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MICROSCOPICAL STUDIES IN A CASE OF PSEUDOHYPERTROPHIC PARALYSIS.[1]

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NOTWITHSTANDING that a great amount of attention has during the last few years been devoted to the subject of primary affections of the muscles, and that a great deal has been accomplished towards the correct classification of the various forms encountered, nevertheless our ideas in regard to the processes and anatomical changes which occur in these affected muscles are still in a condition of undesirable confusion, and it seems to me that, before we can clear up the clouds from the clinical field of vision, we must do so from the pathological one. An affection which we know to be a primary myopathy, for it is well settled that here the central nervous system and the anterior nerve roots are not affected, is the form known as pseudohypertrophic paralysis. But what the histological changes are, as they occur in this affection, is not yet definitely decided. Notwithstanding the numerous examinations of muscles which have been made, there does not appear to be an entire uniformity of opinion as regards the anatomical changes which take place, and it is therefore very probable that these changes vary in different stages of the affection. For this reason every careful and impartial observation must be of value. It is in this spirit that I take the liberty of presenting the results of the microscopical examinations in the following case.

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The pieces of muscle examined were excised from a patient, whose history is a classical one of pseudohypertrophy. The case was a typical one, so that the description can be made very short.

Sept. 30th, 1885. H. P., æt. 15. Family history unimportant. No heredity. Mother had seven children, of which two died. One of these was paralyzed, probably a diphtheritic paralysis. The others, with exception of the patient, were all well. He was brought up at the breast. Began teething at eight months. At thirteen months could walk. At eighteen months he had convulsions, which repeated themselves during four days. Then he was unable to walk for four weeks, but subsequently he walked as well as ever. His mother says he always had "crooked legs." He went to school and did not show any backwardness. At age of 9 years he had a severe fall, which necessitated his confinement to the house for eight weeks. From this time the mother first noticed some awkwardness in hisgait. At the age of 12 years it was noticed that mounting stairs afforded him particular difficulty. His condition gradually grew worse and worse; he fell easily and any slight jar was sufficient to make him lose his balance.

Status Præsens. Upon examination the usual symptoms of pseudohypertrophic paralysis are found, such as, letting himself fall into the chair in sitting down; placing his hand on his knees and drawing himself up when arising; difficulty in mounting stairs, etc. Examination shows hypertrophy to an enormous extent of both vasti externi, of both calves, of the glutei, infraspinati, deltoidei, biceps, triceps, and costal portions of the pectoralis major. No atrophy of any muscles could be made out.

Pat. tendon reflexes absent.

Hypertrophied muscles show reduced excitability to both currents. Otherwise nothing abnormal to be found.

Two pieces of muscle, each of about the size of a bean, were removed from the quadriceps femoris of the left leg. The muscle was placed at once in a one-half per cent solu-

tion of chromic acid, and after a sufficient amount of hardening had taken place it was imbedded in celloidin and transverse and longitudinal sections made. These were then stained with an ammoniacal solution of carmine and mounted in glycerin. Transverse sections examined by low power (200 diam.) reveal a striking variation from normal muscle in the number of muscle fibres as arranged into groups by the perimysium internum. Whereas a normal quadriceps femoris shows between thirty and fifty muscle fibres in a bundle, the diseased muscle averages about

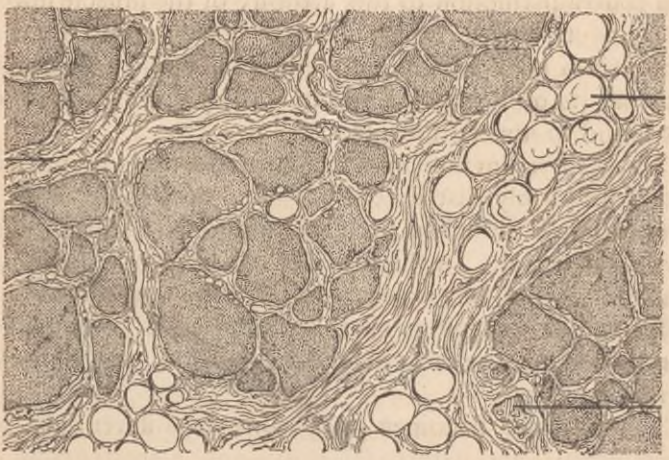

FIG. 1.—Quadriceps femoris from pseudo-hypertrophic muscle. × 300. Transverse section.

