Clinical lecture on a case of progressive muscular sclerosis (pseudo-hypertrophic muscular paralysis of duchenne). / by William Pepper.

CLINICAL LECTURE

ON A CASE OF PROGRESSIVE MUSCULAR SCLEROSIS (PSEUDO-HYPERTROPHIC MUSCULAR PARALYSIS OF DUCHENNE).

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W. E., æt. 20, was admitted to the Philadelphia Hospital, April 19, 1871. He was born in Virginia, and has resided there or in the District of Columbia until the present time. His parents are both dead,—his father from cholera, his mother from some unknown cause. He had two sisters and a brother, all of whom are dead,—two from unknown causes; but one sister had paralysis (apparently hemiplegia), and was unable to walk for some time before her death. The patient himself was a delicate and weakly child so far back as he can recollect. He never suffered either from malaria or rheumatism. He was engaged in the country on a farm, and his strength was overtasked by heavy lifting. He never, however, met with any injury. Six years ago he began to notice gradually increasing loss of strength in the legs, which progressed so slowly that for eighteen months he was still able to run about, though not so actively as other boys. He was not obliged to use a cane until two years ago, and since then only in walking considerable distances. This gradually increasing debility was attended with no pain, formication, or subjective sense of change of temperature in the legs. There were also no contractions or cramps of the muscles. The progressive debility had not continued long before he noticed that it was necessary, when he was standing or walking, to throw his shoulders back and protrude his

abdomen and lower part of the thorax, thus showing that the muscles of the back were affected at a very early date. During this early period he could walk quite naturally, but in running he threw his shoulders far back and stretched his legs widely apart; he assumed the same position also in going up an elevation. Two years later the muscles of the arms became affected in the same way as those of the legs and back. During the first three years he merely noticed that the legs did not grow as they should do, but afterwards atrophy began, first in the muscles of the calves, shortly after in those of the thighs and of the back, and soon afterwards in those of the shoulders and arms. About two years ago, after the atrophy of the muscles of the calves had become very marked, he noticed that they began to increase in size, and this growth has continued until they have acquired a size much greater than they ever had previously. This process of renewed growth next appeared, about one year ago, in the muscles of the forearm, and has continued at a slow rate. During all this time his weakness has steadily increased; he has, however, never been kept in bed by it, but has been able to get about feebly by the aid of a cane. He has never had a sense of constriction about any part of the body. His appetite throughout has been good, his digestion fair, and bowels regular. His urine has always been passed with ease, and has merely been noted to be occasionally yellow. About one year ago he was seized, without any apparent cause, with a severe epileptic convulsion, and since that time he has had similar attacks at intervals of from fifteen to thirty days. He has usually been unable to tell when these fits were coming on, but occasionally he has had a strange feeling in the head, and has thought of foolish things, before the attacks. The fits have been attended with entire unconsciousness, sudden falling to the ground, and muscular convulsion. He has usually been half a day in entirely recovering from them. He has never had more than two convulsions on the same day.

Present condition.—His expression is natural, mind active, and special senses unaffected. The muscles of the face are not involved, and their action is perfect. His tongue is clean and moist, appetite fair, digestion easy, and bowels regular. There is no enlargement of the abdominal viscera. The urine is normal and secreted in normal quantity. His respirations are easy, twelve in the minute, chiefly diaphragmatic: the vesicular murmur is soft and healthy. The cardiac sounds are normal. The pulse is 75, in the recumbent position.

Muscular system.—The muscles of the neck (sterno-cleido-

mastoids and extensors of the head) are of fair size, and their movements are strong and free. The trapezii are feeble, and he retracts the shoulders with difficulty and feebly. The pectoral muscles are moderately wasted and feeble. The scapular group of muscles are less wasted, and the scapulæ do not project markedly from the thorax, so that the serrati magni are probably not much wasted and enfeebled. The deltoids are extremely wasted, and he is unable to raise either arm within thirty degrees of the horizontal plane; when the arm is raised, there is a marked depression below the acromion process. The biceps muscles are also extremely wasted, and he is able to flex the forearm only a little beyond a right angle. The triceps muscles are also very feeble, and the long head of each is greatly wasted, while the external and short heads appear as quite prominent fleshy masses.

The forearms seem unduly large in comparison with the atrophied arms, and are in reality larger than they have ever previously been. They have, moreover, a peculiar blunt and swollen appearance, owing to the sudden enlargement of the muscles above the wrists. The atrophy of the forearms seems never to have reached the degree attained elsewhere, so that the degree of consecutive hypertrophy has not been so marked as in the calves. The grasp of the hands is decidedly weaker than would be expected from the size of the forearms, that of the right being much weaker than that of the left hand. There has been no atrophy of the muscles of the hands.

When he sits up in bed, he is only able to hold the shoulders back with effort; there is increased bowing forward of the vertebral column, with absence of the lumbar depression. There is decided wasting of the erector spinæ muscles on either side. When lying in bed, the lumbar spine is raised, so that the obliquity of the pelvis and hypogastric region is increased. The muscles of the abdomen and thorax are not wasted, and preserve good strength.

