its ends. Under favorable conditions of preparation and light, the body of the fibre appears no longer homogeneous but distinctly fibrillated, the fibrils extending parallel with the long axis of the fibre, and being therefore of varying length (Fig. 3409). They are very fine and appear like a skein of thread, being in many superimposed layers, and not in a single layer, as is shown in Fig. 3409. These fibrils are supposed to be the true contractile parts of the fibre. Between them is a limited amount of clear intermediate substance. According to some authors, the fibrils are directly connected with the intranuclear network.

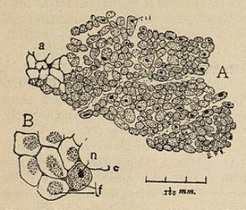


FIG. 3407.—Transection of Part of the Circular Muscular Coat of the Human Duodenum. (Drawn by Mrs. Gage.) This shows the cut ends of the plain muscular fibres and their combination into fascicles. Magnified about 350 diameters. *A*, Camera lucida drawing; *a*, connective tissue between the fibres, the fibres having fallen out—it is a kind of endomysium; *n*, nucleus. A nucleus appears in only part of the cells as only a few are at the level of the section. Compare the longitudinal views in Figs. 3406, 3408, and 3409. *B*, Enlarged view to show the connective tissue between the cells and that the muscle fibres have shrunken considerably. The one at the left is shown unshrunken. *c*, connective tissue between the fibres; *f*, muscle fibres, one shrunken and one unshrunken; *n*, nucleus in the unshrunken fibre.

Sarcolemma. — A thin, homogeneous, elastic sheath or sarcolemma is described by some authors as enclosing the individual smooth muscular fibres (Fig. 3409, *B*). An equal, or greater, number of authors deny the presence of a special envelope or sarcolemma for the smooth muscular fibres of vertebrates.

Blood- and Lymph Vessels of Unstriated Muscular Tissue.—The blood-vessels are less numerous than those of the striated muscles, but they have the same general arrangement, the capillaries forming a network with square or parallelogrammic meshes. The lymphatic vessels have been most investigated in the muscular tissue of the uterus and intestine, where they are in the form of passages and lacunæ which anastomose between the fibres.

Nerves of Smooth or Unstriated Muscular Tissue.—These are abundant and consist of myelinic and amyelinic fibres, which are in many situations in the form of a plexus with ganglia. The special distribution to the individual muscular fibres, and the termination of the nerves, will be discussed under *Nerves* (*q.v.*).

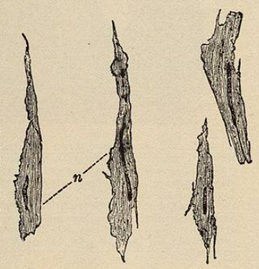


FIG. 3408.—Smooth or Unstriated Muscular Fibres of the Vascular System, to show their Irregular Form and the Rod-shaped Nucleus. From the thyroid artery of man. Magnified 340 diameters. (Schaefer.) *n*, Nucleus.

HISTOGENESIS OF MUSCULAR TISSUE.—Muscular tissue of all forms in vertebrates is developed from cells of the mesoderm or middle germinal layer. The cells are at first rounded and indistinguishable from others of the mesoderm. It is only later, when approximately in the position of the future muscle, that they assume the characteristic form and appearance of the structural elements of the special kind of muscular tissue to which they give rise.

Histogenesis of Striated, Skeletal Muscular Tissue.—The muscles of the trunk are without doubt mainly or entirely derived from special masses of mesodermal cells—*muscle plates* or *myotomes* (*protvertebræ* of older writers). These appear on the dorsal aspect of the embryo, and give it the first appearance of being composed of a series of segments. According to some writers, all the skeletal muscles are derived from the muscle plates, those of the limbs being outgrowths or diverticula of the muscle plates; but working over an exceptionally large collection of human and mammalian embryos of all ages, Bardeen and Lewis[1] could in no case demonstrate definite processes of the myotomes growing into the limb buds. They do not deny the possibility of the entrance of scattered cells from the myotomes entering the limb protons, but the appearance is that the muscles of the limbs arise by a differentiation of a part of the mesenchyma, making up so large a part of the developing limbs.

