v. Merkel u. Bonnet"; "Index Catalogue of the Surgeon-General's Office," "Jahresberichte über d. Fortschritte der Anat.," *Journal of the Roy. Micr. Soc., Zeit. f. mikr. Anat.*

Specific reference has been made to the following:

[1] Bardeen and Lewis: The Welch Book and Amer. Journ. Anat., vol. i., 1902.
[2] Batten, F. E.: Brain, vol. xx., 1897.
[3] Beale: Trans. Royal Micr. Soc., 1864, pp. 94–108.
[4] Bowman: Phil. Trans. R. S., 1840, pp. 457–501.
[5] Busk and Huxley: Translation of Kölliker's Manual of Histology, 1853.
[6] Felix, W.: Festschrift für A. von Kölliker, 1887.
[7] Gage, Susanna P.: The Microscope, vol. viii., 1888. Proc. Amer. Micr. Soc., 1890.
[8] Heitzmann: Wien. Akad. Sitzungsber., lxvii., pp. 141–160.
[9] Herzig und Biesiadecki: Wien. Akad. Sitzungsber., xxx., pp. 73–74; xxxiii., pp. 146–149.
[10] Jardet: Arch. d. Phys. Norm. et Path., 1886, pp. 93–100.
[11] Kölliker: Gewebelehre, sixth edition, 1889.
[12] MacCallum, J. B.: Anat. Anz., vol. xiii., 1897; Johns Hopkins Hospital Bulletin, October, 1898.
[13] Meek, A.: Journ. Anat. Physiol., vol. xxxiii., 1899.
[14] Ranvier: Leçons, 1880, and Traité Technique.
[15] Remak: Froriep's Notiz., 1845, No. 768.
[16] Rollett: Wien. Akad. Sitzungsber., xxi., pp. 176–180.
[17] Salter: Tongue, Todd's Cyc. Anat. Phys.
[18] Schwann: Untersuchungen, 1839.
[19] Weismann: Arch. f. Anat. u. Phys., 1861, pp. 41–63.
[20] Huber and DeWitt, Jour. Comp. Neurol., vol. vii., 1898.

Simon Henry Gage.

MUSCLE, PATHOLOGY OF.—

I. Striated Voluntary Muscle.

From the pathological point of view, the important points to be considered in the structure of striated voluntary muscle are the amount of interstitial connective tissue, the size and shape of the muscle fibres, the striation, and the number and position of the nuclei. Normally the endomysium, or the connective tissue separating the individual fibres, is small in amount, while that separating the fasciculi is considerably larger in amount, varying in different portions of the muscle. The distinctness of the striation depends somewhat on the method of fixation and preparation of the tissue, but in well-fixed preparations the fibres show a distinct transverse striation, due to the difference of refraction of the fibrillar and interfibrillar substances of the fibres, the ultimate fibrils being anisotropic, while the sarcoplasm is isotropic. In cross sections, the muscle fibres present irregular lighter and darker areas, due to the arrangement of the fibrils in columns, known as muscle columns, with a larger amount of sarcoplasm between the columns than is found between the individual fibrils. The muscle fibres are large, showing normally in cross section a diameter of from 10 μ to 100 μ, while they often attain a length of 12 cm. Their free ends are usually pointed, while the end attached to tendon is rounded. The nuclei of white muscle fibres are situated immediately under the sarcolemma and are very numerous, a cross section of a muscle fibre presenting from one to four or five nuclei. The nuclei of red muscle are situated in the sarcoplasm between the muscle columns. Marked variations occur in the number of nuclei, however, as has been pointed out by Morpurgo and Bindi and others. In young muscles, the nuclei are more abundant and more uniformly distributed than in adult muscle. In small adult muscles the nuclei are more abundant than in the larger fibres, while in the large irregular fibres the number is very variable and much smaller than in the smaller fibres or the embryonic muscle. Hence growth of muscle is not accompanied by corresponding increase of nuclei, the small fibres with high coefficient of growth preserving the juvenile character of nuclear abundance. These are the fibres which change most in the process of activity hypertrophy, the abundance of nuclei corresponding to a greater reserve of growth energy.

Under different pathological conditions, any one of these factors may be materially altered. The connective tissue may be increased or diminished in amount. The muscle fibres may be larger or smaller than normal and may change their shape and their relation to each other. The striation may become indistinct or even be lost altogether, the fibres assuming a granular or homogeneous appearance, while the nuclei may be greatly increased in number and very irregularly grouped, so that some sections will contain large numbers of nuclei, while others contain none. The muscle fibres may segment into short discs, or may break up longitudinally into small slender fibrils, which may remain attached at one extremity, giving the appearance of a branching of the parent fibre. The pathology of striated muscle has recently been treated by Professor Warthin in the *American Journal of Pathology*, and with some modifications I have made use of his classification in the following discussion.

Congenital anomalies of muscle concern largely the realm of gross anatomy. Supernumerary muscles may be found or certain muscles may be lacking. Occasionally the origin or insertion of a muscle varies from the normal. Such anatomical variations are considered in a separate article. (See *Muscles, Anomalies of.*)

Circulatory Disturbances.—Voluntary striated muscle has a very rich blood supply; numerous arteries break up into rich, long-meshed plexuses of capillaries, which surround the muscle fibre, each cell being in contact with several capillaries. The free anastomoses of these vessels easily compensate for any local obstructions, thrombosis, or embolism, and prevent any deleterious results, unless an infective embolus is the cause of the obstruction, in which case an abscess results. "In cachectic conditions, fevers, etc., in which the nutrition of the muscle is lowered, an anæmic necrosis may result from arteriosclerosis, deficient heart action, local compression, infiltrations, etc. Such anæmic infarctions are seen in senile gangrene, decubitus, etc." (Warthin). Psoas infarcts, associated with bed-sores, may result from long continuance of the recumbent posture, in which case the main arteries of the muscle may contain obturating thrombi or may show a proliferating endarteritis. In this condition, the entire muscle may undergo Zenker's necrosis, appearing white and translucent, but usually hemorrhages are scattered through the muscle and the necrosed area is surrounded by an extensive extravasation of blood. Scar tissue may replace the necrosed tissue, attempts at regeneration of the muscle fibres being frequently found; if the area becomes infected, however, a psoas abscess may result.

Anæmia of muscle may result from general anæmia or it may be local in origin, being caused by obstruction in the nutrient arteries, compression or arteriosclerosis. The muscle is pale and either soft, as when the affection is local, or dry, when the process is part of a general anæmia. The muscle may, however, be brown from increase of pigment.

