A CONTRIBUTION ON THE MOTOR NERVE-ENDINGS AND ON THE NERVE-ENDINGS IN THE MUSCLE-SPINDLES.

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By far the greater number of all the communications dealing with the ending of nerves in muscle tissues pertain to observations made on muscle tissue impregnated with one or the other of the several gold chloride methods; valuable as such observations have been, they yet leave many of the details more or less unsatisfactorily answered. Since the introduction of the chrome-silver and methylene blue methods, some further facts, tending to clear up some disputed points, have been gathered.

At the outstart however—and without in the least attempting to throw discredit on the many important observations which have been made with the Golgi method, greatly furthering our knowledge of the structure of the central and peripheral nervous system—it may be stated that so far as pertains to the relation of the ultimate endings of the nerve fibers to the structural elements of the several motor tissues, the Golgi method does not seem so applicable as its rival, the methylene blue method. The great advantage which this latter method has over both the gold chloride and the chrome-silver methods lies in the fact that in the most *successfully stained* methylene blue preparations, only the nerve fibers and their ultimate endings are colored, while the other tissues remain practically unstained. The observations on the endings of nerves in motor tissues made with the methylene blue method have revealed most clearly the shape and arrangement of the ultimate branches of the axis cylinder; there exist however differences of opinion as to the relation of such endings to the muscle fiber or muscle cell, its sarcolemma, muscle substance and muscle nuclei. This, we believe, is largely due to the fact that such observations have been made on methylene blue stained tissues fixed in ammonium picrate and cleared in glycerine. Tissues prepared by this method are usually examined in relatively large pieces or in teased preparations and, while many important observations may be made on such preparations, as the results of Dogiel and Retzius may show, the observer is often left in doubt concerning this or that point of interest.

It occurred to us that by using the *intra vitam* methylene blue method of Ehrlich as improved by Bethe, where the stained tissues are fixed in ammonium molybdate, and may then be embedded in paraffin, sectioned and double stained, it would be possible to obtain surface views, longitudinal and cross sections of the motor endings in relatively thin sections, so stained that the nerve and its terminal apparatus would be blue and all other structures red. Such preparations, we hoped, would throw new light on some of the disputed points and confirm facts more or less clearly established. We trust the facts to be presented may substantiate our expectations.

It was our wish to make the investigation more comprehensive, especially that portion which pertains to the motor endings in striped muscle and heart muscle, but other duties have interfered. It is thought however that enough observations are at hand to admit of drawing some general conclusions, and further, that this exposition of the results obtained with this method, may stimulate others to its use in similar investigations.

The material was obtained as follows:

Motor endings:

a. striped muscle, rabbit and frog (Rana halecina);
b. heart muscle, cat;
c. involuntary muscle, cat, tortoise (Chelydra serpentina), and frog (Rana halecina).

Nerve ending in muscle spindle:

Amphibia, frog (Rana halecina);

Reptilia, tortoise (Chrysemys picta and Emys meleagris);

Bird, dove;

Mammalia, dog, cat, rabbit, Guinea pig and rat.

Method: The methylene blue method has alone been used. A 1% solution of methylene blue in normal salt was injected either into the living animal, or (in staining the nerves in muscle spindles, the intrinsic plantar muscles being used almost exclusively) into the abdominal aorta after bleeding the animal. From 45 minutes to an hour after the injection, the tissues to be studied were removed to a slide moistened with normal salt solution, where they remained until the blue color was developed in the nerve fibers, this being controlled under the microscope. As soon as the nerve endings seemed well stained, some of the pieces of muscle were placed in the following fixative:

Ammonium Molybdate	1 grm.
Aqua Dist.	10 c. cm.
Hydrochloric Acid	1 gtt.

This fixative, which is only very slighly modified from that suggested by Bethe, needs to be cooled to nearly zero, before placing the tissues into it; it is therefore well to prepare it before the injection is made, and to surround it with ice, so that it may be properly cooled before using. In this fixative, the tissues remain from 6 to 12 hours; they are then washed in distilled water and hardened in absolute alcohol; embedded in paraffin and cut in serial sections. The sections were fixed to slides with albumen fixative and counter stained in alum carmine or alum cochineal and mounted in balsam. Others of the muscle pieces, especially those stained for the nerve ending in spindles, were fixed in a saturated aqueous solution of ammonium picrate (Dogiel); cleared in equal parts of ammonium picrate and glycerine and teased under the dissecting microscope, and mounted in the picrate-glycerine mixture. In this way, it was often possible to obtain very complex nerve endings, with the nerve fibers going to them, as some of our figures may show. The capsules of the spindles are in this way not shown and the intra-fusal fibers only faintly seen.

Motor endings in striped muscle. It is not our purpose to give a full review of the literature bearing on the motor endings in striped muscle tissue. This has been so well done in the writings of Krause, Kühne and Ranvier that such a summary is here uncalled for. Mention may however be made of the fact that Doyère, as early as 1840, discussed the endings of nerves in striped muscle of insects; describing a granular expansion of the nerve which seemed to be glued to the muscle substance, and which was found under the sarcolemma; the term "*Doyère's elevation*" comes from this account. Kühne discovered in 1862 the branched ending of the axis-cylinder in frog's muscle. In the same year, Rouget described an end-plate, which was said to be under the sarcolemma. This was regarded as the expanded end of the nerve fiber, its nuclei similar to the nuclei found in the nerve sheath. Rouget's observations were made on reptilia, birds and mammals. Further advance was soon made by Krause, who observed that the axis cylinder did not form the end-plate by its expansion, but terminated in a number of pale fibers, in a fibrillar, nucleated capsule, which was regarded as an expansion of the nerve sheath and which was outside of the sarcolemma. A much more accurate account, as we now know, was given by Kühne in 1864, where, especially in his later communication, he states that the nerve ending is under the sarcolemma, the nerve sheath becoming continuous with the muscle sheath. And further states that the myelin stops abruptly, while the axis cylinder divides into a number of branches, which terminate in an elevation on the muscle fiber. In his classical research, which appeared in 1887, Kühne says that at the point of innervation of a striped muscle fiber, the following structures are to be recognized:

1. The telolemma with its granular nuclei.
2. The branches of the axis cylinder—"*Das Geweih.*"
3. The sole ("*Die Sohle*"), consisting of a granulosa with large transparent nuclei.

Consequent on the results obtained with the methylene blue method in staining other nerve end-organs, this method was also employed to stain the nerve ending in striped muscle tissue, and there now exist a number of communications, giving results obtained with this method, of which observations, those of Arnstein, Cuccati, Gerlach, Feist, Dogiel and Retzius will be considered.

In discussing our own observations, those made on the rabbit will first be considered. Here, as in many other vertebrates (Reptilia, Birds and Mammals), a localized ending, a motorial end-plate, is found, presenting a more or less distinct elevation at the point of entrance of the nerve fiber.

The relation of the "motorial end-plate" or the "motor ending" to the muscle fiber may first be discussed. The great majority of all the observers are in accord in regarding the motor end-plate as under the sarcolemma, although some few observers still describe it as outside of the sarcolemma; Kölliker, closing his remarks touching this point, says, "das sowohl eine hypolemmale als eine epilemmale Lage derselben (motorial end-plate), ihre Vertheidiger hat;" while Böhm and Davidoff refer to it as "der am meisten bestrittene Punkt;" and Krause regards the end-plate as the continuation of Henle's sheath, which surrounds the entire end-organ and unites it to the sarcolemma.

Cross sections are of course most suitable for answering this question. No doubt the difficulty experienced by Kühne and van Syckle in making cross sections of motor endings stained in gold chloride has deterred many from further pursuance of this procedure, and yet the results obtained by them, if one may judge from Kühne's account and figures (Fig. 30 to 40, Plate B.) show most clearly that the end plate is under the sarcolemma, as does also Fig. 79 of Böhm and Davidoff's text-book.

In Fig. 6, 7 and 8, are shown three longitudinal sections and in Fig. 9, 10 and 11, three cross sections of motor endings taken from longitudinal and cross sections of rabbit's muscle, the nerves of which had been stained in methylene blue, the sections, about 20 μ in thickness having been counter stained in alum carmine.

A study of these figures will show that, in case the sarcolemma (*S*) is clearly made out, it passes over the motorial end-plate. The sections from which these figures were taken, as also many others, leave no doubt concerning this point.

Most writers have agreed with Kühne in stating that the neurolemma of the nerve fiber terminating in the end-plate is continuous with the sarcolemma, covering the end-plate. This we can confirm in our sections, as Fig. 4, 7, 10 and 11 may show. In these figures, *n. l.*, the neurolemma can be traced with the utmost clearness into *S*, the sarcolemma.

The termination of the axis-cylinder—das Geweih. Writers are agreed that the arborescent figure seen in the motorial end-plate when stained with the various dyes, is the continuation of the axis cylinder of the medullated fiber terminating in the motor ending. This is most clearly seen in a striped muscle, the motor endings in which have been stained *intra vitam* with methylene blue. In well stained preparations, only the axis cylinders and their branched endings are stained blue, all other structures remaining unstained. The branched endings of the axis cylinder in a motorial end-plate may thus be regarded as the end-brush, or more correctly speaking, one of several end-brushes, of the neuraxis of a motor neuron.

Kühne has most carefully studied the structure of these branched endings of the axis cylinder—*das Geweih*—in gold chloride preparations, and, without going into a lengthy account of the results obtained by him, the following brief statement may be given to show his conclusions as to their structure. Kühne describes an axial fiber as axial tree—*Axialbaum*—which stains more deeply in gold chloride and is looked upon as representing the ultimate fibrillæ of the axis cylinder, and a *stroma*, which in the living axis cylinder and end-branches is distributed between the ultimate fibrillæ, but in the gold chloride preparations, forms a peripheral zone, surrounding the axial fibers; this does not stain in the gold solutions or stains only very lightly. This differentiation is well shown in Kühne's figures of the cross sections of the motor endings (Fig. 30 to 40, plate B).

The structure of the end-branches of the axis cylinder in motor endings has further been discussed by Feist, Cuccati and Retzius, based on observations made with methylene blue, and while they consider more particularly the motor endings in amphibian muscle, their results may here be presented. Feist is entirely in accord with Kühne's views. He states that, in methylene blue preparations of frog's muscle, further stained in picro-carmine, the axial thread retains the blue color while, in the stroma, the blue is either entirely displaced by the picro-carmine or it collects in irregular granules. Cuccati describes blue granules in the peripheral part of the branches of the axis cylinders ending in the striped muscle of frog and triton, when stained in methylene blue and fixed in ammonium picrate, and Retzius finds both axial threads as described by Kühne and Feist and the peripheral granules (*Randkörner*) described by Cuccati in frog's muscle similarly treated.

Retzius states however—a point which we will emphasize —in discussing the nerve ending in frog's muscle, that even with very high magnification (Winkel's Imm. Obj. 1-24 and Ocul. 3) "konnte ich keine Structur in den durch Methylenblau gefärbten Endscheiben wahrnehmen. Erst nach dem Zusatz von pikrinsauren Ammoniak trat die üblich 'Differenzierung' hervor." We may finally add the following comment made by Schäfer on Kühne's observations as above given: "Kühne regards the axial part as representing the fibrils of the axis cylinder, but it may be doubted whether the differentiation into axial part and stroma is not due to the shrinking of the axis cylinder under the influence of the reagent."