Pe, Perimysium externum (carrying arteries and veins). *Pi*, Perimysium internum (carrying capillaries). *T*, Tendonlike formations, formed from previous muscle-fibre. *F*, Fat globules.

one-half that number. At the same time it is conspicuous that the size of the single muscle fibres is on an average smaller than normal, but that there are a number of fibres of normal size present. Hypertrophic fibres were sought for carefully in all my specimens, but in vain. Although variations in the thickness of the fibres have been noted by most all observers, some finding atrophic, normal, and hypertrophic, others finding only normal and hypertrophic ones, the majority of later observers, particularly

Schultze and Erb, claim that hypertrophic fibres are always present. Schultze goes so far as to make the principal microscopical differentiation between neurotic and non-neurotic atrophies dependent upon the hypertrophy or non-hypertrophy of muscle fibres. But he says that this hypertrophy may be absent in pseudohypertrophy and analogous affections, if at the time of the examination general marasmus existed. This certainly was not the case in my patient. It must, however, be acknowledged that perhaps a more extended examination of other muscles might have revealed their presence.

In contradistinction to this atrophy of the muscle fibres, the connective tissue constituting the external and internal perimysium is decidedly augmented, to such a degree in fact that its bulk is twice and in some places three times that found in normal muscle.

The perimysium internum in a normal muscle is approximately uniformly distributed between the single muscle fibres, being of sufficient breadth only for carrying a capillary blood-vessel. In the diseased muscle, such a limitation of breadth is but exceptional, and the average bulk is sufficient for carrying several capillaries, in some places even attaining the size of the perimysium externum of normal muscles.

Thus it often becomes impossible to differentiate between internal and external perimysium ; a small group of muscles fibres (as in one specimen ten) being surrounded by a layer of connective tissue fully as broad as the normal perimysium externum.

This latter, in the diseased muscle, is conspicuous by the presence of arteries and veins, and of two kinds of bundles of fibrous connective tissue, the one being the delicate fibrous tissue as seen in normal muscle, and the second being broad and dense, resembling the fibrous connective tissue of aponeuroses and fasciæ.

Besides this, the perimysium externum is, in many places, crowded with or replaced by fat tissue.

The general impression gained at the first glance is that the number of muscle-fibres is reduced, the mass of con-

nective tissue, on the contrary, being decidedly augmented. These facts correspond to reports of all other observers, since first described by Duchenne, and four years later by Griesinger, and form the basis of the name pseudohypertrophy.