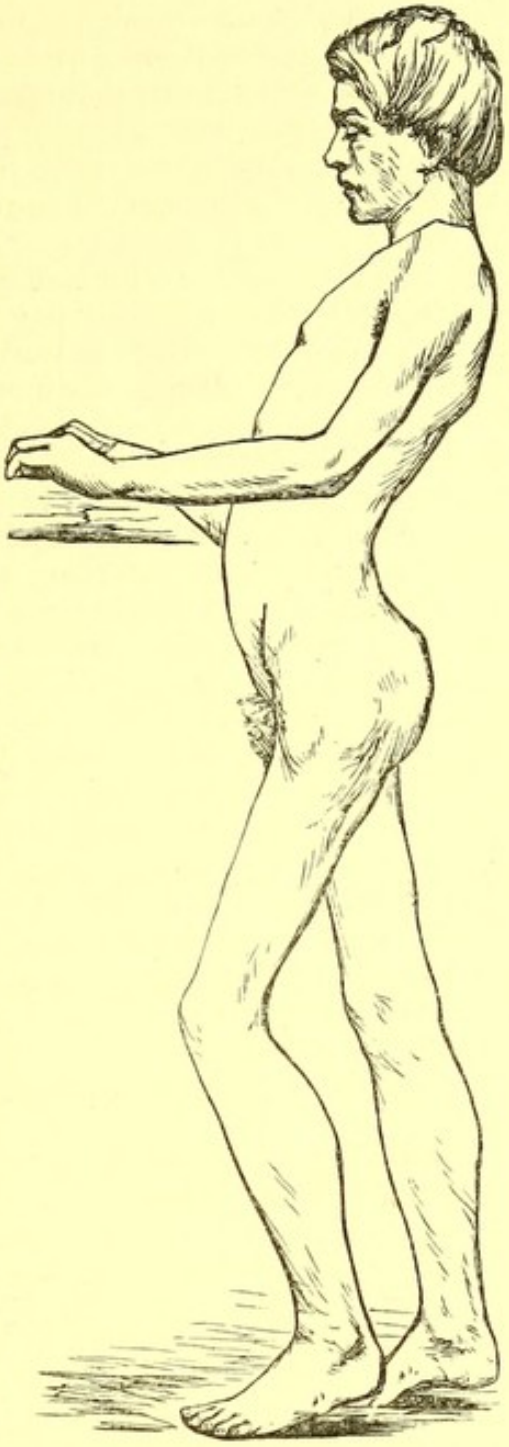
When he is lying down, the feet are strongly extended and adducted (equino-varus), so that the toes point towards each other, while the soles rest on the bed. There is great prominence of the tarsus. The muscles of the thighs are all much wasted, as are those of the buttocks. It is with difficulty that, when lying down, he can draw up the legs by the action of the flexor muscles. He has much more power of extending them by the quadriceps extensors. The rotators, abductors, and adductors of the thighs are much less affected. He can move in bed only by a wriggling motion.

The calves appear as large as those of a vigorous man, contrasting very strangely with the wasted thighs. They feel quite firm, even when relaxed, and when he contracts the muscles they stand out well, and are hard and elastic. The heads of the gastrocnemii especially become prominent, standing out like firm subcutaneous tumors. He has considerable power of flexing, adducting, and abducting the feet, but the extensors are very feeble. The muscles of the right thigh and leg are decidedly stronger than the corresponding ones of the left side.

In rising from the recumbent position into a sitting one, he is obliged to make a very strong effort. When about to stand up, he throws his body forward till it almost rests on his thighs, and then, placing his hands on his knees and rising a little from his seat, he slowly raises his body by sliding his hands up his thighs; and when he has raised himself as far as possible in this way, he places one hand after the other on a chair-back or edge of a table, and leans forward. He then, by jerks of the alternate sides of the body, draws his legs forward, thus assuming more and more nearly an erect position. So soon as he approaches this, the legs are widely separated, the shoulders thrown quickly back, and the abdomen protruded, and, after tottering a few times, he secures his equilibrium in this peculiar position. It is very tiresome for him to stand without some support, and when he does so he bears with his whole weight on the right foot, the sole of which rests flat on the ground, while the left leg is thrown forward in advance, and the heel elevated from the ground. When a support is afforded him, he places both hands on it, and leans forward, rising on the balls of the feet, so that the heels are raised one-half inch from the ground. (See figure.) In this position he stands for half an hour or more at a time. The muscles of the calves are contracted and thrown into prominent relief.

In walking, as in standing, the shoulders are thrown very far back, and the lumbar depression is rendered very deep; the arms hang down by the sides, coming decidedly behind the line of the buttocks. The legs are kept quite widely apart. He advances each one by resting his weight on the opposite foot, and then swinging forward the whole side, the foot describing a slight arc. At the moment of thus swinging forward either leg, he rises slightly on the opposite foot. While standing on the right foot, the whole sole rests on the ground, though the heel merely touches it lightly; but when his

weight is thrown entirely on the left leg, the left heel still does not touch the ground. The effort of advancing each leg is evidently great; the muscles of the thighs tremble and quiver, but those of the calves contract forcibly and are thrown into bold relief. Walking is very tiresome, and gives him pain and soreness in the back. No fibrillar contractions are seen in any of the muscles.