Hyperæmia usually disappears shortly after death, the passive hyperæmia occurring only in the rare cases of extreme vascular stasis, while the congestive form is found in the neighborhood of inflammatory areas. Œdematous muscle is softer and moister than normal muscle, and on microscopic examination clear vacuoles are seen in the protoplasm of the muscle cells, while the connective tissue is much looser than under normal conditions, the connective-tissue fibres being separated by accumulations of clear fluid. In severe cases, the muscle fibres may undergo liquefaction.

Hemorrhages in muscle are far from uncommon; they may result from trauma, from convulsive contractions of the muscle, from increased blood pressure, or from degenerative changes in the vessel walls or in the surrounding muscle. Such changes are common in typhoid or typhus fever, in septic conditions, pernicious anæmia, etc., while small hemorrhages are frequent in the acute infections, phosphorus poisoning, leukæmia, and pernicious anæmia. As a result of the hemorrhage, the muscle fibres are pushed apart and may be destroyed, if the hemorrhage is large. The muscle liquefies or undergoes a coagulation necrosis. Blood clot becomes organized and a pigmented scar remains, only a few regenerated muscle fibres usually replacing a portion of the connective tissue of the scar. The connective tissue

may, however, develop into cartilage and bone, as in some of the cases of traumatic myositis ossificans.

Retrogressive Changes.—Changes in size of the voluntary muscle fibres are among the commonest changes met. Under circumstances of increased nutrition, whether from the general condition or from systematic muscular exercise, the muscle fibres increase in size and we have a true *hypertrophy* of the muscle, while under the opposite conditions of disuse or diminished use of muscle, or when the general nutrition is lowered, the fibres undergo *atrophy*, the diminution in size varying with the degree of the unfavorable conditions. These conditions of true hypertrophy and of simple atrophy are usually transient, the fibre being restored to its normal appearance on the restoration of the normal conditions. If, however, the exercise be continued too long or be carried to an excess, the hypertrophied muscle may become atrophied, and simple atrophy may lead to degenerative changes. Simple atrophy, in its simplest form, occurs in old age, but it is also seen in cachectic states, such as tuberculosis, carcinoma, etc., and it may result from compression of the nutrient arteries. Macroscopically, atrophic muscles appear paler, dryer, and firmer than normal. A brown pigment, hæmofuscin, probably a product of the sarcoplasm of the muscle fibre, may develop in the fibres, giving them a brown color. In some cases, the fibres undergo *hydropic degeneration*, serous atrophy, in which the muscle appears moist and soft.

The clinical aspect of the muscular atrophies will be treated under a separate heading. Regarding the pathological aspect of the muscular atrophies, we may say that atrophic degenerations may be neuropathic, depending on lesions in the spinal cord, or they may be primary or myopathic. In the former case, some of the most interesting changes are those which occur in the spinal cord; the cells of the anterior horn are atrophied and show degenerative changes and the pyramidal tracts are involved. The degeneration may even be traced to cells in the medulla and motor cells of the cerebral cortex. In the myopathic form of muscular atrophy, or the so-called muscular dystrophy, the nervous system shows no essential changes, although varied and irregular alterations are described by certain authors, such as atrophy of the posterior root ganglion cells, some cytoplasmic changes in the ganglion cells of the spinal cord, etc. None of these changes, however, is found uniformly in all cases of muscular dystrophy, and the disease is therefore believed to originate in the voluntary muscle and is probably due to some congenital anomaly of development. Kollaritz describes atrophy of the motor cells and of the fibres of the substantia grisea centralis around the spinal canal, these changes occurring especially in the cervical and dorsal regions. The peripheral nerves were intact. He believes that the changes in the cord and in the muscle occur together and that both probably depend on faulty development. Atrophy of the motor cells is especially characteristic both in his cases and in those of Erb, Schultze, Preisz, Frohmeier and others. This may readily be explained as the result of faulty development, and the development of muscles might well stop if at a certain age the motor nerve cells thus atrophied, while it is not unreasonable to suppose that the motor nerve cells might undergo secondary atrophy, as the result of this degeneration of the muscle fibres. While it was formerly believed that the primary dystrophies could be distinguished microscopically from the neuropathic atrophies, it is now generally conceded that there is no essential difference in the pathological picture presented by the two classes of the disease. The idea that the dystrophies could be differentiated by the fact that the atrophy was uniformly preceded and accompanied by hypertrophy of the muscle fibres has been practically overthrown by the recognition of the fact that in both the neuropathic and myopathic atrophies the atrophy may be preceded by hypertrophy, the fibres being enlarged to a variable extent before the atrophy sets in, and even at the height of the atrophic process some enlarged fibres may be found among the many atrophic cells. In neuropathic atrophy, however, the localization of the degenerative process varies according to the localization of the lesion in the cord.

In a case of traumatic transverse myelitis resulting from an injury to the cord in the lower dorsal region, the psoas muscles showed the most extreme degree of degenerative changes, while the lumbar muscles and the leg muscles contained bundles of extremely atrophic fibres, and the muscle cells of other bundles were normal in size, appearing hypertrophied by contrast with the atrophied fibres. In the psoas muscles, most of the cells were very small, appearing scarcely larger in cross section than involuntary muscle cells. No transverse striation could be observed in any of the fibres and the cross sections appeared either homogeneous or finely granular. Some, however, were vacuolated, some showing very little of the protoplasmic substance of the fibre, appearing to consist of nucleus and sarcolemma, the intervening space being clear. A few of these fibres in cross section presented no nuclei; in the majority, however, one or two deeply stained, relatively large nuclei were seen near the end of the oval cell, while some showed a crescent or corona of nuclear substance at the periphery. Many cells were seen containing numerous nuclei, which were often hyperchromatic and appeared as a dense, fused mass of deeply stained chromatic substance. These giant cell forms or sarcolytes were especially numerous in some fields, while in others very few were found. In longitudinal sections, longitudinal and transverse cleavage could be observed, and in many areas long, narrow, spindle-shaped cells were seen, which contained long rows or chains of deeply stained nuclei. There was also a marked increase of connective tissue, often accompanied by a deposition of fat, especially in the increased connective tissue of the endomysium. This picture may be taken as the typical picture of muscular atrophy, varying in degree, but little in character. The increased connective tissue, the fibrillar forms mentioned, and the multinuclear, giant-cell forms have been the subjects of much discussion. Durante, Kroesing, and others, upholding the view of embryological development of muscle advocated by Hoffmann, Waldeyer and others, that the striated muscle cell is a syncytium developed by the fusion of numerous spindle-shaped cells of the mesoderm, describe the longitudinal cleavage or fibrillation of the muscle fibre as a return to the embryonic condition. They state that these fusiform fibres may form new muscle fibres, but usually degenerate and mingle with the connective tissue, acquiring all its characteristics. To this tissue Kroesing gives the name myogenous connective tissue or connective-tissue state of the muscle fibres. He states that the increase of connective tissue in muscular atrophy is due to the formation of this tissue rather than to an increase of true connective tissue. In preparations stained by Mallory's differential stain for connective tissue, however, it may be plainly seen that this tissue gives the reaction of true connective tissue, so that we may conclude that, if it be derived from muscular tissue, it has acquired, not only the morphological, but also the chemical characteristics of connective tissue. It seems more probable, however, that the muscle degenerates on account of the poor nutrition of the tissue, and that the increase of connective tissue is due to the well-known tendency of connective tissue to replace lost tissues and to fill spaces where it is needed. The fate and significance of the multinuclear forms have been considered by many authors and have been generally regarded as attempts at regeneration. Fujinami, however, believes that in purely degenerative processes, cells morphologically identical with the myoblasts of regenerating muscle may be found, and that in these cases they should not be interpreted as having a regenerative significance, but rather as degenerative forms. While this point seems to need further investigation, Fujinami's view receives confirmation from the fact that these multinuclear forms are quite as numerous in the most extreme degree of muscular degeneration, where no tendency to repair