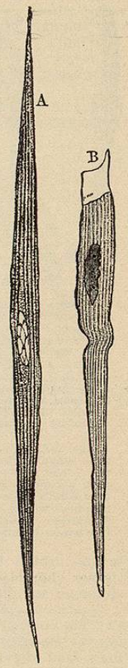


FIG. 3409.—Smooth, or Unstriated Muscular Fibres, to show the Fibrillated Structure and the Intranuclear Network. From the small intestine. Highly magnified. (Schaefer.) *A*, An entire cell or fibre, showing the fusiform shape, the longitudinal fibrillation, the oval nucleus with its intranuclear network, and the conical mass of granular protoplasm at each end of the nucleus. The fibrillæ appear coarse and as if in a single layer; in an actual specimen they are very fine and in many superimposed layers. *B*, A broken fibre, to show the presence of a sheath-like covering or sarcolemma projecting like a hollow sac from the broken end.

Cellular Origin of the Muscular Fibres.—All are agreed that the muscular fibres are derived from mesodermal cells; but there are two views as to the number of cells entering into the formation of a single muscular fibre. These are: (A) That they are *multicellular in origin*. This view originated with Schwann,[18] and is at present held by a considerable number of investigators. It teaches that each striated muscular fibre arises by the fusion of several cells arranged in a row, the nuclei of the fused cells remaining as the muscle corpuscles. The entire fibre is therefore, according to this view, a multicellular structure or *cell complex*. (B) That they are *unicellular in origin*. This view originated with Remak,[15] and is the one adhered to by most later writers. It holds that each striated muscular fibre originates from a single cell, the nucleus of which divides repeatedly with the growth of the cell. According to this view, the muscle corpuscles are formed by the division of the original nucleus, and the entire fibre is an enormous *multinuclear cell*.

Whether the muscular fibres are of multicellular or unicellular origin, the later course of development is as follows: The elongated granular spindles, which are to become muscle fibres, show first a faint longitudinal striation at the entire periphery or at one side, and later a transverse striation; or the two striations appear simultaneously. The nuclei and the unstriated protoplasm occupy the centre or one side of the fibre (Fig. 3412). Gradually the entire protoplasm becomes striated, and in birds and mammals most of the nuclei reach the surface of the fibre; but in the cold-blooded vertebrates they are scattered throughout its entire thickness. Glycogen is very abundant during the later stages of development.

Sarcolemma.—According to Schwann, this is formed by a union of the cell walls of all the cells originating the fibre, the parts of the cell walls which originally came in contact in the interior having disappeared. Others hold that this is the cell wall of the single cell originating the fibre; and still others agree with Busk and Huxley that in the earlier stages of development nothing like a cell wall or sarcolemma is present, but that it is an after development, and arises by a transformation of the protoplasm at the surface of the fibre into formed material or a kind of cuticula. The view of Busk and Huxley seems to be most in accordance with the general teachings of histogenesis and growth.

Growth and Fluctuation in Size of Striated Muscular Fibres.—There are two marked changes in muscular fibres during their development in the embryo: (1) The cells pass from the ordinary reticulated condition of protoplasmic cells to the striated condition; (2) they increase in number until about the time of birth, and the sarcoplasm or undifferentiated part of the cell grows proportionally less, and the striated part gradually greater in amount, while the nuclei increase in number, and in mammals and birds gradually migrate to the surface.

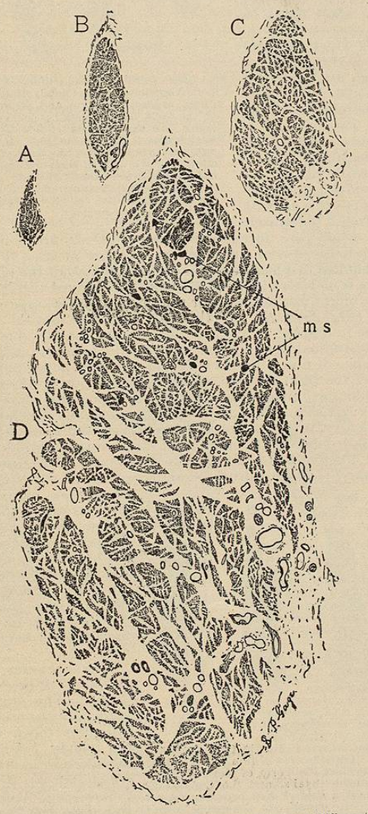


FIG. 3410.—Sections of the Human Sartorius Muscle at Different Ages to Indicate the Change in Size. (Drawn by Mrs. Gage.) The sections were made through the proximal (upper) third in each case, and all were photographed at exactly the same scale. The drawings are from tracings directly from the photographs. The sections are placed with the corresponding edges looking in the same direction. Magnified about 4.5 diameters. *A*, Section from a fœtus 92 mm. long; *B*, section from a fœtus 140 mm. long; *C*, section from a female child at birth; *D*, section of the sartorius of a woman seventy-two years old; *ms*, muscle spindles. There are eight of these in this cross section. Their position is indicated in solid black (*cf.* Fig. 3382 and 3400).

