uncle (III. 34) who died in infancy the family history is negative.

D. DISCUSSION:

The presence of a large proportion of isolated cases in this series is in keeping with the findings of other workers. When this occurs in a disease which has a sex-linked recessive pattern of inheritance, it is assumed that the isolated cases are the result of a new mutation on the X-chromosome. In two of the cases in this series (56 and 57) there has been an autosomal recessive mode of inheritance. If one accepts that these two cases are typical Duchenne-type muscular dystrophy, one can then assume that some of the isolated cases may also have an autosomal recessive mode of inheritance.

In the 14 cases of this series discussed in group 4 above, the mode of inheritance cannot be established with certainty. In cases 32 and 33 there is a possibility that a male cousin (III. 36) was also affected, in which case the latter's mother (II, 11) would also be a carrier and the inheritance would then

be sex-linked recessive. In cases 40, 41 and 42 a sex-linked recessive inheritance is a strong possibility. However, since the two fathers were also brothers, there is a greater chance of them both carrying an autosomal recessive gene than if they were unrelated. While this increases the possibility of an autosomal recessive inheritance, the likelihood is still much less than the sex-linked recessive one.

In the remaining cases of this group various mechanisms are possible. Where multiple male cases occur in one generation only, this may be due to a mutation on the X-chromosome of the mother. The disease might then affect 50% of her sons. The chances of 2 boys being affected would then be 1 in 4, and of 3 boys 1 in 8 (or 1 in 8 and 1 in 16 of all children, male and female). In the rare instances where unrelated parents both carry the same autosomal recessive gene, the chances of a child (of either sex) being affected is 1 in 4. The chances of 2 children being affected would then correspondingly be 1 in 16 and of 3 children 1 in 64. The risk with a sex-linked recessive inheritance is therefore 4 times greater than with an autosomal recessive. In addition the chances of a mother carrying a sex-linked recessive gene are far greater than of both parents carrying the autosomal recessive one.

No instances of an autosomal dominant mode of inheritance occurred in this series.

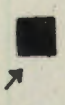
E. CONCLUSIONS.

Muscular dystrophy in childhood of the Duchenne type can be inherited through a sex-linked recessive or an autosomal recessive mechanism. The large proportion of isolated cases are due to new mutations on the X-chromosome or to an autosomal recessive inheritance.

GENETIC CHARTS

KEY:


AFFECTED MALE.

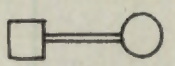

PROPOSITUS.

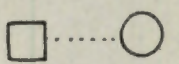

UNAFFECTED FEMALE.

3 INDIVIDUALS, SEX UNKNOWN.


ABORTIONS OR MISCARRIAGES.


STILL-BORN OR DIED IN INFANCY.


CONSANGUINEOUS MARRIAGE.


PARENTS UNMARRIED.

REFERENCE NO. ON CHART, IN THAT GENERATION.

UNAFFECTED MALE AGED 17.


EPILEPTIC.

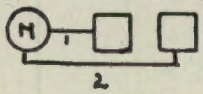

MENTALLY RETARDED.


DEAF AND DUMB.

HYDROCEPHALIC.

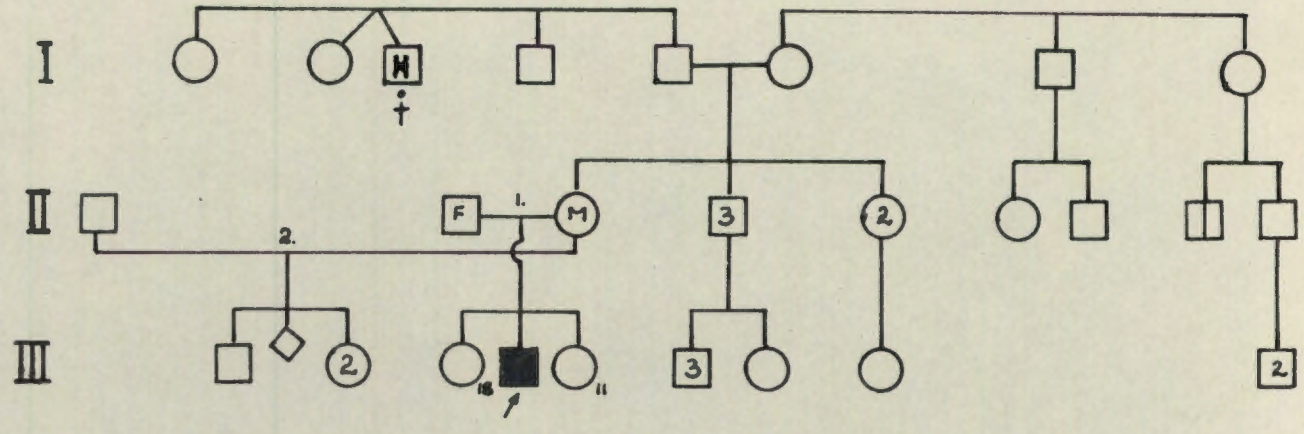
MENTAL DISEASE.

MOTHER.

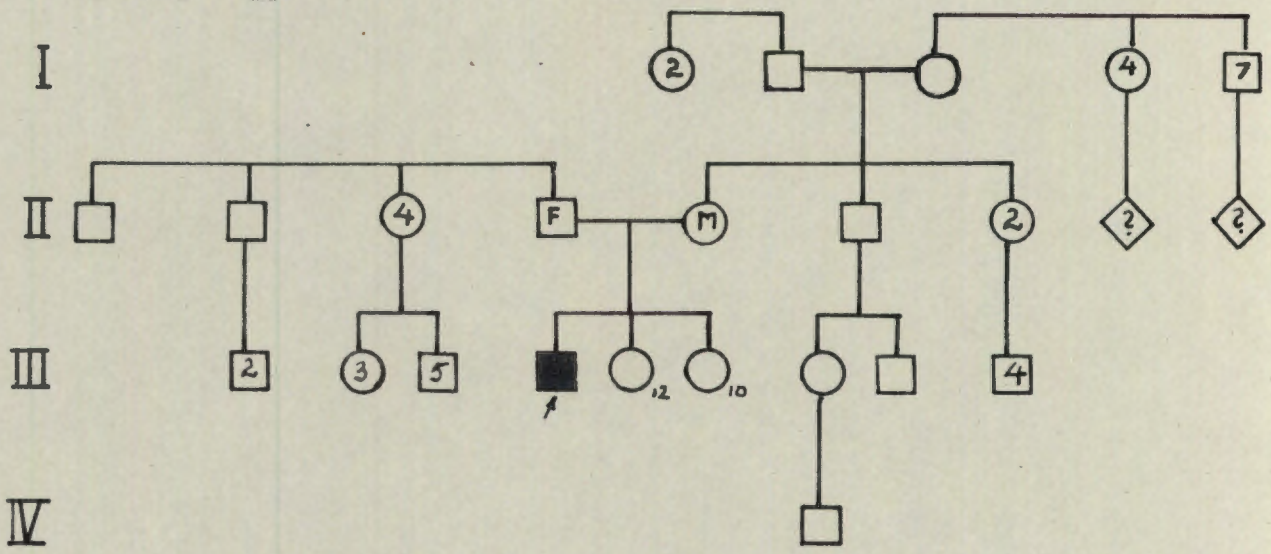


MULTIPLE MARRIAGES.

