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A CONTRIBUTION TO THE PATHOLOGY OF PARAMYO-
CLONUS MULTIPLEX (FRIEDREICH'S TYPE).*

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The peculiar type of muscular contractions described by Friedreich under the name of paramyoclonus multiplex is of very rare occurrence. The uncertain mechanism of its production and the controversy attending its classification and position among the motor neuroses warrant a brief review of the literature as an introduction to the clinical and pathological report which is to follow.

Historical. The history of paramyoclonus multiplex began in the year 1881 with the description of a case by Friedreich,¹ presenting the following peculiarities: The patient was a man with lung tuberculosis, aged fifty, who, following a violent fright, developed quick clonic contractions of the muscles of the proximal segments of the upper and lower extremities. The contractions resembled in character those induced by the electric current, the individual muscles springing forward as though excited by an invisible electrode. It was particularly noted and emphasized that individual muscles, such as the sartorius and supinator longus, would spring forward in independent contractions which singly are incapable of voluntary innervation. Moreover, there was an absence of synergetic muscular action, so that the locomotor effect attending such coördinated muscular contraction was absent. When the contractions were very strong, however, a slight movement resulted. Occasionally, owing to the great rapidity of the contractions, the muscle was thrown into a state of momentary tetanus. There was cessation of the movements during sleep. These muscle contractions were increased by nearly all forms of peripheral and mechanical stimuli. They were diminished or entirely inhibited by voluntary movement, so that little inconvenience was caused by performing acts of everyday life, in this respect presenting a marked contrast to the co-

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ordinated movements of cerebral origin. The knee-jerks were greatly exaggerated. The gross motor power suffered no impairment. The electrical reactions were normal. This was essentially true of the psychical and sensory functions. At times painful flexor spasms of the thigh occurred. There were absolutely no stigmata of hysteria.

The peculiar features of this affection, viz., the spontaneous contraction of individual muscles not singly under the control of the will, and the absence of synergetic muscular action in the affected members, were so at variance with the known characteristics of muscular contractions of cerebral origin as to render some other explanation probable. Friedreich, after a careful consideration of all the possible sources, as the brain, spinal cord, nerves and muscles, proposed the hypothesis which referred the symptoms to an *excessive irritability of the anterior horn cells of the cord*. This theory was in harmony with the special clinical features of the case, i.e., the single muscle contraction, the absence of synergetic action, the great exaggeration of the knee-jerks, and their diminution as the motor symptoms subsided, the great susceptibility of the contractions to peripheral stimuli, and their cessation on voluntary innervation of the part.

In the course of a few years the accuracy of Friedreich's observation was confirmed on many sides by notable observers. Among the earlier recorded cases were those of Löwenfeld,² Remak,³ Seeligmüller,⁴ Francotte,⁵ Homên,⁶ Allen Starr,⁷ Bechterew⁸ and Marie.⁹ It was but natural that Friedreich's description, based on one case, should undergo considerable enlargement and some variation, as the literature was enriched by other observers, and that even new forms and types should be added. Thus, in 1886, Seeligmüller described a congenital case; Unverricht¹⁰ in 1891 added a family form associated with epilepsy, and Gucci¹¹ an hereditary form in 1893. Some of the more important semeiological deviations from the original Friedreich type which have been subsequently described are as follows: That the muscular contractions are *not* limited to the proximal segments of the extremities, but that all the voluntary muscles may be involved with the sole exception of those moving the eyeballs. Voluntary movement has not in all cases seemed to soothe or interrupt the contractions; indeed, the contrary effect has been noted.

In some cases peripheral stimuli have failed to increase the symptoms. The knee-jerks, although usually exaggerated, have been found occasionally of normal intensity or even diminished. In two cases they were absent. The electrical reactions have been essentially normal. In a few cases only was a slight qualitative increase noted. Rarely contractions have persisted during sleep. Pains and paresthesias have been observed accompanying and following the paroxysms. Fright as an etiological factor was by no means constant, and a variety of predisposing and exciting causes are on record.