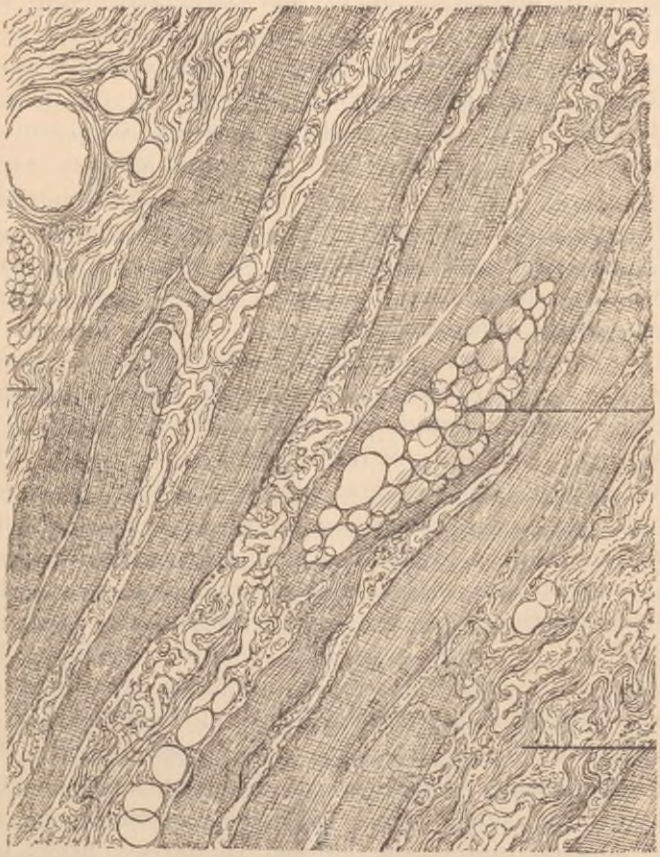

FIG. 2.—Quadriceps femoris from pseudo-hypertrophy. × 300. Longitudinal section. *A*, Artery. *V*, Vein. *C*, Capillaries. *TT*, Tendon-like formations of fibrous connective tissue arisen from previous muscle-fibre. *F*, Fat globules *in* muscle-fibres.

The question which, after such a view, forces itself upon the mind is, Whence comes this augmented connective tissue?

This question is, to my knowledge, not answered satisfactorily by any of the writers upon this subject. They speak of chronic interstitial connective-tissue hyperplasia (Friedreich, Erb), proliferation of connective tissue (Buss), and Schultze describes the microscopical picture as being one in which the muscles are partly replaced by normal fat and normal connective tissue, while the fibres themselves are partly in a state of simple atrophy; and in another place, he speaks of the appearance of large connective-tissue tracts in the muscles. Thus we see no satisfactory explanation is given as to their origin. The fact that the muscle-fibres are decreased in number as well as in size is in itself suggestive of the source of the augmented connective tissue. And, actually, all my specimens go far to prove that the connective tissue has grown, to a great extent at least, at the expense of the contractile substance.

Not only are the nuclei of the muscle-fibres augmented, and here and there arranged in chains, but in many places the peripheral portions of the fibres are transformed into clusters of medullary or inflammatory corpuscles. These clusters are, as a rule, seen along one side of the muscle-fibres only, very exceptionally on both sides. Not infrequently the muscle-fibre, in a *longitudinal section*, appears to be split into smaller pieces by chains of medullary corpuscles, the presence of which leads to a division of the original muscle-fibre into two or more sections. This process of splitting up or dichotomous division is well known since the descriptions of Cohnheim and Knoll, and has been uniformly observed by the latest observers (Erb, Schultze, Buss). Taking these divisions into consideration, we can understand why, in a transverse section of the affected muscle, the number of narrow fibres is so much in excess of those visible in normal muscle, where their presence becomes explicable by the spindle shape of such individual muscle-fibre. Examined with high power, the fact becomes established that the medullary corpuscles have originated from the muscle substance itself. Bay-like, crescentic, or elongated excavations of

the latter are found filled up with medullary corpuscles, and either sharply defined towards the muscle, or gradually blending with it. In the latter case, we observe a breaking up of the muscle-tissue into bodies which are at first homogeneous and later granular and nucleated, and which occupy only the periphery of the muscle-fibre in certain cases, and in others are seen penetrating its entire substance.

In many places, we can observe a gradual transition of the medullary corpuscles into spindles, and through these into fibrous connective tissue. However, not only the delicate, but also the coarse fibrous connective tissue seems to be an offspring of muscle-tissue. This coarse tissue especially is not infrequently seen in tracts of the breadth of original muscle-fibres, and often bordered on either side by the delicate variety. This fact is suggestive, in a measure at any rate, of the origin of the coarse bundles from an entire previous muscle-fibre.