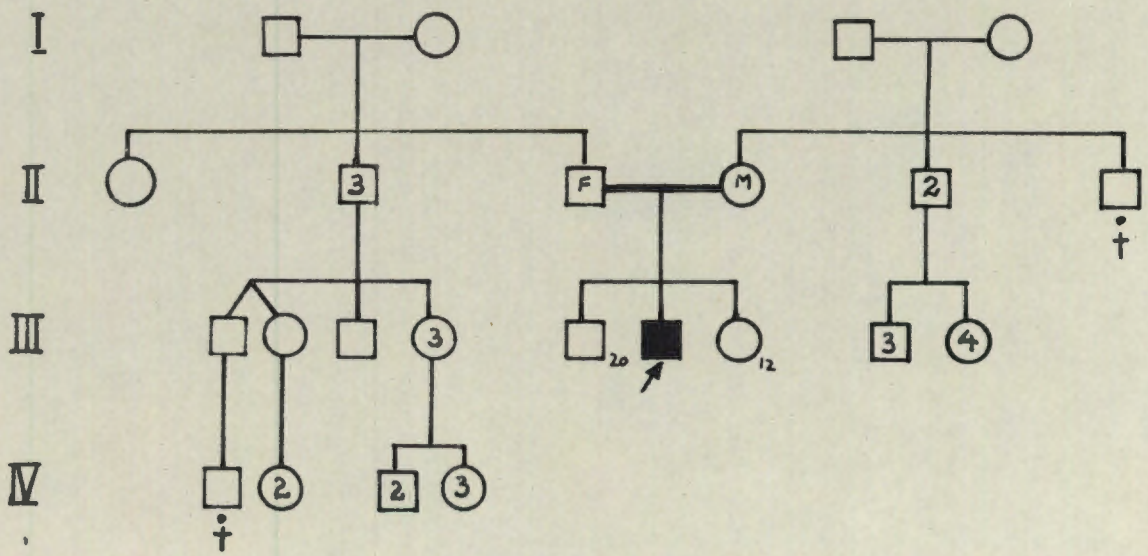
Case 1



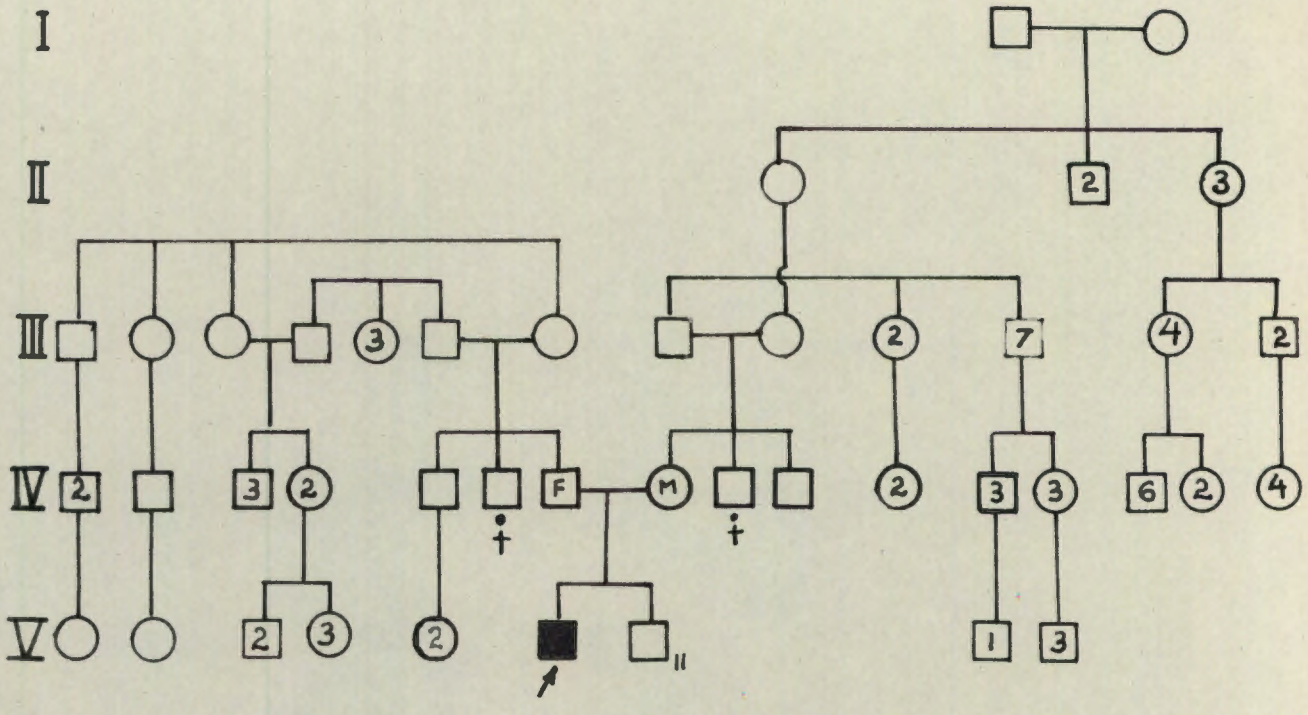
Case 2



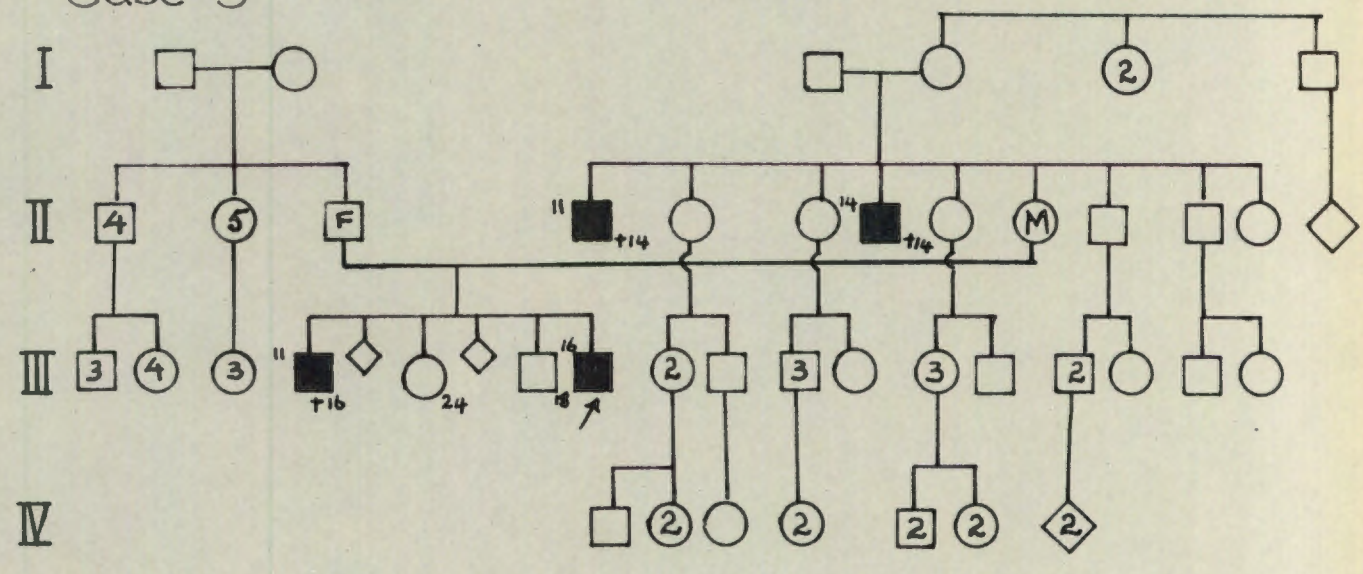
Case 3



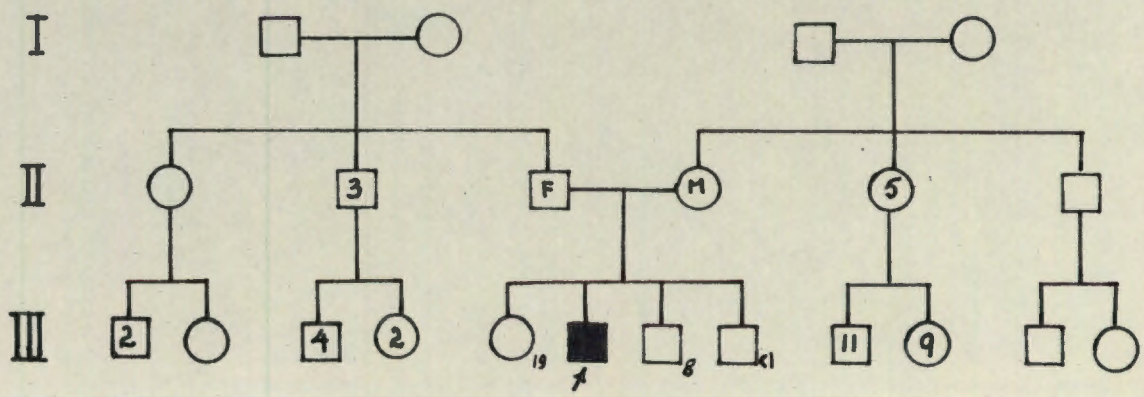
Case 4



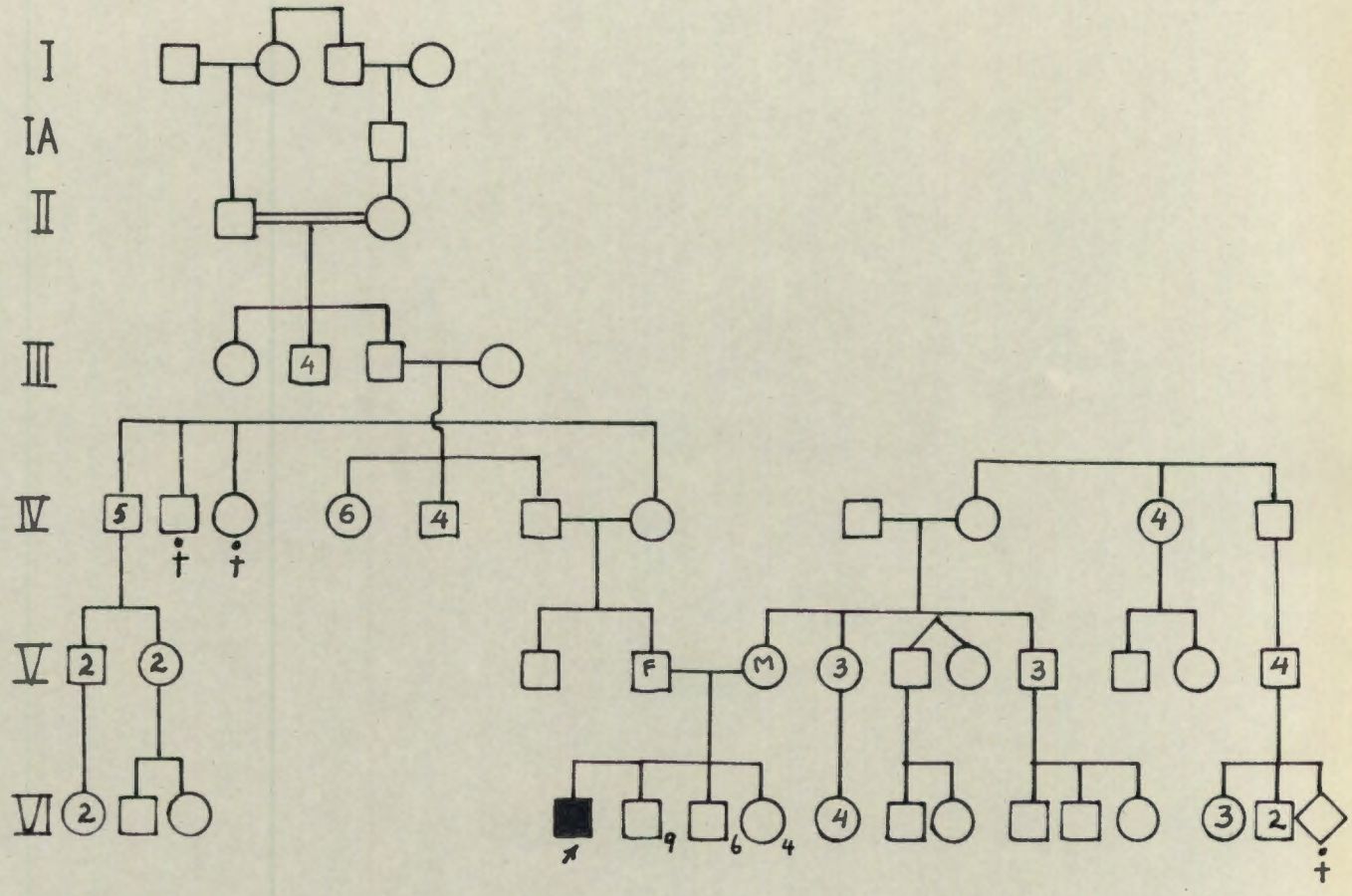
Case 5



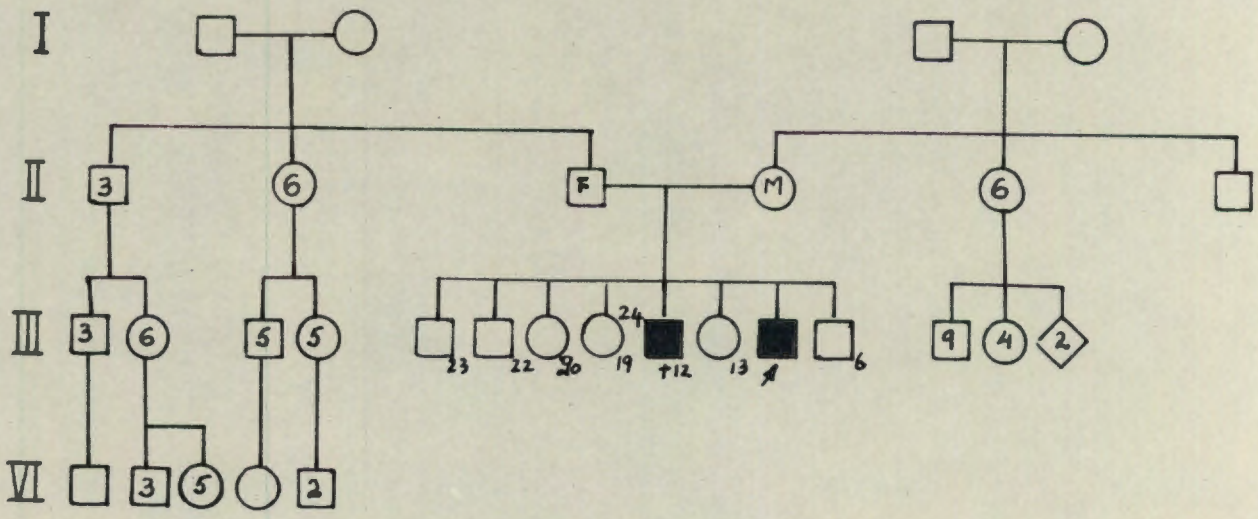
Case 6



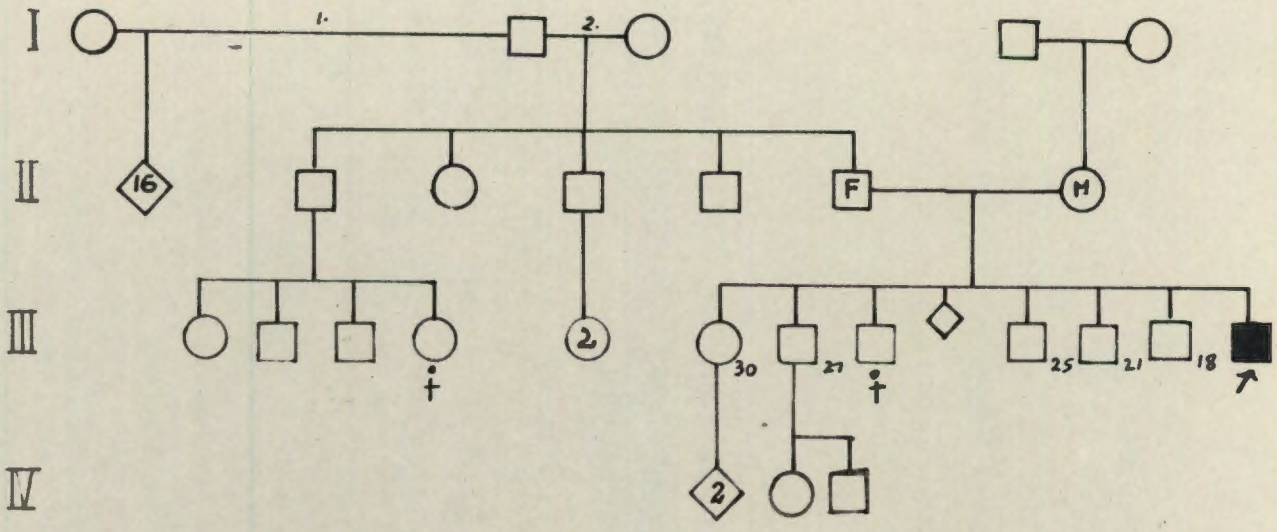
Case 7



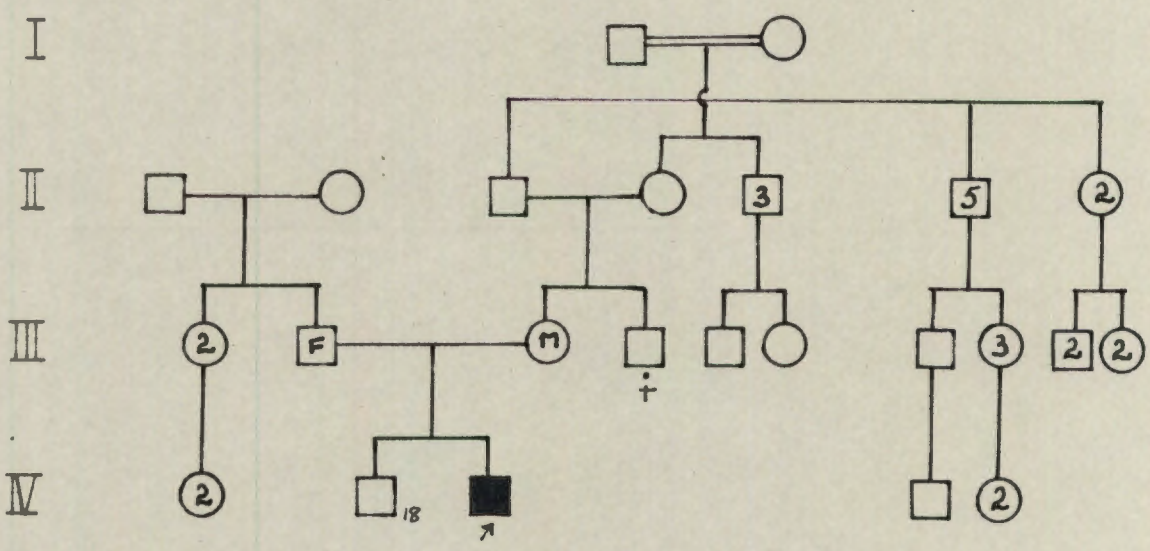
Case 8



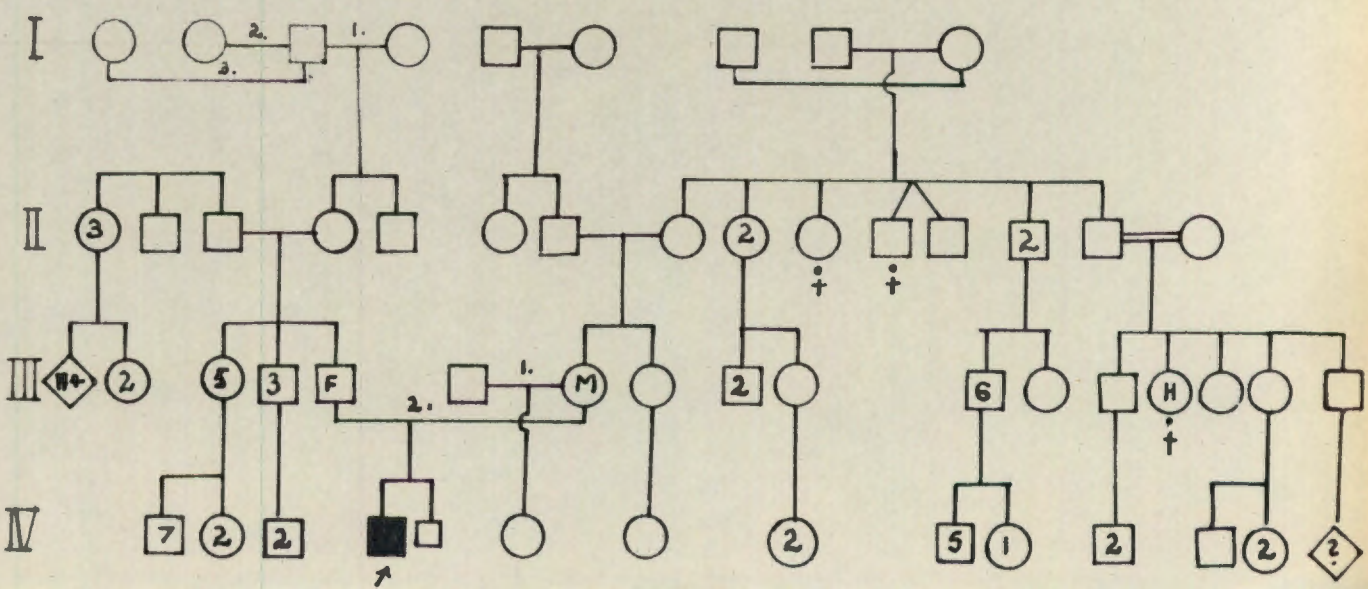
Case 9



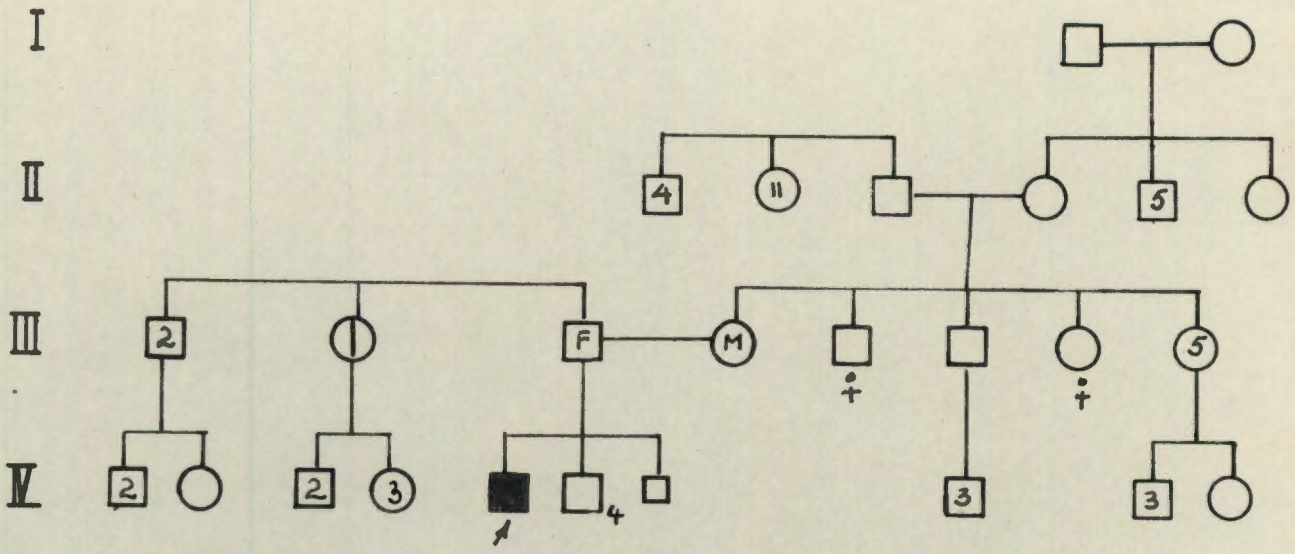
Case 10



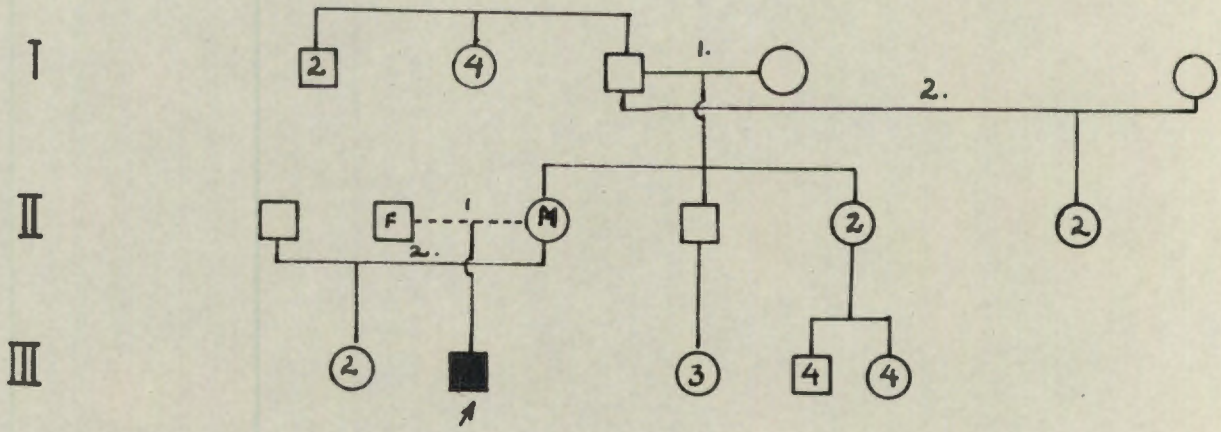
Case 11



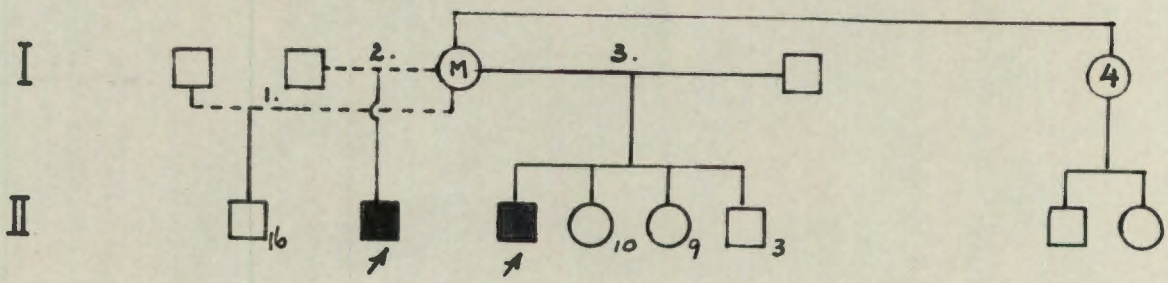
Case 12



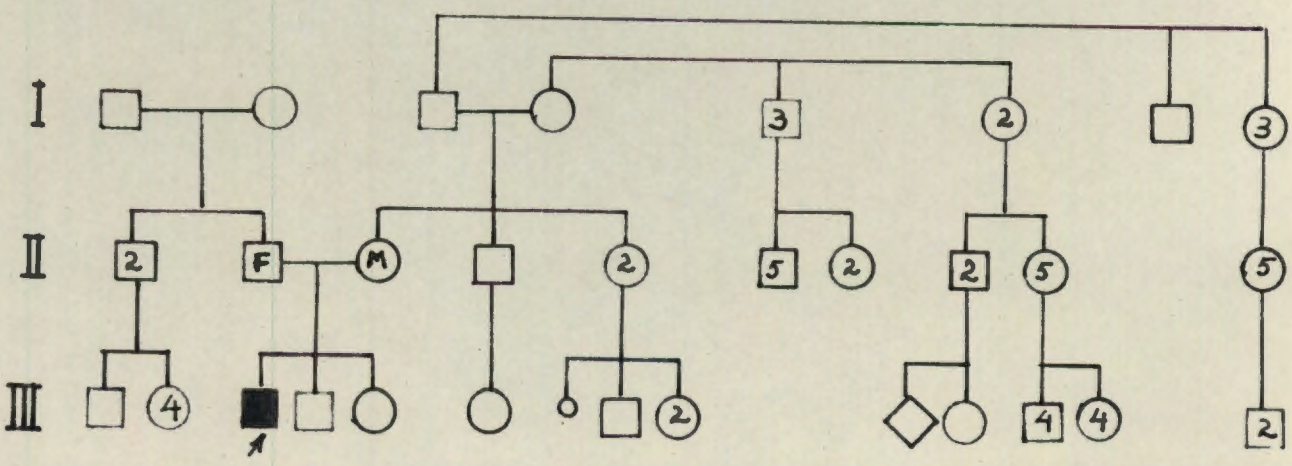
Case 13



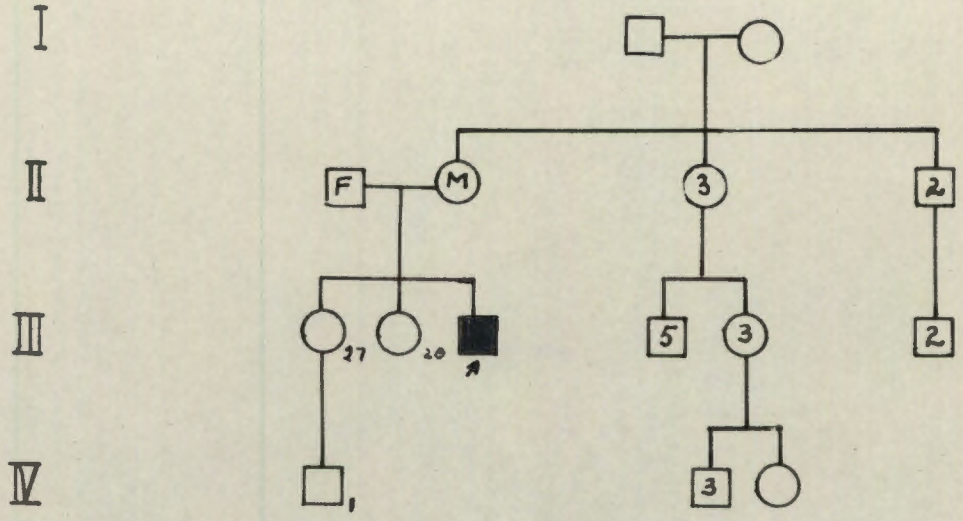
Case 14; 15



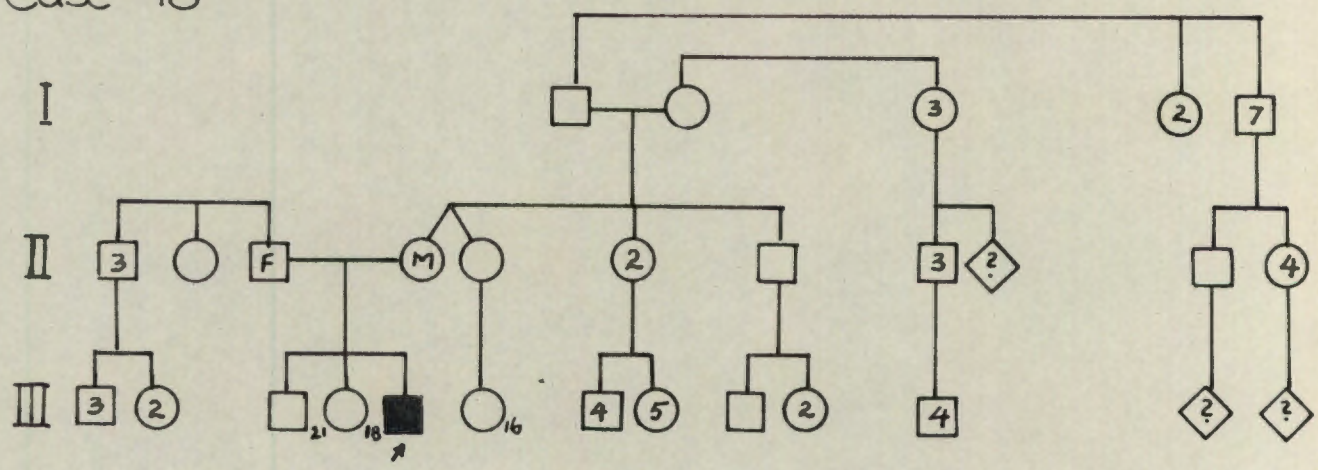
Case 16



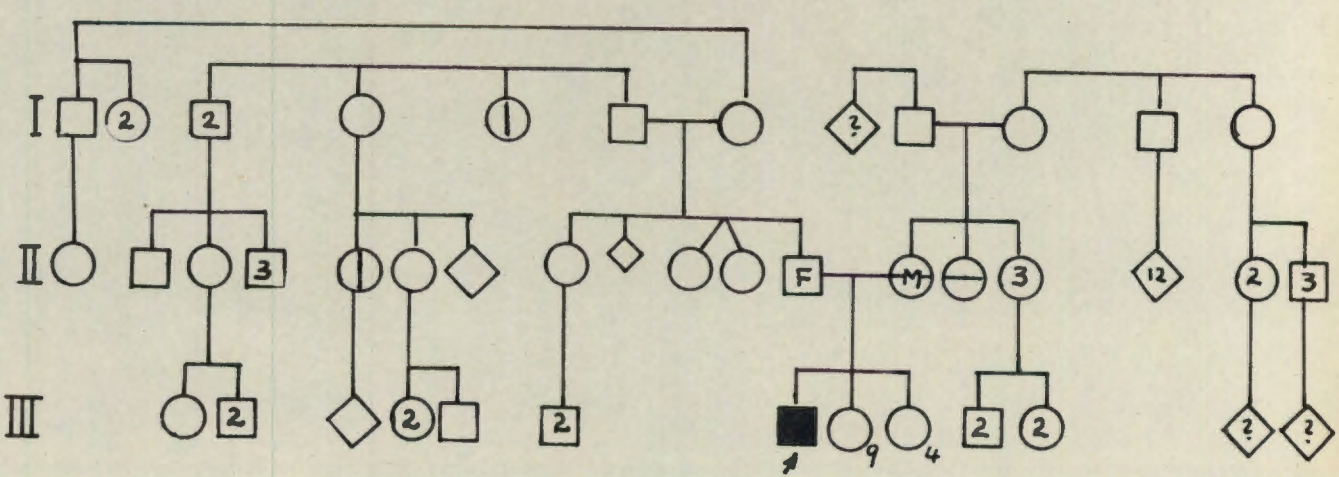
Case 17



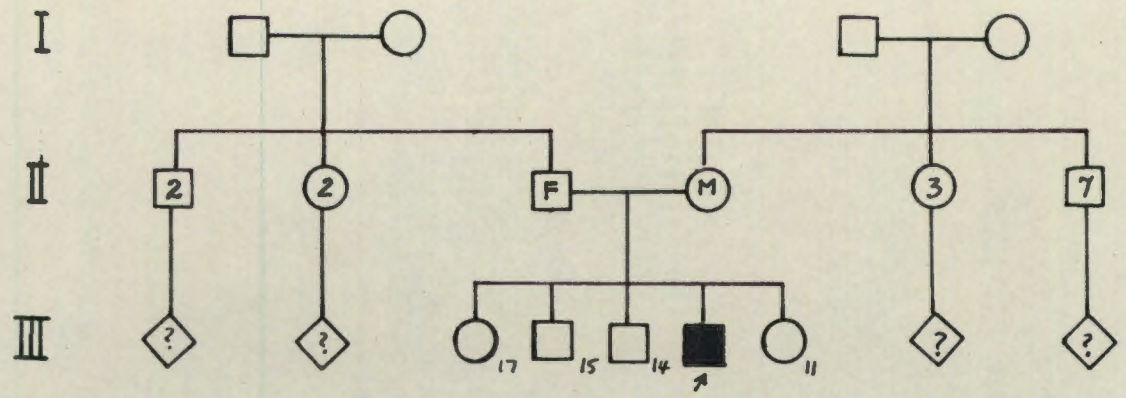
Case 18



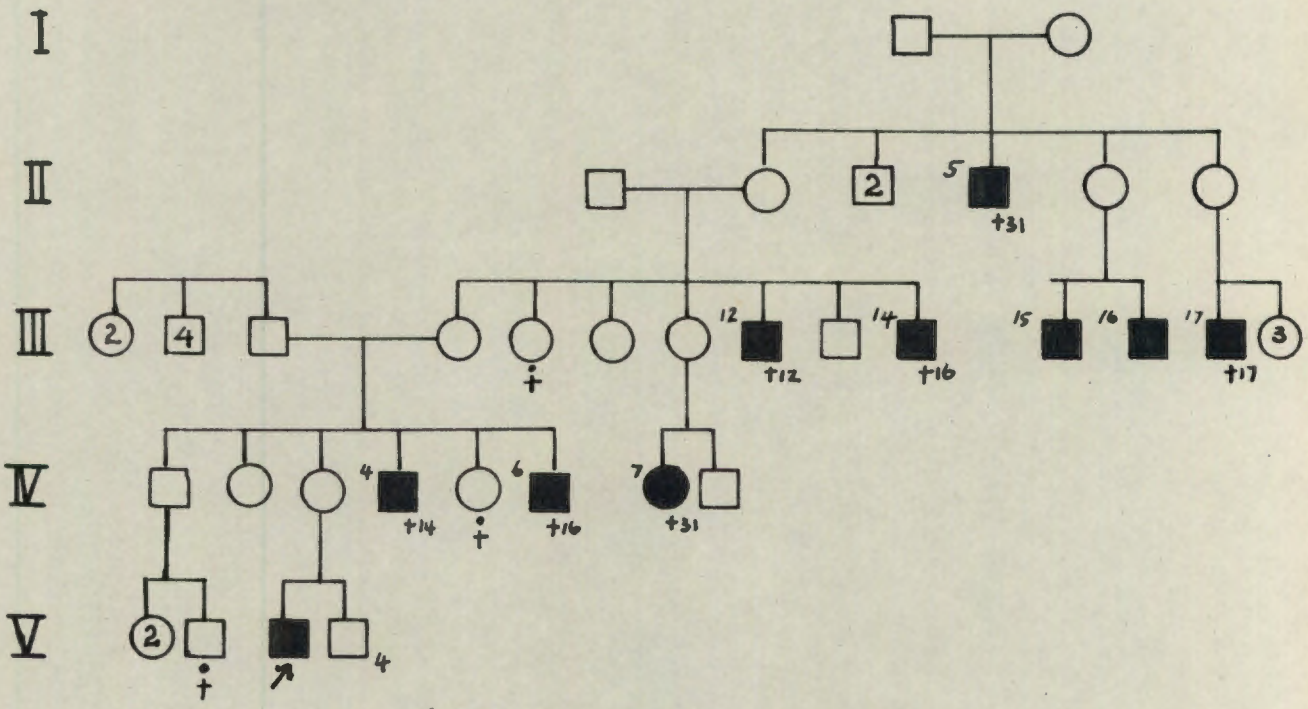
Case 19



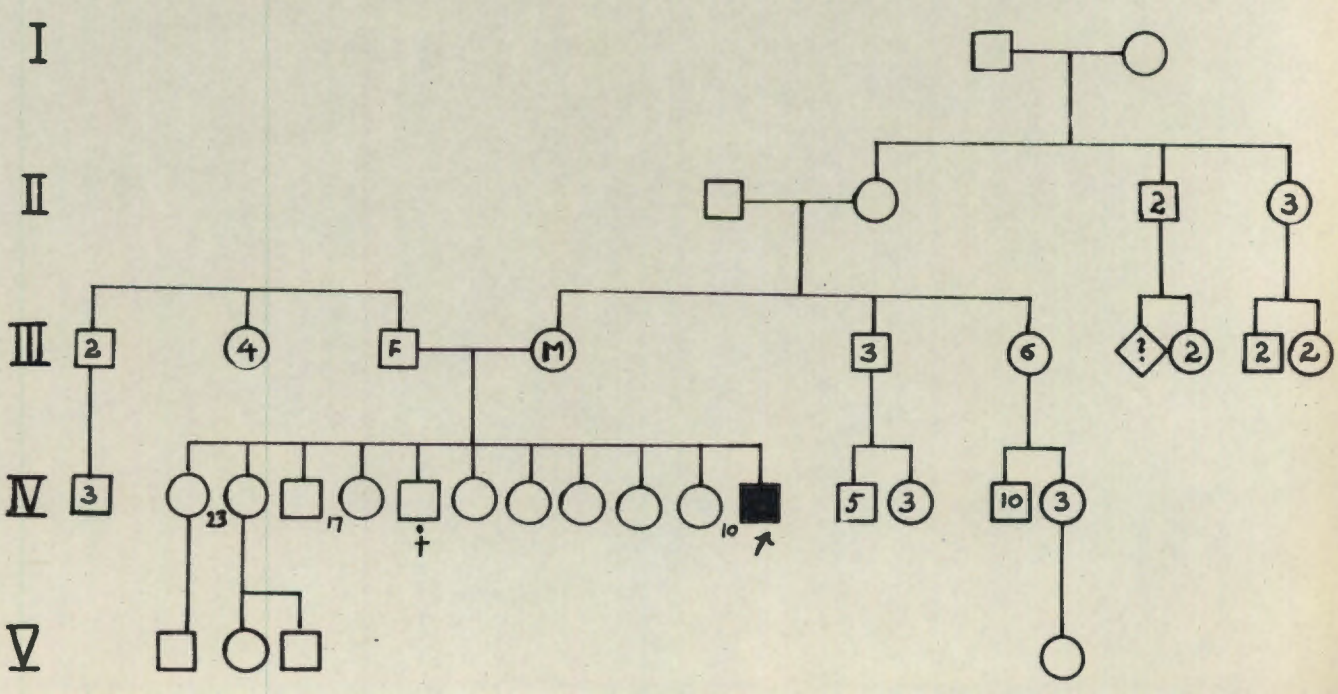
CASE 20



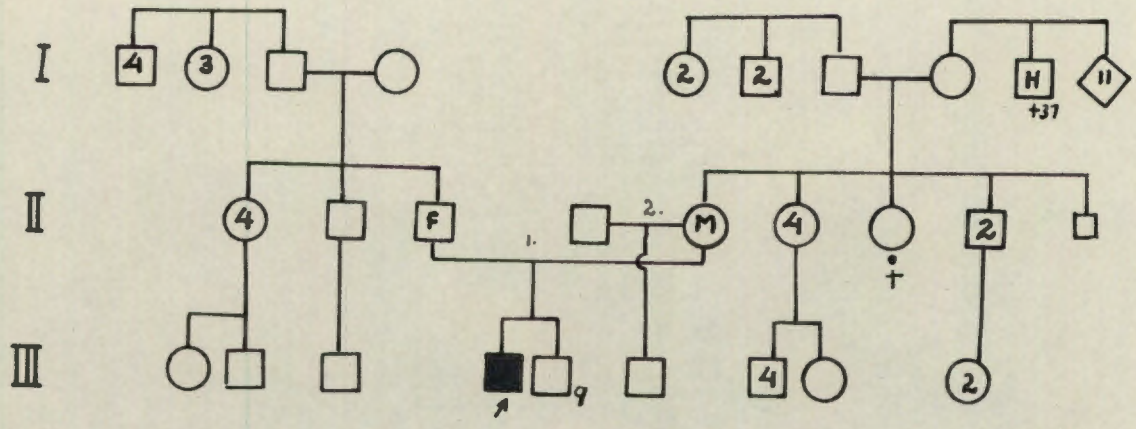
CASE 21



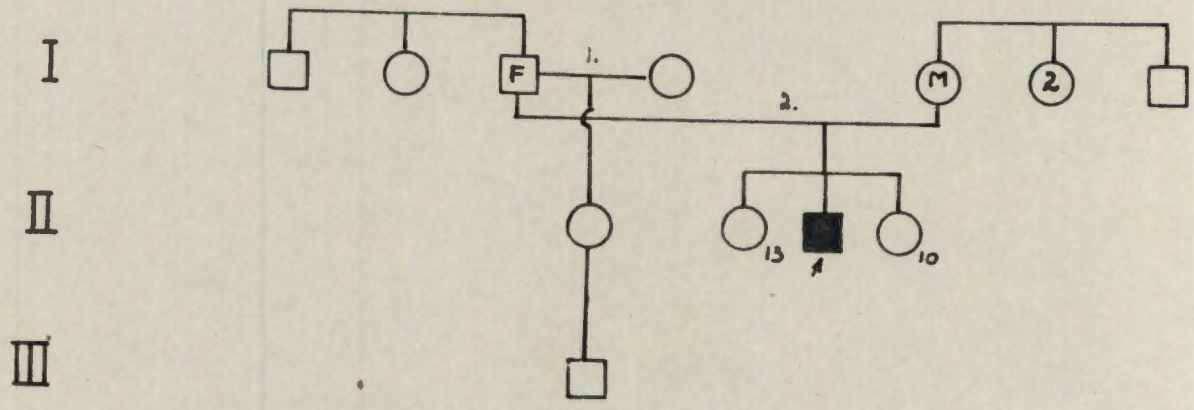
CASE 22



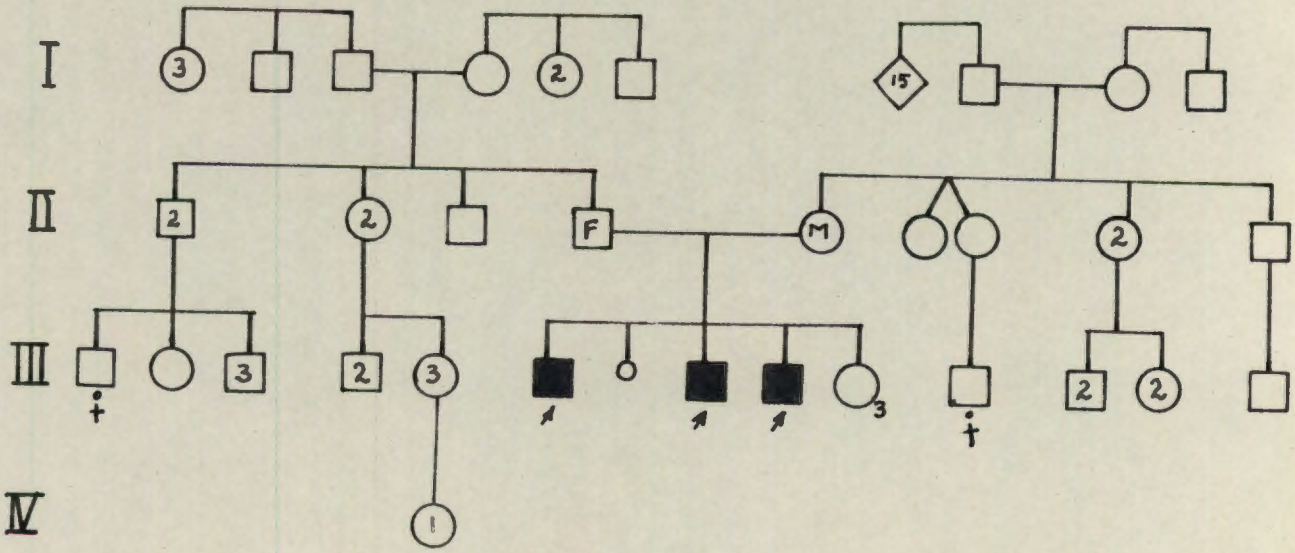
Case 24



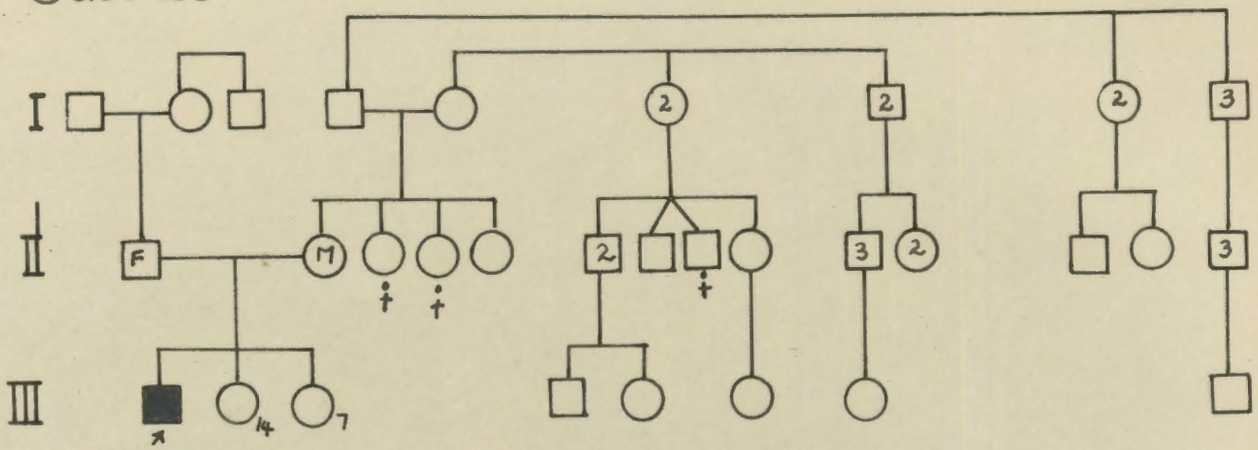
Case 25



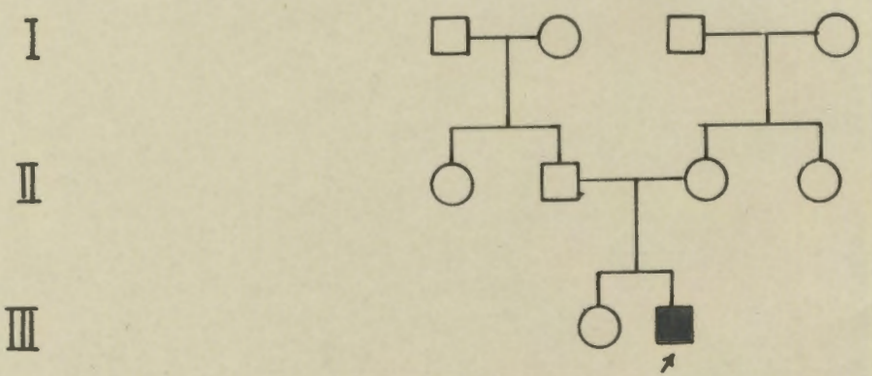
Case 26; 27; 28



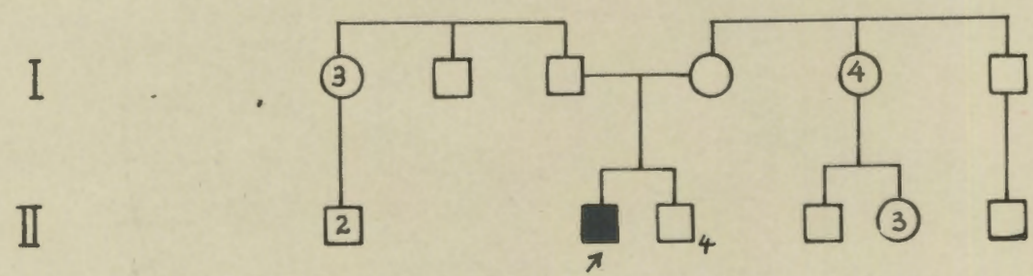
Case 29



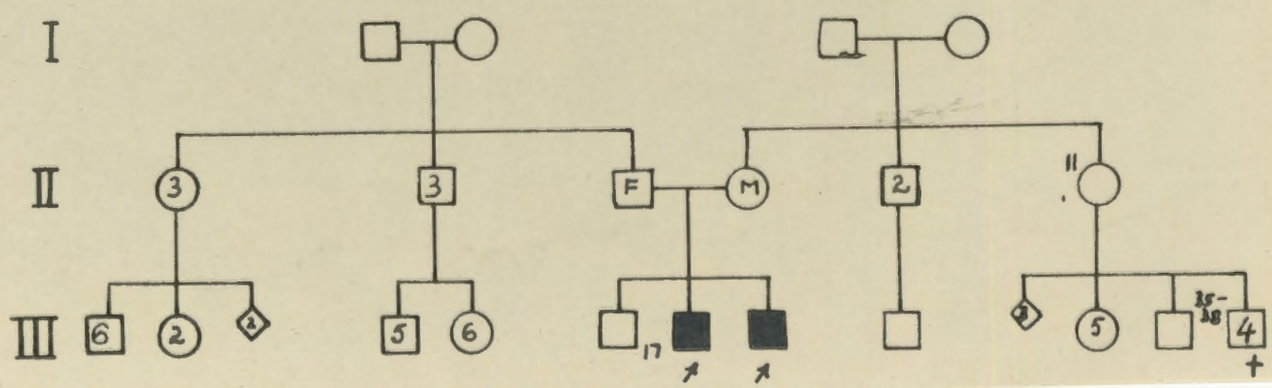
Case 30



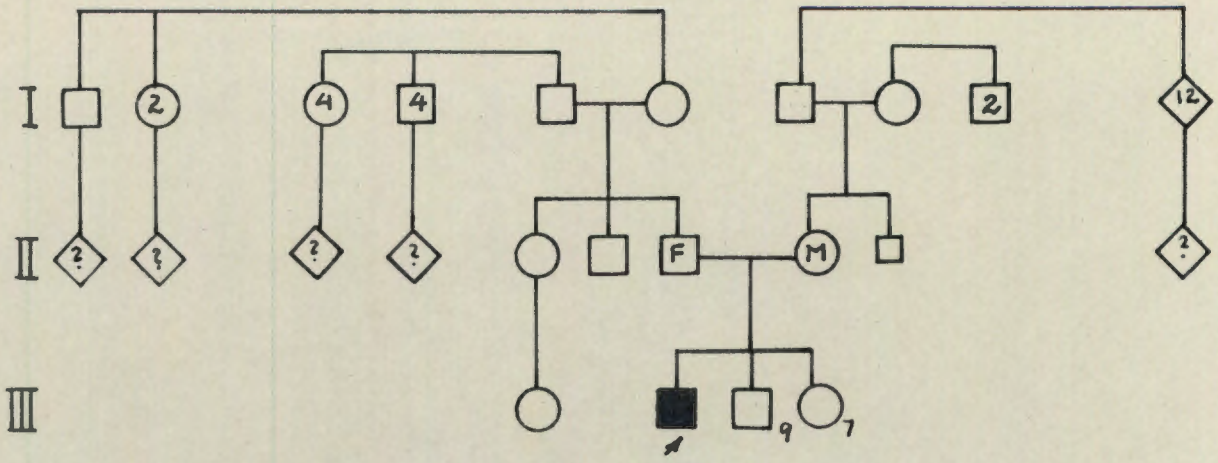
Case 31



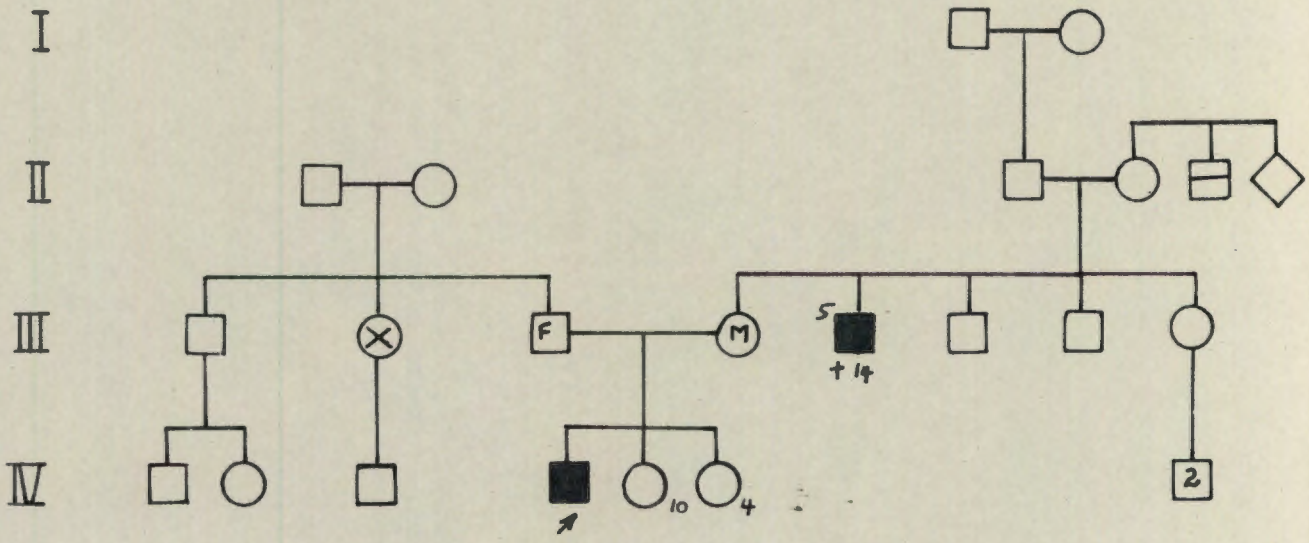
Case 32; 33



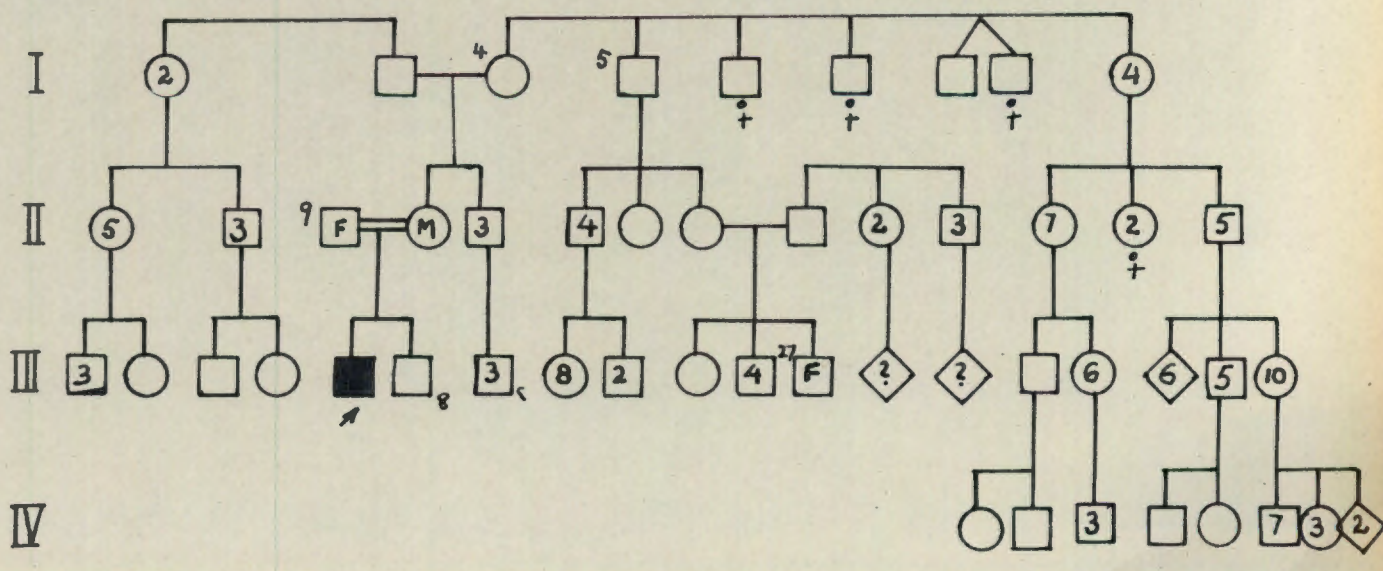
Case 34



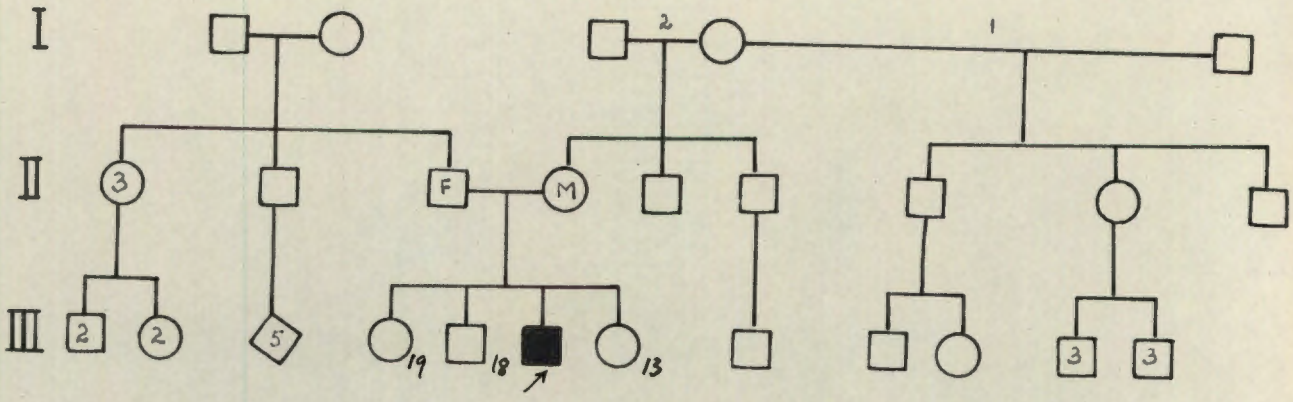
Case 35



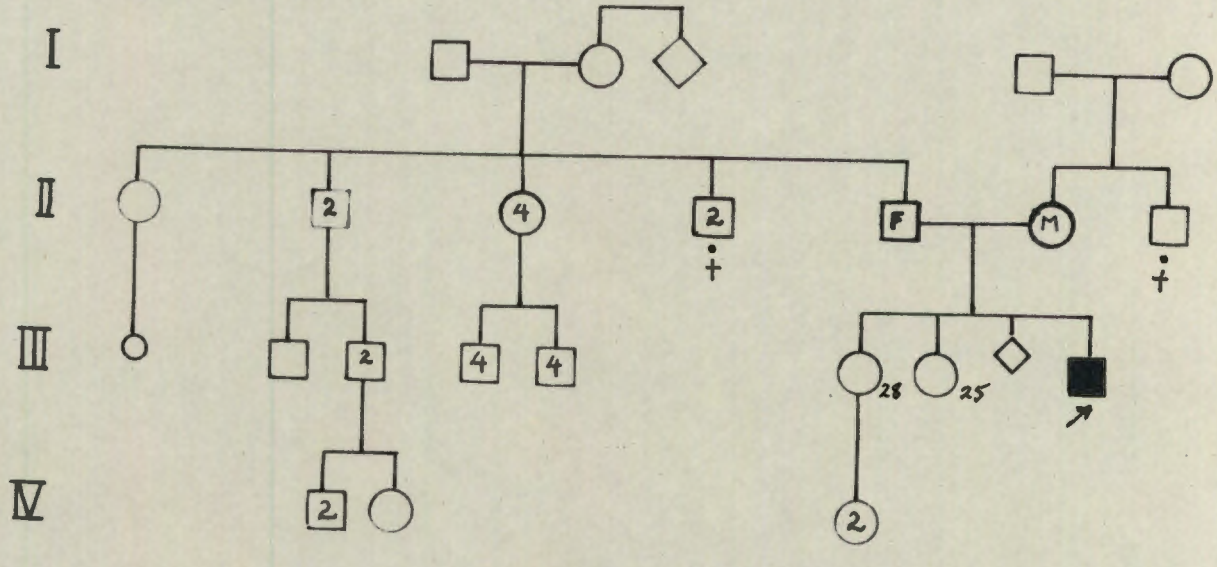
Case 36



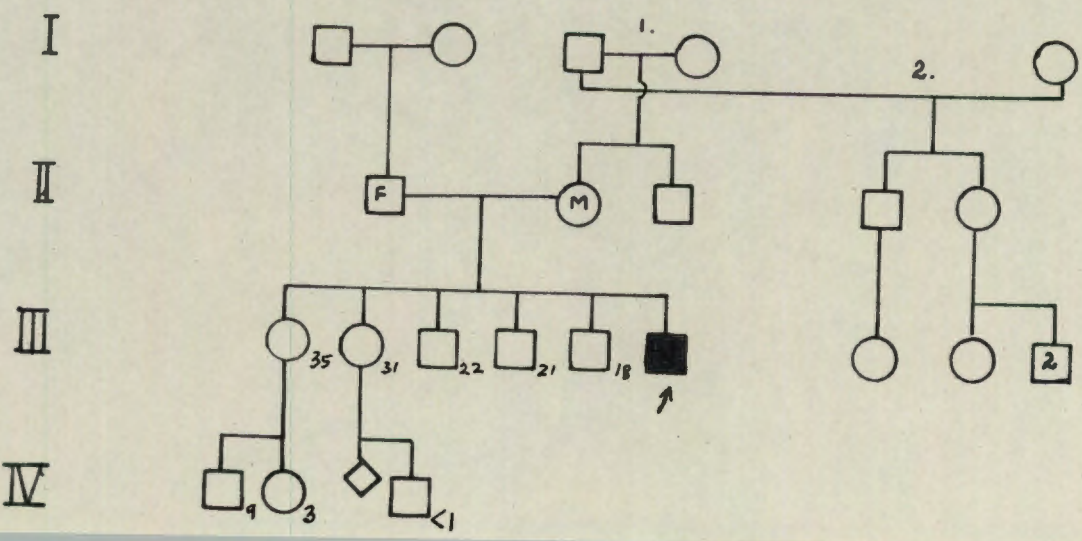
Case 37



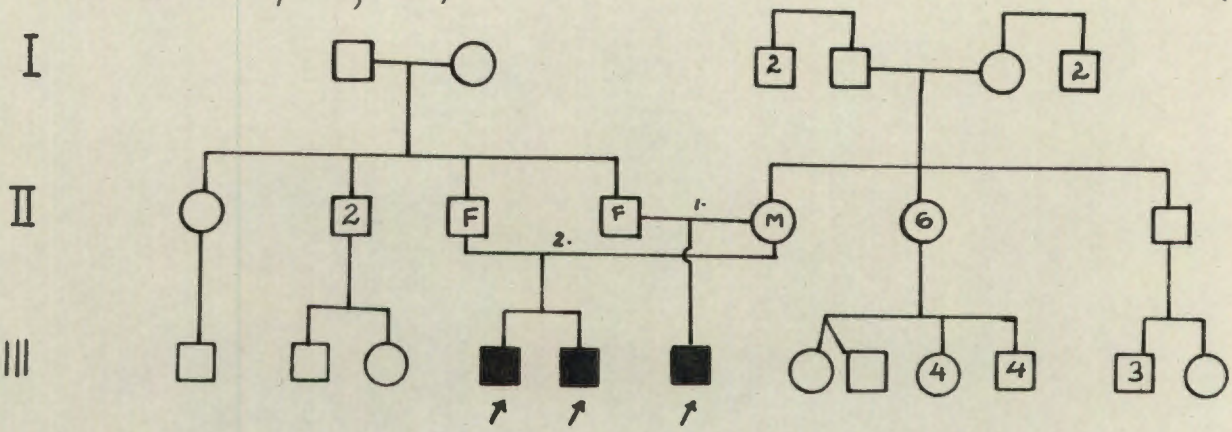
Case 38



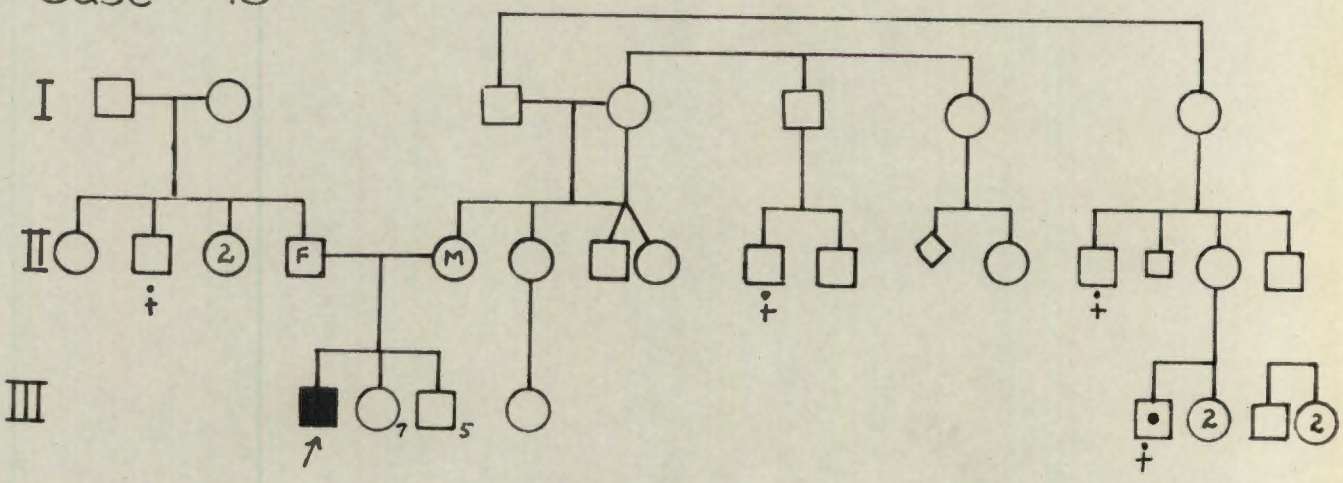
Case 39



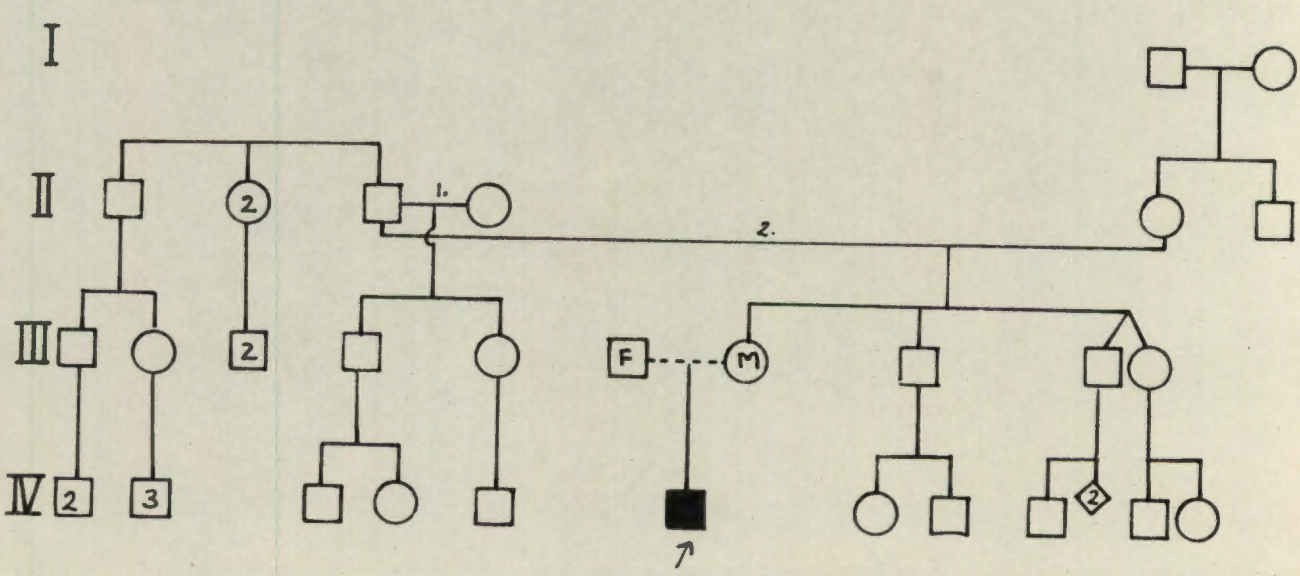
Case 40 ; 41 ; 42 ;



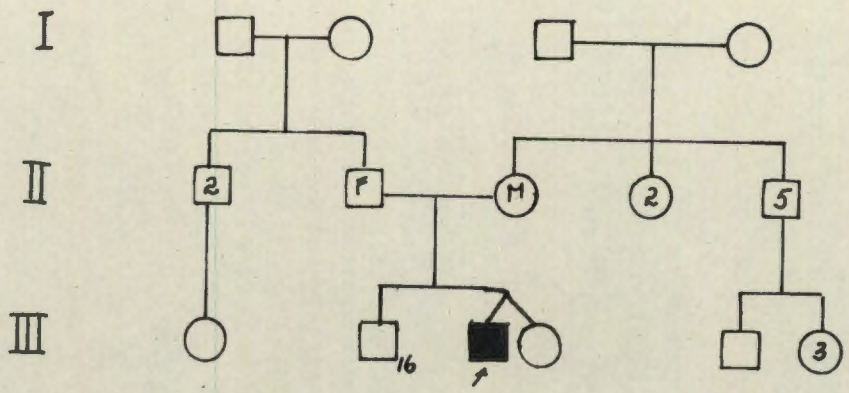
Case 43



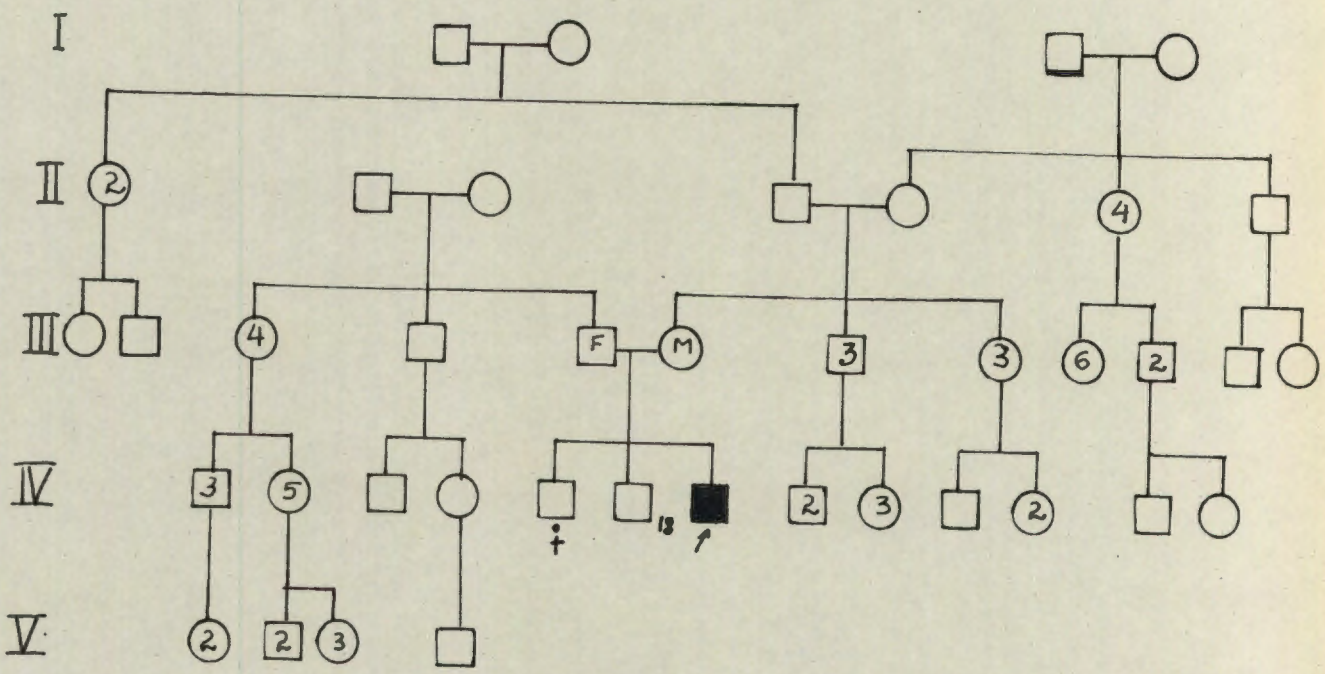
Case 44



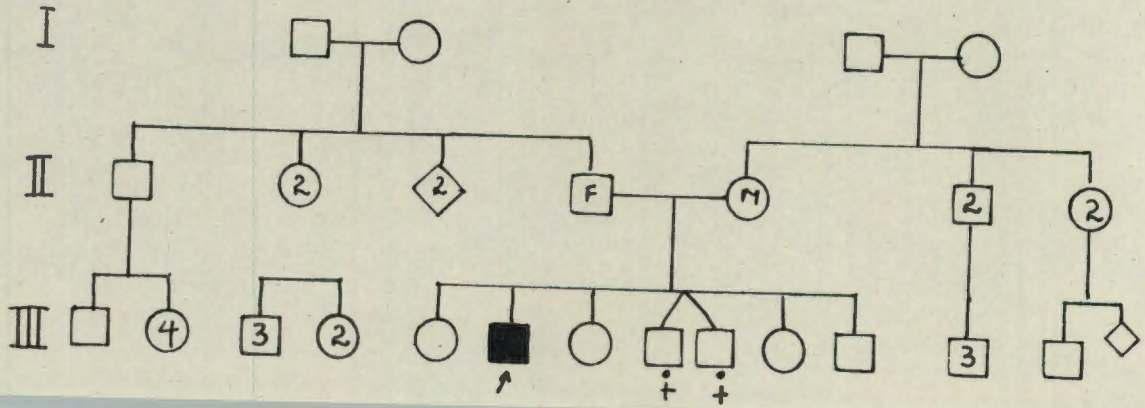
Case 45



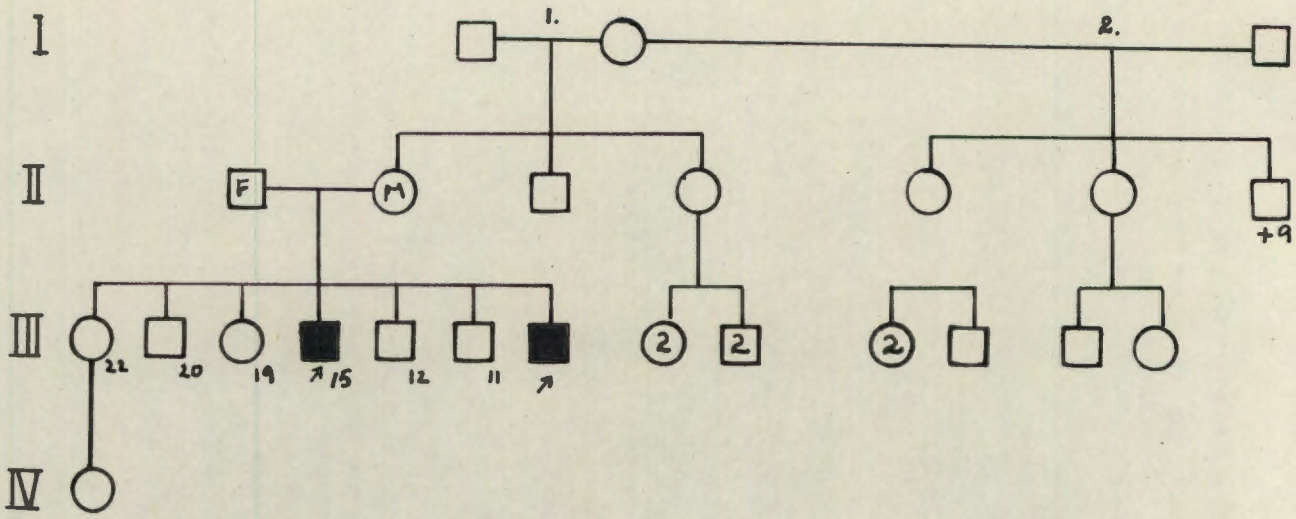
Case 46



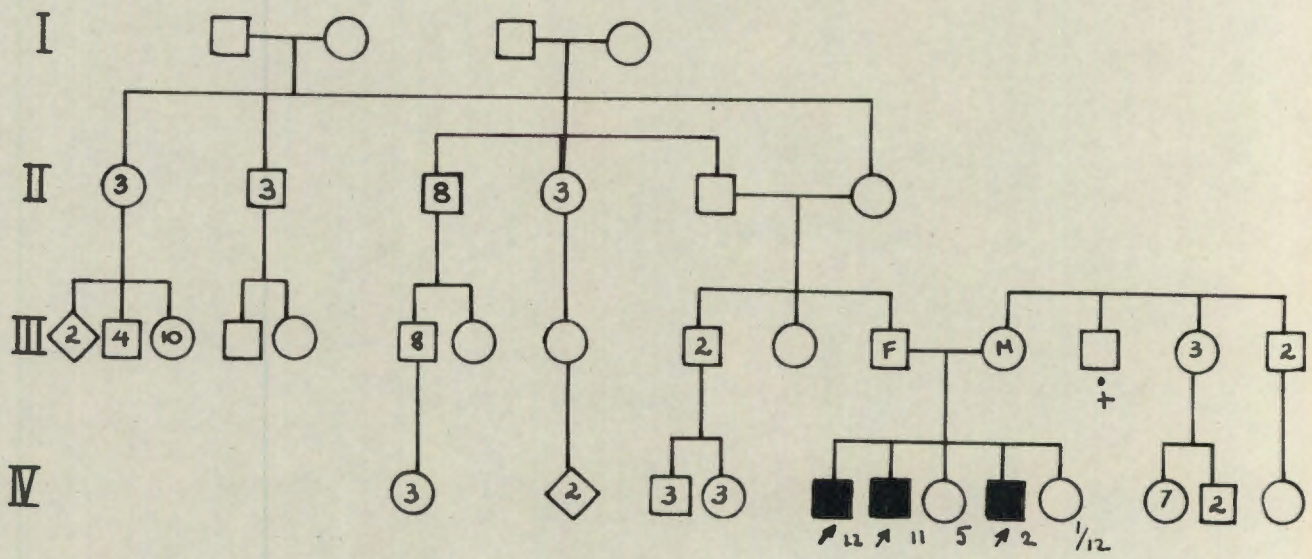
Case 47



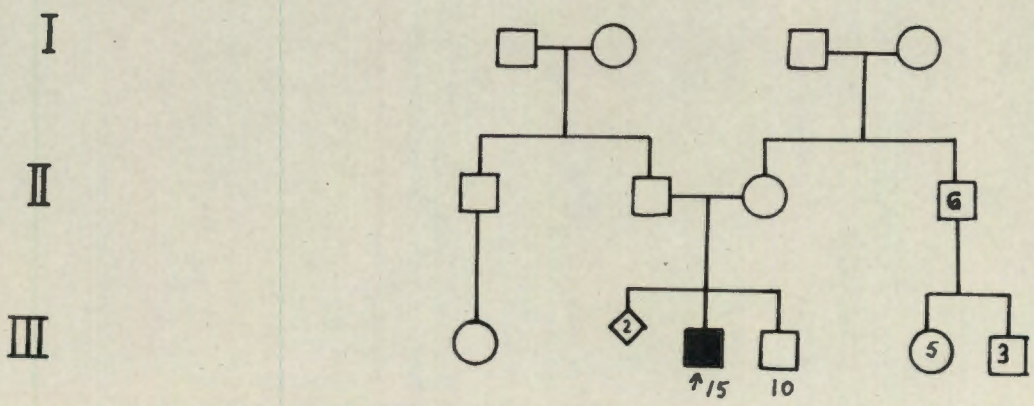
Case 48; 49



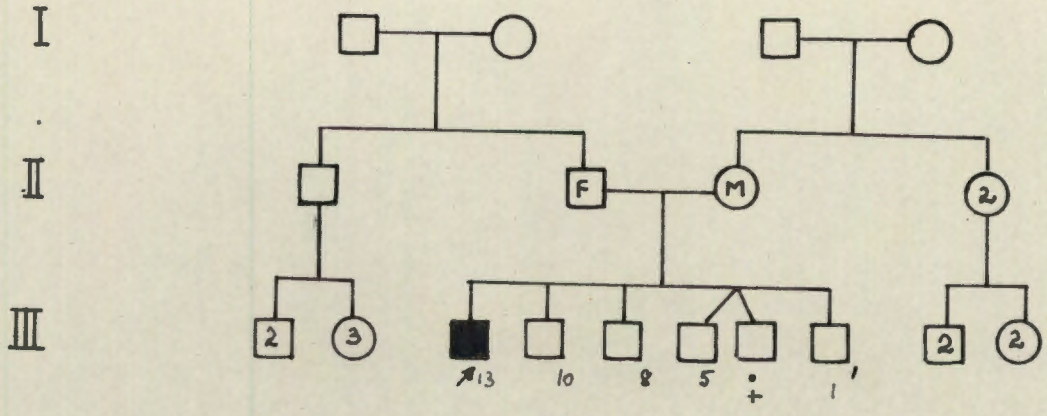
Case 50; 51; 52;



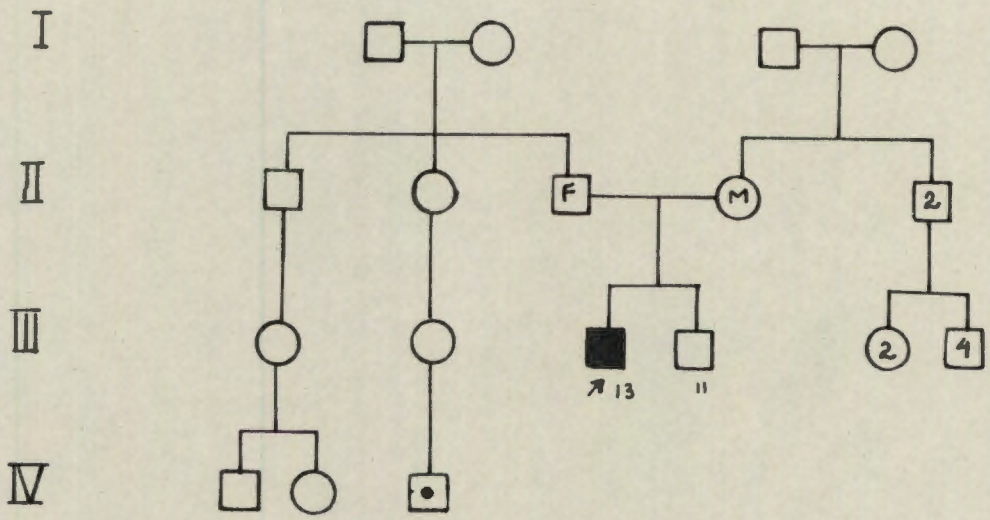
Case 53



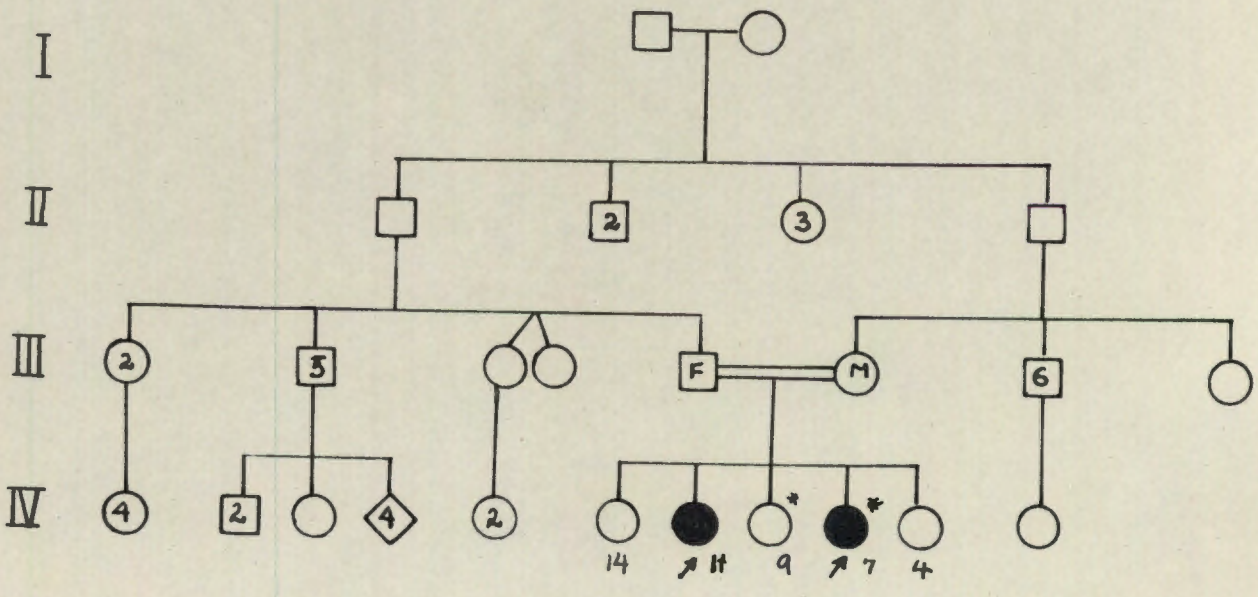
Case 54



Case 55

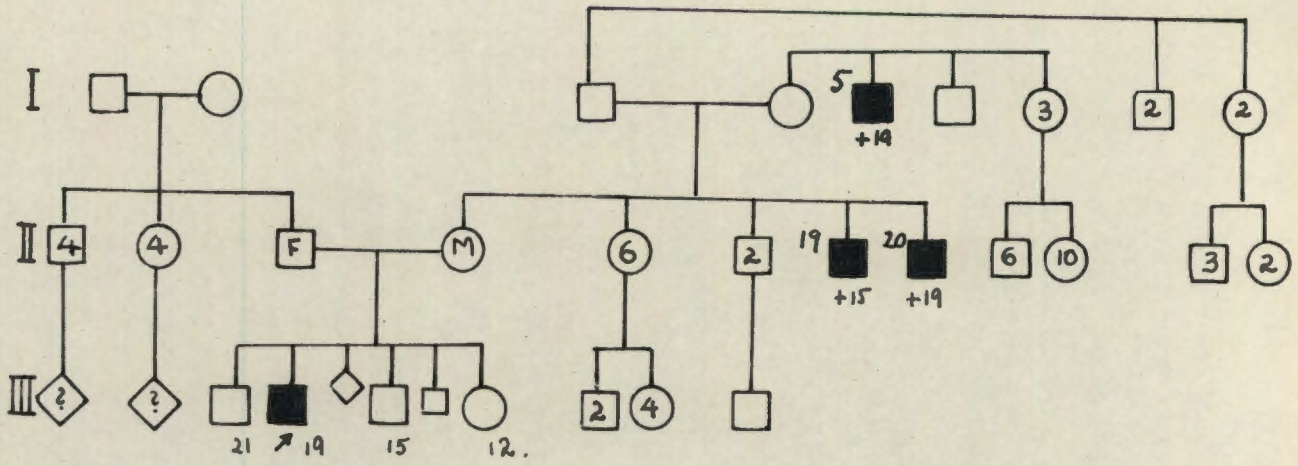


Case 56; 57

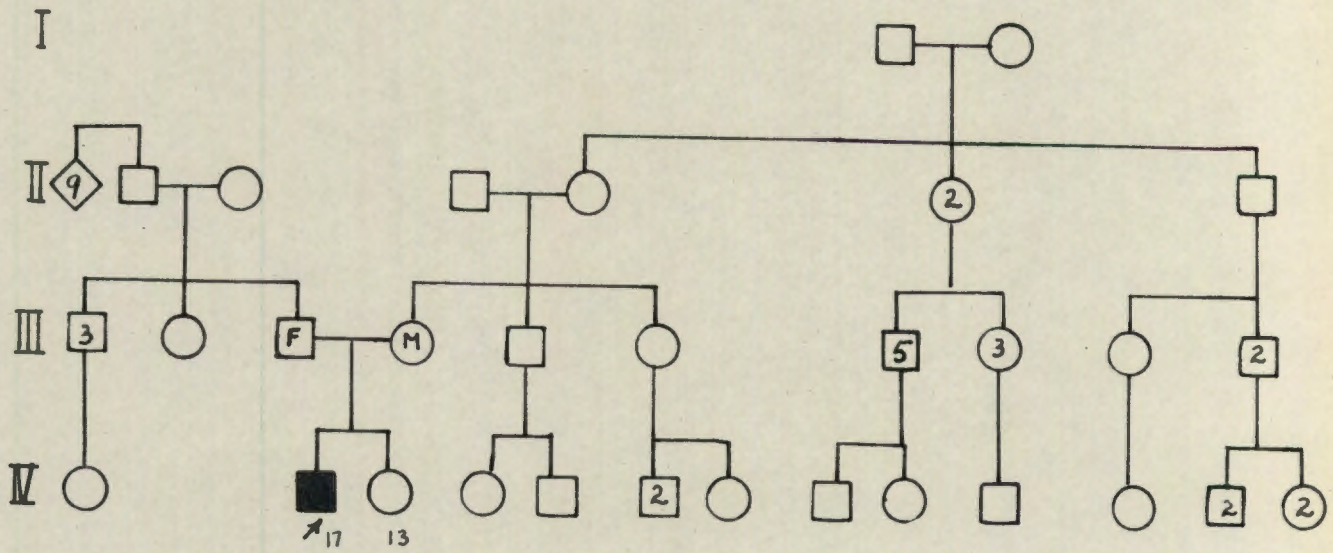


* clawed toes.

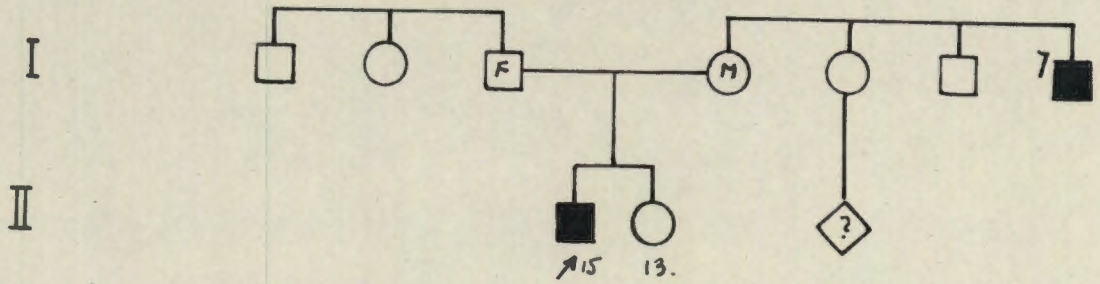
Case 58



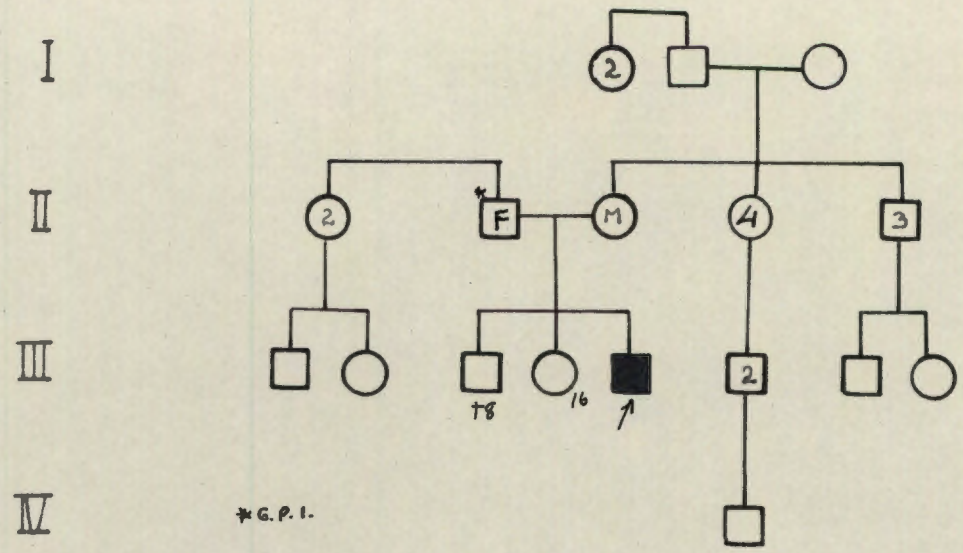
Case 59



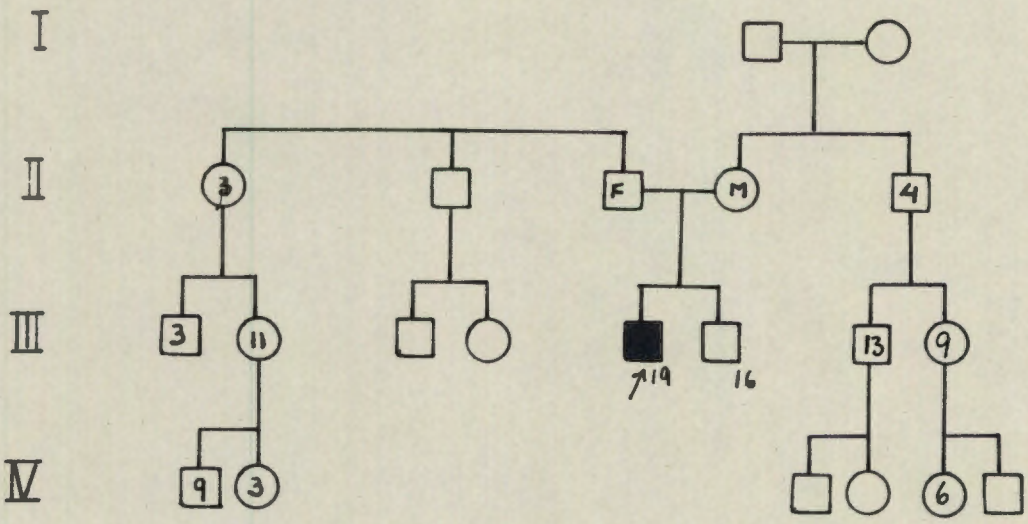
Case 60



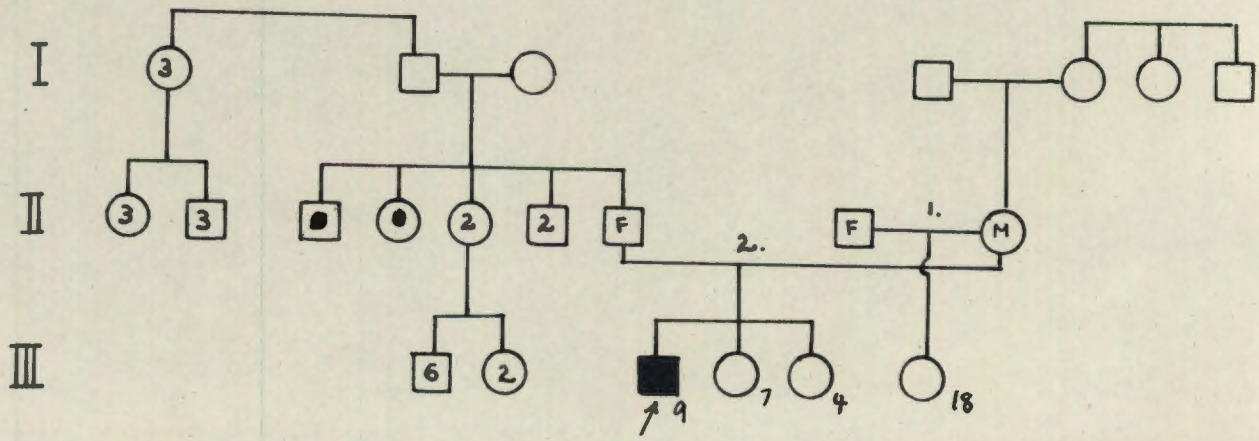
Case 61



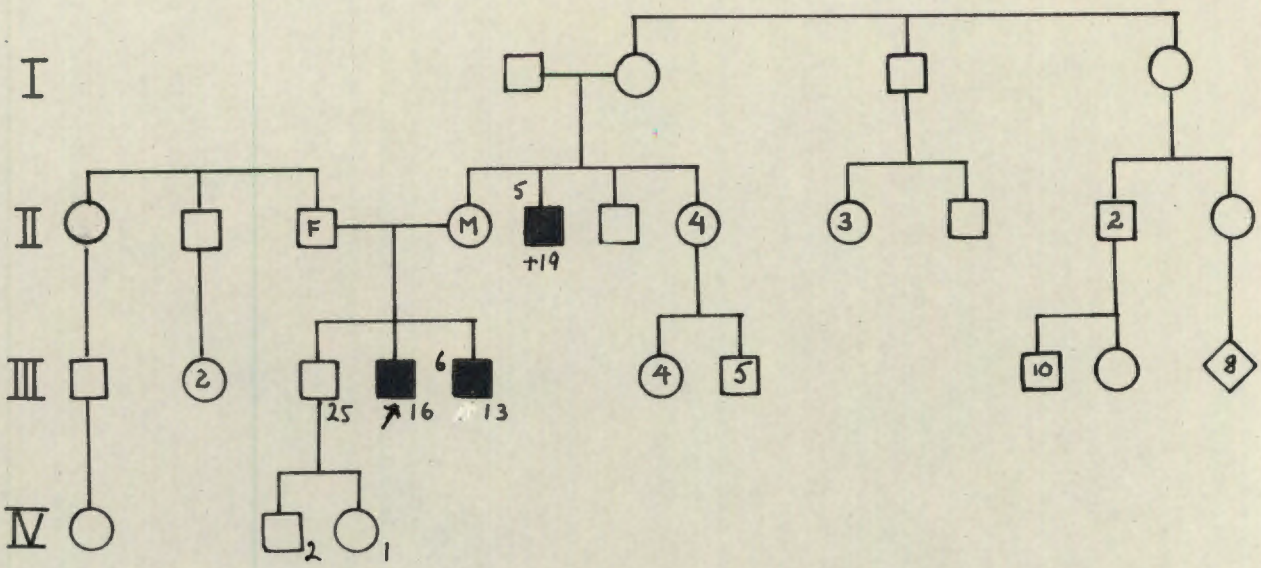
Case 62



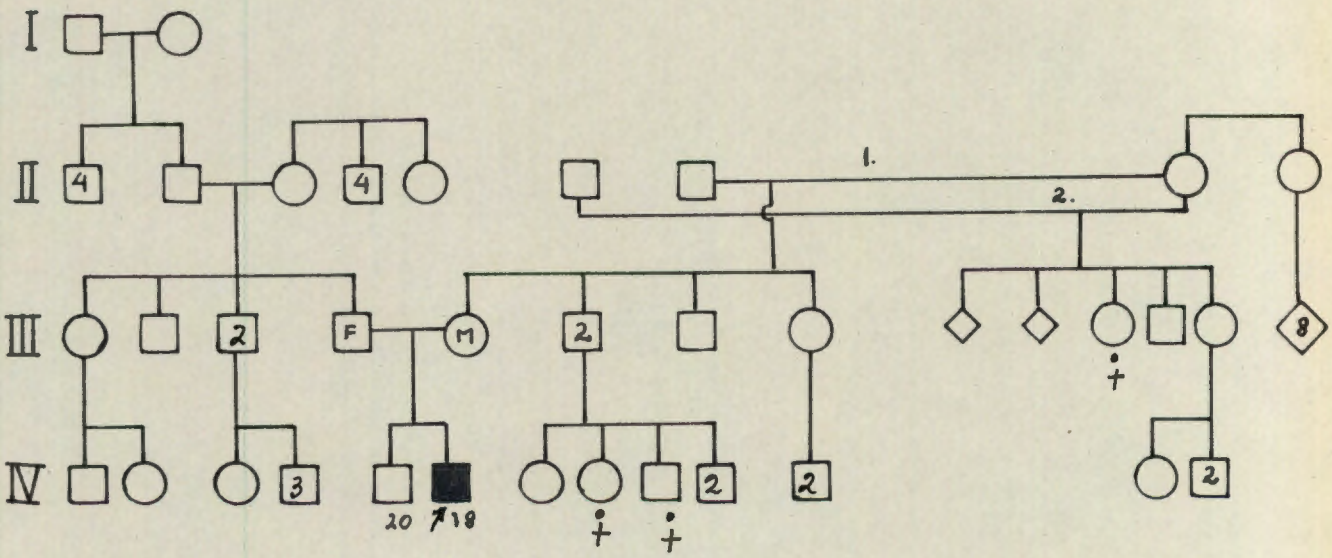
Case 63



Case 64



Case 65



CHAPTER 3.

CLINICAL FEATURES AND COURSE OF THE DISEASE.

MATERIAL AND METHODS:

A detailed clinical assessment and follow-up has been made of 65 cases. These comprise 35 inpatients and 22 outpatients at Queen Mary's Hospital for Children, and 8 inpatients at the Southern Hospital, Dartford. All the patients were males except cases 56 and 57. The onset of the disease in all cases was before adolescence. The ages of the patients at the time of initial examination varied from 3 to 18 years.

The clinical assessment included a detailed history obtained at interview with parents or relatives and supplemented by a questionnaire. At the time of admission a full clinical examination was performed with special accent on the musculo-skeletal system. An assessment of various physical activities such as walking, standing, getting up from the floor, sitting up from the supine position, feeding himself, combing his hair, washing his face and writing was made. The power of various muscle groups was charted, and the presence and extent of skeletal deformities was noted. These criteria and also the reflexes were assessed in all patients at three-monthly intervals, (excepting the 8 patients at the Southern Hospital who were seen only on two occasions).

A history of each case is included in Appendix III and the main clinical features are summarised in the tables of Appendix IV.

RESULTS

A. HISTORY:

Pregnancy. In the present series a history of complications of pregnancy was obtained in only 3 cases. Foetal movements were reduced in 8 cases, increased in 1 case, no information obtained in 2 cases, and normal in the remainder.

TABLE III.1. MILESTONES

Case No.	Sat up	Stood up	Walked	Comment
1.	12	18	18	? Delayed
2.	5	?	12	Normal
3.	9	18	24	Delayed
4.	4	10	15	Normal
5.	9	14	18	Normal
6.	12	36	38	Delayed
7.	8	15	19	Delayed
8.	?	18	24	Delayed
9.	10	10	13	Normal
10.	6	18	24	Delayed
11.	6	10	18	Normal
12.	9	11	12	Normal
13.	6	10	12	Normal
14.	9	11	12	Normal
15.	8	11	12	Normal
16.	9	12	12	Normal
17.	9	13	15	Normal
18.	12	18	22	Delayed
19.	9	24	36	Delayed
20.	9	12	24	? Delayed
21.	?	?	?	?
22.	9	20	4 yrs.	Poliomyelitis
23.	?	?	24	? Delayed
24.	6	13	24	? Delayed
25.	?	?	24	? Delayed
26.	9	24	24	Delayed
27.	7	15	17	Normal
28.	8	18	24	Delayed
29.	12	24	24	Delayed
30.	6	12	18	Normal
31.	5	10	18	Normal
32.	8	15	24	? Delayed
33.	6	12	18	Normal
34.	12	12	24	Delayed
35.	12	18	30	Delayed
36.	9	16	24	Delayed
37.	9	20	24	Delayed
38.	never walked			
39.	? N	? N	12	Normal
40.	15	24	30	Delayed
41.	12	24	27	Delayed
42.	12	18	20	Delayed
43.	8	13	16	Normal
44.	poliomyelitis			
45.	12	18	24	Delayed
46.	16	18	24	Delayed
47.	?	?	24	? Delayed
48.	7	12	18	Normal
49.	6	18	24	Delayed
50.	6	15	18	Normal
51.	5	13	17	Normal
52.	5	10	14	Normal
53.	12	?	18+	Delayed
54.	8	20	22	Delayed
55.	8	14	16	Normal
56.	8	14	16	Normal
57.	8	12	16	Normal
58.	?	11	24	? Delayed
59.	?	12	24	? Delayed
60.	9	36	36	Delayed
61.	?	24	36	Delayed
62.	9	15	18	Normal
63.	8	24	36	Delayed
64.	6	?	15	Normal
65.	6	?	16	Normal

Age is given in months.
Delayed: All milestones delayed; or two milestones delayed one of which is walking.
? Delayed: walking only delayed; or sitting and standing delayed but walking at a normal age.

Milestones. Although the average age for the various milestones is well documented, the upper limit of normal is not clearly defined (Illingworth, 1957). In the present investigation it was found that the milestones most frequently remembered by the parents were the ages of walking, standing and sitting. The age at which the child started to talk was prone to subjective interpretation on the part of the mother and was found to be impossible to assess.

The upper limit of normal for sitting, standing and walking has been taken as 9, 14, and 18 months respectively. Details of the milestones of individual cases as well as the criteria used in classifying them are given in table III. 1.

A definite delay in milestones occurred in 26 cases; a probable delay in a further 8 cases, and 27 cases were normal. Two cases had poliomyelitis in infancy (22 and 44) and in a further 2 cases no information was available.

Age of onset. It is difficult to determine the age of onset of a disease which is insidious. A lot will depend on the powers of observation of the parents and their familiarity with the disease from experience with previously affected sibs.

The first presenting symptom has been used as the criterion for the age of onset. This was not changed when a history of delayed milestones or other symptoms were subsequently obtained on direct questioning. The age of onset of individual cases is shown in Table III. 2 and the number of cases falling into the various ages of onset are given in Fig. 3.1. In 47 cases (72%) the first abnormal symptom presented before the age of 4, while in 13 of these it was present before the age of 2.

TABLE III. 2 : MILESTONES AND EARLY SYMPTOMS.

Case No.	Age of onset	Age of walking	Abnormal gait	Tendency to fall	Difficulty with stairs	Unable to run	Dystrophic manner
1.	1½	1½	1½	1½	D	+	2½
2.	1¼	1¼	15M	4	1½	?	3
3.	2	2	2	2	D	D	+ (?age)
4.	2	1¼	2	2	+	+	4
5.	1¼	1½	1½	1½	+	D	Unable to get up
6.	<1	3/4	3	3	+	+	3
7.	2	19M	2	5	Age ?	Age ?	5
8.	3	2	5	5	3	+	5
9.	2½	13M	?	2½	?	+	5
10.	3	2	2	3	D	+	3
11.	3	1½	3	4	+	+	4
12.	2	13M	2	2½	Age ?	Age ?	5
13.	8	1	8	8	8	polio	
14.	5	1	?	?	5	?	?
15.	3	1	?	?	?	?	?
16.	2	1	3	2	4	D	4
17.	3	1¼	3	5	D	+	5
18.	<1	20M	2	2	+	+	2
19.	2	3	3	3	D	+	3½
20.	2	2	2	2	+	+	Unable to get up
21.	3	?	3	?	D	D	3
22.	5	4	5	5	5	? polio	5
23.	3	2	3	3	3	3	3
24.	2	2	2	2½	+	+	4
25.	2	2	2	2	D	+	+(?age)
26.	2	2	2	2	+	+	5
27.	2	17M	2	2	2	+	2
28.	2	2	2	2	+	D	+(?age)
29.	2	2	2	2	+	+	Unable to get up
30.	5	1½	5	5	5	5	5
31.	2	1½	2	2	4	+	2
32.	3	2	5	5	+	+	?
33.	3	1½	3	4	+	+	5
34.	2	2	2	2	D	+	4
35.	<1	2½	3½	3	+	+	Unable to get up
36.	3	2	3	5	4	+	5
37.	2	2	2	2	+	+	Unable to get up
38.	<1	never walked					
39.	4	1	4	4	4	?	Unable to get up
40.	5	2½	5	5	5	5	5
41.	5	20M	5	5	5	5	5
42.	6	2¼	7	7	7	?	7
43.	3	16M	3	6	3	+	6
44.	8	polio					
45.	5	2	6	5	8	5	6
46.	2	2	2	2	D	+	Unable to get up
47.	2	2	2	?Age	+	+	
48.	5	1½	5	7	5	5	
49.	5	2	5	6	7	+	6
50.	2½	1½	2½	3	D	?	3½
51.	4	17M	4	5	5	5	5
52.	1½	14M	1½	1½	+	+	1½
53.	1½	2	3½	1½	3	+	
54.	<1	20M	2	2	+	+	3
55.	3	16M	16M	6	3	3	6
56.	5	16M	5	6	5	6	6
57.	6	16M	6	6	6	6	6
58.	5	2	5	5	+	+	5
59.	7	2	7	7	7	7	7
60.	3	3	5	5	+	+	
61.	4	3	4	4	+	+	4
62.	2	1½	-	-	+	+	
63.	3	3	3	3	+	4	
64.	5	15M	5	5	5	5	5
65.	<1	16M	4	2½	D	+	4

+:never able to climb stairs or run.
D:was able to climb stairs or run initially,but with difficulty.
Figures indicate age of onset of symptoms in years, unless otherwise indicated.
(M = mo nths)

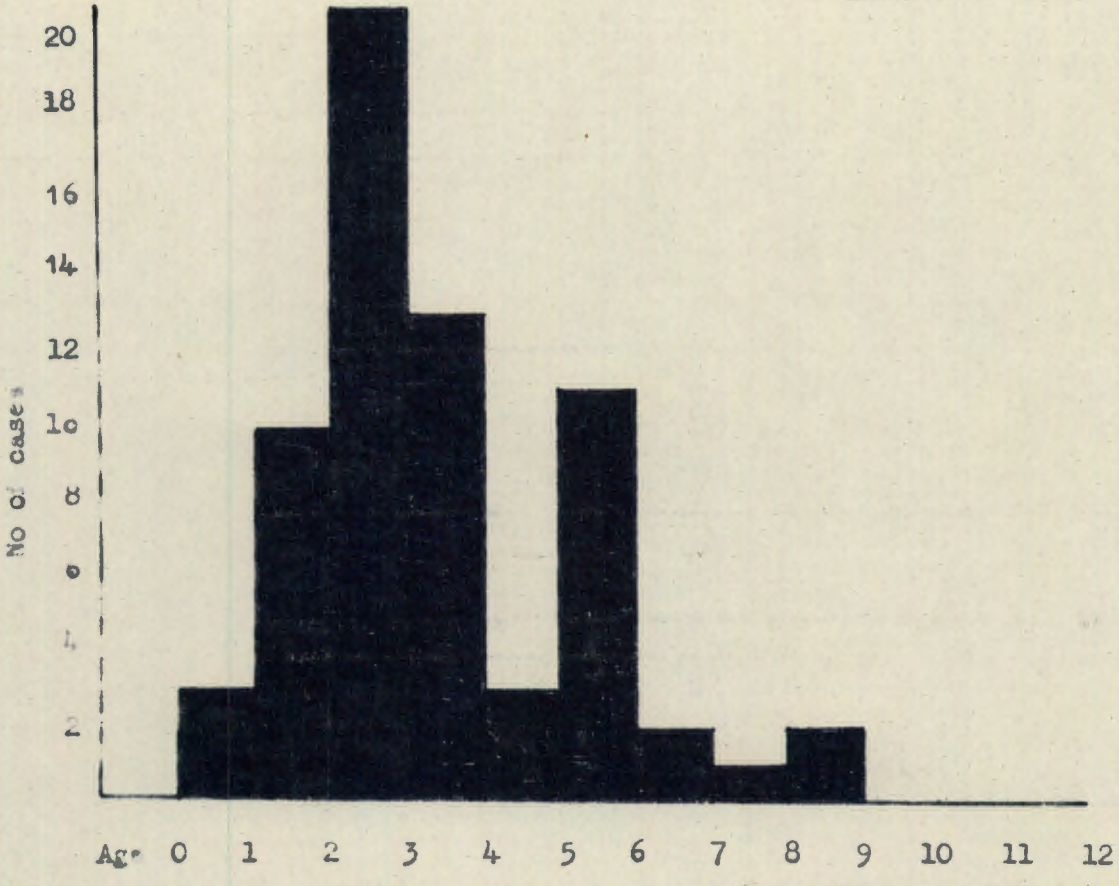


Fig.3.1: INCIDENCE OF ONSET AT VARIOUS AGES

Symptoms. The most frequent initial symptom was an abnormal gait (24 cases), frequent falls (17 cases), and difficulty in climbing steps (6 cases). Other symptoms were deterioration in walking after poliomyelitis (3), reluctance to walk (3), delayed walking (2), floppy infant (2), walking on toes (2), difficulty in getting up (1), difficulty in crawling (1), "sluggish" infant (1), delay in holding head up (1), stiff feet (1) and excessive fatigue (1).

Where abnormality of gait was not the first symptom, it still presented at an early stage of the disease. The descriptive terms used by the parents were "waddling", "swaying", "like a crab", "like a duck", "as if he had a stone in his shoe", while others simply called it a "peculiar gait." "Waddling" as a descriptive term is probably the most accurate.

A history of walking on the toes was obtained in 41 cases, while in 18 this symptom was absent. No information was available in the remaining 6 cases.

Although difficulty in climbing stairs was an initial symptom in only a few cases it was found on direct questioning that there were 22 who had never been able to climb stairs. A history was frequently obtained of difficulty in getting onto a pavement, the child often going down onto all fours in an attempt to do so.

Inability to run was never a presenting feature but was frequently present from early infancy. In only 15 cases was a history obtained of the child being able to run at any stage. An attempt to run usually resulted in marked accentuation of the waddle and frequent falls.

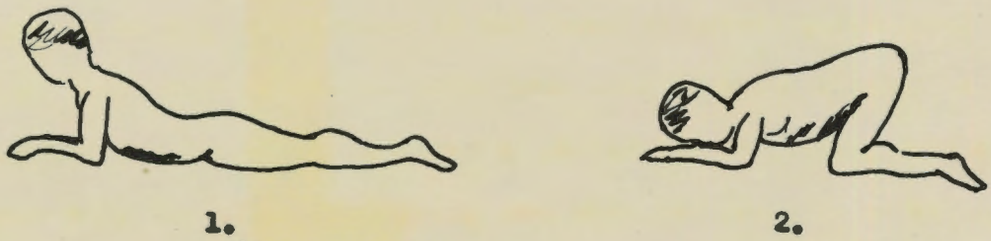
Frequent falls were a constant feature of the early stages of the disease. Although on direct questioning it was found that some cases (7) were never able to get up from the ground without assistance, difficulty in getting up was a presenting symptom in only one instance.

In the present series 43 cases got up in the characteristic dystrophic manner, so vividly described by Gowers and illustrated in Fig. 3.2. When the extensors of the back and hip were not severely affected (cases 21, 42 and 52) the child was still able to get up by simply supporting a hand or elbow on one knee. When the weakness was mor advanced, they "climbed up their thighs" in addition. The symptoms discussed above are correlated with the age of onset and walking in Table III. 2.

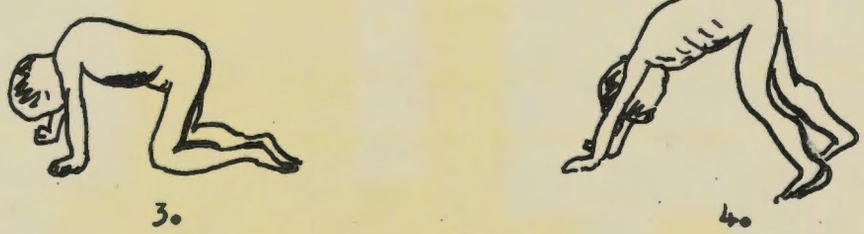
Enlargement of the calves was noted by the parents in 41 cases. In 20 cases this feature was not observed, and in 4 no information was available. Prominence of other muscles was noted in 5 cases. These included the neck (13, 35), the arms (32, 35, 54) and thigh (56, 57) and the back (35).

Weakness of the arms was observed by the parents in 45 cases. In only 3 cases was this symptom noted before the age of five.

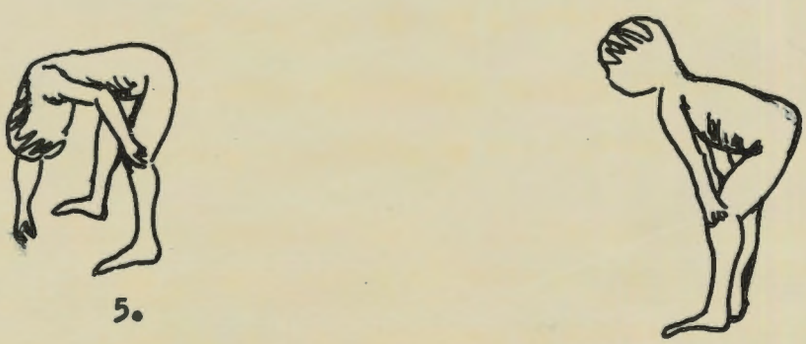
Fig. 3.2 METHOD OF GETTING UP FROM THE GROUND.



1. 2.



3. 4.



5. 6.

7. 8.

1. Lying in prone position.
2. Getting onto hands and knees.
4. Legs and arms extended. Legs brought as close as possible to arms.
5. Hand placed on knee.
6. Both hands on knees. Knees extended.
7. Hands moved alternately up hips. "climbing up himself."
8. Erect posture.

Pain in the muscles was present in 22 cases. It usually involved the legs, and tended to occur with exercise, while the patient was still ambulant. In some instances a history was obtained that the calf muscle went into a state of spasm when the pain occurred and the heels became raised off the ground.

Excessive fatigue was noted in 35 cases. Sphincter control was normal in all cases, and difficulty in chewing observed in only two. Apart from case 65, weakness of the facial muscles was not observed by the parents.

The age of inability to walk varied considerably. At one extreme was case 38 who did not pass the normal milestones and only walked for a short period at the age of eight, while, on the other hand, cases 10 and 14 remained ambulant until the age of fourteen, and case 23 was still walking at the age of sixteen. The number of cases losing the ability to walk at the various ages is given in Fig. 3.3, and its correlation with the age of onset is shown in Fig. 3.4.