Classification. But a small proportion of the cases now reposing in the literature under the title paramyoclonus multiplex or its abbreviated form, myoclonus multiplex, are typical examples of this affection. Many cases are hardly recognizable if Friedreich's conception is adhered to, some observations having more in common with convulsive tic, *maladie de tic*, chorea and hysteria. In some observations the peculiar features which led Friedreich to separate this from the other motor neuroses, i.e., the isolated contraction of a muscle not singly under voluntary control and the absence of locomotor effect, have been completely ignored. Cases are recorded as paramyoclonus multiplex in which the affection was characterized by convulsive movements of a paroxysmal character very far indeed from the individual shock-like muscle contraction which usually first becomes apparent when the surface of the body is exposed, and which interferes but little with voluntary movement. This statement will receive more weight when the tabulations of Unverricht are considered, who collected and classified the cases recorded up to the year 1891. Of the forty-eight cases collected, Unverricht accorded to only six the dignity of paramyoclonus multiplex, and to eleven cases a resemblance only to the paramyoclonus; eleven cases he considered uncertain, and the remainder were grouped with hysteria, chorea, or the tic forms.

A survey of the more recent literature shows the same confusion to prevail. Nearly all forms of myoclonia in the broadest sense of the term are included under this head, while the pure cases of paramyoclonus form but a small minority.

It must be observed, however, that muscular contractions iden-

tical with or closely resembling those of the essential form of paramyoclonus are found associated with or dependent upon other conditions. Thus, in hysteria and the traumatic neuroses, twitchings resembling paramyoclonus are recorded; and as a sequela of joint affections and then presumably of reflex origin. They are also described in conjunction with epilepsy, the so-called myoclonus epilepsy. Rarely muscular spasms of an entirely different type, i.e., the tic convulsif, *maladie de tic*, are accompanied by movements of a paramyoclonic nature.

In the other forms of myoclonia the Friedreich type may be very closely simulated, but attention to the characteristics just outlined usually renders differentiation possible. Dejerine¹² emphasizes the strong resemblance which some hysterical movements bear to this affection. Indeed, some observers, as Moebius,¹³ regard paramyoclonus as a manifestation of hysteria. Moebius, in support of the hysterical nature of the affection, mentions the difficulty incurred in determining the contraction of an isolated muscle not individually under voluntary control when such contractions are lightning-like. This may be true of the periods of great exacerbation, but would hardly be applicable to the whole course of the disease. Furthermore, it is impossible to reproduce these contractions at will, which, according to our present conceptions, would exclude hysteria. Schultze¹⁴ regards the paramyoclonus multiplex as a generalized form of tic convulsif. Many observers, as Oppenheim,¹⁵ Unverricht, Risien-Russell,¹⁶ Allen Starr and Wollenburg,¹⁷ view this affection as an independent form of motor neurosis. Others, as Raymond,¹⁸ would fuse the various myospasms together under a generic term as myoclonia, considering them as allied in nature and differing only in degree, the degenerative tendency representing the common basis and essential factor in the production of them all. This would include the *maladie de tic*, tic convulsif, electric chorea of Henoch-Bergeron, paramyoclonus multiplex, myokymia, and fibrillary twitchings.

Pathogenesis. Diversity of opinion is not confined to the classification of this affection, but the origin and the mechanism of its production are the subject of controversy. Pathological anatomy has thrown no light upon the subject. The theories which today receive serious attention are those of the cerebral and the spinal

origin. Whether the latter consists of a derangement of the motor portion of the reflex arc (Friedreich) or of the sensory portion, as advocated by Vanlair,¹⁹ is secondary to the question at issue.

According to our present knowledge, the evidence is strongly in favor of a spinal origin of the Friedreich type of paramyoclonus multiplex. The electrical stimulation of the motor cortex with the most delicate electrode fails to produce a contraction of an individual muscle. On the contrary, the result is a movement, a synergetic muscular action. We may assume with a certain degree of probability that movements rather than individual muscles are here represented. The medullary centers, on the other hand, have a more individual relation with the respective muscles under their control, although the exact nature of this relation is still a subject under investigation. It will be remembered in this connection, however, that Sano²⁰ advocates an individual muscle representation in the anterior horn cells, based on experimental studies.