Electric examination, April 23, 1871.—The muscles of the forearm (tested on the right side) contract well under a faradaic current of rather unusual strength; they also respond well to faradization of the brachial plexus. Electro-muscular sensibility is not acute, though this may be a mere individual peculiarity. The muscles of the arm, the pectoralis major, and the trapezius all contract on faradization, whether direct or applied to their motor points. It requires rather too powerful a current to produce these effects. A still more powerful current is required to induce contraction of the thigh-muscles, but they all respond, though feebly: the sensibility to the current is impaired. The contractions of the flexors of the leg on the thigh are the most feeble, and are obtained only by very strong currents. The muscles of the leg respond more actively than the muscles of the thigh, whether the electrode

is placed over the nerve in the thigh, or on the motor point of the muscle, or directly over its body.

When tested with a galvanic current, the muscles of the calves of the legs contract with each interruption and renewal of a current of rather unusual strength (twenty cells, Stöhrer), and electro-muscular sensibility is acute. The muscles of the thighs also respond, but with more difficulty, to the galvanic current.

The following measurements were taken:

Right arm, greatest circumference	7 inches.
" forearm, circumference one inch above wrist	6 "
" " " at middle	8¼ "
" " " three inches below elbow, point of greatest thickness	8½ "
" thigh, circumference hand's breadth above knee	10¼ "
" " " at middle	11½ "
" " " close to perineum	12⅞ "
" calf, " at thickest part	12⅞ "
Left arm, corresponding point	7 "
" forearm, " "	6 "
" " " "	8⅛ "
" " " "	8⅝ "
" thigh, " "	10½ "
" " " "	11⅝ "
" " " "	12¾ "
" calf, " "	12¾ "

The general *sensibility* is everywhere normal, and there are no subjective disturbances of sensation. The circulation of the extremities is somewhat feeble, and both hands and feet readily become bluish on exposure to cold. The color of the surface is, however, everywhere normal, without any mottling.

April 30.—He had to-day an epileptic attack, with frothing at the mouth, general muscular spasms, and unconsciousness, lasting for eight minutes. There was deep stupor and sleep for four hours subsequently, and he did not entirely recover until the following morning. The fit was preceded for about a minute by the foolish fancies he has frequently had before.

Ordered Syr. Phosphat. Comp., fʒij, t. d.
Faradization of arms and legs on alternate days.

Remarks.—I have been led, gentlemen, to detail at unusual length the symptoms present in this case, not only on account of its great interest and rarity, but because it is the first case of this disease that has been

carefully studied and described in this country.* In commenting upon these symptoms, I will ask your attention especially to those points which are most highly characteristic.

The mode of invasion of the disease presented a distinct peculiarity. It was marked merely by a progressive loss of power in the muscles of the legs, buttocks, and spinal region, which was so gradual in its development that the patient continued able to run about for eighteen months. In the present case the loss of power involved the muscles of the buttocks and spinal region sooner than usual, since there was a very early development of the next two symptoms characteristic of progressive muscular sclerosis,—peculiarity in the position and gait of the patient, and marked anterior curvature of the lumbar spine. Patients affected with this disease stand and walk with their legs widely separated, as though to enlarge their base of support and thus increase the security of their equilibrium. Duchenne is inclined to think that this position cannot be exclusively due to the weakness of the legs, since in other forms of partial paralysis of the legs the same position is not assumed to an equal degree. It appears to me that the separation of the legs may also be partly accounted for by the extreme obliquity of the pelvis caused by the lordosis of the lumbar vertebræ; and a further cause of this separation of the legs will be found in the mode of walking.

The weakness of the legs and of the gluteal muscles gives to the patient a peculiar gait, which I have attempted to describe. This peculiarity consists essentially in the fact that the patient, in taking a step forward, for instance, with the right foot, throws his entire weight on the left leg, leaning over to that side, and then, by a jerk of the right side of the body, the right leg is thrown or drawn forward, the foot describing a small

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* In the *Boston Medical and Surgical Journal*, November 17, 1870, there is an interesting paper on this subject by Drs. Ingalls and Webber. Unfortunately and unavoidably, the report of the case, which serves as the introduction to the paper, is very meagre. The article contains, however, a valuable tabulated summary of all the cases of this disease on record up to that date. There is also a complete bibliography appended.

arc, and the toe pointing downwards. It is evident that this mode of walking must be an additional cause of the separation of the legs, since, when the weight of the body is thrown on one leg and the other is swung around, the step can be made more readily and much longer when the feet are wide apart.

While the weight of the body rests on either foot, it will be noticed that the heel is raised slightly from the ground, or at most touches it very lightly. It is evident that in such a mode of walking as this the muscles of the leg upon which the whole weight of the body is thrown, and which serves as a fulcrum, must be subjected to a severe strain and be thrown into a state of powerful contraction.