seems to be present or is to be expected, as in areas less severely affected.

Progressive muscular dystrophy, in its simple form, presents a very similar pathologic picture to that described for neuropathic atrophy. The pseudohypertrophic form, however, is characterized by a marked formation of adipose tissue, formed probably from the proliferated cells of the endomysium, although Kroesing states that it arises from a metaplasia of the muscular tissue into adipose tissue. This myogenous adipose tissue is distinguished from true adipose tissue by the presence of fragments of muscle or by remains of muscle structure or arrangement. In this form of atrophy, as in the others, the muscle fibres are more or less atrophied. A true hypertrophy of the muscle may, however, accompany the increase of connective and adipose tissue, as in the case reported by Durante, in which many of the cells attained a diameter of 180 μ; the nuclei were greatly increased in number, being arranged either in long lines or in a circle surrounding the fibre. Vacuolation and granular degeneration were also noted in these fibres. Durante believes that the muscular hypertrophy in this case was congenital or was developed in early life, while the degenerations and elephantiasis were probably of much later growth.

Thomsen's Disease, or Myotonia Congenita, is a special form of muscular dystrophy, which is hereditary and congenital and affects numerous members of the same family. It is characterized clinically by the occurrence of tonic cramps, when the patient attempts to move. A case recently described by Koch may be taken as typical of the affection. The patient was twenty-one years old and his musculature was well developed. The principal symptom of the affection was stiffness, slowness, and difficulty of motion, especially when first beginning to move, but wearing off later as the effort was continued. This symptom had been noticed since early childhood. The cramps are usually painless and may affect the limb muscles, the eye muscles, and the muscles of mastication, but the extremities are the parts most involved. The involuntary muscles are spared. Cold and nervousness may cause an increase of the affection, while systematic muscular exercise is beneficial. The affection is rarely cured, although it does not endanger the life of the patient. Erb describes an increase of the interstitial connective tissue, with marked hypertrophy of the muscle fibres. The finer details of structure may also be slightly altered, the striations being less distinct than normal, the fibres appearing more homogeneous, but often vacuolated. Koch describes a longitudinal cleavage of the muscle fibres, causing an increased number of fibres. He states that amitotic division of the muscle nuclei was observed, resulting in the formation of the long, slender cells containing rows of nuclei, such as are observed in degenerative and regenerative processes.

Degenerations.—While the various forms of muscular degeneration have been variously classified, it may be

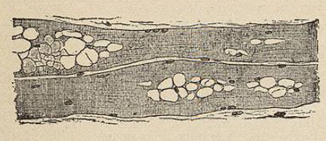

Fig. 3418.—Hydropic Degeneration of Voluntary, Striated Muscle. (Ziegler.)

noted that they all tend to occur together, wherever the muscle is exposed to unfavorable conditions. Progressive muscular atrophy, whether of nervous or of muscular origin, may be accompanied by any or all of the degenerative processes, while inflammations, injuries of muscle, and tumors are all, to a greater or less extent, surrounded by areas of degenerated muscle. One of the most common and at the same time the most serious degeneration affecting striated muscle is the *granular or proteid degeneration*, also known as *cloudy swelling*. The fibre is usually enlarged, the striations are less distinct, the cell appearing distinctly granular. The granules are not fatty, since they do not react to osmic acid nor dissolve in ether or chloroform; they dissolve in acetic acid. Durante distinguishes two forms of granular change—one, which we may regard as physiological, due to excessive activity of muscle, and analogous to the granular change in gland cells during secretion. The fibres are enlarged and the striations are indistinct on account of the thickened layer of granular sarcoplasm lying between the sarcolemma and the fibrils. This condition is usually transitory, the cell returning to its normal state as soon as the conditions which caused the change have been altered. If, however, the cause persists, the cell may undergo fatty degeneration or liquefaction or coagulation necrosis. The second type is a true degeneration, leading to the death of the cell, and occurs in cachexias, infectious diseases, myositis, and other muscular affections.

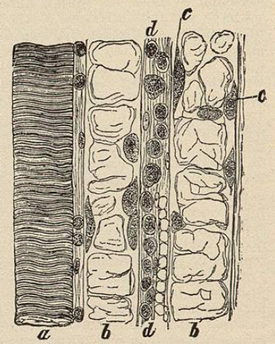

Fig. 3419.—Zenker's Waxy Necrosis. (Ziegler.)

Hydropic degeneration of voluntary muscle occurs especially in suppurative inflammations, chronic œdemas, etc., and is characterized by the presence of clear vacuoles in the protoplasm. Fresh muscle thus affected appears pale and watery. It may be distinguished microscopically from simple œdema of muscle by the fact that the muscle nuclei stain poorly in case of degeneration.

Fatty degeneration occurs in an extreme degree in cases of phosphorus poisoning and to a less degree in tuberculosis, in fevers, intoxications, etc. The muscle cells show fat globules in their protoplasm, which therefore appears peculiarly reticular. These may merge into larger fat droplets. These cells stain poorly in eosin, so that a fibre undergoing fatty degeneration appears hazy and mottled, while, after treatment with osmic acid, the droplets show the characteristic black reaction. The muscle nuclei may also show the characteristic degenerative changes.