Those rare cases in which paramyoclonic twitchings have occurred in the course of organic disease of the cerebral cortex must be considered in this relation. Examples of such are paresis, chronic meningitis with cortical atrophy (Murri²¹), chronic uremic edema of the cortex (Levi and Follet²²), and myoclonus epilepsy (Unverricht, Clark and Prout²³). These cases are by some observers considered confirmative of a cortical origin. If, however, minute pathological changes of the cerebral cortex were capable of inducing this type of muscular contraction, they should be of more frequent occurrence, considering the vast number of such conditions, constantly under observation. In view of this rarity, a coëxisting alteration of the spinal centers is more probable; and in the family affection, characterized by the association of myoclonus and epilepsy, we are dealing with a degenerative affection of the cerebrospinal axis, the epilepsy referable to the upper, the myoclonus to the lower centers. The few cases of hemimyoclonus (Minkowsky,²⁴ Bernhardt,²⁵ and Seeligmüller²⁶), usually cited as evidence of the cerebral origin, weigh but lightly in the balance.

Very interesting and suggestive from an etiological point of view and corroborative of the spinal theory are those cases of paramyoclonus multiplex occurring in conjunction with articular

affections. Chauffard's²⁷ case of hemiparamyoclonus followed directly on an attempt to break up old joint adhesions in the right knee and hip. Levi and Follet report a case of paramyoclonus multiplex complicating spondylose rhizomelique with the usual joint manifestations. The articular muscular atrophies and the old theory offered in explanation, the perversion of the functions of the anterior horn cells (Paget, Charcot) arise in this connection. Raymond²⁸ demonstrated experimentally that if the posterior roots are cut before the articulation is disturbed, this atrophy will not occur. This is almost indisputable proof of its reflex origin. If pathological reflex stimuli from the articulation can affect the trophic function of the anterior cells, is it not reasonable to infer that the motor function may be perverted in a similar manner with a resulting hyperexcitability? It is a common observation that the tendon jerks are exaggerated in muscles which are the seat of this atrophy, the knee-jerks in affections of the knee joint, the Achilles jerk in ankle joint disease. This exaggeration would hardly be expected in atrophic muscle groups unless accompanied by an unusual irritability of the reflex centers. Gowers²⁹ cites an interesting case in this connection. A young man, following an injury to the left knee, developed an acute atrophy of the quadriceps extensor. When seen two years later the atrophy still persisted, the left knee-jerk was exaggerated, and there was in addition a well-marked ankle clonus upon the left side. This same condition was persistent one and a half years later, and with the associated ankle clonus would seem to prove that the functional and trophic changes in the anterior horn cells in joint affections may not only be of long duration, but may extend to neighboring centers. The muscles from a case of articular atrophy were examined by Darkschewitz³⁰. A majority of the muscle fibers were found to have undergone a diminution in size, averaging about half the normal diameter. These atrophic changes in the muscle fibers, in an affection where presumably the trophic function of the anterior horn cells has been restricted by some inhibitory influence, receive additional significance from the muscle changes found in my case of paramyoclonus multiplex, an affection presumably due to an exaggeration of the function of the anterior horn cells. Here the diameter of the muscle fibers was two or three times in excess of the normal.

As further evidence in favor of the spinal origin of the peculiar contractions under consideration may be mentioned the relationship existing between paramyoclonus multiplex, myokymia and fibrillary twitchings. Between the fascicular contractions and the muscle waves and the individual muscle contractions of paramyoclonus there are transition forms; a series of gradations, so that one condition merges imperceptibly into the other. The myoclonus fibrillaris multiplex of Kny³¹ represents such a transition form. Thus, in one case the affection may bear the stamp of a myokymia, yet simple fibrillary waves occurring and occasionally the whole muscle undulating; so in paramyoclonus certain undulations may occur. Dana,³² in a recent communication, emphasizes the relationship of myokymia and paramyoclonus multiplex. The dependence of myokymia and fibrillary contractions on disease of the lower nervous mechanism is fairly well established, and has been recently discussed by Walton.³³ The etiology in some of the recorded cases (cited by Walton): lead-intoxication (Huber); following in the wake of old poliomyelitis (Williamson, Walton), low grade neuritis (Biancione), sciatica (Gowers), bear no other interpretation. This receives additional weight from the accompanying pains, paresthesias and electrical disturbances not infrequently observed.

There is still another peculiarity observed in these three forms of muscle contraction, and that is the passive attitude manifested by the patient towards them. The muscle contractions and undulations are felt as such, but otherwise cause little or no disturbance, save occasionally a cramp or a pain. This is largely accounted for by the usually complete preservation of the power of performing voluntary acts and the absence of strong convulsive movements of a coördinated type. It is also possible that their origin in the lower centers, far removed from the psychical sphere, may also play a rôle.