Our own observations on this point are as follows: In striped muscle tissue from the rabbit, stained *intra vitam* in methylene blue, removed to a slide and examined at once, (1-12 oil imm. and No. 3 ocul. Leitz), no structure whatever can be made out in the arborescent nerve ending. All the branches of the axis cylinder have a homogeneous blue color, and while they often show slight thickenings and here and there short side branches, they are nevertheless of a very regular contour. If the same preparation is set aside for a short time, 10 to 15 minutes, and is again exposed to the air by the removal of the cover glass, and then again examined, small blue granules and now then an axial thread may be seen in many of the end-branches of the axis cylinder.

In tissues fixed in ammonium molybdate, sectioned and double stained in alum carmine, the branches of the axis cylinder present different appearances. In some, motor endings, Fig. 3, a distinct axial thread and stroma may be made out; this is, however, only rarely seen. More often the branches of the axis cylinder present a fine granular appearance; irregular granules varying in size and the intensity with which they are stained, and distributed, sometimes evenly through the end-branches, or again only in their peripheral portion, may be seen. Fig. 4 to 8 show this. It may in fact be stated that the end-brush of a motor nerve, meaning by that the branched ending of an axis cylinder in a motorial end-plate, is structurally very similar to the nerve fibers and their branches in other nerve endings when stained in methylene blue and fixed in ammonium molybdate. We are therefore led to conclude, basing this statement on a somewhat extended experience with the *intra vitam* methylene blue method, that the differentiation which has been observed and described, in the structure of the end-brush of a nerve fiber ending in the motorial end-plate, depends, to some extent at least, on the method used to stain it; and, if the methylene blue method is used, on the time intervening between their successful staining and their fixation, and also on the fixative used. In this connection, it may further be said that a comparison of the figures given by observers using the methylene blue method in staining the motor endings with those current in our text books and with Kühne's excellent and numerous figures will show that the branches of the axis cylinder appear much smaller in methylene blue preparations than in those stained with gold chloride; the former method, it would seem, portrays much more nearly the actual conditions. This at least seems to be the case when such motor endings are compared with nerve endings in other tissues. Thus far in our discussion, no mention has been made of the behavior of the myelin of the medullated fiber ending in the motorial end-plate. This, as is well known, stops abruptly as soon as the sarcolemma is reached by the nerve fiber; this fact is confirmed in our preparations, the myelin often staining faintly blue.

Before leaving the discussion of the ending of the axis cylinder in the motorial end-plate, attention needs to be drawn to some curious endings now and then seen among the endings thus far described. One such is shown in Fig. 2. As may here be seen, the axis cylinder terminates in an ending which does not in the least resemble the ones shown in the other figures. Instead of fine branches which may clearly be made out, we have here short, coarse and very granular fibers which seem to anastomose. We are thus far unable to give any explanation of these structures, the more so since they have been met only a few times, but always in muscle in which the great majority of the motor endings seemed in every way normal. They are mentioned here simply as a curious anomaly.

The sole and its nuclei. The granular mass, in which the nerve fiber terminates, was at first looked upon as the expanded end of the nerve fiber—Doyère, Engelmann and also Kühne in his earlier writings. Kühne deserves the credit of the discovery that the axis cylinder terminates under the sarcolemma in the nucleated granular substance which he described as the sole (*Sohle*); the nuclei, as sole nuclei (*Sohlenkerne*).

This granular sole differs greatly in its behavior toward staining reagents, even in its reaction to the same stain in different parts of the same preparation. In some of the gold chloride preparations, it remains entirely unstained, in others, is only faintly stained, and in still others, it takes a reddish color somewhat deeper than the muscle substance yet less deep than the branches of the axis cylinder; usually the nuclei of the sole may be made out more or less clearly. Kühne, and it seems to me very correctly, makes the following comment on this point: "Ohne Zweifel sind in der Deutung der Gold-bilder die gefährlichsten Irrthümer dadurch entstanden dass man die genannten Inhaltbestandtheile des Nervenhügels nicht genügend unterschieden hat, indem man sich vor allem die Möglichkeit nicht klar gemacht hat, dass die dem Geweih wie ein Teig anklebende Granulosa diesem zugehörig erscheinen muss, wenn sie durch die Färbung nicht genügend davon unterschieden ist." In motor endings stained in methylene blue and examined at once, or fixed in ammonium molybdate and studied in sections, no trace of a granular sole is seen. Both Retzius (for rabbit) and Dogiel (for reptilia) state that in unfixed muscle (stained in methylene blue) the granular sole and its nuclei are not seen. It may however, as they have shown, be brought out with picro-carmine. Opinions still differ as to the nature of the sole. Böhm and Davidoff state that "The substance of the sole may be regarded as an accumulation of neuroplasma, its nuclei corresponding, very probably, to the nuclei of the sarcolemma and those of the neurolemma."

Kölliker, whom we will quote in his own words, has this to say concerning the fine granular substance of the sole. "Entweder entsteht dieselbe durch eine Wucherung der Zellen der *Schwann*'schen Scheide, die auch bei den Endplatten die Endäste oder Achsencylinder bekleiden und würde sich so erklären, dass diese granulierte Substanz Kerne enthält, die nicht an den Endfasern direkt ansitzen. Oder es ist dieselbe sammt den eben erwähnten Kernen eine Fortsetzung der *Henle*'schen Nervenscheide, welche wie Krause annimt, die gesammte Endplatte umhüllt und mit dem Sarcolemma verbindet, eine Aufstellung, die eine epilemmale Lage der Rouget'schen Endplatten voraussetzen würde."

In his later writings, Kühne, if we understand him correctly (pages 91-92), suggests the hypothesis that the granular sole might be looked upon as muscle protoplasm—sarcoglia or sarcoplasm, while the nuclei of the sole might be likened to muscle nuclei. This interpretation of the granular sole and its nuclei suggested itself to us before Kühne's similar observation was definitely understood.

In all our sections of striped muscle of the rabbit, in which the motor endings were well stained in methylene blue and in which the sections were further stained in alum carmine, nothing is seen of a granular sole; as, for instance, Figs. 1, 3, 4 and 5 may serve to show. In longitudinal or cross sections of the motor endings in rabbit's muscle (stained as above indicated) what has been described as a granular sole may be observed as a nearly homogeneous substance, continuous with the sarcoplasma found between the muscle fibrillæ and staining in every way like it, as may be seen in Fig. 6 to 11.

Such observations have led to the conclusion that what has been described as the granular sole may be regarded as an accumulation of sarcoplasma continuous with the sarcoplasma of the muscle. The nuclei of the sole are in structure very similar to the muscle nuclei, and we have regarded them as such. As our figures may serve to show, especially those showing a longitudinal or cross section of the motorial end-plate, the branches of the axis cylinder—the end-brush of the neuraxis of a motor neuron—terminate in this mass of sarcoplasma, the muscle nuclei, which are here found in relatively large numbers, being both above and below the terminal branches of the axis cylinder. Schäfer states that "applied to the branches of the ramifications, small granular nuclei are seen at intervals; these nuclei of the arborization are different from the clear nuclei of the bed and also from the flattened nuclei of the sheath, which lie directly under the sarcolemma covering the end-plate, and which resemble the nuclei of the sheath of Schwann covering the nerve." Nuclei applied to the branches of the axis cylinder have also been described by Ranvier and Kölliker, while Kühne does not recognize them. In none of our preparations made from rabbit's muscle were such nuclei (*Geweih-kerne*) seen. In our sections, nuclei which seemed in very close apposition to some one of the terminal branches, were now and then seen. Such nuclei had not, however, a distinctive structure.

The telolemma nuclei described by Kuhne and others, were now and then recognized in our sections. They are more oblong and stain more deeply than the muscle nuclei. See *t, n,* of Figs. 3, 4, 5, 7, 9 and 11.

The motor ending in striped muscle of amphibia. As is well known, in amphibia the axis cylinder of the motor fibres terminating in striped muscle does not end in a localized area (birds, reptilia and mammalia), but ramifies over a proportionately much larger area, forming the so-called "*Stangen-geweih,*" as was first correctly pointed out by Kühne. The form of this ending is so well known that a further description seems superfluous. There is, however, one point, concerning which investigators are still not agreed; namely, the relation of the end-branches of the axis cylinder to the sarcolemma of the muscle fibers. We trust our observations may be of some value in settling this point.

Following Kühne, many observers have stated that the ramifications of the axis cylinder of the motor nerves terminating in striped muscle of amphibia are under the sarcolemma, while Krause, Kölliker, Sihler and, to some extent, also Retzius contend that these endings are wholly or in part outside the sarcolemma.

Kölliker has this to say concerning these endings: "Die Nervenfasern gehen zuletz in blasse Endfasern über, die alle aus einer Fortsetzung der *Schwann'schen* Scheide und des Achsencylinders bestehen und da und dort dieselben Kerne zeigen, die auch in der Schwann'schen Scheide der noch dunkelrandigen angrenzenden Nerven sich finden." "In Betreff der Lage dieser Endäste stehen sich immer noch zwei Ansichten gegenüber, indem die Einen mit Kühne dieselben zwischen das Sarcolemma und die Substanz des Muskelfaser verlegen, die anderen *mit mir* und *Kraüse* der Meinung sind dass dieselben auf dem Sarcolemma ihre Lage habe."

Sihler, in two publications giving the results of observations made with two methods which he himself has devised (see his accounts for these methods), expresses himself very strongly in favor of an epilemmal ending of the nerve fibers in frog's muscle.

The conclusions expressed in his earlier communication may serve to show his position. "The whole nerve ending is situated on the outside of the sarcolemma, and, like the capillaries, embedded in the gelatinous connective tissue." This opinion is very largely confirmed in his second paper.

In the account given by Retzius, who has worked on the motor nerve endings in frog's muscle with methylene blue the following statement may be found: "An den Methyleneblaupräparaten konnte ich ferner nie sicher sehen, ob die Endplatten auf oder unter dem Sarcolemma liegen, so dass ich zur Lösung dieser alten Streitfrage nichts beitragen kann." And again,—"Die leichte, reine Färbung der Nervenfasern und ihrer Endscheiben, ohne gleichzeitige Färbung des Inhalts der Muskelfaser, scheint mir indessen für eine Anhaftung an der Aussenseite des Sarcolemmas zu sprechen, denn an den abgerissenen Enden der fraglichen Muskelfasern sah ich in der Regel gleichzeitig eine diffuse Bläuung des Muskelfaserinhalts."

This question, it seemed to us, might be most satisfactorily answered in cross and longitudinal sections of the motor endings in amphibian muscle stained in methylene blue and further treated as designated. Two such cross sections are shown in Figs. 13 and 14. It may here be seen that the ramifications of the axis cylinder are under the sarcolemma terminating in a relatively thin layer of sarcoplasma, which layer of sarcoplasma is continuous with that found between the muscle fibrillæ.