The newly-formed connective tissue itself is seen, in various places, to be the seat of an inflammatory infiltration, and in this condition exhibits the characteristic adenoid or myxomatous structure, that is, clusters of globular shining corpuscles imbedded in the meshes of a delicate fibrous network.

The muscle-fibres themselves are conspicuous by their longitudinal striation, which signifies a prevailingly longitudinal arrangement of the sarcous elements. These are invariably extremely minute in size. Their arrangement into groups, due to the embryonal sarcoplasts, is not very marked; hence, also in transverse section of the fibres the traces of Cohnheim's fields are rather indistinct.

This fact would, according to my judgment, indicate the existence of a malformation of the muscle-tissue existing from the earliest stages of its development.

In some muscle-fibres, the centre is occupied by clusters of coarse, shining granules, likewise a pathological feature, indicative either of a reformation or of a beginning inflammation in the centre of the fibre.

Exceptionally there are present narrow muscle-fibres

in which all striations are lacking, which have a marked gloss and are deeply stained with carmine.

This is the change which, by previous observers, has been described as colloid or hyaline degeneration of the muscle fibre.

The fat tissue, as already mentioned, is present in a

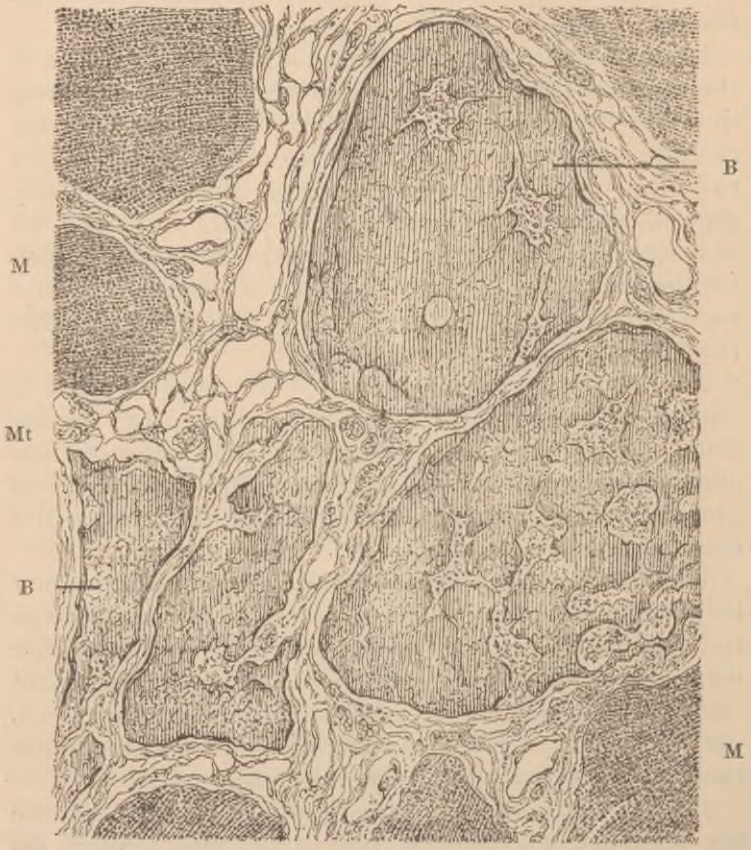

FIG. 3.—Quadriceps femoris from pseudo-hypertrophy. × 500. Transverse section. *MM.* Muscle-fibres, cut obliquely. *Mt*, Myxomatous tissue of perimysium. *BB*, Transverse sections of bundles of tendinous tissue, resembling fields of hyaline cartilage. (In a granular, partly homogeneous basis substance are imbedded branching protoplasmic bodies, in part interconnected.)

large quantity in the newly-formed connective tissue. Exceptionally, however, fat globules are seen in the interior of the muscle-fibre. That the fat globules are ac-

tually in the centre of the fibre, and not on the surface, can easily be ascertained in longitudinal sections where the clusters of fat globules are seen to be bordered on all sides by striped muscle-tissue. Obviously, the inflammatory change has in this instance led to a new formation of myxomatous tissue, whose meshes then became the seat of fatty deposit.