Remarks. I. The term paramyoclonus multiplex, or myoclonus multiplex, should be reserved for that form of myospasm characterized by multiple, spontaneous, isolated contractions of individual muscles.

II. This type is peculiar and distinctive, and receives its most logical explanation in a disturbance of the spinal centers.

III. This type should be carefully separated from the cerebral type of the myospasms which are characterized by movements of a more or less coördinated type, as are observed in the *maladie de tic*, *tic convulsif* and the convulsive tremor of Pritchard and Hammond.

IV. The contractions of *paramyoclonus multiplex* are closely related to the *myokymia* and fibrillary contractions.

V. *Paramyoclonus multiplex* may occur as an idiopathic or a deuteropathic affection, in the latter complicating various organic and functional diseases of cerebral and spinal origin.

CASE REPORT.*

These observations were made in the surgical wards of Bellevue Hospital, service of Dr. B. B. Gallaudet, through whose courtesy I was permitted to study and publish the case.

History. July, 1901. The patient was a man, aged forty-nine years, Hungarian by birth, tailor by occupation. His admission to the surgical ward was for the treatment of a tuberculous affection of the left ankle joint, which was discharging from several sinuses. An operation had been performed upon the joint at the New York Hospital a few months before. This was his sole complaint on admission, and the surgeons discovered by accident the curious muscular contractions with which he was afflicted and which apparently caused him no concern. It was ascertained that these had made their appearance about six months before without pain or paresthesia, first in the upper, soon after in the lower extremities. There had been no preceding illness except the joint affection before alluded to. He was of moderate habits, denied venereal disease, and no family neurotic taint was discoverable, but owing to his long exile from Hungary his knowledge in this direction was imperfect. No member of his family, to his knowledge, had ever had a convulsion. A few months before the onset of the disease, being poor and in feeble health, he had written to Hungary requesting money from his family with which to return home. This had been promised him, but in due time instead of a money order he received a letter containing a refusal. He despaired of ever being able to return to his native land, became sad and depressed, and a few weeks later the twitchings began. As he related this story his eyes filled with tears, and on subsequent allusion to it he always showed profound emotion. The twitchings had not interfered with the ordinary acts of life, as dressing, walking or holding a newspaper, and had caused him but little annoyance; toward the end of the day he would feel rather fatigued.

*Read, with presentation of specimens, before the New York Neurological Society, February, 1903.

Physical Examination. The man is of medium height, well made, body weight well preserved. Facial expression is quiet and melancholy. Skin pallid, mucous membrane a fair color. The face free from tremor or movement of any kind. Dressed and sitting in a chair, as when I first saw him, no abnormal movements of any kind were visible, except an occasional playing of the fingers. Locomotion and station were naturally somewhat interfered with by virtue of the joint affection, but were entirely unaffected by the muscular contractions. The pupils and pupillary reactions were normal, as were all the cranial nerves. No nystagmus. After removal of the clothing, the picture presented by the patient was a strange and unusual one. The muscles of the arms and shoulder girdles, thighs and buttocks displayed the greatest activity, individual muscles springing forward in contraction with the greatest rapidity and variation; sharp, shock-like contractions following one another with regularity and rhythm. The whole body of a muscle contracted as if stimulated by an invisible electrode. These contractions were unaccompanied by any locomotor effect. Occasionally, a barely perceptible flexion, extension or supination resulted from a particularly violent or prolonged contraction. It was further noted that while symmetrical muscles were involved, the contractions were by no means synchronous or isochronous. The movements were all clonic, no tonic contractions being noted. Contractions were noted in the following muscles: Deltoids, pectorals, scapular group, biceps, triceps, supinators, gluteal groups, extensors and flexors of the knee, and the sartorius; an occasional contraction was noted in the forearms and in the calves of the legs. The greatest play of movement was in the proximal segment of the extremities. The abdominal muscles and the diaphragm were quite free. The intensity and rapidity of these contractions could be modified in various ways. Mechanical stimulation of the skin and muscle increased them, while a coördinated act, such as grasping or picking up an object, caused their cessation or a very marked diminution. In walking and standing this diminution in the lower extremities was very noticeable. The contractions were most severe in the recumbent posture, less while standing, and almost disappearing while walking to and fro. An unusual and important peculiarity of these spasms was the contraction of individual muscles, as the sartorius and supinator longus, the isolated contraction of which cannot be produced at will. There were apparently isolated contractions of the brachialis anticus and coraco-brachialis, but this could not be determined with certainty. The muscular system was quite well developed and showed no evidence of pathological hypertrophy or atrophy. The gross motor function was undisturbed. The myotatic irritability

was increased. No electrical examination was made. Sensation was undisturbed. The tendon and skin reflexes were all present and very active; the knee-jerks especially were much exaggerated. Flexor response to plantar stimulation. No stigmata of hysteria.