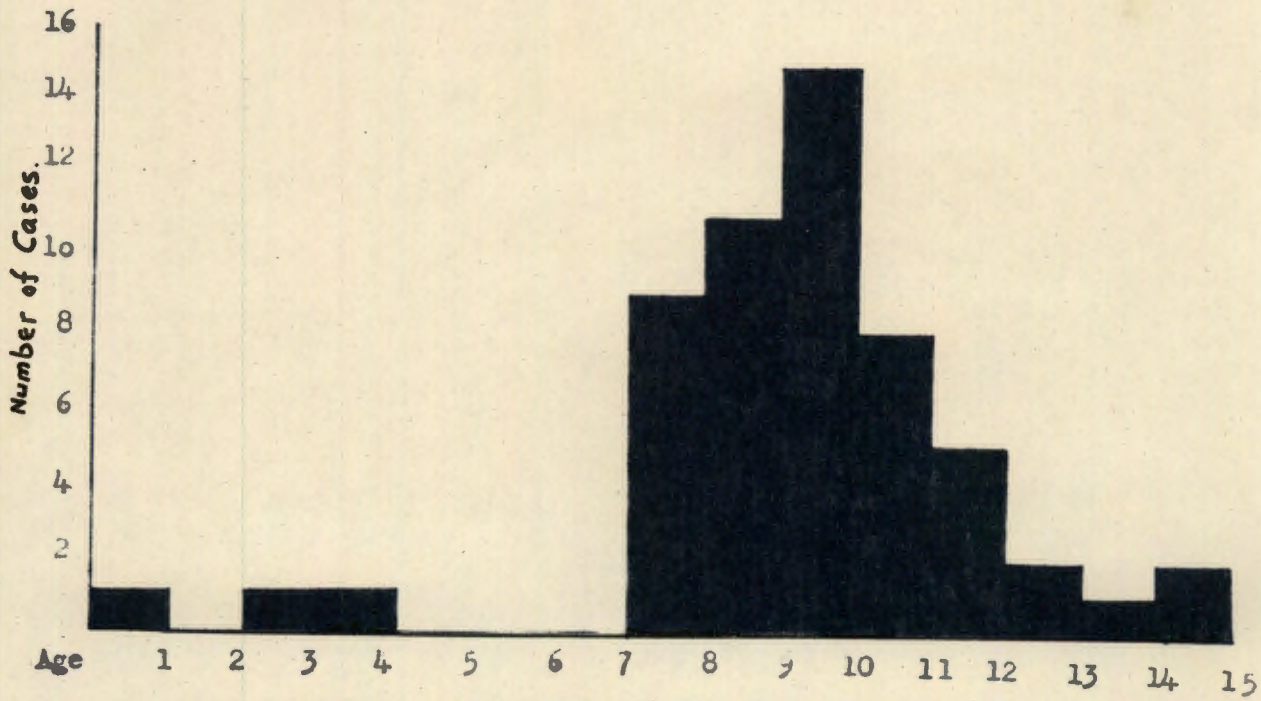
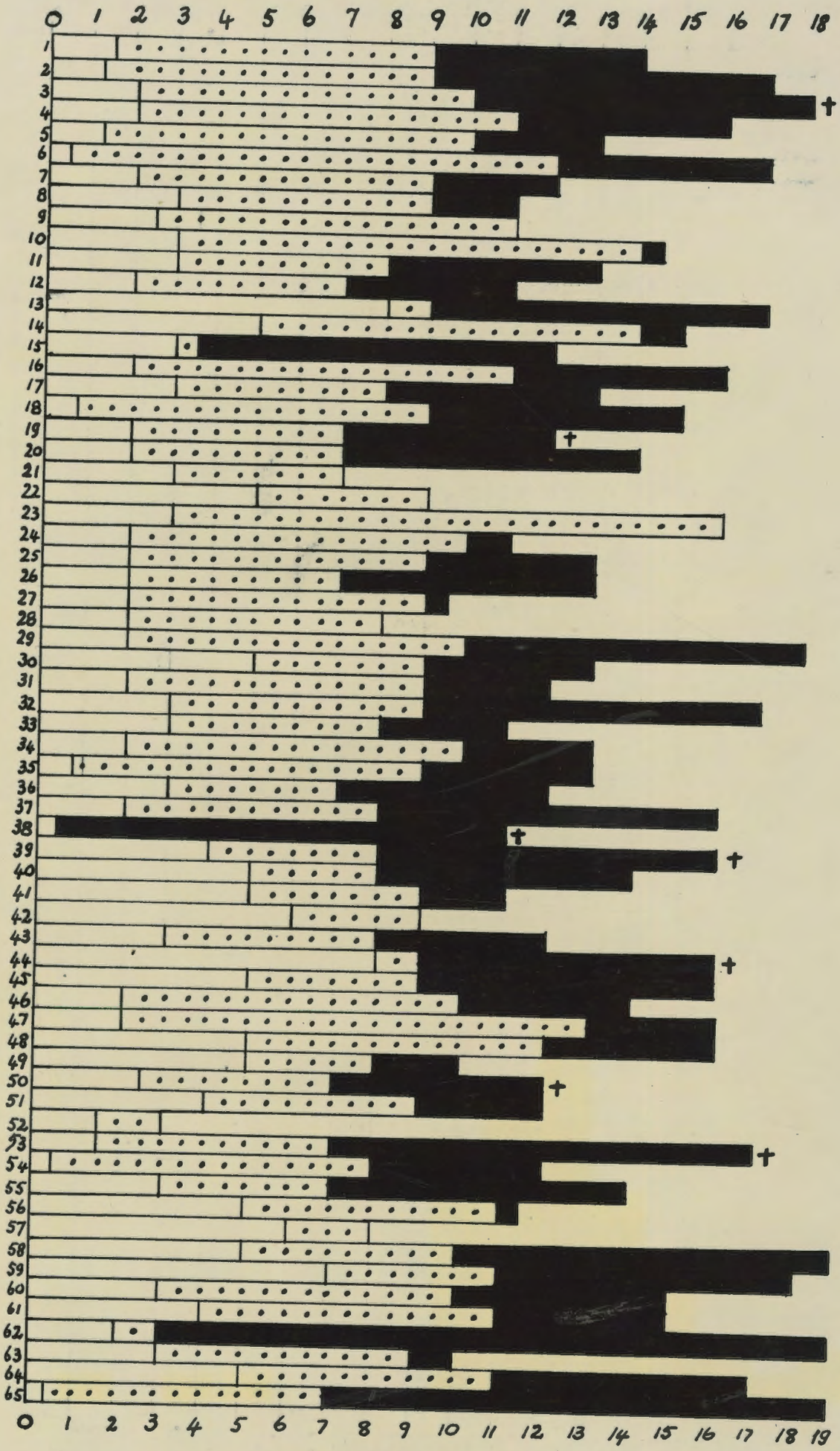
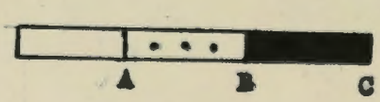


Fig.3.3; INCIDENCE OF LOSS OF ABILITY TO WALK AT VARIOUS AGES

Fig. 3.4 COURSE OF THE DISEASE IN 65 CASES.



KEY:



A : Age of onset (first symptom)

B : Age of inability to walk.

C : Present age or age at death (†)

In the present series the loss of ability to walk was directly caused by some precipitating factor in 13 cases. These are summarized in Table III. 3 below:

TABLE III. 3 : FACTORS PRECIPITATING INABILITY TO WALK.

Case No.	Age.	Precipitating Factor.	Duration of immobilization.
8	9	Fall (bruising)	2 weeks
12	7	Tonsillitis	3 days
24	10	Cold	6 days
29	10	Appendicitis	3 weeks
30	8	Elongation of tendo achilles	6 weeks
32	9	Appendicectomy	2 weeks
33	8	Fractured femur	2 months
34	10	Measles	7 days
35	9	Sprained ankle ?	1 week
39	8	Influenza	2 weeks
43	8	Fracture ankle	3 weeks
55	7	Rubella	2 days
62	$2\frac{3}{4}$	Measles	2 weeks

Furthermore, in case 26 there was a very marked deterioration in walking after 2 months' immobilisation in plaster of Paris for a fractured tibia, and eventual inability to walk six months later. In a number of cases (e.g. case 56) the parents noted a definite deterioration in muscle power following a relatively minor illness or injury.

A history of mental retardation was obtained from the parents in 17 cases.

A positive family history of the disease occurred in 24 cases.

B. CLINICAL FINDINGS:

The general appearance of the patient in the early stages of the disease was usually normal. In the later phases, the majority were very obese (e.g. cases 4 and 36) but some were extremely wasted (e.g. case 48). The facies, apart from being rotund in the obese patient, was usually normal in the early stages. Of the patients with more advanced disease, marked weakness of numerous facial muscle was observed in 12 cases, while a further 8 had a limited (horizontal) smile.

The size of the tongue was difficult to assess owing to the wide variation in normal people. However, there was gross enlargement in 21 cases and it was a common sight to see a patient with his tongue protruded, especially when concentrating on some effort. An atrophic tongue, but without fasciculation was present in Case 32.

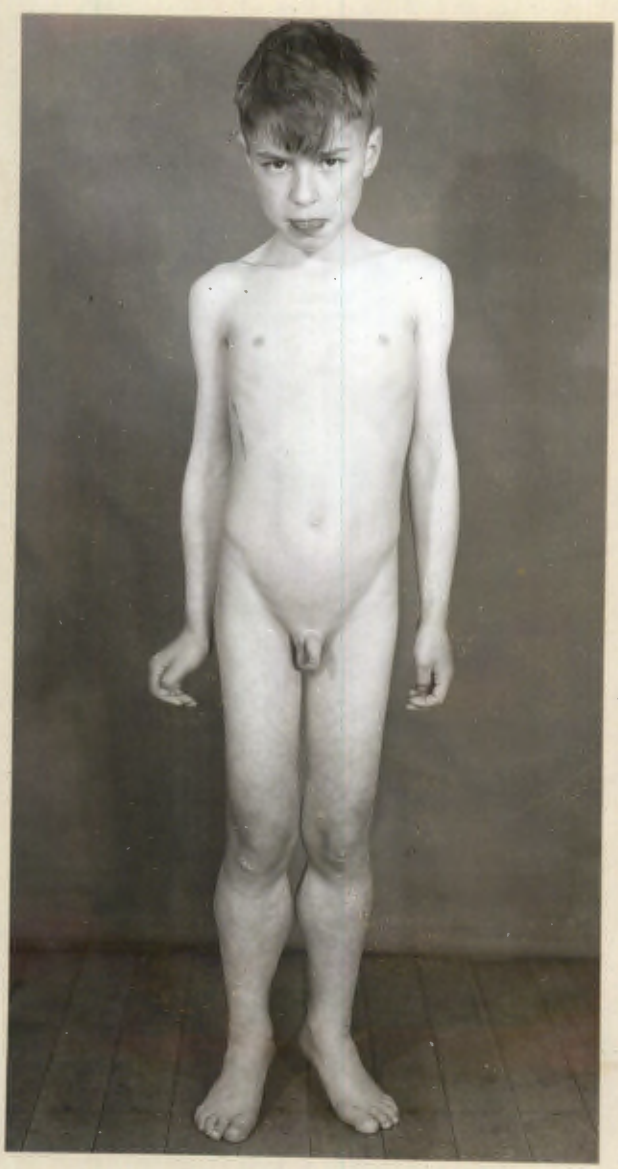
It was also noted that a large proportion of cases had broad mandibular and maxillary arches, with wide separation of the teeth.

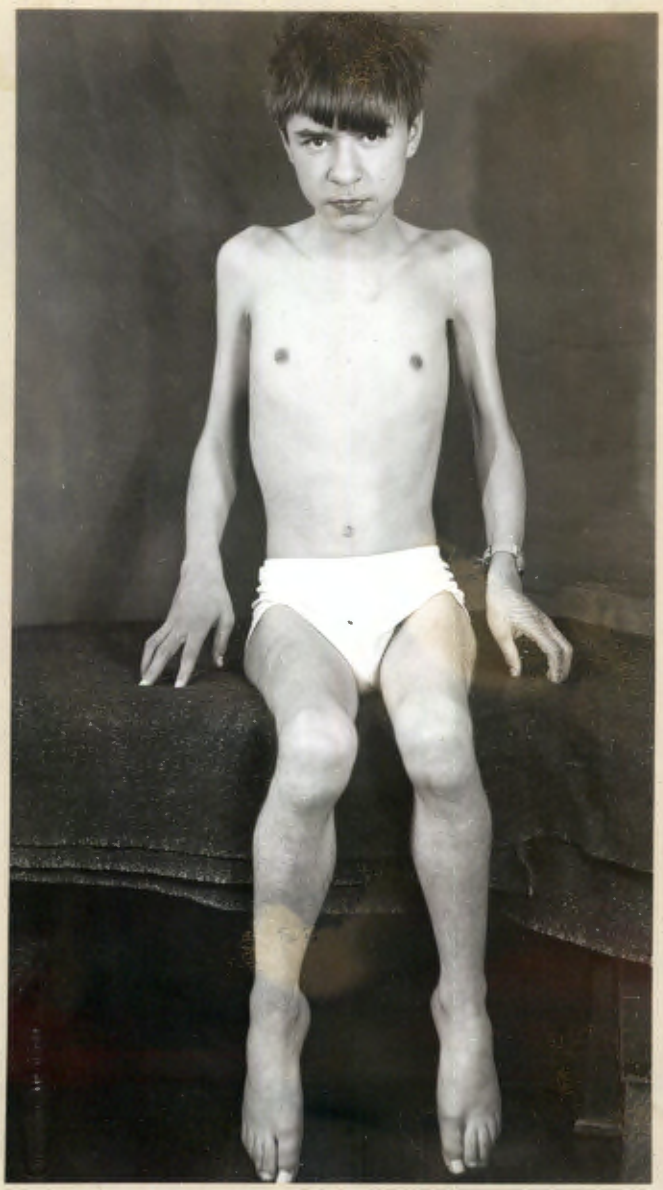
Apart from asymmetry of the ears in case 19, no congenital abnormalities were observed.

The skin over the limbs, especially the legs, was frequently mottled and had a dusky cyanotic tinge. (See photographs of cases 10, 22, 53, Appendix III). They often were objectively cold, although the patient made no complaint. It was associated with non-pitting oedema of the dorsum of the foot in some cases (e.g. 22, 36, 44, 53).

On examination of the musculo-skeletal system, there was a marked variation; not only at different stages of the disease, but also in different patients at a comparable stage. In the early phases the child usually appeared to have a normal muscular development, or even gave the impression of being "well-built", owing to the enlargement of various muscles (cases 21, 28, 42, 52, 57). Case 38 was the one exception. He had no enlargement of any muscles and from the onset of his illness

(before the age of one) there was marked generalised atrophy. The enlargement of muscles usually persisted until the patient was unable to walk, after which there was a progressive wasting (See Figs. 3.5 and 3.6).





Figs. 3.5 and 3.6: DIFFERENCE IN APPEARANCE WITH PROGRESSION OF DISEASE. (3 YEARS).

The incidence of enlargement or wasting of individual muscles is shown in Appendix IV, Table IV.1. While some of the early cases had generalised enlargement of muscles, those in the later stages usually had a more extensive atrophy. Of the muscles which remained relatively prominent in the later stages, the calves were the most common (10 cases). Others included the deltoid (10 cases) and two or three bellies of serratus anterior (10 cases). (Fig. 3.7).

FIG. 3.7 : PROMINENCE OF SERRATUS ANTERIOR AND DELTOID.

In case 14, there was a generalised enlargement of the muscles. During the two years prior to going off his feet, the circumference of his calves increased by over 2 inches and there was a further increase of an inch in the 6 months after he lost the ability to walk. (Fig. 3.8)

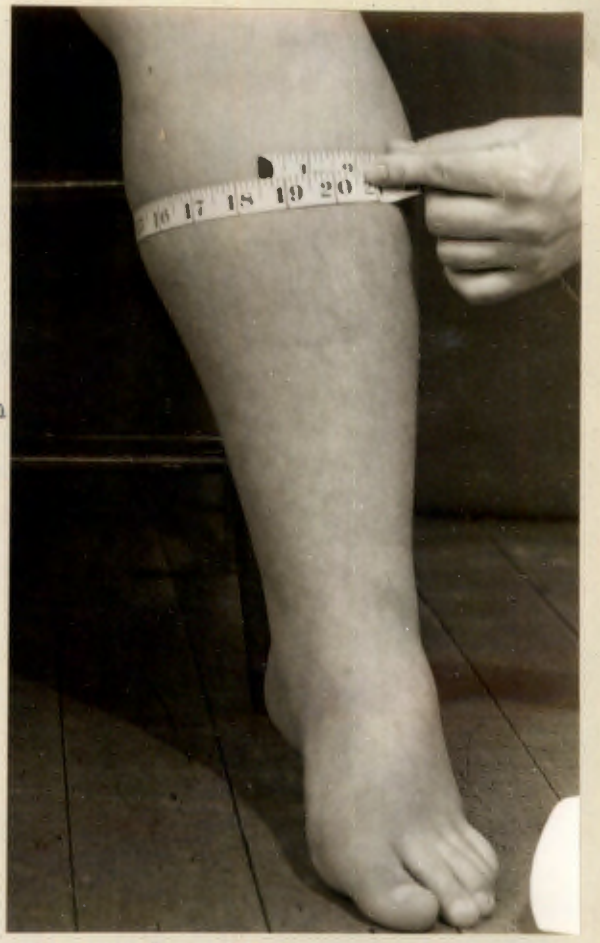


Fig. 3.8 : ENLARGEMENT OF CALF.

In a number of cases, wasting of some muscles was already apparent in the early stages of the disease. The rhomboids and the sternal head of pectoralis major were frequently involved, but various other muscles were also affected. In some cases, the disease process produced an almost selective symmetrical wasting of particular muscles, leaving adjacent ones unaffected. (Fig. 3.9)

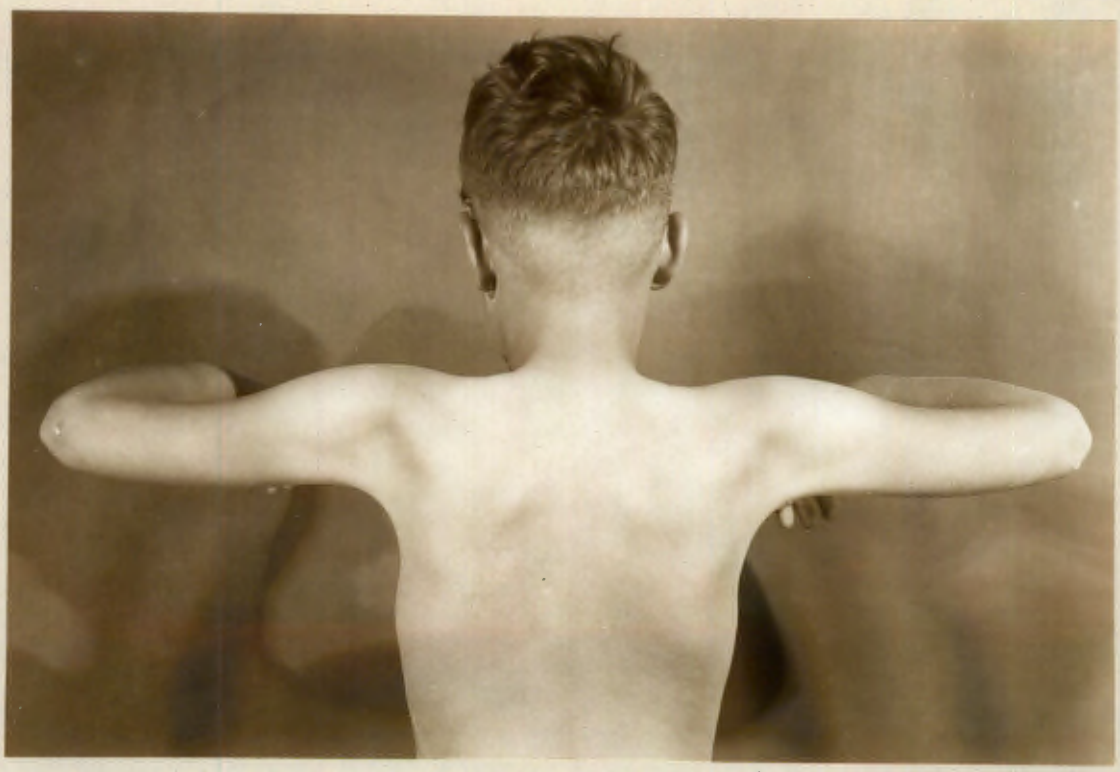
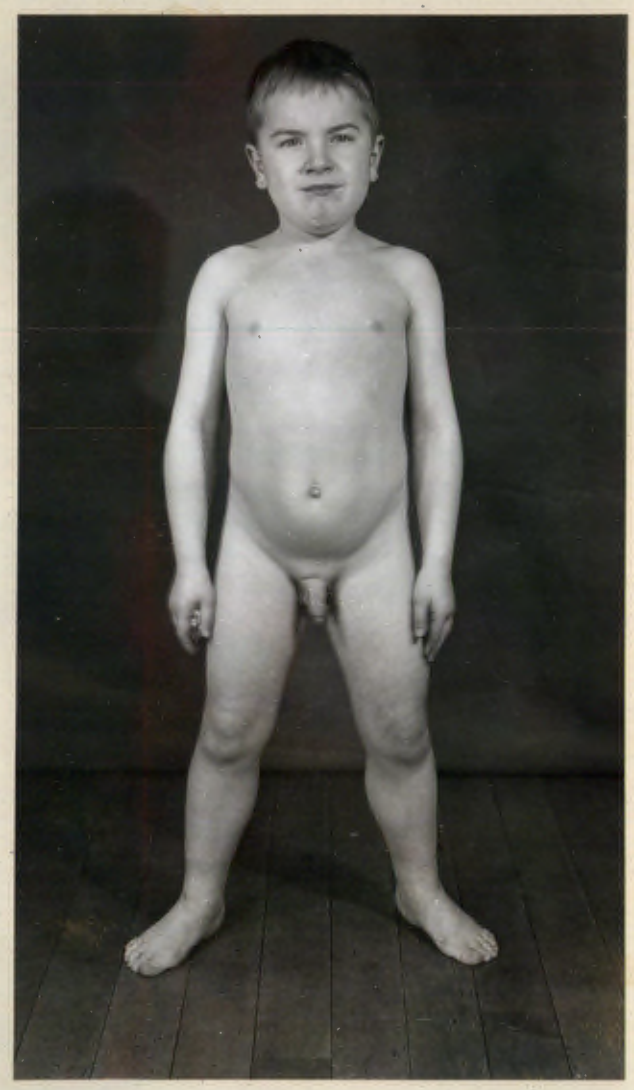


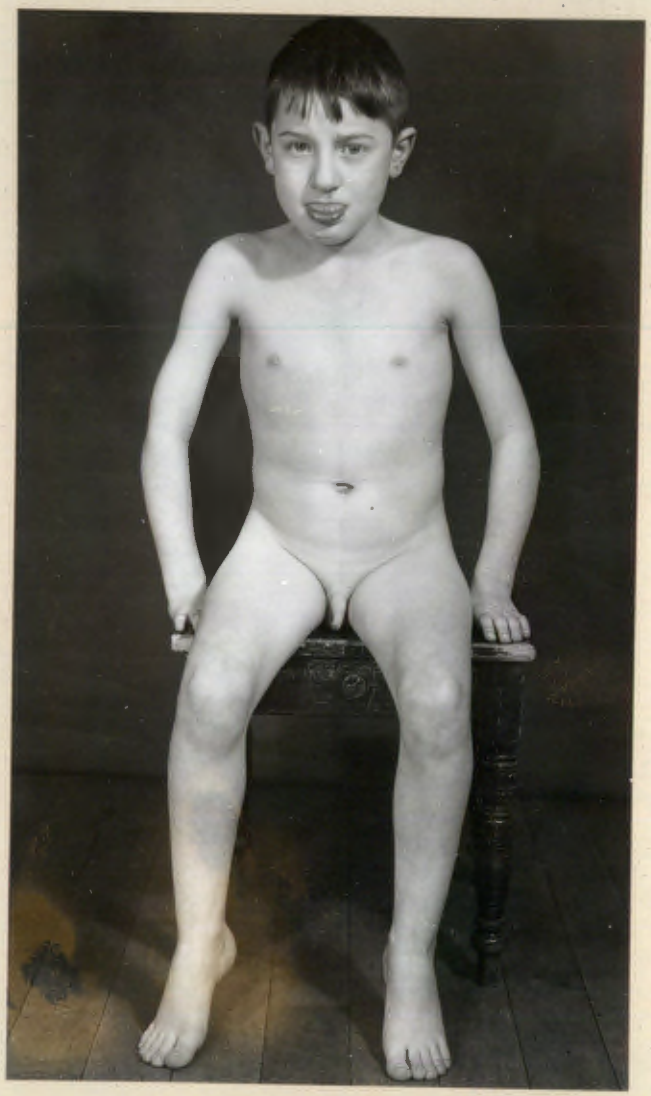
Fig. 3.9 : LOCALISED SYMETRICAL WASTING

A comparative picture of the disease at various stages was well shown in a number of families with more than one affected child. In cases 26, 27 and 28, the disease started at the same age. Although there was a marked difference in the muscle power between these three brothers (see Appendix IV), their general appearance was similar (Figs. 3.10, 3.11 and 3.12). The prominence of the musculature shown by the youngest child was also present in the other two. Cases 50, 51, and 52 on the other hand, presented a remarkable contrast (Figs. 3.13, 3.14 and 3.15). While case 52 with early disease was similar in appearance to case 28, the second child had marked atrophy of the upper arms, shoulder girdle muscles and thighs. The eldest sib had gross generalised wasting of the muscles of the trunk and limbs, with sparing of only the face and neck. An even more striking contrast was shown by two brothers, cases 48 and 49. (Fig. 3.16 and 3.17).

The most common deformities noted were scoliosis of the spine and contractures of the limb muscles. The contracture of the calf muscles with shortening of the tendo Achilles usually started while the patient was still ambulant. The other deformities only developed after the patient had lost the ability to walk.

Scoliosis was present in 34 cases, the concavity being to the left in 21 cases, and to the right in 13 cases. Limitation of extension of the knees due to contractures of the hamstrings was present in 47 cases; most of these also had some limitation of flexion. Flexion alone was limited in 1 case. Contractures at the knee usually developed within a few months of inability to walk and were slowly progressive, until extension was ultimately limited beyond 90° or 100°. Limitation of extension at the elbows was present in 41 cases and a number of these also had limitation of supination. The hips showed contractures of the flexors in 22 patients and limitation of rotation in 2 cases. The shoulder was affected in 4 cases and the wrist in 8. In all cases





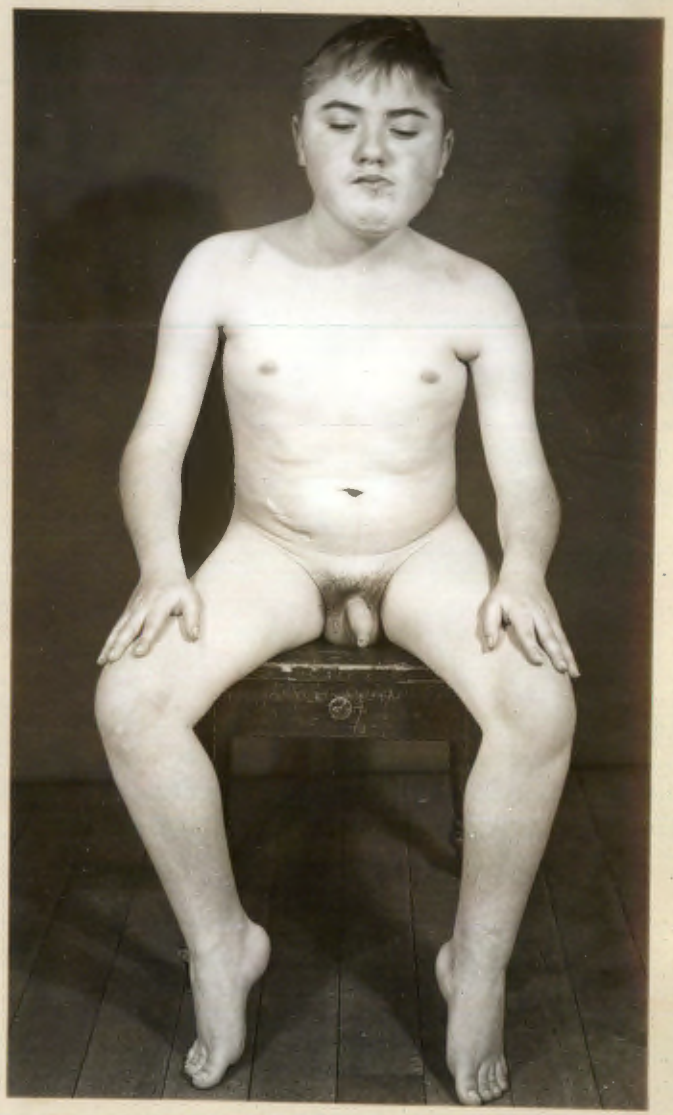
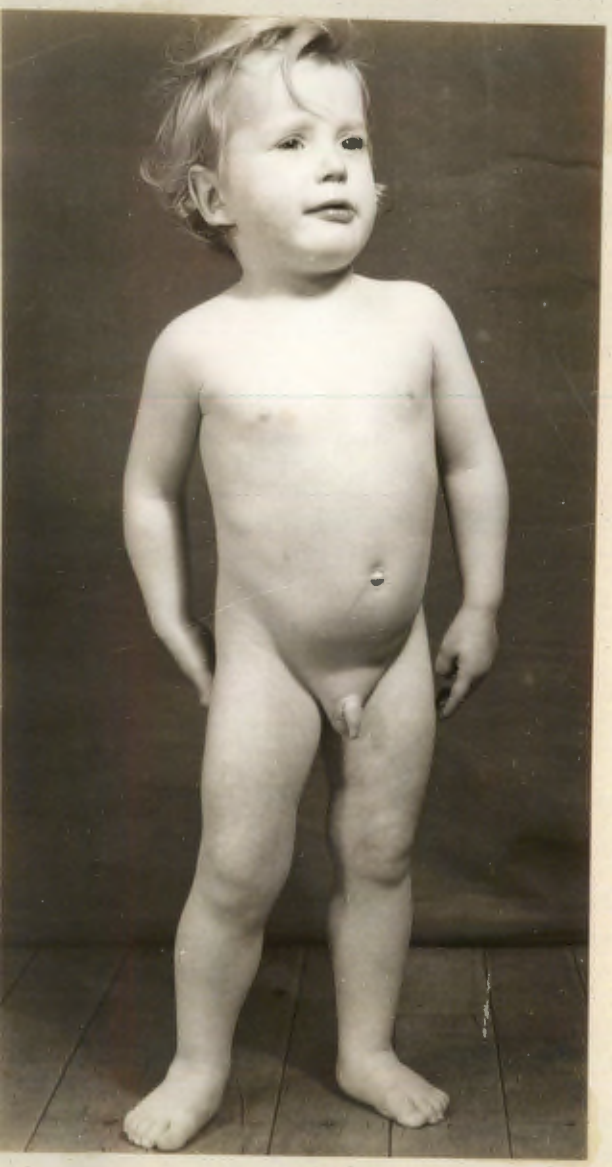
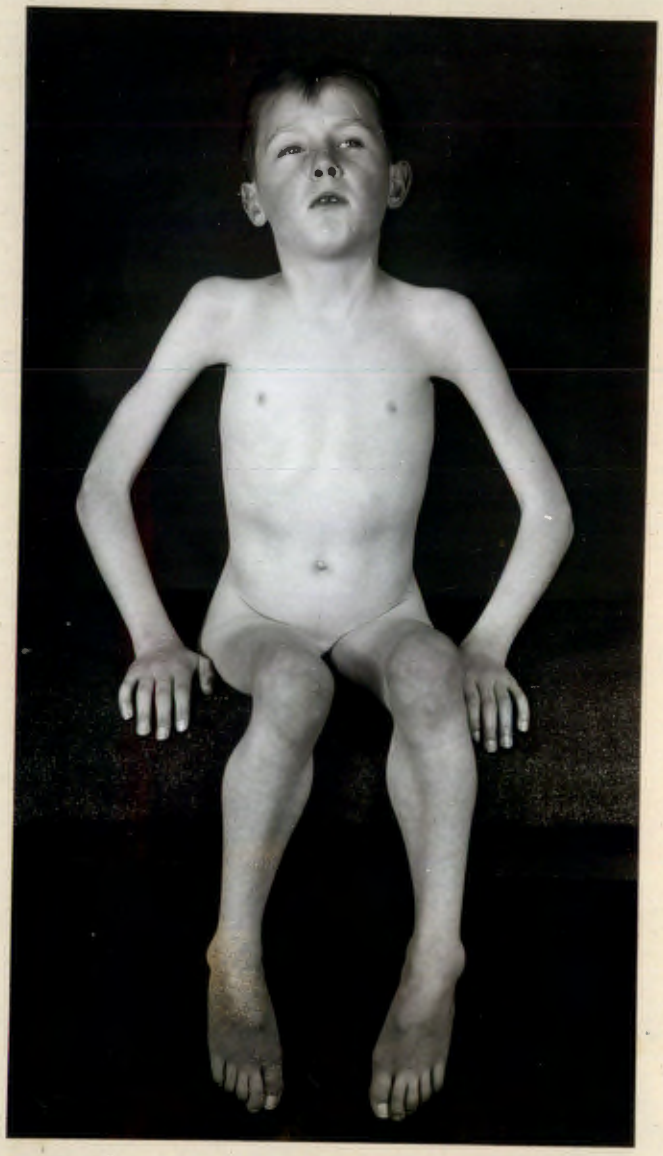


Fig. 3.10 - 3 .12. SIMILARITY IN APPEARANCE OF THREE BROTHERS (Case 26-28)





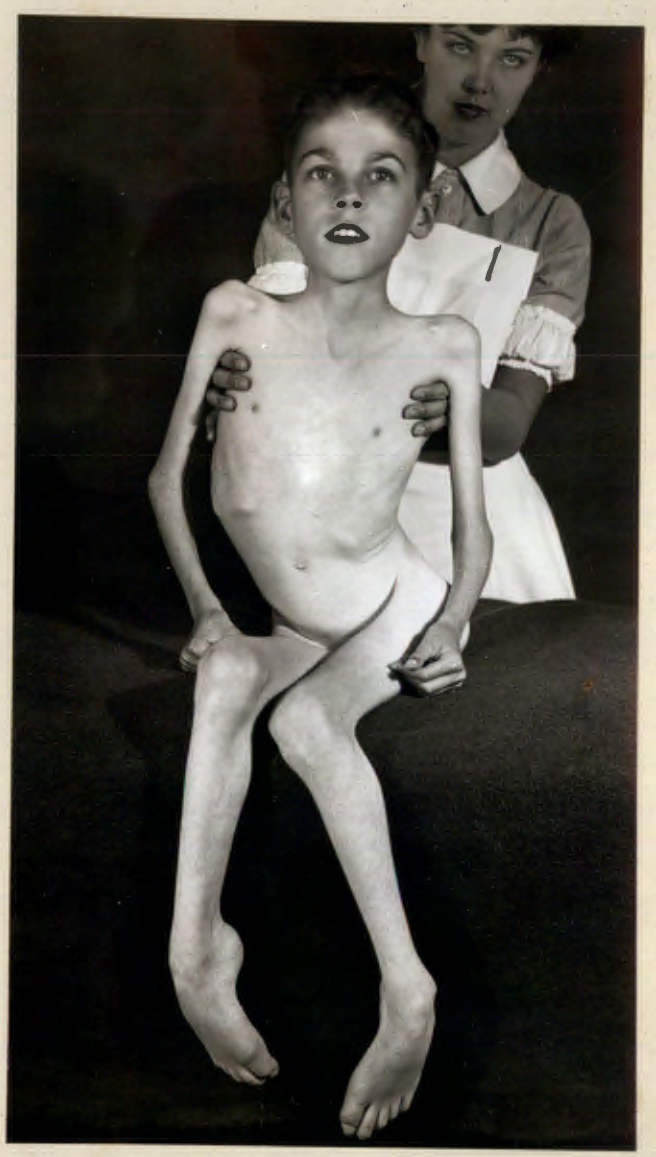


Fig. 3.13 - 3.15. DIFFERENCE IN APPEARANCE OF THREE BROTHERS WITH THE SAME DISEASE (Case 50-52)

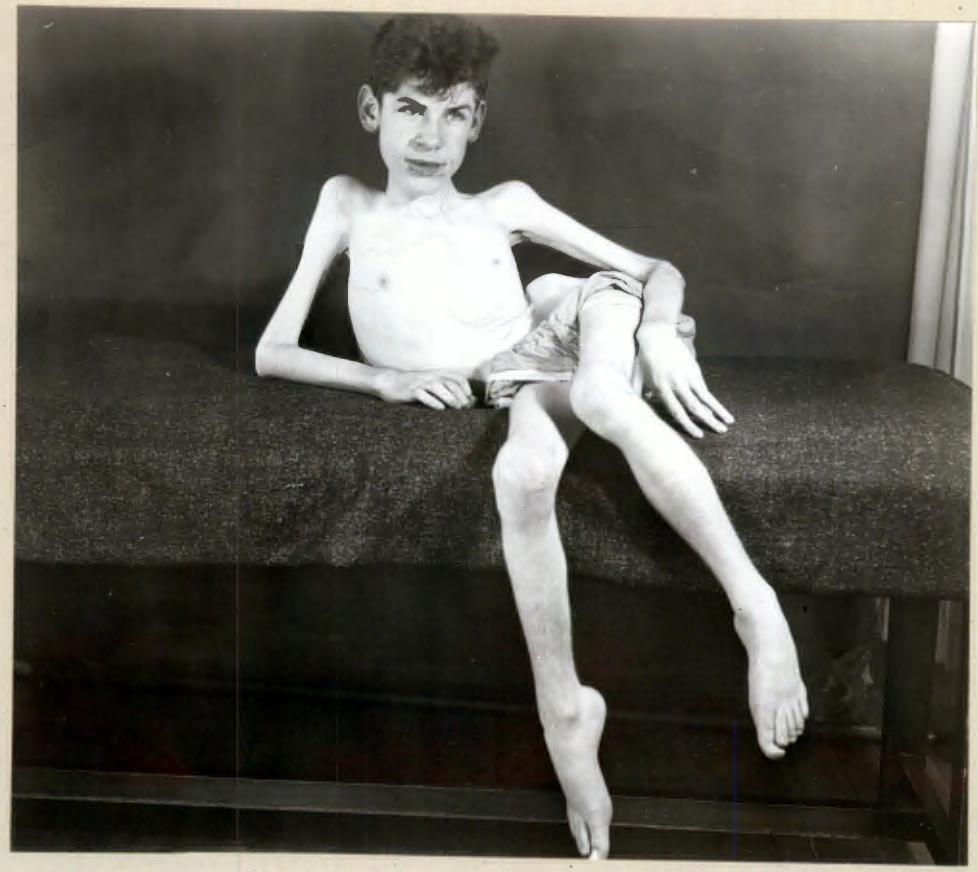


Fig. 3.16 - 3.17. CONTRASTING APPEARANCE IN TWO BROTHERS

there was fairly uniform involvement of the two sides. Equinus deformity of the ankles was present in 52 cases. In some of the more advanced ones, the deformity reached 180°. Details of the deformities are given in Appendix IV, Table IV.2.

In the early stages of the disease (cases 21, 52 and 57) the weakness was mainly limited to the back and hip muscles. At a slightly later stage the shoulder girdle muscles also became weakened while that of the lower limb progressed further (cases 28 and 42). In the very late stages of the disease there was practically no movement left in any of the limb or trunk muscles apart from the hands and the feet. (e.g. Cases 50 and 53). The extent and distribution of muscle weakness in individual cases is summarized in Appendix IV, Tables IV.3 to IV.7.

In the present study a number of interesting observations were made in connection with the reflexes. The deep tendon reflexes in the arms were absent in all but 4 cases, which are summarized in Table III.4.

TABLE III.4 : REFLEXES IN UPPER LIMBS.

Case No.	Biceps.		Triceps.		Supinator.	
	R	L	R	L	R	L
21	+	+	+	+	++	++
28	0	0	0	0	+	+
42	+	+	+	+	+	+
57	+	+	0	0	0	0

All four were early cases. It was noteworthy that in the two elder brothers of case 28 (cases 26 and 27), the two elder brothers of Case 42 (cases 40 and 41), and the elder sister of Case 57 (case 56), the deep reflexes in the arms were all absent.

The knee jerks were present in 7 cases and in a further 2 cases were elicited on one side only. In all the patients who had

a positive knee jerk, the ankle jerks were also present, with the one exception of case 56 whose ankle jerks were absent. (See Appendix IV, Table IV.8.)

The ankle jerks were present bilaterally in 40 cases and unilaterally in 5. In 25 of these cases the ankle jerks were abnormally brisk, and unsustained clonus was present in 3 of them.

It was observed in one of the patients that a tap on the lower half of the tibia produced a brisk contraction of the calf muscle, resembling the usual response of the ankle jerk. This reflex, "the tibial tap", was subsequently assessed as a routine procedure in all cases. When present, it could be elicited by a light tap at the junction of the middle and lower thirds of the anterior aspect of the tibia. When brisk, it also resulted from a tap over any part of the lower third of the tibia, and at times even on the dorsum of the foot or the lateral aspect of the lower leg.

The tibial tap was present in 26 cases. It was more frequently elicited in those cases where the ankle jerk was brisk, and the ankle jerk was invariably present where the tibial tap could be elicited. In a comparative examination of the reflexes in 9 children with cerebral diplegia the tibial tap was positive bilaterally in 7 cases and in the other 2 unilaterally. All 9 cases had abnormally brisk ankle jerks and in 5 the tibial taps were brisk as well. In a series of 50 children with no evidence of nervous or muscular disease the tibial tap was invariably absent. The ankle jerk could also be elicited by a brisk tap on the sole of the foot held in a dorsi-flexed position. This was done routinely on every case and found to closely parallel the ankle jerks elicited in the usual way. (Appendix IV, Table IV.8).

The plantar response was flexor in all cases.

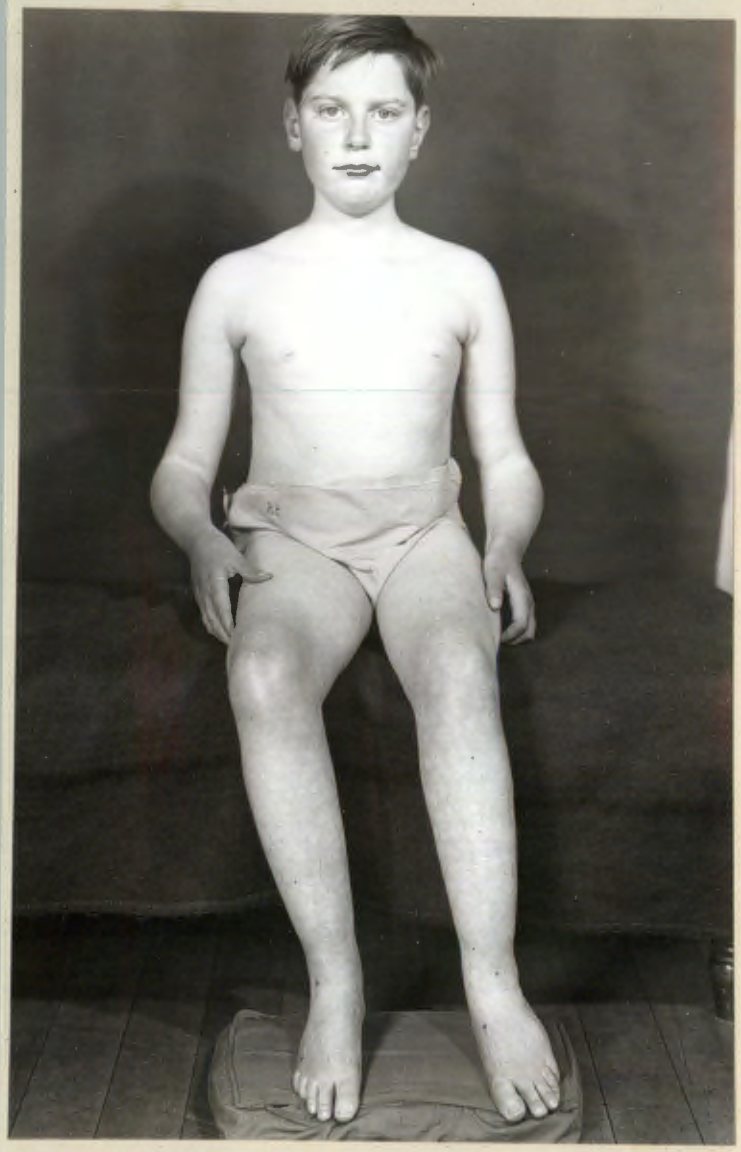
Of the superficial reflexes, the abdominals were present in

27 cases and the cremasteric reflexes in 29 cases. Allowing for the normal variability of these superficial reflexes, and the frequent presence of obesity in the cases of progressive muscular dystrophy, which makes the abdominal reflexes more difficult to elicit, these are probably within the normal limits.

C. COURSE AND COMPLICATIONS.

Various complications were common in the course of the disease. Mild upper respiratory infections, especially during the winter months, frequently led to pneumonia unless treated. A history of previous fracture of a long bone was obtained in 19 cases. In a number of cases, multiple fractures had occurred. Fractures often followed on a relatively minor injury, such as a bump on the knee, (case 4), or a fall on the floor (case 28). The fractures observed in the course of this investigation all united well within a short space of time.

Although there is a suggestion of some uniformity in the clinical pattern of the disease (see Fig. 3.4), considerable variation occurred in individual cases. The majority of patients showed a steadily progressive course, in which the decline was scarcely noticeable in periods of less than 6 months or a year. In others, however, the course was quite dramatic. In case 44, after a relatively gradual progression until the age of 14, there was a sudden change and he went rapidly downhill. The weakness and deformities increased and the wasting became extreme (Figs. 3.18 and 3.19). Prior to his death at the age of 16, there was no residual active movement in practically any of the trunk, limb and neck muscles and he had difficulty in swallowing. This patient had previously had poliomyelitis which might have influenced the course of the disease. However, a very similar picture was shown by case 39 who did not have poliomyelitis (Figs. 3.20 and 3.21.)



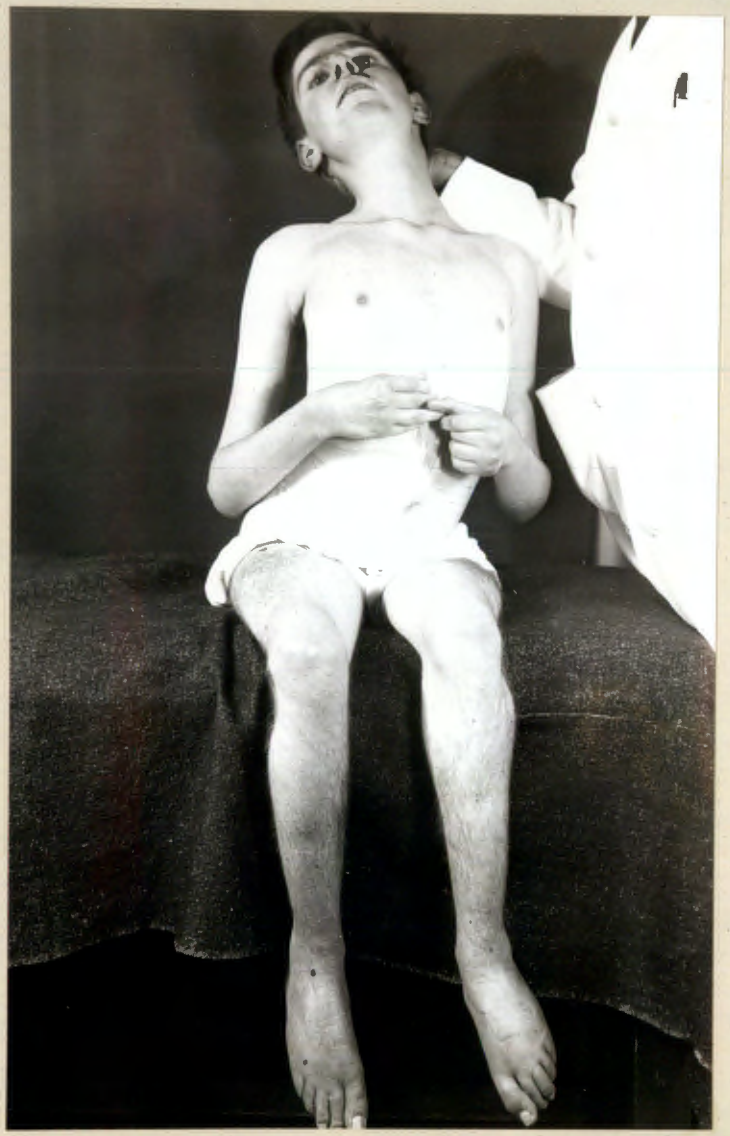


Fig. 3.18 - 3.19. CASE 44. RAPID PROGRESSION OF THE DISEASE (3 years)

Of the 7 cases who died during this study, six had pneumonia whilst in the other (case 44) death was probably due to cardiac failure (see Chapter 6). On clinical grounds, it was thought that a cardiac cause of death was likely in cases 39, 44, and 53 because of the sudden collapse and state of shock in the final stages, reminiscent of the picture in acute myocardial infarction.

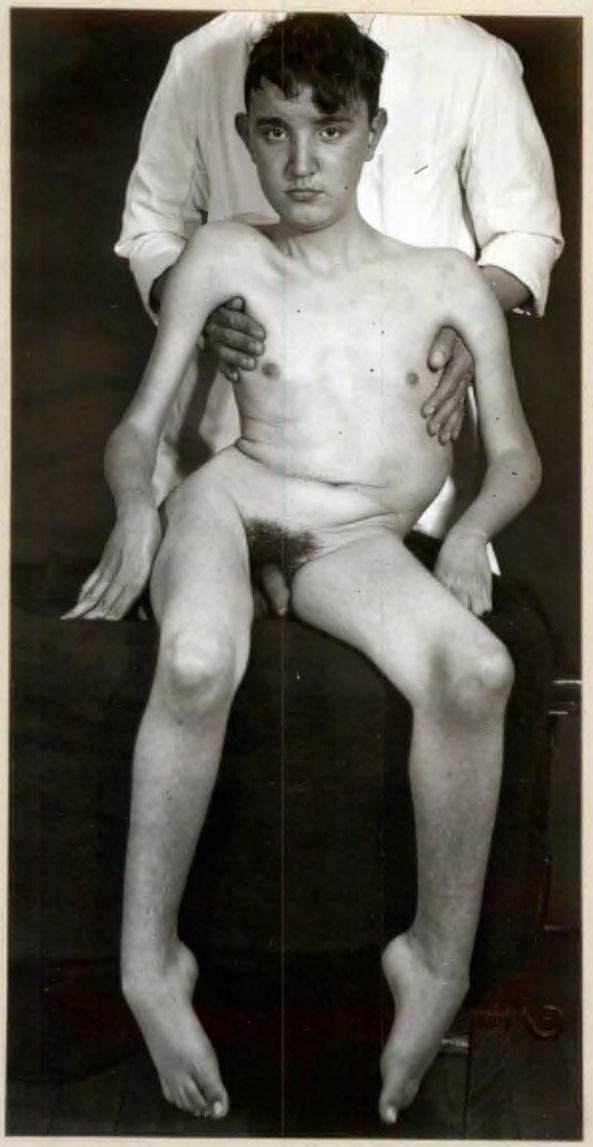


Fig. 3.20 - 3.21 CASE 39 RAPID PROGRESSION OF THE DISEASE
(2 years)

DISCUSSION.

In the majority of cases in this survey, the presenting features and manifestations followed the same pattern as that described for the Duchenne type of dystrophy by previous authors. A number of points of special interest have, however, arisen in the course of this study.

The presence of enlargement of some muscles in the early stages of the disease followed by their later atrophy, as well as the occurrence of patients in the same family with either predominant enlargement or wasting of muscles, supports the view that these differences in appearance do not imply a different disease. For this reason the term "pseudohypertrophic" should not be used to designate a particular type of dystrophy.

Many of the characteristic early features of the disease can be explained on the basis of muscular weakness. The waddling gait is due to the weakness of the gluteus medius and minimus muscles (Duchenne, 1867). These muscles normally support the pelvis when one leg is raised off the ground. When they are weak, as in progressive muscular dystrophy, the body is tilted towards the leg on the ground when the other one is raised, in order to bring the centre of gravity over that leg. The lordosis is due to the weakness of the spinal extensors plus the flexion of the pelvis on the hips (Gowers, 1879) due to the weakness of the hip extensors. Gowers has analysed the manoeuvre by which the dystrophic child characteristically gets up from the ground (see Fig. 3.2). There are two components. Firstly the hands are placed on the knees in order to extend the knees and thus take the weight of the body off the knee extensors. This can also be done by placing the legs widely apart and gradually moving the hands backwards along the ground until the weight of the trunk is over the legs. A hand

supported on the knee then helps in the second part of the manoeuvre which is to extend the hips. If the hip extensors are not strong enough this is achieved by moving the hands alternately upwards along the thighs. This is usually referred to as "climbing up himself." These manoeuvres are a reflection of a consistent pattern of muscular weakness and not pathognomonic of muscular dystrophy, as suggested by Gowers. I have observed the identical picture in a boy of 6 years who had acute poliomyelitis 2 years previously, severely affecting the back and hip muscles. He had a slightly waddling gait and climbed up himself in the "characteristic dystrophic manner." His weakness was non-progressive so that the question of a superadded muscular dystrophy did not arise.

Deformities are a common feature of the disease. With the exception of the contracture of the calf muscle with shortening of the tendo Achilles, the contractures all occur late in the disease. The shortening of the calf muscle has been considered by previous authors as the result of fibrosis of the muscle (Gowers 1879), or due to asymmetrical power between the calf muscles and the weak anterior tibial group (Eulenburg 1865).

The resultant walking on the toes has been looked upon as being secondary to the contracture of the calves. In my opinion the shortening of the muscle is secondary to the abnormal posture. In an early case (52) it was observed that the child walked on his toes in spite of the fact that full dorsi-flexion of the ankle was possible. If the back is held in a lordotic position to compensate for the weakness of the trunk and pelvic girdle muscles, it is much easier to maintain the balance in an upright posture when standing on the toes, than when the heels are on the ground. The reason for these children walking on their toes is, therefore, to maintain their

balance and thus compensate for the weakness of the back muscles and hip extensors. This leads to constant plantar flexion of the feet, with resultant shortening of the calf muscles. (Lockhart (1960) has mentioned the permanent shortening of the tendo Achilles in normal subjects wearing high heels.) The mechanism of the contractures is probably the same in all muscles affected, namely relative immobilization in a fixed position. Thus after the patient becomes chairbound, the extension of the knees becomes limited beyond about 90°. Similarly extension of the elbows becomes limited and there is also limitation of supination, because the elbows are kept in a position of constant flexion and partial pronation.

The scoliosis is due to the fact that the child usually leans to one or other side in his wheel-chair. An early curvature of the spine as a result of this has been observed within a few months of the patient going off his feet. Although Gowers commented on the fact that the scoliosis (the concavity) in all cases was to the right, this was probably coincidental and not due to the muscles always being weaker on the left. In the present series 21 cases had a scoliosis with concavity to the left and 13 cases had a scoliosis to the right. Scoliosis did not occur in children who were still ambulant.

After the child goes off his feet the contractures are progressive, but usually do not go beyond 90° flexion of the knees and elbows. The hips and shoulders may also show some limitation of certain movements. Most commonly a limitation of about 45° in extension of the hips, while in the shoulders the movements most commonly affected are abduction and external rotation. The ankles invariably have a marked, progressive, equinus deformity which may eventually reach 180°. Contractures of the flexors of the wrist and fingers are not a common feature of progressive muscular dystrophy,

although in a few cases limitation of dorsi-flexion of the wrist beyond 180° was noted. In the one case in which flexion contractures of the fingers occurred (44) it was probably related to the previous poliomyelitis. The absence of contractures in the muscles of the hands supports the hypothesis that contractures only occur in muscles habitually held in a relatively fixed position.

The reflexes are usually said to be lost or diminished. Gowers (1879) found that, apart from the knee jerk which was diminished when atrophy of the knee extensors was considerable, the tendon reflexes were unimpaired. Walton and Nattrass (1954), on the other hand, observed normal deep tendon reflexes in only one of their 48 cases. All the reflexes were absent in 6 cases, while in the remaining 41 the ankle jerks were present but the other deep reflexes in all four limbs were absent or depressed. Adams, Denny-Brown and Pearson (1953) maintain that the tendon reflexes are lost when the muscles concerned become involved.

In the present investigation it was observed that the tendon reflexes of the upper limbs were absent in the vast majority of cases. It is difficult to understand why the deep reflexes of the arms should disappear before those of the legs, and even at a stage of no apparent muscular weakness or wasting.

The ankle jerks, on the other hand, were present in 62% of the patients, which included all stages of the disease, and were abnormally brisk in more than half of these cases. The presence of the ankle jerk reflects the less marked wasting or weakness of the calf muscle in comparison with the quadriceps. This was usually borne out on charting of muscle power. However, the difference in power between the calf muscles and the anterior crural group of muscles, did not seem sufficient to explain the increased ankle jerks.

The positive "tibial tap" is not easy to interpret. At first sight one might ascribe it to a stretching of the tendo Achilles caused by a transmitted impulse from the tibia. However, in many cases where it was brisk it could quite readily be elicited by a very light tap on the tibia or even a tap in the lateral direction over the lower part of the fibula, which did not appear to cause any movement of the tibia. The fact that it was present in all the cases of cerebral diplegia suggests that it is associated with an increased ankle jerk. This was also the case in 18 of the cases of progressive muscular dystrophy where the ankle jerk was abnormally brisk. In the remaining 8 cases with a positive tibial tap, however, the ankle jerk was of normal intensity. On the other hand, in 6 cases where the ankle jerk was brisk, a tibial tap could not be elicited.

Four cases of the present series had poliomyelitis (13, 22, 44 and 49). In case 22 this occurred in infancy, resolved completely, and the subsequent course of his muscular dystrophy was not exceptional. Case 49 had poliomyelitis after the onset of his muscular dystrophy, and it probably influenced his comparatively early inability to walk (at the age of 8). In cases 13 and 44 the muscular dystrophy developed after the poliomyelitis and only became apparent at a relatively late age (8 years in both cases). The course of the disease was rapidly progressive after that and both patients were off their feet within a year. In case 13 disproportionate wasting of the left deltoid and greater weakness of the left arm than the right were evidence of the previous poliomyelitis. (Fig. 3.22)

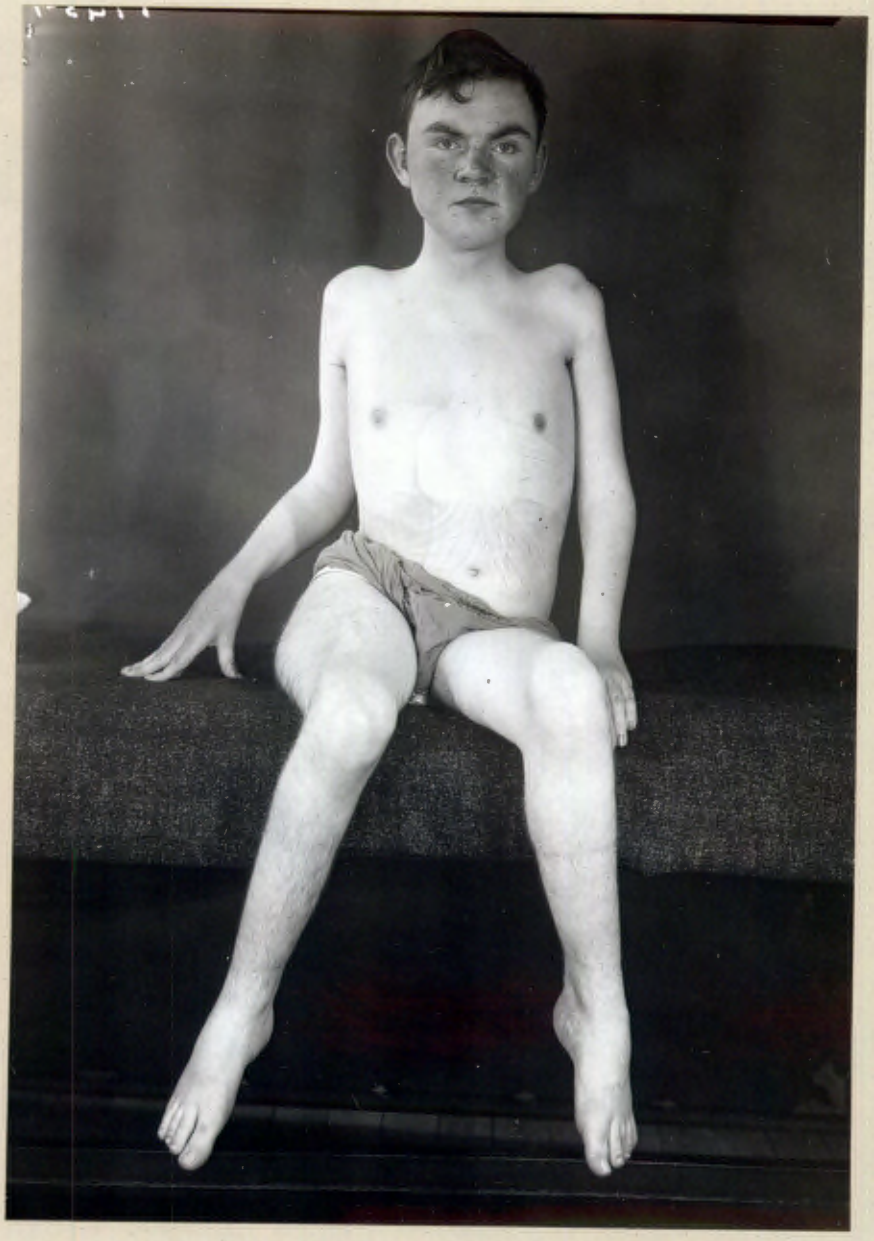


Fig. 3.22 : UNILATERAL WASTING OF DELTOID (POLIOMYELITIS).

In case 44 there was no asymmetry of the musculature on inspection. The muscle charting showed a more extensive unilateral weakness of isolated muscle groups. (See Appendix IV, Table IV.6).

In these 2 patients the diagnosis of poliomyelitis was confirmed on electromyography. In case 13 the left deltoid showed the characteristic denervation pattern, while the right tibialis

anterior had a typical myopathic pattern (Buchtal, 1957). In case 44 a denervation pattern was present in the left tibialis anterior and a myopathic pattern in the right.

Electromyography was also done on a further 22 patients. In 20 a typical myopathic pattern was observed. In the other 2 patients (20 and 39) the electromyographic changes were inconsistent with the clinical diagnosis. Both showed a denervation pattern in the right, as well as the left, tibialis anterior. The clinical diagnosis was, however, confirmed at biopsy in case 20 and at autopsy in case 39. In another patient (case 38), on the other hand, the diagnosis of a myopathy, rather than a neuropathy, was based on the E.M.G. findings.

Case 38 had an atypical course. Generalised wasting and weakness was already present in the first year of life and the clinical appearance was reminiscent of Werdnig-Hoffmann's disease. However, in the light of the E.M.G. findings, a congenital form of myopathy (as first described by Batten, 1910) may be the best diagnosis.

The majority of patients studied showed a fairly uniform pattern, with onset of the initial symptom before the age of 4 and a steady progression, with inability to walk usually by the age of 12. The 7 patients who died ranged in age from 11 to 18 years. These cases conform to the Duchenne type as defined by Stevenson (1953). The course in some patients, on the other hand, was much slower. Cases 10 and 14 walked till the age of 14, and case 23 was still ambulant at 16. In addition, 3 patients were still alive at the age of 19. These findings support the view of Walton and Nattrass that some cases of Duchenne-type dystrophy may have a slower progression. The variation in the course of the disease in affected sibs is of interest. Case 15 lost the ability to walk by the age of 4, while his brother walked till the age of 14. Similarly, case 49 went off

his feet at 8, while his brother did so only at 12. It thus seems impracticable to divide cases into a severe and mild groups on the basis of being able to walk at the age of 11 (Blyth and Pugh).

Fig. 3.23 : DUCHENNE TYPE DYSTROPHY IN FEMALES, (56, 57). CLAWED TOES IN CASE 57 AND UNAFFECTED SIB (CENTRE).

Two females, cases (56 and 57) had a similar pattern of disease to that occurring in the males (Fig. 3.23). The presence of clawed toes in one of these patients (57), as well as in a sib unaffected by muscular dystrophy, is of added interest.

MANAGEMENT.

The nursing attention of these children is no small task. In the later stages of the disease the weakness is so generalised and extreme, that any active movements which remain are usually confined to the hands and feet. The majority can manage to feed themselves and to write, as long as their elbows rest on a table to allow for the weakness of the shoulder muscles. As a rule they are unable, however, to wash their faces or comb their hair after the age of about 12 or 13. There are also many small things which they require help with - things which one normally takes for granted - such as lifting out an arm from under the bed-clothes, scratching the nose, using a handkerchief and so forth.