The conditions here presented being therefore very similar to those found in such vertebrates as present a localized motorial ending, with the distinction that in the latter the axis cylinder terminates in a localized elevation—the sole—which has been interpreted as being a circumscribed accumulation of sarcoplasma, while in amphibia the sarcoplasma surrounding the ramified ending of the axis cylinder, extends, like it, over a larger proportionate area of the muscle fibre.

The figures here shown, and many others that might be sketched, would seem to confirm most fully the belief in a hypolemmal ending of the axis cylinder in striped muscle of amphibia. In fresh methylene blue preparations of the motor endings, studied in a thin muscle, as for instance the cutaneus pectoris (Ecker), the axis cylinders of the medullated nerves may be traced with the utmost clearness into the ramifications, which we believe are under the sarcolemma. The terminal branches which are non-medullated, are entirely devoid of any sheath; even under the 1-12 in. oil imm., no trace of the sheath of Schwann, which, according to Kölliker, accompanies such branches to their termination, can here be made out. The same may be said of muscle stained in methylene-blue and cut parallel to the long axis of the muscle fibers, the sections being further stained in alum carmine, The terminal branches (hypolemmal fibers) are, as Fig. 12 may show, devoid of any covering of their own. The neurolemma becomes continuous with the sarcolemma as soon as the nerve fiber passes under the latter. See Fig. 14, *n. l.* Sihler would, if these observations are correct, be in error when he states that neither the sheath of Schwann nor Henle's sheath is continuous with the sarcolemma.

The myelin of the medullated fiber stops abruptly as soon as the axis cylinder passes under the sarcolemma; this point needs no further discussion.

Concerning the structure of the hypolemmal branches of the axis cylinder in frog's muscle, the statements above made on the hypolemmal nerve branches in rabbit's muscle are equally applicable. Kühne and Feist describe an axial thread and stroma; Cuccati, peripheral granules; and Retzius finds sometimes an axial thread, and again the granules mentioned by Cuccati, in picrate of ammonium fixed methylene blue stained muscle tissue, but not in such tissue examined before such fixation. In our sections of frog's muscle, stained in methylene blue and alum carmine, the appearance most generally seen is shown in Fig. 12. The hypolemmal branches present a fine granular appearance, are often more or less varicose and often show marked differences in thickness in the course of a branch. Now and then what might have been interpreted as an axial thread was seen, this, however, very seldom and only in some of the hypolemmal branches.

In sections giving a surface view of the muscle fibers of the frog, double stained in methylene blue and alum carmine, it may be seen that the muscle nuclei are more numerous in that portion of the muscle fiber receiving the ramified ending of the motor nerve. Many of these nuclei are found in the thin layer of sarcoplasma in which the axis cylinder branches terminate. These nuclei are comparable to the so-called sole nuclei, which, it will be remembered, were also regarded as nuclei of the sarcoplasma—muscle nuclei.

In our sections, we have recognized the nuclei described by Kölliker, Ranvier and others, which form a part of what has been regarded as the hypolemmal portion of the axis cylinder. The nuclei in question are described by Kölliker as the nuclei of the sheath of Schwann accompanying the ramifications of the axis cylinder. That the terminal branches of the axis cylinder are not invested with a continuation of the sheath of Schwann, we have already tried to show; such nuclei, if present, could not, therefore, be regarded as nuclei of this sheath. In our sections, nuclei are sometimes found very near one or the other of the hypolemmal branches of the axis cylinder, as *a*, and *á* of Fig. 12, may show. The differential staining used by us, and the use of the micrometer screw of the microscope enable us to state that such nuclei are not a part of the terminal branches, but are always more or less distinctly separated from them. Such nuclei have no doubt been interpreted as nuclei of the hypolemmal branches in gold chloride preparations, where such differentiation is not always possible.

Before closing the discussion of the motor endings in amphibian muscle, attention needs to be drawn to a view expressed by Gerlach, namely, that the nerve fibers terminate in an intramuscular network which pervades the entire muscular substance, which network is in connection with the contractile portion of the sarcolemma contents. That we may state Gerlach's opinion correctly, we give here his own words on the subject: "Es existirt innerhalb des Sarcolemmas ein Axenfasernnetz, welches die contractile Substanz durchzieht, das intravaginale Nervennetz. Bei günstiger Goldeinwirkung, erscheint der ganze Muskelfaden von strichartigen Punkten durchsetzt und zwar haben diese gesprenkelten Stellen ganz dieselbe Farbe, wie die intravaginalen Nerven. Demnach muss in dem contractilen Inhalt des Sarcolemmas eine Substanz vorhanden sein, welche Goldsalze in derselben Weise reducirt, wie die intravaginalen Nerven. Durch weitere Behandlung der Goldpräparate mit Cyankali gelingt es den sicheren Nachweis zu führen, dass zwischen den intravaginalen Nerven und diesen Sprenkelungen directe Continuitätsbeziehungen existiren." This view is defended by Gerlach in his second communication based on observations made with methylene blue. It would seem to us, from Gerlach's descriptions and figures, that both in his gold chloride and in his methlyene blue preparations, he has stained the sarcoplasma, in which, as we believe, the axis cylinder terminates. But the mere fact that, in methylene blue, for instance, certain granules and other substances are tinged blue, is not proof positive that these are of a nervous nature; as it is well known that, under certain circumstances, elements other than nerve fibers are stained in methylene blue, even when the blue is injected into the circulation of a living animal. Red blood cells may be stained blue or show blue granules; connective tissue cells; intracellular cement substance; and now and then most clearly yellow elastic fibers may in this way be stained. In well stained motor endings, before fixing or after fixation in ammonium molybdate, when examined under the 1-12 oil imm., not a trace is seen of Gerlach's "intravaginal network" in methylene blue preparations. Dogiel discusses this point in the following words: "Bei einer gehörig gelungen Tinction normaler Muskelfasern ist nichts derartigen zubemerken."

As our observations pertain exclusively to the ultimate ending of the motor nerves in striped muscle, and, as our preparations were made with that end in view, we do not desire here to touch on the general distribution of the motor fibers in striped muscles, on their branching, etc. For answering these questions surface preparations are far more suitable than sections. Our observations admit, we believe, of our drawing the following conclusions as to the structure of the motor endings in striped muscle in the vertebrates examined, and we would venture to suggest that such conclusions apply equally well to motor endings of such other vertebrates as show a structure similar to those here discussed.

(1) The ramified terminations of the axis-cylinder in the motorial endings of striped muscle are the end-brushes of the neuraxes of motor neurons, and are similar in structure to the end-brushes of other cerebro-spinal fibers.

(2) This end-brush (*das Geweih,* Kühne) terminates in the sarcoplasma, therefore under the sarcolemma of the muscle fibers. At the place of ending of the nerve fibers, the sarcoplasma may be accumulated in a circumscribed mass, forming an elevation, more or less distinct, on the side of the muscle fiber, as in reptilia, birds and mammalia, or spread out over a proportionately greater area of the muscle fiber, as in amphibia. In the mass of sarcoplasma, the muscle nuclei (sole nuclei of other writers) are relatively more numerous than in other parts of the muscle fiber.

(3) The neurolemma of the nerve fiber terminating in the motorial ending becomes continuous with the sarcolemma at the point of entrance of the said nerve fiber into the sarcoplasma. Over the endings, sarcolemma or neurolemma nuclei—telolemma nuclei—are seen.

4. The neuraxis of the motor neuron loses its medullary sheath before piercing the sarcolemma.

Motor endings in cardiac muscle. No attempt will here be made to discuss the whole question of the innervation of the mammalian heart nor even to refer to the now extensive literature dealing with the subject; for this, the interested reader may consult the articles of Retzius and Berkley and especially the very recent communication by Jacques who has reviewed the literature very extensively.

We wish here simply to refer to the ultimate ending of the motor nerves on the heart muscle cells and to draw attention to a method for staining them which we believe will give more satisfactory results than the methods hitherto used. We refer here to the method used in staining the nerve ending in voluntary muscle; namely staining in methylene blue, fixing in ammonium molybdate, embedding in paraffin and sectioning, and further staining such sections in alum carmine. In heart muscle, prepared after this manner, the nerve fibers are blue, muscle and nuclei, red. The shape and structure of the ultimate nerve endings and their relation to the heart muscle cell may, it seems to us, be more clearly made out in preparations thus prepared, than in methylene blue stained tissues fixed in ammonium picrate, or in preparations stained after the chrome-silver method.

Our results were briefly as follows:

In sections of cat's auricle from 10 to 20 μ in thickness prepared as above stated, portions of the intramuscular plexus, or pericellular plexus, described by authors are abundantly seen. The nerve fibers of this plexus are, as far as we have determined, non-medullated. They vary, however, much in size, and in the size and number of the varicose enlargements seen on them. They often show relatively large sheath nuclei, clearly seen with these stains; these nuclei stain red, the axis cylinder blue. The strands of the intra-muscular plexus may consist of single fibers or small bundles of fibers. We have now and then been able to trace such a small bundle to some one of the sympathetic ganglia situated in the wall of the auricle. Some of the non-medullated fibers of the intra-muscular plexus are therefore, no doubt, the neuraxes of sympathetic cells situated in the auricular wall. Whether they all are, or what particular intra-muscular fibers are, is a subject concerning which further research is needed. From this intra-muscular plexus, one may now and then trace a nerve fibril to its ending on a heart muscle cell. Such fibrils are usually very varicose and terminate in endings which vary in complexity. In Figs. 15 to 20, several such endings are reproduced. They may be very simple, consisting of a small terminal bulb, as shown in Fig. 15; these, it may be stated, are most numerous; or again, the fibril may branch just before it terminates, into two short filaments, each of which ends in small bulbar enlargements, as seen in Fig. 16. The endings may however be much more complex, the nerve fiber terminating in 4 to 8 small filaments, and ending in a terminal enlargement, as is shown in Figs. 17 to 20. The terminal end-bulbs in these more complex endings are usually grouped in more or less compact clusters as a majority of the figures show; they may however sometimes be spread out over a proportionately larger area, see Fig. 20, and especially the upper cell of this figure. Sometimes it may be seen the terminal fibrils supply more than one heart muscle cell; this is indicated in Fig. 16, where the fiber sends off a small branch, ending on the cell shown, the fiber itself going on. In this way a fibril of the intra-muscular plexus may innervate four or five successive cells. Figs. 19 and 20 also show this ending of such fibrils on more than one cell. That the endings here described are on the heart muscle cell may be seen in Fig. 21, showing cross sections of heart muscle cells through the nerve ending.

We have not been able to associate these several types of endings with nerve fibers showing any peculiar or characteristic structure. Wherever it was possible to trace the fibril terminating in any one of the above described endings for some distance away from the cell on which it terminated, such a fibril or fiber always presented the appearance of a non-medullated, more or less varicose nerve fiber, the latter characteristic—the varicosity of the fiber—although very constant for non-medullated fibers, not being looked upon as showing any inherent structural differences. We are reminded here of what Dogiel has said of the structure of the ultimate branches of nerve fibers. He describes these as consisting of one or several ultimate fibrillæ, which stain deeply in methylene blue, surrounded by an interfibrillar substance, which stains only faintly in the blue; then follows this statement: "Letztere (interfibrillar substance) lagert sich in überlebendem Nervengewebe als eine gleichmässig, dünne Schicht an der Peripherie aller Nervenästchen und Fäden ab, während sie mit dem Eintritt der postmortalen Veränderungen wahrscheinlich ein wenig aufquillt und in abgesonderten Klümpchen sich ansammelt, welche sich auf dem Verlauf der genannten Aestchen vertheilen und ihnen ein charakteristisches Bild geben." If this be so, the difference in the degree of varicosity would depend largely on the rapidity with which such terminal fibers are fixed after the removal of the "*überlebend*" tissue.