It is curious to observe in our patient that, while the wasted thigh-muscles tremble and contract feebly, the muscles of the calves appear to contract very powerfully, and stand out in bold relief. I shall return to this point, but will now merely call attention to the further proof of the greater power of these calf-muscles, shown by the elevation of the heel from the ground at the very moment that the whole weight of the body is resting on the same leg. This elevation of the heel is not a voluntary act, intended to give greater height, so that the sweep of the other leg may be more readily effected, but is the unavoidable result of the marked superiority in power of the extensors of the foot over the flexors.

The next striking peculiarities about patients with this disease are the mode of rising from the sitting to the standing position, and the posture assumed while standing. Nothing could more strikingly demonstrate the great weakness of the extensors of the back than the manner in which our patient gradually raises himself into the erect posture by the power of his arms. The weakness of the same muscles compels him, when standing, to counteract the tendency to fall forward by throwing the shoulders far back, while the lumbar spine projects forward, thus deepening greatly the lumbar depression, and producing the deformity known as "ensellure," or "saddle-back." Duchenne calls attention to a peculiarity of the spinal lordosis in this disease,

as distinctive from that seen in atrophy or paralysis of the muscles of the abdominal walls, in the fact that a vertical line dropped from the most prominent spinous process falls behind the plane of the sacrum. This peculiarity is very clearly shown in the accompanying wood-cut, which illustrates the position my patient assumes when standing and leaning on a support.

I have already alluded to the disproportionate strength of the muscles of the calves; and this is also clearly seen in the existence of double equino-varus. It is impossible to ascertain the precise period when this deformity began, but it is probable that, as is usually the case in this affection, we may class it as one of the later symptoms. At all times, but especially when the patient walks, the tendo-Achillis on each side appears unusually tense, prominent, and large; but there can be no doubt that the tendency to club-foot is due solely to the superior strength of the muscles of the calf (the extensors of the foot) as compared with that of the flexors. Thus, on directing the patient to make various movements with his feet, it is readily perceived that the movements of flexion of the foot are very feeble, while those of extension and adduction are quite vigorous.

Finally, it remains, in studying the symptomatology of this case, to examine carefully the relation which the atrophy and hypertrophy of the muscles bear to each other. I desire to call more particular attention to this point, since, in the cases of this disease hitherto recorded, muscular atrophy has either not been present, or has not attracted the careful study it merits, at least from a theoretical point of view. The changes in the muscles have invariably been preceded, as in the present case, by a stage of progressive debility of varying duration, after which the first alteration observed in the muscles has been, in a majority of cases, a gradual increase in their bulk. In a few cases, atrophy of certain groups of muscles has coincided with enlargement of others. In the present case, however, the processes have been differently related. In all of the muscles affected, including those of the extremities, of the buttocks, lumbo-spinal region, and shoulders, the first change noticed has been a slowly developing

atrophy, which has advanced in the case of certain muscles (*e.g.* the biceps flexors of the arms and the calf-muscles) to an extreme degree. Thus, wherever enlargement of the muscles is noted, it has been developed as a secondary change consequent upon a primary process of atrophy, a fact which appears to me highly important as bearing on the affinities of the disease we are considering.

The modes of distribution of these two conditions are, however, quite dissimilar. Thus, in the case of the atrophic change, it has advanced from the feet upwards, successively involving the muscles of the calves, thighs, buttocks, lumbo-spinal region, shoulders, arms, and forearms. On the other hand, the process of consecutive enlargement, having also appeared first in the muscles of the calves, has affected in addition only the muscles of the forearms and two of the heads of the triceps muscles. This irregularity in the distribution of the excessive muscular growth has been noted in other cases, in some of which it has remained limited to the legs, or has involved in addition the arms and even the face. The usual rule is, however, for it to affect the legs first, and thence to extend to the truncal muscles.

The statement is made by several observers that the weakness of the muscles increases with the increase in their bulk; and in certain cases this would appear to have been the case. More usually, however, no direct relation exists between the loss of power and the apparent enlargement of the muscles; and it may even happen, as in the present case, that those very muscles are by far the strongest which have undergone most marked secondary enlargement. This is clearly seen in the production of double equino-varus by the over-action of the extensors of the feet, and is no less true of the muscles of the forearms. It is important to note carefully this fact, since it shows conclusively that, whatever may be the nature of the change in the muscle which leads to its enlargement, its first and direct effect is not to weaken the contractile power.

The affected muscles in this disease give different results when tested with faradaic and with galvanic currents; the results also vary at different stages of the

same case. In the present instance, the results accord with those obtained in a number of cases, especially in those studied by German observers; that is to say, the muscular contractility, as tested by faradization, is impaired in all the affected muscles, those which are hypertrophied, however, contracting more actively than those which are atrophied. The galvano-contractility is also slightly impaired. The electro-muscular contractility has been found unimpaired in the earlier stages of the disease; but later it diminishes, the muscles continuing, however, to respond actively to galvanism after they have partly lost their power of responding to faradization.

Electro-muscular sensibility has been found normal or impaired in different cases: in my patient it is diminished to faradization, but remains acute to galvanism. The temperature of the affected parts remains normal in some cases, while in others it is lower than that of the trunk, and the skin has then been observed, in a few cases, to be marbled or mottled.