The amount of fat may vary from the presence of a few globules to that of large clusters, which latter lead to a corresponding increase of the diameter of the muscle-fibre at that point. These observations correspond entirely with those of other writers.

Peculiar interest is attached to formations which are seen in the perimysium, and which, at the first view, convey the impression of fibrous connective tissue devoid of striation. These formations are conspicuous by their high refracting power, their composition of small angular pieces, their wavy contour, and their deep staining with carmine.

In some places they are so numerous that the muscle-fibres are completely replaced by them, it being noticeable, however, that they correspond in breadth and general configuration with these fibres.

High powers (5–600 diam.) show that these tracts are composed of bluntly angular lumps between which interstices of various sizes are visible, filled with protoplasm. The angular fields again are made up of smaller pieces indistinctly separated from each other, and corresponding in size with the medullary corpuscles.

Cross sections of these tracts are at once recognizable by their high refracting power and their deep carmine stain.

The protoplasmic bodies visible in the interior of these tracts are sometimes narrow and branching, like tendon corpuscles in transverse section, sometimes, on the contrary, they are oblong or slightly irregular, without larger offshoots, closely resembling the appearance of cartilage corpuscles. There cannot be the slightest doubt as to the

origin of such tracts from previous muscle-fibres (Figs. 4 and 5).

I have, in many places, seen transverse sections of these tracts surrounded by a delicate perimysium, a portion of the tracts still exhibiting all the characteristic features of

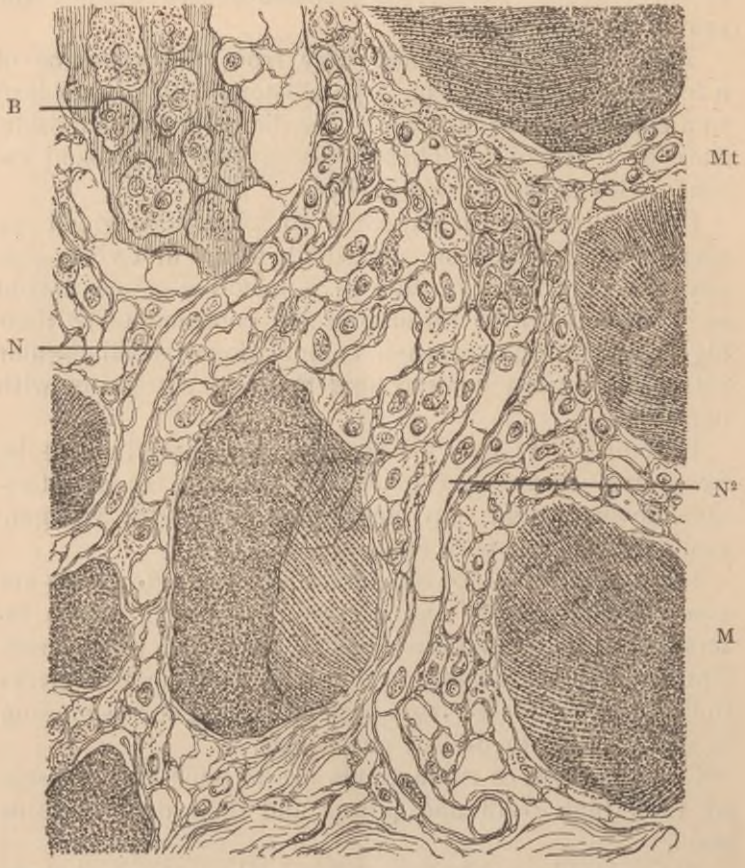

FIG. 4.—Quadriceps femoris from pseudo-hypertrophy. × 500. Transverse section. (Nerves.)

N^1, Medullated nerve-fibre terminating in a hilly formation composed of myxomatous tissue, possibly a muscle-plate. N^2, Medullated nerve-fibre terminating in a cluster of inflammatory corpuscles. (Neuritis.)