In cases of inflammations, fevers, intoxications, and in the neighborhood of malignant tumors may be found fibres undergoing *simple necrosis;* these are larger than normal, show no transverse striations and no nuclei, and the entire fibre takes an indifferent bluish-red color, when stained with hæmatoxylin and eosin. In chronic œdema, suppurative inflammation, etc., the muscle fibres may undergo *liquefaction necrosis*. The fibres at first appear enlarged, vacuolated, or granular, and finally dissolve in the fluids in the surrounding tissues. Zenker has also described a *waxy or hyaline necrosis* of the muscle fibres, occurring in typhoid fever. It may also occur in any severe fever, in acute tuberculosis, in sepsis and variola, and also in wounds, inflammations, and to a limited degree in all the pathological processes which may result in the degeneration of voluntary muscle. If the degeneration is of wide extent, the affected muscle is soft, white and translucent, resembling fish-flesh. The softening may lead to more or less extensive hemorrhages in the muscle. The muscles most frequently severely affected are the psoas, the abdominal muscles, and the muscles of the thigh. The muscle fibres are of irregular size and form, many of them being swollen. The cross striation is lost, at least in many areas, and a peculiar

hyaline or waxy mass appears in the protoplasm, the fibre finally breaking up into irregular hyaline masses, which are afterward absorbed. The hyaline mass usually stains poorly with the ordinary stains, but may resemble fibrin in its reaction to Weigert's fibrin stain, while in the Van Gieson stain it may react like colloid. The hyaline mass may fill the entire cell or occupy only certain areas, these peculiar homogeneous areas being surrounded by granular sarcoplasm, while some areas may appear striated and quite normal. The nuclei may entirely degenerate, while in milder cases they may proliferate and lead to the regeneration of the muscle fibre. A leucocytic infiltration of the intermuscular connective tissue may precede or accompany this degeneration. In senile gangrene, decubitus, infective inflammations, burns, freezing, and in lowered nutrition of the skin and subcutaneous tissues, the voluntary muscles may undergo gangrenous changes, the muscles becoming brownish, black, or greenish in color, breaking up into shreds or liquefying, or, if exposed to the air, undergoing mummification. Microscopically, the muscle fibres present the picture of liquefaction or coagulation necrosis, the fibres losing their form and striation. A marked leucocytic infiltration accompanies this process, while blood pigment and crystals of cholesterin and triple phosphate are often found. In mummification, the cells shrink and lose their form and nuclei and finally appear like horn. Not unlike a liquefaction gangrene is the degenerative process described by Hoen as occurring in the striated muscle fibres of the uvula. This is characterized by a bleb-like change, associated with pigment formation and nuclear proliferation. The sarcolemma is raised by the vesicles, each of which contains a nucleus, so that the liquefying process seems to begin in the undifferentiated sarcoplasm surrounding the nucleus. Cross striation can still be seen in places, but the longitudinal striation is replaced by wavy and undulating lines, due to the twisting of the fibrillæ. The final stage of the degenerative process shows masses of large blebs, containing small, large, and misshapen nuclei, with pigment, through the middle of some of which runs a shadow suggestive of a muscle fibre. Even in such a mass, some fibrils may be found which still show striæ.

Fragmentation and Fibrillation.—In necrosis and in most of the degenerative and other pathological states of muscle, fibres may be found which are breaking up either longitudinally into long fusiform fibrils, or transversely into irregular plates or discs of muscle substance. Often the fibril can be traced to the point where it joins the parent fibre. The process results in the atrophy of the main fibre, while the fibril which has been split off may either develop into a new muscle fibre, as in the regeneration of muscle by the proliferation of its nuclei, or it may still further degenerate, either shrinking into threads so that the tissue closely resembles fibrous connective tissue, or undergoing fatty degeneration and forming a tissue resembling adipose tissue. Warthin states that "*amyloid degeneration* of voluntary striated muscle is rare and occurs especially in the muscles of the tongue and larynx. The deposit begins in the capillary walls of the endomysium and may extend around the sarcolemma, causing an atrophy of the fibre. The atrophic fibre then appears as if surrounded by a glassy hyaline substance. Ultimately the fibre disappears and the confluence of the deposit leads to the formation of nodular masses." The presence of pigment in voluntary muscle fibres, in the so-called brown atrophy, has already been mentioned. The pigment, known as hæmofuscin, appears as brown or yellow granules in the neighborhood of the nuclei and it indicates a degeneration of the muscle substance. The degenerative processes in voluntary muscle caused by experimental section of the nerve have been well described by Ricker and Ellenbeck. Chromatin granules appeared in the nucleus on the twenty-third day. The nuclei appeared shorter and broader, even spherical, with loosening of the chromatic network. The muscle and nuclei showed œdematous changes. The division of the nuclei was by direct fragmentation, no mitotic figures being found. The authors regard this nuclear fragmentation as a degenerative process, not leading to the regeneration of the muscle. The muscle fibres showed atrophy, but very slowly developing, while the protoplasm showed vacuolation and transverse cleavage, with diminishing distinctness of striation. There was at first an increase in the amount of fat in the intermuscular connective tissue, followed by diminution. The muscle was at first hyperæmic and œdematous, but later became anæmic. There were also an increase of connective tissue and a narrowing and hyaline deposition in the intermuscular capillaries. The changes were believed to be due to disturbances of circulation rather than to direct influence of nerve section.

Schujeninoff has carefully studied the processes involved in the *calcification* of striated muscle, both experimentally in animals and by observation of men. He concludes that the lime salts are deposited in muscle under certain conditions, as after the suture of a wound in the muscle. The calcification takes place after the fibres have undergone a colloid degeneration. When the lime salts are absorbed, the calcified fibre disappears. The calcification of muscle is therefore a local, secondary process, which stands in relation with the local disturbance of circulation.