There is an entire want of disturbance of the general health in this singular disease. The appetite remains good until a late period, digestion is well performed, and the action of the bowels is regular. Neither the rectum nor the urinary bladder becomes paralyzed. The disease is not attended by any pain or alteration of general sensibility.

It is a singular fact that in a notable proportion of the cases progressive muscular sclerosis has occurred in children of feeble intelligence or in idiots. There is, however, no necessary connection between it and any kind of cerebral disturbance, since in some cases the disease has existed in a well-developed form in conjunction with a normal condition of the mental functions. The complication of epileptiform convulsions, which is presented in the case before us, is a hitherto unobserved one. It is, however, associated with such perfect retention of memory, such activity and clearness of mind, and such integrity of all the special senses, that I cannot regard it as any evidence of an organic affection of the brain. I shall, however, return to this point hereafter.

I have thus dwelt upon the various symptoms of this disease, which we have seen to be characterized by a

period of gradually increasing debility, soon followed by peculiarities in the mode of standing and walking, by lordosis of the lumbar spine, and by equino-varus; while later still the enfeebled muscles either undergo atrophy, with a subsequent remarkable enlargement of a greater or smaller number of them, or they pass into this state of enlargement without undergoing any previous diminution in size. The subsequent course of such cases, so far as known, may be told in a few words. In all instances where the disease has reached the stage in which the symptoms are fully developed, a fatal result has followed. The disease is a slow one, and may occupy several years in reaching the period of its full development; it then remains stationary for several years longer; but finally a stage ensues in which the loss of power rapidly increases and extends, with or without accompanying atrophy, to muscles previously unaffected. The sufferer is soon confined to bed, and death occurs in one or two years, either from sheer prostration or from some intercurrent disease.

When we come now to ask ourselves what relation this disease bears to the various forms of paralysis or of muscular atrophy, we are met by the difficulty that, until the present time, but one careful post-mortem examination has been made of the body of a patient dying from this malady. In this instance the nervous centres were examined by Cohnheim, but with entirely negative results. But although, therefore, there is still great need of further examinations of the internal organs, nerve-centres, and ganglia of the sympathetic nerve, much light can be thrown upon the question by the careful examination of the tissue of the affected muscles. This is secured by the use of a little instrument, devised by Duchenne, and termed an "emporte-pièce,"* by which fragments can be obtained from the substance

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* This useful little instrument is shaped like a trochar. The blade is, however, a hollow cylinder, composed of two parts, one of which, bearing the point, is fixed, while the other can be withdrawn a little by sliding a movable button on the handle. The trochar is introduced closed into the substance of the muscle, the button withdrawn, so as to open the cylinder and allow a fragment of muscle to project into it; the button is then pushed forward, cutting off and securing the little morsel of tissue.

of any superficial muscle and subjected to microscopic examination.

I have thus obtained a fragment from each of the gastrocnemii and from the left deltoid muscles, and have found the following appearances, after careful microscopical examination of each piece.

The fragment removed from the left deltoid was of a slightly pale reddish color. When examined microscopically, a large majority of the fibrils showed distinct, though often fine and delicate, transverse striation. In a few instances, striation was entirely absent, the fibrils looking homogeneous and much like ground-glass cylinders. In a very few fibrils, also, distinct longitudinal striation was visible, and in others there was multiplication of the nuclei in the sarcolemma. In not a single fibril was there any trace of fatty degeneration. The fibrils varied in size from $\frac{1}{465}''$ to $\frac{1}{230}''$, or even, in a few cases, $\frac{1}{160}''$. The striation was particularly faint, or at times even absent, in the largest fibrils. There was a large amount of interstitial white fibrous tissue, with abundant granular matter containing many oval nuclei. In places there were small collections of minute fat globules or refracting granules.

The fragments removed from the gastrocnemii presented closely analogous conditions. The muscular tissue was merely rather paler red than normal. The muscular fibrils varied greatly in appearance and in size. The transverse striation was in some fibrils perfectly healthy, but in a majority it was altered, though in various ways. Thus, in some it was very faint and difficult to distinguish; in others, it was wholly absent, the fibrils presenting the appearance of fine ground glass. In other fibrils there was a marked appearance of longitudinal striation, due to delicate fibres or very fine fusiform cells arranged in the long axis of the muscular fibril. In many fibrils there was distinct excess of the nuclei of the sarcolemma, which appeared as large oval nuclei with a punctiform nucleus. A few fibrils presented streaks of minute fatty granules along their centres, and a very small number were decidedly fatty. The muscular fibrils varied greatly in size also. Many were about $\frac{1}{250}''$ to $\frac{1}{330}''$ in diameter; but a number were $\frac{1}{450}''$ to $\frac{1}{400}''$, while others were as much as $\frac{1}{125}''$, $\frac{1}{140}''$, $\frac{1}{200}''$ in width. There was a large excess of interstitial tissue, in places taking the form of long, narrow, wavy bands of pure white fibrous tissue; in others, appearing

as abundant granular stroma, thickly strewn with oval nuclei. There was also some curly, elastic fibrous tissue. There was a considerable amount of interstitial fat, existing as scattered globules, or arranged in patches of large, closely aggregated fat-globules. In places isolated muscular fibrils lay imbedded in this fibroid tissue so as to be scarcely visible; but in other places a number of fibrils lay directly in contact with each other, forming a little bundle, around which the excessive growth of interstitial tissue had occurred. The arterioles and capillaries appeared healthy. No nerve-fibrils were detected.