The man was quiet and uncomplaining and shunned the society of his fellow-patients. He presented no evidence of mental enfeeblement. A few weeks later acute symptoms developed, death ensuing apparently from a generalization of the tuberculous process; as the thoracic and abdominal cavities were not opened, the immediate cause of death must remain unknown. It is interesting to note that the muscular contractions persisted the whole time during which he was under observation, varying, however, in intensity, and, according to the statement of the house-surgeon, were observed for twenty minutes after the respiratory and cardiac functions had ceased. According to the nurse's statement, the contractions ceased during sleep.

Histological Examination. The autopsy was performed forty-eight hours after death. The brain, spinal cord, and the right radial and anterior crural nerves were removed and placed in 10 per cent formalin solution. Portions of the right supinator longus, right sartorius, and left trapezius muscles were also removed.

Brain. Sections were prepared from the Rolandic area on both sides and from the frontal, temporal and occipital lobes, according to the Nissl, Weigert-Pal, Marchi and Van Gieson methods. No evidences of pathological changes were discoverable in nerve structures, meninges, vessels or glia. The outlines of the cortical cells and their processes are well preserved. A few cells are moderately pigmented. The nuclei, nucleoli and their refractive bodies are quite distinct. The nuclear network, however, is broken up and appears granular and homogeneous, remaining unstained or receiving a faint bluish tint. The Nissl granulations are coalescent and rather clumpy, staining intensely blue. The slight alterations in the nuclei and Nissl bodies are dependent on cadaveric changes.

Spinal Cord. Sections were prepared from various levels of the cord by the Nissl, Weigert-Pal, Marchi and Van Gieson methods. They were essentially normal. The spinal stichochromes of the anterior horns were absolutely normal. Cell bodies, processes, nuclei and nucleoli, no excess of pigmentation. The Nissl granulations, while somewhat coarse and rounded, are normal in distribution and arrangement. The vessels of the gray matter of the cord, especially in the cervical and upper dorsal regions, are distinctly thickened. The vessels in the lateral columns are also slightly sclerosed. This thickening involves chiefly the adventitia; nowhere was obliteration of the lumen observed.

The capillaries of the brain and cord are distended with blood.

Peripheral Nerves. The peripheral nerves, the inter-muscular nerve fibers and the muscle spindles were normal.

Muscles. The muscles were fixed and hardened in formalin, alcohol and Müller's fluid, and stained by the carmine, hematoxylin, Van Gieson and the Marchi methods. The supporting structures (endomysium and perimysium) were normal, as were the blood vessels.

majority in any given field, the diameter averages 150 micromillimeters and, in many, 175 micromillimeters. In contrast to this are very small fibers having crescentic forms or flattened out on the periphery of the large fibers. Of these smaller fibers some are below the normal standard. The fields of Cohnheim are quite distinct. Instead of finding the nuclei of the sarcolemma sheath