The fibres at about the time of birth are more uniform in diameter than in earlier stages or in the adult (Fig. 3411, *A–D*).

Until recently investigations have not been made to determine whether the increase in the total size of a muscle from the new-born to the adult was due to an increase in the size only of the individual fibres or to an increase *both in size and in number*. That the size of the individual fibres is greatly increased (three to five times) is very evident to any one who examines new-born and adult muscle under the microscope (3411, *C–D*). But whether or not the fibres are increased in number as well as in size with the increase in bulk from the embryo to the adult (Fig. 3411), requires a most laborious investigation, and it is necessary in the investigation to keep in mind the possible difference in size of a fibre at different parts of its length, and to the fact that many fibres end by pointed or branched terminations wholly within the muscle, never reaching either tendon of origin or of insertion (Figs. 3388, 3389); also to the possible longitudinal shifting of fibres during the growth of the muscle in length. During the last five years careful investigations have been undertaken by Meek[13] and by MacCallum[12] to determine the changes taking place from birth to maturity. The work of Meek was directed to the lower animals with special reference to the elucidation of the principles underlying the most economical and satisfactory rearing of animals for food. He found that during growth there was an actual lessening, in a given cross section, of the number of fibres in a muscle, amounting in many cases to more than one-half.

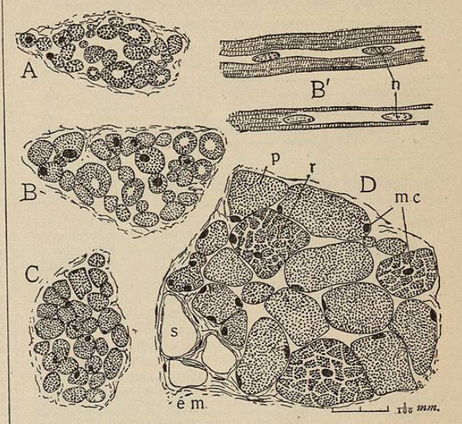


FIG. 3411.—Sections to show Fascicles of Striated Muscle at Different Stages of Development. (Drawn by Mrs. Gage.) Magnified about 350 diameters. *A*, Transection of a fascicle of the sartorius of a human fœtus 92 mm. long; *B*, fascicle of the sartorius of a human fœtus 140 mm. long; *B'*, two fibres from *B* in longitudinal section to show the striation of the fibrils and the central nuclei (*n*); *C*, transection of a fascicle of the sartorius muscle of a female child at birth. Here the nuclei are at the surface in most cases, and the fibres are more compact and more uniform in size than in *A*, *B*, or *D*; *D*, transection of a fascicle of the sartorius of a woman seventy-two years old. It will be noted that the fibres show great diversity in size. The drawing is diagrammatic only in showing some red fibres with abundant sarcoplasm. In the original the fibres were all of the pale variety. *em*, Endomysium surrounding the fibres; *mc*, nuscle corpuscles; *p*, pale fibre with evenly distributed sarcoplasm and fibrils; *r*, red fibres with abundant sarcoplasm and evident muscle columns.

In the following table the kitten at nine days is taken as representing the normal number of fibres—one hundred per cent. It will be noticed that the number of fibres in a given cross section of a muscle decreases as the age increases, and that the mother possessed the smallest

number of fibres, although the sectional area of the muscle was very much greater than that in any of the kittens. The results obtained from the vole, rat, and sheep were equally striking.