Similar examinations have, as before stated, been made in a number of the cases of this disease, and have yielded results agreeing in all essentials with those I have found in the muscles of this patient. The points which I desire to dwell upon as of capital importance in their bearing on the pathology of the disease are, in the first place, that the primary fundamental change in the affected muscles is an excessive growth or hyperplasia of the interstitial connective tissue. This is found to have taken place even in those muscles which have not undergone any increase in bulk, or which are even reduced in size (for instance, the left deltoid in this case). In the latter case it is evident that the process cannot have advanced far, and it also appears probable that there is a certain amount of simple atrophy of the muscular fibrils developed simultaneously. This, however, does not appear to be the only change in the muscular fibrils, which are also found to begin to lose their transverse striation, and to present increase in the nuclei of their sarcolemma, or distinct longitudinal striation. Observe, however, that there is not the slightest tendency to a primary fatty degeneration of the muscular fibril. It may happen that this interstitial growth never reaches such an extent as to cause apparent enlargement of the muscle, so that only certain muscles may thus enlarge. Thus, as a rule, the muscles of the calves are the first to undergo this subsequent change, and they may be the only ones in which it appears, although numerous other muscles may present the first stage of the process.

In those muscles which do undergo this subsequent enlargement, the hyperplasia of interstitial connective tissue is found to have reached an extreme degree. The

appearances presented indicate that the entire process has been one of sclerosis, in which there has been rapid growth of nucleated fibro-cellular tissue, with the development of bands of wavy fibrous tissue, and even some curly elastic fibres. It is easy to recognize, therefore, the identity of this process with the other sclerotic inflammations, as of the connective tissue of the nervous centres (sclerosis of brain and spinal cord), of the lungs, liver, and kidney (cirrhosis), and of the subcutaneous tissue (scleroderma). There is, however, one point in which this affection of the muscles appears to differ from the other sclerotic conditions mentioned. In the latter, we constantly observe that, with the progress of the change, a tendency to organization and contraction of the newly-formed fibrous tissue soon manifests itself, while the essential elements of the part (nerve-tubules, liver-cells, or uriniferous tubules) are compressed and undergo atrophic degeneration. In the disease we are now considering however, there is a simultaneous change in the muscular fibrils, even in the early stage; but this does not appear to depend wholly on the hypertrophy of the interstitial connective tissue, nor does it maintain any definite or constant relation with this latter change throughout the course of the disease.* Indeed, as is seen in this patient, those very muscles which present the greatest degree of sclerotic enlargement may be the strongest of the whole series which are implicated in the disease. It is true that the muscular fibrils of such muscles present a further stage of the change begun in the first period of the disease. Their transverse striation is still more delicate and faint, or is even, in a number of fibrils, entirely lost. But they do not seem to have undergone any further atrophy; indeed, the measurements I have made, and the increased strength in the muscles of the patient's calves, would point to the belief that the muscular fibrils may temporarily share the exaggerated nutrition

* It may be that in some cases where there is marked loss of power, with general preservation of the size and striation of the muscular fibrils, the sclerotic change in the connective tissue compresses the branches of the motor nerves as they traverse the muscular tissue.

of the surrounding connective tissue, and undergo a delusive increase in size and power.* Thus, I find that the fibrils in the gastrocnemii muscles of this patient are fully one-third wider than those in his left deltoid, and that some of the former have acquired the enormous size of $\frac{1}{125}''$ in transverse diameter.

Whether this transitory stage usually exists or not, the sclerotic change does not depart from its inevitable law of development. Already in this second stage we have seen patches of fat-globules appearing in the interfibrillar spaces, and as the disease passes into the final stage, this fatty degeneration of the muscle advances with varying rapidity, even leading in some cases to such an accumulation of fat as to be visible to the unaided eye as yellowish streaks. This extreme condition is, however, very rare, and much more frequently the accumulation of fat is moderate. Even when very great, however, it is found to be far more due to increase of the interstitial fat than to a true fatty degeneration of the muscular fibrils. Their nutrition must be, however, very gravely impaired, so that they undergo atrophy, and in many places entirely disappear, leaving their sheaths empty. This change coincides with the rapid extension of paralysis which characterizes the final stage of the disease.

This detailed account of the muscular lesion naturally leads to the question of the pathology of this curious affection. It cannot be held that the disease depends upon or is essentially connected with any cerebral lesion. It is true that in a number of cases the patients have been idiotic, or at least exhibited marked impairment in intellectual development: in the present case, also, epileptic convulsions are present as a complication. It must, however, be remembered that cerebral disturbances of any kind whatsoever are not uniformly present, that disorders of special sense are rare, and that some cases of the disease have been observed associated with a normal state of the intellectual faculties; and, finally, that in the one case where the nervous centres have been

* This enlargement of the size of the fibrils of the gastrocnemii has also been observed by Leyden (loc. cit.).

examined, the brain was found healthy. The peculiar character of the muscular lesion and its symmetrical distribution are additional proof, if more were wanting, of the absence of all connection between the disease we are discussing and any cerebral lesion.