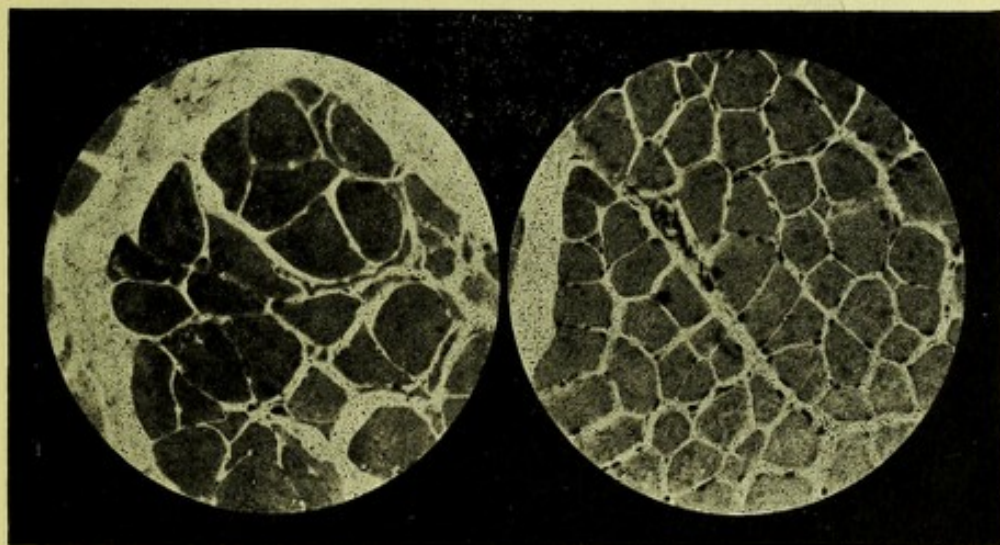


Fig. 1.

Fig. 2.

The picture presented by the muscles on transverse section is striking, the diameter of the muscle fibers reaching an unusual size (see Figs. 1 and 2). Of the larger fibers which form the

Fig. 1—Right supinator longus muscle from case of paramyoclonus multiplex.

Fig. 2—Normal muscle. Same enlargement as Fig. 1.

confined to the periphery of the muscle fiber and just beneath this membrane, as is customary in man, they are found scattered as well between the sarcous elements (Fig. 3). This is not true of all the fibers, but is observed in a large number and in all sections studied. Sometimes as many as three or four nuclei occupied a central position in a single fiber, usually only one or two. They are identical in staining properties with those of the sarcolemma sheath. On longitudinal section the transverse striation is distinct

and well preserved (Fig. 4). In the smaller fibers only is it at times indistinct or absent, these showing in addition a tendency to longitudinal cleaving. The nuclei of the sarcolemma sheath are increased in number; their structure and size are normal. Small clumps of a dark brown or yellow pigment are observed scattered over both the transverse and longitudinal sections, in the

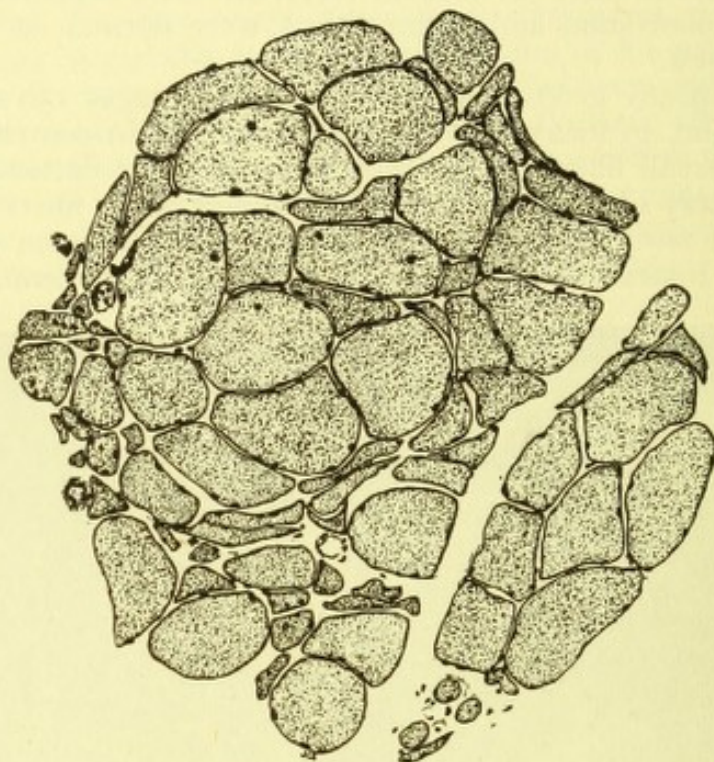


Fig. 3—Sartorius muscle. Paramyoclonus multiplex. Fibers hypertrophied with centrally situated nuclei.

latter especially in relation with the sarcolemma nuclei. No degeneration and no vacuolization of the sarcous substance is present. No degenerations were demonstrable by the Marchi method.