TABLE OF THE NUMBER OF STRIATED MUSCULAR FIBRES IN A CROSS SECTION OF THE BICEPS BRACHII OF THE CAT (FELIS DOMESTICA) AT DIFFERENT AGES. ALL FROM THE SAME FAMILY. (Meek.[13])

Age.	Sex.	Area of section.	Number of fibres.	Per-centage of fibres.
9 days	Male	8.4 mm.	83,514	100
20 days	Male	8.1 mm.	64,108	77
240 days	Female	22.8 mm.	37,830	45
3 years 5 months.	Female (mother of above).	41.5 mm.	32,039	38

In the investigations of MacCallum on human muscle, especially the *sartorius*, while a marked decrease in fibres was not noticed, it was brought out with great clearness that the increase in cross section of the muscle was due to the increase in size of the individual fibres, and not to an increase in number. Naturally an investigation of this kind is not so satisfactory on human beings as the same rigorous methods cannot be adopted as with the lower animals, where a whole family may be investigated. Individual variation within a single litter is considerable, but where specimens must be taken from different families, the variation would naturally be greater.

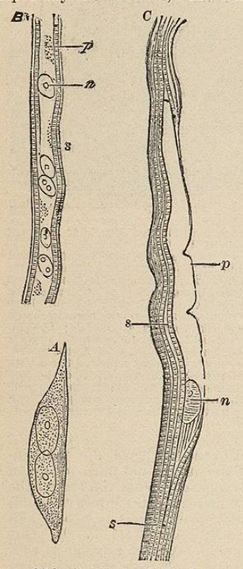


FIG. 3412.—Developing Striated Muscular Fibres, showing Different Stages of Development and Different Positions of the Unstriated Protoplasm. *A*, Elongated cell with two nuclei; the longitudinal striation is beginning to show on the right side. From a foetal sheep. (Wilson Fox.) *B*, Developing muscular fibre, showing both longitudinal and transverse striations at the periphery, and a central unstriated cylinder of protoplasm containing several nuclei. From a human fœtus near the third month. (Ranvier.*) *n*, Nucleus (there is usually a mass of glycogen near each nucleus); *p*, central unstriated protoplasm; *s*, peripheral striated substance; *C*, developing muscular fibre, showing a lateral position of the unstriated protoplasm. From a three months' human fœtus. (Ranvier.) *n*, Nucleus; *p*, unstriated protoplasm at one side of the fibre; *s*, striated sarcous substance with longitudinal and transverse striations.

In the lower animals it was found that the decrease in number was greater with a muscle called upon for great exertion than in one less actively employed; and as a natural sequence, the muscles of the right side showed a greater decrease in fibres than the corresponding muscles of the left side, although the actual bulk of the muscles on the right is usually greater than that on the left.

The conclusions of Meek are as follows: "Up to the time of birth, in at any rate the higher mammals, perhaps in all *eutheria*, hyperplasia characterizes the growth of muscle; while after or about birth hyperplasia ceases, and extra-uterine life brings about a selection of some of the fibres at the expense of their neighbors. In other words, during extra-uterine life muscle, according to its position, suffers more or less a reduction in the number of its fibres, the degree of which is expressive of its functional importance. The surviving elements are at the same time greatly hypertrophied, and the extent to which this takes place is also expressive of the work which the muscle performs, or of which it is capable."

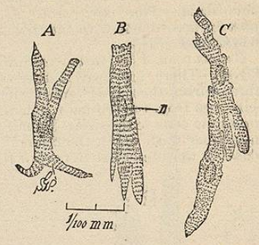


FIG. 3413.—Cardiac Muscle Cells of the Left Ventricle of a Newly Hatched Chick, to show the Form and Structure of the Cells, their General Appearance being like that of Adult Cold-blooded Vertebrates. *A*, Branched cell; *B*, cell with proportions nearly like those of the adult; *C*, two cells in their natural relations, the lower end is fusiform and the transverse striation obscure; *n*, nucleus. In all the cells the striations extend across the nucleus.

While the above investigations indicate clearly that in passing from birth to maturity the increase in size of the individual fibres determines the increase in size of the muscle as a whole, the decrease in number of the fibres in a given cross section may be due, in part at least, to a mechanical displacement along the long axis of the muscle as it increases in length. This mechanical displacement might also account for the fibres with two tapering ends (Fig. 3388, *B*). While it is conceivable that the decrease in number in a given cross section may be due to a longitudinal displacement, and not to an actual disappearance of fibres, the fact that in the more active muscles of the right side the apparent diminution in fibres is considerably greater than in the corresponding muscles of the left side, where the length is practically the same, can be explained only on the hypothesis that there is an actual decrease in the number of fibres during growth.