We have been led to mention these facts, since Berkley has quite recently described two distinct kinds of nerve fibers, with distinctive nerve endings in heart muscle. In the intermuscular plexus, these nerve fibers are described by him as follows:

1. Varicose nerves of "longitudinal main fibers with right angled branching; the terminations being on short ramuscules from the finer filaments." These fibers are stained a "brownish black" in the chrome-silver method used by Berkley. "The end-apparatus of the varicose network is usually very simple, being represented almost without exception by a minute ball-like arrangement at the terminal point of the end branches."

2. Fibers that stain a "uniform jet black" and "run for a long distance with but very few side branches and exceedingly rarely develop upon themselves any knotty thickenings." "They are characterized not uncommonly by the presence of a round or elongated ball not far distant from the end apparatus." "The end apparatus of the second type of fiber, presents, in complete contrast to the fibers of the network, an end apparatus of complex form." Fig. 4, 5 and 6, of Berkley's article show these more complex endings, which are of pennate form, some simpler, others more complex. The account here given has reference to Berkley's observations on the mouse heart. In his description of the endings in the dog's heart, he states that they correspond in the main with those found in the mouse. In about 120 successfully stained sections from the heart of the dog, Berkley found about 10 endings of a more complex nature. "These expansions were of considerable size, covering the breadth of two or three muscular fibers and varied slightly in form." Berkley's interpretation of these more complex endings and also his opinion of the bulbar enlargement on the fibre thus ending, may be given in his own words: "In all these nodal structures, which are always most deeply stained, it is impossible to discover anything of a cellular nature, yet, as they are several times larger than any of the ordinary varicose knots that are met with on the fibers of the first class, and have little

that is common in appearance with them, we think, after every allowance has been made for visual error, that they may be considered bipolar cells situated in the path of the fibers, and that the end apparatus should be looked upon as their terminal expansion. However the number so far seen is too few to enable us to regard them from other than a somewhat hypothetical standpoint." As our observations were made on the cat and more particularly on the auricle, we are not fully prepared to discuss Berkley's results. We may however be allowed the following critical remarks: In the first place, in the cat at least, as our figures may show, the ultimate nerve endings in the heart muscle can not be divided into two distinct types—simple and complex; intermediate stages of complexity are found between these two extremes. Furthermore the endings described by us are all endings of varicose fibers, which, it is true, may not always show the same degree of varicosity; yet this difference is not regarded as of any essential importance, as we have above stated. The suggestion may further be made, as has been done by one of us in another place, that the nodular enlargements, which Berkely has interpreted as the cell bodies of bipolar cells, may, after all, be nuclei of the sheath of Schwann of non-medullated and not medullated fibers. When we compare the size of the nodular enlargements pictured by Berkley with the size of some of the nuclei found on non-medullated fibers, stained in methylene blue and counter-stained in alum carmine, when viewed under about the same magnification, we are led to disagree with him when he states that "this swelling in the pathway of the nerve is far too large to be thought of as a varicosity or as the nucleus of the myelin sheath of the nerve fiber, supposing such a sheath to occur in this situation."

These considerations make us somewhat skeptical as to the existence of two distinct kinds of nerve fibers with characteristic end-apparatus; and while we have no desire to discredit Berkley's observations in this direction, we can but feel that methods other than the chrome-silver method where the structure of the fiber, etc., may be determined with greater certainty, are more suitable for the investigation of this problem.

Arnstein, who first stained the cardiac muscle in methylene blue, describes their ending on the heart muscle cells without an end-bulb. "Dann sieht man den varicosen Faden sich an die Muskelzelle ansetzen ohne eine Endausschwellung zu bilden," are his words on this point. Jacques, who has quite recently reported on the heart muscle nerves as seen when stained with methylene blue, makes the following general statement concerning their ending: "From the intra-muscular fibers, terminal fibers arise, which penetrate between the cells of the muscle bundles and enter into communication with them by means of terminal and lateral branches of varied form and size, comparable for the most part to the terminations described in striped muscle of invertebrates." The endings sketched by him in Fig's. 10, 15 and 16 (young rat) and Fig. 14 (cat) of Plate XVIII, while resembling somewhat those given by us, are all somewhat coarser, showing larger end-bulbs—mushroom-like endings as stated by him—when compared with ours.

The simple ending shown in Fig. 15 resembles very closely the endings shown in Fig's. 6 and 7, Plate XV, of Retzius' article, showing the nerve ending in the cardiac muscle of the mouse when stained with the Golgi method. The more complex endings mentioned are not discussed nor diagramed by him.

Further contributions on the cardiac nerves stained with the Golgi method have been made by Ramon y Cajal and Azoulay; their results are however known to us only through reviews. Ramon y Cajal, who has stained the cardiac nerves of reptilia, batrachians and mammals, recognized a pericellular plexus, comparable to that found in smooth muscle. He states that the fibrils are devoid of myelin and beset with varicosities and attach themselves to the striated substance and end on its surface in small enlargements. Azoulay has studied the cardiac nerves in the human embryo; but reached no definite conclusion as to their ultimate ending.

Motor endings in involuntary muscle tissue. The endings of nerve fibers in involuntary muscle tissue have been the subject of numerous contributions. Since their first description in 1862 by Kölliker, they have been repeatedly investigated by all the current methods. It is thought best to dispense with a review of the now somewhat voluminous literature treating of this subject, since a number of the recent writers, among whom may be mentioned Lustig, Erik Müller, Retzius, Brenheim and Schultz, have covered the ground very completely. It is now very generally believed that the nerve fibers ending in the involuntary smooth muscle tissue are the neuraxes of sympathetic neurons, situated in, or at some more remote point from, the smooth muscle in which such endings are found. Indeed quite recently, Arnstein was able to sketch an entire sympathetic neuron, the neuraxis of which terminated in the muscle tissue found in the wall of the trachea; and one of us, as stated in another place, was able to see this now and then, in the sympathetic cells found in Auerbach's plexus in some fishes and reptilia examined by him. This is, however, usually not possible, as the neuraxes and, to some extent, the dendrites also of the sympathetic neurons found in involuntary muscle tissue, are interwoven into such intricate plexuses, that the tracing of a single neuraxis through its terminal branchings becomes impossible. Many writers, following Arnold, have described three plexuses thus formed in involuntary muscle tissue,—a *ground* plexus, an *intermediary* plexus, surrounding the fasciculi or bands of smooth muscle; and an *inter-muscular* plexus found between the spindle shaped cells. These plexuses are said to anastomose with each other. There is, however, probably no actual anastomosis of the nerve fibers constituting these several plexuses, but rather an interlacement of such fibers. It is, however, not our purpose to dwell on these facts, as they may be quite readily ascertained in gold chloride, chrome silver or methylene blue preparations; but rather, to discuss briefly the more disputed question of the ultimate ending of these nerves in the involuntary muscle tissue. Concerning this point, two very contradictory views have been expressed: on the one hand it is asserted more or less positively by Kölliker, Löwit and Gescheiden and in more recent years by Arnstein, Retzius, Erik Müller, Dogiel and Schultz, that the nerve fibers terminate on the spindle shaped cells; while, on the other hand, Frankenhäuser, Lustig, Obregia and Brenheim find that the nerve fibers terminate in the muscle cell, on or in the nucleus. Arnold and Obregia go so far as to say that the nerve fibers may pass through or over the nucleus and appear again in the inter-muscular plexus (Arnold), or pass on and end in the nucleus of some neighboring cell (Obregia).

Our own results confirm the observations of those writers who contend for a free ending of the terminal fibers *on* the spindle shaped cells of involuntary muscle. Our sections were obtained from the muscular coat of the stomach and intestine of kittens, tortoises and fishes, stained in methylene blue and alum carmine, the method here being the same as used for the other motorial endings previously discussed. The sections were from 5 to 7 μ in thickness. In such sections, studied under the 1-12 oil imm., the cell outline of the spindle shaped muscle cells, as also their nuclei, may readily be made out; they are stained red; the nerve fibers, blue. Figs. 22 and 23 may serve to show the results obtained; both sketches were made from preparations obtained from the muscular wall of a kitten's stomach. Preparations made from the intestine of the tortoise and fish, show essentially the same kind of an ending, so that it did not seem necessary to duplicate the figures.

In Fig. 22, may be seen at *a*, a small varicose fibril from the intramuscular plexus. The terminal fibers of this plexus usually, as shown here, run parallel with the long axis of the muscle cells, seemingly embedded in the inter-cellular cement substance. Such terminal branches may, in sections 15 to 20 μ in thickness, be traced under a 1-12 in. oil imm., through several fields of the microscope. From place to place, short side filaments are given off from such terminal fibers, which may be traced to a muscle cell, on which they terminate in one or two nodular enlargements; one such is shown in *b*, of Fig. 22. A terminal fiber may, in this way, send side filaments to 6 or 8 muscle cells, as it courses along in the intercellular cement. Occasionally two or three short filaments end on one cell, each in a small end-bulb, as may be seen in Fig 23; this is, however, rarely seen. That the endings are *on* the cells, and not *in* them or in the nucleus, may be ascertained in the occasional cross sections through the muscle cells and nerve endings which are here and there met, or perhaps more clearly in the oblique sections now and then obtained. See Fig. 24; also shown in Fig. 44 of Schultz's article.

These results, as may be seen from the following quotation, agree very closely with the results obtained by Müller with the Golgi method: "Die feinen Zweige endigen mit einer keulen oder birnenförmigen Anschwellung die sich auf eine Muskelzelle legt. Diese Anschwellungen sind sehr konstant und regelmässig ihrem Aussehen nach, so dass ich keinen Anstand nehme, sie als ein der Wirklichkeit entsprechendes Structurverhältniss anzusehen. Es ist indessen nicht nur an den Enden der Fäden, wo sich solche befinden. Man findet nämlich oft die Fäden ihrer ganzen Länge nach mit dergleichen kleinen Platten versehen, oft an kleinen kurzen Stielen sitzend und eine jede mit ihrer besonderen Muskelzelle in Verbindung tretend."