Regeneration of Voluntary Muscle.—In embryonic life, striated muscle fibres develop from mesodermic cells, each fibre being formed by endogenous proliferation of the nuclei of a single cell. This is the view advanced by Remak, Schultze, Kölliker, Zenker, and many others, who contend that the growth both in length and thickness takes place by this nuclear proliferation, while the protoplasm changes into the contractile substance of the muscle fibre. This view is opposed by Hoffmann, Waldeyer, Kroesing, Durante, and many others, who believe that the muscle increases in length only by endogenous division of the nuclei, while the increase in thickness is brought about by the apposition and fusion of numerous fusiform cells. Experimental degeneration of muscle has been brought about by tenotomy, by neurotomy, and by sectioning the muscle fibre itself. Numerous experiments have also been undertaken in the transplantation of portions of muscle taken both from the same animal and from other animals, even those of a different species. Salvia transplanted muscle from a rabbit to fill the space made by removing portions of a dog's muscle. He states that the result was perfectly satisfactory, as the new muscle replaced the old perfectly both anatomically and functionally. Others have claimed equal success in similar experiments, but Capurro, in a series of experiments recently reported, gained results which were only partially satisfactory. The result of transplanting free pieces of muscle was negative. By using only a portion and leaving a pedicle attached during the union, he was able to secure satisfactory functional results. He observed degenerative changes in the muscle, such as simple atrophy, Zenker's necrosis, fibrillation, increase of connective tissue, leucocytic infiltration, etc. In these cases, as well as in wounds of muscle, granulation tissue is first formed. The muscle nuclei proliferate, both by mitotic and by amitotic division, and buds of sarcoplasm containing the new nuclei grow out from the ends or body of the muscle fibre into the granulation tissue. These buds at first show no striation, but contain many large nuclei and appear like epithelioid cells. Then in the sarcoplasm, fibrils are formed and thus the fibre becomes striated. Several new fibres may be formed from one bud or myoblast. In addition to these myoblasts, free multinuclear cells are formed, known as sarcolytes. These are not in connection with the original fibre, and while some may form new fibres or unite either with the old fibre or with new ones, most of them probably undergo fatty degeneration or necrosis. The sarcolytes may resemble the myoblasts in section and give the appearance of regenerative effort, even when the conditions are so unfavorable that no attempt at regeneration is to be expected. A perfect regeneration of muscle appears to be possible only when the contrac-

tile substance is but slightly injured and the sarcolemma and muscle nuclei are intact, as after freezing, after the degenerative changes of typhoid fever, sepsis, and trivial traumatic injuries in which but little of the contractile substance is lost. In more severe injuries the regeneration is only partial, muscle fibres growing out from the

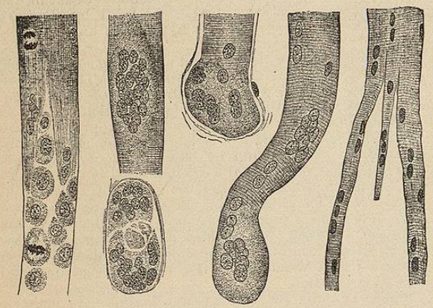

FIG. 3420. — Regeneration of Muscles, Myoblasts, and Sarcolytes. (Ziegler.)

ends of the old fibres into the granulation tissue which at first replaces the destroyed muscle (Warthin). Volkmann states that regeneration is functionally important only after typhoid fever and freezing, while after injuries the regeneration is so slight that function is not restored unless the wounds are small. Larger wounds heal by the formation of scar tissue, which is muscularized from both sides and ends, but only for a short distance. Transplanted pieces of muscle degenerate and are replaced by scar tissue, which is in the same way muscularized for a short distance from the sides and ends. Kümmel, however, reports a case in which he sutured the ends of muscle which were from 8 to 10 cm. apart, and secured almost perfect restoration of function after six months. The differences in the reported results may depend upon different nutritive or nervous conditions, but it would seem from the majority of the reports that, while voluntary muscle does regenerate by both mitotic and to a limited extent amitotic division, its power of proliferation is extremely limited and does not extend to the complete restoration of large areas of destroyed muscle fibre.

CHANGES IN THE MUSCULAR NERVE ENDINGS.—The subject of degenerative changes in voluntary muscle can scarcely be fully treated without some consideration of the changes occurring in the motor and sensory nerve terminations in this muscle. I am not familiar with any work reporting the changes in the motor endings in human muscle occurring under pathological conditions, but Huber has recently reported the results of some experiments on rabbits, in which he crushed the posterior tibial nerves, afterward studying the motor and sensory nerve endings in the interossei muscles by means of the *intravitam* methylene blue method. Till the end of the first day after crushing the nerve, the motor endings presented a normal appearance and the muscle responded to electrical stimulation of the nerve applied below the point of injury. During the second day, changes began to appear in the motor endings, ushered in by relatively large, usually round or oval, deeply staining enlargements, or varicosities, varying in number, size, and shape, which were found on the arborizations of the motor endings. These changes did not affect all the motor endings at the same time; but when a majority of all the motor endings in the muscle showed the nodular enlargements, the muscle failed to respond to electrical stimulation. At the same time the nerve fibre showed degenerative changes at its distal end. Later, the arborizations disappeared or failed to stain differentially, although the so-called sole plate sometimes stained a faint blue. The regeneration of these endings was observed about thirty days after the experiment, beginning with the formation of fine, varicose fibres ending in a small granule, and passing through various transition stages to an ending which is in every respect like the original ending. Not until numerous regenerated motor endings were found, did the muscle again respond to electrical stimulation. The neuromuscular nerve end-organs are the most interesting of the sensory nerve endings found in voluntary muscle and have been subjected to the most careful investigation. Sherrington sectioned the sciatic nerve, causing degeneration of the nerve fibres and complete atrophy of the muscle fibres, but found the intrafusal muscle fibres of the spindle well preserved and the striation retained one hundred and fifty days after the section. Eichhorst reports the presence of fat globules in the intrafusal muscle fibres of neuromuscular spindles in a case of phosphorus poisoning. Grünbaum found the muscle fibres atrophied and surrounded by hyaline substance in some of the spindles in a case of pseudo-hypertrophic paralysis, while Gudden observed atrophy of the intrafusal fibres in a case of alcoholic neuritis. Batten examined the condition of the neuromuscular spindles in cases of infantile paralysis, tabes dorsalis, myopathy, progressive muscular atrophy, and peripheral neuritis, and found the muscle spindles normal, except in one of the three cases of tabes examined. After injury of the brachial plexus, however, which resulted in complete loss of motion and sensation, he found changes in the spindles one year after the traumatism. The spindles were small, the intrafusal fibres were atrophied and granular with indistinct striation, while the nerve fibres going to the spindles were poorly stained. Batten therefore concludes that after injury or section of the nerve the neuromuscular spindles undergo degenerative changes in time, but much later than the surrounding muscle fibres. Laslett and Warrington found the spindles unaltered in a case of lead paralysis examined by them. Batten, in a series of experiments upon animals, showed early degenerative changes in the nerve terminations within the neuromuscular end-organs, with later changes in the form, calibre, and arrangement of the intrafusal muscle fibres, but he was unable to reproduce the fatty change of the intrafusal muscle seen by him in the case of tabes dorsalis. Huber, in the experiments previously described, found that the myelin of the large sensory nerve fibres going to the neuromuscular and neurotendinous end-organs showed segmentation, and that the nerve fibres within the organs were broken up into irregular, deeply staining fragments, which gradually disappeared. The changes in the sensory nerve end-organs did not, however, take place until the third day after the crushing of the nerve. No degenerative changes in the muscle fibres of the spindle were mentioned by him. Regenerating sensory endings were seen by him on the forty-first day after the experiment, but it was not until the end of the second month or the beginning of the third month that the nerve endings in these organs presented an appearance similar to that found in the normal organs. In the case of transverse myelitis previously described, the neuromuscular nerve end-organs showed œdema, the layers of the capsule being widely separated by clear fluid, and the muscle fibres also being crowded apart. The muscle fibres of the spindle did not, however, show any marked pathological changes. In the neurotendinous nerve end-organs, also, Cattaneo and others have demonstrated early changes in the nerve endings.