An elucidation of the processes involved in the disappearance of fibres during growth, and in the every-day occurrence of use-hypertrophy and disuse-atrophy, belongs to the domain of physiology and still awaits investigation, although Morpurgo and Schiefferdecker have made a beginning.

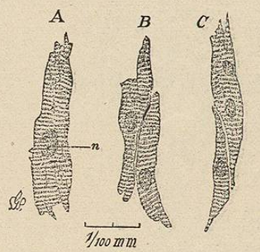


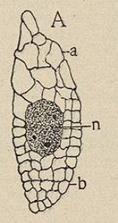
FIG. 3414.—Cardiac Muscle Cells from the Left Ventricle of a Kitten Three Weeks Old, to show the Form of the Cells, their Structural Details, and the Commencement of a Close Union between Two of them. *A*, Large cell possessing nearly the proportions of those of the adult; *B*, two cells in their natural relations; about opposite the nucleus of the upper one the cells are closely united as in the adult (compare Figs. 3397, 3403); *C*, two cells in their natural relations, the upper one has two nuclei; *n*, nucleus. The transverse striations cross the nucleus in all the cells.

Histogenesis of Cardiac Muscular Tissue.—This originates, like the other muscular tissue of the body, from mesodermic cells which are at first rounded and indistinguishable from the surrounding cells. These pre-muscle cells increase in size and elongate and become spindle-shaped. They contain a large nucleus and reticulated protoplasm. The reticulum is at first irregular, but later it becomes more regular; and when the cell has assumed a spindle shape, the appearance is given of clear bodies with rather definite outlines, arranged in somewhat regular longitudinal rows. These clear bodies are the sarcoplasmic discs of MacCallum.[12] As the cells continue to elongate, the striated fibrils so characteristic of striated muscular tissue appear in the cells, always appearing first near the periphery and gradually fill up the cell, so that finally the entire mass is pervaded by them (Figs. 3415, 3405).

* This figure is almost identical with the one of developing striated muscles published by Schwann[3] in 1839 (Pl. XIV., Fig. 3).

Th: further differentiation, besides the complete fibrillation of the cell body, consists in great increase in size, the production of branches or processes, and the fusion, apparent or real, of neighboring cells at various points to produce the anastomosing fibres of adult heart muscle. It is a very interesting fact that the heart beats rhythmically and vigorously for a considerable time before there is any sign of the striated fibrils in the cells.

Fibres of Purkinje.—In the heart of many adult animals (especially ruminants; also in the heart of the pig, horse, dog, cat, hedgehog, marten, and some birds; also, according to Gegenbaur, sometimes in the human heart) there appear, in the muscular substance next the endocardium, chains or groups of cells with a granular, nucleated central part and a striated periphery (Fig. 3417). These cells are supposed to be cardiac muscle cells in course of development into those of the ordinary, elongated, adult form, with branches and striation of the entire contents.



Histogenesis of Smooth or Unstriated Muscular Tissue.—The cells which develop into unstriated muscular tissue are derived mostly from the splanchnic layer of the mesoderm. The cells are at first rounded and granular; they elongate in two directions, thus forming the characteristic fusiform, smooth, or unstriated muscular fibres. The development of the longitudinal fibrillation has not yet been traced. The physiology of muscular tissue will form a separate article (*q.v.*).

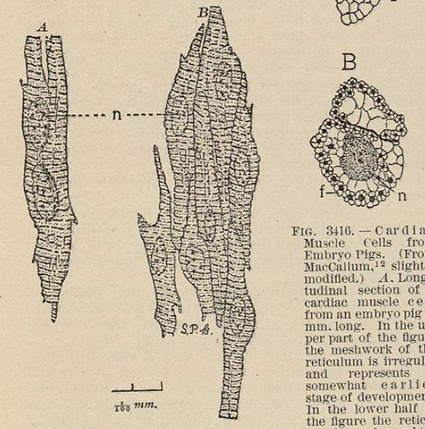


FIG. 3415.—Cardiac Muscle Cells of the Left Ventricle of a Child at Birth (Full Term), to show the Form of the Cells, their Structural Details, and their Relations to One Another, and their General Agreement with those of Cold-blooded Vertebrates. *A*, Large cell with two nuclei; this cell has nearly the proportions of those of the adult; *B*, group of cells in their natural relations; at the right of the middle cell are two spaces or fissures (compare Fig. 3397). *n*, Nucleus. The transverse striations cross the nuclei in all the cells, and each nucleus possesses several nucleoli.