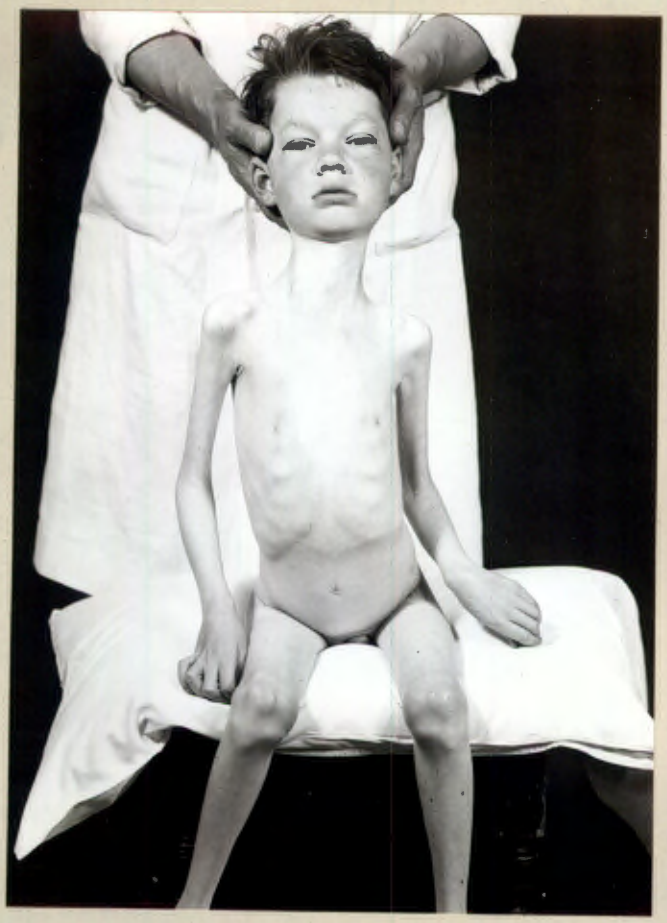
Owing to the great tendency to put on weight after becoming immobilized, it is quite a problem lifting these children in and out of bed or their wheel-chairs. Mechanical hoists are available but are very time-consuming and hardly practicable on a unit of 20 patients.

Many authors have written on the value of splints for weakened muscles and tenotomy of contracted tendons. I am convinced that while the child is still mobile, no active procedures are advisable. It has been pointed out that both the lordosis and the plantar flexion of the feet with walking are compensatory. It will, therefore, only make matters worse to attempt to treat the compensatory lordosis, in view of the associated weakness of the hip extensors. Similarly, if the tendo Achilles is lengthened in order to bring the ankle up to right angle and allow the heel to be placed on the ground, it is often found that the child has even more difficulty in maintaining his balance (see case 8, Appendix III). Once the patient is no longer

able to walk the problem is a different one. The tendency to develop contractures is rapid and extreme; thus they develop very marked scoliosis and also equinus deformity of the feet. This is the result of the position in which they are constantly kept. When the patient is seated in the wheel-chair he will usually lean towards one or other side because of the difficulty in sitting erect. This will result in a scoliosis with concavity of the spine to that side. I do not believe that the scoliosis is a result of asymmetrical weakness of the back muscles and have not observed any scoliosis in any child who was still walking. The scoliosis can be prevented by fitting a moulded support to the trunk. At Queen Mary's Hospital for Children a light-weight celluloid jacket is cast for each patient as soon as he is no longer able to walk. This is worn under the clothing and is taken off at night. It was originally designed for the long-term management of tuberculosis of the spine. Where this procedure has been adopted before the onset of scoliosis, the back has usually remained straight, even for 5 years or more (Fig. 3.24 and 3.25). The special support has done much to improve the patient's comfort and also reduced the liability to respiratory infection. Apart from these considerations it also improves the appearance of the patient.

The progressive equinus deformity can be controlled to some extent by fitting firm boots which strap up around the ankle. After the child ceases to walk these will help keep the ankle at the right angle and prevent the deformity.

The contractures of the elbows and knees are no disadvantage. With the elbows at 90° and the forearms in partial pronation, the limbs are in a position of optimum function for writing, feeding and such movements. Similarly with the knees unable to extend beyond



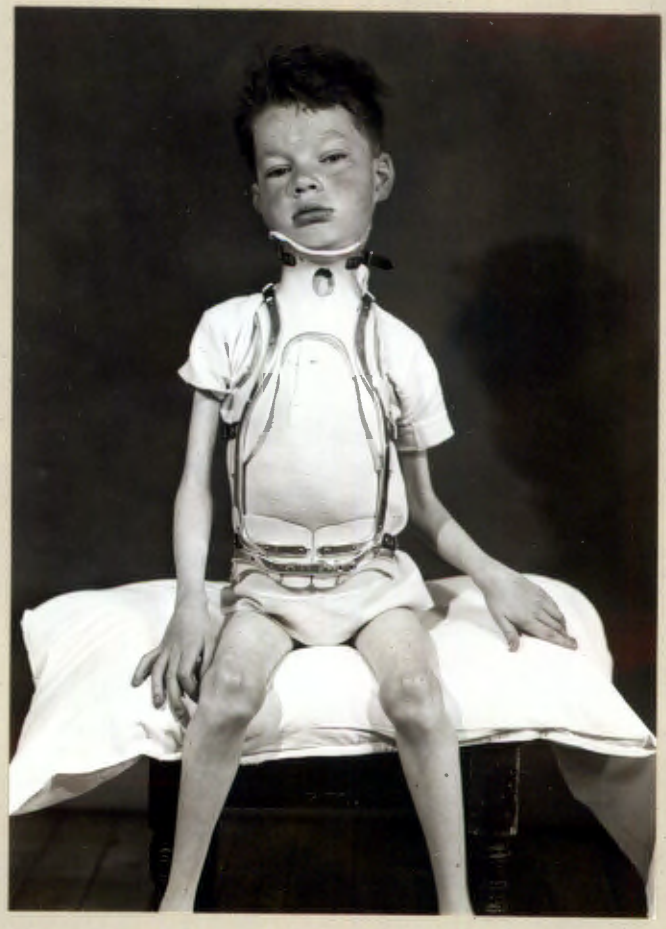
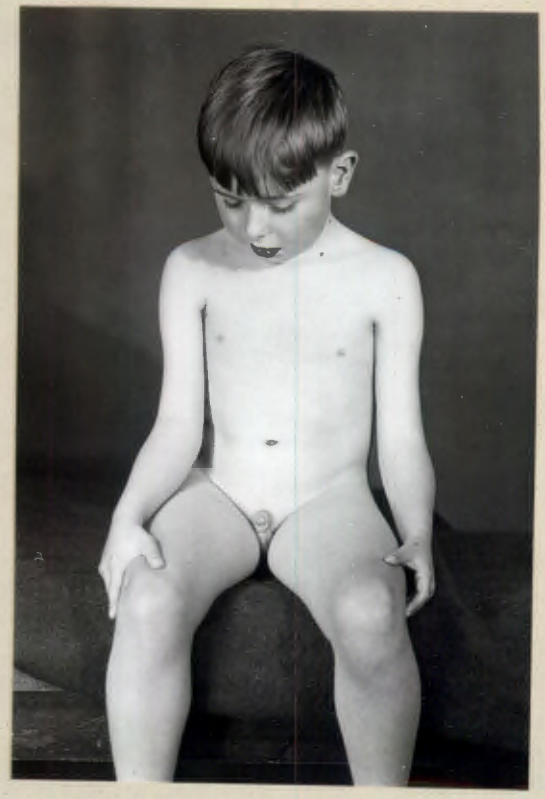


Fig. 3.24 and 3.25 . PREVENTION OF SCOLIOSIS
BY USE OF CELLULOID JACKET.



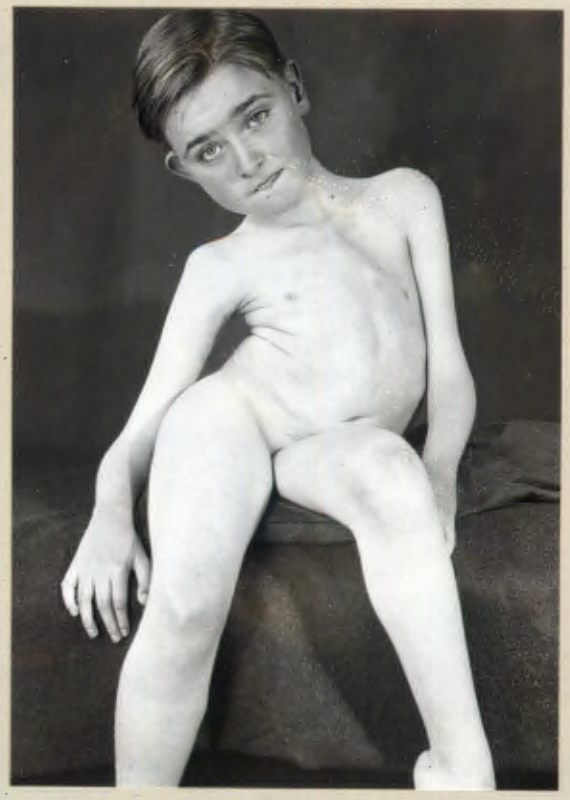


Fig. 3.26 and 3.27 . DEVELOPMENT OF SCOLIOSIS
(OVER 4 YEARS).
SPINAL SUPPORT NOT WORN.

90° there is no real disadvantage, because the patient can sit comfortably in the wheel-chair, and is also comfortable when sleeping on his side. In one patient, an orthopaedic surgeon attempted to improve things by cutting the hamstrings and stretching the legs. The result was an ankylosis with the knees at 180°, and the child required an extension to his wheel-chair to support his legs in this unphysiological position, and also experienced marked discomfort at night.

While it is an advantage for a physiotherapist to take the joints through their range of passive movements at regular intervals to maintain as much mobility in them as possible, there is no advantage in attempting to stretch contractures which have occurred. This only causes discomfort to the patients and will not increase the range of movement.

It has been mentioned that immobilization even for short periods may lead to marked deterioration in the power of the muscle. For this reason the child should be encouraged to remain ambulant (within the capacity of his weakened muscle). For minor illnesses it is better to keep the child semi-mobile rather than confined to bed. Similarly for sprains and fractures an attempt should be made to get the child mobile as soon as possible and, when he has to be confined to bed, active physiotherapy is essential.

These children are very prone to chest infections which commonly follow a relatively minor upper respiratory infection. This is the most frequent cause of death. Because of the diminished chest movement a slight limitation of respiratory capacity can have dire results. The cough is weak and ineffective, and they are unable to clear their respiratory passages of secretions. It is thus advisable to treat even minor upper respiratory infection

with antibiotics and intensive physiotherapy.

It is of utmost importance to try and maintain the morale of these helpless children. It has been my impression that in the majority of cases there is a definite advantage in being placed in a special unit rather than being at home. The main reason is that, with a large number of children with a similar affliction, they are less conscious of their handicap and do not have to compete with normal children as would occur at home. In the early stages of the disease, on the other hand, while the child is still ambulant, he is better off at home. In 5 cases of this series where the child initially was admitted for a short period, either for an upper respiratory infection or a fracture or while the mother was ill, the parents were so impressed by the change in temperament of the child that they requested permanent hospitalization.

The muscular dystrophy unit at Queen Mary's Hospital is run on the lines of a residential school for handicapped children. In addition to nursing and medical attentions, the inpatients have a full schooling programme, and usually go home for the school vacations. They are also allowed a fair amount of latitude as regards going out for week-ends. This is probably the most satisfactory compromise under the circumstances.

CHAPTER 4.

MENTAL DEFECT AND MUSCULAR DYSTROPHY

HISTORICAL REVIEW:

Mental retardation in association with progressive muscular dystrophy in childhood was observed by a number of the early authors (Duchenne, 1861, 1872; Gowers, 1879; Speilman, 1872; Erb, 1884, 1891). For this reason Duchenne (1861) used the descriptive title "Paraplegie hypertrophique de l'enfance de cause cerebrale" for the first case he described. The series of 13 cases he subsequently recorded (Duchenne, 1872) included 5 with mental retardation. Only two of the 24 cases described by Gowers (1879) were mentally backward, and he was of the opinion that mental defect was not a part of the disease, but that the muscular affection was more common among children with mental defect than among others. Erb's extensive series (1891) contained 23 case histories conforming to the Duchenne type. Mental retardation was recorded in 5 of these (cases 24, 25, 27, 32 and 33). The intelligence was normal in 7 (cases 2, 22, 26, 28, 29, 30 and 80) and there was no comment in the remainder (cases 1, 3, 4, 23, 31, 34, 52, 53, 54, 55 and 81).

In a detailed clinical assessment of 48 cases of "Duchenne-type" muscular dystrophy, Walton and Nattrass (1954) commented that at least 10 patients had a peculiarly coarse, "brutish", appearance, while another 6 were "dull, unresponsive and monosyllabic". However, they concluded that no patient was mentally defective, only 4 were slightly backward, and psychometric testing in 6 who looked particularly dull showed them to be of above normal intelligence. They thought that much of the impression of mental retardation could be attributed to loss of education or to the

reaction of these patients to their physical disability.

PRESENT INVESTIGATION:

Because of the apparent difference of opinion on the presence or absence of mental defect and its interpretation in muscular dystrophy, this feature has been investigated in the present series of cases.

The parents were directly questioned about the mental progress of the child. An assessment was also made at the clinical examination and the patients were placed into one of three categories:- A: definitely retarded, B: probably retarded and C: of average or above average intelligence. Category B included those cases where it was thought that optimum schooling facilities and encouragement might have placed the child in a higher intelligence bracket than at present. In addition the intelligence of 27 inpatients was more accurately assessed by the Terman-Merrill revision of the Stanford-Binet Test (Form L).

RESULTS:

In 17 of these 65 cases, the parents thought that the child was mentally retarded. This ranged from gross mental retardation in some cases to an inability to keep up with their schooling.

Clinical assessment revealed that 30 (46%) of the 65 children were of average or above average intelligence; 21 (32%) were definitely mentally retarded, and 14 (22%) probably retarded.

Table IV.1 shows that 10 of the 27 inpatients (37%) have a normal I.Q. (above 70), 14 (52%) are educationally subnormal (I.Q. 50-70) and 3 (11%) ineducable (I.Q. of less than 50).

In comparing the patients who had I.Q. tests with their clinical assessment (see table IV.1) there are a few differences. Of the patients with I.Q.'s over 70, there are 3

TABLE IV. 1. INTELLIGENCE QUOTIENT AND CLINICAL ASSESSMENT OF INTELLIGENCE IN 27 CASES OF MUSCULAR DYSTROPHY.

Case No.	Chronological Age	Mental Age	I.Q.	Clinical Rating	History of Retardation.
16	16+	17.9	118	C	
4	15.2	15.7	103	C	
36	12.6	12.7	101	B	+
31	12.4	12.2	99	C	
43	12.2	11.2	92	C	
37	16.1	12.2	81	C	
12	11.6	8.10	77	C	
20	12.7	9.6	76	A	
27	9.5	6.10	73	A	+
48	16+	10.8	71	A	+
45	15.10	10.0	67	A	
55	14.6	9.2	65	C	
1	14.1	8.10	64	B	
28	8.0	5.1	64	A	+
22	9.9	5.10	60	A	+
42	9.9	5.10	59	A	+
33	11.8	6.10	59	A	
35	13.2	7.6	57	A	+
23	15.6	8.4	56	A	
15	10.8	6.2	55	A	
41	11.3	6.0	53	A	+
53	16+	8.0	53	A	
40	14.7	7.2	51	A	+
14	12.8	6.6	51	A	
25	12.11	6.2	48	A	
32	15.7	7.0	47	A	+
26	12.11	5.5	42	A	+

who were thought, on clinical assessment, to be definitely retarded and one possibly retarded. Of the educationally subnormal group, one case had been classed as possibly retarded and another as of average intelligence. In the cases with an I.Q. below 60 there is no discrepancy between the clinical assessment and the accurate testing.

If one makes a further allowance for possible lack of educational facilities and the psychological effect of the physical disability, and considers an I.Q. below 60 instead of 70 as a subnormal level, it will be noted that 12 of the 27 (44%) cases fall into this category.

If one compares the group of inpatients with the series of patients as a whole it will be noted that 37% of the former have a normal intelligence as compared with 46% of the latter. If 60 instead of 70 is accepted as the lower limit of normality for this group there are then 56% of normals in the select group.

DISCUSSION:

The series of inpatients on whom an assessment of intelligence was done may be selective, in so far as parents may be less likely to seek permanent hospitalization for an intelligent child than for a retarded one with the same physical disability. For this reason the incidence of mentally backward children in this series may be higher than that occurring with muscular dystrophy in general. In spite of this possibility the incidence of a subnormal intelligence in 63% of this group is not much greater than the clinical estimate of 54% in the whole series of 65 cases.

The presence of mental retardation in association with muscular dystrophy raises some interesting points relative to aetiology. Progressive muscular dystrophy is a genetically

determined disease. If the associated mental retardation is also genetically determined, it is possible that both conditions may be caused by the same gene through a possible common mechanism,such as an enzymic defect. On this basis, however, it would be difficult to explain why in some typical cases of muscular dystrophy the intelligence is completely normal or even above average. This may be due to different degrees of the same defect. Thus, for example, a certain critical level of the defect may cause the muscular paralysis while a much lower level might be necessary for an associated mental defect. The other possibility is that two separate genes are involved but that these are closely linked and frequently co-exist in muscular dystrophy. In this case the particular gene for mental retardation is commonly found in association with that of progressive muscular dystrophy.

CHAPTER 5.

PATHOLOGY.

A. Historical Review.

An account of the morbid anatomy and hypotheses on the nature of the pathological process appeared in many of the early papers.

Meryon, (1852) and (1864), recorded the autopsy findings in two cases. He commented on the extensive involvement of the skeletal muscle and the fact that the nervous system was normal. He thought the changes were primarily due to a fatty or granular degeneration within the muscle fibre itself. In 1865 Billroth reported on the first muscle biopsy ever done (Griesinger, 1865). He attached prime importance to the extensive adiposity of the muscle and thought that the surviving fibres were normal and showed no evidence of intrinsic degeneration.

The importance attached at that time to the increase in adipose tissue is reflected in the names suggested for the disease: "paralyses avec surcharge graisseuse interstielle" (Fritz, 1865), "lipomatosis luxurians musculorum progressiva" (Heller, 1866), "Muskellähmung in folge von Hypertrophie des interstitiellen Fett-und bindegewebes" (Sigmundt, 1866), "atrophia musculorum lipomatosa" (Seidel, 1867).

In a detailed autopsy report, Eulenburg and Cohnheim (1866) also stressed the importance of the increase in adipose tissue. In addition they were the first to observe that while some fibres were atrophic others were larger than normal, and that occasional fibres appeared to be subdividing in their longitudinal axis.

Duchenne (1868) thought that the proliferation of fibrous tissue in the early phases of the disease was of more

significance and suggested the name "paralysie myosclérosique." After Duchenne introduced his ingenious "emporte-piece histologique," a trochar with a sliding blade, muscle biopsies could be more readily undertaken and greatly facilitated histological studies.

The first comprehensive account of the microscopic features of dystrophic muscle was given by Erb in 1891. He described hyperplasia of the interstitial connective tissue and fat which varied from one case to another; hypertrophy or atrophy of muscle fibres; marked proliferation of nuclei in the fibres; formation of vacuoles in the fibres; and division of fibres in their longitudinal axis. He thought that the presence of enlarged fibres amidst the atrophic ones was of special significance. He also drew a clear distinction between these changes and those observed in the muscle in association with degeneration of the lower motor neurone. Erb agreed with Meryon and Eulenburg and Cohnheim that there were no pathological changes in the central nervous system in progressive muscular dystrophy.

Erb's descriptions have formed the basis of recent texts on the subject (Adams, Denny-Brown and Pearson, 1953; Greenfield, Shy, Alvord and Berg, 1957). The latter authors have reviewed the variations in the histological features of normal muscle and they compared these with dystrophic muscle.

B. Pathological Study of 18 cases of progressive muscular dystrophy.

The pathological studies in this series are based on the autopsies of 5 of the 7 patients who died during the present investigations and on 14 muscle biopsies.

The autopsies and their routine histological study were performed by Professor Daniel and members of his staff. The discussion on the macroscopic features in these cases is based

on their findings.

Sections of various affected muscles from two of the autopsy cases (3 and 53) as well as the 14 muscle biopsies were prepared and studied personally. The discussion of the histological features is based on personal observations.

Macroscopic features.

Details of the autopsy findings of the five cases (cases no. 3, 39, 44, 50 and 53) are given in appendix III with the corresponding case histories.

In all the 5 cases generalised involvement of the skeletal muscles was noted. The proximal limb muscles and those of the trunk were most severely effected, and were in most instances almost completely replaced by fat. The more distal muscles, as well as the intercostal muscles and the small muscles of the neck, still retained some resemblance to normal muscle in colour and structure (but showed marked microscopic involvement).

In case 44 the tongue was grossly enlarged. In three of the cases (3, 44, 53) areas of fibrosis were observed in the myocardium. (Cardiac changes are discussed in chapter 7).

Evidence of respiratory infection was present in 4 cases (3, 39, 50 and 53). In case No. 44 there was no consolidation, but the lungs were oedematous. In this case passive congestion of the liver was also noted.

The macroscopic appearances of the nervous system were normal in 4 cases, while in case 44 there was evidence of degeneration of the anterior nerve roots in the left lumbo-sacral and right lumbar regions, consistent with his previous poliomyelitis.

Microscopic Features:

Muscle biopsies were obtained from the lateral head of gastrocnemius in 13 patients (cases 1, 3, 12, 14, 15, 20, 22, 23,

26, 27, 35, 44, 48) and from the deltoid in one (case 28). All biopsies were done under general anaesthesia except case 44 where a local anaesthetic was used. Specimens from several muscles were also obtained 20 hours after death in case 53, and 12 hours after death in case 3. Frozen sections were prepared according to the techniques described by Dubowitz and Pearse (1960, 1961). Haematoxylin and eosin, and haemalum and van Gieson stains were done in each case. The main histological characteristics are summarised in tables V.1 and V.2.

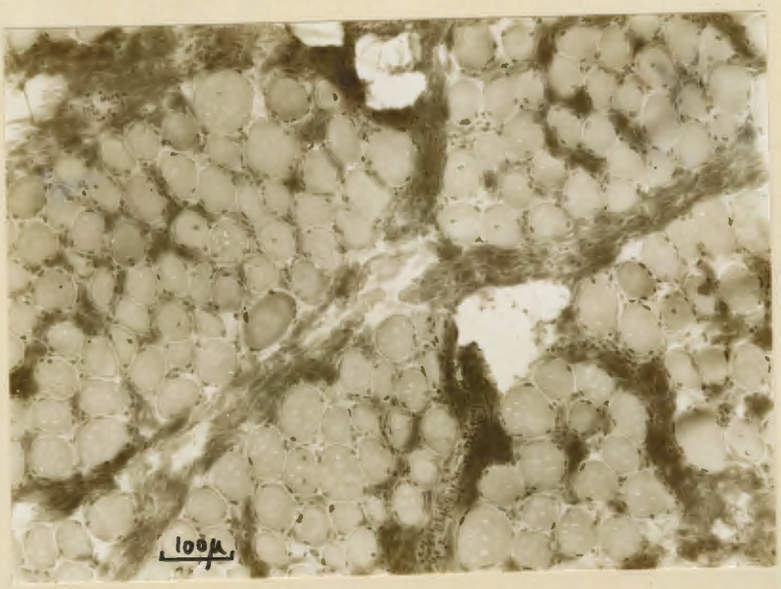


Fig. 5.1 CASE 28. SHOWS EXTENSIVE PERI- AND ENDOMYSIAL CONNECTIVE TISSUE (DARKER AREAS); VARIATION IN FIBRE SIZE; INTERNAL NUCLEI. (Van Gieson)

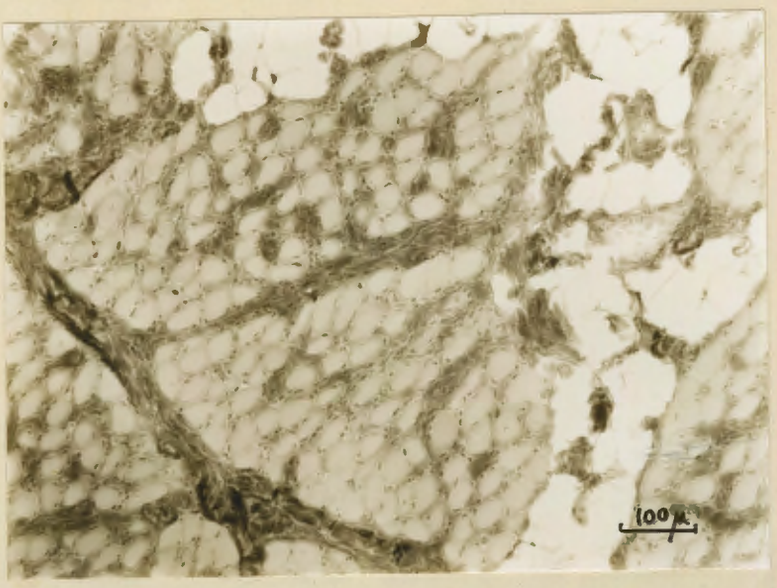


Fig. 5.2 CASE 27. SHOWS CHANGES SIMILAR TO FIG.5.1, BUT INCREASE IN PERIMYSIAL FAT. (V.G.)

In some of the early cases (12, 22, 27, 28, 35) the muscle fibres were still arranged in bundles. The main abnormality in most of these was a marked increase in the endo-, peri- and epimysial connective tissue (Fig. 5.1 and 5.2). In most of the patients with advanced disease on the other hand (3, 20, 44, 48, 53) sections were composed mainly of adipose tissue interspersed with islets of surviving fibres (Figs. 5.3. and 5.4).

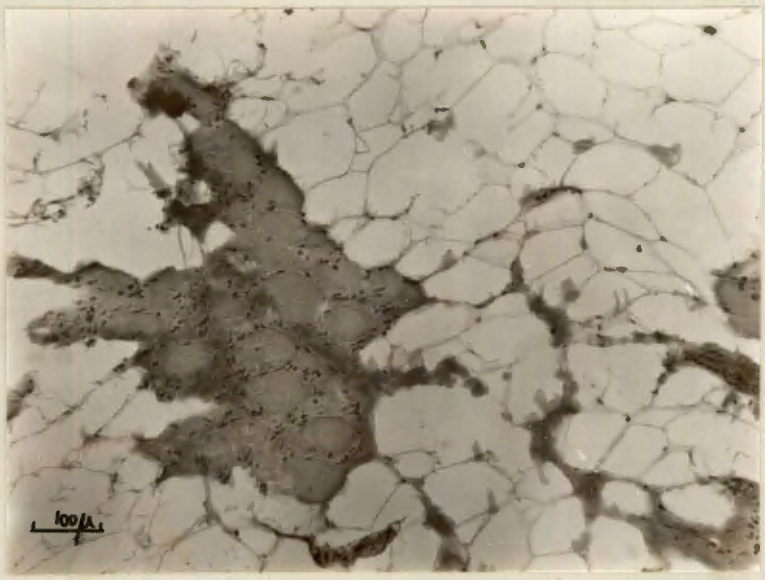


Fig. 5.3 CASE 53. (AUTOPSY), SHOWING EXTENSIVE ADIPOSE TISSUE.(V.G)

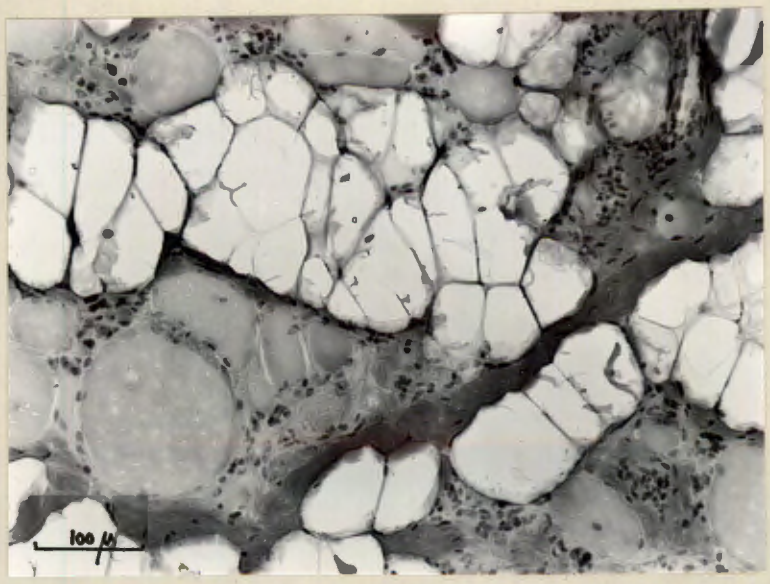


Fig. 5.4 CASE 48. SHOWS EXTENSIVE ADIPOSE TISSUE; VARIATION IN FIBRE SIZE; CELLULARITY. (V.G.)

TABLE V.1. : CORRELATION OF HISTOLOGICAL FEATURES OF MUSCLE BIOPSIES WITH CLINICAL DATA.

Case No.	Age	Duration of Symptoms (years)	Clinical State of Gastrocnemius	Histological Features		
				Range of Fibre Size (μ)	Fat	Connective Tissue
1	14	12	**P	25-150	++	++
3	17	15	A	10- 75	++++	+
12	11	9	P	25-100	++	+++
14	14	9	P	15-100	++++	++
15	12	9	P	10- 50	+++	+
20	14	12	A	25-100	++++	++
22	9	4	P	25-125	+++	+
23	15	12	P	25-135	-	-
26	12	10	P	25-150	+++	++
27	9	7	P	25- 60	++	++++
*28	8	6	P	25- 75	-	++++
35	13	8	P	10-125	++++	++++
44	16	8	A	25-150	++++	++
48	14	9	A	10-110	++++	++

* Biopsy of deltoid
* * P - "pseudohypertrophy"
A - atrophy

TABLE V.2. : HISTOLOGICAL FEATURES OF MUSCLE OBTAINED AT AUTOPSY.

Case No.	Age	Duration of Symptoms (years)	Muscle	Histological Features		
				Range of Fibre Size (μ)	Fat	Connective Tissue
53	16	14	Gastrocnemius	20-100	++++	+++
			Peroneus brevis	20-125	++++	++
			Sternomastoid	20-160	++++	++
			Thenar muscles	20- 90	+	+++
			Diaphragm	20-175	+	++++
			Tongue	20-135	+	+++
3	18	16	Gastrocnemius	10- 80	++++	+
			Sternomastoid	20- 90	+++	++
			Diaphragm	20-120	+	++++

The amount of connective tissue in these advanced cases varied from slight (e.g. case 3) to extensive (e.g. case 15). In case 23, whose disease had progressed much more slowly than average, and who was still ambulant at the age of 15, there was no increase in either fat or connective tissue.

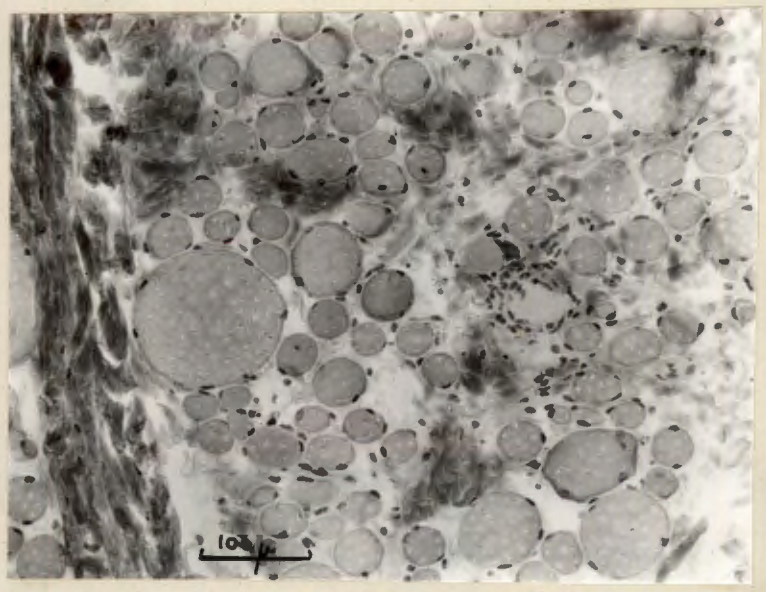


Fig. 5.5 CASE 26. VARIATION IN FIBRE SIZE; ROUNDING OF FIBRES. (V.G.)

The muscle in all the cases showed a marked variation in fibre size (Figs. 5.4 and 5.5). Fibres of varying size were scattered at random throughout the sections, without any semblance of a fixed pattern. Abnormally large fibres (over 75μ) were present in the majority of muscles examined. The absence of these large fibres in some instances (cases 3, 15, 27 and 28) bore no relation to the duration of the disease or to the presence or absence of clinical pseudohypertrophy. In all cases there were also numerous fibres which were relatively small.

Most of the fibres had lost their normal shape (Fig. 5.5). The polygonal shape of normal muscle fibres is probably due to mutual pressure by adjacent fibres. The absence of this factor in dystrophic muscle, where the fibres become separated from each other by connective tissue or fat, would explain the rounded appearance of many of the dystrophic fibres in transverse section.

Some fibres appeared to have subdivided along their longitudinal axis, each subdivision having its own sarcolemmal membrane and sarcolemmal nuclei, but all being ensheathed by a common endomysial layer (Fig. 5.6).

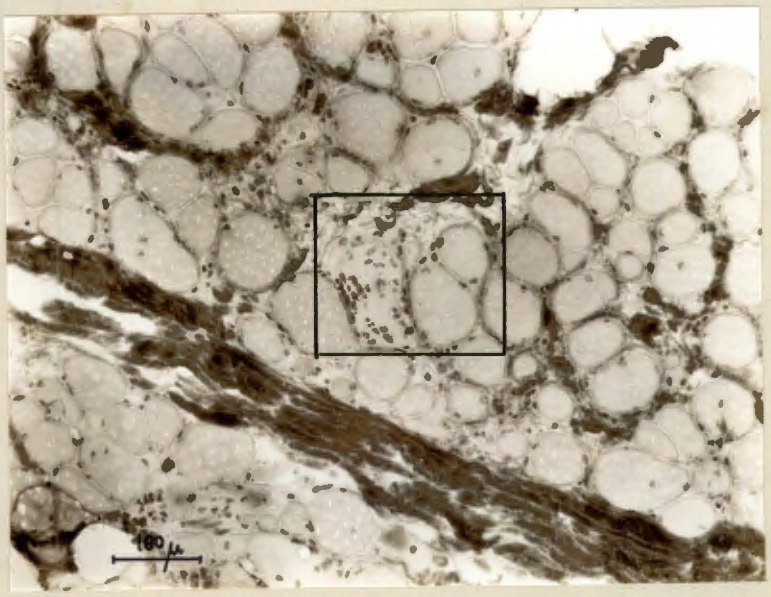


Fig. 5.6 CASE 1. NOTE LONGITUDINAL SPLITTING OF FIBRES. (V.G.)

The sarcolemmal nuclei were increased in size and in some fibres also in number. Internal nuclei were present in occasional fibres in every section. Although infrequent, they were more numerous in every case than 3 per 100 fibres.

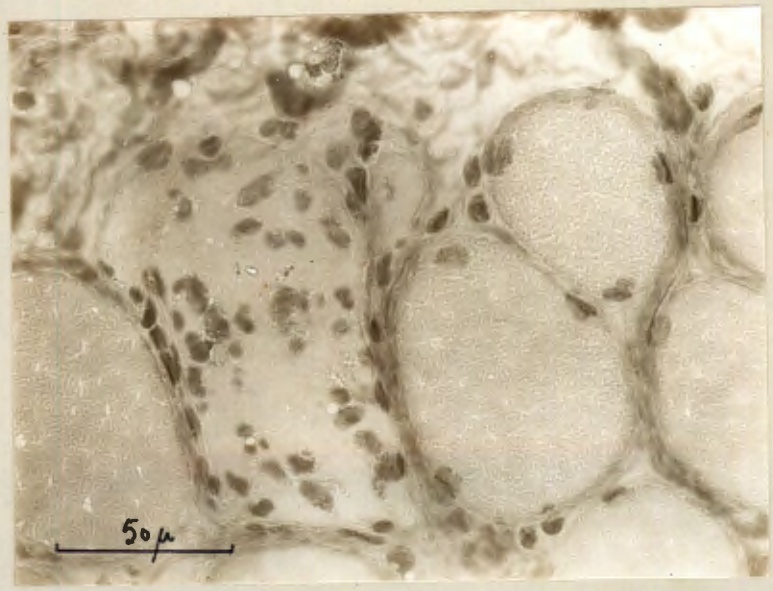


Fig. 5.7 CASE 1. (PART OF FIG. 5.6). SHOWS PHAGOCYTOSIS OF DEGENERATING FIBRES. (V.G.)

In many sections there were degenerating fibres, some hyaline, others granular in appearance, which were completely swamped with nuclei (Fig. 5.7). The latter were morphologically similar to fibroblast or macrophage nuclei and these fibres were probably undergoing phagocytosis. Fibroblasts were numerous in the endomysial connective tissue, particularly around degenerating fibres (Fig. 5.5). Occasional lymphocytes were also present.

In case 44, the muscle biopsied had previously been affected by poliomyelitis. Histologically the features were identical to those of the other cases of muscular dystrophy. No recognisable evidence of neurogenic muscular atrophy (as illustrated in Fig. 5.8) was present in the sections. The features in the muscle due to the previous poliomyelitis were probably completely obliterated by the changes of advanced muscular dystrophy.

Fig. 5.8 LONGSTANDING NEUROGENIC ATROPHY. NOTE UNIFORMLY SMALL ATROPHIC FIBRES AND ISOLATED LARGE FIBRE. (V.G.)

In case 53 (autopsy) the changes in the gastrocnemius, sternomasteid and peroneus brevis were similar to those in the biopsy specimens. (Table V.2 and Fig. 5.3). In the thenar muscles early changes were present. The fibres were still arranged in

bundles. They varied in diameter and many were rounded. There was marked proliferation of connective tissue particularly in the perimysium and to a lesser extent in the endomysium. Adipose tissue was present in a few areas in the perimysium. There was a striking increase in endomysial cellularity, consisting mainly of fibroblasts. No inflammatory cells were seen. A number of muscle fibres were markedly infiltrated with nuclei.

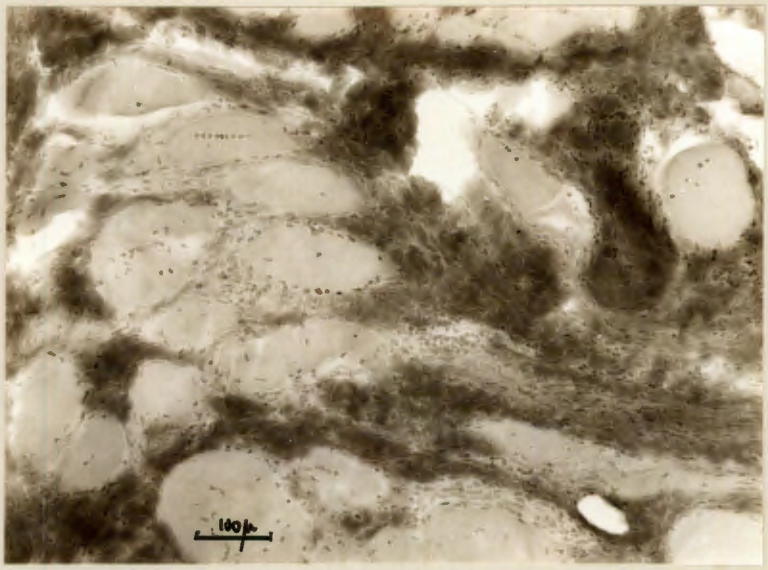


Fig. 5.9 CASE 53. DIAPHRAGM. NOTE EXCESSIVE CONNECTIVE TISSUE; GIANT FIBRES; CENTRAL NUCLEI. (.VG.)

The diaphragm was severely affected by the disease. There was a striking proliferation of connective tissue which was mainly endomysial (Fig. 5.9). A slight excess of adipose tissue was also noted. The fibres varied markedly in size and there were a large proportion of giant fibres. Internal nuclei were frequent and in many instances were arranged in longitudunal chains. Many degenerating fibres were swamped with nuclei. With such gross involvement it is surprising that the diaphragm was capable of any function at all.

Fig. 5.10 CASE 53. NOTE VARIATION IN SIZE OF FIBRES; MARKED CELLULARITY OF FIBRES AND INTERSTITIAL TISSUE; INCREASE IN PERIMYSIAL FAT AND CONNECTIVE TISSUE.

The tongue was also involved (Fig. 5.10). There was a marked increase in connective tissue, mainly perimysial, and a slight increase in adipose tissue. The fibres varied in size and many were undergoing degeneration and were infiltrated by fibroblasts and macrophages. The endomysium was very cellular but no inflammatory cells were present.

In case 3 (autopsy) the gastrocnemius and sternomasteid also showed advanced changes with extensive fatty infiltration. The changes in the diaphragm were similar to those in case 53, but the fibres were not as markedly enlarged. In addition there was more marked cellularity of the endomysium, composed mainly of fibroblasts.

The myocardial lesions in cases 3 and 53 are discussed in Chapter 7.

In addition to the involvement of the muscles mentioned above, changes were also noted in the autopsy specimens of the external ocular muscles in cases 39 and 44, and the striated muscle of the oesophagus in case 44. These changes consisted of variation

in fibre size, degeneration of fibres, proliferation of sarcolemmal nuclei and an increase in endomysial connective tissue. These changes correspond to the early changes in the skeletal muscle.

Discussion.

The macroscopic features are in keeping with the observations of numerous previous authors.

The cause of death in 4 of the cases was a respiratory infection. In case 44, on the other hand, there was no evidence of infection but the lungs were oedematous. The cause of death in this patient was probably cardiac failure.

Involvement of the striated muscle of the oesophagus is an unusual feature of progressive muscular dystrophy. It has however, been previously recorded (Bevans 1945). Its apparent rarity may merely reflect infrequent study of the oesophagus at autopsies.

The most consistent changes in the affected skeletal muscles were the variation in fibre size and the eventual loss of muscle architecture. Initially there seemed to be more proliferation of connective tissue, while in the later stage, adipose tissue was the major component.In one case with a relatively benign form of the illness, the fibres varied in size but the bundles retained the normal architecture and there was no increase in connective tissue or fat. It would be difficult in this case to diagnose progressive muscular dystrophy on the histological features alone. A firm diagnosis, however, was possible on clinical grounds and supported by the electromyographic studies.

On histological grounds there appeared to be no difference between muscles which were clinically pseudohypertrophic, and those which were atrophic. Pseudohypertrophy is usually due

to excessive adipose tissue. This was indeed the explanation in case 14 whose calf circumference was 18½ inches and had increased by over 3 inches in the 12 months prior to his going off his feet. The biopsy was done shortly after he went off his feet. In other cases, however, with muscles which were more prominent clinically the main abnormality was proliferation of connective tissue (e.g. cases 27 and 28).

Excessive cellularity was common in the endomysial tissue in most cases. Although comprising mainly fibroblasts, there were also numerous lymphocytes, sometimes occuring in the form of focal collections, and occasional polymorphs. It is important to recognise this fact, as one may otherwise suggest a diagnosis of polymyositis on histological grounds, especially where clinical details may be inadequate.

In the interpretation of muscle pathology, transverse sections are of more value than longitudinal ones. They have the advantage of easier measurement and comparison of fibre size and also contain more fibres per field. The proliferation of fat and connective tissue can also be more readily assessed.

Many of the features of diseased muscle on which diagnosis is based require careful assessment. Although variation in fibre size can be readily observed and its distribution noted, the interpretation of size of the individual fibre presents more difficulty. There is a great variation in normal muscle, both from one muscle to another, and in the same muscle at different ages. The average diameter of the fibres in most muscles is 40-50μ (Adams, Denny-Brown and Pearson, 1953). In the sartorius, Wohlfart (1937) found a range of 10-50μ at 11 years of age and 20-70μ at 20 years. Greenfield et al. (1957) observed no fibres

of less than 25μ in diameter in the normal vastus lateralis of the adult. Some small fibres are bound to be present in a cross section of normal muscle because of the tapering of the end of the fibre, but will only comprise a small percentage of the fibres.

The interpretation of an increase in sarcolemmal nuclei also presents difficulty. If one accepts 8 nuclei per fibre in transverse section as the upper limit of normal (Greenfield et al), there have been very few fibres in the present study with excessive sarcolemmal nuclei (see Figs. 3.5 and 3.6).

The main reason why fibres are often thought to have excess of sarcolemmal nuclei in routine paraffin preparations is possibly because of the artefactual shrinkage of the muscle fibre away from the sarcolemma. Internal nuclei were more frequent than 3 per 100 fibres (Greenfield et al).

Any attempt to explain the curious pathological changes in the muscle will raise many interesting points. While it has become accepted that progressive muscular dystrophy is a primary disease of muscle, we still do not know the mechanism by which the changes are produced. The excessive proliferation of connective tissue in the early phases of the disease surely reflects an active process and can hardly be looked upon as merely a replacement of degenerating fibres. It is far more extensive than I have seen in any other disease process affecting muscle, such as neurogenic atrophies and the benign congenital hypotonias (Dubowitz & Pearse, 1961). If one assumes that brothers afflicted with the same disease undergo the same pathological sequence of events, it is of interest that the excess connective tissue in the early phases of the disease in case 27 and 28 should have been replaced by fat in the later stages, as apparent in their elder brother (case 26).

The proliferation of adipose tissue is equally interesting. In the early stages it may be so marked as to visibly increase the bulk of the muscle. Unlike the connective tissue it persists throughout the course of the disease and in advanced phases is the main component of the muscle. The possible reason why muscles which are apparently enlarged at an early phase of the disease may become atrophic later, is that the muscle fibres gradually disappear while the initial proliferation of fat does not increase. Even the very atrophic muscle is composed mainly of fat.

Fat replacement is not specific to progressive muscular dystrophy. I have seen extensive adiposity in the muscle in cases of longstanding benign congenital hypotonia and slowly progressive spinal muscular atrophies (Dubowitz & Pearse, 1961).

CHAPTER 6.

HISTOCHEMICAL INVESTIGATION.

In order to investigate the possibility of an enzymic defefect in progressive muscular dystrophy, various enzyme systems were studied, according to the techniques described by Dubowitz and Pearse (1960), (1961), in the 14 biopsy specimens and in the muscle obtained from two of the autopsy cases (see chapter 5). Muscle from 6 normal children obtained at routine orthopaedic operations was used as a control.

RESULTS:

In normal muscle two groups of fibres were observed. One, usually of smaller diameter, had a high content of various oxidative enzymes associated with the Krebs Cycle, and a low content of phosphorylase, while the other had a low content of oxidative enzymes and a high content of phosphorylase (fig. 6.1).

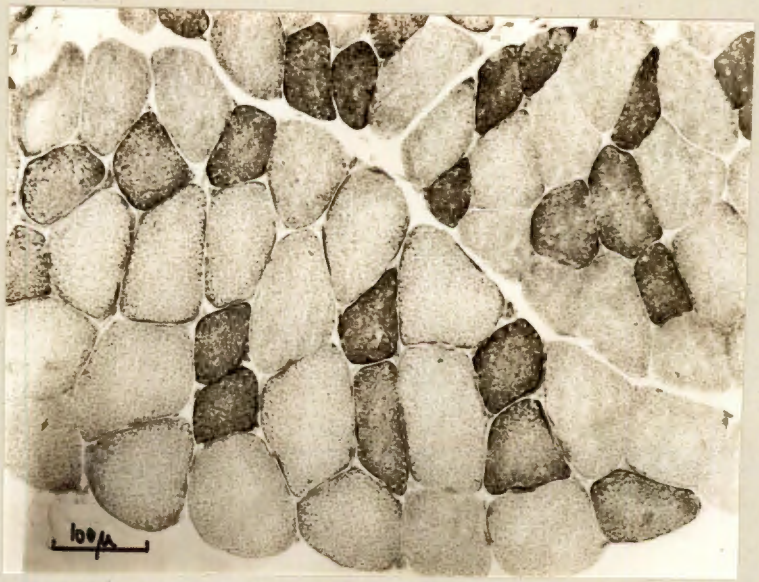


Fig. 6.1. NORMAL MUSCLE. LACTATE DEHYDROGENASE. NOTE STRONGER REACTION IN SMALLER FIBRES.

This reciprocal relationship between phosphorylase and oxidative enzyme content of individual fibres was consistently present (fig. 6.2 and 6.3). (Dubowitz and Pearse, 1960).

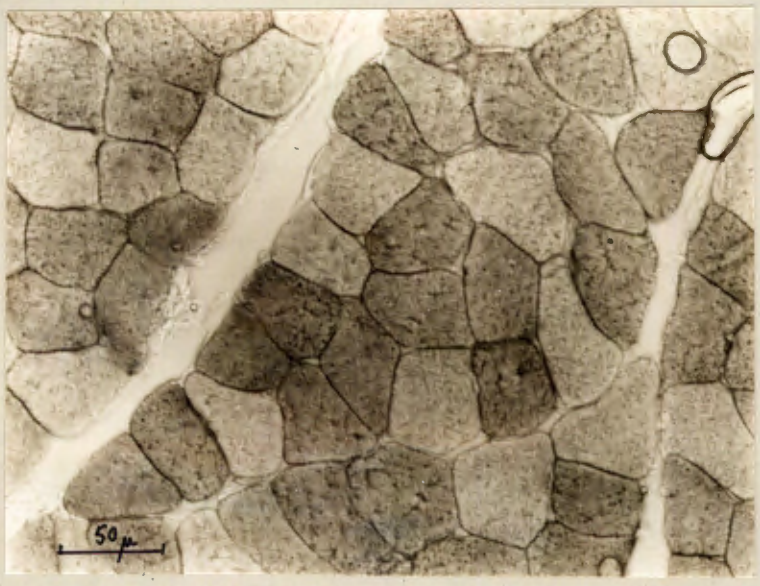


Fig. 6.2 NORMAL MUSCLE. LACTATE DEHYDROGENASE. SHOWS SOME FIBRES MORE REACTIVE THAN OTHERS BUT NO VARIATION IN SIZE.

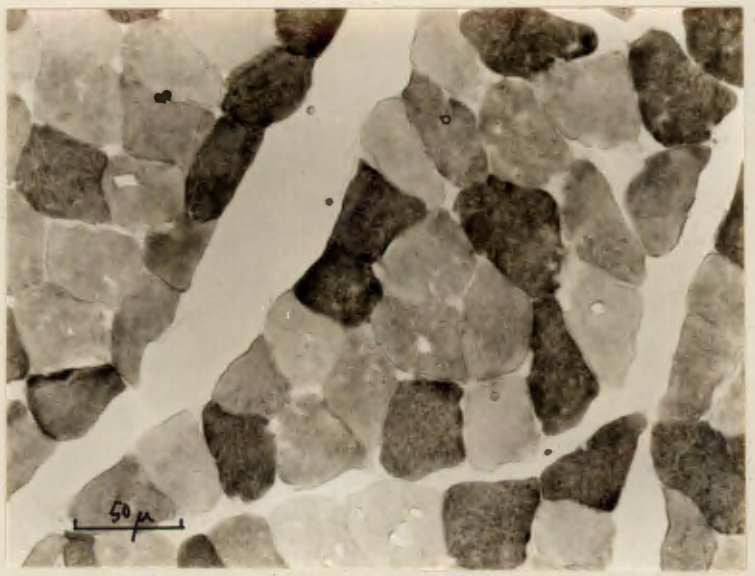


Fig. 6.3 NORMAL MUSCLE. PHOSPHORYLASE. SERIAL SECTION TO FIG. 6.2 . NOTE RECIPROCAL ACTIVITY OF FIBRES.

In dystrophic muscle there was no apparent absence or deficiency of any of the enzymes studied. Most of the abnormally large fibres (greater than 75μ) were found to be rich in phosphorylase and poor in oxidative enzymes, while the small atrophic fibres (less than 30μ) had a high content of oxidative enzymes and a low content of phosphorylase (figs. 6.4 and 6.5).

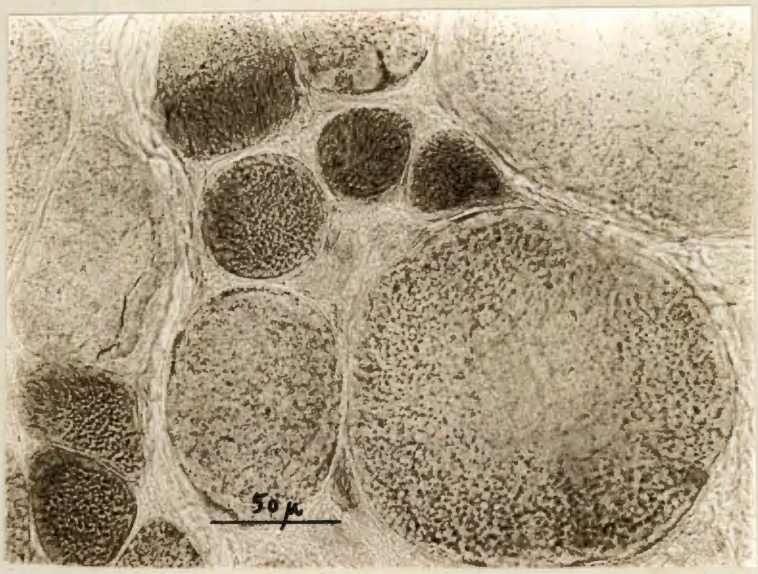


Fig. 6.4 CASE 26. DPN-DIAPHORASE. NOTE MORE INTENSE REACTION IN SMALL FIBRES.

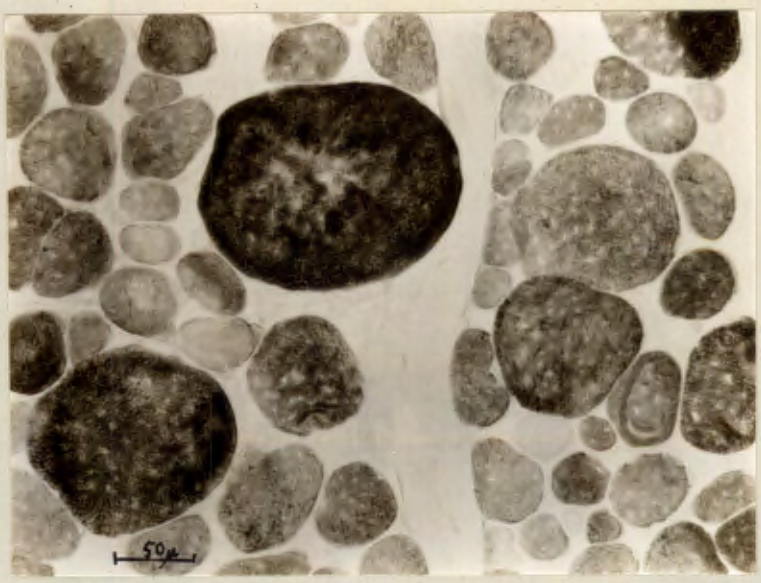


Fig. 6.5 CASE 26. PHOSPHORYLASE. NOTE MORE INTENSE REACTION IN ABNORMALLY LARGE FIBRES.

As in normal muscle there was a reciprocal relationship between the phosphorylase and oxidative enzyme content of individual fibres.

In cardiac muscle from one of the autopsy cases (53) there were scattered areas with loss of oxidative enzyme activity (Fig. 6.6). These areas showed no apparent changes on routine van Gieson or Haematoxylin and eosin staining of serial sections. The reaction for phosphorylase was negative in all post-mortem specimens.

In the second autopsy case studied (3) there were no areas of loss of enzymic activity.

Fig. 6.6 CASE 53. DPN-DIAPHORASE. SHOWS AREA WITH LOSS OF ENZYMIC ACTIVITY.

DISCUSSION:

If phosphorylase activity reflects the breakdown of glycogen, it is possible that the fibres with high phosphorylase content depend on the glycogen cycle for their energy. The fibres rich in oxidative enzymes, on the other hand, may preferentially use the substrates of the Krebs cycle, and possibly utilize fat as their source of energy.

It appears that the hypertrophic fibres in muscular dystrophy correspond to the larger fibres in normal muscle which have a high content of phosphorylase, while the atrophic fibres correspond to the smaller fibres with high content of oxidative enzymes. These two fibre types may respond in a different way to the fundamental process responsible for muscular dystrophy, and this may account for the striking variation in the size of the fibres. Furthermore a varying proportion of these fibre types in different muscles may explain why some muscles are affected more readily by the dystrophic process than others.

The changes observed in the cardiac muscle are similar to those observed by Wachstein and Meisel (1955) in cardiac muscle from patients dying of myocardial infarction.

CHAPTER 7.

CARDIAC INVOLVEMENT IN MUSCULAR DYSTROPHY.

HISTORICAL REVIEW.

Although Coste and Gioja (1838) suspected cardiac hypertrophy in one of their cases, it was not until 1883 that the myocardial lesion in progressive muscular dystrophy was first described. Ross (1883) noted atrophy of the muscle fibres and an increase of the interstitial connective tissue in a 12 year old boy.

Meerwein (1904), Globus (1923) and Zatuchni et al. (1951) reviewed the literature for clinical and pathological evidence of cardiac involvement in case reports of progressive muscular dystrophy. (It is noteworthy that in the single personal case reported by Zatuchni et al., the histological features of the skeletal muscle, illustrated in the photomicrograph, are characteristic of neurogenic muscular atrophy and not muscular dystrophy, as assumed by these authors).

A detailed description of the myocardial lesions in 6 autopsies was given by Nothacker and Netsky (1950), while Rubin and Buchberg (1952) reviewed the clinical and electrocardiographic features of the same series. Weisenfeld and Messinger (1952) surveyed a series of 44 cases.

A shortcoming of all these reports is that they are either a retrospective assessment of hospital records, a report of a single case, or a review of the previously reported cases of muscular dystrophy, in which the evidence for cardiac involvement was often merely incidental and usually incomplete.

The accounts given of the myocardial lesions were fairly consistent, and resembled the early changes in dystrophic skeletal muscle (Bevans, 1945). The predominant lesion was the

TABLE VII.1.

CARDIAC INVOLVEMENT IN MUSCULAR DYSTROPHY.

Author	Total No. of cases investig.	Total No. of abnormalities	Heart rate	Abnormal rhythm	P	P-R	QRS /amplitude/ & duration	Q	$R+V_1$	ST segment changes	T flat: - inverted:	BP
MEERWEIN (1910)	480	89	↑(50%)									
PUDDU and MU SAFFIA (1931)	30	2		Wolff-Parkinson-White (1)								
BOAS and LOWENBURG (1931)	7											
ZATUCHNI (1951)	156	94	↑(No?)	Extrasystoles $\frac{2}{105}$ Parex.tachyc.(No?)	↑$\frac{2}{105}$	↑$\frac{2}{105}$	↑$\frac{3}{105}$	+	+	+		↑$\frac{10}{24}$
RUBIN (1952)	33		↑(3)			↓$\frac{5}{17}$		+		"serial changes"		
WEISENFELD (1952)	44	85%	↑(No?)									
MOORE (1954)	(Review)						BBB			"diffuse changes"		N
SCHOTT (1955)	6 (childhood type)	6					↑ amplit.					
GRANDELL (1956)							↑ amplit.			+		
MANNING (1958)	28				N	N	N	+	+	+	+	↑(1)
PRESENT SERIES	56	8e% +		Wolff-Parkinson-White ?(1)	↑$\frac{3}{56}$	↓(1)	BBB $\frac{6}{56}$	+	+	+	+	↑$\frac{5}{65}$

Key: N : Normal.
↑ : Increased.
↓ : Decreased.
$\frac{2}{105}$: 2 cases out of 105.
(3) : 3 cases.

fibrosis of the myocardium. This ranged from microscopic proliferation of the connective tissue to large areas of scarring. It was associated with degeneration of the muscle fibres, which sometimes showed variation in fibre size. There was a variable increase in adipose tissue. The coronary arteries were not diseased.

The clinical evidence was far less clear-cut. In a large proportion of cases the cardiovascular system was clinically normal (Rubin and Buchberg, 1952). The more consistent abnormalities recorded were tachycardia, abnormal rhythms, increase in heart size, systolic murmurs and congestive cardiac failure. It is noteworthy, as pointed out by Tournisire et al. (1955), that many of the reported cases also suffered from other known cardiac diseases such as rheumatic fever.

In recent years much interest has been shown in the electrocardiographic changes in muscular dystrophy. (Puddu and Mussafia, 1939; Zatuchni et al., 1951; Rubin and Buchberg, 1952; Weisenfeld and Messinger, 1952; Manning and Cropp, 1958; Giannini et al., 1959). The abnormalities recorded by these authors are summarised in Table VII.1.

Catheterization studies on 10 cases (Gailani, 1958) revealed that some patients were on the verge of congestive cardiac failure. There was no evidence of pulmonary hypertension to possibly explain some of the E.C.G. changes.

PRESENT INVESTIGATION.

In order to assess the incidence and nature of the cardiac involvement in this series of cases, the following studies have been made.

Post-mortem examination of the heart was performed

in 5 cases (3, 39, 44, 50, 53). A histological study of the myocardium was personally undertaken in two of these cases (3, 53) and in addition various histochemical investigations on them were performed (see chapter 6). A full clinical examination of the cardiovascular system was made in each case. In addition electrocardiograms were done on 56 cases.

PATHOLOGY. Details of the autopsy findings are given with the respective case histories in Appendix III. The heart was enlarged in 4 cases (3, 44, 50, 53) and in 3 there were numerous areas of fibrosis (3, 44, 53). There was a patch of atheroma in the proximal 1 cm. of the right coronary artery in case 44; the coronary arteries of the remaining cases were normal. On routine histological examination there was a varying degree of proliferation of connective tissue and fibrosis of the myocardium.

In cases 3 and 53 the histological features observed were extensive proliferation of the connective tissue with numerous plaques of collagen. The residual muscle fibres had a normal appearance, although there was some variation in fibre diameter in case 3. The muscle nuclei were prominent and irregular. There was marked cellularity in the interstitial tissue, consisting mainly of fibroblasts and lymphocytes (fig. 7.1)

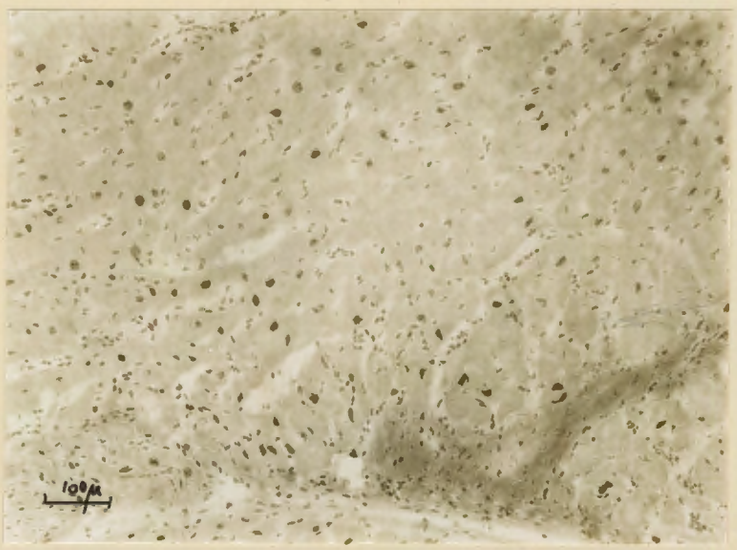


Fig. 7.1. CASE 3. PROLIFERATION OF CONNECTIVE TISSUE; PROMINENCE OF MUSCLE NUCLEI; CELLULARITY OF INTERSTITIAL TISSUE.

Clinical Features:

There was no history of symptoms referable to the cardiovascular system.

Dyspnoea on effort was difficult to assess because of the severe limitation in locomotion. Fatigue was a feature of some cases, but was probably due to muscular weakness. No patient complained of palpitations and there was no history of swelling of the feet.

On examination there was no central cyanosis but mottling of the skin of the legs with slight cyanosis was a common feature in the later phases of the disease.

The peripheral pulses were palpable in the majority of cases.

Swelling over the dorsum of the foot was frequently observed in chairbound cases. It was usually non-pitting.