Nor is the argument more strong in favor of a spinal lesion as the cause of this affection. It is true that the first idea which will arise, on learning from a patient that his malady began with gradual loss of power of both legs, is that there is some disease of the anterior columns of the spinal cord. When, however, as in the present case, we further find that there has been no alteration of sensibility, no loss of co-ordination of muscular movements, no subjective sensations, such as of formication or of constriction, no implication of either bladder or rectum; when also we learn on careful examination that the loss of power was not in reality the primary symptom, but was preceded by and existed only in proportion to certain muscular changes,—we must conclude that the disease is not dependent upon any affection of the spinal cord. The most important fact to be clearly apprehended here is that in reality there is no paraplegia, in the strict and only correct significance of the word, present in the disease we are studying. It is of course true that a paralyzed muscle will often undergo atrophy or fatty degeneration, but these changes are then dependent upon loss of function and of innervation, and are essentially secondary to the interruption of the transmission of motor power. Widely different, however, is the relation which here exists between the loss of power and the alterations in the muscles. There is throughout the course of the disease no real loss of motor nerve-power, nor any interference with its transmission, but merely an interference with its manifestation, owing to a progressive sclerotic change in certain muscles. This change has been slowly advancing for some time before the loss of power is so marked as to attract the notice of the patient; and just in proportion as it progresses, do the muscles become more and more weak, until, when the final stage of the sclerosis is attained, their contractile power is so completely lost that the patient is bedridden and almost motionless. It is on account

of the radical difference between this process and any form of paraplegia that I object to the name "pseudo-hypertrophic paralysis," applied by Duchenne to this disease, and greatly prefer "progressive muscular sclerosis," as expressing accurately the pathological condition present.

Having, then, excluded the possibility of either a cerebral or spinal origin for this disease, I can only offer the somewhat unsatisfactory view of its pathology, that it consists essentially in a perverted nutrition of the muscles affected, probably dependent upon a lesion of the branches of the sympathetic nerve which are distributed to the tissues involved. This opinion that the sympathetic nerve is primarily affected, does not, it is true, rest on any positive or convincing evidence. In a certain number of cases, however, especially in those observed in Germany, there have been symptoms noticed, such as reddish or bluish discoloration of the skin of the affected parts and variations in their temperature, which would certainly indicate some marked disturbance in the vaso-motor supply of the cutaneous vessels, and have accordingly led many of the observers of this disease to adopt this view of its pathology. It must be confessed, however, that such symptoms are not constant, or at least are not present at all stages of every case: thus, in the present instance, the most careful examination fails to determine them. Still, for the present, in fault of any exact knowledge or of any more satisfactory explanation, this view of the pathology of progressive muscular sclerosis may be accepted.

I may add that no additional light is to be derived from a study of its causes. It is eminently a disease of infancy and childhood, making its appearance in the vast majority of cases between the ages of five and thirteen years. It has, however, been observed to begin in one case at the age of fourteen years; in the present case it was first noticed at the age of fifteen years; and in two cases observed by Benedikt (loc. cit.), and in one by Laycock (loc. cit.), the disease seems to have originated in adult life. The disease is much more common in the male than in the female sex; and, finally, it frequently affords evidence of a hereditary tendency, two or even

four cases having been more than once observed in a single family. It usually appears spontaneously, not appearing to depend upon any particular external causes. In single instances it has been attributed to such causes as the influence of cold and damp, or an attack of some eruptive fever. In my own case, the cause assigned by the patient, protracted over-exertion in doing work too heavy for his years, is far more likely to have really influenced the development of the disease. It must be conceded, however, that in its etiology, as well as in its pathology, this curious affection still presents an unsolved problem.

Let me now invite your attention to the relation which this disease bears to other affections. I shall not occupy your time by any lengthy discussion of the diagnosis between progressive sclerosis of the muscles and atrophic infantile paralysis. The suddenness of attack in this latter affection, frequently associated with fever or with some cerebral disturbance, as convulsions, the occurrence of complete and more or less extensive paralysis, the gradual disappearance of the paralysis in some parts, while in others it remains permanent, the diminution and ultimate loss of electro-muscular contractility, the occurrence at a later period of fatty degeneration and atrophy of the affected muscles, with arrest in the development of the bones and marked deformities, and the entire absence of any secondary enlargement of the parts involved, constitute a series of distinctive features so clear and decisive as to render the differential diagnosis easy and certain.

A disease from which it is much more important to carefully distinguish progressive sclerosis of the muscles is progressive muscular atrophy occurring in childhood. The especial importance of the relations of these two diseases depends on the fact that both are alike diseases of nutrition of the muscles, thus constituting a group quite distinct from all the forms of true paralysis. In both the disease begins—usually without any apparent cause—insidiously, and progresses slowly but surely. In both the loss of motor power is secondary to the changes in the muscular tissue; in both the muscular degeneration and consequent loss of power almost invariably

progress steadily to a fatal result. In progressive muscular sclerosis the positive anatomical proof is still wanting, but analogy, theory, and some special symptoms lead us to believe in the existence of a lesion of the sympathetic nerve system. In progressive muscular atrophy, careful post-mortem examination has repeatedly demonstrated the actual presence of such a lesion. These two diseases, then, stand related to each other as being alike caused by disturbance of the trophic nervous system, but they are at the same time most positively separated from each other by marked differences in their course and symptoms.