INFLAMMATIONS.—The inflammatory processes in voluntary muscle may be acute, subacute, or chronic. The true inflammatory conditions are largely interstitial, involving the connective tissue of the endomysium and perimysium and the capillaries, while the muscle fibres undergo degenerative changes as a result of the changed nutritive conditions brought about by the presence of the inflammatory exudate. The inflammations may be the result of the extension of an inflammation from neighboring tissues, or germs may be carried into the muscular tissue through the blood current. Traumatism, disturbance of nutrition, and vascular changes may also act as powerful indirect etiological factors. Myalgia or so-called rheumatic myositis or muscular rheumatism often affects the muscles of the back, neck, or the intercostal muscles. In most cases it is probably not a myositis but a neuralgia, due to slight twisting or laceration of some of the muscle fibres. Its one common symptom is pain in the muscles. It usually quickly subsides, often spontaneously. If necessary, anodynes or hot applications will generally give relief.

In *acute parenchymatous myositis*, the muscle fibres show granular, hydropic, and fatty degeneration, Zenker's necrosis, fragmentation, fibrillation, etc. The endomysium contains large numbers of leucocytes and is œdematous, while the capillaries and blood-vessels are distended and filled with blood cells. If the degenerative changes in the muscle fibres are not too severe, recovery usually takes place with complete restoration of structure and function of the affected muscle. This comparatively mild form of inflammation occurs after slight injuries, in disturbances of circulation, in typhoid fever, and in the neighborhood of new growths. Trichina cysts, anthrax pustules and other irritating conditions may produce similar processes in neighboring muscles. A similar form of myositis has been called by Froriep *monomyositis*. It arises on a traumatic or infectious basis and may lead either to muscular abscess or to an indurative interstitial inflammation which ends either in repair or in the formation of a muscle tumor. The course may be acute, subacute, or chronic. The symptoms consist of extreme pain in the affected muscle, generally preceded by chill and slight rise of temperature. There are some swelling and œdema of the skin over the affected part, with swelling and extreme tenderness of the affected muscle, which soon becomes very hard. There is also contracture of the affected muscle, with some diminution of the electrical excitability. A more severe and generally fatal inflammatory affection is known as *primary acute polymyositis*. This is infectious in character and is accompanied by œdema and marked swelling of the overlying connective tissue and hyperæmia and even exanthema of the overlying skin. The clinical symptoms are fever, pain, tenderness, and loss of function in the affected muscles. These symptoms suggest trichinosis, and Hipp suggests the name pseudo-trichinosis. The resemblance indeed is at times so striking that a differentiation can be made only by removing portions of the affected muscle and subjecting them to microscopical investigation. This form of myositis is sometimes known as dermatomyositis, because of the simultaneous involvement of the skin and muscles. Polymyositis may also be hemorrhagic in character, since a marked extravasation of blood may be found between the muscle bundles. This usually runs a chronic course, death resulting from involvement of the heart. A case of this kind has been described by Bauer: The affection started with severe pains in the legs, after which swellings gradually developed in various regions of the body. The general condition was poor, sleep disturbed, appetite impaired: the patient had fever, and his face was reddened but not œdematous. The muscular swellings were painful, circumscribed, and surrounded by a doughy, indurated area. These showed areas of pigmentation surrounded by a violet zone. Death occurred from asthenia. At the autopsy, the muscle in places presented a brownish-red appearance, with punctate and linear pigmentation and in other places a waxy-yellow appearance. The muscle fibres were partly normal and partly degenerated with proliferation of the nuclei. These were separated by a hemorrhagic exudate, which in some places showed large numbers of leucocytes, so that a purulo-hemorrhagic effect was produced. In this case, the staphylococcus was found. In certain septic cases a diffuse, purulent infiltration of various muscles may occur, this condition being rarely regarded as primary and terminating in gangrene of the muscle. Ziegler describes a case of phlegmonous inflammation of the subcutaneous and intermuscular connective tissue near the pectoral muscle, resulting from an infected wound. Skin phlegmons, erysipelas, decubitus, and purulent arthritis may also cause similar suppurative muscular affections. The muscle is swollen and softened and may be mottled yellow, brown, red, and greenish in color. The pus infiltrates the endomysium and may burrow along the sheaths of the muscles for considerable distances. Small, circumscribed abscesses, either single or multiple, are found throughout the muscle in various regions in case of hæmatogenous infection. These small abscess cavities are filled with pus and tissue débris, and are surrounded by œdematous and degenerating muscle. These small abscesses may be absorbed or become encapsulated, while larger ones break and discharge their contents, being replaced by scar tissue, which gradually contracts and is partly replaced by new-formed muscle fibres. The scar tissue may undergo calcification, while the encapsulated forms may become either calcified or liquefied. On exposure to the air, this greenish-black, gangrenous muscle evaporates or undergoes mummification. Stierlin has described a case of septic total necrosis of muscles resulting from wound infection with obstruction of the artery and therefore interference with the nutrition of the part. The bacteria were gas-forming, putrefactive bacteria. Fragments of the necrotic muscle filled the abscess cavities. The entire process was limited to the musculature, the skin being unaffected. The connective tissue and lymph and blood capillaries were filled with innumerable cocci, forming a network around the muscle cells, which appeared in cross section as homogeneous red discs in which no nuclei could be seen. Very few cocci had penetrated the muscle cells. An *acute interstitial or productive myositis* may also be distinguished; it is progressive in character and generally passes into the chronic form. It

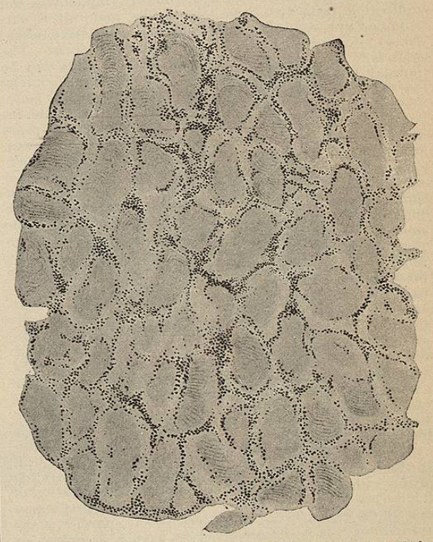

FIG. 3421.—Purulent Myositis, with Necrosis of Muscle. (Stierlin.)

occurs in typhoid fever, chronic irritations, etc. The primary changes are in the connective tissue, which proliferates and causes a secondary degeneration of the muscle fibres.