In the majority of cases the blood pressure was normal but a diastolic pressure of over 100 mm. Hg. was noted in 5 cases.

Tachycardia was a variable feature on routine examination. The sleeping pulses of 29 inpatients were recorded daily for a period of 1 week. The rate varied from 62 to 110 with an average of 81.

Definite cardiomegaly was observed in only one case (44), where it developed shortly before death.

Apart from grade I to grade II systolic murmurs in some cases, no abnormalities were observed on clinical examination of the heart.

In 3 of the patients who died, a cardiac cause was thought likely on clinical grounds, because of the sudden collapse and state of shock, with hypotension, pallor and sweating, in the terminal phases. There was no complaint of chest pain, but the picture was nevertheless reminiscent of acute myocardial infarction.

Electrocardiographic Changes.

Electrocardiograms were done on 56 patients. These consisted of the standard limb and chest leads in 54 and only the limb leads in 2. The main data from the electrocardiographic tracings are tabulated in Appendix IV.

In the present survey the patients have been subdivided into the age groups of Ziegler (1951), namely; I, over 12; II, 8-12; III, 5-8 and IV, under 5. All analyses have been based on the normal standards given by Ziegler.

Heart rate: A definite elevation of the heart rate was present in 8 cases, while in a further 5 it was borderline. The remaining cases, although individually within the normal range, had a mean which was significantly higher than normal in the two age groups I and II. (92.7 and 104.8 respectively). In the other age groups the number of cases was too small for statistical analysis.

Rhythm: No abnormality of cardiac rhythm, except for the tachycardia and occasional extrasystoles, was noted.

P wave: Abnormally large P waves were recorded in 3 cases (24, 30 and 44).

P-R interval: The P-R interval was shorter than normal in one case (14) and borderline in 5 (15, 16, 18, 25 and 44). The

remainder, although individually within normal limits, had a mean value which was significantly lower than normal in groups I (0.125) and II (0.128)

QRS complex: Bundle branch block was present in 6 cases (4, 23, 29, 45, 53, 55). Abnormal Q waves occurred in a high proportion of the cases. These were most frequently seen in the left precordial leads (V_{4-7}) and in leads II and III. In 12 cases the Q waves were definitely abnormal in leads V_{4-7} and II and III. Of these 7 also had a Q wave in V_3. Flattened T waves and /or depression or elevation of the S-T segment was observed in all the cases with abnormal Q waves. In one case (27) Q waves were only present in V_3 and there was an S-T depression in V_1 and V_2.

The R/S ration in aVR was greater than unity in 3 cases (1, 36, 44). The R/S ratio in V_1 was greater than normal (for the age) in 20 cases. This was associated with B.B.B. in 4 instances. The R/S in V_5 was normal in all cases.

Right ventricular hypertrophy (R.V.H.) has been assessed on the criteria of Hollman (1958). Definite R.V.H. was present in 4 cases (18, 24, 30, 35) while in a further 16 it was a strong possibility.

S-T segment: Depression or elevation of the S-T segment was present in 10 cases. Flat T waves occurred in 10 cases and abnormal inversion of the T wave was noted in 2.

U waves: Prominent U waves were present in 18 cases. They were most marked in V_{1-3}.

In 5 patients more than one E.C.G. was done. In two the records were similar but the others showed interesting changes.(Figs. 7.2 - 7.4). In case 4 the initial E.C.G. (23.6.58) showed the following features. The rate was 136 per minute. The Q wave was prominent in lead III and V_6 and 7. The QRS was wide in V_1 (0.12 sec.)

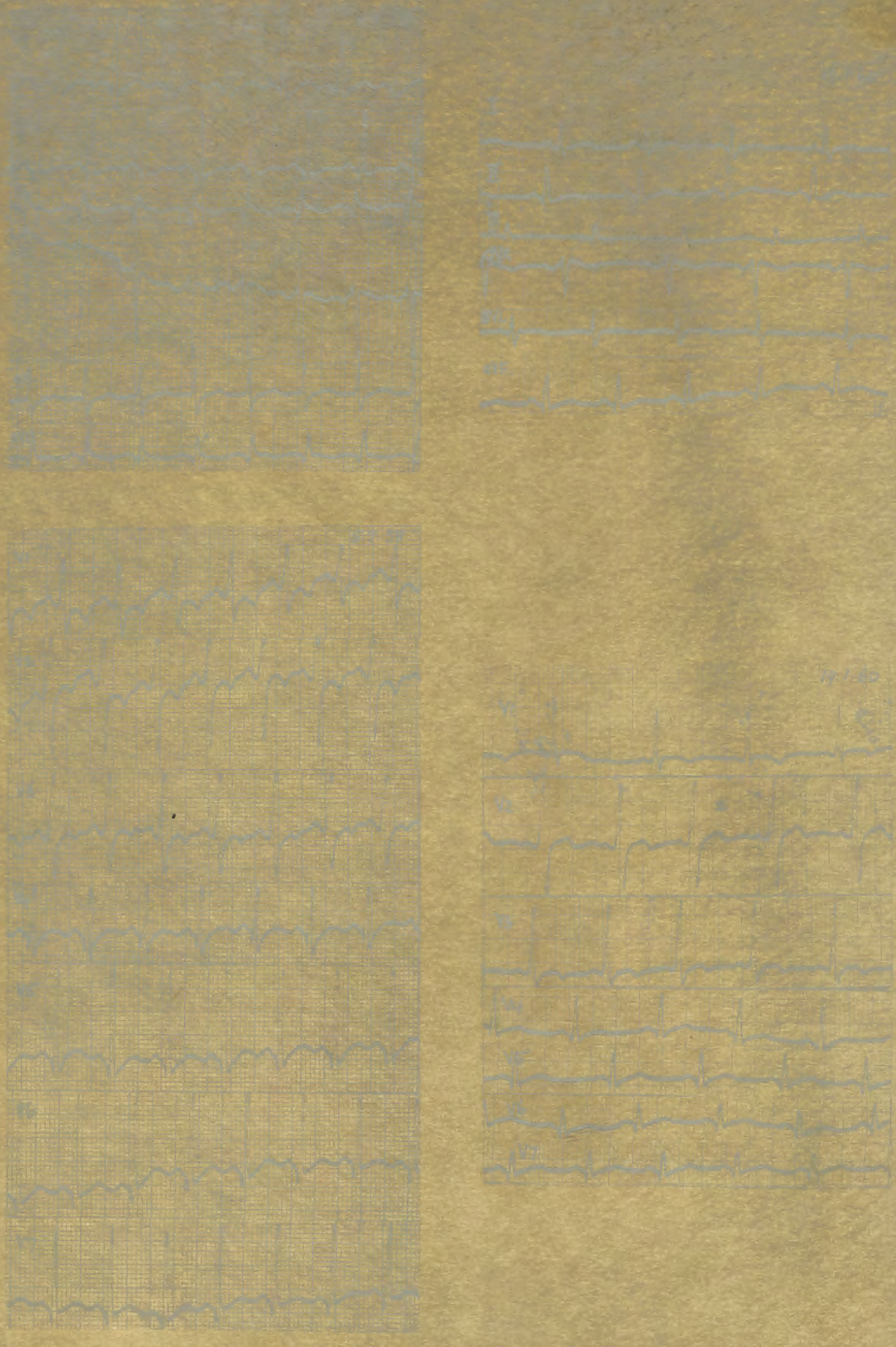
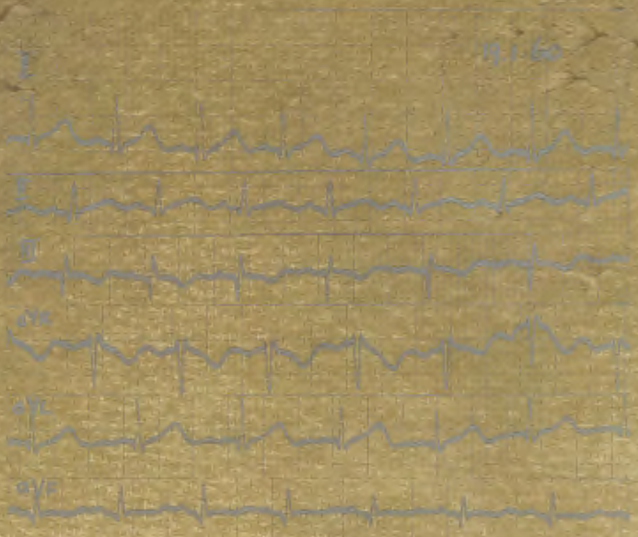
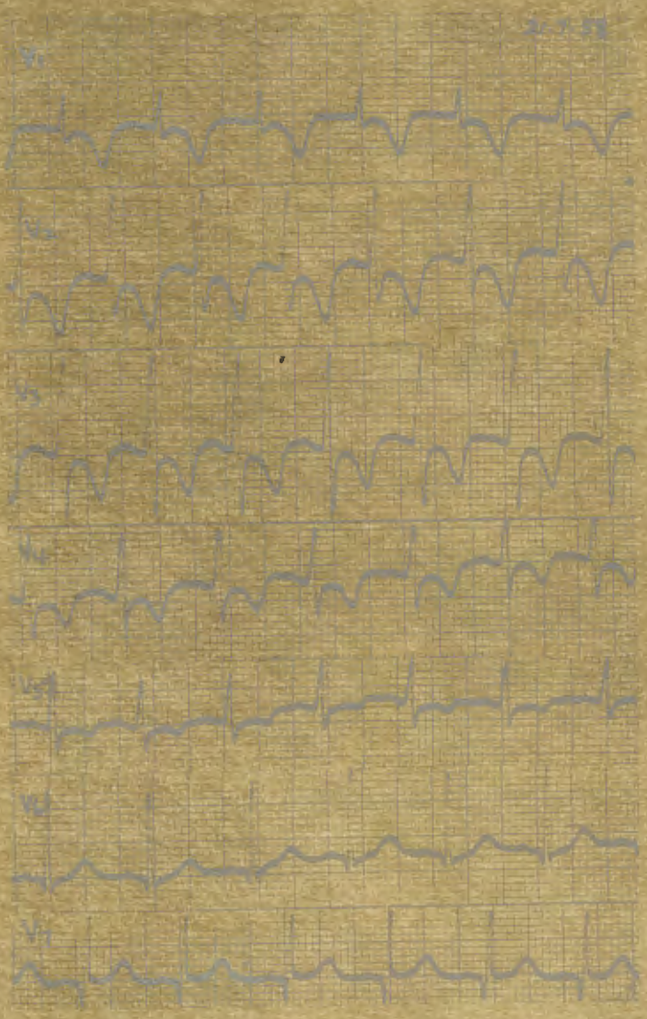


Fig. 7.4. Case 6. Serial ECGs.





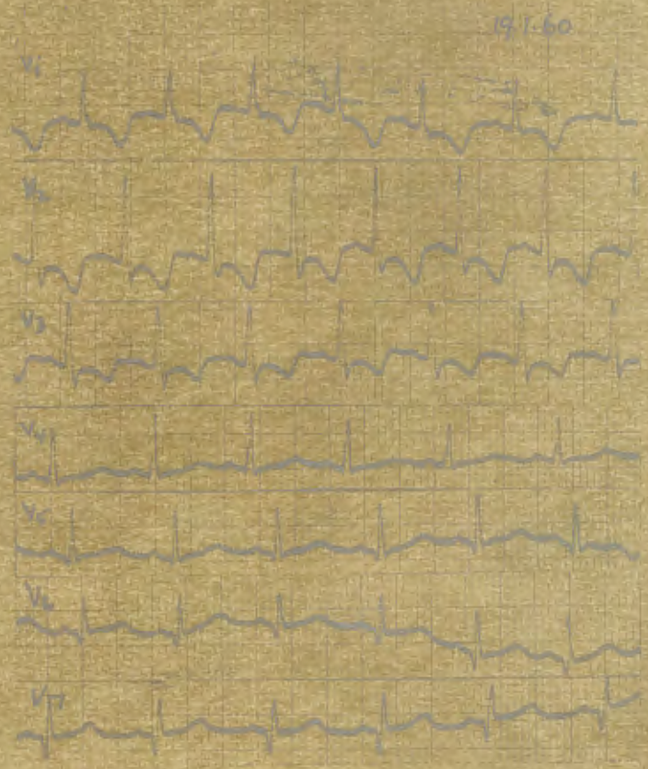


Fig. 7.3 Case 36. Serial ECGs

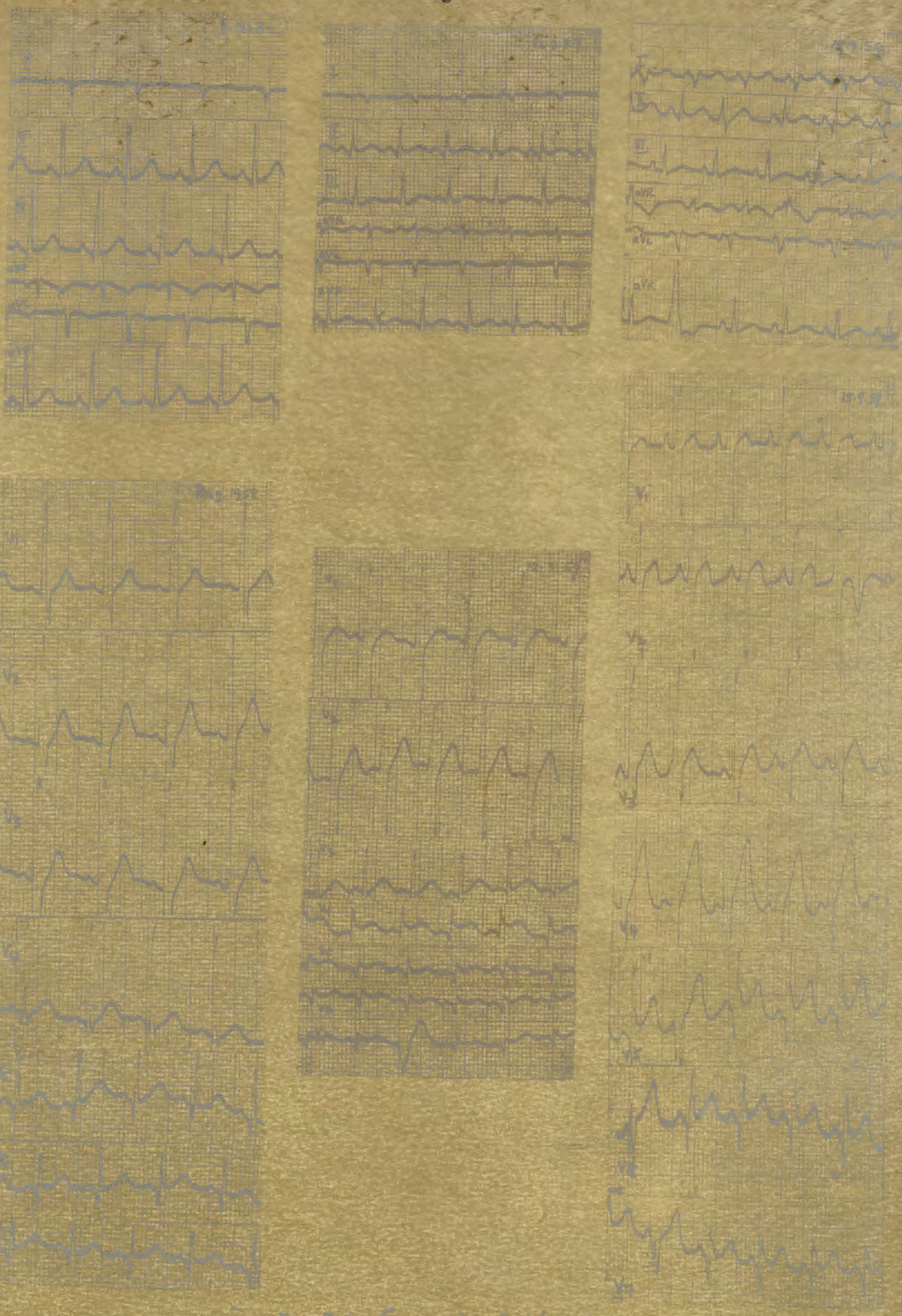


Fig 74. Case 44 Serial ECGs

The R/S ratio in V_1 was 1.6. The T wave was flattened in lead II and inverted in III, $-V_1$-3. These changes were interpreted as indicating left ventricular damage and right ventricular hypertrophy, with a possible bundle branch block. Eighteen months later (19.1.60) the heart rate was 79. The RVH was more marked, with an R/S ratio in V_1 of 6.0. The S-T changes, however, had shown considerable improvement over the right precordial leads. The Q waves were also less striking. It thus appeared that the "acute" muscle damage present at the time of the first E.C.G. had resolved.

Case 36. The initial E.C.G. (21.7.58) showed a rate of 125 per minute. Abnormal Q waves were present in lead III. The R/S in V_1 was 4.0. The T wave was inverted over V_3-5 and there was S-T depression over the right precordial leads. The extensive T wave inversion seemed out of proportion to the R.V.H. and suggested R.V. damage. In the second E.C.G. (19.1.60) the heart rate was 125. The changes in the Q waves were similar to previously but the inverted T waves were less conspicuous and there was now an upright T wave over V_4. The S wave had disappeared in V_1, so that R/S approached infinity. Depression of S-T was still present in V_1-3. The change in the T waves suggested some improvement in the right myocardial damage.

Case 44. August, 1958: Sinus rhythm with a rate of 100/minute. Right axis deviation ($+ 100^{\circ}$). Abnormal Q waves present over V_5-7. R/S ratio in V_1 of 3.3. Low voltage T wave over lead I. Interpreted as representing R.V.H. and extensive damage of the myocardium of the left ventricle.

March, 1959: Heart rate 136. Ventricular ectopic beats. Elevated S-T segment over V_4-6. Suggestive of acute myocardial damage over left ventricle.

September, 1959. Heart rate 125 per minute. Abnormal P wave in lead III and right ventricular leads. Q waves were present in lead I and were very striking over the left ventricular leads. R wave larger than S in aVR.

R/S ratio less than previously in V_1 (0.6). S-T segment elevated in $V_{5,6}$. The changes suggest extensive damage of the myocardium, and the R. atrial hypertrophy reflects right ventricular decompensation.

DISCUSSION.

The pathological changes observed in the cardiac muscle are similar to those described by previous authors. All 5 patients showed microscopic evidence of cardiac involvement, while in 3 cases the fibrosis was so extensive as to be evident to the naked eye. The patches of fibrosis are similar in appearance to healed infarcts. However, with one exception, the coronary arteries were all normal.

Histochemically one case showed patchy areas of loss of enzymic activity where serial sections revealed no histological change. These resembled the changes described in patients dying of acute myocardial infarction.

The presence of tachycardia in this series is in keeping with the findings of previous authors. Apart from this sign there were no abnormal symptoms or signs of note. This may, however, not give a true reflection of the patients cardiac state as he is at constant rest and not putting much strain on the heart.

The fact that these patients appear to have a sudden cardiac type of death in the course of a respiratory infection, supports the findings of Gailani, that these patients may be on the verge of cardiac failure. Though the shock-like state has been partly attributed by previous authors (Zatuchni et al.) to abnormality of rhythm, this factor has not been observed in the present series.

The E.C.G's have shown evidence of "recent" myocardial damage in certain cases and on serial investigation in 2 cases there appeared to be some resolution of the changes, comparable to what one might expect with a healing infarct. The abnormal Q waves also suggest cardiac ischaemia.

Conduction defects have been described by previous authors but there have been conflicting views. Zatuchni et al. found a prolonged or normal P-R, while Rubin and Buchberg found it to be shortened. In the present study there has been no direct evidence of an abnormally short P-R interval, but the mean valve was significantly lower than the normal which supports this view.

The occurrence in one patient (case 14) of a short P-R (0.09) in association with a long cycle length (heart rate 60) suggests a Wolff-Parkinson-White syndrome.

Bundle branch block has been observed in isolated cases by previous authors. In the present series there was a high incidence (10%) of undoubted bundle branch block.

The presence of Q waves has previously been noted over the left ventricular leads. The occurrence of Q waves in V_3 in the present series is exceptional.

CONCLUSIONS:

Although it is not always easy to interpret changes in the electro cardiogram, there can be no doubt that involvement in the myocardium is a common feature in progressive muscular dystrophy in childhood. In this series there were less than 10 cases out of 56 investigated, who had a completely normal E.C.G. The electrocardiographic changes suggest extensive involvement of both ventricles and right ventricular hypertrophy.

The pathological findings confirm the E.C.G. evidence.

In all 5 cases examined there were fibrotic changes in the myocardium.

The absence of clinical symptoms or signs in a large percentage of these cases is probably a reflection of their inactivity and it is likely that if they were subjected to any effort comparable to normal activity it would probably produce cardiac failure.

CHAPTER 8.

I. SERUM ALDOLASE AND TRANSAMINASE.

Aldolase is an enzyme which catalyses the reversible splitting of fructose - 1 : 6 - diphosphate into two triose esters, glyceraldehyde - 3 - phosphate and dihydroxyacetone phosphate.

Schapira, Dreyfus and Schapira (1953) reported a raised serum aldolase level in 26 out of 29 children and in all of 11 adults with different types of muscular dystrophy. They found no correlation between the serum aldolase activity and the rate of progression of the disease or the degree of the muscle wasting.

Evans and Baker (1957) found that the aldolase was invariably raised in their 13 cases of pseudohypertrophic dystrophy. They were of the opinion that the increased serum aldolase level does not reflect a primary biochemical abnormality in muscular dystrophy, but merely represents a generalized loss of water-soluble protein from the affected muscle fibres.

Pearson (1957) reported a raised serum level of glutamic oxaloacetic transaminase in 47 out of 87 cases of muscular dystrophy (54%).

Of the 46 patients under 18 years of age, however, the enzyme level was above normal in 90%. He concluded that, as in the case of aldolase, the high serum transaminase level merely reflects a leakage from the damaged muscle fibre, and is of no etiological significance.

Material and Methods.

The serum aldolase was estimated by the method of Evans and Baker (1957) on 39 cases, and the serum glutamic oxaloacetic transaminase, by the method of Cabaud et al. (1956), on 16 cases

of progressive muscular dystrophy. Aldolase estimations were also done on the parents and sister of cases 26-28, the three sibs of case 7 and one of the sibs of cases 56 and 57. These relatives were clinically unaffected by the disease. All the estimations were done by the Department of Chemical Pathology at Guy's Hospital.

Results.

The enzyme levels are correlated with the age of the patient and the duration of symptoms in Table VIII.1.

The aldolase level was raised (above 11 units) in 32 cases and was within normal limits in seven. The serum transaminase level was raised (above 1.4 micromoles per ml.) in 15 cases and within normal limits in one case. Of the 15 cases with a raised transaminase level, 12 cases also had a raised aldolase level, while in one (case 53) the aldolase was normal. In the other 2 (cases 56, 57) the aldolase was not estimated. The normal transaminase level in one patient (case 37) was associated with a normal aldolase level.

All the relatives investigated had normal enzyme levels with the exception of one of the sibs of case 7 (Table VIII.2.) This 5-year old boy had a slightly raised aldolase level (12.5 units) but showed no evidence of the disease on clinical examination.

TABLE VIII.1: SERUM ALDOLASE AND TRANSAMINASE LEVELS IN 41 CASES OF PROGRESSIVE MUSCULAR DYSTROPHY.

Case No.	Age.	Duration of Symptoms.	Aldolase (normal: 0-11 units)	Transaminase (normal: 0.2-1.4 units)
1	13	11	12.5	
2	16	14	61.9	2.35
4	13	11	4.83	
6	15	10	35.2	3.0
7	10	8	29.9	
10	13	10	29.5	
11	12	10	13.3	
12	10	8	13.3	
13	15	6	14.2	
14	13	8	21.2	3.74
15	11	8	14.1	1.87
16	15	13	24.8	2.24
19	12	10	12.4	
20	13	11	16.8	
23	14	11	42.0	3.47
24	10	8	23.3	
25	11	9	11.9	
26	11	9	20.0	
27	8	6	23.9	
28	6	4	25.5	
29	16	14	18.6	1.7
30	12	9	10.5	
31	11	9	18.3	
32	15	12	13.7	3.68
33	10	7	23.7	2.34
37	14	12	8.0	.88
38	10	9	5.4	
39	16	12	22.2	1.87
40	13	7	23.3	
42	8	2	61.5	
43	11	8	14.2	2.34
44	14	6	15.5	
45	14	9	17.7	2.59
47	14	12	19.2	
50	12	10	7.3	
51	10	6	9.3	
52	2	1	51.7	
53	15	13	8.9	2.45
55	13	11	12.7	
56	11	6		1.91
57	7	1		2.93

TABLE VIII.2.
SERUM ENZYME LEVELS IN UNAFFECTED RELATIVES.

Case No.	Age	Aldolase (normal 0-11 units)	Transaminase (normal 0.2-1.4 units)
Family of cases 26-28			
Mr. J.	39	4.33	
Mrs. J. (F.)	32	6.98	
S.J. (F.)	3	5.31	
Family of case 7			
C.C.	8	3.1	
G.C.	5	12.5	
B.C. (F.)	3	5.7	
Family of cases 56-57			
S.T. (F.)	9		0.69

Discussion:

Of the 7 patients with a normal aldolase level, 6 conformed to the usual pattern of the disease and did not differ from cases with raised aldolase levels in respect of severity of the disease, rate of progression, or the extent of pseudo-hypertrophy or atrophy.

Case 38, on the other hand, did have some unusual features.

The disease was already manifest within the first year of life and had a more rapidly progressive course than is usually observed. In addition there was extreme wasting of the muscles of the limbs, trunk and neck.

Of special interest are the normal aldolase levels in cases 50 and 51 and the very high level in their younger sib (case 52). This suggests that the enzyme level may be raised early on in the disease and come down to a normal level at a later stage. A higher level was also recorded in case 28 than in his two older sibs (both of whom, however, had abnormally high levels); and in case 42 as compared with his older sib (40). Although the early cases seemed to have higher levels than those of longer duration this was not invariable. Thus the highest aldolase level was observed in a patient with disease of long duration (case 2).

There does not appear to be any correlation between the clinical state of the patient and the aldolase level. Thus, cases 4, 37 and 53 have normal levels while cases 13, 16, 31 and 45 of comparable age and severity, have raised levels.

Conclusions:

The serum aldolase levels were invariably high in the early stages of the disease. Later in the course of the disease normal results were obtained in a number of cases, irrespective of the clinical state of the patient. These results are in disagreement with those of Evans and Baker where high levels were obtained in all 9 cases of "pseudohypertrophic muscular dystrophy" (aged from 5 to 10 years).

Aldolase estimations may be of value in differentiating some early cases of muscular dystrophy from neurogenic atrophy or benign congenital hypotonia. In the latter conditions the enzyme level is normal.

The serum transaminase level corresponded to the aldolase level in 13 of the 14 estimations.

II THERAPEUTIC TRIAL.

INTRODUCTION

There is no drug available which is known to influence the course of progressive muscular dystrophy. Walton and Nattrass (1954) reviewed the numerous forms of therapy for which claims have been made. In 1958 Manzini and Frattola reported that a crude extract of hog's stomach caused a significant drop in the serum aldolase level of 11 patients with various forms of progressive muscular dystrophy. A daily dose of 200 or 300 mgms. of the extract was used, and treatment was continued for variable periods ranging from 10 to 53 days. An aldolase estimation was done prior to commencement of, and again after completion of, therapy. There was an associated gain in weight in all but one case. They interpreted these results as being due to a direct anabolic protective action of the extract on the muscle cell and thus slowing down the degenerative process.

MATERIAL AND METHODS.

In order to assess to the validity of these results and the therapeutic value of the extract of hog stomach, a blind clinical trial was undertaken. Crude mucopolysaccharide extract of hog stomach was obtained from The Evans Biological Institute.

Sixteen inpatients with varying stages of the disease were divided into two similar groups on the basis of age and duration of symptoms (Table VIII.3). Two separate batches of unidentified capsules (A and B), one being the crude mucopolysaccharide extract and the other similar capsules containing lactate were administered to the two groups in a dosage of 1 capsule twice daily (equivalent to 500 mgms. of the crude extract). In addition 4 control cases convalescent from rheumatic fever (cases A and B) or tuberculosis (cases C and D) were given known mucopolysaccharide.

TABLE VIII.3. TRANSAMINASE LEVELS DURING THERAPEUTIC TRIAL.

Case No.	Age	Category	Muscle Power		Transaminase.					
			9.6.59	13.7.59	1.6.59	8.6.59	15.6.59	22.6.59	29.6.59	6.7.59
12	11	A	6	6	1.43	2.52	1.6	1.74	2.00	1.97
14	14	A	18	18	1.69	2.15	2.08	3.13	1.70	2.31
15	12	B	6	7	1.67	1.63	1.12	1.67	2.08	1.60
16	15	B	8	11	1.57	2.24	1.84	1.94	1.70	2.86
22	9	B	17	10	2.06	2.89	2.58	2.98	3.91	3.20
25	12	B	3	6	2.04	1.94	2.04	2.11	2.18	2.58
26	12	A	5	7	2.48	2.65	2.0		3.5	2.82
27	9	A	10	11	2.34	2.69	2.96	3.3	2.42	2.86
28	7	A	13	14	3.58	6.41	4.45	6.55	8.1	5.10
32	16	B	5	5	0.97	1.84	1.22	1.40	1.26	1.90
33	11	B	6	12	2.32	3.03	2.86	2.42	2.1	3.57
35	12	B	12	13	2.06	3.71	2.58	3.26	2.76	2.00
37	15	A	3	6	0.75	1.16	1.12	1.36	1.30	1.26
43	12	A	6	8	1.23	1.36	1.97	2.14	1.94	2.10
45	15	A	8	9		1.36	1.80	1.60	1.29	2.08
55	14	B	4	9	0.98	1.26		1.26	1.26	0.95
A	8	M	17	14	1.16	1.42	1.63	1.56	1.26	2.21
B	10	M	25+	20	0.80	1.83	0.95	0.92	1.02	1.36
C	14	M	20	21	0.55	0.65	0.95	1.06	0.99	1.67
D	14	M			0.45	0.75	0.48	0.82	0.58	

Serum transaminase levels were done weekly, commencing 2 weeks before tablets were given. Transaminase was measured because it had been found it closely paralleled the aldolase level in other cases of the series. Clinical assessment included subjective evidence of improvement. Muscle charting at the beginning and end of the trial and, in addition, a rough measurement of muscle power was obtained by measuring on a spring balance attached to a holster around the head, the resistance of the extensors of the neck and back to a forward pull with the patient in the sitting posture. Although a crude method, it did give fairly consistent readings. The trial was continued for 4 weeks. Table VIII.3 summarizes the transaminase results and muscle testing.

RESULTS.

There was no clinical improvement and no significant reduction of the transaminase levels in either group of patients. Category A was the active substance and category B the control.

CONCLUSIONS.

Mucopolysaccharide extract of hog stomach does not appear to be of any value in the treatment of progressive muscular dystrophy.

SUMMARY AND CONCLUSIONS.

This thesis contains the results of my observations on a number of aspects of progressive muscular dystrophy in childhood.

The variable clinical pattern of the disease has been stressed and it has been shown how the disease may differ in presentation, in the same patient at different stages, in different individuals at a comparable stage, and in affected sibs.

The inheritance has been investigated and the views of previous authors substantiated. The majority of cases are isolated and of those with a positive family history most are inherited through a sex-linked recessive mechanism. However, two female cases have been presented with the characteristic features of Duchenne-type muscular dystrophy but an autosomal recessive mode of inheritance. It has been suggested that some of the isolated cases may also have an autosomal recessive inheritance and not be due to new mutations on the X-chromosome.

The clinical impression of a high incidence of mental defect in association with progressive muscular dystrophy has been confirmed by psychometric testing of 27 inpatients. If both the mental defect and the myopathy are due to the same fundamental defect, with a genetic basis, this raises various possibilities in relation to etiology.

The pathology of the disease has been briefly reviewed and the main histological features discussed. No difference in histological pattern was evident between cases with clinical pseudohypertrophy and those with atrophy. Pseudohypertrophy was usually associated with abundant adipose tissue in the muscle, but some early cases with this clinical feature had only an excess of collagen.

The application of modern histochemical techniques has produced interesting results in regard to both normal and dystrophic muscle. The presence of different types of fibre in normal muscle, and the way in which these are related to the enlarged and the atrophic fibres of dystrophic

muscle, has been discussed. It is possible that the variation in the proportion of the different fibre types, which differ in their metabolism, may explain the consistent distribution pattern of the muscular weakness, as well as the earlier affection of some muscles than others.

Involvement of the cardiac muscle has been shown to be a common feature of progressive muscular dystrophy in childhood. Post-mortem examination of the heart in 5 cases revealed fibrotic lesions in all of them. The extensive abnormalities observed in the electrocardiographic tracings have been recorded and an attempt made to interpret them.

Serum aldolase and transaminase levels were consistently raised in the early than in the later stages of the disease. In some instances normal values were obtained in otherwise typical cases. A crude mucopolysaccharide extract of hog stomach, which had been claimed to be of value, was tested but found to produce no clinical improvement or reduction in the abnormal serum enzyme levels.

APPENDIX I.

CLASSIFICATIONS.

APPENDIX I.

CLASSIFICATIONS.

Landouzy and Déjerine (1885)

Progressive Muscular Atrophies.

A. Myopathic Atrophies.

1. Progressive Atrophic Myopathy.

a. Progressive muscular atrophy of childhood.

b. Facio-scapulo-humeral type.

c. Scapulo-humeral type.

d. Femoro-tibial type.

2. Pseudo-hypertrophic Myopathy.

a. Classical pseudo-hypertrophic paralysis.

b. Leyden-Möbius type.

c. Juvenile form.

B. Neuropathic Atrophies.

Erb (1891)

A. Dystrophia musculorum progressiva infantum.

1. Hypertrophic form.

a. with pseudo-hypertrophy.

b. with true hypertrophy.

2. Atrophic form.

a. with primary facial involvement.

b. without facial involvement.

B. Dystrophia musculorum progressiva juvenum et adultorum (juvenile form).

Batten (1910)

1. Simple Atrophic type. (Myopathic form of Oppenheim's Myatonia congenita (1904).

2. Pseudo-hypertrophic type (Duchenne).

3. Juvenile type (Erb).

4. Facio-scapulo-humeral type (Landouzy and Déjerine)

5. Distal type (Gowers 1902).

6. Myatonia atrophica type (Thomsen, 1876; Steinert, 1909)

7. Mixed and transitional type.

Milhorat and Wolff (1943)

Progressive muscular dystrophy. (No sub-classification).

Bell (1943)

A. Cases with pseudo-hypertrophy at some stage but without facial involvement.

B. Atrophic group with no evidence or history of pseudo-hypertrophy and no facial involvement.

C. All cases with facial involvement, irrespective of the presence of pseudo-hypertrophy.

Tyler and Wintrobe (1950)

1. Childhood type. (Duchenne's pseudo-hypertrophic type; Leyden-Möbius' atrophic pelvi-femoral type).

2. Facio-scapulohumeral type (including scapulo-humeral or "juvenile" type).

Levison (1951)

1. Scapulo-humeral type (Erb).

2. Facio-scapulo-humeral type (Landouzy and Déjerine).

3. Lower extremity type (Duchenne; Leyden-Möbius).

Stevenson (1953)

1. Duchenne-type rapidly progressive muscular dystrophy of young boys.

2. Autosomal limb-girdle type

a. with facial involvement.

b. without facial involvement.

Becker (1953, 1957).

1. Shoulder-girdle or descending form.
2. Pelvic-girdle or ascending form.
   a. Malignant X-chromosomal type.
   b. Benign X-chromosomal type.
   c. Auto somal recessive type.

Walton and Nattrass (1954)

1. Duchenne type (including childhood pelvi-femoral type)
2. Facio-scapulo-humeral type.
3. Limb-girdle type (scapulo-humeral, pelvi-femoral, and late juvenile (Nevin, 1936).

Blyth and Pugh (1959)

(Muscular Dystrophy in childhood.)

A. Childhood type.
   1. Severe group.
      (i) those "off their feet" by the age of 11.
      (ii) those under 11 showing rapidly progressive difficulty in walking.
   2. Mild Group.
      (i) Still ambulant after 11.
      (ii) Those under 11 with slowly progressive condition.

B. Adult Types.

APPENDIX II.

ROUTINE QUESTIONNAIRE.

QUEEN MARY'S HOSPITAL FOR CHILDREN, CARSHALTON, SURREY

QUESTIONNAIRE FOR MUSCULAR DISEASES

A. PREGNANCY

1. Was there anything unusual about the pregnancy ? .....

2. Did you have any illness during pregnancy ? .....

3. Were the movements normal, more than normal, less than normal ? .....

4. Was an X-ray taken ? .....

B. LABOUR

1. Was the labour normal, long, very short ? .....

2. Were instruments used ? .....

3. Were there any complications ? .....

4. Was the child normal at birth ? .....

5. What was the birthweight ? .....

6. Did he cry normally ? .....

7. Was he breast fed ? ..... How long ? .....

8. Did he suck normally ? .....

9. Was he an active child ? .....

10. Was there anything unusual about his appearance ? .....

C. MILESTONES

At what age did he :

1) Hold his head up ? .....

2) Sit up unsupported ? .....

3) Stand on his own ? .....

4) Crawl ? .....

5) Walk ? .....

6) Start talking ? .....

D. ILLNESS

1. What was the first abnormality you observed ? Describe in detail ? Give age ? .....

2. Was there anything unusual about his mode of walking ? .....

D. ILLNESS (continued)

3. Did he walk on his toes ?
At what age ? .....

4. Was he able to run normally ?
climb upstairs normally ? .....

5. Did he tend to fall ? From what age ? ....

6. Was he able to get up after falling ?
Did he do this in a normal manner ?
.....

7. Did you note enlargement or wasting of any muscles ? Specify which muscles ?
At what age ?
.....

8. Did he complain of pain in his muscles ? .....

9. Did he tire readily ? .....

10. At what age did he go off his feet ?
Did any illness or episode cause this ? .....

11. Did you observe any weakness of his

arms ? ..... At age of .....

face ? ....

neck ? ....

back ? ....

12. Have you noted any abnormality of his tongue ? .....

13. Has there been any difficulty with chewing or swallowing ? .....

14. Has he gained or lost weight ? ..... From age of .....

15. Has he ever had a squint or double vision ? .....

16. Has he ever had a persistent skin rash ? .....

17. Has his mental development been normal ?
.....

18. At what age was the diagnosis first made ? .....

E. PAST ILLNESSES

1. Give age of previous illnesses (including childhood illnesses) .....

operations .....

fractures of bones .....

2. Did any of these affect his muscular weakness ? .....

F. FAMILY HISTORY

1. Give ages of his brothers and sisters and parents.
.....

.....

F. FAMILY HISTORY (continued)

2. Has any other member of the family on either side had a similar illness ? .....
Describe in detail.

.....

.....

.....

3. If father and mother married previously, give details of children .....

.....

.....

4. Do any relatives have mental illness, epilepsy, nervous disease or other illness of note ?

.....

.....

5. Have there been any marriages between cousins or near relatives in the family at any time ?

.....

6. Tabulate brothers and sisters of his mother and father from eldest to youngest, and give details of children of each, stating sex and age.

Father : Brothers and Sisters	Children (Sex and Age)
.....	.....
.....	.....
.....	.....
.....	.....
.....	.....
.....	.....
.....	.....

Mother : Brothers and Sisters	Children (Sex and Age)
.....	.....
.....	.....
.....	.....
.....	.....
.....	.....
.....	.....
.....	.....

APPENDIX III.

CLINICAL HISTORIES.

CASE NO. I BORN: 20.8.45

HISTORY: Recurrent vomiting during most of pregnancy; otherwise normal. Labour and neonatal period normal.

Milestones: Sat up: 1 year; Stood: 18 months; Walked: 18 months. When he started walking abnormal gait observed. At 2¼ "knock knees" diagnosed. Prominence of the calves was noted at the age of 3. Weakness of the arms first noted at 3 when he was unable to lift heavy objects. He then had a marked waddle to his gait, tended to fall frequently and had difficulty in getting up. "Climbed up himself" in the typical dystrophic manner. He had difficulty in getting onto a kerb; when going up steps supported a hand on his lower thigh. He was never able to run or jump. Occasional cramps in his legs while walking.

A diagnosis of muscular dystrophy was made at 4.

His weakness gradually progressed. Difficulty walking up incline. Wasting of the arms and thighs was first noted at 8. He went off his feet at the age of 9. There was no precipitating factor.

Although his mental development was not grossly retarded, his younger sister surpassed him.

Three attacks of confusion since July, 1957 and withdrawal lasting about 4 weeks. During these attacks he sometimes became hallucinated and noisy, at other times mute and apathetic and disinterested in his surroundings and food. Chewing, swallowing and sphincter control normal. Tongue normal in appearance. No skin rashes.

COURSE: Psychotic attacks lasting 3-6 weeks at intervals of approximately 3 months. Probably Schizophrenia. Muscle power showed no demonstrable deterioration over period of a year.

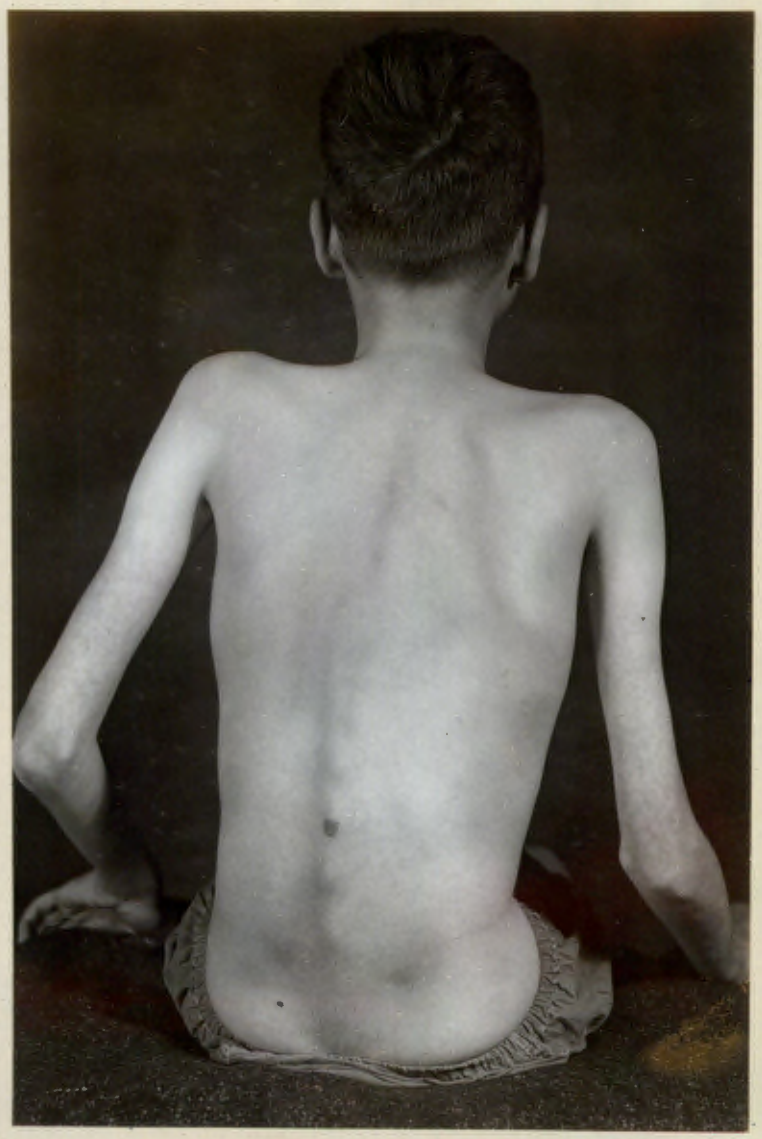


Fig. 1-2 : NOTE PROMINENCE OF CALVES, SERRATI ANTERIOR; WASTING TRAPEZII AND UPPER ARMS; EQUINUS OF FEET.

CASE NO. 2. BORN: 16.2.42

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 5 months; Walked: 12 months.

At 15 months twisted his foot and limped for 3 months. At 18 months unable to climb steps. At a kerb went down on all fours and crawled up. Appeared stable on his feet. Calves became prominent. The mother noticed that his socks became too tight around the top. His walking gradually deteriorated. At 4 he started to fall frequently.

Would suddenly drop while walking "as if legs gave way under him." Got up "like a cow." Walked on his toes with feet inverted and associated lordosis. At age of 5 diagnosis of "knock knees and stiff toes." Steel brace fitted to spine; unable to walk with it. Diagnosis of muscular dystrophy at 6.

Weakness of shoulder abductors at 7. Walking gradually deteriorated until he was unable to walk at 9. Able to sit unsupported till 10. Weakness of neck also noted. Became obese after going off his feet. Extremities became blue and cold, but no subjective symptoms. Intelligence normal.

PAST ILLNESSES: Measles, Pertussis and Chicken-pox (5) did not set him back.

COURSE: Over a period of 2 years there was very little change in his condition.

CASE NO. 3. BORN: 14.5.42

HISTORY: Pregnancy, labour and neonatal period normal. Won prize at baby show at 6 months.

Milestones: Sat up: 9 months; Stood: 18 months; Walked: 2 years. (Sister at 10 months, brother at 13 months).

From the time he started walking he had a waddling gait and "his body used to move as if he were being energetic and not getting anywhere." Unable to climb stairs. Able to run but with marked waddle. Fell frequently. Initially able to get up normally, but later got up in typical dystrophic manner.

Calves were prominent at 2. He walked on his toes and tended to overbalance backwards when on his flat feet. His tongue was large and he tended to keep it protruded. Diagnosis made at 5.

After starting school at 5 fell more frequently. "Legs simply gave way under him." The weakness slowly progressed. More rapid decline from age of 9. Weakness of arms noted. Used wheelchair intermittently. Unable to walk after 10. Back and neck noted to be weak after age of 10.

Developed a scoliosis. Although always thin, striking loss of weight from age of 13.

No pain in muscles.

PAST ILLNESSES: Measles (14 months), Chicken-pox (16 months), Pertussis (2), Rubella (2), Tonsillectomy (3) did not set him back.

COURSE: Admitted in March, 1959 for lobar pneumonia. Discharged home after one month, during which time his temperament and interest in things improved considerably. A muscle biopsy showed the characteristic changes of muscular dystrophy. (see

CASE NO. 3 (contd.)

chapter 5).

Re-admitted November, 1959 with mental disturbance of one week's duration. Aware of his surroundings but withdrawn and spoke irrationally. Mental state returned to normal after 2 months. Muscular condition showed minimal deterioration over period of one year. Died suddenly in May, 1960 following inhalation of vomitus.

Autopsy Report: The muscle groups were extremely wasted but the proximal muscles were more severely affected than the distal. The diseased muscles were pale and flabby. The small muscles of the hands and the neck muscles were relatively well preserved. The heart was enlarged (207 g.) and there were visible areas of fibrosis in the left ventricle and septum. . The coronary arteries and great vessels were normal. There was an acute tracheobronchitis and aspirated food was present in the trachea and major bronchi. The right lower lobe was consolidated. The left lung was normal. The bones were rather soft. The marrow present appeared normal. Apart from the slight generalised ventricular dilatation the central nervous system was macroscopically normal. The endocrine glands, gastrointestinal and genitourinary systems appeared normal.

Personal observations on the histological features of the cardiac and skeletal muscle are contained in chapters 7 and 5 respectively.

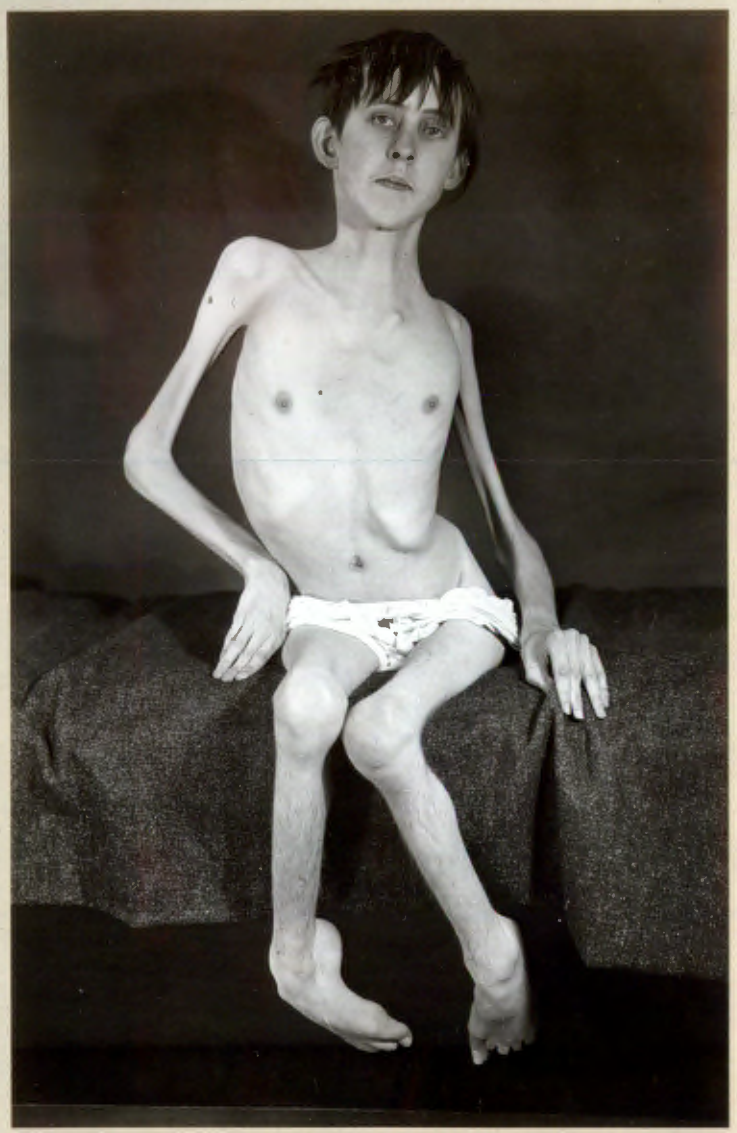


Fig. 3 and 4. GENERALISED WASTING. SCOLIOSIS. EQUINOVARUS DEFORMITY.

CASE NO. 4. BORN: 8.11.44

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 4 months; stood: 10 months; walked: 15 months.

His walking initially appeared normal but he had difficulty getting up steps. From the age of two he walked with "a hollowed back, stomach out and legs rather splayed." He fell frequently and had difficulty in getting up. Did so by pulling onto some object or "climbing up himself". Diagnosis first made at 4.

Gradual progression in weakness. Never able to run normally. At the age of 5 he began to walk on his toes. Slight prominence of the calves noted at that stage. At the age of 6 bilateral extension of the tendo achilles and subsequent plantar fasciotomy on the right foot performed. He was able to walk on the flat of his feet thereafter and seemed more stable. Lordosis of back became less prominent. Weakness of arms first noted at age of 7.

Put on Vitamin E age of 10. Mother thought it improved his general condition. Went off his feet at 11. No precipitating factor.

After being confined to a wheel-chair put on weight and developed contractures of the knees. Slow decline in muscle power. Sphincters and chewing normal. Intelligence normal.

PAST ILLNESSES: Measles, Chicken-pox, Pertussis and Mumps at age of 4 had no deterious affect on muscle weakness.

COURSE: Muscle charting at 3 monthly intervals over a period of 18 months showed hardly any deterioration in power.

Two days prior to admission he fell out of his

chair and bumped his right knee. X-ray revealed a supracondylar fracture of the femur with no displacement. It healed well after 3 weeks in a plaster cylinder.

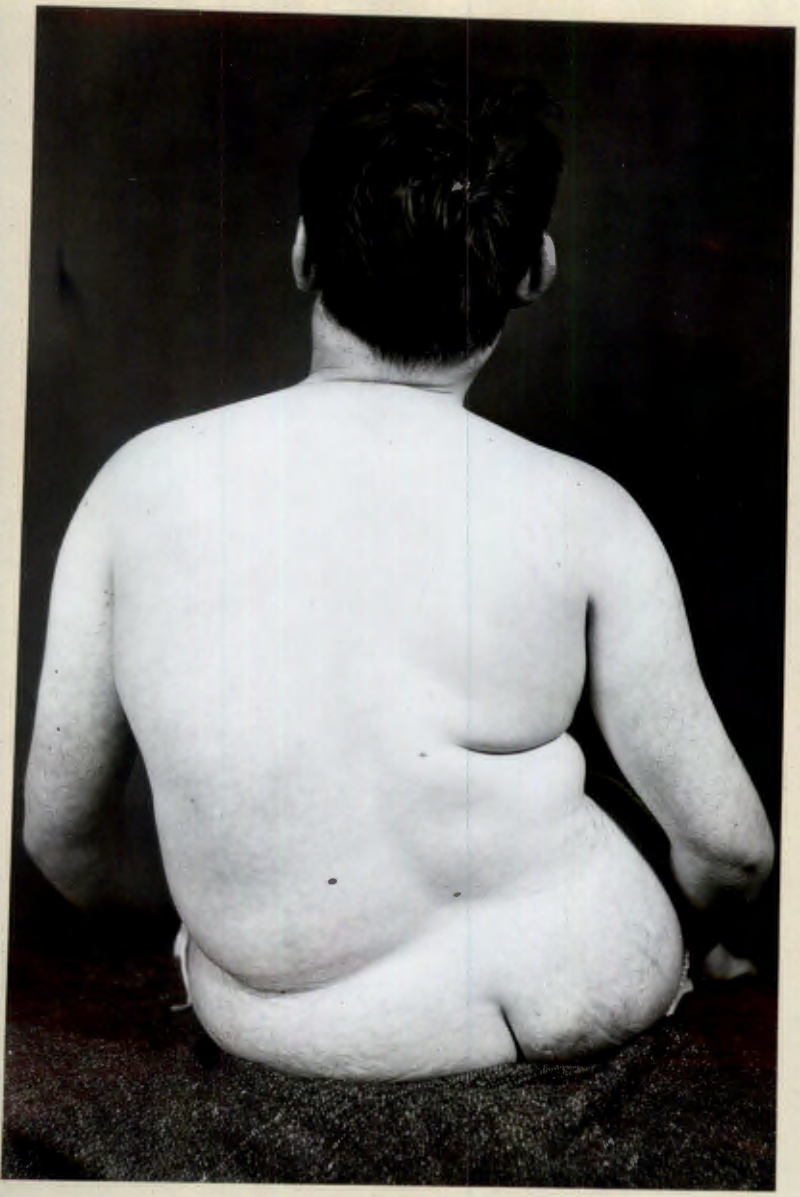


Fig. 5 and 6. GENERALISED OBESITY. SWELLING OF THE DORSUM OF FEET. MOTTLING OF SKIN.

CASE NO: 5. BORN: 25.2.46

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 9 months; Stood and Crawled: 14 months; Walked: 18 months. (Affected brother had not walked till 2 years, while his 2 normal sibs had walked at 1 year.)

At the crawling stage mother thought he had muscular dystrophy because his movements resembled those of his affected brother. He was unsteady on his feet after starting to walk, and fell frequently. "His legs just seemed to give way under him". After falling he was never able to get up by himself. All activities seemed an effort to him.

One foot became inverted at 2 and improved with a special boot support. He was unable to run normally and unable to walk up steps. He either crawled up or had to be helped. His calves became prominent at the age of 3 and weakness of arms was noted at that time. At 5 he was able to walk 100 yards uphill to school. Children knocked him down at school and derided him. Transferred to a school for the physically handicapped at 8. He seemed to tire readily and occasionally complained of cramp in his legs. There was a gradual deterioration in power until he went off his feet at the age of 10. No precipitating cause. Still able to feed himself.

After going off his feet curvature of spine developed and there was progressive gain in weight. (His affected brother, on the other hand, became very thin in spite of a good appetite). From the age of 12 he was unable to move his shoulders. His intelligence was normal.

PAST ILLNESSES: Measles (4) did not set him back.

FAMILY HISTORY: Positive. A brother and two maternal uncles were similarly affected.

CASE NO. 6. BORN: 1.12.42

HISTORY: Pregnancy, labour normal. Inactive in neonatal period.

Milestones: Held head up: 6 months; Sat up: 12 months; Crawled: 24 months; Stood: 36 months; Walked: 38 months.

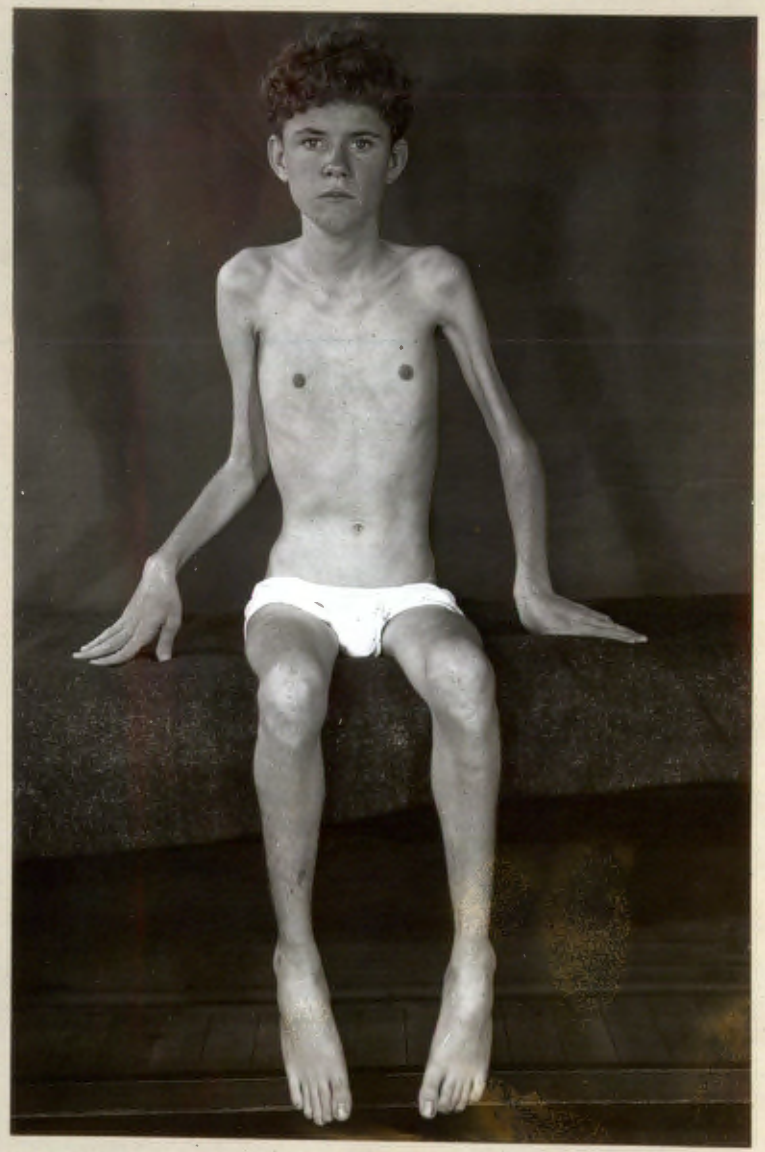
Mother noted abnormality when not sitting by 8 months. "Floppy infant" who did not move his limbs. When he started walking he had "a strange swaying gait with feet placed widely apart." He did not walk on his toes. Unable to run or climb stairs. Fell frequently. Climbed up himself in typical dystrophic manner. Tired readily and complained of pain in calves with walking.

Prominence of calves noted at 5. Other muscles appeared to waste progressively. Weakness of arms noted at 5. Diagnosis made at that stage.

Gradual progression of weakness. Went off his feet at 12. Weakness of back observed soon afterwards. Appeared to have difficulty with chewing. Sphincter control normal. Intelligence normal.

PAST ILLNESSES: Recurrent respiratory infections from infancy. Greenstick fracture of ankle at 5 years.

COURSE: Slight deterioration of muscle power over period of 2 years.



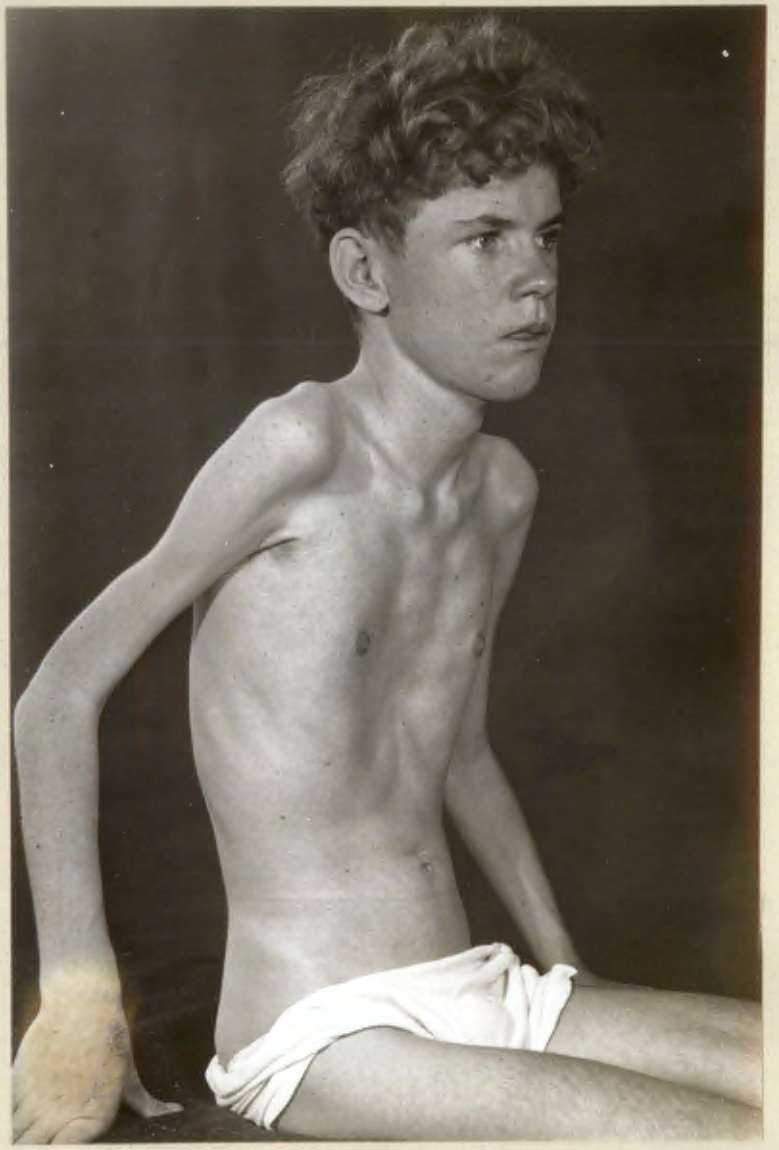


Fig. 7 - 8 GENERALISED WASTING. PECTUS EXCAVATUM.

CASE NO. 7 BORN: 30.10.47

HISTORY: Pregnancy, labour and neonatal period normal. Milestones: Held head up: 4 months; sat up: 8 months; stood: 15 months; walked: 19 months. Speech retarded. From the beginning his gait had a waddling character. Diagnosis of flat feet suggested at 2½. Initially he was stable on his feet and was able to run and climb stairs. After the age of 5 he began to fall. Got up in typical dystrophic manner. Callipers were prescribed which further handicapped his walking and made him more unstable. At the age of 6 plaster casts were applied to his feet to correct the eversion and he was immobilised for about 2 months. His legs were weaker after that but he could still walk. The following year his feet were again manipulated and kept in plaster for about 3 months. His walking gradually deteriorated. Weakness of the arms was first observed at the age of 7. A diagnosis of muscular dystrophy was made after a biopsy at the age of 8. He was still able to walk short distances; there was a marked lumbar lordosis and waddling gait. Never walked on toes. At the age of 9 he had a bilateral Souttars operation. He went off his feet shortly after that. There was no enlargement of any muscles. After going off his feet his calves became wasted and to a lesser extent also the thighs and arms. There was no muscular pain. He did not tire. Chewing, swallowing and sphincter control were normal. His intelligence was grossly subnormal.

PAST ILLNESSES: Rubella (2), Measles (4), Chicken-pox (4), did not set him back.

COURSE: Over a period of 18 months there was only slight deterioration in the muscle power. He was still able to crawl about and could get into sitting position by rolling on his side and

gradually working his way up with his arms.