Schultz, who has more recently worked on the question, with both the Golgi and the methylene blue method, reaches identical results as to the ending of the motor fibers in involuntary, smooth muscle. He describes, however, another system of nerve cells and nerve fibers, which may here be briefly mentioned, although somewhat foreign to the subject in hand. Schultz states that in methylene blue preparations, he has observed a large number of nerve cells in the muscular tissue of the intestinal wall., From these, longer or shorter processes are given off, which pass out between the muscle cells. These processes show varicosities and swellings toward the end of the branches, to some extent also along the processes; these swellings and nodules are looked upon as an end-apparatus. In the more fortunate preparations, he has recognized longer processes, which are not varicose and do not branch, and which could now and then be traced into a neighboring nerve bundle. These cells, according to Schultz, form the sensory nerve supply of smooth muscle; and he states that we may find in them an explanation of the severe pain which is now and then experienced when the hollow organs are diseased. Schultz seems not to be aware of the fact that sensory, cerebro-spinal nerves have been traced into the epithelium of some of the hollow organs. One of us has quite recently pictured such sensory endings in the wall of the frog's bladder, where, with methylene blue, they may be most clearly shown. And Smirnow has pointed out the existence of sensory nerves in the walls of the heart. We have no doubt that many of the larger medullated fibers which accompany the sympathetic nerves to the viscera will be proved to end in free endings in or under the epithelial lining. We are, therefore, entirely in accord with Kölliker, when he states that "Alle weit in die Peripherie entstrahlenden markhaltigen Fasern, wie z. B. die in den Milz-nerven der Weideskauer, im Gekröse des Darmes, in der Leber, u. s. w. betrachte ich als sensible Elemente." Attention needs further to be drawn to the fact that Dogiel has quite recently described a "second type of sympathetic cells" found in the ganglia of Auerbach's and Meissner's plexus, which cells are spoken of as sensory sympathetic cells. If we understand Dogiel correctly, they are not regarded as of carrying sensations of pain to the cerebro-spinal centres, but rather as functioning in local reflexes, etc. Structurally, these cells differ markedly from those described by Schultz as sensory sympathetic cells. The question may here be asked whether the cells described by Schultz as sensory sympathetic cells are not identical with the cells described by Dogiel as the "cells of Ramon y Cajal". Such cells, Dogiel states, resemble very closely sympathetic nerve cells, and stain very readily in methylene blue, and are, if one may judge from Fig's. 5 and 6 of his article, very numerous. These cells are described by Dogiel as having varicose processes; he was however unable to find processes not beset with varicose enlargements, and not branching. It is true, he adds, and we give here his own words, "Dass zuweilen irgend ein Fortsatz in Vergleich zu den übrigen feiner erschient, mit einer grossen Anzahl Varicositäten besetzt ist und gewissermassen an einen Axencylinderfortsatz erinnert. Allein ein solcher Fortsatz unterscheidet sich dadurch scharf von einem wirklichen Axencylinder einer Nervenzelle des Auerbach'schen oder Meissner's chen Geflechtes, dass er bedeutend dicker und mit varicosen Verdickungen besetzt ist; zu dem ist er stets nach Verlauf einer oft sehr kurzen Strecke aufs neue einer Teilung unterworfen." Such cells, as Dogiel has shown by injecting the intestinal wall with gelatine, form a perivascular plexus surrounding the intestinal arteries, veins, capillaries and lymphatic vessels, and have no connection with the plexuses of Auerbach and Meissner. They are, if we understand him correctly, although he is not explicit on this point, not to be looked on as nerve cells. These cells have now and then been seen by us, especialy well in some methylene blue preparations of the frog's stomach, and, in several instances, showed a very distinct granulation, the granules being relatively large and resembling very closely the granules sometimes stained in methylene blue, in cells which were looked upon as containing basophile granules. Attention must here again be drawn to the fact that not all structures staining blue in methylene blue, even when this stain is injected into the circulation of the living animal, should be looked upon as nervous in nature. This stain does stain nerve cells and nerve fibers most beautifully in some instances, leaving nothing more to be desired, yet, unfortunately, often stains other structures also, and the investigator is often at a loss how to interpret any particular preparation before him. There is, it is true, very often a slight color differentiation, which in some cases is helpful; the nerve fibres and nerve cells staining a more purplish blue than the other tissues; this is especially noticed in the axis cylinders of nerve fibers; yet this statement is open to many exceptions. These facts will, we believe, explain many of the discrepancies noticed in the accounts of writers, working with similar methods and on the same tissues.

We are therefore led to agree with Dogiel in considering the cells described by Schultz as other than nerve cells, probably cells of connective tissue origin. And while we have not been able to add materially to the observations of Erik Müller, Retzius and Dogiel, and to that portion of Schultz's account which pertains to the endings of motor nerves in involuntary muscle, we trust that our confirmation of their results with methods differing somewhat from the ones they used, may prove of some value.

Muscle-Spindles. In 1862, Kölliker described in the cutaneus pectoris of the frog, peculiar bundles of small muscle fibers, to which, at an expanded portion of the bundle, a relatively large medullated nerve fiber was attached. They were designated "muscle-buds" (Muskelknospen), and were regarded as showing a longitudinal division of muscle fibers and a consequent division of the muscle nerve.

In the following two years, in three communications, Kühne mentions similar structures in the muscles of adult rats, house mice, rabbits, lizards and snakes (Coluber natrix) and also in the frog. These structures were described by him as "muscle-spindles" (Muskelspindeln) and, while not assigning to them any definite function, he suggests the possibility of their being other than growth centers. His own words read as follows: "Sind dieselben Apparate mit einer noch unbekannten physiologischen, für den Zuckungsvorgang des Gesammtmuskels wichtigen Function, oder stellen sie nur ein Stadium noch nicht vollendeter Entwickelung einer Muskelfaser dar? Für das Letztere spricht der Umstand, dass der Spindel zuweilen bis hart an den Nerveneintritt hin Querstreifen zeigt, während für das Erstere die unverkennbare Aehnlichkeit des nicht gestreiften Abschnittes mit den Balken des Schwammgewebes vieler pseudoelektrischen Organe sprechen würde."

Since the discovery of these structures by Kölliker and Kühne, they have been repeatedly found and variously interpreted. We shall not attempt, however, to do more than give a brief summary of the opinions current in the literature concerning the muscle-spindles and similar structures. And this may perhaps best be done by classifying them as follows:

1. They have been regarded as *growth-centers*, following Kölliker in this respect, by Bremer, Felix, v. Franque, Trinchese, Tanhoffer and Volkmann, also by Schäfer and Schifferdecker. The majority of these investigators have recognized

the large medullated nerve fibers going to the muscle-spindles, but have not ascribed to them any characteristic nerve ending, and have usually regarded them as in process of division, preparatory to the innervation of the resultant muscle fibers of the spindles.

2. Other investigators, following Fränkel in this respect, who found them especially numerous in phthisical subjects and who speaks of structures very similar to the muscle-spindles as "encapsuled bundles" (umschnürrte Bündel), have regarded them as pathological structures, the result of inflammatory degeneration. We may here mention Eisenlohr, who found them in cases suffering with infantile paralysis, and Millbacher, who has studied the structural changes in striped muscle in cases succumbed to one or the other of several chronic diseases. In his article, he speaks of three types of "umschnürrte Bündel."

a. Incompletely encapsuled bundles;

b. Completely encapsuled bundles enclosing muscle fibers plainly visible;

c. Completely encapsuled bundles, enclosing muscle fibers highly atrophic.

These three forms are regarded as developmental stages of one and the same process; and the capsule is looked upon as the result of the proliferation either of the internal perimysium, or of the adventitia of adjacent blood-vessels.

Eichhorst has described muscle-spindles, or very similar structures, judging from his figures, in the striped muscle of alcoholists. He also attaches pathological significance to them in so far that he traces the development of the capsule to the greatly proliferated neurolemma of the muscle nerves, which were found markedly diseased. We may yet mention Santesson, who found, in a case of dystrophia muscularis progressiva, numerous muscle-spindles, especially in the more atrophied muscles; they were regarded as showing an attempt at regeneration in diseased muscle. "S. Mayer and Babinski similarly ascribe them to degeneration, although considering them physiological rather than pathological, inasmuch as due to a degeneration of normal occurrence within active muscle." (Quoted from Sherrington.)

3. Muscle-spindles, or similar structures, have further been described by a number of writers, who have been more guarded in attaching any especial significance to them, and have described them as "physiological structures," without assigning them any definite function.

We may here mention Mays, who, in two communications, has drawn attention to them. In his first, the possibility of their being sensorial end-organs is discussed; in his second, he contents himself with the following statement: "Da ich somit die Frage, was die Muskelspindeln eigentlich seien noch nicht für entscheiden halte, so kann ich auch heute der Ansicht noch nicht unbedingt beipflichten, welche sie mit grosser Bestimmtheit als sensible Organe auffasst." Roth, who has designated them "neuro-muscular bundles" (Neuromusculäre Stämmchen), has found them in man, cat, dog, and rabbit, but ascribes to them no definite function.

Blocq and Marinesco found "neuro-muscular bodies" in atrophied muscles of poliomyelitis and polyneuritis, and have described quite accurately the capsular sheath, ascribing however no definite function to them. Pilliet has described similar structures in cases of alcoholic paralysis, amyotrophic lateral sclerosis, and progressive muscular atrophy, and draws attention to a similarity in their structure to that of the Pacinian bodies. He suggests that they may represent the end-apparatus of centripetal nerves, peculiar to striped muscle, and more easily found in atrophied than in normal muscle. Christomanos and Strössner, in a carefully prepared article, state that they were not able to satisfy themselves that the muscle-spindles were growth centres, neither could they ascribe to them any pathological significance; they are inclined therefore to regard them as a peculiar nerve end-apparatus.

4. Finally we may mention those writers who have, with more or less confidence, described the muscle-spindles as sensorial end-organs, and have, consequently, given more attention to the relation of the nerve fibers to the spindles, and to their

mode of ending. We may here mention Kerschner, who, in his first communication, mentions that he had found in connection with motor endings on the muscle fibers of the muscle-spindle, very complicated endings of the large medullated fibers which had been traced to the muscle-spindles. By reason of their resemblance to the Golgi tendon-spindles, with which they are often associated, he regards the muscle-spindles, and we may here use his own words, "als komplicirte sensible Endorgane, welche den Muskel-sinne dienen dürfen."

In a second paper which appeared in the same year, he described the ending of the large medullated nerves more fully. The following is taken from his account: "The sensory fiber, or several of them (in man), divides soon after it enters the capsule, di- or tri-chotomously. The resulting branches, which may be far distant from the entrance of the nerve fibers, are wound around the muscle bundle or its individual muscle fibers; the windings above mentioned are especially numerous in man. Here and there an end-fiber can be found, which terminates in an end-bulb; the motor fiber (or several such), which may enter the capsule separately, or with the sensory fibers, runs parallel to the muscle bundle, and ends at a considerable distance from the sensory endings, in a small motor ending." Kerschner's preparations were demonstrated and described by von Ebner, at the Vienna meeting of the "Anatomische Gesellschaft" in 1892. Von Ebner here states that he concurs in Kerschner's interpretations of the muscle-spindles. About the same time, Ruffini gave an account of his observations on the nerve ending in muscle-spindles in man and cat, and gives the only figures, with which we are familiar which may be at all compared with the ones accompanying this article. (The cut given in Kölliker's text-book, showing the ending of a nerve in the muscle-spindle of a rabbit, seems to us sketched from an incompletely stained preparation.) Ruffini makes this statement concerning the ultimate ending of the nerve fibers on the muscle fibers of the spindle: "J'ai pu ramener ces terminaisons finales de la fiber nerveuse à trois types principaux, que j'appellerai terminaisons à anneaux, à spirales et à fleurs." His account of these endings will be more fully considered subsequently. In still another article, Kerschner reiterates his former views as already given, and, while giving a summary of the literature appearing before that time, adds little to what he had stated concerning the ending of the nerve fiber in these structures. Kerschner here, however, promises an extensive monograph on the sensory endings in muscle and tendon-spindles, with numerous plates. This, if it has appeared, we have not been able to consult, as we have not found any reference to it.