Remarks. The peculiar character of the muscular contractions in the case just described entitles it to a place among those rare cases of essential paramyoclonus multiplex. The histological examination of the spinal cord and biceps muscle from the original Friedreich case was carried out by Schultze.³⁴ The result was an entirely negative one. This and my own case constitute, I believe, the only examples on record of this type of paramyoclonus multiplex with systematic histological examination. The examination of the nervous system in my case was entirely normal. The muscle fibers, on the other hand, while

retaining their normal structure, were considerably hypertrophied. They were twice or three times the size of normal fibers from corresponding muscle utilized as control preparations. Muscle fibers vary considerably in size even under normal conditions. In

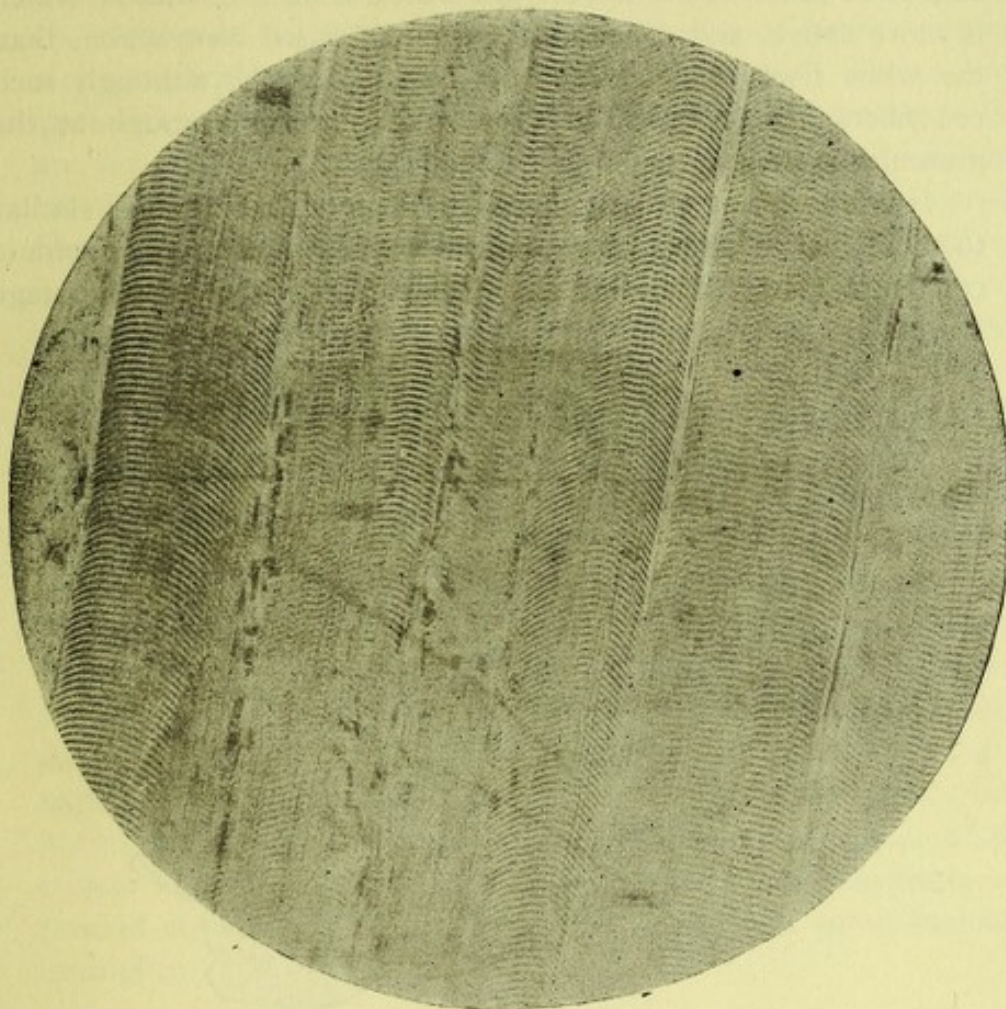


Fig. 4—Muscle showing transverse striations. *Paramyoclonus multiplex*.

general, the larger the muscle the larger is the muscle fiber. In man the minimum diameter is given as 10 micromillimeters; the maximum as 100 micromillimeters. In the case under consideration, the larger proportion of the muscle fibers on transverse section averaged a diameter of 150 micromillimeters, many measuring 175 micromillimeters. This increase in size of the fibers was not universally distributed over the microscopic field. In round numbers, two thirds may be said to have presented this change.

Many of those remaining were below the normal standard, so that the contrast was very evident.