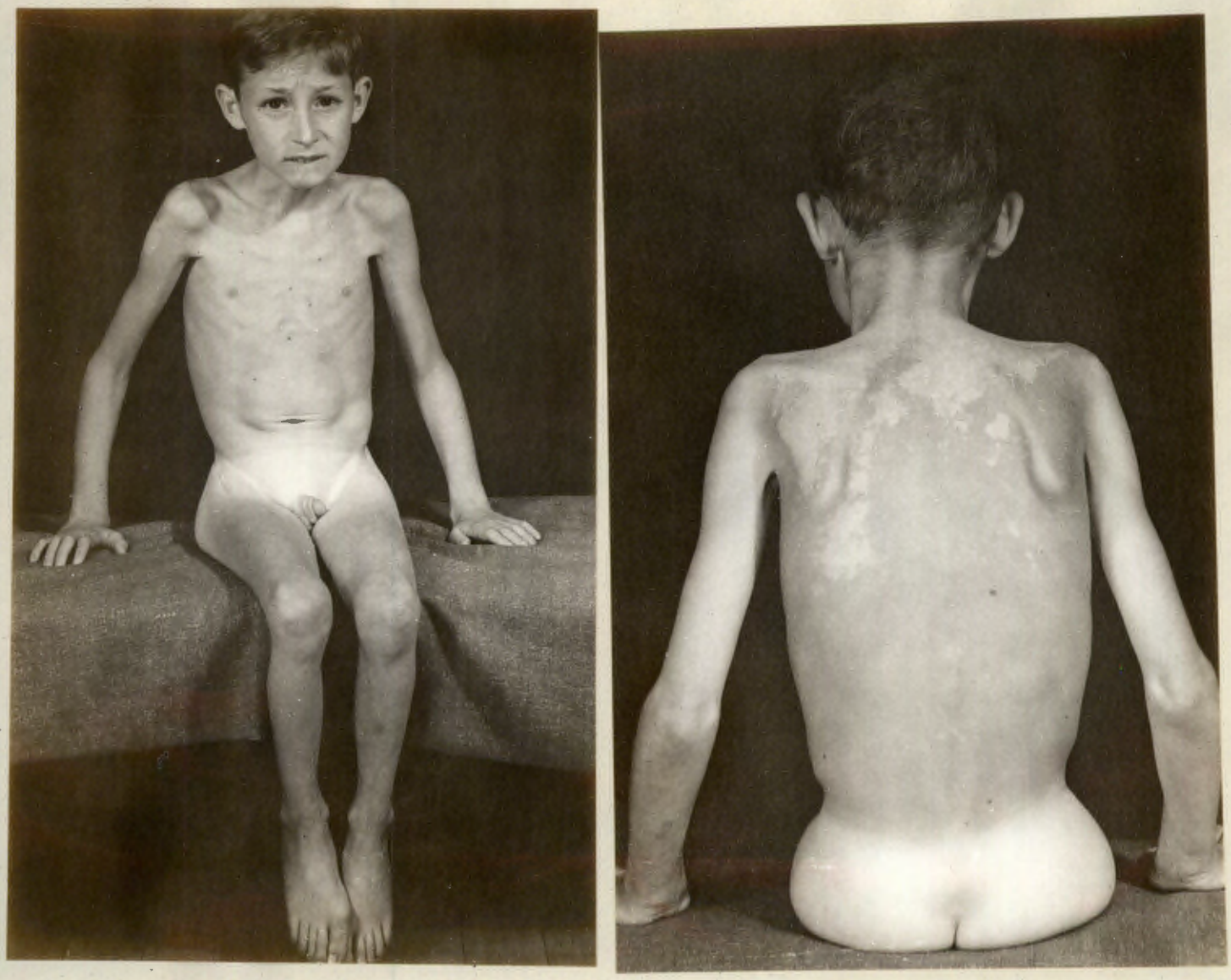


Fig. 9 - 10 : NOTE GENERALISED WASTING; MOST MARKED AROUND SHOULDER GIRDLE. (MOTTLING IS SUNBURN).

CASE NO. 8 BORN: 25.7.48

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Crawled: 9 months; Stood: 18 months (sibs. at 10-12 months); Walked: 2 years.

Initially quite stable on his feet and gait appeared normal. At 3 able to climb stairs but only by holding onto the railings; difficulty stepping onto pavement or bus. Never able to run normally and tended to fall when attempting to do so. Initially he was able to get up from the ground normally, but after the age of 5 "climbed up himself". Difficulty in walking uphill but managed reasonably well on the level. After starting school at 5 he fell frequently and was readily knocked over. When walking he frequently just slumped down as if his legs gave way under him. He tired readily but made no complaint of pain.

Although an older brother was similarly affected, his parents overlooked these symptoms till the age of 5. Weakness of the arms was first noted at 6, and there was flaccidity of the shoulders when they tried to lift him. Diagnosis at 6.

Swelling of his calf muscles was first noted at 7. When walking the calves became more prominent and seemed to contract, his feet became plantar flexed and he was unable to put his heels to the ground. This was less marked after rest.

Slow gradual progression of his weakness. Marked exacerbation when confined to bed for 2 weeks at the age of 9 following a broken nose and bruises sustained from a fall. He was unable to walk again after that but still rode a tricycle for a few months.

Put on a lot of weight after going off his feet.

Chewing and sphincter control normal. Although a fairly bright child he lagged behind at school.

COURSE: No marked change over period of a year.

CASE NO. 9. BORN: 7.6.48

HISTORY: Pregnancy and neonatal period normal. Adopted by a cousin at 6 months.

Milestones: Crawled at 9 months; Sat up and stood: 10 months; Walked: 13 months.

His gait initially appeared normal. He was able to climb up stairs but could never run in a normal manner. At the age of 2½ noted to be unstable on his feet and was falling frequently. No change in his condition until he started school at the age of 5 when he was readily knocked over by other children. He also fell frequently, often simply slumping down "as if someone had chopped his feet from under him." He got up with great difficulty by "climbing up himself." Prominence of the calves was also first noted at the age of 5. Diagnosis of muscular dystrophy was made at 6.

Gradual progression of weakness. From the age of 9½ he started to walk on his toes. When seen at age of 11 he could still walk about ¾ mile on level ground. He tired readily and occasionally complained of pain in the calves. No weakness was observed in the neck, face or arms. Chewing and swallowing were unimpaired and sphincter control was normal. He was of average intelligence.

PAST ILLNESSES: Measles (6) and Mumps (10) did not set him back.

COURSE: No follow-up possible.

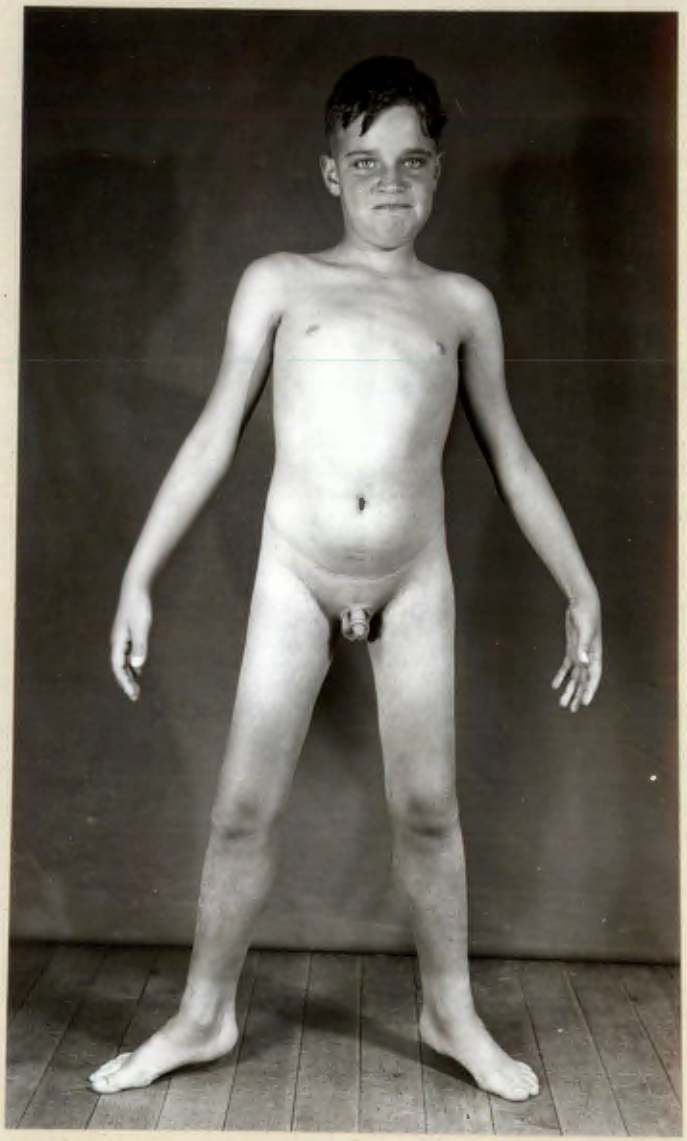




Fig. 11 - 13. TYPICAL STANCE - ON TOES; BROAD BASE; LUMBAR LORDOSIS.NOTE ATROPHY OF RHOMBOIDS.

CASE NO. 10. BORN: 12.4.45

HISTORY: Pregnancy, labour and neonatal period normal. Milestones: Sat up: 6 months; Stood: 18 months; Walked: 2 years. In infancy already it was noted that his calves were very prominent and formed "a little hard knot behind his leg." From the time he started walking he fell frequently and had difficulty in getting up. He "climbed up himself" in the characteristic dystrophic manner. His gait seemed normal until the age of 3, after which he walked on a wide base and swayed from side to side. He had difficulty climbing up steps and was never able to run normally. There was a slow gradual progression of the weakness with no periods of arrest or improvement. No weakness of the arms was noted till the age of 11, when he had difficulty in lifting heavy objects. There was no difficulty with chewing or swallowing. Sphincter control was normal. Intelligence normal.

PAST ILLNESSES: Measles, Chicken-pox and Whooping Cough at 2, when starting to walk, did not set him back. Fractured clavicle (9).

COURSE: When first examined at the age of 12 years 10 months he was still walking, on his toes, on a wide base, and with a marked waddle. There was marked lumbar lordosis. His calves were prominent ($14\frac{1}{2}$").

His weakness gradually progressed. A year later he had much more difficulty with walking and was readily bumped over. He could only get up when holding onto something. Boots with wedged heels to conform to his raised heels with walking, were fitted but did not improve his stability. He was still able to walk about $\frac{1}{4}$ mile at that stage but was already using a wheel-chair intermittently. He continued to walk for almost another

CASE NO. 10 (contd.)

year before becoming chairbound at the age of 14. There was a deterioration in the power of most of the muscles of the lower limbs, more particularly those around the pelvic girdle.

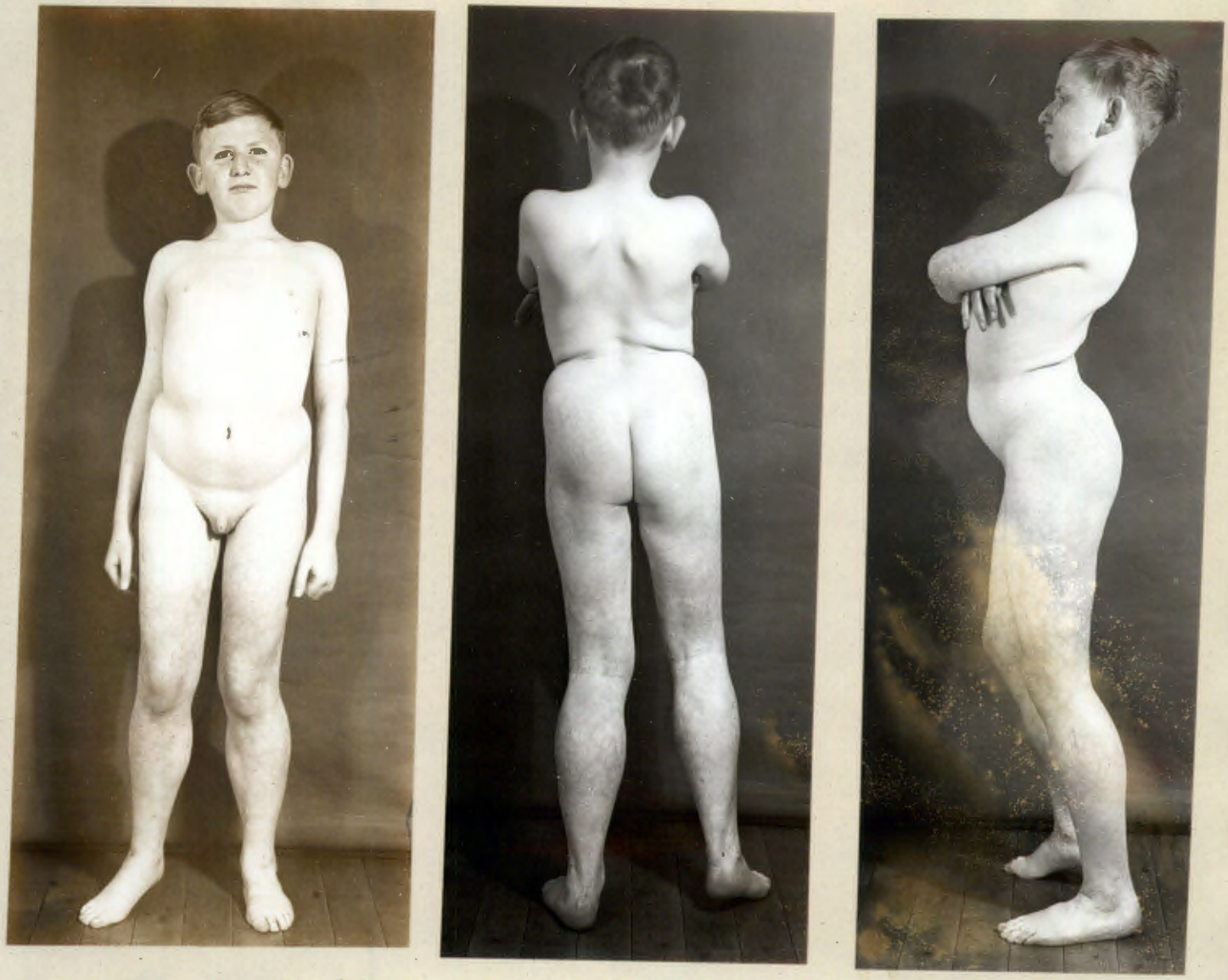


Fig. 14 - 16. SLIGHT OBESITY. MARKED LORDOSIS, RAISED HEELS. "MARBLING" OF SKIN.

CASE NO. 11. BORN: 22.3.46

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 6 months; Stood: 10 months; Walked: 18 months.

Initially his gait was "slow and ponderous". Stable on his feet. Never able to climb steps or run. From early infancy calf muscles prominent and firm. At 2½ it was remarked that he had "boxer's legs."

At age of 4 parents concerned at his difficulty with walking. Tired readily, but no complaint of pain. Developed swaying gait, walked on his toes, and fell frequently. Difficulty in getting up. "Climbed up himself." After starting school at 5, fell more frequently. It is interesting that through his father's encouragement he became a keen boxer and won some contests at school!

His walking gradually deteriorated. Unable to walk after the age of 8. Weakness of arms noted after that and progressed fairly rapidly. He continued to crawl until the age of 10.

Weakness of neck apparent at 11. Intelligence average.

PAST ILLNESSES: Measles (2), Mumps and Pertussis (3), Chicken-pox (4) did not set him back. Stretching of tendo achilles and hamstrings at the age of 10.

COURSE: Deterioration of trunk and girdle muscles observed over a period of 18 months.

CASE NO. 12. BORN: 8.3.48

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 8 months; Stood up: 12 months; Walked: 13 months.

The gait initially was normal and he was quite stable. He seemed able to get about and get up steps quite normally. At the age of 2 his mother noted that he tended to wobble from side to side when he tried to run. From the age of 2½ he began to fall frequently - his legs simply gave way under him. He got up after falling without any apparent difficulty. His gait gradually became more waddling. He never walked on his toes. He did not complain of any pain, but tended to tire readily and could not walk long distances. There was no apparent enlargement of any muscles.

After starting school at 5 he fell more frequently and had difficulty in getting up. He did this in a typical dystrophic manner. Diagnosis of muscular dystrophy made at 6. After the age of 6 he could no longer get up from the ground. Weakness of the arms first noted at that stage. He also had difficulty in abducting the shoulders and feeding himself. After 6 there was gradual progression of his difficulty with walking and he tended to support his hands on his hips while doing so. At the age of 7 he lost the ability to stand or walk after being confined to bed for 3 days with tonsillitis. The progression was very slow. After going off his feet he was still able to crawl until the age of 9. Contractures of knees from age of 7. Mental development normal.

PAST ILLNESSES: Rubella (2) did not set him back. Influenza (9)

COURSE: There was a slight progression of the weakness of all muscle groups in the course of 2 years and the development of a slight scoliosis concavity to the right.

Muscle Biopsy: Typical changes of progressive muscular dystrophy.

CASE NO. 13. BORN: 16.8.42

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 6 months; Stood and Crawled: 10 months; Walked: 12 months.

No abnormality was noted prior to poliomyelitis at 3. This affected mainly his left arm, back and both legs. He steadily improved and on discharge from hospital at age of 5 he was walking satisfactorily although there were slight residual contractures of the hamstrings, hip flexors and calf muscles. There was marked weakness of the left upper arm.

At the age of 8 it was noted his walking was deteriorating and he had increasing difficulty in climbing stairs.

At the age of 9 the right tendo Achilles was elongated and an attempt made to stretch his hamstrings and hip flexors. His walking became worse and he developed a marked lumbar lordosis. 6 months later he was falling frequently and had difficulty getting up from the ground.

The contractures of the hips and knees became more marked. He was unable to walk before he was 10. His arms became progressively weaker from that time. No enlargement of any muscles noted.

PAST ILLNESSES: Fractures: left tibia and fibula (July 1953); Surgical neck of left humerus (Nov., 1955); right femur (Feb. 1956).

EXAMINATION: The muscular weakness had the typical distribution of progressive muscular dystrophy with more marked involvement of the trunk, girdle and proximal limb muscles. There was no enlargement of any muscles. There was marked wasting of the left deltoid and the muscles of the left arm were weaker than those of the right. There was 2 inches of shortening of the left arm.

CASE NO. 13 (contd.)

Electromyography: Left deltoid: typical denervation pattern.
Left and right tibialis anterior: typical myopathic pattern.

COURSE: Minimal deterioration was noted in his muscle power.

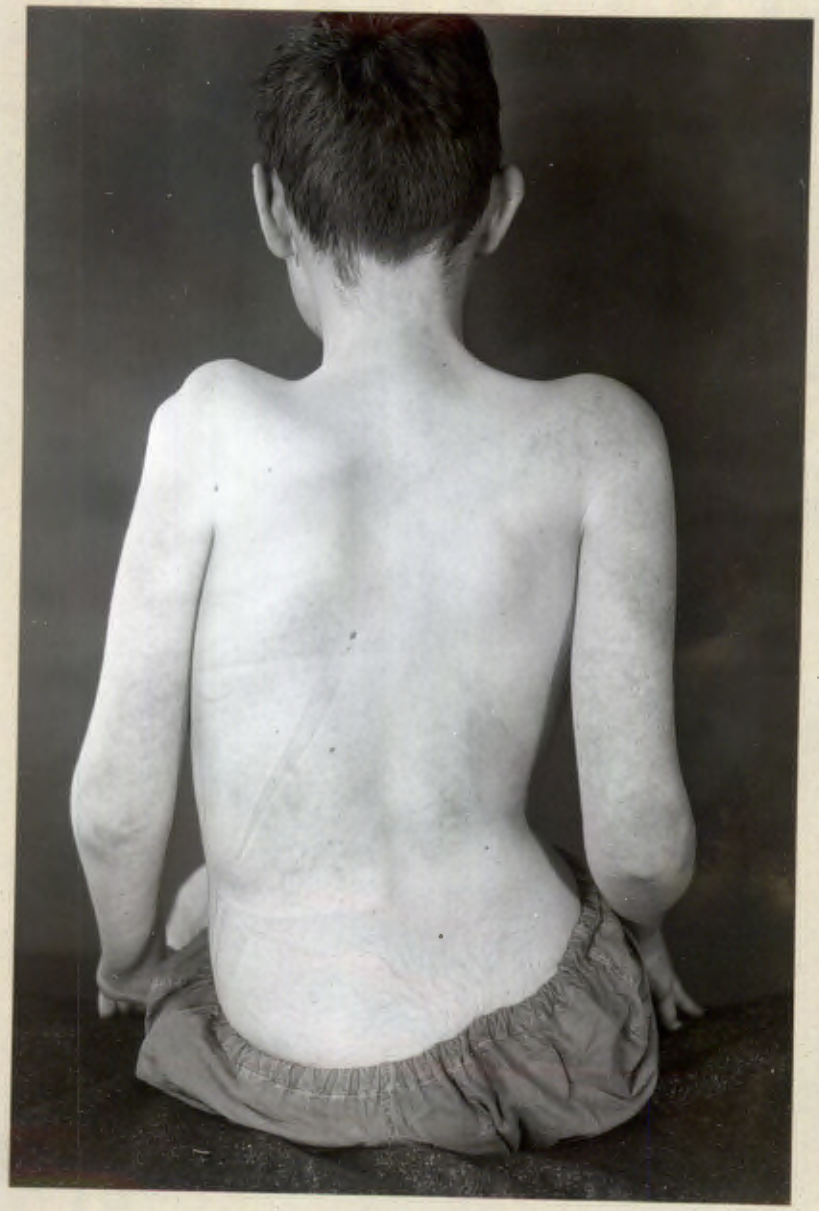


Fig. 17 : NOTE WASTING OF LEFT DELTOID.

CASE NO. 14. BORN: 24.2.45

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 6 months; Sat up: 9 months; Stood: 11 months; Walked: 12 months.

The child was fostered out at the age of 5. At that time only abnormality observed was difficulty in climbing steps.

PAST ILLNESSES: Fracture left arm.

COURSE: When first examined at the age of 12 he was still ambulant with a marked waddle and lordosis of the lumbar spine. He got up from the floor in the characteristic manner. There was a generalised prominance of his muscles, more especially of the calves, quadriceps, forearms and deltoids. A year later he was still walking but tended to fall more frequently. He walked on his toes and was developing an equinus deformity of both feet. He was unable to get up off the floor but could get into a sitting posture with the use of his arms. The calves had increased in size ($14\frac{1}{2}$"/$15\frac{1}{2}$" to 15"/$15\frac{3}{4}$" circumference). When standing the calves were extremely hard but tended to be flabby and soft when supine. Over the next 6 months there was a further decline in his muscle power and a phenomenal increase in the size of his calves ($17\frac{1}{2}$"/$16\frac{1}{4}$"). (No hospital pyjamas could be found to fit.) His walking had deteriorated and he could only just manage when helped onto his feet. He went off his feet at $13\frac{1}{2}$, after which the muscles tended to become flabby and he gained weight. The calves steadily increased in girth and were $18\frac{1}{2}$"/$18\frac{3}{4}$" after a further 6 months. There was progressive loss of muscle power. The only deformity at that stage was a limitation of dorsiflexion of the feet beyond 100^{o}.

Muscle Biopsy: Characteristic changes of muscular dystrophy. Marked excess of adipose tissue.

CASE NO 14.

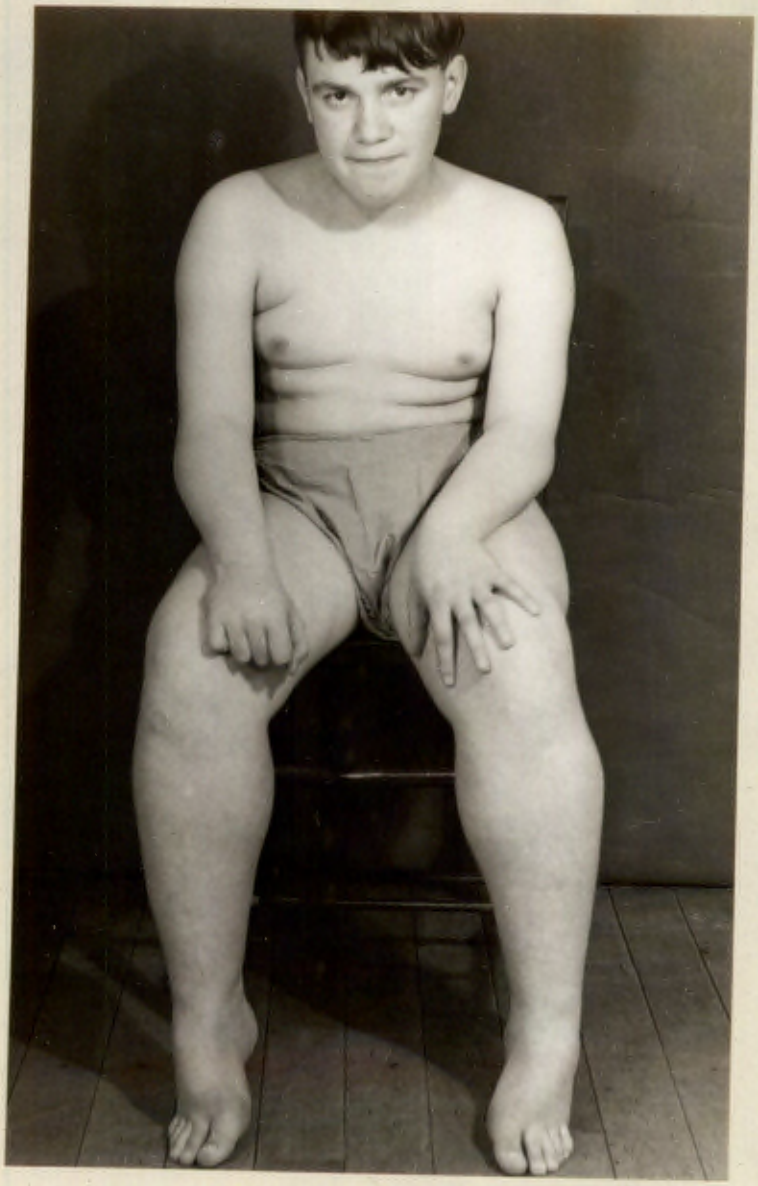


Fig.18 : ENLARGEMENT OF CALVES, QUADRICEPS, DELTOIDS AND FOREARMS.
EQUINUS DEFORMITY OF FEET.

CASE NO. 15. BORN: 1.3.47

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 5 months; Sat up: 8 months; Stood up: 11 months; Walked: 12 months.

The mother did not observe anything unusual in his mode of walking and he was able to perform all activities. Fairly stable on his feet. At the age of 3 he was reluctant to walk and stopped walking 3 months later. He was fostered out at an early age.

PAST ILLNESSES: Measles (7) did not set him back.

FAMILY HISTORY: Half brother affected (Case 14).

COURSE: Over a period of two years there was a marked deterioration in his muscle power and a slight increase in his scoliosis. There was also a progression of the muscle wasting.

Muscle Biopsy: Typical changes of advanced muscular dystrophy.

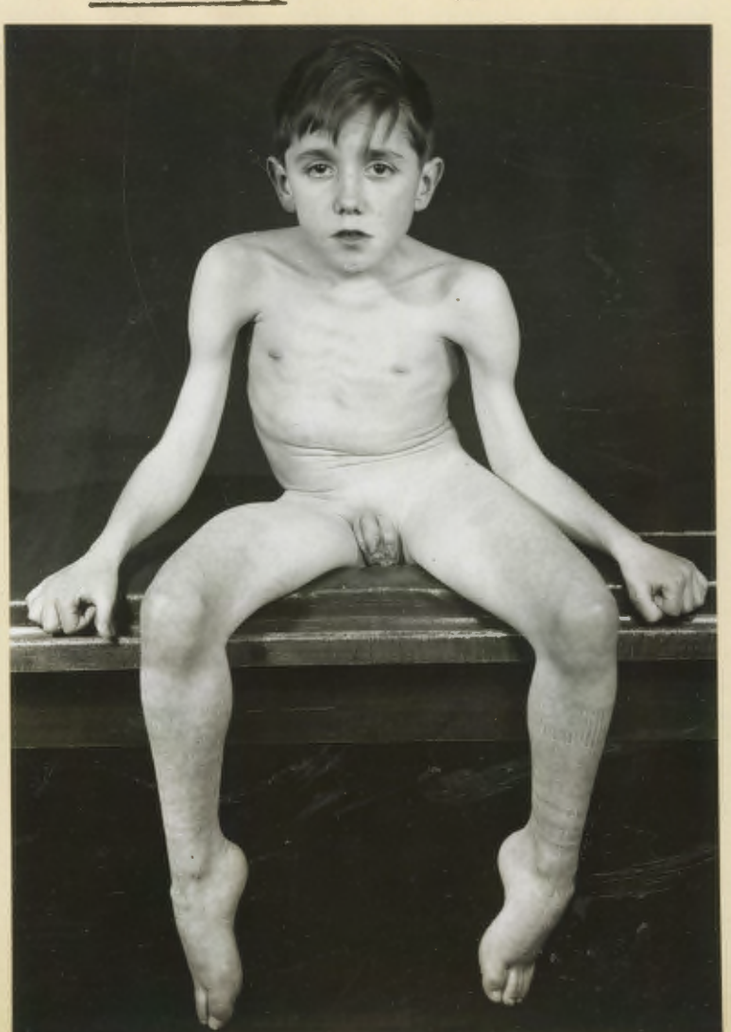


Fig. 19.
PROMINENCE OF DELTOID AND CALVES.
WASTING OF UPPER ARM.
EQUINUS DEFORMITY.

CASE NO. 16. BORN: 8.9.43

HISTORY: Foetal movements reduced, otherwise pregnancy, labour and neonatal period normal.

Milestones: Sat up: 10 months; Stood: 12 months; Walked: 12 months.

Although his gait seemed normally initially, and he was able to negotiate steps, he tended to trip a lot and was unable to run. He leaned forward when walking. He was able to get up after falling in a normal way. At the age of 3 attended Casualty Department for a cut lip and was told that his gait was abnormal, and diagnosis of muscular dystrophy was made. At that stage he was walking with a marked waddle and a "straight back" and his calves were prominent. His walking gradually deteriorated, and he fell more frequently. From the age of 4 he climbed stairs on all fours and he got up from the ground in a typical dystrophic way. Could not be lifted up by the axillae which were "floppy."

From the age of 5 he walked on his toes. No complaint of pain in muscles, but tired very readily. There was a gradual progression of his weakness until he finally went off his feet at the age of 11. No weakness of arms noted. Sphincter control normal. Tendency to constipation. Mental development normal.

PAST ILLNESSES: Measles, Rubella and Chicken-pox did not set him back.

COURSE: Over a period of 3 years there was slight deterioration in the power of most muscle groups. There was a progressive atrophy of various muscles and the circumference of the calves declined by 2 inches. He also lost weight.

CASE NO. 17. BORN: 4.9.46

HISTORY: Foetal movements reduced. Otherwise pregnancy, labour and neonatal period normal.

Milestones: Sat up and crawled: 9 months; Stood: 13 months; Walked: 15 months.

Up to age of 3 his gait was normal and he was stable on his feet. He was never able to run and had difficulty climbing stairs. From the age of 3 he walked with "his stomach prominent, his back arched and his shoulders held well back."

No change until 5 when he started school. Began to fall frequently and got up in typical dystrophic manner. Diagnosis made at 5. Weakness of arms noted at 6. Slow progression of weakness. Off his feet at 8 during a period at a Convalescent Home where he was apparently confined to bed. Pseudohypertrophy was not noted at any time and there was no complaint of pain.

Intelligence below average.

PAST ILLNESSES: Measles (6 months); Chicken-pox, Rubella (6); did not set him back.

COURSE: Slight deterioration over period of a year.

CASE NO. 18. BORN: 11.7.44

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 9 months; Sat up and crawled: 12 months; Stood: 18 months; and Walked: 22 months.

His mother was concerned at the delay in his milestones and his apparent sluggishness as an infant. His gait was abnormal from the beginning. He walked on his toes on a wide base with a marked waddle and the back arched. He seemed reluctant to walk and cried when encouraged to do so. He fell frequently and got up in the characteristic dystrophic manner. After the age of 4 he was no longer able to get up from the ground.

He was unable to run and was only able to get up steps by crawling. He could not step onto a pavement or bus unaided. His calf muscles became very prominent at the age of 4 and were very firm on palpation. His neck muscles also seemed unduly large. Muscular dystrophy diagnosed at age of 4.

At the age of 5 he had an operation for lengthening of the tendo Achilles. It took him a long time to regain the ability to walk after the operation, but he appeared more stable on the flat of his feet.

The weakness of his legs gradually deteriorated until he was unable to walk at the age of 8. Weakness of the arms was first noted at the age of 11 when he was unable to abduct the shoulders. Contractures of the knees developed at the age of 11. Weakness of the neck and back noted at the age of 13.

COURSE: Slight deterioration over period of a year.

CASE NO. 19. BORN: 1.3.46

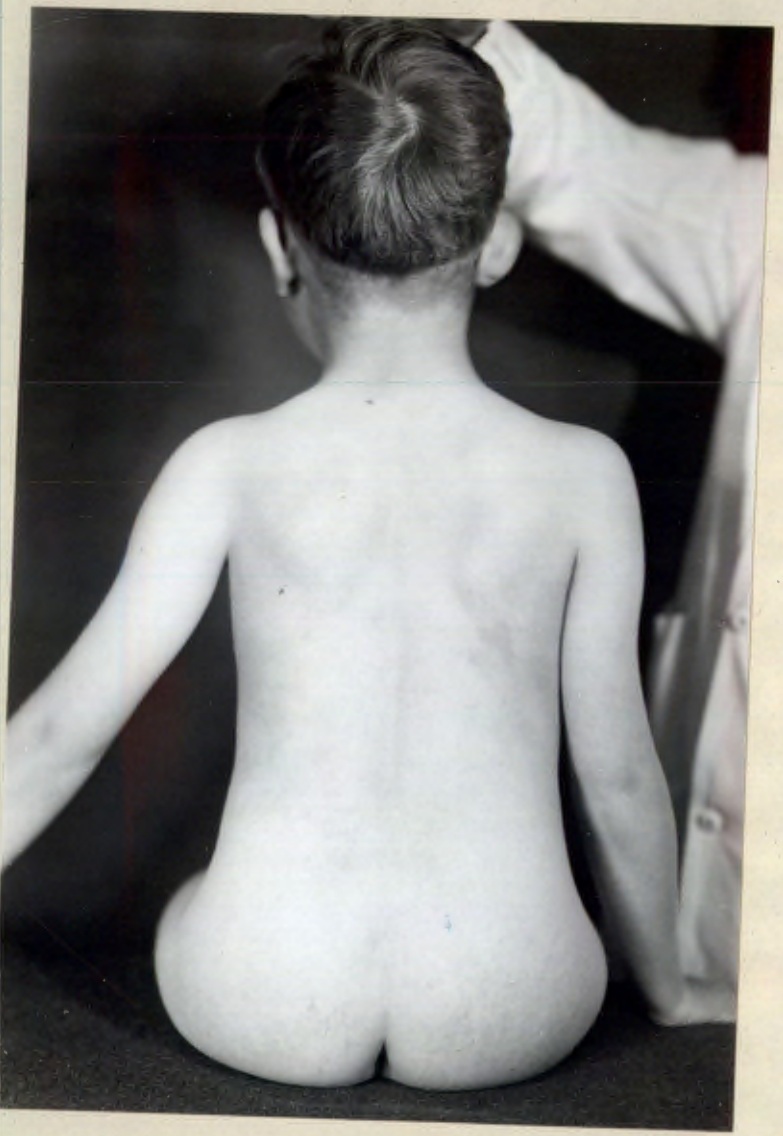
HISTORY: Pregnancy, labour and neonatal period normal. Milestones: Sat up: 9 months; Stood up: 2 years; Walked: 3 years. Parents were concerned at delay in Milestones. His gait was abnormal from the beginning. He walked on his toes with a marked waddle, lumbar lordosis. He fell frequently and got up in the typical dystrophic manner.

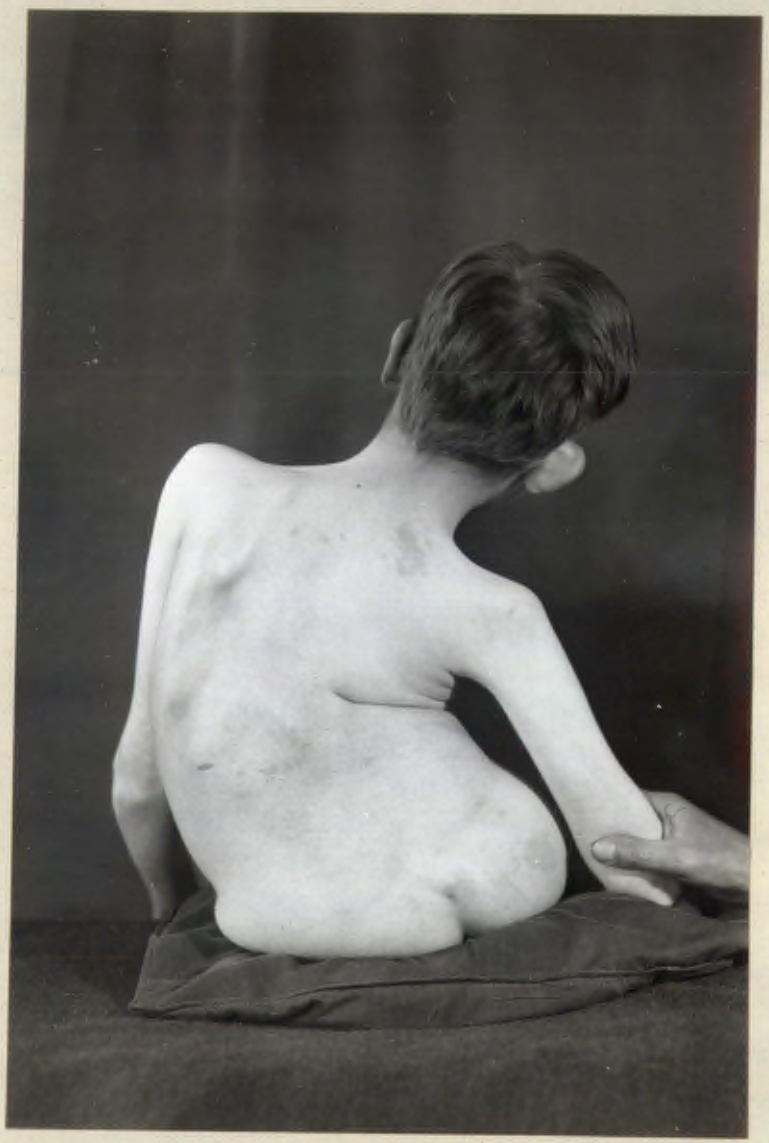
He was able to ascend steps by supporting a hand on his thigh. He could not run. Diagnosis at age of 3.

Weakness of the arms and neck was noted at about 5. His intelligence was normal. His weakness progressed steadily. After the age of 6 he was unable to get up from the ground and he went off his feet at the age of 7. Prior to that he was only able to walk about 100 yards. The calves were prominent from early infancy and were firm on palpation. He occasionally complained of pain in the legs.

PAST ILLNESSES: Gastro-enteritis (1), Measles (2), Whooping Cough (5), Chicken-pox (6) did not affect his muscle power.

COURSE: This child was an inpatient in 1954 but was transferred to a residential school at the parents' request. The spinal jacket was discarded. When reassessed in 1958 there had been a severe deterioration in his condition with generalised wasting and marked scoliosis. There was a slight progression of weakness in the next 6 months. He died of pneumonia in November, 1958. No autopsy.





Figs. 20 - 21 PROGRESSION OF SCOLIOSIS IN 4 YEARS.

CASE NO. 20. BORN: 31.3.45

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 9 months; Stood: 12 months; Walked: 2 years. Frequent falls from the beginning. Left foot inverted and tended to trip him. Difficulty in holding him by armpits. He was never able to get up from a sitting or lying position without support. At the age of 5 his calves were very prominent. Weakness of the arms and hands was first noted at the age of 6 and has been slowly progressive. From the age of 6 he began to fall more frequently. At the age of 7 he had an operation on his left foot for pes cavus. Callipers and boots were fitted. He was still able to stand and walk with sticks for a short time, but went off his feet shortly after. The calves gradually became soft and flabby after going off his feet. There was a progressive gain in weight after he became chair-bound.

PAST ILLNESSES: Whooping Cough (2½) set him back considerably.

COURSE: Gradual progression of weakness and wasting over period of two years.

Electromyography: Denervation pattern.

Muscle Biopsy: Characteristic changes of muscular dystrophy.

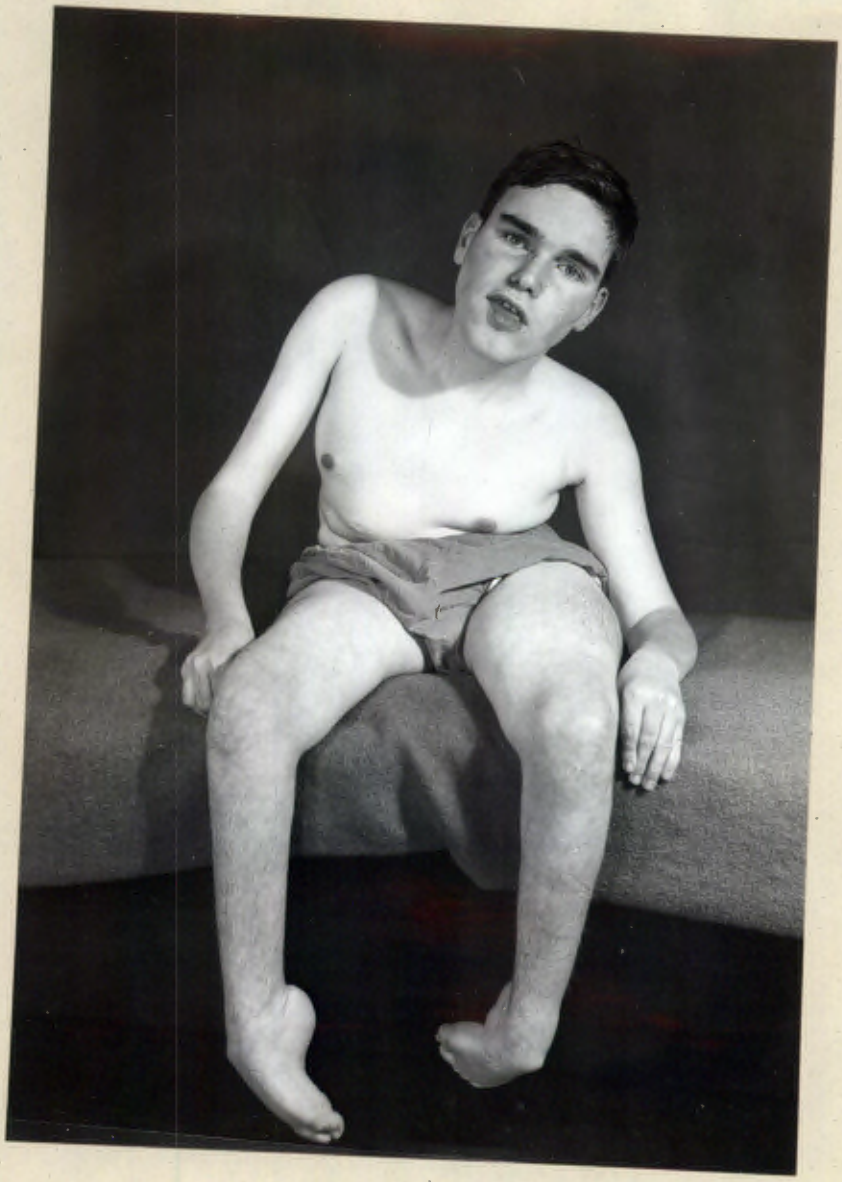


Fig. 22. NOTE EXTREME EQUINO-VARUS DEFORMITY; WIDELY SPACED TEETH; LARGE TONGUE.

CASE NO. 21 BORN: 1952

HISTORY : This child was brought to outpatients by his grandmother who suspected he might be suffering from muscular dystrophy, which had affected various other members of the family. Apart from the slight awkwardness of his gait, and difficulty in running and getting up steps no abnormality had been observed. The mile stones had apparently been normal, but no details were available.

EXAMINATION : Active child. Intelligence seems normal.

Deformities: No skeletal deformities. Contractures - slight shortening of the right tendo achilles, with limitation of extension at 90°. Walks with wadling gait, slight lordosis and heels slightly raised. Gets up from sitting to standing posture by supporting hand on knee. Gets up from floor in typical dystrophic manner. Difficulty in climbing steps. Pseudohypertrophy present in both calves and in both vastus lateralis muscles.

Power: There is slight weakness present of the trunk muscles and also muscles of the pelvic girdle.

Reflexes: All present. The ankle jerk, tibial taps and plantar taps are brisk, the others within normal limits.

Other systems normal.

A definite diagnosis of progressive muscular dystrophy was made.

CASE NO. 22. BORN: 15.2.50

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 9 months; Stood up: 20 months;

Walked: 4 years.

A few days after second inoculation for diphtheria at 10 months, the child became ill, limp and lifeless. Over a few weeks his condition gradually improved, but the mother noticed incurving of left foot. Seen at a hospital at the age of 2 when it was noted left ankle was smaller than right and there appeared to be loss of tone. Given intensive physiotherapy and gradually improved. (? attack of poliomyelitis). His mental development was also retarded and he was late in talking.

At the age of 4 his gait was slow, but appeared normal in character. There was no tendency to fall, no limp, and the left foot was normal in function. At the age of 5, after starting school, he began to fall frequently for no apparent reason - "legs simply gave way under him." At that stage he got up in the typical dystrophic manner after falling. The mother also noted difficulty in climbing stairs. Unable to negotiate a high pavement or get onto a bus. Unable to run normally. Prominence of calf muscles noted at age of 7. Diagnosis made at that time. He occasionally complained of pain in the calves, especially during cold weather. Weakness of arms noted since age of 8. Intellectual development markedly retarded. Unable to read or write, but able to copy things.

PAST ILLNESSES: Measles in infancy. Chicken-pox (2 months). Respiratory infection (March, 1959) did not set him back.

COURSE: When first seen at age of 9 he had a typical waddling gait and walked on his toes. There was no evidence to suggest previous poliomyelitis.

CASE NO. 22 (contd.)

Over a period of 18 months there was a marked decline in his muscle power and he could only walk short distances. He was no longer able to get up from the ground.

Muscle Biopsy: Typical changes of muscular dystrophy.

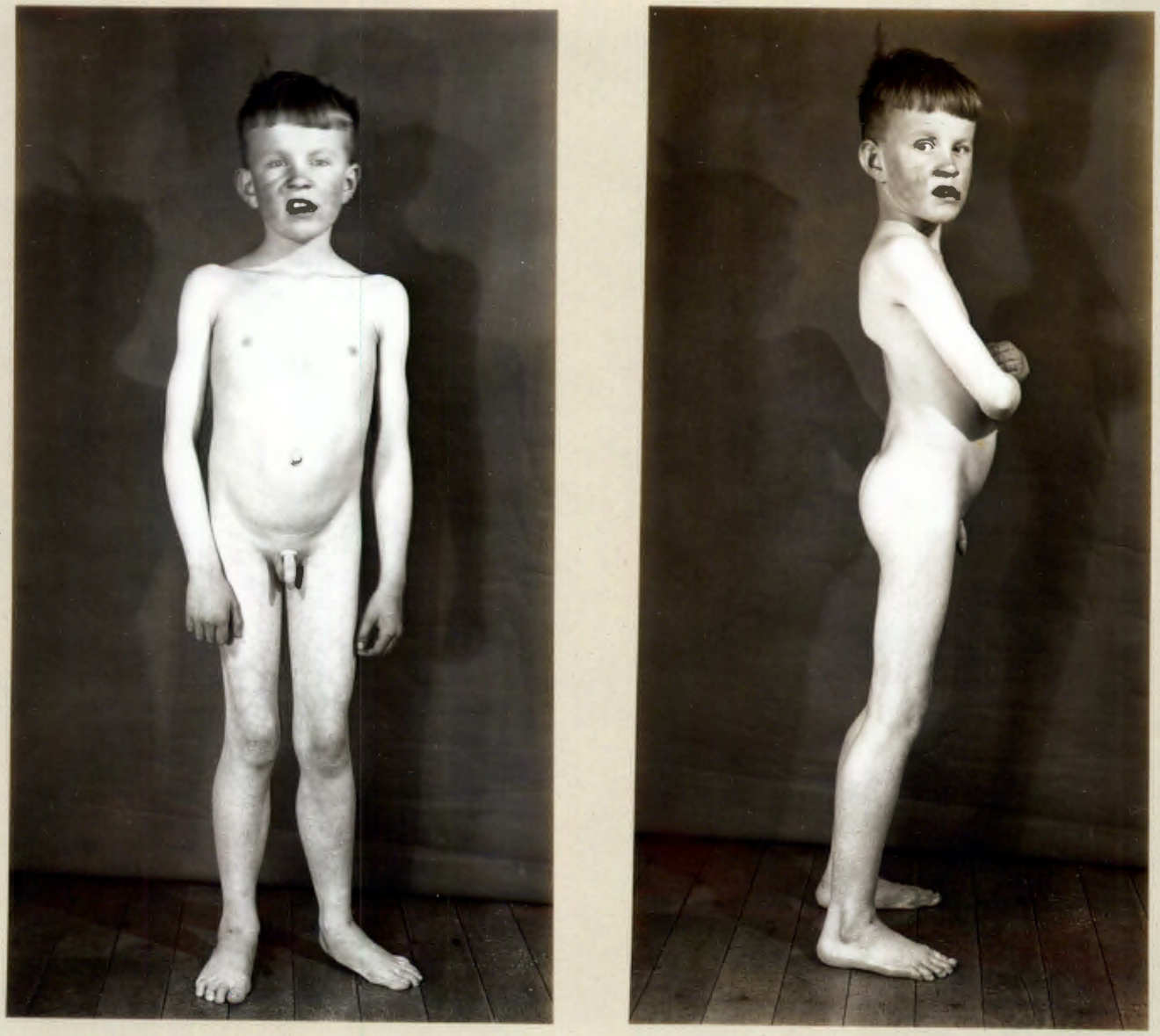


Fig. 23 - 24. PROMINENCE OF CALVES. LOCALIZED WASTING OF ARMS. LUMBAR LORDOSIS.

CASE NO. 23 BORN: 21.11.43

HISTORY: Illegitimate child. Adopted at the age of 6 months. The pregnancy, labour and neonatal period are said to have been normal.

Milestones: Sat up: 7 months; Stood up: 12 months; Walked: 14 months.

No abnormality was noted till the age of 3. He then began to walk on his toes and to fall frequently. After falling he got up in the typical dystrophic manner. He had difficulty in climbing up stairs and was unable to run. There was striking enlargement of his calves. He started school at the age of 5 and was found to be mentally retarded. A diagnosis of muscular dystrophy was made at that stage.

His weakness progressed very slowly. At the age of 10 he was still able to walk the half mile to school without tiring. At the age of 13 he had a McEwens osteotomy on the right femur and elongation of the right tendo achilles for contractures of the hamstrings and calf muscle. After being immobilised in plaster for 2 months he gradually became mobile again. He appeared to be more stable on his feet. There was no history of pain in his muscles. No weakness of the arms was observed. Sphincter control, chewing and swallowing were normal. From childhood he was prone to temper tantrums and could not tolerate being teased.

PAST ILLNESSES: Measles (4), Whooping Cough (5), Chicken-pox (7) did not influence his illness.

COURSE: When first admitted at the age of 13½ he was still able to walk. There was marked weakness of the pelvic girdle muscles and to a lesser extent of the shoulder girdle. The calves were enlarged. The quadriceps and upper arms were wasted.

CASE NO. 23 (contd.)

A month later he sustained an oblique fracture of his right femur. This united well. After 3 months immobilisation he had difficulty in regaining the ability to walk. During this period he was quite a behaviour problem and had to be transferred to a psychiatric unit for a period of 3 months. On re-admission intensive physiotherapy and encouragement led to gradual improvement in his walking.

His walking appeared to improve and a year later he was able to get about for long distances without a stick. Objective testing revealed no improvement or deterioration in the muscle power. A 2" raise on his right boot to compensate for shortening of his femur (from the fracture) helped his walking further. His temperament vacillated between co-operation and complete obstinancy. Six months later he was still walking well. His gait had the typical waddle and was associated with a lumbar lordosis. He was unable to get up from the ground in spite of an extreme effort. Muscle power of individual groups showed no change on testing.

Muscle Biopsy: Early changes of muscular dystrophy.

CASE NO. 24. BORN: 29.4.48

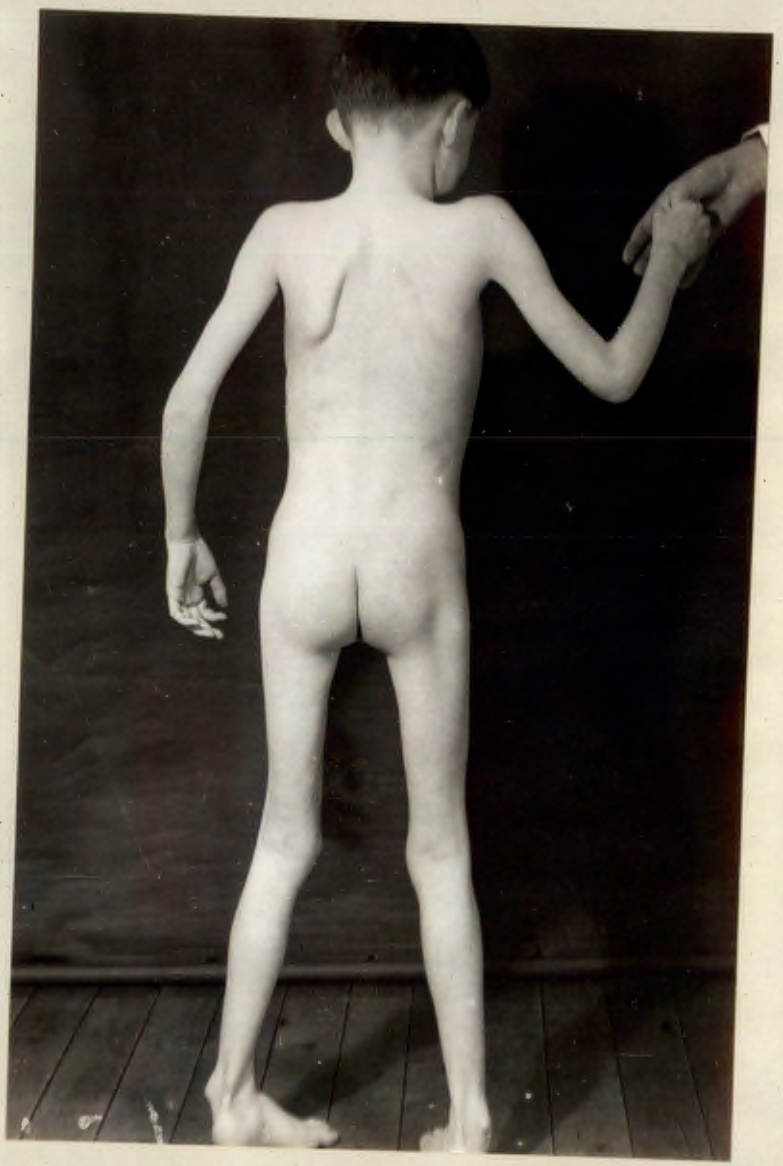
HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 4 months; Sat up: 6 months; Stood: 13 months; Walked: 2 years.

Gait was waddling from beginning and thought to be due to flat feet. At the age of 2½ mother suspected some abnormality because of frequent falls. Shoulders appeared floppy. Mother unable to lift him by axilla. He tired readily when walking. (Maximum distance 200 yeards.) At the age of 3 diagnosis of flat feet and knock knees made. Diagnosis of muscular dystrophy at age of 4. Never able to run or climb steps. After falling, climbed up himself in typical dystrophic manner. Weakness was slowly progressive. Weakness of arms noted at 5. No pain in muscles. No evidence of pseudohypertrophy. Mental development seemed retarded.

PAST ILLNESSES: Dislocation of left shoulder (3).

COURSE: When first examined at the age of 10 he was still walking: typical waddling gait on his toes with marked varus deformity of both feet and lumbar lordosis. Unable to get up. Had to be placed on feet in order to walk. There were no contractures apart from limitation of dorsi-flexion of ankles. His weakness gradually progressed. 6 months later, following a chest cold for which he was kept in bed for 6 days, he was unable to walk any longer. In the course of the next year he developed progressive contractures of the knees and the elbows.



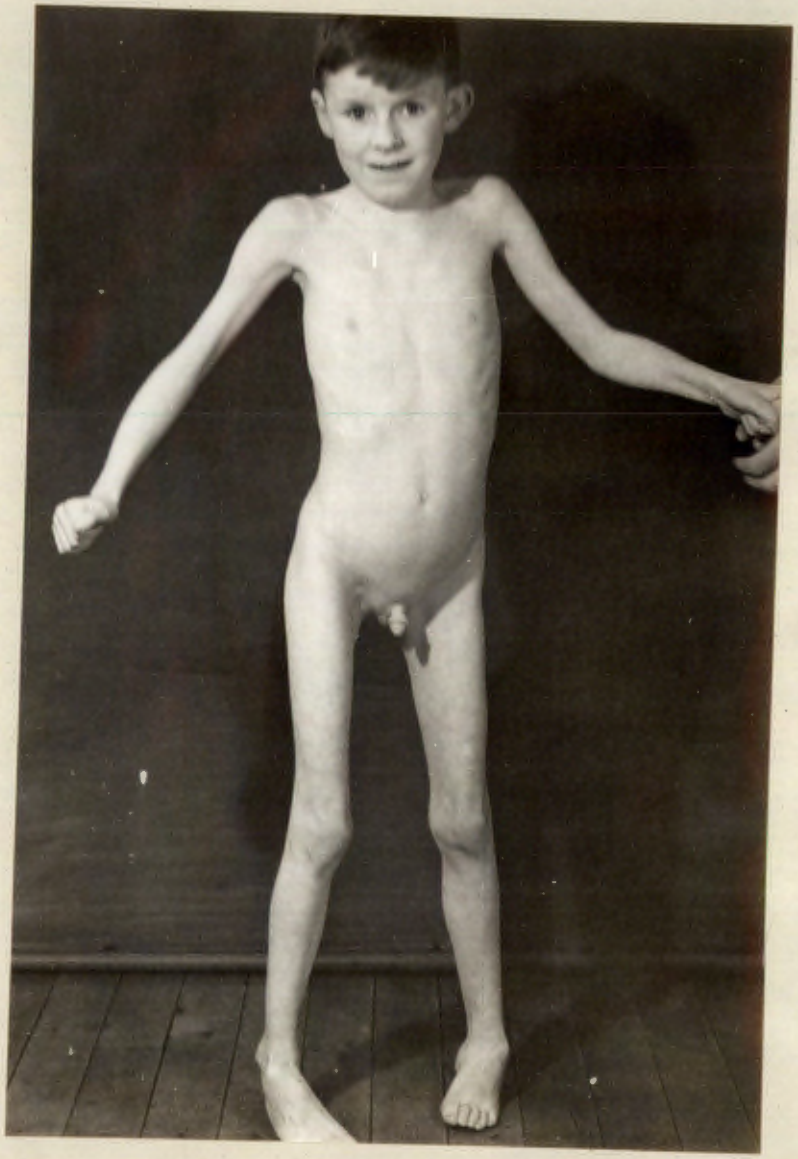


Fig. 25-26. GENERALISED WASTNG.EQUINOVARUS DEFORMITY.

CASE NO. 25 BORN: 9.10.46

HISTORY: Pregnancy and labour apparently normal, (no history available). Mother died when he was 3. In Nursery since age of 1. Walked at 2. Tended to be unstable on his feet from the beginning. No swelling of muscles noted. Always thin. Diagnosis of muscular dystrophy at 7. According to sister, walked with marked lordosis. Fell frequently. Unable to get up. Only got as far as kneeling position. Stopped walking at age of about 9. Developed contractures of knees following this. Elongation of hamstrings and division of fascia latta on right side was performed which partially corrected leg deformities but he was unable to get back on his feet again. Associated mental retardation. (Sisters have low normal intelligence).

PAST ILLNESSES: Measles, Chicken-pox, Mumps, Rubella, Pneumonia and Gastro-enteritis did not apparently affect muscular condition.

COURSE: Over a period of 2 years there was not much deterioration in his muscle power, but his scoliosis tended to be progressive.

CASE NO 25.

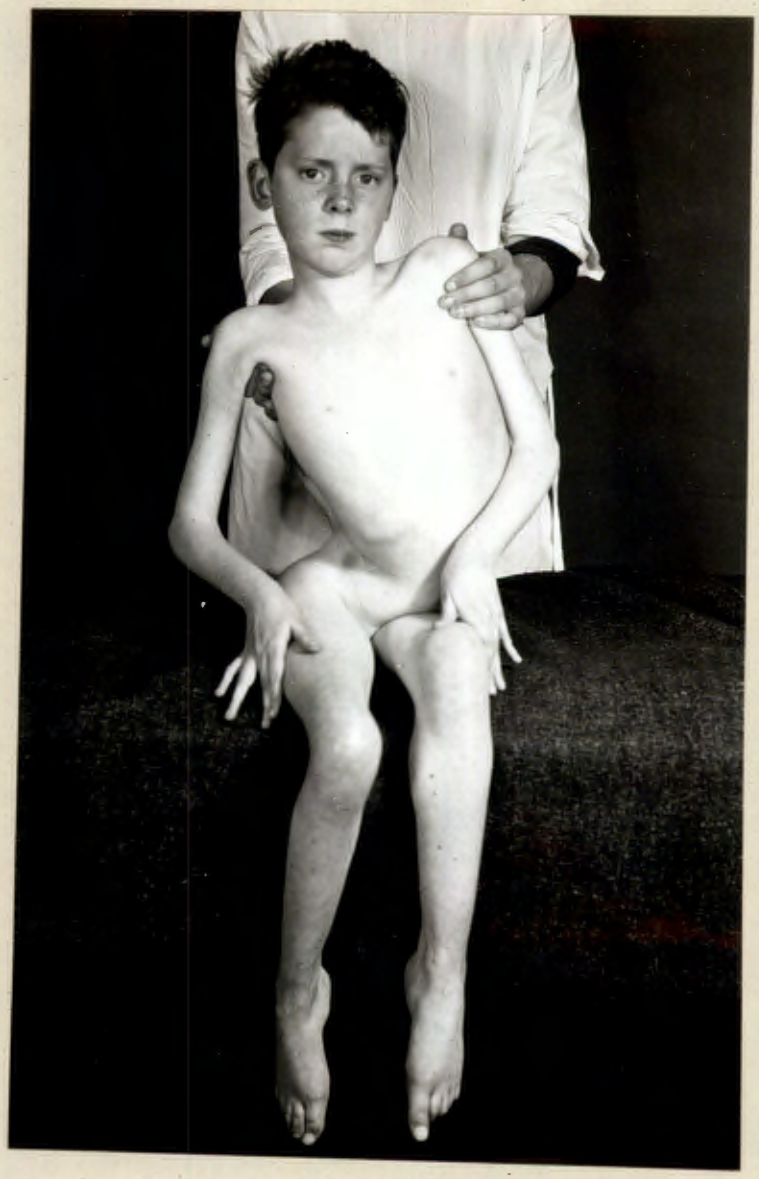


Fig. 27. GENERALISED WASTING AND SCOLIOSIS.

CASE NO. 26 BORN: 30.11.46

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 5 months; Sat up: 9 months; Stood: 2 years; Walked: 2 years.

His gait was waddling from the beginning and he fell frequently. He seemed to get up normally after falling. He was unable to run or to climb stairs or negotiate a kerb. He crawled up and down stairs. From the age of 4 he walked on his toes with an associated lumbar lordosis. After starting school he got up from the ground in the characteristic dystrophic manner. Weakness of the arms was also noted and he had difficulty in holding a pencil firmly or doing up his buttons. A diagnosis made at 6 after a muscle biopsy. Enlargement of the calves was striking at that time. At 6½ he fell and fractured his right tibia. After 2 months in plaster his walking deteriorated considerably and he went off his feet 6 months later. After going off his feet calves became thinner. The weakness of his arms progressed gradually. After the age of 9 no longer able to get up from the supine. His mental development was markedly retarded. He was referred to a mental home for a few months prior to his admission.