Sherrington deserves the credit of having conclusively shown, by experimental means, that the nerve fibers going to the muscle-spindles are sensory. We quote from him as follows:

"My own experiments have been suitable for examining the effect of degeneration of the motor spinal roots upon the nerve fibers supplying the muscle-spindles; they demonstrate that the muscle-spindle is supplied with nerve fibers arising in cells of the spinal root-ganglion. In muscles from which all motor fibers have been entirely removed by degeneration I have never in a single instance failed to find every spindle met with in the muscle still possessed of perfectly sound myelinate nerve-fibers. The myelinate fibers are traceable from the sensory roots, and penetrate into the spindles and terminate within them. The muscle-spindle proves therefore to be a sensorial organ as argued by Kerschner and as indicated by the histological analysis of the nerve-ending by Ruffini."

We may further mention Dogiel's work, who has described very accurately the endings of the spindle-nerves in the muscle-spindle of the frog, as seen when stained with methylene blue; he, while mentioning that the spindle-nerves have no connection with the motor nerves of the muscle, dismisses his account without making any statement as to the probable function of the muscle-spindles. Sihler, who has quite recently worked on the ending of the spindle-nerves in the muscle-spindle of snakes, defends the view that this is a sensorial end-apparatus which subserves the muscle sense.

Our own observations pertain more particularly to the ending of the spindle-nerves in the muscle-spindles. The method used by us was selected with this end in view; the method, while showing the general structure of the muscle-spindles, was not the method which would have been selected, had this been the more particular aim of the research. Our observations on the general structure of the muscle-spindle confirm, in the main, observations previously made, and more particularly those made by Sherrington and given in his account of these structures; this account will here be followed.

Capsule of muscle-spindle. The capsule or perimysial sheath of some writers, has essentially the same structure in all vertebrates examined, although it varies much in thickness. It may be said to be made up of concentrically arranged layers of white fibrous tissue, the several layers being often in close apposition, or again more or less distinctly separated one from the other, leaving larger or smaller clefts between them. The number of these concentric layers varies; Sherrington places it at six to eight, which number holds good for many of the muscle-spindles seen by us, especially those found in mammalian muscle. In amphibia, reptilia, and birds, the capsule of the spindle may be said to be relatively thinner, consisting often of only two to four concentric layers; thicker capsules are, however, also met. The fibrous tissue of the concentric lamellæ is white fibrous, practically devoid of yellow elastic tissue. This may be seen in muscle-spindles overstained in methylene blue, our experience having taught us that in tissues thus overstained, the yellow elastic fibers are often clearly brought out; it is also seen in sections stained after Unna's method; neither of these methods shows any elastic fibers in the capsule of the muscle-spindle. At the beginning of the muscle-spindle (proximal end), the capsule becomes continuous with a somewhat thickened perimysial sheath, which surrounds the muscle fibers about to enter the muscle-spindle. The behavior of the capsule at the distal end of the muscle-spindle depends somewhat on its relative position in the muscle. The spindle may be embedded in the muscle substance, in which case, as Sherrington correctly states, "its long axis lies parallel to the muscle fibers amid which it is embedded;" here the distal end of the capsule seems again to become continuous with the internal perimysium. This, it would seem, is the more usual disposition of the distal end of the capsule in amphibia and reptilia, and is now and then found in birds and mammalia.

In case the muscle-spindle lies near the tendinous insertion of the muscle, in which case the long axis may also be parallel to the muscle fibers amid which it is embedded, or may be at an angle to them, the distal end of the capsule becomes continuous with the fibrous tissue septa, or with the tendon; this we have found to be the more common ending of the spindle-capsule in mammalia, but has been seen also in birds and reptilia (tortoise).

More immediately surrounding the enclosed muscle fibers, designated by Sherrington as "*intrafusal fibers,*" there is found a connective tissue sheath which he has described as the "*axial sheath,*" consisting of thin bands or plates of white fibrous tissue in which nuclei are numerous.

Between the capsule and the axial sheath is found a relatively large lymph space—Golgi and Sherrington—designated by the latter as the "*periaxial space*;" this, he correctly states, is "bridged across and partially subdivided in many points by extremely tenuous membranes and filaments." The periaxial lymph space is broadest near the middle of the muscle spindle, generally tapering off toward the ends. The intrafusal fibers are sometimes in the middle of this space and again eccentric. The space also shows buddings here and there, which seem, however, in a large measure due to foldings in the capsule, the result of contraction of the contiguous muscle fibers.

Intrafusal muscle fibers. The intrafusal muscle fibers differ in size and structure from the muscle fibers of striated muscle. Their number varies. In the snake, only one intrafusal fiber is found, as has been stated by Kühne, Mays, and Sihler; similar spindles have been found in the lizard by Bremer, Trinchese and Cattaneo. In the other vertebrates examined, the number varies from two to ten, and, as Sherrington has stated, in some of the larger spindles—compound spindles—as many as twenty may be found. It is stated (Sherrington) that the muscle fibers destined to form intrafusal fibers are of the red variety, rich in protoplasm. In muscle-spindles containing more than one intrafusal fiber, one, two, three, and perhaps even more muscle fibers enter the proximal end of the spindle, and at once divide into two, three, or even four daughter fibers, of round or oval shape; these are the intrafusal fibers. They usually have a more or less parallel course in the spindle, although in longitudinal sections, they now and then give the appearance of a loose braid, showing that the intrafusal fibers may now and then be more or less twisted in the spindle. The intrafusal fibers are, so far as our observations allow us to assert, enclosed in a sarcolemma, although this is not always distinctly made out in sections, and Sherrington states that "some of the intrafusal fibers are devoid of sarcolemma." The intrafusal fibers show a more or less distinct longitudinal and cross striation, which may usually be made out through the entire length of the fiber. In the middle third of the spindle, the portion described by Sherrington as the equatorial region, the intrafusal fibers possess, according to this observer, the following structure: "The intrafusal fiber often becomes somewhat smaller in diameter and is nearly always circular in section. Its surface zone soon gets thickly encrusted with or almost completely occupied by a sheet of nuclei. Whether these nuclei are strictly part of the muscle fiber is not clear to me. The nuclei are spherical or slightly oval, are clear, and measure about 6 μ in diameter. Cross-sections reveal beneath the nuclear sheet a thin tubular layer which is fibrillated. This tubular layer itself invests a central core (4μ-5μ) of hyaline substance, which runs rod-like along the axis of the intrafusal fiber in this region. The cross-section of the fiber thus often displays a nearly complete zone of four to six nuclei around a hyaline centre." We have quoted thus freely from Sherrington's account, because our own observations are not fully in accord with what he has here described. The sheet of nuclei mentioned by him, is not, we believe, a part of the intrafusal muscle fiber, as, in instances where it was possible to make out a sarcolemma on the intrafusal fibers in the equatorial region of the muscle-spindle, the nuclei above referred to, seemed outside of this sheath. They seem to belong to a connective tissue sheath, which surrounds each intrafusal fiber; a sheath inside of the axial sheath, with which it is partly fused, or to which it may be partly united by means of bands or septa of fibrous tissue. In longitudinal sections of muscle-spindles, the arrangement of the nuclei is such that they seem to belong to endothelial cells lining the fibrous tissue sheath surrounding the intrafusal fibers. On this point, however, we possess no conclusive observations. The hyaline core mentioned by Sherrington, we have interpreted as sarcoplasma, the intrafusal fibers, especially in the equatorial region, often showing fibrillation only in the peripheral zone. In the central of the intrafusal fibers, also more apparent in the equatorial region, a row, or sometimes two parallel rows of nuclei are found. We can confirm the statement of Christomanson and Strõssner, of Kerschner and Sherrington, that these nuclei are resting nuclei, which show no sign of karyokinetic cell division. The main differences which we have observed between the structure of the intrafusal fibers in the equatorial region and that in the other parts of the spindle—proximal and distal polar regions—are that in the former, the cross and longitudinal striation is not so apparent, the central "hyaline core" is more clearly made out, and the nuclei are more numerous. The intrafusal fiber in the equatorial region resembles in structure a developing striated muscle fiber. In cases where the muscle-spindle is situated near the tendon of the muscle or near a fibrous septum, the intrafusal fiber becomes tendinous and seems to fuse with the distal part of the spindle capsule. In the simpler muscle-spindles, containing one intrafusal fiber, this becomes less distinctly striated and shows more nuclei, when within the spindle. In the snake, the muscle fibers destined to become intrafusal fibers are throughout very much smaller than the other striated muscle fibers, about 8 to 10 times smaller, as correctly stated by Sihler. After entering the spindle, it may retain its former size or become slightly larger, less distinctly striated and show more nuclei, the nuclei being found in an axial core, not striated and probably sarcoplastic in nature. The capsule of these simpler spindles consists of two to three concentrically arranged membranous lamellæ of fibrous tissue, between which clefts or spaces may now and then be made out. These lamellæ are not, we believe, elastic in nature ("mehrere Lagen elasticher Membranen"), as Sihler has stated.

We may finally refer to the fact that the muscle-spindles have, according to Cattaneo, a distinct blood supply. One or two relatively large vessels go to each spindle. The vessels pass along the border of the spindle either on or in the capsule and give off branches which have a spiral or wavy course. Our own observations on this point are confined to the muscle-spindles found in the rabbit. In relatively thick sections of one of the intrinsic plantar muscles previously injected with gelatine blue, these spindle-vessels may readily be seen. From the larger branches found in the capsule of the spindle, secondary branches are given off, which have a spiral or wavy course and anastomose to form an open network surrounding the spindle; from this, relatively long, straight branches may be traced between the intrafusal fibers of the spindle.