Another peculiarity was the presence of sarcolemma nuclei between the sarcous elements. This is a peculiarity of the so-called red fibers of the lower vertebrates, a form of muscle which is more active, and capable of more prolonged contraction, than the white fibers which constitute human muscle, although such red fibers are scattered in very small number throughout the muscular system in man.

It is interesting and significant to observe that changes similar to those just mentioned have been described in cases of myotonia congenita (Erb,³⁵ Dejerine and Sottas³⁶), the hypertrophic stage

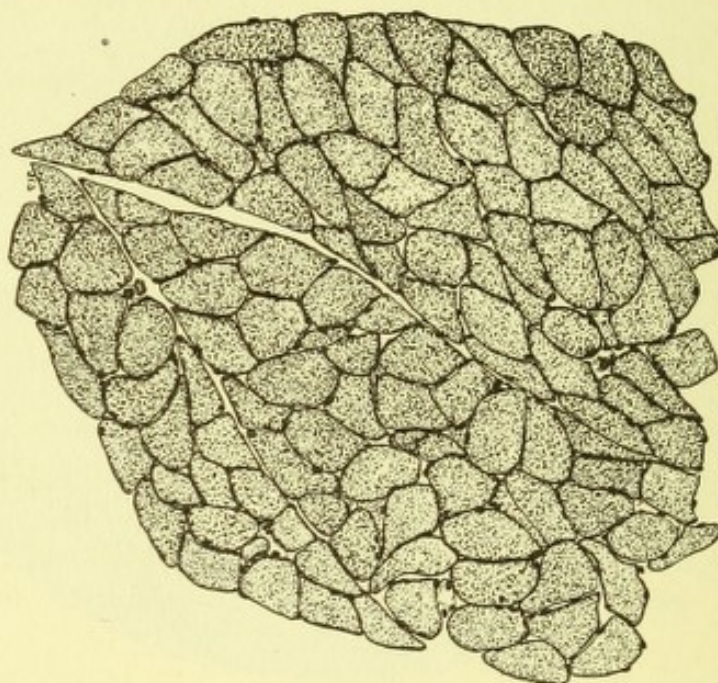


Fig. 5—Sartorius muscle from a case of chronic progressive chorea [control preparation]. Same enlargement as Fig. 3.

of the muscular dystrophies, and in those rare cases of true muscular hypertrophy, of which examples have been described by Friedreich,³⁷ Auerbach,³⁸ and Berger³⁹. If such alterations in the size and nuclear constituents of the muscle fiber were simply the result of overaction, and secondary only to violent and prolonged muscular action, they should occur in long-standing spasmodic affections of cerebral origin. In one of the cases used as a control preparation in the present study, a chronic progressive chorea

of fifteen years' duration, the muscles were found absolutely normal (Fig. 5). It is suggestive that in the muscular dystrophies and hypertrophies and in myotonia and in paramyoclonus multiplex, which represent obscure affections of the muscular and neuromuscular systems respectively, muscle changes essentially similar should be encountered. Hajos' ⁴⁰ case of paramyoclonus multiplex with the electrical reactions of Thomsen's disease is of interest as furnishing clinical evidence of this relationship. We are far from understanding the true significance of the relations existing between the peripheral motor neurone and the muscle fiber, tissues having a different structure and derivation and yet intimately related; the fate of the one resting entirely upon the integrity of the other—the so-called *trophic function or influence of the anterior horn cells*.

In articular muscle atrophies, this trophic influence in some obscure way appears to undergo a reflex inhibition. In the Darkschewitz case the muscle fibers had suffered a reduction of one half their natural size.

As this trophic influence may under certain conditions be so perverted as to cause disintegration or atrophy of the muscle fibers, it is reasonable to assume the possibility of an increased trophic function with a resulting hypertrophy. If the Friedreich theory of the irritability of the anterior horn cells is accepted in explanation of the motor phenomena of paramyoclonus, these muscle changes may well represent a concomitant increase of the trophic function of these same cells, and this would constitute important objective evidence of the spinal origin of paramyoclonus multiplex.

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NOTE.—For further bibliographical references consult the monographs of Unverricht ("Die Myoklonie," 1891) and Gaupp ("Ueber Myoklonie," Inaugural Dissert., Tübingen, 1898), also Risien-Russell (Albutt's "System of Medicine"), and Wollenburg (Nothnagel, *Spec. Path. u. Ther.*).