PAST ILLNESSES: Bronchopneumonia (6 weeks), Measles (5) and Chicken-pox (6) did not affect his muscle power. Perforated appendix (12).

COURSE: There was minimal deterioration over a period of a year.

Muscle Biopsy: Characteristic of advanced muscular dystrophy.

CASE NO. 27 BORN: 17.6.50

HISTORY: Pregnancy, labour and neonatal period normal. (Increased foetal movements).

Milestones: Held head up: 4 months; Sat up: 7 months; Stood: 15 months; Walked: 17 months.

Seemed to walk quite normally initially but had difficulty in getting up steps. Able to run but fell when doing so. Got up after falling in typical dystrophic manner. Initially he walked on his flat feet, but from the age of 6 walked on his toes. There was progressively more difficulty with running and he fell more frequently. Had greater difficulty getting up. Did not complain of pain. Calves were prominent but not as marked as his elder brother (Case 26). Weakness of the arms was first noted at the age of 6. Tongue very large and "seems to get in his way". Able to feed himself. Backward at school but more intelligent than elder brother.

PAST ILLNESSES: Measles (3), Chicken-pox (3) did not set him back. Fractured clavicle (9).

COURSE: When first examined at the age of 9 he was still able to walk short distances. His gait was typical. He was just able to get up from the ground (in the characteristic dystrophic manner.)

There was a gradual decline in his power until he lost the ability to walk 6 months later. During the following year there was some deterioration in the power of the pelvic girdle and lower limb muscles.

Muscle Biopsy: Characteristic changes of early dystrophy.

CASE NO. 28 BORN: 11.11.51

HISTORY: Pregnancy, labour and neonatal period normal.

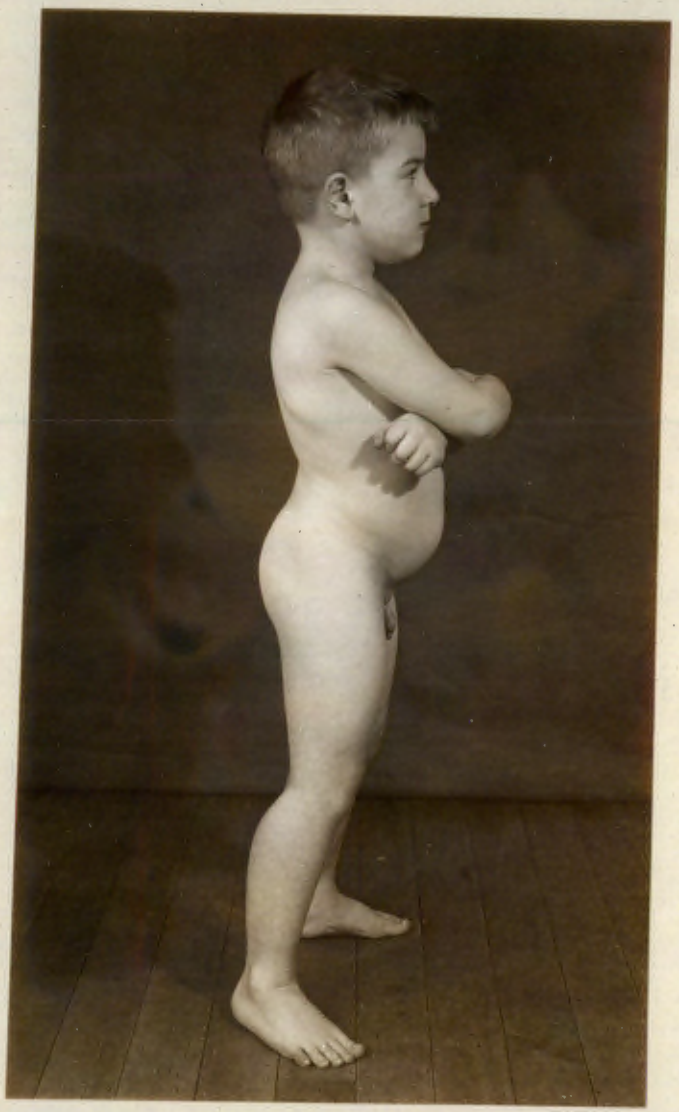
Milestones: Held head up: 4 months; Sat up: 8 months; Stood: 18 months; Walked 2 years.

From the beginning his gait was abnormal. There was a typical waddle and lordosis and he walked on his toes. He was never able to get up steps or a kerb. He tended to fall frequently and got up in a typical dystrophic manner. Marked swelling of calves was noted at that stage. The weakness gradually progressed and he fell more frequently. Occasionally complained of pain in the feet. No apparent weakness of arms. Tendency to gain weight. Has a large tongue and dribbles a lot. Mental development definitely retarded. "Always seems tired and without energy."

PAST ILLNESSES: Chicken-pox (2), Measles (2) did not set him back.

COURSE: In December, 1958, he fell and sustained a fracture of the shaft of the left femur. After 2 months immobilization in a Thomas's Splint, during which time he had intensive physiotherapy, he gradually regained the ability to walk and was back to his previous activity after 3 months. On muscle charting there was a slight deterioration of the power of both legs after the fracture, which was more marked on the left.

Muscle Biopsy (Deltoid): Characteristic changes of early dystrophy.



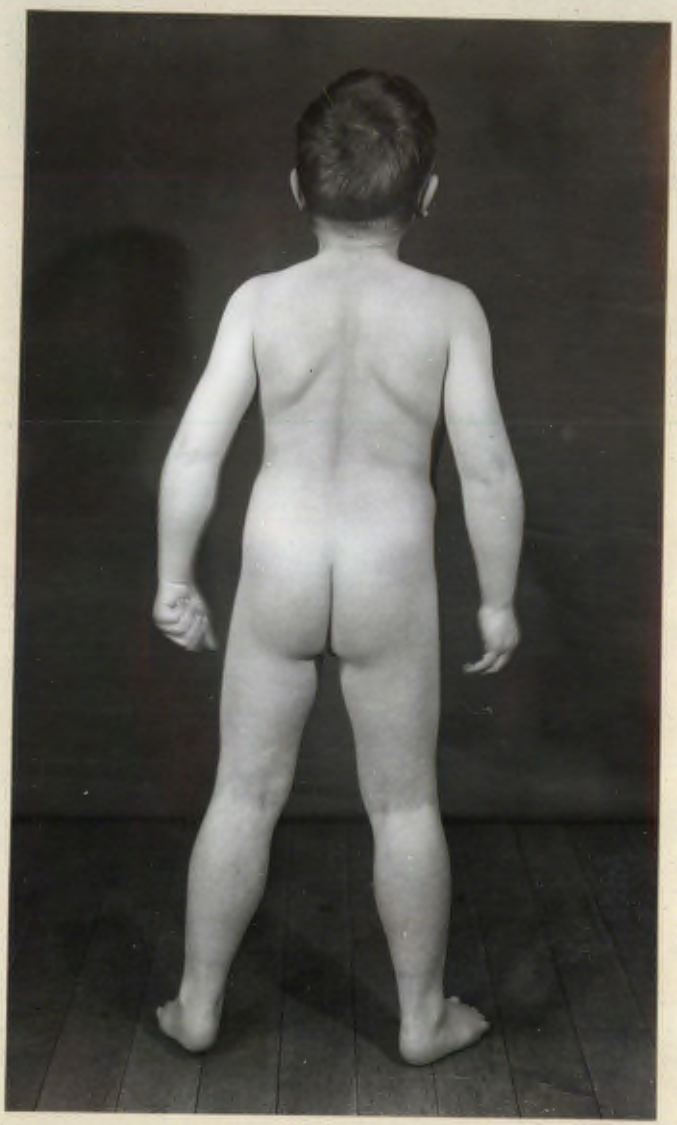


Fig. 28 - 29. PROMINENCE OF MUSCLES. RAISED HEELS. LORDOSIS.

CASE NO. 29 BORN: 17.12.41

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 1 year; Stood: 2 years; Walked: 2 years. Tended to walk on tips of toes from beginning and supported his hands on the backs of his hips. Waddling gait. Tended to fall frequently. Able to rise on own after falling down but needed a support. Never able to climb stairs. Gradual progression of weakness. At age of 5, taken to school in wheel-chair, but walked ½ a mile home. Still walking on toes. Fracture of femur at age of 7. Off feet for 4 months. Abnormal gait after fracture had set. Took long time to get back to activity. Not quite as well as before. Falling more frequently. Occasional pain in thighs. Unable to walk again after appendicitis at age of 10 (in bed 3 weeks). Weakness of arms only noted at 14. Was able to manipulate a wheel-chair prior to that. Difficulty in getting hand to mouth for feeding from age of 16.

PAST ILLNESSES: Fractured femur (7). Appendicitis (10). Appendicectomy (13).

COURSE: Over the course of 2 years there was a progressive wasting of the muscles, a deterioration in the power of most muscle groups and an increase in the deformities. The following contractures developed:- Elbows 145°, Hips 140°, Knees 95°, Ankles - limitation of dorsi-flexion at 90°.
A positive ankle jerk was elicited on a number of occasions.

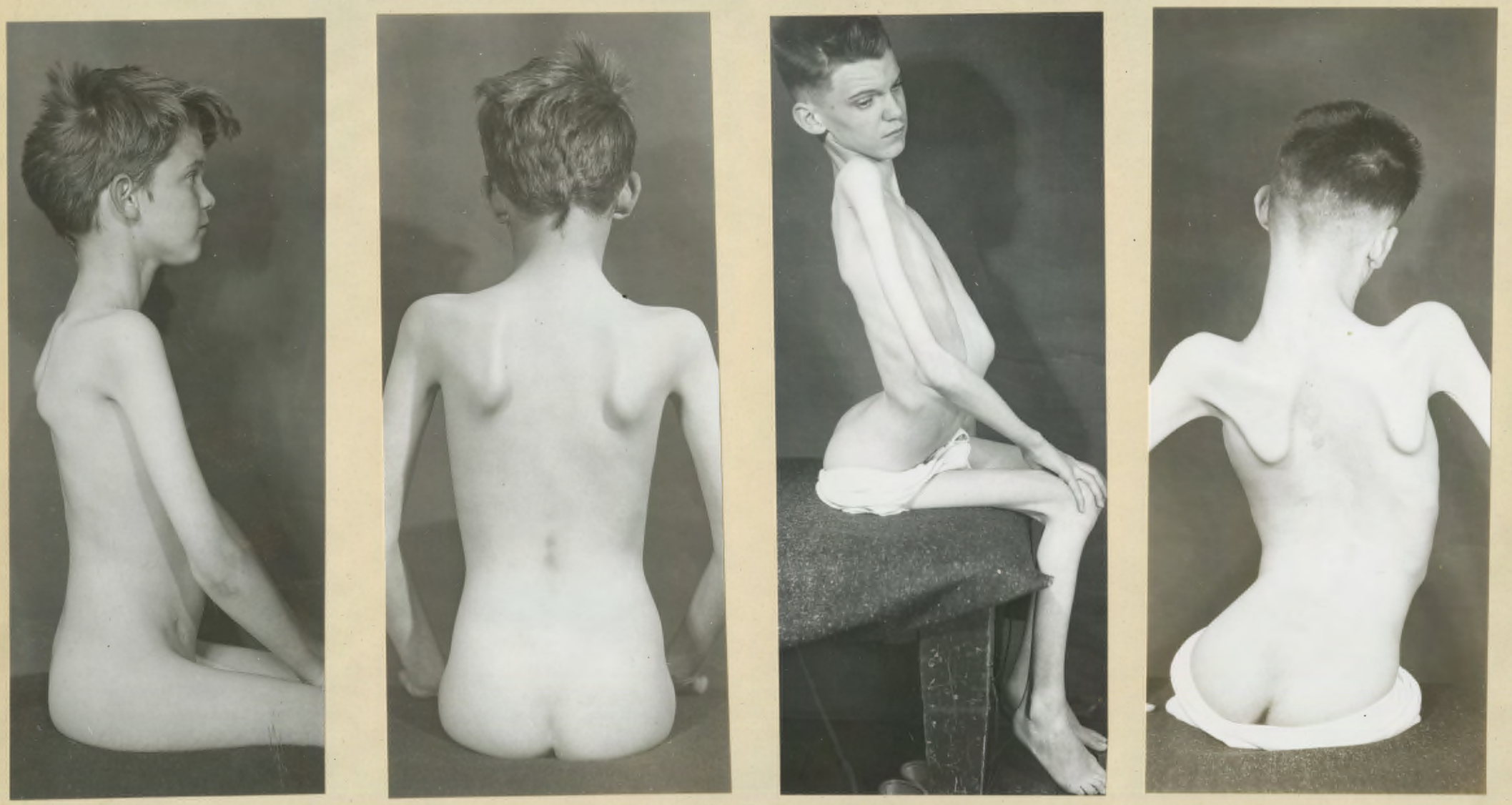


Fig. 3o - 33 PROGRESSION OF THE DISEASE IN THREE YEARS.

CASE NO. 30 BORN: 17.12.41

HISTORY: Pregnancy, labour and neonatal period normal. (Foetal movements vigorous).

Milestones: Held head up: 4 months; Satu up: 6 months; Walked: 18 months.

His gait seemed normal and he was able to run and climb stairs. No abnormality was noted until the age of 5 when he began to fall frequently. He had difficulty getting up from the ground which he did in the characteristic dystrophic manner. At the age of 7 his calves became more prominent and he began to walk on his toes with an associated lumbar lordosis. Occasional pain in calves. At the age of 8 elongation of the tendo Achilles bilaterally was carried out to correct the equinus deformity. After 6 weeks immobilisation he never regained the ability to walk. He was only able to get about with the aid of sticks for a few months post-operatively. Weakness of the arms was first noted at the age of 10. There was a gradual decline in his muscle power.

PAST ILLNESSES: Greenstick fracture right tibia (8 months). Fractured jaw (10). Fracture left femur (12). Chicken-pox and Measles (4).

COURSE: There was a generalised slight deterioration in the power of his limb muscles over the period of one year.

CASE NO. 31 BORN: 15.5.47

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 2 months; Sat up: 5 months; Crawled: 8 months; Stood: 10 months; Walked: 18 months.

At the age of 2 his mother observed that, when he bent down to pick something up he had difficulty in getting erect and put his hands on his knees. He had a waddling gait from that time. He fell frequently, his legs just seemed to give way under him. After falling he had difficulty in getting up, which he did in a typical dystrophic manner. He tended to walk on his toes. His back was "straight" and abdomen protuberant. He was never able to run or climb steps. Calf muscles looked very prominent and felt hard to the touch. They increased in size as he got older. There was no complaint of pain. Weakness of the grip developed at the age of $2\frac{1}{2}$ or 3, but he was able to lift his arms and able to carry a chair. Diagnosis made at 3.

He tended to tire readily. Started at School for Physically Handicapped at the age of 5. Became progressively weaker until he went off his feet at the age of $9\frac{1}{2}$ (No precipitating factor). Face and general body became fatter and larger after that. Weakness in neck muscles observed after becoming chair-bound. Intelligence normal.

PAST ILLNESSES: Whooping Cough (2), Measles (5), Chicken-pox (5), Mumps (7) did not affect his weakness.

COURSE: There was no obvious deterioration in his condition over the period of 18 months.

CASE NO: 32. BORN: 16.11.42

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 8 months; Stood at: 1 year;

Walked: 2 years.

Fractured skull at the age of 3. Speech still retarded at that stage. Psychiatrist thought him mentally retarded. His walking was unstable after that. From the age of 5 he walked with a definite waddle and on his toes. He fell frequently. He was unable to run and could not ascend stairs. His calves and arms were prominent. His weakness progressed slowly. Weakness of the arms first noted at the age of 6. Diagnosis at 8. Following an appendicectomy at the age of 9, for which he was in bed for 2 weeks, his walking deteriorated markedly and he had great difficulty in standing and getting up from a sitting posture. He went off his feet shortly after. He was found at that time to be mentally retarded with an I.Q. of 54.

PAST ILLNESSES: Measles, Appendicitis, Fractured Skull.

FAMILY HISTORY: Positive.

COURSE: There was only slight deterioration of muscle power over a period of 3 years.

CASE NO: 33. BORN: 25.1.48

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 6 months; Stood: 12 months;

Walked: 18 months.

Mother first noticed "weakness" at about 3 years of age. Walking was slow and he tended to walk on toes. Unable to jump or run. Difficulty climbing stairs. At the age of 5 had marked difficulty in getting up from the floor which he did in a typical dystrophic manner. He fell frequently from the age of 4 or 5. There was no apparent enlargement of any muscles and the muscles of the legs tended to get gradually thinner. He occasionally complained of pain in the muscles and tended to tire readily. His weakness progressed gradually. Diagnosis at 7. At the age of 9 he sustained a fracture of the right femur necessitating immobilization in Thomas's splint for 2 months, after which he was no longer able to walk. No weakness of arms observed. Put on weight from time of going off his feet. Mental development thought to be normal.

FAMILY HISTORY: Positive.

COURSE: There was a slight deterioration over a period of 3 years.

CASE NO. 34. BORN: 13.10.46

HISTORY: Pregnancy normal but foetal movements less than with sibs. Normal labour. In the neonatal period he appeared to be "lazy and inactive."

Milestones: Sat up: 1 year; Stood: 1 year; Walked: 2 years.

The gait was abnormal from the beginning. He "waddled like a duck" and tended to fall frequently - initially backwards but subsequently into a cross-legged sitting position. When walking his abdomen was protuberant and he did not bring his heels to the ground. He was never able to run normally and had difficulty climbing stairs, which he managed by supporting a hand on the hip. After the age of 4 he got up from the floor in the typical dystrophic manner. His calf muscles became prominent. He sometimes complained of pain in his calves with walking and his mother noted that the calves then became hard and contracted "like tennis balls." When the pain occurred he seemed to go up on his toes. Although the parents suspected some abnormality when he started walking it was initially diagnosed as "flat feet" and it was not till the age of 6 that muscular dystrophy was diagnosed.

The weakness progressed steadily. Whenever he was nervous or excited his walking was worse and he fell more frequently. He went off his feet at the age of 10 following one week in bed with measles. He was still fairly mobile prior to that illness. Weakness of the arms was first noted at 10 years. No weakness of hands. In childhood he was thin with prominent calves. After going off his feet he became obese. His intelligence seemed normal but his progress at school was below average.

PAST ILLNESSES: Whooping Cough and Mumps (10) did not set him back; Measles (10) set him back considerably. Chicken-pox (10) after going off his feet.

COURSE: No apparent change over period of 1 year.

CASE NO. 35 BORN: 19.7.46

HISTORY: Pregnancy - vaginal bleeding at 3 months required admission to Hospital for 2 days. Otherwise normal. Labour normal. Neonatal period "lazy" baby.

Milestones: Held head up: 6 months; Sat up: 1 year; Stood up: 18 months; Walked: 2½ years.

At the age of 10 months the mother already suspected that he might have muscular weakness because her brother had suffered from muscular dystrophy. From the time he started walking his gait was abnormal. He walked with legs astride, abdomen prominent and back arched backwards, and wobbled from side to side. He was stable on his feet at that stage. Never able to run or climb stairs. He was unable to get up from the ground even in infancy. There was no prominence at that stage of any muscle groups. From the age of 3 walked on toes. Diagnosis of muscular dystrophy made then. Weakness gradually progressed. After starting school at 6, very unsteady and fell frequently. Tired readily while walking. Great difficulty in walking uphill. Did not complain of pain in muscles. Enlargement of calf muscles and deltoids as well as the back of the neck on both sides first noted at the age of 8. Muscles felt firm and hard. Weakness progressed steadily until the age of 9, when he fell and sprained his ankle. Strapped with elastoplast and after being confined to a chair for a week, unable to stand or walk again. After going off feet became generally obese, without change in appetite. Weakness of arms first noted at the age of 10. Unable to raise them. Intellectual development retarded. Did not make normal progress at school - only learned to read at age of 12.

PAST ILLNESSES: Measles, Chicken-pox and Whooping Cough (5) did not set him back.

CASE NO. 35 (contd.)

COURSE: There was not much deterioration in muscle power over the period of 18 months.

Muscle Biopsy: Characteristic changes of advanced dystrophy.

FAMILY HISTORY: Positive.

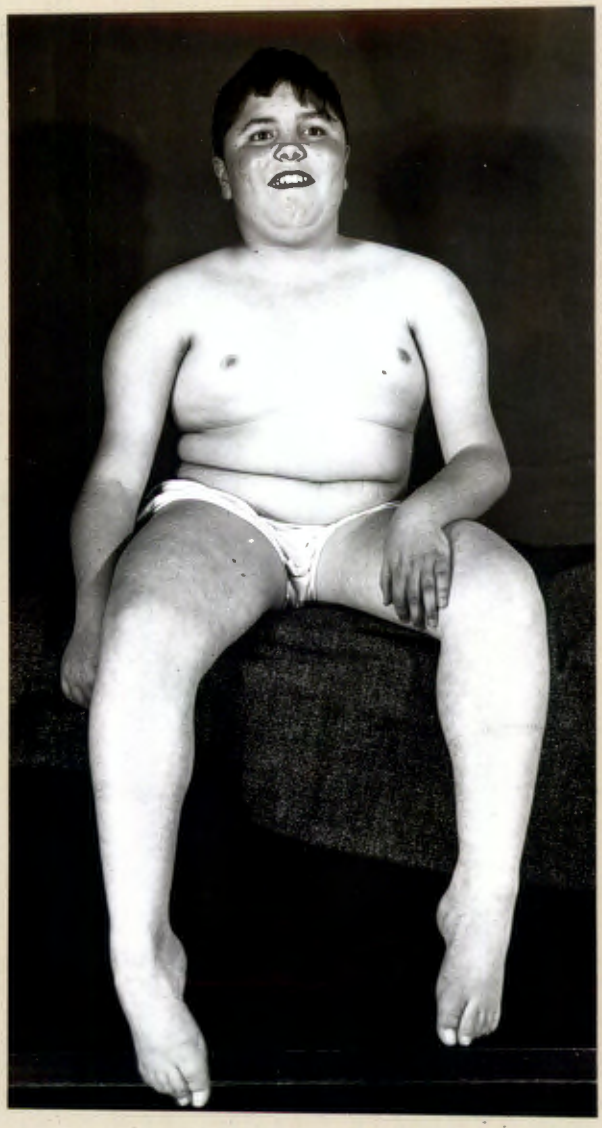


Fig. 34. : NOTE GENERALISED OBESITY; ENLARGEMENT OF DELTOIDS, WASTING OF ARMS.

CASE NO. 36. BORN: 16.4.57

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 9 months; Crawled: 13 months; Stood: 16 months; Walked: 2 years.

At about 3 noted that he tended to "plonk his feet down as if flat-footed." He was never able to run normally. Initially seemed to go up steps normally. Muscles normal in appearance. At 4 years the calves became "firm, fat and rounded" and a diagnosis of dystrophy was made.

At the age of 5 he had a definite waddling gait with lordosis of the spine. The calves seemed to be increasing in size and became very hard. Still walking on the flat of his feet. From the age of 5 he got up in the typical dystrophic manner. After starting school he tended to be knocked over more readily. From the age of 6 he walked on his toes and from that time was also unable to get up after falling. No pain in muscles. Tired readily and his limit came down to about 50 yards. Went off his feet at the age of 7½. "Suddenly he was unable to walk one morning." Marked increase in weight from 8. From the age of 10 weakness of the arms noted and also weakness of the neck. Mental development rather slow.

PAST ILLNESSES: Whooping cough (4) and Mumps (5) did not set him back. Measles (5) made him considerably weaker. Appendicectomy (8).

COURSE: No apparent change in 2 years.

CASE NO 36.

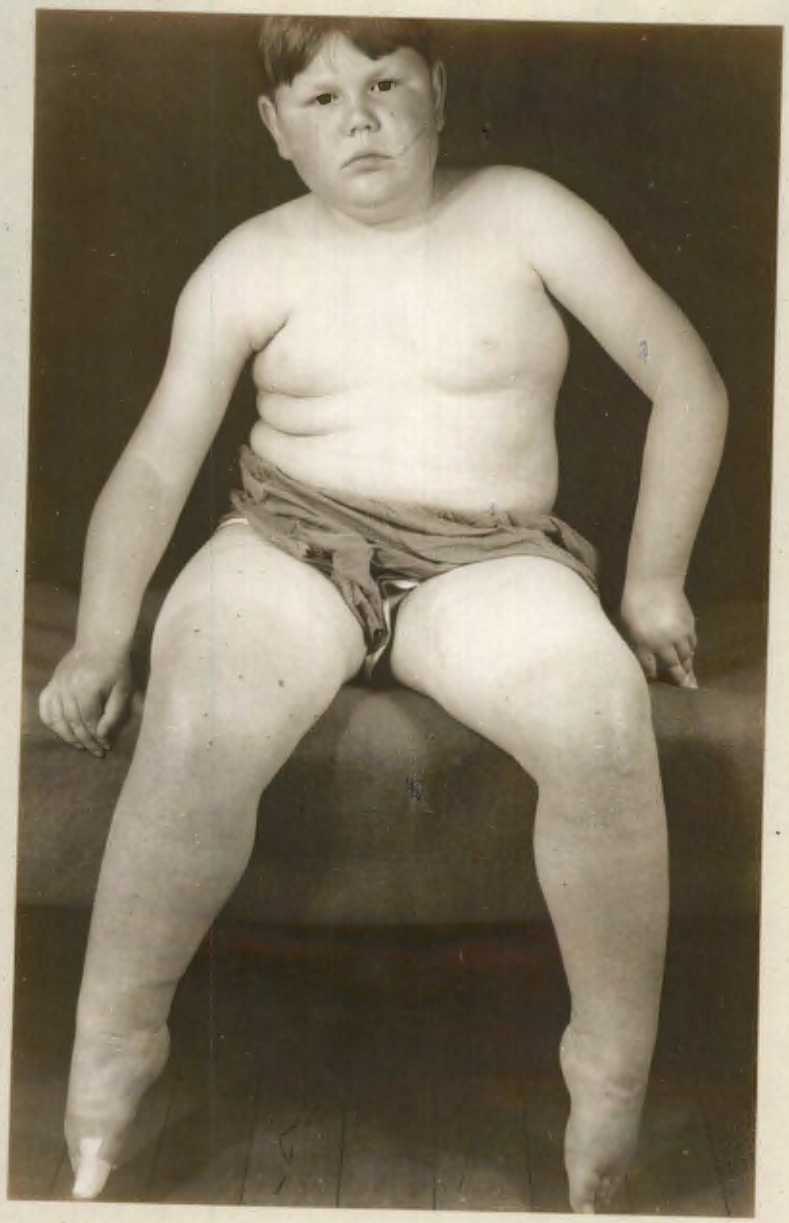


Fig. 35. GENERALISED OBESITY.

CASE NO. 37 BORN: 22.8.43

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 9 months; Stood: 20 months;

Walked: 2 years.

Walking was slow but gait normal. He tended to fall frequently and was unable to get up. ("no muscles in his arms"). Never able to climb stairs. Definite weakness of arms at 7. Walked reasonably well till 8. Had to be pushed to school in a pram, but walked home alone ($1\frac{1}{2}$ miles). After 8 walked on toes and waddled from side to side. Weakness progressively worse. More frequent falls. Stopped walking soon after 8. Continued to crawl for a period after that. No difficulty in swallowing. No swelling of muscles. No pain.

PAST ILLNESSES: Measles, Mumps, Rubella, Chicken-pox did not set him back.

COURSE: Prone to repeated bouts of upper respiratory infection. Slow progression of muscular weakness. Contractures also present in finger flexors and right thumb flexors with no apparent progression.

CASE NO 37.

Fig. 36 - 37. EQUINOVARUS DEFORMITY. HYPOTONIA OF HIPS.

CASE NO. 38

BORN: 21.9.47

HISTORY: Pregnancy, labour and neonatal periods normal.

Milestones: Moved his limbs but made no effort to hold his head up or to sit up. When lifted by the armpits he was flabby and slipped through. He sucked normally and had no difficulty with swallowing. He had normal sphincter control after the age of 2.

From about 1 year he shuffled along on his buttocks when put into a sitting posture. At 3 he learnt to ride a tricycle. His muscle weakness appeared to be stationary. At 5 years he was first admitted to hospital. He was unable to sit up from the supine position but could maintain a sitting posture when helped up. He had difficulty in abducting the arms. Power in the hands was relatively good. Bilateral elongation of the tendo Achilles was performed for his equinus deformity of the feet and a bilateral Souttar's operation for contractures at the hips. A celluloid spinal jacket and neck support were supplied. Post-operatively he was able to walk with a walking machine. His condition continued unchanged and he was able to walk short distances holding onto objects. At the age of 8 he managed to walk a distance of 10 yards unaided. He repeated this several times. The following day he was less proficient and was unable to repeat it after that.

The power in his arms and legs showed little change. He could still ride a tricycle and was able to feed himself with his elbows supported. No enlargement of any muscles was noted at any time. He was always slightly built and the muscles seemed to be wasted. His intelligence was normal.

PAST ILLNESSES: Prone to recurrent coughs and colds since infancy. Pneumonia on 3 occasions.

CASE NO. 38 (contd.)

COURSE: There was no obvious change in his condition over a period of 6 months. He was bright and cheerful and of normal intelligence. He died of pneumonia at another hospital in February, 1959. No autopsy was performed.

Electromyography: Typical myopathic pattern.

Serum aldolase: 5.4 units (normal).

COMMENT: This case, although atypical, has been included on the basis of the electromyographic pattern as a possible congenital form of the disease.

Fig. 38 : NOTE EXTREME GENERALISED WASTING; WEAKNESS OF NECK; ABSENCE OF DEFORMITIES IN FEET.

CASE NO. 39.

BORN: 9.2.42

HISTORY: During the second month of pregnancy mother had a mild cerebrovascular episode affecting the left side of her body; recovered within 3 days. Foetal movements were normal. Caesarian section at term. Neonatal period normal.

Milestones: Sitting up and standing were not delayed (age not remembered); walked: 1 year.

No abnormality was noted till the age of 4 when he had difficulty in climbing stairs. His gait became waddling. A diagnosis of 'neurasthenia' was suggested. His calves were prominent. The weakness in the legs gradually became worse. He began to fall and was unable to get up from the ground without assistance.

After the age of 6 the falls became more frequent. A diagnosis of muscular dystrophy was made at that stage. At the age of 8 he was confined to bed for 2 weeks with severe influenza. He developed contractures at the knees and was unable to walk again. Equino varus deformities of the feet developed after that.

Weakness of the arms was first noted at the age of 10, and by 11 he was unable to abduct or flex the arm at the shoulder and "had to advance his hand along a table by stepwise movements of the fingers and palm."

He gained weight after going off his feet and at one stage reached 10 stone. From the age of 14 he developed anorexia and his weight declined steadily and was only 6 stone on admission in 1956. Intelligence seemed normal but he made little progress with home tuition.

PAST ILLNESSES: Measles (1), Pertussis (1).

COURSE: When first examined (September, 1957) there was marked generalised wasting and emaciation. His weight had declined to

CASE NO. 39 (contd.)

4½ stone. There was almost complete paralysis of all limbs and active movements were restricted to the hands and feet. The facial muscles were also severely affected. In the course of the next 6 months there was a further decline in his weakness.

In July, 1958 he died of pneumonia and a pleural effusion which failed to respond to treatment.

AUTOPSY REPORT: All the muscles of the neck, thorax and abdomen, and the four limbs were grossly wasted and had a distinctly yellow colour. The small muscles of the hands and feet were less affected but did have a yellowish tinge. The glutei maximi appeared to be completely replaced by fat. The heart showed no macroscopic abnormality and the coronary arteries and great vessels were normal. Both pleural cavities contained considerably quantities of fluid, that on the left was straw-coloured and clear while that on the right side was cloudy and haemorrhagic and looked like an early empyema. The larynx, trachea and the large and small bronchi contained considerable amounts of tenaceous mucopus. Both lungs were oedematous and the right lower lobe showed early pneumonic consolidation. The surface of the brain appeared congested but showed no other abnormality on section.

Histology: Of the muscles examined, the tibialis anterior, sacrospinalis, biceps brachii and gluteus maximus were more severely affected than the psoas and gastrocnemius. In all these muscles there was extensive replacement of muscle by fat with varying numbers of small groups of muscle fibres running through it. The muscle fibres varied in size, some being enlarged and rounded and containing internal nuclei, while others were extremely small. The cross striations were preserved. There were a number of collagenous septa between the groups of muscle fibres and a condensation of collagen around the blood vessels and nerves.

CASE NO. 39 (contd.)

The lumbrical muscles were also affected and contained fibres of varying diameter. There was a striking increase of collagen but no fatty infiltration. The sternomastoids also showed early involvement with some enlarged fibres, some in a stage of acute degeneration and some very small. There was no fatty infiltration. The external ocular muscles also showed early changes with enlarged rounded fibres and proliferation of sarcolemal nuclei. The tongue was also affected by the disease. The myocardium contained extensive plaques of collagen which were apparent ot the naked eye in the Van Gieson preparations.

Other organs: Sections of the suprarenals, thymus, thyroid, pituitary, kidneys, testis, gasserion ganglion and superior cervical ganglion showed no abnormality.

CASE NO. 40. BORN: 7.2.45

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 8 months; Sat up: 15 months; Crawled: 15 months; Stood on own: 2 years; Walked: 2½ years.

No abnormality noted until the age of 5 when he started to walk on his toes and fell frequently. He wobbled from side to side. Unable to run or climb stairs normally. Difficulty in getting up after falling. Climbed up his legs in typical dystrophic manner. No enlargement of any muscles noted. Occasional pain in muscles. Tired readily. Weakness of the arms first noted at the age of 6 and a diagnosis was made at that stage. Went off his feet at the age of 9 followed by increase in weight. Gross mental retardation; ineducable; certified as mentally defective.

PAST ILLNESSES: Measles, Mumps, fractures of left femur (5/57), right femur (9/57).

FAMILY HISTORY: Positive.

COURSE: There was a slight decline in muscle power over a period of 3 years.

Fig. 39. OBESITY. MENTAL DEFECT.

CASE NO. 41 BORN: 2.7.48

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 6 months; Sat up: 1 year; Crawled: 18 months; Stood: 2 years; Walked: 2 years 3 months.

From the age of 5 he tended to walk on his toes and fell frequently. Waddled from side to side. Unable to run or climb steps. Difficulty in getting up after falling. Did so in typical dystrophic manner. No enlargement of muscles noted. Complained of pain in muscles. Tired readily. Diagnosis at 6. Went off his feet at the age of 9 after gradual progression of weakness. Weakness of arms observed at age of 11. Similar appearance to elder brother (case 40). Mental development retarded.

PAST ILLNESSES: Measles, Mumps did not set him back.

COURSE: There was a slight progression of the weakness over a period of 18 months; and early contractures of the knees developed.

CASE NO. 42. BORN: 28.2.50

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 6 months; Sat up: 1 year; Crawled: 15 months; Stood: 1½ years; Walked: 1 year 10 months.

The onset seemed slightly later than his two elder brothers (cases 40 and 41). A diagnosis was suggested at 6 but the parents did not notice any abnormality till the age of 7 when he was walking on his toes and fell frequently. There was a marked waddle to his gait. When falling he got up by supporting his hands on his legs. He was unable to run or to climb steps normally. Weakness was noted in the shoulders at the age of 8. No swelling of any muscles was noted. He did not complain of pain in the muscles, but tended to tire readily. Mental development retarded.

PAST ILLNESSES: Measles and mumps (? age) did not set him back.

FAMILY HISTORY: Positive.

COURSE: When first seen at the age of 8 he walked with a slight waddle which was accentuated with attempts to run. He was able to negotiate broad stairs one at a time, and got up from the ground with relative facility; he momentarily supported the left elbow on the left knee while doing so. In the course of two years there was a slight but definite decline in his muscle power, and increased difficulty in getting up from the ground. His back muscles were relatively strong and he did not "climb progressively up his thighs with his hands." There was a more marked waddle to the gait. He still walked on the flat of his feet.

CASE NO. 43. BORN: 29.3.47

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 4 months; Sat up: 8 months; Stood: 13 months; Walked: 16 months.

At the age of 3 he walked "as if he had a stone in his shoe." There was also difficulty in lifting his feet and in getting up steps. He seemed hesitant and nervous to climb. He did not fall much. No abnormal appearance of muscles. At age of 4 walking became worse and he dragged his left foot. Still stable on feet. At age of 4½ diagnosis of flat feet made and shoes wedged. Weakness progressively increased. After tonsillectomy at 5½ (in bed 8 days) his muscle power deteriorated considerably. This was followed by measles (in bed for a week) which set him back further. He was still able to walk on the level but had great difficulty climbing stairs or getting onto a bus. Walked on soles with waddling gait. From the age of 6 began to fall more frequently and got up in a typical dystrophic manner. After age of 7 no longer able to get up from ground on own. Diagnosis of muscular dystrophy then made. Enlargement of calves noted at that time. Trial of Vitamin E at the age of 8 without effect. At the age of 8 he fractured his right ankle. After being immobilised for 3 weeks he was unable to walk again. He continued to crawl for a few months. No weakness noticed in arms. Average intelligence.

COURSE: There was no marked change in his muscle power over a period of 2 years.

CASE NO. 44 BORN: 12.2.43

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up unsupported at 6 months.

At the age of 9 months he contracted poliomyelitis affecting mainly the left leg, the neck and the abdominal muscles. After 6 weeks at another hospital he was transferred to Q.M.H., in December, 1943. His muscular weakness improved very slowly. He developed a marked valgus deformity of the left foot, for which an elongation of the peroneus longus was performed in February, 1947. The deformity recurred and the foot was manipulated and kept in plaster for a prolonged period. He was very slow in learning to stand and walk.

By December, 1947 he was able to get about with the aid of crutches. There was weakness of the right leg as well. The walking gradually improved. A double walking calliper was fitted in February, 1948.

By February, 1949 he got about with only a left calliper and sticks and in April, 1949 he could walk without a calliper or sticks. He still had a valgus deformity of the left foot. In June, 1949 there was a flexion contracture of the left hip which was treated with traction and physiotherapy. A closed tenotomy of the peronei was performed for the deformity of the foot. He was able to walk after that with a left calliper and sticks. During the following year he developed contractures of the right hip flexors and the hamstrings on both sides. This handicapped his walking and by April, 1951 he could scarcely walk or stand at all. The flexion contractures at the hips could not be improved by stretching and a bilateral Souttar's operation was performed with unsatisfactory result. In October, 1951 he had a bilateral manipulation and stretching of the hip flexors and tendo Achilles. Tenotomy of the tendons behind the knee was also performed. Post-operatively he had great difficulty in standing or walking.

CASE NO. 44 (contd.)

In April, 1952 weakness was noted in the upper limbs and the back. In view of the apparent deterioration in his weakness a diagnosis of muscular dystrophy was suggested. A year later he could only get about with the aid of a walking machine. At that stage it was suggested that the whole clinical pattern might fit in with one diagnosis, progressive infantile spinal muscular atrophy (Werdnig-Hoffmann's disease).

In May, 1954 he lost the ability to get about with the walking machine. His muscular weakness deteriorated steadily, and by December, 1956 there was marked generalised weakness with practically no active movement present in the shoulder, hips, knees and elbows, and there was marked talipes equino valgus deformity of the feet. There was a gradual decline in his weight.

EXAMINATION: (January, 1958).

Musculoskeletal System: Gross generalised wasting of limb and trunk muscles. No enlargement of any muscles.

Deformities: Contractures were widespread and there was limitation of movement in the following joints:

Shoulders	:	Abduction	90°	90°
		Flexion	45°	45°
		Extension	20°	20°
Elbow	:	Extension	80°	80°
		Flexion	full	
		Supination: fixed position with no pronation of supination possible.		
Wrists	:	Flexion	30°	0°
		Extension	0°	30°

Finger flexors all had marked contractures.

Back : Fixed contractures of spinal extensors causing uniform lordosis.

CASE NO. 44 (contd.)

Hips (Range of movements) 80°- 135°; 80°- 150°

Knees " 95 - 135°; 95 - 135°

Ankles : marked equinus deformity. 5° range of residual movement.

Toes : Contractures of flexor muscles; more severe on left.

POWER: There was gross generalised weakness. Active movements in limbs almost restricted to the wrists, fingers, ankles and toes. Facial muscles and tongue normal.

Reflexes; All absent.

Other Systems: Cardiovascular: No apparent cardiomegaly but apex beat heaving in nature. Harsh systolic murmur at apex and pulmonic area. Second sound at pulmonic area markedly accentuated. Blood pressure 120 systolic; diastolic ?. Peripheral pulses present. Mottling and dusky cyanosis of both feet and legs, which felt objectively cold. Skin of hands and feet smooth and atrophic. Chest expansion limited to 1 inch. Lungfields clear. Secondary sex characters normal. Intelligence above average.

COURSE: By December, 1958 there was a further rapid deterioration in his condition. The wasting was more profound and the contractures more marked. He complained of difficulty with swallowing of solids and to a lesser extent, of liquids. Fluids sometimes regurgitated through the nose. On examination there was no apparent weakness of the tongue or palate.

In September, 1959, he had an episode of nasal regurgitation of fluid. This was followed by intermittent dyspnoea at rest, slight peripheral and central cyanosis and evidence of right sided consolidation of the lung. There was a marked tachycardia and cardiomegaly, but no other evidence of cardiac failure. X-ray of the

CASE NO. 44 (contd.)

chest showed an enlarged heart but no consolidation of the lungs.

He died two days later.

At autopsy the findings were consistent with an advanced myopathy. The heart was enlarged and showed a severe degree of fibrosis.

SPECIAL INVESTIGATIONS:

Electromyography: Typical myopathic pattern in right, and denervation pattern in left tibialis anterior.

Consistent with diagnosis of myopathy + old poliomyelitis.

Serum Aldolase: 15.5 units (raised).

AUTOPSY REPORT: All the skeletal muscles with the exception of some of the suboccipital muscles were severely affected. The tongue was large (weight 115 g). The heart was enlarged (130 g) with dilatation of the left ventricle and hypertrophy of the right. In the anterior wall of the left ventricle there were a number of areas of fibrosis resembling old infarcts. The consistency of the muscle was firm and rubbery. The coronary arteries were small. There was a patch of atheroma in the proximal 1 cm. of the right coronary artery. The great vessels were normal. The lungs were oedematous but there was no evidence of consolidation. The liver showed chronic passive congestion. The spinal cord looked normal externally but the anterior nerve roots in the left lumbar-sacral region were markedly thin and grey and the right lumbar anterior roots were slightly grey.

HISTOLOGY: Muscles of the arms and legs showed severe involvement by the dystrophic process with almost entire replacement by fibrous tissue and a variable amount of fat. Muscle spindles appeared normal. The muscles from the left leg showed almost complete replacement by fat and the residual fibres showed no evidence of denervation consistent

CASE NO. 44 (contd.)

with poliomyelitis in infancy. Sections from the diaphragm and rectus capitis major showed less severe involvement than the limb muscles. The striated muscle of the oesophagus was also affected by the dystrophic process. There was variation in fibre size, internal nuclei, necrosis of fibres and intersitial fibrosis. The smooth muscle was normal. The smooth muscle of the bladder and ileum was not affected. The cardiac muscle contained numerous patches of collagen and extensive diffuse interstitial fibrosis. No evidence of active myocarditis or recent infarction was present.

CASE NO. 45 BORN: 18.11.45

HISTORY: Pregnancy, labour and neonatal period normal. First of twin (vertex).

Milestones: Sat up: 1 year; Stood: 18 months; Walked: 2 years. Nothing abnormal noted until 5 when he began to fall frequently. Able to get up on his own after falling. Laughed at himself. After the age of 6 he became weaker and tended to fall more frequently. Diagnosis made at that age. Climbed up himself in typical dystrophic manner. Walked on his toes from the age of 7. No longer able to get up from the floor after the age of 8. Crawled about actively after that. Unable to climb stairs unaided. Went off his feet at the age of 9. Not precipitated by any episode. No weakness of arms noted. No swelling of muscles apparent. Complained of muscle pain. Rapid increase in weight after going off his feet. Mental development apparently normal.

PAST ILLNESSES: Chicken-pox, Whooping cough, Measles did not set him back. Fracture of left tibia at 10.

COURSE: There was minimal change in his condition over a period of 3 years. There was mottled cyanosis of the hands and feet and non-pitting oedema on the dorsum of the feet.

CASE NO. 46 BORN: 13.6.45

HISTORY: Pregnancy normal. Foetal movements less than previous child. Labour and neonatal periods normal.

Milestones: Held head up: 14 months (but was not floppy); Sat up: 16 months; Stood: 18 months; Walked: 2 years. (Elder sister had normal milestones).

His gait was abnormal from the beginning. He walked on his toes with forward stoop. He seemed unable to walk erect. He was never able to run and could not climb stairs without gripping some support. He fell frequently; "his legs simply gave way under him." He was unable to get up from the ground without some support. The calf muscles were prominent. He tired readily after walking short distances. His weakness progressed gradually, he fell more frequently and had increasing difficulty with walking. He went off his feet at the age of 10. Weakness of his arms was first noted 2 months later and has gradually increased. Mental development appeared normal but little progress with home tuition.

PAST ILLNESSES: Rubella (4) had no effect on muscle power.

COURSE: No follow-up possible.

CASE NO. 47. BORN: 2.10.43

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 6 months; Stood: 7 months;

Walked: 2 years.

From the beginning his gait seemed abnormal. He was unstable and had a sway. Always complained of tiredness. Did not fall much. Nothing unusual in appearance of muscles. No complaint of pain. Gradual progression of weakness. Had to be helped up steps. Managed to walk to school nearby. Diagnosed at 4. Prominence of calves noted at 10. No weakness observed in arms until after going off his feet at the age of 12. Intelligence normal.

COURSE: His rate of progression was slower than average. At age of 15 he could get from his wheel-chair into his bed, and also able to turn over. No deterioration was observed over a period of $2\frac{1}{2}$ years.

CASE NO. 48. BORN: 23.1.43

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 6 months; Sat up: 7 months; Stood: 12 months; Crawled: 12 months; Walked: 18 months.

Mother did not observe any abnormality in gait or activity until he started school at 5. Then noted that his gait was unusual and he tended to lean forward on his toes. Abdomen prominent with walking. Walked to and from school (½ mile) without tiring. He was unable to run normally and had difficulty in climbing steps. From the age of 7 fell frequently. Unable to get up unsupported after doing so. Walking gradually deteriorated, and he tired readily and complained of occasional pain in leg muscles. Weakness and wasting of arms and weakness of back noted at 9. At the age of 11 he was still walking, but only short distances and with great difficulty. He went off his feet at the age of 12. No enlargement of any muscles noted. His tongue was abnormally large. After going off his feet his weight declined. He developed progressive scoliosis and was fitted with a brace which he did not wear. Mental development normal.

PAST ILLNESSES: Chicken-pox and measles (infancy) did not set him back. Pneumonia (14).

FAMILY HISTORY: Positive.

COURSE: Slight deterioration of power over period of 18 months.

Muscle Biopsy: Characteristic changes of advanced dystrophy.

CASE NO. 49 BORN: 6.3.49

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 4 months; Sat up: 10 months; Stood: 18 months; Walked: 2 years.

His gait appeared to be normal and he was stable on his feet. However, he was unable to walk fast and tired readily.

In November, 1954, he attended another hospital with his elder brother. It was noted that he had "poor posture" and was "slightly retarded." In March, 1955 they recorded that he "tends to be slow and ungainly in rising from floor. Calves large and tight."

In November, 1955 he was admitted to hospital with paralytic poliomyelitis which affected mainly the left arm and both shoulder girdles and to a lesser extent the right upper arm and thighs. He made satisfactory progress and was discharged in January, 1956. His walking was good but very slow. In January, 1957 he injured his left ankle. A below knee plaster was applied in which he got about quite well for 6 weeks. He was fitted with a high calliper, and walked with difficulty. His left foot tended to invert. His walking deteriorated rapidly and after June, 1957 (aged 8) he could no longer walk. There was some weakness of the back and arms at that time. There was no pain in the muscles. His intellectual progress was subnormal.

PAST ILLNESSES: Poliomyelitis (5), Ankle injury (7).

FAMILY HISTORY: Positive.

COURSE: Previous poliomyelitis indicated by absent reflexes in the left leg and brisk ankle jerks, tibial taps and plantar taps on the right side. The power of some muscles on the left was slightly less than on the right. No deterioration was evident over a period of 1 year.

CASE NO. 50. BORN: 5.5.46

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 3 months; Sat up: 6 months; Stood: 15 months; Walked: 18 months.

Initially no abnormality was noted but at $2\frac{1}{2}$ his mother observed that his gait was waddling. He was never able to run normally and had difficulty in negotiating steps and even the pavement. He fell frequently and from the age of $3\frac{1}{2}$ climbed up himself. At that stage he could walk the $\frac{1}{4}$ mile but tended to tire. There was prominence of the calf muscles.

He gradually became weaker and fell more frequently. At the age of 4 he was unable to sit up from the supine and there was also weakness of the arms. By 5 his walking had deteriorated markedly and he had a marked waddle and lumbar lordosis. After the age of 7 he could no longer walk. The power in his arms gradually declined after that. At the age of 9 he developed a scoliosis of the spine and there was weakness of the neck and back. He could sit unsupported till the age of 10. His feet tended to become blue and cold. From the time of going off his feet he became thinner and his muscles became wasted. No difficulty with swallowing but "chewing seemed an effort." Intelligence seemed normal and he was sharp and bright but he was behind in his schooling.

PAST ILLNESSES: Whooping Cough (1), Measles (7), chronic constipation (7) did not affect his muscle power.

FAMILY HISTORY: Positive.

COURSE: There was a steady decline in his muscle power. He was prone to constipation to the extent of requiring colonic washouts. He died of a respiratory infection.

CASE NO. 50. (contd.)

AUTOPSY REPORT: Symmetrical wasting of entire musculature except for face; especially marked in shoulder girdle, upper arms and thighs. Muscles very pale, rather fibrous and occasionally fatty. Intercostals approached normal colour. Nervous system - brian moderately congested; spinal cord: no external abnormality. Respiratory system - collapse of both lower lobes. Fibrous thickening of parenchyma of lungs. Purulent exudate in bronchi which were moderately inflamed. Cardiovascular system: heart (128 g); myocardium, valves, coronaries healthy. Colon contained numerous scybali. Liver normal.

Histology: There was sub-pericardial fatty infiltration and patchy fibrosis of the myocardium and sub-endocardial fibrosis in papillary muscles. Fibrosis also seen around vessels. Tongue: some variation in fibre staining, ? significant. Several foci of abnormal fibres with macrophages or inflammatory cells around them. Central Nervous System - no abnormality.

CASE NO. 51 BORN: 16.12.47

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 3 months; Sat up: 5 months; Stood: 13 months; Walked: 17 months.

Initially his gait and muscle power appeared to be normal. He could run and get up and down steps. At the age of 4 he began to walk on his toes and his calf muscles became prominent and hard. He was unable to walk on his flat feet when encouraged to do so. He was stable on his feet until the age of 5 when he began to waddle and was prone to fall. He got up in the typical dystrophic manner. A diagnosis was made at that stage.

He continued to walk to school until the age of 7 (300 yards). At that time there was some weakness of the arms. During the following year he became more unstable on his feet and was transferred to a special school. The deterioration in his walking was gradual but became more rapid prior to going off his feet at 9. He continued to crawl about for some time. Intelligence normal.

PAST ILLNESSES: Measles (6), and Chicken-pox (8) did not affect his muscle power.

COURSE: There was a slight progression of weakness over a period of 6 months.

CASE NO. 52. BORN: 15.9.56

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 2 months; Sat up: 5 months; Stood: 10 months; Walked: 14 months.

Initially he seemed quite normal, but from the age of 18 months he walked with a slight waddle and was prone to fall. He was able to get up from the floor, but with some difficulty. No apparent deterioration in the following 6 months.

COURSE: He had the characteristic features of early disease. No follow-up possible.

CASE NO. 53. BORN: 5.12.42

HISTORY: Foetal movements reduced. Pregnancy, labour and neonatal period otherwise normal.

Milestones: Sat up: 1 year. Slow in sitting up - not before 1 year. Walked: approximately 1½-2 years.

From the beginning walking was hesitant and he seemed to lack confidence. Gait appeared normal initially and he was able to walk up steps but tended to fall frequently. At age of 3½ diagnosis of rickets suggested for slowness and unsteadiness of gait. Gradual deterioration in walking. Progressive difficulty climbing steps and got up from floor by pulling himself up against a chair or object. After starting school at age of 5 he walked on his toes, was less stable on his feet and fell more frequently. Diagnosis at 5½. No apparent swelling of any muscles. No pain in any muscles. Weakness of arms observed at 6.

Unable to walk after age of 7. Weakness noted in neck at 9 years and back at 10 years. Mental development retarded; considered to be educationally subnormal.

PAST ILLNESSES: Chicken-pox and measles did not set him back.

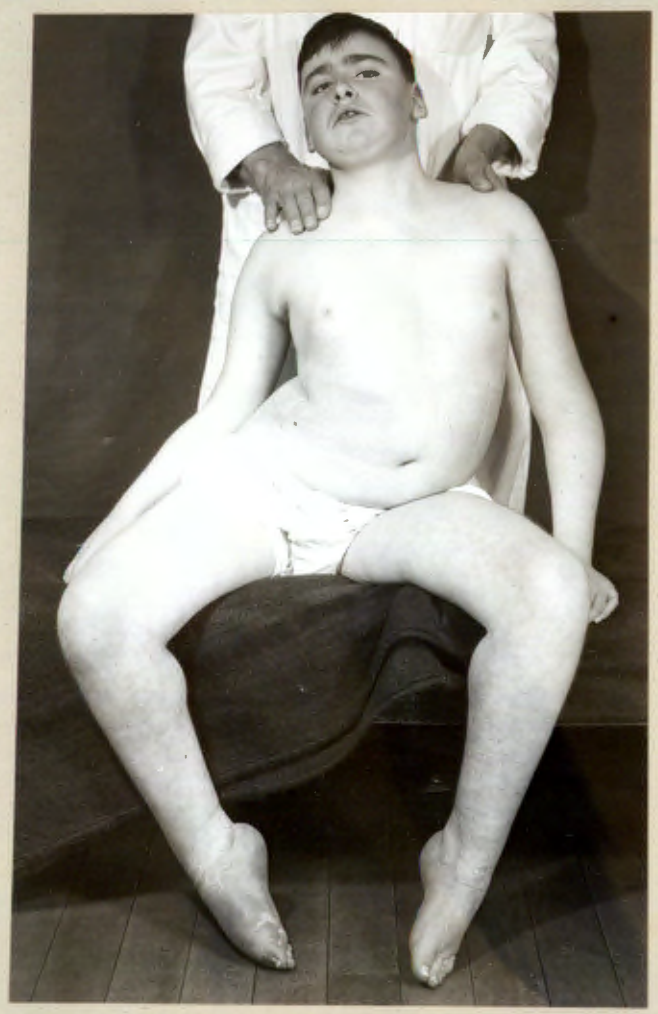
COURSE: There was a gradual decline in his muscle power over a period of 2 years. In November, 1959, following coryza for 2 days, he collapsed, was distressed and cyanosed and became unconscious. There was a tachycardia, and crepitations were present over both lungfields. He died 3 days later.

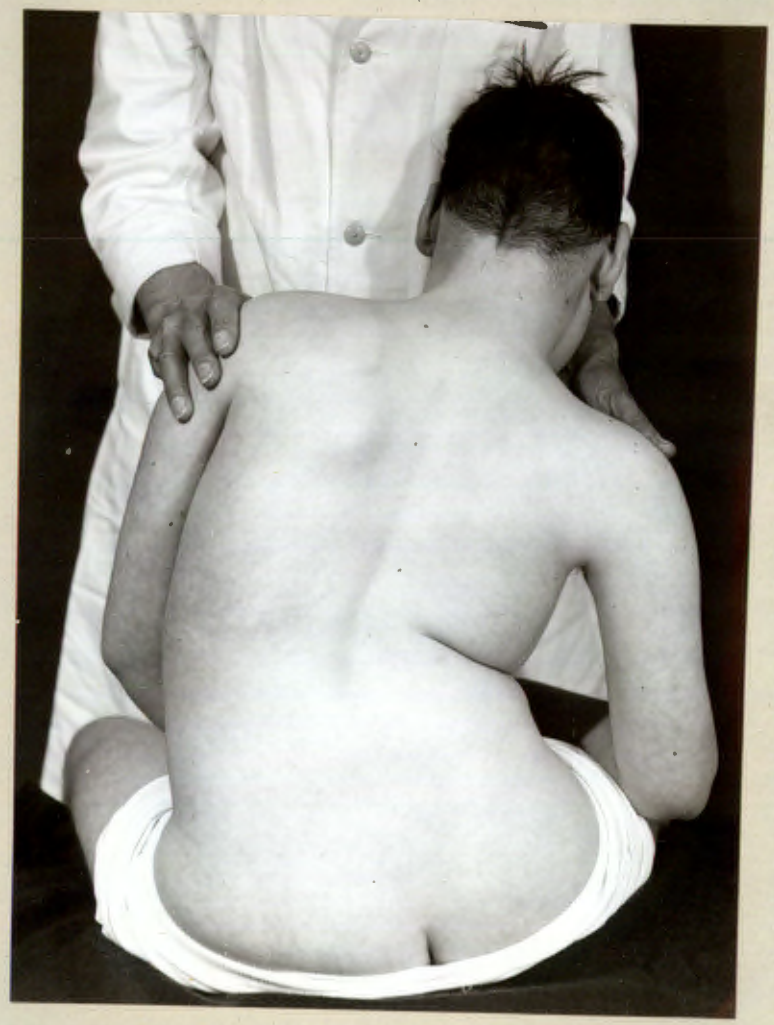
AUTOPSY REPORT: There was a thick layer of subcutaneous fat. Most of the proximal limb muscles were very wasted and almost completely replaced by fat. The forearm muscles, the intercostals and the diaphragm were less severely affected. The small muscles of the hands and the feet, the sternomastoids and

CASE NO. 53 (contd.)

the strap muscles of the neck and larynz were relatively well preserved. The heart was not enlarged but the myocardium of the left ventricle contained several areas of fibrosis. The coronary arteries and great vessels were normal. The trachea and bronchi contained abundant mucopurulent secretion. The left lung was markedly compressed by the scoliosis and the lower lobe was almost airless. The right main bronchus contained thick tenaceous mucus and the upper lobe was collapsed. Generalised acute fibrinous peritonitis was present and the spleen was covered by an acute fibrinous exudate. The endocrine glands, the testes and the genito-urinary tract were normal. The brain and spinal cord appeared normal.

HISTOLOGY: The muscles showed the changes of advanced muscular dystrophy. The lumbricals, diaphragm and temporalis muscle were less severely affected. The central nervous system was normal.





ig. 40 - 41 SLIGHT OBESITY. PROMINENT CALVES. EQUINUS DEFORMITY AND SWELLING OF FEET.

CASE NO. 54 BORN: 2.11.47

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 4 months; Sat up: 8 months; Stood: 20 months; Walked: 22 months.

His mother was worried by the delay in holding his head up and thought that there was some abnormality. When he started walking his gait seemed unusual and he waddled from side to side. He fell frequently and got up by climbing up his legs. He was unable to climb stairs normally and could not run. His calf muscles and shoulders were prominent at 3. Diagnosed at 4.

His walking gradually deteriorated, particularly after the age of 5. He tired very readily. There was no pain in his muscles at any time. He was no longer able to walk after the age of $8\frac{1}{2}$. No weakness apparent in the arms. He occasionally had difficulty with swallowing and tended to choke when eating. His tongue appeared abnormally large. He gained weight after going off his feet. His intelligence was difficult to assess because he was always "of a dreamy temperament and very introverted."

PAST ILLNESSES: Pertussis (4), Scarlet fever (5), Chicken-pox (6) and Measles (11) did not affect his muscle power.

COURSE: No change observed in course of 6 months.

CASE NO. 55. BORN: 13.4.45

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 6 months; Sat up: 8 months; Stood: 14 months; Walked: 16 months.

Initially his gait was unusual in that he walked on his toes with his arms above his head. However, his parents were not disconcerted about it at that stage. He seemed able to get about and run normally, but tired after walking long distances. From the age of 3 became hesitant to step down from the pavement or down stairs. He had great difficulty in getting up steps and did so on all fours. When starting school at the age of 5 he had great difficulty in walking to school uphill and had to be taken in a push-chair. Tended to be knocked over very easily at school. After the age of 6 started climbing up himself in a typical dystrophic manner. Had very well developed calves at that stage. From the age of 6 he walked on his toes and seemed unable to put his feet flat. Diagnosed at 6½.

At the age of 7, after being in bed for 2 days with rubella, he was unable to walk again. No apparent weakness of arms. No pain in muscles at any time. Feet became deformed and calves tended to waste after going off his feet. Did not put on weight. Hands and feet tended to be cold and mottled. Mental development apparently normal.

PAST ILLNESSES: Chicken-pox,(5), rubella (7).

COURSE: Over a period of 2 years there was no gross deterioration in his muscle power and no marked change in the deformities.

CASE NO. 56 BORN: 12.7.48

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 8 months; Stood: 14 months; Walked: 16 months.

Initially her gait was normal and she was able to skip and run. Prominence of the lateral aspect of both thighs was noted at 4 and at 5 she began to walk on her toes and had difficulty with ascending steps. At school she could not keep pace with her mates. She was unable to walk fast and tired readily. She walked on her toes with a waddling gait and an associated lordosis of the spine. From the age of 6 she fell frequently and climbed up herself in the typical dystrophic manner. Weakness of the arms was noted at the age of 7. Diagnosed at 8.

There was a gradual progression of the weakness and a marked deterioration at the age of 10 following confinement to bed for 3 weeks with influenza. She was of normal intelligence.

PAST ILLNESSES: Measles, Chicken-pox, Whooping Cough and Mumps in infancy and Tonsillectomy (5) did not set her back. Influenza (10) caused marked deterioration.

FAMILY HISTORY: Positive.

COURSE: When first seen (April, 1959) she was still able to walk but had to be helped onto her feet. She walked on her toes, on a wide base, with a waddling gait and marked lumbar lordosis. She was unable to get up from the floor or sit up from the supine position. When re-examined 4 months later she was unable to walk. This had followed a minor injury to her knee. There was a deterioration in most of the trunk and proximal limb muscles.

CASE NO. 57. BORN: 10.11.51

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 8 months; Stood: 12 months; Walked: 16 months. No abnormality noted till the age of 6 when her mother observed that her feet appeared stiff and she had difficulty in putting on her shoes. From that time she had difficulty in climbing stairs and tired readily on walking with a tendency to inversion of the feet. She fell frequently and got up with considerable difficulty in the typical dystrophic manner. There was no apparent weakness of the arms. From the age of 7 she had difficulty in getting up from the supine position. Her walking gradually deteriorated. Her intelligence was normal. From the age of 7 she attended a school for Physically Handicapped children. Sphincter control, chewing and swallowing were unaffected.

PAST ILLNESSES: Measles and Mumps did not set her back.

FAMILY HISTORY: Positive.

COURSE: When first examined in April, 1959 she walked with a slight waddle and associated lumbar lordosis. She got up from the floor with difficulty in the typical dystrophic manner and was able to sit up from the supine with the use of her hands. When re-examined 4 months later there was a marked deterioration. She was no longer able to get up from the floor and was much less stable on her feet. Her walking had deteriorated. There was also a decline in the power of many of the girdle muscles.

Fig. 42 - 43 CASE 56 and 57. DIFFERENT PHASES OF THE DISEASE.

CASE NO. 58 BORN: 13.4.50

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Stood up: 11 months; Crawled: 11 months; Walked: 2 years. (previous child walked at 11 months).

The exact age of onset is in doubt. The mother was concerned at the delay in walking. His gait was said to be quite normal initially but in retrospect the mother recalled that there was prominence of the calves at 2 and that he was unable to run or climb stairs. She did not suspect any abnormality till 5, when he started to fall frequently and got up in the typical dystrophic manner. His gait became waddling. Diagnosis at 6. Lordosis of the spine was striking at 7.

Weakness was slowly progressive. After 6 unable to get up from ground. At age of 10, marked difficulty with walking and he used a wheel-chair most of the time. Unable to walk soon after. Still crawled for about 3 months after that time. Always tired rapidly after walking but no pain present. Weakness in arms only noted at age of 12 but previous difficulty in manipulating wheel-chair. Contractures of knees after age of 12. Mental development apparently normal.