Figs. 3413 to 3415 are at a uniform magnification of 500 diameters. The drawings were made with a camera lucida, and the finer details of structure determined with a $\frac{1}{12}$ homogeneous immersion objective, and added free-hand. (Drawn by Mrs. Gage.)

FIG. 3416.—Cardiac Muscle Cells from Embryo Pigs. (From MacCallum,[12] slightly modified.) *A*, Longitudinal section of a cardiac muscle cell from an embryo pig 10 mm. long. In the upper part of the figure the meshwork of the reticulum is irregular and represents a somewhat earlier stage of development. In the lower half of the figure the reticulum is regular and the sarcoplasm is arranged in rows of disc-like bodies. *a*, Irregular reticulum; *b*, regular reticulum; *n*, nucleus; *B*, cross section of two cardiac muscle cells from an embryo pig of 20 mm. The upper cell is cut above or below the level of the nucleus, while the lower cell is cut through the nucleus. *f*, Striated fibrils appearing at the periphery, the sarcoplasm forms kind of a mantle or coating for the fibrils; *n*, nucleus of the lower cell.

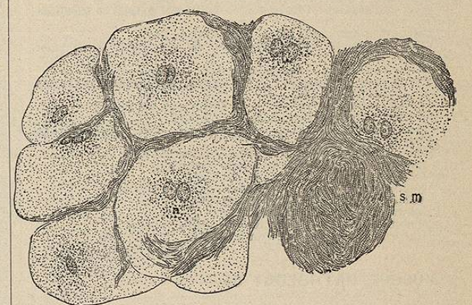


FIG. 3417.—Fibres or Cells of Purkinje from the Heart of a Sheep. Magnified about 300 diameters. (Modified from Ranvier.[14]) At the left the cells are shown in optical section with the peripheral striated fibrils between the cells. On the right is a cell viewed from the surface to show the striated mantle covering the whole cell. *n*, nucleus. Most of the cells contain two nuclei; *sm*, striated mantle at the surface of the cells.

Methods.—Isolation of the structural elements for all forms of muscular tissue is accomplished by soaking the tissue from one to three days in a mixture of 23 c.c. of concentrated nitric acid and 77 c.c. of water, and then for a day or more in a half-saturated solution of alum with five per cent. chloral hydrate. For cardiac muscle, soaking in a mixture of 40 gm. caustic potash and 60 c.c. water for fifteen to sixty minutes proved more satisfactory for isolation than the acid. Cardiac muscle must be perfectly fresh in order to obtain satisfactory results.

Acid specimens were mounted permanently in a mixture of glycerin, 75 c.c.; picrocarmine solution, 25 c.c. Permanent preparations of the caustic-potash specimens were obtained by washing away the caustic potash with a sixty-per-cent. solution of acetate of potash. The cells may be kept in this indefinitely, and mounted in this or in glycerin or glycerin jelly. For the fibrillation of the smooth muscular fibres, a piece of the perfectly fresh muscular coat of the small intestine of a cat was kept from one to three days in 100 c.c. of twenty-five-per-cent. alcohol, containing three-fourths of a gram of picric acid. Preparations were mounted in seventy-five-per-cent. glycerin. Serial sections were made to determine the relations of the striated muscular fibres to one another throughout the entire length of a muscle, and to determine the relative size and number of the fibres in a fascicle at different levels.

(For the general methods of histological investigation, the reader is referred to the article on *Histological Technique*, vol. iv.)

Bibliography.—The bibliography of muscular tissue is so extensive that it would be out of place to give it all in a work of reference like the present. For a more complete discussion of special points, and for the bibliography, reference may be made to the following: *Human Anatomy:* Allen, Gerrish, Gray, Morris, Quain. *Histology and Histogenesis:* Böhm-Davidoff-Huber, Heitzmann, Klein, Kölliker, Leydig, Piersol, Prudden, Ranvier, Schaefer, Stricker. *Embryology:* Balfour, Hertwig, Kölliker, Kollmann, Minot. For monographs one is referred to special papers in the transactions of learned societies, and in the anatomical and embryological periodicals. The bibliography is given in the *Anatomischer Anzeiger, Bibliographie Anatomique;* "Ergebnisse

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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