Thus, in progressive muscular atrophy, the disease nearly always begins in the upper extremities, and invades subsequently the trunk and lower extremities. Indeed, Duchenne has pointed out that when this disease appears in childhood, which is quite rare, it begins in the face, where it produces atrophy of the orbicularis oris and the zygomatici, and does not extend to the trunk and extremities until after a period varying from two to three years. It then follows the same descending course seen in cases occurring in adults. The atrophy usually affects the muscles irregularly, so that various deformities and vicious positions of the parts involved are developed. Microscopic examination shows a progressive fatty degeneration and atrophy of the muscular fibrils, and in proportion as this increases there is loss of power and of electro-muscular contractility. One further symptom of high diagnostic value is the frequent occurrence of fibrillar contractions in the affected muscles. Finally, the muscles which have progressively atrophied never undergo any secondary enlargement, nor does microscopic examination reveal any lesion of the interfibrillar connective tissue. In all of these particulars, then, progressive muscular atrophy differs widely from progressive muscular sclerosis, which is almost exclusively a disease of childhood, beginning in the muscles of the lower extremities and advancing upwards, producing a peculiar mode of standing and walking, and in which the affected muscles, with or without a stage of atrophy, undergo remarkable enlargement, without fibrillar contractions, and with pre-

servation of electro-muscular contractility till a comparatively late period of the disease. Microscopic examination also shows, even in the early stages of the disease, a marked hypertrophy of the interstitial connective tissue in the affected muscles, together with peculiar changes of the muscular fibrils, not at all resembling fatty degeneration ; while later, this sclerotic process terminates in fatty degeneration of the interstitial tissue, and increasing degeneration and atrophy of the muscular fibrils. There is also a want of constant relation between the degrees of sclerosis, of the changes in the muscular fibrils, and of the impairment in muscular power. This hasty summary of the main distinctions between these two affections will show how readily a differential diagnosis can be established.

In regard to the prognosis of progressive muscular sclerosis, the disease may be pronounced incurable, unless treatment is instituted during the earlier stages, before the affected muscles have become markedly enlarged. Even when, however, it has progressed to an advanced stage in certain muscles, its progress in other portions of the body may probably be arrested. The duration of the disease is rarely less than six years, and may extend to upwards of fifteen or twenty. Thus, in the present case, the disease has been in positive existence for five years, and yet has only passed into the second stage, and would probably, even were no treatment adopted, require several more years to run its course. When a fatal result is produced, it is either by the extreme prostration and lowered vitality of the patient, by weakening of the respiratory muscles, favoring pulmonary engorgement, or by some intercurrent disease.

Fortunately, however, it may be safely asserted that treatment, when instituted early and faithfully pursued, exercises a powerful control over the progress of the disease. Unless there are special concomitant symptoms, such as anæmia, epileptiform convulsions, digestive derangement, or the like, there is no clear indication for internal medication, nor has the use of any drugs been followed by decided benefit. Those which may be given most rationally, as tending to modify the nutrition of the nervous system, are the alterative nerve

tonics, of which I should be disposed to especially recommend the nitrate of silver. Of course, in addition, care must be taken to improve the state of the blood, if it be anæmic, and to correct any disturbance of digestion. If the case is complicated with epileptiform convulsions, as in my patient, a course of bromide of potassium may be directed with advantage, The remedy, however, from which most good is to be expected, is electricity. This has been used with very great benefit, in the form of faradization by Duchenne, and in that of galvanization by Benedikt and others. I have pointed out to you that the electro-muscular contractility is usually preserved until late in the disease, though very different results are obtained in some cases by the use of the different varieties of current,—the muscles sometimes contracting most powerfully under the application of a faradaic, and at others under that of a galvanic, current. I should recommend the employment of whichever form is found to secure the most active muscular contractions. If the faradaic current be used, it should be applied directly to the affected muscles, or one electrode may be applied over the motor point of the muscle (*i.e.* over the trunk of the motor nerve before it enters the muscle) and the other over its body. If the galvanic current be indicated, one electrode (the copper pole) should be applied over the carotid fossæ, along the anterior border of the sterno-cleido-mastoid muscles, since in this region the cervical portion of the sympathetic nerve is most readily accessible; and the other electrode (the zinc pole) may be applied along the lumbar spine, or over the motor point of the affected muscles. In some cases it may also be advantageous to combine the galvanization of the cervical sympathetic with faradization of the affected muscles. In the present case, I have directed the muscles to be thoroughly faradized every other day. I have told you that the muscles responded quite actively to the stimulus of this current; and already there is a positive improvement in the power of his legs and in his ability to walk. I am therefore encouraged to persevere in this treatment, in the hope that by its prolonged use the progress of the disease may be ultimately arrested.

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