PAST ILLNESSES: Whooping Cough (2), Measles and Chicken-pox (4) did not affect his muscle power.

FAMILY HISTORY: Positive.

CASE NO. 59 BORN: 1.5.41

HISTORY: Reduced foetal movements. Pregnancy, labour and neonatal period otherwise normal.

Milestones: Stood up: 1 year; (Whooping cough at that stage set him back). Crawled: 18 months; Walked: 2 years.

Gait quite normal initially and stable on his feet. Big calves and people commented on good shape. Able to run and get up quite readily from the prone and supine position and mother did not suspect any abnormality till the age of 7, when he had difficulty in getting up stairs. Supported one hand on the knee to lift the other leg up. Diagnosis of flat feet. Frequent falls with difficulty in getting up, which he did in typical dystrophic manner. "Fell suddenly at times without tripping - legs just gave way under him." Diagnosis at 8.

From 10 lordosis of lumbar spine more marked with prominence of gluteal region and inturning of toes. Afraid to turn round for fear of falling. No change in appearance of calves or other muscles. No pain. Gradual deterioration in muscular power.

Walking deteriorated considerably at 11 after 1 week in bed with influenza, and he went off his feet 3 months later. Unable to manipulate wheel-chair himself. No weakness noted in arms prior to that. Contractures of knees developed after going off his feet. Operation performed on both legs in order to straighten them. (Forrester's knee hinges applied). Extension on his wheel-chair required in order to manage legs in that position.

After age of 10 progressively lost weight. Over a period of 4 years face and body changed from plump appearance to thin and wasted one. Appetite remained good.

CASE NO. 59 (contd.)

The tongue was enlarged from an early age. Mental development apparently normal.

PAST ILLNESSES: Whooping Cough 1 year delayed his ability to stand. Measles (4), Tonsillectomy (6), Chicken-pox (10) no affect on walking. Influenza (11) set him back.

CASE NO. 60 BORN: 6.7.44

HISTORY: Foetal movements reduced. Pregnancy, labour and neonatal period otherwise normal.

Milestones: Sat up: 9 months; Stood: 3 years; Walked: 3 years.

From the beginning he had a waddling gait and was unable to climb stairs. He was unstable on his feet and fell frequently. He had difficulty getting up from the ground. From the age of 5 his weakness was more marked and at school he was readily knocked over. His calves became prominent at that time.

There was a gradual progression of the disease until he went off his feet at the age of 9. No weakness of the arms was apparent. His mental development appeared normal.

PAST ILLNESSES: Measles and Scarlet fever.

FAMILY HISTORY: Positive.

CASE NO. 61 BORN: 15.5.44

HISTORY: Pregnancy - mother has congenital cystic kidneys. No complications of pregnancy but cerebrovascular accident post-partum. Foetal movements less than previous pregnancies. Prolonged labour. Child required resuscitation. Milestones: Unknown as he was reared in Nursery till 2 years. Stood: 2; Walked: 3.

Gait appeared normal initially but he was never able to get up stairs or to run. From age of 4 he fell frequently. Initial diagnosis of backwardness; later flat feet. At 5 tired readily and complained of aching in the legs. Fell frequently - "legs gave way under him." Progressive difficulty in getting up which he did in typical dystrophic manner. Diagnosis at 6.

Swelling of calves noted at age of 8. Calves felt hard. Gait became waddling "like a crab." Buttocks prominent and back lordosed. Gradual progression of weakness and went off feet at age of 11. Put on weight after that. No weakness of arms or face noted. Mental development initially backward but appeared to catch up with chronological age.

CASE NO. 62. BORN: 16.1.40

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 4 months; Sat up: 9 months; Crawled: 9 months; Stood; 15 months; Walked: 18 months.

From early age seemed lazy or "sluggish" with walking. Aged 2 tended to flop on floor and look up at his mother for help. Encouraged to walk. Nothing abnormal about gait initially. Calves appeared normal. Frequent falls. Unable to run at any stage and flopped onto the floor when doing so. At age of 2¾ fit lasting half an hour. Three days later he developed measles and after being in bed 2 weeks refused to walk again. Diagnosis made at age of 7.

Able to sit up normally and continued to crawl after going off feet. Muscles felt firm. Tone in shoulder girdle normal. No apparent weakness of arms, neck or back. Muscles not enlarged or wasted. No complaint of pain. After going off feet became progressively more obese. This became more marked after the age of sixteen. Wears size 20 collars and specially made trousers. Mental development normal.

COMMENT: Unusual features in this case were the early inability to walk, the absence of contractures at the elbows, and the limitation of flexion of the knees beyond 140°, with full extension. There was marked weakness of the toes and feet. In view of the apparent normality prior to the onset, which was relatively late, a diagnosis of muscular dystrophy is more likely than either amyotonia congenita or Werdnig-Hoffman's Disease.

CASE NO. 63. BORN: 18.6.49

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Held head up: 3 months; Sat up: 8 months; Stood up: 2 years; Walked: 3 years.

Mother thought walking delayed. From the beginning he seemed to limp to one side. He fell frequently, but was able to get up without difficulty. The muscles were normal in appearance. He had difficulty with running at 4 but walked reasonably well till 5. One foot turned inwards. Progressive difficulty with getting up after falling which he did in typical dystrophic manner. At age of 6 more rapid progression of weakness and diagnosis of muscular dystrophy made. Went off his feet at age of 9. No weakness noted in arms. Intelligence normal.

PAST ILLNESSES: Pneumonia (2), Mastoiditis (8 months).

CASE NO. 64 BORN: 16.6.42

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 6 months; Stood: 10 months;

Walked: 15 months.

Nothing abnormal noted till the age of 5. Able to walk with normal gait. Able to run normally and get up steps. No abnormal tendency to fall. From age of 5 walked with shoulders back, abdomen prominent and had a "stilted unnatural gait." Difficulty in getting up stairs. Did so with one hand on the knee and the other on the rail. Difficulty in getting up from the floor. Did so in typical dystrophic manner. Unsteady on feet. Fell frequently. Often fell without tripping. "Legs simply gave way under him." Calves were hard and prominent. No complaint of pain in muscles. No prominence of other muscle groups. Diagnosis at age of 5. Able to walk approximately ¾ mile to school at 5, but tired readily. Walking gradually deteriorated. (Weakness of arms first noted at 7). Gradual progression of weakness. Inability to walk after 11. Always big and plump. No change after going off feet. Intelligence normal.

PAST ILLNESSES: Chicken-pox, Measles (4) did not set him back.

CASE NO. 65 BORN: 6.10.40

HISTORY: Pregnancy, labour and neonatal period normal.

Milestones: Sat up: 6 months; Crawled: 9 months; Walked: 16 months.

From early age tended to tire easily when walking and at age of 3 asked to be carried after walking short distances. His gait was normal. General appearance of musculature normal.

At age of 4, left foot became inverted and left leg appeared smaller than right. No apparent limp. Started falling frequently at that age. Treated as polio in 1945. Feet became more inverted, were manipulated and put into plaster. Walking irons applied, which were more of a handicap. Walking steadily worse. Gait unsteady. Went up steps very slowly, one at a time. Legs always seemed tired. From age 2½ fell frequently but still able to get up on own. This became progressively more difficulty. From age 4 get up in typical dystrophic manner. Never able to run. Gradual progression in weakness. Went off feet at age of 7. Diagnosed at 8. Continued to crawl till age of 9. Back became uniformly lordosed. From age of 8 tended to get about by sliding on buttocks. Intelligence normal. Able to read and tell time before the age of 5. Passed G.C.E.

Facial muscles seemed affected at early age. Never able to close eyelids. Eyes turned up when sleeping. Mother thinks facial muscles were already affected when he was teething at 4 months. Never able to smile normally. Photographer commented on this when he was a toddler. In recent years jaw has drooped. No apparent weakness of arms. Able to hold onto father's neck when being lifted. No contractures of knees or elbows until recently. Muscles not enlarged at any stage. No localised wasting apart from

CASE NO. 65 (contd.)

left leg. No history of pain.

PAST ILLNESSES: Whooping cough (3) set him back. Measles (5), mumps (6) did not set him back.

EXAMINATION: Expressionless face. Pouting lower lip. Generalised facial weakness. Ocular muscles normal. Tongue atrophic.

Musculoskeletal system: Generalised hypotonia. Diffuse lordosis of spine. Slight scoliosis, concave right. Lies forward in comfort with abdomen flat on bed. Able to "roll" from supine into sitting position. Hyperextensibility of interphalangeal joints, more on right than left.

Contractures:

Neck	: Limitation of rotation and flexion.		
Elbows	:	135°	110°
Wrists	: (range)	0-100°	90-180°
Knees	: (range)	45-180°	45-180°
Ankles	: marked bilateral varus deformity with slight equinus.		

Right leg larger than left - measurements: greater trochanter to end of fibula 35", 32"; Circumference of thigh (maximal): 26", 21", calf: 15", 14".

No apparent enlargement of any muscle groups. Generalised obesity, except in face. Generalised weakness of shoulders, arms, trunk and lower limbs. Gross wasting of right deltoid, bilateral wasting of sterno-mastoids. Gross wasting of both pectorals.

Other features: high-arched palate, narrow jaw. Penis small. Testes descended, but undersized. Pubic hair scanty. Other systems normal.

CONCLUSIONS: The sequence of weakness in this case seems to have been facial muscles, pelvic girdle and trunk and then upper limbs.

CASE NO. 65 (contd.)

It is difficult to explain the discrepancy in size between the two legs, and the unilateral wasting of the delteid. There is no clear-cut history of poliomyelitis. While the progression of the weakness of the pelvic girdle and lower limbs conformed to the usual Duchenne type, the weakness of the face resembled that seen in facio-scapulo-humeral muscular dystrophy. The sexual hypoplasia is also an unusual feature in association with muscular dystrophy.

APPENDIX IV.

TABLES.

APPENDIX IV. TABLE IV.1.

Case No.	ENLARGEMENT Calf	ENLARGEMENT Other	WASTING. (On examination) SM	T	R	I	S	L	P	D	UA	FA	G	Th	C
1	+	SA.		+							+				
2	+	-		+	+				+		+	+			
3	-	-	Generalised wasting.												
4	+	thigh SpC		+											
5	+	-							+						
6	+		Generalised wasting.												
7	-		Generalised wasting.												
8	+	SA.							+		+			+	
9	+	D			+	+		+	+		+				
10	+	-			+				+				+		
11	+	SA.		+	+				+	+				+	
12		SA.D.							+		+				
13	-	-													
14	+	D.FA.Q			+				+		+				
15	+	SA.D.FA			+				+		+				
16	+	triceps													
17	-	-		+	+				+		+				
18		SA.SpC.		+					+	+				+	
19	+	D	+	+	+						+				
20	-	-		+	+				+					+	
21	+	vast lat.			No wasting.										
22	+	-			+	+		+	+						
23	+	-			+				+		+	+	+	+	
24	-	-			+				+		+			+	
25	+	-			Generalised wasting.										
26	?+	-							+					+	
27	+	SA.			No wasting apparent.										
28	+	SA.			No wasting apparent.										
29	-	-													
30	-	Q							+	+				+	
31	+	-							+	+					
32	-	-			Generalised wasting										
33	-	-			Generalised wasting (slight).										
34	-	-	+		+				+		+				
35	+	D.SA.Sp.C							+	+	+				
36	+	-							+						
37	-	-		+	+					+		+			
38	-	-			Generalised wasting.										
39	-	-			Generalised wasting.										
40	-	-			Generalised wasting.										
41	-	-							+						
42	+	-			No wasting										
43	-	-			No wasting										
44	-	-			Generalised wasting.										
45	-	-			No wasting										
46	+	-							+						
47	+	-			+	+	+	+	+						
48	-	-			Generalised wasting										
49	?	-							+						
50	-	-			Generalised wasting										
51	+	-		+	+				+	+					
52	+	-			No wasting										
53	+	-			Generalised wasting										
54	+	D	+	+	+						+				
55	-	F.A.									+				
56	+	D.Q.			+	+		+	+				+	+	
57	?	vast. lat, Q			No wasting										
58	-	-								+	+	+			
59	-	-			Generalised wasting										
60															
61	+	D.FA.			No wasting										
62	-	-	+							+					
63	-	SA. D.								+	+				
64	-	-									+			+	
65	-	-	+									+			

key: SA. Serratus ant. SpC. Splenius capitis. D. Deltoid. FA. Forearm. Q. Quadriceps. SM. Sternomastoid. T. Triceps. R. Rhomboids. I. Infraspinatus S. Supraspinatus L. Latissimus dorsi P. Pectoralis UA. Upper arm. G. Glutei. Th. Thigh. C. Calf.

APPENDIX IV. TABLE IV.2. : DEFORMITIES.

Case No.	Scoliosis L	Scoliosis R	Shoulder	Elbow R/L	Wrist R/L	Hip R/L	Knee R/L	Ankle	Tongue enlarged	Weakness of face
1								EV	-	+
2	+			*120°			100/140°	EV	-	+
3	+			120(S)		90°(R)	85	EV	-	+
4		+		160		140	110	EV;90	+	S
5		+		175		160	150	90	-	-
6	-			145			120	EV	-	-
7	-					150	100	100	-	-
8	-					160	140	90	-	S
9	-							E sl.	+	-
10	-								?	-
11	-			170		140	120	90	+	-
12	-					150	150	EV;110	-	-
13		+		160			90/110	110	+	-
14	-							100	+	-
15	+						110	EV	-	+
16				160			110	90	-	-
17	+			170(S)		150	100	EV	-	S
18	+		+	120		110	90	EV	-	-
19		+		**160/170		90	150/160	EV	-	-
20	+			100		150	90	EV	+	+
21		-						E sl.	-	-
22		-							-	-
23		+							-	-
24		-		150			160/150	100	-	+
25		+		120			90/100	EV	-	-
26		-		175(S)		110	90	85/75	+	+
27		-						E sl.	+	-
28		-							+	-
29	+			145		140	90	90+	-	-
30			+	100(S)			80/60		-	-
31		-		170		150/170	110/160	EV	-	-
32	+			110/130			85/105	E	↓	-
33	+			110/140			90		-	-
34	+			175		150	160/130	130	-	-
35		-		170			175/150	E	-	S
36		-		160		170	160	E	-	S
37	+			160/120			90	EV	-	+
38	+			150/135		160			-	-
39			+	110	+		120	EV	-	-
40			+	130/140			140	EV	+	-
41		-					160		-	-
42								90	?	-
43	+			150			80	EV	-	-
44		-		poliomyelitis				E	-	-
45		-		150	+	120/90	140/130	EV	-	-
46		-		135			110	95	+	-
47		-					160		-	-
48	+		+	110(S)	+		90/110	110	+	-
49		-		175		160/170	140/160	95	+	-
50	+			135	+	90/100	90	180	-	-
51			+	135			90	E	-	-
52		-							-	-
53			+	170			100		+	S
54	+			170			170	EV	+	+
55	+			110	+	(R)	110	EV	-	-
56		-						90	+	-
57		-							-	-
58	+		+	130/120	+		110	EV	+	S
59	+			110	+	85	90/110	EV	+	+
60	+						140/170	EV	-	-
61	+						160	EV	+	+
62			+	+			180 ext.		+	+
63		-					170	E	-	-
64		-		145		160	100	EV	+	+
65			+	135/110(S)	+				-	+

* Figure indicates angle of maximal extension. (same both sides)
** 1st figure represents right side.
(S)= Limitation of Supination -
R : Limitation of Rotation.
EV : Equinovarus.
S: Limited smile only.

APPENDIX IV.

TABLE IV.3 - 7. MUSCLE POWER CHARTS.

CASE NO	1	2	3	4	5	6	7	8	9	10	11	12	13
NECK:													
Flexors	3	2	2	2	3	2	2	2	3	3	1	1	1
Extensors	3	2	3	3	4	3	3	3	3	4	3	3	3
Sternomastoid	2	2	2	3	3	2	3	3	3	3	2	2	2
TRAPEZII:													
Rhomboids	1	1	2	0	4	2	2	0	2	2	1	0	0
SHOULDER:													
Abductors	2	1	2	2	3	2	3	3	4	4	1	2	2/0
Adductors	2	1	2	2	2	2	3	2	3	3	1	1	1/1
Flexors	2	1	2	2	2	2	3	2	3	3	1	2	1/0
Extensors	2	1	2	2	3	2	3	2	3	3	1	1	1/0
External Rotators	2	1	2	2	3	2	3	2	3	3	2	2	2/1
Internal Rotators	2	1	2	2	3	2	2	2	3	3	1	2	2/2
Pectorals	2	0	1	1	3	2	2	2	3	3	0	1	1/1
ELBOW:													
Flexors	2	2	3	3	4	3	3	3	3	4	1	2	3
Extensors	2	1	2	2	3	2	3	3	3	3	0	2	3/2
Pronators	3	2	3	4	4	2	3	3	4	4	2	3	3
Supinators	3	2	3	4	4	2	3	3	4	4	2	3	3
WRIST:													
Flexors	3	2	4	4	4	3	3	4	4	4	2	3	4
Extensors	3	2	4	4	4	2	3	4	4	4	2	3	3
Finger flexors	3	2	3	4	4	3	3	4	4	4	2	3	4
Extensors	3	2	4	3	4	3	3	4	3	4	2	2	3
Abductors	3	2	3	3	4	3	3	4	3	4	2	3	3
Adductors	3	2	3	3	4	3	3	4	3	4	2	3	3
Thumb muscles	3	2	3	3	4	3	3	4	4	4	2	3	4
TRUNK:													
Flexors	2	1	2	2	2	2	2	2	3	3	1	2	2
Extensors	2	1	1	1	2	3	2	2	3	2	1	0	1
HIPS:													
Flexors	3	1	3	1	3	3	2	2	3	3	1	3	2
Extensors	1	1	2	1	2	2	1	1	2	2	1	1	1
Abductors	2	1	3/2	1	3	3	3	2	3	3	1	2	1
Adductors	2	1	2	1	2	2	3	2	3	2	2	2	1
External Rotators	2	0	2/1	1	3	2	3	2	3	3	1	2	2
Internal Rotators	3	1	1/3	1	2	2	3	2	3	2	1	2	2
KNEE:													
Flexors Medial	3	2	3	2	4	3	3	3	4	3	2	3	3
Flexors Lateral	3	2	2	2	4	3	3	3	3	3	1	2	2
Extensors	2	1	2	2	3	3	2	2	3	3	2	2	2
ANKLE:													
Dorsiflexors	2	1	3	3	4	3	3	3	4	3	2	3	3
Plantar flexors	4	2	4	4	5	3	3	4	5	4	3	3	4
Foot Inverted	3	2	2	3	4	3	3	4	4	4	2	2	3
Foot Everted	2	2	2	2	4	3	3	3	4	4	2	2	3
Toes Dorsiflexion	2	2	3	2	4	2	3	3	4	3	2	3	3
Toes Plantar flexion	3	4	4	4	5	3	3	4	5	3	3	3	4

Table.IV.3. Chart of muscle power. (cases 1 - 13)

Strength of Contraction:

0. No contraction.
1. Flicker only.
2. Contraction but not against gravity.
3. Contraction against gravity.
4. Contraction against gravity and resistance.
5. Normal contraction.

CASE NO.	14	15	16	17	18	19	20	21	22	23	24	25	26
NECK:													
Flexors	3	2	2	2	2	2	1	4	2	4	2	1	2
Extensors	4	3	3	3	2	2	3	4	4	4	2	2	3
Sternomastoid	4	2	3	2	2	2	2	5	3	4	2	2	2
Trapezii	3	2	3	3	2	2	2	5	3	3	3	1	2
Rhomboids	2	0	0	2	1	1	1	5	2	3	1	0	0
SHOULDER:													
Abductors	3	2	2	2	1	1	2	5	3	4	3	1	2
Adductors	3	2	2	2	2	2	2	5	3	4	3	2	2
Flexors	3	2	2	2	1	1	1	5	3	4	3	1	2
Extensors	3	2	2	2	1	1	1	5	3	3	3	1	2
External Rotators	3	2	2	2	1	2	1	5	3	3	3	2	2
Internal Rotators	3	2	2	2	1	2	0	5	3	3	3	1	2
Pectorals	2	2	2	2	1	1	0	5	3	3	3	1	2
ELBOW:													
Flexors	3	3	3	3	3	3	3	5	4	3	3	2	3
Extensors	3	2	3	2	3	2	2	5	3	3	3	2	3
Pronators	4	3	3	3	3	3	3	5	4	4	4	2	3
Supinators	4	3	3	3	3	3	3	5	4	4	3	2	3
WRIST:													
Flexors	4	3	4	4	3	3	3	5	4	4	4	4	3
Extensors	4	3	3	4	3	3	3	5	4	4	3	3	3
Finger Flexors	4	3	3	4	3	3	3	5	4	4	4	3	3
Finger Extensors	3	3	3	3	3	3	2	5	4	4	3	3	3
Finger Abductors	3	2	3	3	3	3	2	5	3	4	3	2	3
Finger Adductors	3	3	3	3	3	3	2	5	3	4	3	2	3
Thumb muscles	3	3	3	3	3	3	3	5	4	4	3	3	4
TRUNK:													
Flexors	3	1	2	2	1	1	0	3	2	3	1	1	2
Extensors	3	0	1	2	1	1	0	4	3	3	2	0	1
HIPS:													
Flexors	3	2	4	2	1	1	1	4	3	3	3	1	2
Extensors	3	2	3	2	2	1	0	4	2	2	2	0	2
Abductors	3	2	2	2	2	1	0	4	3	3	3	1	2
Adductors	3	2	3	2	2	0	0	4	3	3	3	1	3
External Rotators	2	2	3	2	2	1	0	5	4	3	3	1	2
Internal Rotators	2	2	3	2	2	1	0	5	3	3	3	1	2
KNEE:													
Flexors Medial	3	2	4	3	3	2	2	5	4	4/3	4	2	3
Flexors Lateral	3	2	3	2	3	2	1	5	3	3/2	3	1	3
Extensors	4	2	2	2	2	2	1	4	3	3	3	2	2
ANKLE:													
Dorsiflexors	3	2	3	3	3	2	1	5	4	3	4	1	2
Plantar Flexors	4	2	4	3	4	3	2	5	4	4	4	2	3
Foot Inversion	3	2	3	3	3	3	1	5	4	3	4	1	2
Foot Eversion	3	1	3	3	3	2	1	5	4	3	3	1	2
Toes Dorsiflexion	3	3	3	3	3	2	1	5	4	3	3	2	2
Toes Plantar Flex.	4	3	4	4	4	3	2	5	4	4	4	3	3

Table.IV.4... : Chart of muscle power. (cases 14 - 26)

Strength of Contraction:
0. No contraction.
1. Flicker only.
2. Contraction but not against gravity.
3. Contraction against gravity.
4. Contraction against gravity and resistance.
5. Normal contraction.

	27	28	29	30	31	32	33	34	35	36	37	38	39
NECK:													
Flexors	3	3	2	2	3	1	2	2	2	1	1	3	0
Extensors	4	4	4	2	3	3	3	3	2	2	2	0	2
Sternomastoid	3	3	3	2	3	2	3	2	2	2	2	1	2
Trapezii	3	3	2	2	2	1	2	2	2	1	0	3	0
Rhomboids	2	2	1	2	1	0	1	1	1	0	0	2	0
SHOULDER:													
Abductors	4	3	2	2	3	1	3	2	2	2	1	2	1
Adductors	4	3	2	2	2	1	3	2	2	2	1	2	0
Flexors	3	3	2	1	3	1	3	2	1	2	0	2	0
Extensors	3	3	2	1	3	0	3	2	1	2	0	2	0
External Rotators	3	3	3	1	2	0	3	2	1	2	0	2	0
Internal Rotators	3	3	2	1	2	0	3	2	1	2	0	2	0
Pectorals	3	3	2	1	2	1	3	1	1	1	0	2	0
ELBOW:													
Flexors	4	4	3	3	3	2	3	3	3	3	1	3	1
Extensors	3	3	3	3	2	1	3	3	3	2	2	1	1
Pronators	4	4	3	3	3	2	3	3	3	2	2	2	1
Supinators	4	4	3	3	3	2	3	3	3	2	2	2	1
WRIST:													
Flexors	4	4	3	3	3	3	4	4	4	3	3	3	1
Extensors	4	4	3	3	3	3	4	4	3	3	3	2	0
Finger Flexors	4	5	4	3	4	3	4	4	4	3	2	3	2
Finger Extensors	3	4	3	3	3	3	4	4	3	3	2	2	2
Abductors	3	4	3	3	3	2	3	3	3	3	2	2	2
Adductors	3	4	3	3	3	2	3	3	3	3	2	2	2
Thumb Muscles	4	5	3	3	3	2	3	4	4	3	3	3	2
TRUNK:													
Flexors	2	3	2	2	2	0	2	2	2	1	0	2	1
Extensors	3	4	2	1	2	0	2	2	1	0	0	2	1
HIP:													
Flexors	3	3	2	2	2	1	3	2	1	1	0	3	1
Extensors	2	2	1	2	2	0	1	2	1	0	0	1	1
Abducters	3	4	2	2	0	1	2	2	2	1	0	3	1
Adducters	3	3	2	2	1	1	2	1	2	1	1	2	1
External Rotaters	3	4	3	2	2	1	3	3	2	1	0	3	0
Internal Rotaters	3	4	3	2	2	1	3	2	1	1	0	3	0
KNEE:													
Flexors Medial	4	4	3	3	3	2	4	3	2	2	2	3	2
Flexors Lateral	3	4	2	2	3	1	2	3	2	0	1	3	1
Extensors	3	3	2	2	2	1	2	2	3	2	0	3	1
ANKLE:													
Dorsiflexors	4	4	2	3	3	2	4	3	3	2	1	3	1
Plantar flexors	5	5	3	3	3	2	4	4	4	2	2	2	2
Foot Inversion	3	4	3	2	3	2	3	3	3	2	2	2	1
Foot Eversion	3	4	3	2	3	0	3	3	3	1	0	2	1
Toes Dorsiflex.	3	3	2	3	3	2	4	3	3	1	1	3	1
Toes Plantar flex.	4	4	3	3	3	2	4	4	4	3	2	2	2

Table..IV.5... : Chart of muscle power. (cases 27-- 39)

Strength of Contraction:
0. No contraction.
1. Flicker only.
2. Contraction but not against gravity.
3. Contraction against gravity.
4. Contraction against gravity and resistance.
5. Normal contraction.

CASE NO.	40	41	42	43	44	45	46	47	48	49	50	51	52
NECK:													
Flexors	1	2	4	2	0/1	2	2	4	2	3	1	2	5
Extensors	2	3	5	3	3	3	3	4	3	3	1	3	5
Sternomasteids	1	3	4	3	2/1	2	2	4	2	3	1	2	5
Trapezii	1	2	4	2	1	2	3	4	2	3	3	3	5
Rhemboids	0	0	3	0	0	0	2	2	0	2	1/0	1	5
SHOULDER:													
Abducters	1	3	4	2	1	2	2	3	2	3	0/1	3	5
Adducters	1	2	4	2	0	2	2	3	2	3	1	3	5
Flexors	1	2	4	2	1	2	2	4	2	3	1	3	5
Extensors	1	2	4	2	1	2	2	3	2	2	1	3	5
External Rotaters	1	3	4	2	0	2	2	3	2	2	1	3	5
Internal Rotaters	1	1	4	2	0	2	2	3	2	3	1	3	5
Pecterals	1	2	4	1	0	1	2	3	2	3	1	3	5
ELBOW:													
Flexors	2	3	5	2	3/2	3	3	3	2	3	1	3	5
Extensors	2	3	4	1	2	3	3	3	2	3	1	2	5
Prenaters	2	3	5	2	0	3	3	4	3	3	2	3	5
Supinaters	2	3	5	2	0	3	3	4	3	3	2	3	5
WRIST:													
Flexors	3	4	5	4	3	4	4	4	3	3	3	3	5
Extensors	3	4	5	3	3	4	3	4	3	3	3	3	5
Finger Flexors	3	4	5	3	3/2	4	4	3	4	3	3	4	5
Finger Extensors	3	3	5	3	3	3	3	3	3	3	2	3	5
Abducters	2	3	5	2	2	3	3	3	3	3	2	4	5
Adducters	2	3	5	2	2	3	3	3	3	3	2	4	5
Thumb Muscles	3	4	5	3	3	4	3	3	4	3	3	4	5
TRUNK:													
Flexors	1	2	4	1	1	2	2	2	0	2	0	3	5
Extensors	0	1	4	2	0	1	1	2	2	2	0	2	4
HIP:													
Flexors	1	1	4	2	2	3	2	3	2	3	1/0	2	5
Extensors	0	1	3	1	1	2	1	2	0	2	0	1	5
Abducters	0	0	4	0	0/1	2	1	3	1	3	0	2	5
Adducters	1	1	4	0	2/1	3	1	3	1	2	1	2	5
External Rotaters	0	1	4	2	0/1	3	3	3	2/0	3	0	2	5
Internal Rotaters	0	1	5	2	2	3	2	3	2/0	3	0	2	5
KNEE:													
Flexors Medial	1	3	5	3	3	4	3	4	4	4	2	4	5
Flexors Lateral	0	0	5	0	1/2	2	3	3	2	3	2	3	5
Extensors	1	2	5	2	1/0	2	2	2	2	3	0	2	5
ANKLE:													
Dorsiflexors	1	3	4	3	2	4	3	3	2/3	3	1	2	5
Plantar flexors	2	4	5	3	3	4	4	3	4	4	2	4	5
Feet Inversion	1	3	4	0	2/1	3	3	3	2	3	2	2	5
Feet Eversion	1	3	4	0	3	3	3	3	2	3	1	3	5
Toes Dorsiflex.	2	3	5	2	2/1	3	3	3	3/0	3	1	2	5
Toes Plantar Flex.	2	4	5	3	4	4	4	3	3	4	3	4	5

Table. IV.6. .. : Chart of muscle power. (cases 40 - 52)

Strength of Contraction:
0. No contraction.
1. Flicker only.
2. Contraction but not against gravity.
3. Contraction against gravity.
4. Contraction against gravity and resistance.
5. Normal contraction.

CASE NO.	53	54	55	56	57	58	59	60	61	62	63	64	65
NECK:													
Flexers	1	1	1	4	3	2	2	3	3	3	2	3	0
Extensors	2	3	2	4	4	2	3	3	3	2	3	3	3
Sternomastoids	2	2	2	5	4	4	3	4	4	3	3	3	3
Trapezii	0	1	2	4	4	2	3	3	3	3	2	3	1
Rhomboids	0	0	2	2	4	0	3	2	3	2	2	2	1
SHOULDER:													
Abductors	2	1	2	3	4	0	2	2	3	2	3	2	2
Adductors	2	1	2	3	4	0	2	2	3	2	3	2	3
Flexors	2	1	2	3	4	0	2	2	2	2	3	2	2
Extensors	1	1	1	3	4	0	2	2	2	2	3	2	3
External Rotators	0	2	1	3	4	1	2	2	3	2	2	2	2
Internal Rotators	1	2	1	3	4	1	2	1	3	2	2	2	2
Pectorals	1	0	1	3	4	1	2	0	3	1	1	2	1
ELBOW:													
Flexors	1	3	3	4	5	2	2	3	3	3	3	4	3
Extensors	1	3	1	4	4	2	2	3	3	3	3	3	2
Pronators	2	3	3	5	4	2	2	3	4	3	3	4	3
Supinators	2	3	3	5	4	2	2	3	4	3	3	3	1
WRIST:													
Flexors	3	3	3	5	5	3	3	3	3	3	4	4	3
Extensors	3	3	3	5	5	3	3	3	3	3	3	4	2
Finger Flexors	3	3	3	5	5	3	4	4	3	3	4	4	3
Finger Extensors	3	3	3	5	5	3	4	4	3	3	3	3	2
Abductors	3	4	3	5	5	3	3	3	3	3	3	4	2
Adductors	3	4	3	5	5	3	3	3	3	3	3	4	2
Thumb Muscles	3	4	3	5	5	3	4	3	3	3	4	4	3
TRUNK:													
Flexors	0	1	1	2	4	2	1	1	2	2	3	3	2
Extensors	0	1	0	2	3	2	1	2	2	2	2	3	2
HIP:													
Flexors	0	1	2	3	4	1	3	1	2	2	2	2	3
Extensors	0	1	1	3	4	0	1	1	2	3	1	2	2
Abductors	0	0	1	2	4	1	2	2	2	1	2	2	4
Adductors	0	1	2	2	4	1	2	1	2	1	2	3	4
External Rotators	0	1	1	3	4	1	2	2	3	2	2	2	3
Internal Rotators	0	1	0	3	4	1	2	2	3	2	2	3	3
KNEE:													
Flexors Medial	2	2	3	4	5	2	4	3	3	1	3	4	4
Flexors Lateral	1	2	0	4	4	3	3	3	2	1	3	3	3
Extensors	0	1	2	4	4	2	3	2	2	1	3	3	3
ANKLE:													
Dorsiflexors	1	1	0	5	5	2	2	3	3	1/2	3	3	3
Plantar Flexors	2	2	3	5	5	4	2	4	4	1	3	3	3
Foot Inversion	1	3	2	5	5	3	2	3	4	1	3	3	3
Foot Eversion	1	2	0	5	5	3	2	3	3	1	3	3	3
Toes Dorsiflex.	0	3	1	5	5	2	3	2	3	0/2	3	3	3
Toes Plantar Flex.	1	4	3	5	5	3	3	3	4	1/2	3	4	3

Table.IV.7.... : Chart of muscle power. (cases 53-- 65)

Strength of Contraction:
0. No contraction.
1. Flicker only.
2. Contraction but not against gravity.
3. Contraction against gravity.
4. Contraction against gravity and resistance.
5. Normal contraction.

APPENDIX IV.

TABLE IV. 8 : REFLEXES

Case No.	Knee Jerk	Ankle Jerk	Tibial Tap	Plantar Tap
1	- / -	+ / +	- / +	- / +
2	- / -	++ / ++	++ / ++	++ / ++
3	- / -	+ / -	+ / -	+ / -
4	- / -	+ / +	- / -	+ / +
5	- / -	++ / ++	+ / +	++ / ++
6	- / -	+ / +	- / -	+ / +
7	- / -	- / -	- / -	- / -
8	- / -	++ / ++	+ / +	+ / +
9	- / -	++ / ++	+ / +	+ / +
10	- / -	++ / ++	- / -	++ / ++
11	- / -	++ / ++	+ / -	+ / +
12	- / -	++ / ++	++ / ++	+ / ++
13	- / -	++ / ++	- / -	- / +
14	- / -	+ / +	- / -	+ / +
15	- / -	- / -	- / -	- / -
16	- / -	- / -	- / -	- / -
17	- / -	++ / -	+ / -	- / -
18	- / -	- / -	- / -	- / -
19	- / -	- / -	- / -	- / -
20	- / -	- / -	- / -	- / -
21	+ / +	++ / ++	++ / ++	++ / ++
22	- / -	- / -	- / -	- / -
23	- / +	+ / ++	- / -	- / +
24	- / -	- / +	- / -	- / -
25	- / -	+ / +	- / -	- / -
26	- / -	++ / ++	++ / ++	++ / ++
27	+ / +	+++ / +++	++ / ++	++ / ++
28	+ / +	++ / +++	+ / +	+ / +
29	- / -	+ / +	- / -	- / -
30	- / -	+ / +++	+ / +	+ / +
31	- / -	+ / +	+ / -	- / -
32	- / -	+ / +	+ / +	- / -
33	+ / +	++ / ++	++ / ++	++ / ++

Case No.	Knee Jerk	Ankle Jerk	Tibial Tap	Plantar Tap
34	- / -	- / -	- / -	- / -
35	- / +	++ / +	- / +	+ / -
36	- / -	+ / +	++ / ++	+ / +
37	- / -	+ / -	- / -	+ / +
38	- / -	- / -	- / -	- / -
39	- / -	- / -	- / -	- / -
40	- / -	- / -	- / -	- / -
41	- / -	++ / ++	++ / +	++ / +
42	++ / ++	++ / ++	++ / ++	++ / ++
43	- / -	+ / +	- / -	+ / +
44	- / -	- / -	- / -	- / -
45	- / -	- / -	- / -	- / -
46	- / -	++ / +	- / -	+ / +
47	- / -	- / -	- / -	- / -
48	- / -	++ / ++	+++ / ++	++ / +
49	- / -	++ / +	- / -	+ / -
50	- / -	+ / +	+ / +	+ / +
51	?	?	?	?
52	- / -	+ / +	++ / ++	+ / +
53	- / -	- / -	- / -	- / -
54	- / -	+ / +	+ / -	+ / +
55	- / -	- / -	- / -	- / -
56	+ / +	+ / +	- / -	+ / +
57	+ / +	- / -	- / -	- / -
58	- / -	- / -	- / -	- / -
59	- / -	++ / +	++ / -	+ / -
60	- / -	+ / +	- / -	- / -
61	- / -	+ / +	- / -	+ / +
62	- / -	- / -	- / -	- / -
63	- / -	+ / +	- / -	+ / +
64	- / -	++ / ++	++ / ++	++ / ++
65	- / -	- / ++	- / -	- / -

APPENDIX IV. TABLE IV. 9. E.C.G. CHANGES (case 1-33)

Case No.	Heart rate	P - R	P>3 in II; P>2.5 in others	QRS	Q + in V_1	R/S V_1	R/S V_5	R/S AVR	ST segment elevated depressed	T flat; or inverted;	U waves	QTC	Scoliosis	Age
1.	100	0.12				4.1	∞	0.14		All leads		0.39	-	13
2.	78	0.12				1.4	3.2	0.6				0.39	-	16
3. a.	136	0.12				0.7	∞	0.5					L	16
b.	136	0.12				0.7	∞	0.5				0.39	L	17
4. a.	136	0.13		BBB	III, $V_{6,7}$	1.6	6.6	0.14		II, III, V_{1-3}		0.40	R	13
b.	79	0.12				6.0	6.0	0.5					R	15
5.	108	0.13			III	1.0	∞	0.6		L.V.		0.44	R	13
6.	84	0.13				1.2		0.14				0.35	-	15
7.	94	0.12				4.0	5.6	0.14				0.39	-	10
8.	116	0.12										0.38	-	10
9.	100	0.16				1.0	∞	0.2		I, V_3	V_2	0.38	-	11
10.	125	0.12				0.6	∞	0.2		Ly.		0.38	-	13
11.	86	0.15				2.6	6.0	0.4				0.37	-	12
12.	108	0.12				4.0		0.14				0.36	-	11
13.	84	0.12				12.0	12.0	0.16				0.42	R	16
14.	60	0.09		?W-P-W.*		1.0	4.0	0.5			?	0.38	L	14
15.	100	0.10				1.3		0.14			?	0.36	L	12
16.	86	0.15			V_3	1.4	8.0	0.3		V_3, V_7	V_2;3;7.	0.36	-	15
17.	116	0.10			$V_{1,3-7}$			0.25				0.38	L	12
18.	125	0.10				2.0	2.0	1.0				0.44	L	15
19.	108	0.12			V_{3-7}	0.9				V_{1-3}		0.40	R	12
20.	84	0.14			II, V_{3-7}	1.1	∞	1.0		V_{3-7}		0.39	L	14
21.	92	0.12				1.1	3.6	0.2				0.38	-	7
22.	94	0.12				0.5	∞						-	7
23.	84	0.12		BBB								0.42	R	15
24.	100	0.12	+		V_{3-7}	∞	∞	0.14			V_2	0.39	-	11
25.	100	0.12			II, III, V_{4-7}	0.8	21.0	0.25	↓ III			0.39	R	12
26.	150	0.12				1.5	∞	0.38	↓ I, II		V_2	0.37	-	11
27.	125	0.12			III	2.0	8.0	0.25				0.40	-	8
28.	80	0.12			II, III, V_{3-7}	∞	∞					0.37	-	6
29.	75	0.13		BBB								0.40	L	16
30.	116	0.12	+			11.0	∞	0.4			V_{1-3}	0.38	L	12
31.	120	0.14				1.8	25.0	0.13				0.40	-	11
32.	74	0.12				1.5	8.0					0.37	L	14
33.	108	0.14				1.0	1.0	0.25			V_{1-3}	0.39	L	10

* Wolff-Parkinson-White Syndrome.

APPENDIX IV. TABLE IV. 10. E.C.G. CHANGES (case 34-57)

Case No.	Heart rate	P - R	P>3 in II; P>2.5 in others	QRS	Q + in V_1 >2mm in others	R/S V_1	R/S V_5	R/S AVR	ST segment elevated↑ depressed↓	T flat or inverted	U waves	QTC	Scoliosis	Age
34.	100	0.13				1.0	∞	0.6				0.40	L	12
35.	108	0.14				9.0	1.0	2.0	↓V_1	V_{3-7}		0.38	-	13
36.	125	0.13			I, III, V_3.	∞	8.0	0.3	↑III, ↓V_2			0.40	-	12
37. a.	84	0.12				1.2	∞	0.3			V_{1-7}		L	14
b.	84	0.14				1.0	4.0				V_{1-2}		L	16
38.	100	0.10											L	10
40.	116	0.12				0.13	2.5	0.08			V_{2-3}	0.41	R	13
41.	116	0.14				1.0	∞	0.13		L.V.	V_1	0.38	-	10
42.	108	0.14				1.0	∞	0.3			V_2		-	9
43.	106	0.12			II, V_{3-7}	1.0		0.25					L	11
44. a.	100	0.12			V_{5-7}	3.3	∞	0.25		I	V_{1-4}		-	15
b.	136	0.10				2.0		1.0	↑V_{4-6}				-	16
c.	125	0.12	+		I, V_{5-7}	0.6		1.0	↑ $V_{5,6}$				-	16
45.	68	0.12		BBB	V_7							0.38	-	14
46.	108	0.12				3.5	∞	0.2		All leads		0.41	-	13
47.	88	0.12				0.7	∞	033			V_{2-3}	0.41	-	15
48.	136	0.12			II, III, V_{3-5}	0.5	∞	0.44		I, V_1		0.40	L	16
49.	98	0.12			II, III, V_{4-7}	1.0	∞	0.3				0.39	-	9
50.	108	0.12				0.2	∞	0.2				0.36	L	12
51.	100	0.12				1.2	∞	0.14			V_2	0.39	R	10
52.	136	0.13				-	-	0.14				0.39	-	3
53.	84	0.14		BBB								0.40	R	17
54.	136	0.12				1.0	∞		↓ V_{1-3}				L	12
55.	100	0.12		BBB								0.38	L	13
56.	94	0.14				0.9	∞	0.14				0.38	-	11
57.	136	0.13				0.9	∞	0.5	↓ V_1		V_2	0.39	-	7

A C K N O W L E D G E M E N T S.

Without the help and co-operation of many people this work would have been impossible, and I welcome this opportunity of recording my sincere thanks and gratitude to them.

First and foremost, Dr. David Lawson, Physician Superintendent at Queen Mary's Hospital for Children. Throughout the course of this study his guidance, advice and constructive criticism have been of inestimable value. I am also grateful to him for the opportunity of studying the patients under his care on the Muscular Dystrophy Unit, and appreciate all the excellent facilities he has made available to me.

I am indebted to Professor P.M. Daniel of The Institute of Psychiatry at Maudsley Hospital, for his stimulating interest in this work and for teaching me the fundamentals of muscle pathology. I appreciate his advice and encouragement and am also grateful to him and members of his Staff for the Autopsy examinations.

I wish to express my appreciation to Dr. A.G. Everson Pearse, of the Post-graduate Medical School, for opening up new pathways for me in the realm of histochemistry. His enthusiasm and intellect have been a great source of inspiration. I am also grateful to him for the excellent facilities he has given me in his department.

I also wish to record my gratitude to the following persons who have contributed much to this work.

Mr. R.M. Metcalfe and Mr. R.G. Thomas, Consultant Orthopaedic Surgeons at Queen Mary's Hospital, for their encouragement and advice, and for the opportunity of examining a large number of children with muscular dystrophy under their care.

Dr. W.E.R. Budd, Physician Superintendent at the Southern Hospital, Dartford, for the opportunity of studying patients in his care.

Dr. C.E. Thornton and Dr. Arthur Hollman (Post-graduate Medical School) for their expert advice in the interpretation of the electrocardiograms.

Professor R.H.S. Thompson and Dr. Brian McArdle, of Guy's Hospital, for their help and advice with the serum enzyme estimations and the therapeutic trial.

Dr. A.T. Richardson, of the Royal Free Hospital, for the electromyographic studies.

A number of surgical registrars at Queen Mary's Hospital for their ready help with the muscle biopsies. I am also grateful to all my colleagues on the medical staff at Queen Mary's Hospital, for their help and encouragement. I wish to thank especially Dr. Marjorie Semmens for the assistance, advice and constructive criticism she has given me on numerous occasions in the course of this work.

Mr. R.J.S. Reynolds, Superintendent Physiotherapist at Queen Mary's Hospital, who was in a large part responsible for initially stimulating my interest in this disease, for all his help, advice and many suggestions. Also to the various members of his Staff who gave me invaluable assistance with the assessment of the patients.

Miss E.J. Shearn, Deputy Headmistress at Queen Mary's Hospital School, for the enthusiasm and efficiency with which she helped me in the assessment of intelligence of the children.

Sisters F.J. Rayment and E. Daniels and Staff Nurse E. Parks, as well as all the other members of the nursing and auxillary staffs, for all the help and co-operation and for the efficient way in which they have played their part in many of the investigations.

Miss Mary Pugh has contributed all the excellent clinical photographs and has also done the electrocardiographic tracings.

The most arduous task of preparing the manuscript has been undertaken by Miss Anne Faulds and I appreciate the most efficient manner in which she has coped.

I gratefully acknowledge the generous financial support, in the form of a research fellowship, which has been given me by the Muscular Dystrophy Group.

Last, but not least, I have a special debt to my wife, not only for the immense amount of direct help in the preparation of this thesis, but also for her tolerance and good humour, in what must certainly be looked upon as a novel way of spending a honeymoon.

BIBLIOGRAPHY.

ADAMS, R.D., DENNY-BROWN, D., and PEARSON, C.M. (1953)
Diseases of Muscle - A Study in Pathology. New York : Hoeber.

ADAMS, W. (1868), Trans. Path. Soc. Lond. 19, 11 (case report)

ARAN, F.A. (1850). Réchèrches sur une maladie non encore décrite du systéme musculaire. (Atrophic musculaire progressive).
Archiv. Gén. de Med. 24, 5, 172.

BADHAM, J., (1835).Paralysis in childhood; four remarkable cases of suddenly induced paralysis in the extremeties occurring in childhood without any apparent cerebral or cerebro-spinal lesions.
Lond. med. Gaz. 17, 215.

BATTEN, F.E., (1910). The myopathies or muscular dystrophies.
Quart. J. Med. 3, 313.

BAY, N.H., (1877). Tre tilfaelde af pseudohypertrofia muscularis.
Hosp. tid. 4, 441

BECKER, P.E., (1953). Dystrophia Musculorum Progressiva. Ein genetische und klinische Untersuchung der Muskeldystrophien.
Stüttgart : Thieme.

BECKER, P.E., (1955). Zur Genetik der Myopathien.
Dtsch. Z. Nervenh. 173, 482.

BECKER, P.E., (1957). Neue Ergebnisse der Genetik der Muskeldystrophien.
Acta. genet. 7, 303.

BELL, C., (1830). The Nervous System of the Human Body.
Longmans : London. Appendix p. 161.

BELL, J., (1943). On Pseudohypertrophic and allied types of Progressive Muscular Dystrophy. The Treasury of Human Inheritance (4)
London : Cambridge Univ. Press.

BERENBAUM, A.A., AND HOROWITZ, W., (1956). Heart involvement in progressive muscular dystrophy; report of a case with sudden death.
Amer. Heart J. 51, 622

BERGENON, (1867). Hypertrophie Musculaire. Gaz. des Hosp. 40, 249

BEVANS, M., (1945). Changes in the musculature of the gastrointestinal tract and in the myocardium in progressive muscular dystrophy.
Archiv. Path. 40, 225.

BLYTH, H., AND PUGH, R.J., (1959). Muscular dystrophy in childhood. The genetic aspect. Ann. hum. Genet., Lond., 23, 127.

BOAS, E.P., and LOWENBERG, H., (1931). The heart rate in progressive muscular dystrophy. Arch. int. Med. 47, 375.

BRAMWELL, E. (1925). The muscular dystrophies, sympathetic system, and endocrine glands. Lancet, 2, 1103.

BRÜNNICHE, (1874). Tilfaelde af pseudohypertrofisk muskelparalyse.
Nord. Med. Ark., 2, 257.

BUCHTAL, F., (1957). An introduction to electromyography. Copenhagen : Gyldendal. (pp 43).

CABAUD, P., LEPER, R., and WROBLEWSKI, F., (1956). Colorimetric measurement of serum glutamic oxaleacetic transaminase. Amer. J., clin. Path. 26, 1101.

*COSTE and GIOJA. (1838). Ann. clin. esp. incur. Nap. (Quoted by: Schmidt, 1839).

DARWELL, J. (1830). Cases of a peculiar species of paralysis. Lond. med. Gaz. 7, 201.

DAVIDENKOW, S., (1930). Ueber die Vererbung der Dystroph. musc. prog. und ilurer Unterformen. Arch. Rass. Gesellsch. biol. 22, 169.

DIEHL, F., HANSEN, K., and v. UBISCH, G., (1927). Der Erbgang der Dystroph. musc. progr. Dtsch. Z. Nervenh. 99, 54.

DUBOWITZ, V. (1960). Progressive muscular dystrophy of the Duchenne type in females and its mode of inheritance. Brain, in press.

DUBOWITZ, V., and PEARSE, A.G.E. (1960). Reciprocal relationship of phosphorylase and oxidative enzymes in skeletal muscle. Nature, 185, 701.

DUBOWITZ, V., and PEARSE, A.G.E. (1961). Enzymic activity of normal and dystrophic muscle. A histochemical study. J. Path. Bact., in press.

DUCHENNE, G-B., (1861). De l'Electrisation Localisée et son Application à la Pathologie et à la Thérapeutique. Paris : Baillierr et Fils, 2nd. ed.

DUCHENNE. G.B. (de Boulogne). (1867). Physiologie des Mouvements. Paris : J.-B. Bailliere et Fils. pp. 872.

DUCHENNE, G-B., (1868). Recherches sur la paralysie musculaire pseudohypertrophique ou paralysie myosclerosique. Arch. Gén. Méd., 6 sér., 11: 5, 179, 305, 421, 552.

DUCHENNE, G-B., (1872). De l'Electrisation localisée et son application à la Pathologie et à la Thérapeutique. Paris : Bailliere et Fils, 3rd ed.

ERB, W.H., (1884). Ueber die "juvenile form" der progressiven Muskelatrophie; ihre Beziehungen zur sogenannten Pseudohypertrophie der Muskeln. Dtsch. Arch. klin. Med., 34, 467.

ERB, W.H., (1891). Dystrophia muscularis progressiva. Klinische und pathologisch - anatomische Studien. Dtsch.Ztschr. Nervenh. 1, 13, 173

EULENBURG, A. von., (1865). Ueber muskelhypertrophie. Berl. klin. Wschr. 2, 490.

EULENBURG, A. von., and COHNHEIM, R., (1866). Ergebnisse der anatomischen Untersuching einer Falles von sogenannter Muskelhypertrofie. Verh. Berl. Med. Ges., 191, 210.

EVANS, J.H., and BAKER, R.W.R., (1957). Serum aldolase and the diagnosis of myopathy. Brain, 80, 557.

* This reference could not be traced in the journal cited.

FOSTER, B.W., (1869). Paralysis with apparent muscular hypertrophy. Lancet i, 629.

FRIEDREICH, N., (1873). Ueber Progressive Muskel atrophie, uber wahre und falsche Muskelhypertrophie. Berlin : Hirshwald.

FRITZ, (1865). Remarques sur les paralysies avec surcharge graisseuse interstitielle. Gaz. hebdom. 34, 529.

GAILANI, S., DANOWSKI, T.S., and FISCHER, D.S. (1958). Muscular dystrophy. Catheterization studies indicating latent congestive heart failure. Circulation. 17, 583.

GIANNINI, A., and DEL CARLO GIANNINI, G., (1959). Ricerche elettrocardiografiche nelle distrofia muscolare progessiva. Sast. nerv. 11, 291.

GLOBUS, J.M., (1923). The pathelegical findings in the heart muscle in progressive muscular dystrophy. Arch. Neurol. Psychiat., 9, 59.

GOWERS, W.R., (1879). Clinical lecture en pseudehypertrephic muscular paralysis. Lancet, ii, 1; 37; 73; 113.

GOWERS, W.R., (1879). Pseudehypertrephic muscular paralysis. A clinical lecture. London : J.A. Churchill. pp. 66.

GRANDELL, F., (1956). The heart in progressive muscular dystrophy. Amer. J. med. Sei. 231, 659.

GREENFIELD, J.G., SHY, G.M., ALVORD, E.C., and BERG, L., (1957). An Atlas of Muscle Pathology in Neuromuscular Diseases. London : E. & S. Livingstone, pp. 104.

GRIESINGER, W., (1865). Ueber Muskelhypertrophie. Arch. d. heilk. 6, 1.

HALDANE, J.B.S., (1935). The rate of spontaneous mutation of human genes. J. Genet. 31, 317.

HANHART, E., (1949). On a large Swiss family with simple recessive progressive muscular dystrophy. (Duchenne-Griesinger's type). Hereditas, Lund. Supl. vol. p.586.

HELLER, A., (1866). Klinische Beobachtunger uber die bisher als "Muskelhypertrophie" bezeichnete Lipomatosis luxurians musculerum progressiva. Dtsch. Archiv. f. klin. Med. 1, 616.

HELLER, A., (1867). Nachtrag zu den klinischen Beobachtungen über die bisher als Muskelhypertrophie bezeichnete Lipomatosis luxurians musculerum progressiva. Dtsch. Archiv. f. klin. Med. 2, 603.

HILLIER., (1868). Trans.Path. Soc. Lond. 19, 12 (case report).

HOFFMANN, J., (1892). Ueber familiäre progressive spinale muskelatrophie. Arch. Psychiat. Nervenh. 24, 644.

HURWITZ, S., (1936). Primary myopathies. Report of 36 cases and a review of the literature. Arch. Neurol. Psychiat. 36, 1294.

ILLINGWORTH, R.S., (1957). The Normal Child. London : Churchill.

INGALLS, W., and WEBBER, S.G., (1870). A case of progressive muscular sclerosis, with a paper on the same. Boston med. surg. J. 6, 321.

KAULICH, (1862). Muskelhypertrophie mit paralyse. Prag. Vierteljahrsschr. 73, 113.

KENNEDY, M., (1841). Observations on Paralytic affections met with in Children. Dublin med. Press. 6, 201.

LANDOUZY, L., and DÉJERINE, J., (1884). De la myopathie atrophique progressive (myopathie héréditaire) débutant, dans l'enfance, par la face, sans altération du système nerveux. Comp. Rend. Acad. Sci., Paris. 98, 53.

LANDOUZY, L., and DEJERINE, J., (1885). De la myopathie atrophique progressive; myopathie sans neuropathie, debutant d'ordinaire dans l'enfance, par la face. Rev. de Med. 5, 81, 253.

LANGDON-DOWN, (1870). Med. Times, 1, 376. (case report).

LEVISON, M., (1951). Dystrophia Musculorum Progressiva, Clinical and Diagnostic Criteria; Inheritance. Copenhagen : Moller.

LEYDEN, E., (1876). Klinik der Rückenmarks - Krankheiten. Berlin : Hirschwald, 2, 447.

LOCKHART, R.D., (1960). The Anatomy of Muscles and their relation to Movement and Posture. London : Acad. Press. 1960, p.1. In "Structure and Function of Muscle." Edit: G.H. Bourne.

MANNING, G.W., and CROPP, G.J., (1958). The electrocardiogram in progressive muscular dystrophy. Brit. Heart J. 20, 416.

MANZINI, B., and FRATTOLA, L., (1958). Azione di estratti di mucosa gastrica du maiale nella distrofia muscolare progressiva proropatica. Boll. Soc. ital. Biol. sper. 34, 23.

MEERWEIN, (1904). Verhaltnisse von Herz und Zunge bei den primaren myopathien. Dissertation. Basle. 1904. (Quoted by Beas and Lowenberg, 1931.)

MERYON, E., (1852). On granular and fatty degeneration of the voluntary muscles. Med. Chir. Trans. 17, 73.

MERYON, E., (1864). Practical and Pathological Researches on the various forms of Paralysis. London : J. Churchill.

MILHORAT, A.T., and WOLFF, H.G., (1943). Studies in diseases of muscle. Hereditary of progressive muscular dystrophy; relationship between age at onset of symptoms and clinical course. Arch. Neurol. Psychiat., Chicago, 49, 641.

MINKOWSKI, M., and SIDLER, A., (1928). Klinische und genealogische Untersuchungen zur Kenntnis der progr. Muskeldystrophie. Arch. d. Julius Klaus Stift. 3, 239.

MÖBIUS, P.J., (1879). Ueber die hereditären Nervenkrankheiten. Samml. klin-Vertr., (inn. med)., 171, 1505.

MOORE, W.F., (1954). Cardiac involvement in progressive muscular dystrophy. J. Pediat. 44, 683.

NATTRASS, F.J., (1954). Recovery from"Muscular Dystrophy." Brain. 77, 549.

NOTHACKER, W.G., and NETSKY, M.G., (1950). Myocardial lesions in progressive muscular dystrophy. Arch. Path. 50, 578.

OPPENHEIM, M., (1904). Ueber einen Fall von Myatonia Congenita. Berl. klin. Wschr., 41, 255.

PARTRIDGE. (1847). Lond. med. Gaz. 40, 944.

PEARSON, C.M., (1954). Serum enzymes in muscular dystrophy and certain other muscular and neuromuscular diseases. I. serum glutamic oxaleacetic transaminase. New Engl. J. Med. 256, 1069.

PIETZ, D.G., and PINSKY, S.T., (1956). Progressive muscular dystrophy with involvement of the heart; a case report. J. Ind. Med. Ass. 49, 161.

PUDDU, V., and MUSSAFIA, A., (1939). L'electrocardiogramme dans la dystrophie musculaire progressive. Arch. Mal. Coeur, 32, 958

ROSS, J., (1883). On a case of pseudo-hypertrophic paralysis. Brit. Med. J., 1, 200.

RUBIN,I.L., and BUCHBERG, A.S., (1952). Heart in progressive muscular dystrophy. Amer. Heart J. 43, 161.

RUSSELL, J., (1869). Two cases of Duchenne's paralysis and muscular degeneration, or paralysis with apparent hypertrophy - family history of concurrent paralysis : microscopic appearance of the affected muscles. Med. Times, 1, 571.

SCHAPIRA, G., DREYFUS, J.C., and SCHAPIRA, F., (1953). L'elevation du taux de l'aldolase serique: test biochimique des myopathies. Sem. Hôp. Paris. 29, 1917.

SCHOTT, J., JACOBI, M., and WALD, M.A., (1955). Electrocardiographic patterns in the differential diagnosis of progressive muscular dystrophy. Amer. J. Med. Sci. 229, 517.

SCHMIDT, C.C., (1839). Krankhafte Hypertrophie des Muskelsystems. Jahrbücher der In-und Aüslandischen gesamenten Medicin, 24, 176.

SEIDEL, M., (1867). Die Atrophie Musculorum Lipomatosa. (Segenannte Muskelhypertrophie). Jena.

SIGMUNDT, C., (1866). Ueber Muskellähmung in folge von Hypertrophie der interstitiellen Fett-und Bindegewebes. Dtsch. Arch. Klin-Med. 1, 630.

SJÖVALL, B., (1936). Dystrophia musculorum progressiva. Eine erblich keits medizinische und klinische Studie. Acta Psychiat. Neurol. Suppl. 10.

SMITH, W., (1871). On paralysis with apparent hypertrophy of the muscles. Austr. Med. J. 16, 161.

SPIELMAN, (1862). (Quoted by Griesinger, 1865).
Gaz. Méd. Strassbourg, 5, 85.

SPILLER, W.G., (1913). The relation of the myopathies. Brain, 36, 75.

STEINERT, H., (1909). Myopathologische Beitrage: 1. Ueber das klinische und anatomische Bild des Muskelschwunds der Myotoniker. Dtsch. Z. Nervenheilk. 37, 58.

STEPHENS, F.E., and TYLER, F.H., (1951). Studies in disorders of muscle; inheritance of childhood progressive muscular dystrophy in thirty-three kindreds. Amer. J. Hum. Genet. 3, 111.

STEVENSON, A.C., (1953). Muscular Dystrophy in Northern Ireland. 1. An account of the condition in fifty-one families.
Ann. Eugen. Lond. 18, 50.

STEVENSON, A.C., (1955). Muscular dystrophy in Northern Ireland. II. An account of nine additional families.
Ann. Hum. Genet., Lond., 19, 159.

STEVENSON, A.C., (1958). Muscular dystrophy in Northern Ireland. IV. Some additional data.
Ann. Hum. Genet., Lond., 22, 231.

TOURNIAIRE, A., FOURNIE, G., BLUM, J., and SEMET, J., (1955). Le coeur dans la myopathie. Arch. Mal. Coeur, 48, 738.

THOMSEN, J., (1876). Tonische Krämpfe in willkürlich beweglichen Muskeln in folge von ererbter psychischer Disposition. (Ataxia muscularis?). Arch. Psychiat. Nervenk. 6, 702.

TYLER, F.H., and STEPHENS, F.E., (1950). Studies in disorders of muscle. II. Clinical manifestations and inheritance of facio-scapulo-humeral dystrophy in a large family.
Ann. Int. Med. 32, 640.

TYLER, F.H., and WINTROBE, M.M., (1950). Studies in disorders of muscle: 1. The problem of progressive muscular dystrophy.

UNDERWOOD, M., (1784). A Treatise on diseases of children.
J. Matthews, London. ed. 1. (1797) ed. 3.

UNDERWOOD, Michael, (1826). A Treatise on disease of children.
ed. 8. Edit. by J. Merriman. p. 439.

VAN PHAN, N., and ERDMANN, T., (1959). Herzmuskelveranderungen bei progressiver Muskeldystrophie. Z. Kinderheilk, 82, 412.

WACHSMUTH, A., (1855). Ueber progressive Muskelatrophie.
Zeitsch. Rat. Medicin. 7, 1.

WALTON, J.N., (1955). On the inheritance of muscular dystrophy.
Ann. Hum. Genet., Lond., 20, 1.

WALTON, J.N., (1956). The inheritance of muscular dystrophy: further observations. Ann. Hum. Genet., Lond., 21, 40.

WALTON, J.N., and ADAMS, R.D., (1958). Polymyositis. London : Livingstone.

WALTON, J.N., and NATTRASS, F.J., (1954). On the classification, natural history and treatment of the myopathies. Brain, 77, 169.

WEISENFELD, S., and MESSINGER, W.J., (1952). Cardiac involvement in progressive muscular dystrophy. Amer Heart J. 43, 170.

WEITZ, W., (1921). Ein Schlusswort zur Frage des Erbganges der Dystrophia musc. progr. Dtsch. Z. Nervenh. 107, 316.

WERDNIG, G., (1891). Zwei fruhinfantile hereditare Falle von progressiver muskelotrophie unter den bilde der dystrophie, aber auf neurotischer grundlage. Arch. Psychiat. Nervenh. 22, 437.

WERNICH, A., (1867). Fall von Muskelhypertrophie. Dtsch. Archiv. f. klin. Med. 2, 232.

WEST, CHARLES. (1847). Lecture on the disease of infancy and childhood. Lon. med. Gaz. 40, 605.

ZATUCHNI, J., AEGERTER, E.E., MOLTHAN, L., and SHUMAN, C.R., (1951). The heart in progressive muscular dystrophy. Circulation, 3, 846.

ZIEGLER, R.F., (1951). Electrocardiographic studies in normal infants and children. Springfield : Thomas.

ADDENDUM.

GOWERS, W.R. (1902) A lecture on myopathy and a distal form. Brit.med.J. 2, 89.

NEVIN, S. (1936) Two cases of muscular degeneration occurring in late adult life, with a review of the recorded cases of late progressive muscular dystrophy (late progressive myopathy). Quart.J.Med. 5, 51.

WOHLFART, G. (1937) Über das Vorkommen verschiedener Arten von Muskelfasern in der Skelettmuskulatur des Menschen und einiger Säugtiere. Acta psychiat.Kbh., Suppl.12.