MM, Muscle-fibres in transverse and oblique sections. *Mt*, Myxomatous tissue of perimysium exhibiting all the features of granulation tissue. *B*, Tendon or cartilage-like bundle with numerous and large protoplasmic bodies.

striped muscle-tissue, whereas the surrounding mass was made up of medullary corpuscles more or less advanced in their transformation to basis substance. As regards the nature of these tracts which, at least to my knowledge, represent a novel feature, not only in the study of pseudo-hypertrophy, but in the pathology of muscle-tissue in general, I can say that some of them have the appearance of coarse aponeurotic connective tissue, others that of hyaline cartilage. The morbid process has led to a transmutation of the muscle-fibres into varieties of connective tissue, either aponeurotic or cartilaginous. Obviously this change has not taken place through an immediate transformation, but through the intermediate stage of medullary tissue which, in its turn, has been infiltrated with a chondrogenous basis substance, and thus has led to such a peculiar result.

The vascularizations of the perimysium, that is, the delicate connective tissue only, is, in some places, rich, and evidently surpassing that of normal muscle.

The capillaries form plexus around the muscle-fibres, and are conspicuous by their large calibres and their tortuous course.

I do not doubt that many of these capillaries are newly formed.

I have traced a number of medullated nerve-fibres, which in part were unchanged, and terminated in the usual motor hill on the surface of the muscle-fibre. Other nerves, on the contrary, exhibited augmented nuclei in Schwann's sheath, or they were broken up into rows of medullary or inflammatory corpuscles, or they were lost in fibrous connective tissue, identical with that of the perimysium. The general number of medullated nerve-fibres is, in all of my specimens, noticeably decreased.

If, now, from the results of this examination I may be allowed to draw conclusions without, at the same time, generalizing, I shall, in a measure, differ with other observers.

I am convinced that in my patient the disease is essen-

tially a chronic inflammation invading *both the perimysium and the muscle-tissue.* It is impossible to say what the cause of this process may be, unless it is to be sought for in a congenital malformation of the muscle-tissue itself. Such a malformation is at least indicated by the strikingly small size of the sarcous elements, as we are accustomed to see them in the earliest stages of embryonal development. However this may be, the pathological process consists in a gradual reduction of the muscle-fibres into medullary or inflammatory corpuscles, which in time go to build partly fibrous, partly cartilaginous, and partly fat connective tissue. The process, which is extremely slow, gradually leads to an augmentation of myxomatous or other varieties of connective tissue at the expense of the muscle-tissue. I may here say that I cannot agree with Gowers and Buss, that the proliferation of connective tissue is the primary, and the disease of the muscular tissue the secondary process. Either the reverse of this is true, or the process occurs simultaneously both in the muscle and in the perimysium.

I do not hesitate to place the entire process, as seen in my specimens, in the same category with the process termed *myositis ossificans progressiva*, and had I to describe it in a few words would call it a myositis progressiva hyperplastica.

Of the various investigators of the subject during the last few years, Jurgens is the only one who also considers the process a myositis; but he looks upon it as an interstitial myositis alone, and says that he is not prepared to give an opinion regarding the changes in the muscle-fibres themselves.

The more frequently careful microscopical examinations are made of the muscular tissue in the various dystrophiæ, the more are we obliged to come to the conclusion that, either from a microscopical examination alone we cannot always make a distinct diagnosis between the various affections, or that they are, as is largely admitted to-day, all varieties of one and the same process, which imperceptibly blend with one another.

What particularly impressed me in this connection was that my examination differed so decidedly from descriptions of pseudohypertrophic muscles as given by others, yet, notwithstanding that the case was clinically a perfectly clear one, agreed almost entirely with the description given by Friedreich of the muscle from a case of progressive muscular atrophy (case 10, page 37), which affection, as is well known, he classed as a primary myopathy, and considered the process to consist of a chronic progressive myositis.

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