Spindle-nerves. Nearly all writers who have given observations on muscle-spindles, have recognized large medullated nerve fibers going to these organs, and have described a branching of these nerve fibers, either before entering the spindle, or after their entrance. Sherrington, as previously stated, was the first to show conclusively that such fibers are spinal ganglion—sensory—fibers, which do not degenerate when all the motor nerve fibers going to the muscle have been removed. We find his account of the general distribution of the spindle-nerves very accurate and applying not only to the mammalia studied by him—cat and monkey—but also, with very little modification to other vertebrates possessing muscle-spindles containing more than one intrafusal fiber. As he has stated, usually more than one large medullated fiber, "7 μ—18 μ" (or even longer) in diameter, is distributed to one spindle; two to four may be given as the number for the smaller spindles and five to eight for the larger spindles—compound spindles. The number seems often, however, greater in the immediate vicinity of the larger spindles, due to the fact that now and then, one or the other of the large medullated fibers going to a spindle branches at a very acute angle at some distance from the muscle-spindle. The fibers may approach the muscle-spindle singly, in which case, as is well known, they are surrounded by a thick sheath of Henle, or in small bundles enclosed in a thick connective tissue sheath. The nerve fibers usually enter the spindle from the side, in the smaller spindles, near the center, slightly toward its proximal end, though in the larger compound spindles (see Fig. 39) some of the fibers may enter near the proximal end. In the tortoise now and then, and in the snake more generally, the spindle-nerves enter at the proximal end of the spindle. A portion of Henle's sheath of the spindle-nerves, or of the fibrous-tissue covering of the small bundles of such nerves, becomes continuous with the capsule of the muscle-spindle. Within the capsule, the still medullated nerve fibers, which cross the periaxial space usually obliquely to reach the axial portion of the spindle, are also surrounded by a connective tissue sheath (Henle's sheath), containing many nuclei, which becomes continuous with the axial sheath, where the nerve fibers penetrate it. The course of the spindle-nerves in the periaxial space varies. They may pass obliquely across the periaxial space to reach the axial sheath, which they may penetrate at once or along which they may run for a short distance before penetration; they may have a serpentine course in the periaxial space and may be spirally wound around the axial portion of the spindle. The spindle-nerves remain medullated until they have penetrated the axial sheath, within which they may lose the medullary sheath soon after passing through the axial sheath, or may run along a longer or shorter distance between the intrafusal fibers, having a straight, serpentine, or spiral course, before they lose the sheath of myelin. It has above been intimated that the medullated fibers going to the muscle-spindles may branch; our own observations on this point, as also those on the structure of the spindle nerves, are wholly in accord with the statements regarding these points made by Sherrington; we may therefore give here his words: "I have seen spinal-ganglion fibers branch both when close outside and when quite within the thickness of the capsule. The branching is usually by dichotomous division at a node of Ranvier, and the angle of divergence of the two branches is usually quite small. While approaching the spindle the length of the sheath segments (internodes) of the spinal-ganglion fiber is from 600 μ to 900 μ; at a variable distance within the spindle [We also find before the spindle nerve pierces the capsule], the segments suddenly become much shorter, 80 μ to 130 μ. At the same time, dichotomous subdivision becomes much more frequent, the myelin-sheath becomes much less thick, and the diameter of the axis cylinder considerably greater, e. g. 14 μ instead of 9 μ." The ultimate ending of the spindle-nerves, i. e. the ending of the non-medullated branches of the intrafusal portion of the spindle-nerves, may best be described separately for each of the classes of vertebrates studied. They have, however, this in common: the ultimate endings of the non-medullated branches of the spindle-nerves are found outside of the sarcolemma surrounding the intrafusal fibers, between this sheath and the connective tissue sheath which, as above stated, surrounds each intrafusal muscle fiber.

On the ultimate ending of nerve fibers in muscle-spindles. Amphibia. Our preparations were made from muscle-spindles found in the *cutaneus pectoris, port. sternalis anterior* and *posterior* of *m. pectoralis*, and the *sartorius*. Especially in the first named muscle, which so far as we may judge, contains from 4 to 5 muscle-spindles, the spindle-nerves may be readily stained in methylene blue. Some of the preparations thus obtained were fixed in ammonium picrate and mounted in glycerine-ammonium picrate; others were fixed in ammonium molybdate, embedded in paraffin and sectioned. Dogiel has described and sketched the ending of the spindle-nerves in the muscle-spindles of the frog. A comparison of Fig. 8 of his article with our Fig. 36, shows that we have corroborated his observations. One, two, or even three large medullated fibers are distributed to each muscle-spindle. Occasionally, while yet outside the capsule, more often in the periaxial space, the spindle-nerves undergo branching; the resultant branches consist of one, two, three, or even more, short internodal segments. These branches course along the surface of the axial portion of the spindle, in part outside, in part within the axial sheath and may here have a straight or serpentine course or may be partly wound around the axial portion of the spindle. Within the axial sheath, the medullated nerve fibers may lose their medullary sheath at once or after passing a longer or shorter distance between the intrafusal fibers, where they may undergo further branching. The non-medullated continuations of the medullated nerve fibers break up into fine fibers, richly beset with large varicose enlargements. These, the terminal branches, are in contact with the intrafusal muscle fibers, along which they extend for longer or shorter distances and may often be traced to the poles of the muscle-spindle. In longitudinal sections of muscle-spindles, Fig. 25 (double stained in methylene blue and alum carmine), but especially in cross section, Figs. 26 and 27, it may readily be seen that these terminal fibers are just outside of the sarcolemma of the intrafusal fibers, between it and the connective tissue sheath surrounding these fibers.

Snake. Our preparations showing the nerve endings in the muscle-spindle of the snake were made by injecting the methylene blue (1% solution in normal salt), through the heart. Strips of the back muscles, in which, as Kühne and Sihler have shown, muscle-spindles may be found, were removed to a slide. In these ribbon-like muscles, a muscle-spindle showing a stained spindle-nerve may now and then be found; and we were thus able to obtain a number of muscle-spindles showing the ending of the spindle-nerves. The muscle-spindles of the snake and lizard, as previously stated, are simple, containing only one intrafusal muscle fiber, surrounded by a capsule and axial sheath. One, or, at the most, two medullated nerve fibers have been traced to such a spindle, and, in the preparations obtained by us, the nerve fiber usually enters the spindle at one or the other pole. If two nerve fibers go to the same spindle, these, in the few instances seen by us, enter by opposite poles. In Fig. 37, may be seen such a muscle-spindle receiving two nerve fibers; these, as may be seen, approach the spindle in two quite distinct nerve trunks. (In the figure, only the intrafusal muscle fibers and the nerve fibers are shown. The sketch is from a methylene blue preparation, fixed in ammonium picrate and cleared in glycerine-picrate. In the preparation, the fibrous capsule, as also the fibrous connective tissue sheath around the nerve fibers continuous with the capsule, could be made out, although not very distinctly; also the fact that in the portion of the intrafusal fibre not distinctly striated in the figure, there were about 10 or 12 nuclei. It was, however, found that if all these structures were reproduced in one figure, the ultimate ending of the nerve fibers, which we hope here to show more especially, would come out indistinctly by reason of the fact that it would be covered up by nuclei, etc.) The medullated spindle-nerves lose their medullary sheaths soon after entering the capsule; the ultimate endings are therefore non-medullated, and are, we believe, under the axial sheath in contact with the intrafusal fiber. We have not been able to make longitudinal or cross sections of the muscle-spindles of the snake; the number of successfully stained endings was not sufficient to admit of this. Yet in optical sections of the spindles, a connective tissue sheath, inside of the capsule, which we regarded as the axial sheath, seemed to be outside of the ultimate ending of the nerve fibers.

The ultimate ending of the spindle-nerve is as follows:

The non-medullated continuation of the spindle-nerve divides, soon after its entrance, into two or three branches; these branches may be traced on the intrafusal muscle fiber for some distance, giving off in their course band-like offshoots, which may partly enclasp the intrafusal fiber (*a*, Fig. 36), or almost completely encircle the intrafusal fiber (*b*, of the same figure); the fiber itself ending in one or two large disc-like expansions, *c*, of the figure. The non-medullated fiber, before giving off the band-like offshoots above mentioned, may present one, two, or three flattened expansions, of round, oval, or spindle shape, as may be seen in the figure. The ultimate endings of the spindle-nerves in the muscle-spindles of the snake seen by us, do not all present the same configuration; yet the type is essentially as above described. Sihler, as he himself has stated, was not able to make out clearly the ultimate ending of the nerves in the muscle-spindle of the snake; in some few instances, however, he was able to make the following observation: "Es giebt nämlich auch Spindeln, wo die Querstreifung des Muskels im Spindelmantel nicht verloren geht, wo bloss im inneren des Muskels ein Streifen der dunkeln Substanz sich findet. In solchen—freilich seltenen—Spindeln konnte ich mehrere feine Nervenzweige von myelinhaltigen Nerven abgehen sehen, und glaube ich kaum, dass optische Schnitte der *Henle'schen* Scheiden mich getäuscht haben." The nerve fibers mentioned by Sihler may be the branches of the intrafusal, non-medullated fibers above referred to, his stain not bringing to view the ultimate endings. Other writers, who have given observations on the simple muscle-spindle—designated by Kerschner as "Kühnische Organe"—(Kühne, Bremer, Mays, Trinchese and Cattaneo) have given no definite observations on the ending of the spindle-nerves.

Tortoise. The preparations of muscle-spindles made from these reptiles, were obtained from the vasti muscles. A one per cent. solution of methylene blue in normal salt was injected into the abdominal aorta, and the muscle exposed about an hour after the injection, cut into strips and placed on a slide and examined from time to time, until the endings of the spindle-nerves seemed stained. The tissues were either fixed in ammonium molybdate and sectioned, the sections being further stained in alum cochineal, or were fixed in ammonium picrate and teased, cleared and mounted in glycerine-picrate. The general structure of the spindles is very much as previously described. The intrafusal muscle fibers, from two to eight in number, are surrounded by an axial sheath, periaxial lymph space and capsule, each intrafusal fiber being further surrounded by its own connective tissue sheath, which is partly fused to the axial sheath, or connected with it by bands or septa of fibrous tissue. In the tortoise, many of the muscle-spindles are compound, showing more often two, occasionally three areas of nerve distribution. One, two, or three large medullated nerve fibers go to the smaller muscle-spindles, or to each area of nerve distribution in the compound spindles. The spindle-nerves are surrounded by a sheath of Henle, which (see Fig. 28 and 30) becomes continuous with the capsule and with the axial sheath. The spindle-nerves are medullated until they are within the axial sheath, and also show the short internodal segments, mentioned by Sherrington for mammalia, as previously quoted. Once within the axial sheath, they soon lose their medullary sheath, may now undergo further branching, and may be traced for longer or shorter distances by the side of, or between the intrafusal fibers. The ultimate ending is on the intrafusal fibers, outside of the sarcolemma, but within the connective tissue sheath surrounding the intrafusal fiber. This may be seen in Figs. 29 and 30. The configuration of the ultimate ending of the non-medullated end-branches of the spindle-nerves is shown in Fig. 28, a portion of a compound muscle-spindle of Emys meleagaris, stained in methylene blue and alum cochineal. In this figure, the ending of the non-medullated fiber (terminal branch of a spindle-nerve) designated by *a*, may be regarded as typical. These endings are somewhat difficult to describe and may perhaps be best understood by reference to the figure. They may be likened to a strip of paper, which has, from place to place, been cut nearly in two, the various paper segments thus produced being further trimmed and scalloped into irregular, triangular, oval, or spindle-shaped forms, which are connected by narrow uniting bridges; the whole ending, as thus described, has a somewhat serpentine course on an intrafusal muscle fiber, the irregular, broader portions being moulded to the side of the intrafusal fiber. Only one complete ending is shown in the figure above referred to, and portions of other endings; this is inevitable in sections.

In preparations of muscle-spindles stained in methylene blue, fixed in ammonium picrate and teased, cleared and mounted in glycerine-picrate, it may be seen that a spindle-nerve may have several, two, three or four, or perhaps even more such endings; and these are not always on the same intrafusal fiber, the non-medullated branches going to this or that intrafusal fiber before ending.