Chronic Myositis.—In progressive muscular atrophy, whether neuropathic or myopathic, there is a marked increase of the intermuscular connective tissue, so that the

small muscle bundles are separated by thick bands of connective tissue, or the muscle may be entirely replaced by connective tissue. This constitutes the condition known as chronic interstitial myositis or fibrous myositis. It may also occur in the neighborhood of chronic inflammatory or irritative processes, as ulcers, tumors, parasites, foreign bodies, etc. It may also attack the muscles in the neighborhood of inflamed joints, as in inflammatory rheumatism, gout, etc. Acute purulent myositis may be followed by a condition in which the abscesses are walled in by granulation tissue and we may speak of it as a chronic purulent myositis. This occurs most frequently in the psoas muscle. While the condition may follow an ordinary pyogenic infection, it is far more common after specific infections, such as tuberculosis, syphilis, actinomycosis, glanders, gonorrhœa, leprosy, etc.

Tuberculous Myositis may and frequently does occur in muscles in the neighborhood of a tuberculous abscess or some focus of infection, the process extending directly into the muscle from the infected area, as in the muscles surrounding a psoas abscess or caseating lymph gland, or in the intercostal muscles in pyothorax and in miliary tuberculosis of the pleura. Primary or hæmatogenous tuberculosis of muscle is, however, rare—a fact which is explained by the bactericidal action of the muscular fluid, which, as Tria states, is more efficient in its action than the fluids of any other tissues. Cases of hæmatogenous tuberculosis of the muscles have, however, been described by Habermaas, Müller, Delorme, Reverdin, and Lanz and Quervain, and Steinthal, the latter having collected eight cases of primary tuberculosis of the abdominal muscles. The tuberculous nodules found in the intermuscular connective tissue present usually a caseated necrotic centre surrounded by a zone of lymphocytes and epithelioid cells with some giant cells, and this is surrounded by a zone of lymphocytes and connective tissue. Blood-vessels are poorly developed in these areas. The muscle in the neighborhood of one of these areas may be normal, but is usually atrophied, while the muscle nuclei are increased in number and surrounded by a clear zone; the protoplasm of the muscle diminishes as the nuclei increase in number, so that finally the sarcolemma appears filled with nuclear masses. As the muscle degenerates, it is replaced by connective tissue into which the tuberculous foci extend. Here they consist of lymphocytes mostly, with a few epithelioid cells. According to Petit and Guinard, the tuberculous process originates in the intermuscular connective tissue, the degeneration of the muscle resulting from the presence of cells called myophages, which send processes between the contractile fibrils and gradually destroy them. In none of these cases were the tubercle bacilli demonstrated microscopically, but the history of the case, the microscopic appearance of the tissue, and the positive results gained by injecting the contents into guinea-pigs made the diagnosis unquestionable. Tuberculous myositis must be differentiated from syphilitic myositis, interstitial myositis, actinomycosis, echinococcus, and benign and malignant tumors. A tuberculous abscess may also be found in muscle, consisting of muscular and cellular débris surrounded by a thin wall of granulation tissue poor in blood-vessels.

Syphilitic Myositis may be diffuse or circumscribed. In the former case there is a primary diffuse infiltration of the connective tissue with a secondary degeneration of the muscle fibres. It occurs especially in the later stages of syphilis and attacks by preference the muscles of the extremities. It is characterized by a painful, indurated swelling of the affected muscle, which is easily differentiated from other muscular affections by its prompt response to antisyphilitic treatment. Muscle gummata, while not infrequent in the later stages of syphilis, have not often been described. They may, as in the case reported by Eger, develop many years after the syphilitic infection. If no regressive changes have taken place, they are usually indolent in their course, causing no pain, no disturbance of function, and no alteration in electric excitability, unless by their excessive growth they press upon nerves or blood-vessels. They are influenced more or less readily by the potassium-iodide medication. The large tumors may caseate, forming deep ulcers or abscesses, which heal readily but leave indurated scars, which may disturb the function of the muscle. In the earlier stages, the gummas consist of very vascular granulation tissue which may be mistaken for sarcomatous tissue, but later the characteristic three zones develop, the outer consisting of vascular granulation tissue, the inner caseated zone, and the intermediate zone of mature connective tissue. Giant cells may be present or absent. The rich blood supply, the absence of tubercle bacilli, and the response to antisyphilitic medication will readily differentiate these nodules from those of tuberculosis.

A Case of Gonorrhœal Myositis involving the latissimus dorsi has been described by Ware. The microscope revealed a picture of interstitial inflammation, with cloudy swelling of the muscle fibres, though in some places the striation was still distinct. There was some proliferation of the muscle nuclei, showing a possible tendency to regeneration of the muscle fibres. The connective tissue was so greatly increased that the muscle fibres were crowded apart and compressed. No germs were found except the diplococci. This form of myositis is characterized by the intense sclerotic process, which is so marked a feature of gonorrhœal inflammation in other localities. The process generally heals by the formation of connective tissue, which usually undergoes resolution, although cases have been reported of ossification of the affected muscles. If an abscess forms, it is probably due to a mixed infection. The localization of gonorrhœal myositis is probably generally due to extension from neighboring joints and bones, though it may sometimes result from metastasis.

Leprous Myositis.—Fujinami describes the changes which take place in voluntary muscle in cases of leprosy. The muscle is crossed by white strands consisting of connective tissue containing many fat cells and numerous brown pigment granules arising from degenerated muscle fibres. The muscle fibres are atrophied, showing either a very irregular arrangement of the striation or a granular and pigment degeneration. The nuclei are increased in number, enlarged, and very irregularly arranged, while many of them take the stain intensely and show indistinct outlines, so that they appear as fused, hyperchromatic masses. The changes are similar to those observed in muscular atrophy, in the neighborhood of tumors, in inflammatory processes, and are probably due, not to the direct action of the bacilli, but to disturbance of the nutrition of the muscle, perhaps brought about by chemical changes in the lymph caused by the growth of the bacilli. Colonies of leprosy bacilli are seen between the atrophic muscle fibres and in the connective tissue, and they are sometimes seen within the connective-tissue cells or leucocytes.

Actinomycotic Myositis is not at all common, but in rare cases a focus infected with the ray fungus may, either by direct extension or by metastasis, lead to an infection of voluntary muscle. The infection results in the formation of nodules of granulation tissue, which may undergo fatty degeneration or suppurate and form abscesses. The healing of these nodules leaves areas of induration which are not easy to distinguish from the scars of syphilitic myositis. An inflammatory affection of muscle may also be due to an infection with the *glanders* bacillus. This leads to the formation of many small, grayish abscesses, containing a thin fluid in which the germs are found. The muscle may become infiltrated with pus and chronic ulceration or abscess may result.

Animal Parasites.—Varieties of chronic myositis may also result from the presence of certain animal parasites, one of the commonest of which is the *Trichina spiralis*. When found in muscle, it is in the encysted stage of its development, which is known as a measle. The poorly cooked measly pork is eaten, the capsules dissolve in the gastric juice, the embryos develop in the intestine six or seven days after the ingestion of the meat.

These pass into the muscles, showing a preference for the diaphragm, tongue, intercostal muscles, neck, larynx, and thigh muscles. The worm penetrates the muscle fibre, which degenerates, the fibrillæ appearing swollen, granular, and with indistinct striæ. The worm is soon surrounded by a clear, homogeneous capsule, which later becomes calcified. There are at first evidences of acute interstitial inflammation in the intermuscular connective tissue, which later disappear. The clinical symptoms consist of irregular fever, gastro-intestinal disturbances, typhoid symptoms, œdema of ankles, pain and tenderness in the muscles. Brown notes a marked leucocytosis in acute cases, the eosinophile cells being most markedly increased, reaching 68.2 per cent. of all the white blood cells present. Muscular changes take place similar to those in chronic myositis—increase of connective tissue, fibrillation and segmentation of the muscle fibres, with granular and hydropic degeneration of the muscle fibres, with proliferation of nuclei and thickening of the sarcolemma are the most marked changes noted. Death may result in the acute stage of trichinosis, or the worms may become encysted within calcified capsules and create no further disturbance, remaining innocuous during the life of the individual. The *Cysticercus cellulosæ* may sometimes be found encysted in muscle, the cyst being surrounded by a firm fibrous capsule, the whole being surrounded by a zone of inflamed muscle tissue. The *Echinococcus* may be encysted in muscle, although it is far more prevalent in the liver and lungs. The capsule is dissolved in the gastric juice, the embryo developing and making its way through the wall of the stomach or intestine and either passing through the portal circulation to the liver and thence to the heart and lungs, which are the regions infected in sixty-five to seventy-five per cent. of all cases, or wandering actively to the muscles and other regions. Gerulanos has recently collected from the literature two hundred and fourteen cases of muscle echinococcus, one hundred and ninety-five of which were single, while nineteen were multiple. Most of these were, however, very limited in number, while the cysts in the case described by Gerulanos were very numerous, varying in size from a pinhead to a man's head. Some of the largest had suppurated and contained masses of pus, while others showed the scolices and hooks, and others contained nothing except a clear yellowish fluid. The tumors were white, opaque, and either smooth or lobulated, surrounded by a fibrous capsule. The question of the origin of the multiple cysts is one of considerable importance. It is claimed by some that each cyst develops from a single embryo, by others that one cyst, containing an embryo, is formed from which daughter cysts are given off; others believe that the rare cases of multiple echinococcus cysts are due to rupture of a fertile cyst and hence a reinfection of the surrounding tissues. Gerulanos, however, thinks that in his case at least the multiple infection was due to an active wandering of the embryos, which follow the paths of the loose connective tissue surrounding the large vessels, in the neighborhood of which these colonies were usually found. In the case reported by Scholtz, however, the hydatids were found on the outer side of the thigh, far removed from the great vessels. In several of the cases reported, trauma was described as an etiological factor, but probably, as Gerulanos suggests, the trauma has simply called attention of the patient to a latent tumor which has existed for a long time. The diagnosis of this condition must be based on the presence of an elastic, fluctuating, dense, slightly sensitive tumor. The sensitiveness will of course depend on the exact location of the hydatid. It must be differentiated from neoplasms and cold abscesses. The elasticity and fluctuation indicate fluid contents, while the lobulated, multilocular feeling and the history of the case will generally distinguish the echinococcus cyst from the cold abscess, although the cyst may also sometimes be smooth and spherical. The treatment consists in extirpation of the tumors.

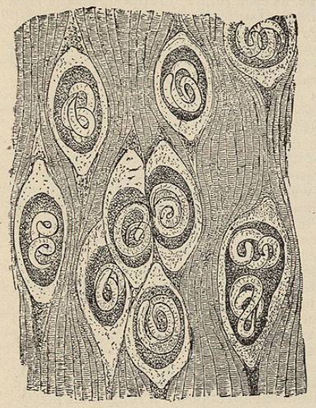

Fig. 3422.—Trichinæ Encysted in Voluntary Muscle. (Ziegler.)

Myositis Ossificans.—Myositis ossificans, as its name implies, is a disease in which an inflammatory affection of the muscles terminates in ossification. Long regarded as a pathological curiosity, it is still a comparatively rare disease, the character and etiology of which are not beyond controversy. Cases of pathological ossification naturally divide themselves into two great classes: those in which bone is formed in connection with bone, an abnormal activity of the cells of the periosteum being the apparent causative factor, and those in which bone is formed in the softer tissues, having no connection, primarily at least, with the skeletal bones or their periosteum. Myositis ossificans occupies a very prominent position in this second group of cases. Two types of this disease are sharply differentiated—a progressive and a stationary form. The progressive type, known as myositis ossificans progressiva, is distinguished from the localized form by the facts that many series of muscle groups are attacked, that it begins in youth and advances with occasional periods of apparent repose followed by exacerbations, which may or may not be attributable to any known exciting cause. This type is much more easily recognized than the second, so that most of the cases mentioned in the literature belong to it. The ear-

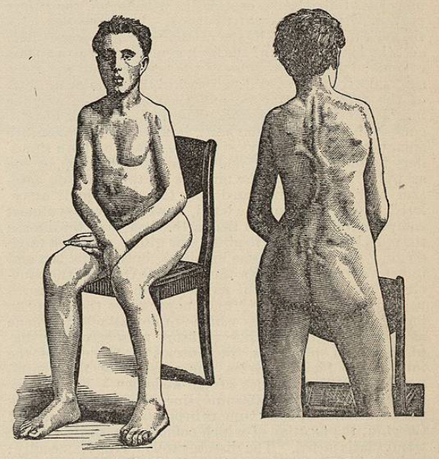

Fig. 3423.—Myositis Ossificans Progressiva, Showing Multiple Osseous Tumors, Forming an almost Continuous Ledge along the Spinal Cord, Fixation of the Head, Microdactylie, etc. (Bremnsohn.)