Birds. Our observations on the muscle-spindles of birds are confined to the dove, and the muscles more particularly studied were several small muscles on the posterior surface of the metatarsus. A 1 % solution of methylene blue in normal salt was injected into the aorta; the muscle exposed about one hour after the injection and observed from time to time until the spindle-nerves seemed completely stained. The tissues were fixed in ammonium molybdate, embedded in paraffin, and cut longitudinally and transversely, the sections being further stained in alum cochineal. We may here add that we have found the methylene blue method somewhat unsatisfactory for staining the endings of the spindle-nerves in birds. For some reason which we can not at present explain, it seems to stain the nerve endings in birds less readily than in the other vertebrates we have examined.[1] It is usually necessary to expose the previously injected muscle pieces quite a long time to the air, sometimes 30-45 minutes, before the blue color develops in the axis cylinders and their endings; as a result, the muscle fibers and other structures of the muscle are often stained quite deeply blue, before the nerve fibers are properly stained. In some few instances, however, what we have regarded as a successful stain of the endings of the spindle-nerves has been obtained, and the observations here given are based on such preparations. The general structure of the muscle-spindles of birds is as has been previously described. They contain from two to six relatively small intrafusal fibers; these are surrounded by an axial sheath, periaxial space, and a capsule consisting of three to five concentric layers of fibrous tissue. The intrafusal fibers are further enclosed, each in a separate, thin, fibrous tis-

[1] In some of our later work we now and then found that the nerve fibers were stained a very short time after the removal of the tissue; but also found that such stained fibers bleached very quickly. This may be an explanation as to why we so often failed in staining the spindle-nerves in the bird.

sue sheath; this sheath and the axial sheath contain many nuclei. Many of the muscle-spindles of birds seen by us have only one area of nerve distribution, but now and then those with two areas have been found. One, two, or three medullated fibers are distributed to each of the smaller spindles or to each area of nerve distribution in the larger—the compound spindles. They are surrounded by a sheath of Henle, which ends, partly in the capsule and partly in the axial sheath. The branching, course, and structure of the spindle-nerves in the bird is as previously described in discussing in a general way the spindle-nerves, and need not here be repeated. They lose their medullary sheath within the axial sheath, the non-medullated continuation of the spindle-nerves now and then subdividing into two or three branches. The ending of such non-medullated branches is shown in Fig. 31; the fiber *a*, presenting, we believe, a typical ending. As may here be seen, the axis cylinder (non-medullated terminal branch) ends in an irregular expansion resting on the intrafusal fiber; from this, processes which resemble somewhat a repeatedly folded ribbon are given off. These processes show successive broader expansions of round, oval, or irregular shape, united by narrower bridges, and extend for some distance on the intrafusal fiber. In preparations of the whole spindle or in longitudinal sections of a spindle, these processes are seen on the intrafusal fibers, in optical section by the side of the intrafusal fiber (*b* of Fig. 31), and also under the fiber. The ending therefore surrounds the intrafusal fiber. Now and then, the non-medullated terminal branches of the spindle-nerves break up at once into two or three processes having the above structure, or, apparently, may continue into such a process; the latter condition may however be due to imperfect staining.

In birds also, a spindle-nerve may have an ending as above described, on more than one intrafusal fiber; on as many as three fibers; that these endings are outside of the sarcolemma may be seen in Fig. 32, a cross section of a small muscle-spindle of a bird, stained in methylene blue and alum cochineal.

They are within the connective tissue sheath surrounding each intrafusal fiber.

Mammalia. In mammalia we have stained the nerves going to muscle-spindles in the dog, cat, rabbit, Guinea pig, and rat, and lately we have confined our attention to the spindles found in the intrinsic plantar muscles, where, as Sherrington has stated, they are very plentiful. The spindle-nerves were stained by injecting a 1 % solution of methylene blue in normal salt into the abdominal aorta, after bleeding the animal. The intrinsic plantar muscles were exposed about one hour after the injection, removed to a slide and observed until the nerve endings seemed stained; the tissues were fixed in ammonium molybdate and sectioned in paraffin, the sections being further stained in alum carmine or alum cochineal; other muscles were fixed in ammonium picrate, teased, cleared, and mounted in glycerine-picrate. The former method brings out very clearly the relation of the ultimate ending of the spindle-nerve to the intrafusal fibers; the latter, the course and the structure of the spindle-nerves as they approach the spindle, as also their general distribution in the spindle.

In all mammalia examined by us, muscles with only one area of nerve distribution and those with several areas in which spindle-nerves terminated—compound spindles—were found. The latter were more numerous in the dog, cat and rabbit than in the smaller mammals—Guinea pig and rat—examined by us. In the dog, several very large muscle-spindles were found, having as many as four areas of nerve distribution.

The general structure of the muscle-spindles of mammalia, as also the distribution and structure of the spindle-nerves, has been discussed in the preceding pages. We may here, however, reiterate the following points regarding the spindle-nerves:

From one to four large medullated nerves end in the smaller spindles and from five to eight in the larger, compound spindles.

Single spindle-nerves are surrounded by a thick sheath of Henle; small bundles of spindle-nerves, by a connective tissue sheath, which becomes in part continuous with the capsule, in part, with the axial sheath. The spindle-nerves remain medullated until they are within the axial sheath, the internodal segments becoming shorter as the muscle-spindle is approached; but this is more especially noticeable after they have penetrated the capsule. After losing the medullary sheath (within the axial sheath), the non-medullated continuation of spindle-nerves undergoes further subdivision, before the ultimate ending is reached. The general course and structure of the spindle-nerves may be seen in Fig. 39, a sketch of a compound muscle-spindle from the intrinsic plantar muscles of a dog, stained in methylene blue and fixed in ammonium picrate, teased and cleared in glycerine-ammonium-picrate. See also Fig. 38, a smaller spindle, also from the dog, and prepared in the same way. In both the figures, only the intrafusal fibers, with the spindle-nerves and their endings are shown. Observations on the ultimate ending of the non-medullated terminal branches of the spindle-nerves have been made by Kerchner (who mentions in his account observations on man, cat, rabbit, rat, and mouse) and by Ruffini (man and cat) and by Kölliker, who mentions briefly and diagrams the ending of a spindle-nerve in the muscle-spindle of a rabbit. The observations of these investigators were made on tissues stained in gold chloride, and, while we are not able to add materially to the accounts which Kerschner and Ruffini have given, yet, as our observations were made on tissues stained in methylene blue, and, to some extent (cat and rabbit) on tissues stained in methylene blue, fixed, sectioned and double stained in alum carmine and cochineal, we may here present our results as corroborative evidence.

Ruffini, whose account we may here follow (as the few figures he gives are the only ones with which we are familiar, comparable to the ones given by us), describes for the cat, three types of ultimate endings of the spindle-nerves—spiral, circular, and flower-like endings ("terminaisons à spirales, à anneaux, et à fleurs"). Of these, the spiral endings may be first considered, as they seem to us the most typical. The non-medullated terminal branch of the spindle-nerve thus ending, flattens out into a ribbon-like ending, more or less irregular, which is spirally wound around the intrafusal fiber, this spiral extending for a longer or shorter distance along the intrafusal fiber; the spiral turns are sometimes so close together that they almost touch each other, or again, farther apart, so that they can be clearly made out. This mode of ending may be seen at *a*, in Fig. 38 and also in various places in Fig. 39. These spirals have also been described by Kerschner, who very correctly adds that from place to place offshoots proceed from the spiral, which may end on the intrafusal fiber surrounded by the spiral, or on some contiguous intrafusal fiber. The "ring shaped" endings of Ruffini have, we believe, been correctly interpreted by Kerschner, when he states: "Die meisten der 'ringförmigen Endigungen' Ruffini's entsprechen Seitenansichten flacher Spiralwindungen." Such ring shaped endings may however now and then be formed by short side branches of the non-medullated terminal branches, which almost completely, or completely, encircle an intrafusal fiber; several such endings may be side by side on an intrafusal fiber. (See *b*, of Fig. 38.) The flower-like endings mentioned by Ruffini, are, no doubt, as suggested by Kerschner, the terminal endings of the spirals, or of branches from the spirals; they may, however, now and then be seen as branches from the terminal, non-medullated continuation of the spindle-nerves, which have a zigzag course on an intrafusal fiber without forming a spiral; see *f* of Fig. 39. In the rat, Guinea pig, and rabbit, spirals are not so apparent as in the dog and cat above described. One, two, or three spiral turns of the ending may now and then be seen. The endings of the non-medullated terminal branches of the spindle-nerves, are, in the rabbit, Guinea pig, and rat not so ribbon-like as in the dog and cat, are much more irregular—"knorrig oder knotig" as Kerschner expresses it, and are much more given to subdivision. We give in Fig. 33, a portion of a compound muscle-spindle of a rabbit. This spindle has three areas of distribution; one (to the left of the figure), and a portion of another (to the right of the figure) are shown in the section from which the sketch was made, the third is in the succeeding section of the series. As may be seen in the figure, no distinct spirals are here shown, the ending consisting of broad, irregular main stems resting on the intrafusal fiber, from which side branches are given off which partly or completely encircle the intrafusal fibers.

That the endings, as above described, are outside of the sarcolemma of the intrafusal fibers may be seen in Figs. 34 and 35; they are, however, within the connective tissue layer surrounding each intrafusal fiber. Spindle-nerves may end on more than one intrafusal fiber, as is shown in Figs. 33, 38 and 39, and especially well shown in Fig. 34, a sketch of a somewhat oblique section of a large muscle-spindle of a cat. The large medullated fiber shown in this figure divides into two non-medullated branches, one of which may be traced to five relatively small intrafusal fibers.

It needs to be stated, however, that, while a spindle-nerve may end on several intrafusal fibers (on an average 3 or 4), other spindle-nerves going to the same area of nerve distribution, or to other areas in the compound spindle, may and often do end on the same intrafusal fibers. Figs. 38 and 39 may serve to show this. In some of the larger muscle-spindles containing 12 to 15 intrafusal fibers, a number of spindle-nerves end in one area of nerve distribution, surrounding three, four, or five intrafusal fibers in one portion of the spindle, another small bundle of spindle-nerves ending on another group of intrafusal fibers in another portion of the spindle; the whole spindle being surrounded by one capsule.

We have not found opportunity to investigate the endings of spindle-nerves in the muscle-spindles of man. That these structures are present in man has been abundantly shown. Investigators who have regarded them as pathological structures have worked on human material, and the figures they give leave no room for doubt as to the identity of the structures they have described, with what has been described as muscle-spindles in other vertebrates. Kerschner and Ruffini have studied the nerve endings in muscle-spindles of man with the gold chloride method. They both state that the annulo-spiral endings are not found here. The ending seems compact, and from what may be gathered from their brief descriptions, it may resemble the endings found in the rabbit.

Sherrington asks the following question: "Is the intrafusal muscle, like the rest of the muscle, connected directly with motor nerves?" In attempting to answer this question with the gold chloride method, he states that he was unable to find motorial end-plates on the intrafusal fibers. He found, however, that by degenerating *all* the nerves going to a muscle (cutting the sciatic nerve of a cat under the gluteus muscle), the striated muscle-fibers of the gastrocnemius and intrinsic plantar muscles were completely degenerated, while the intrafusal muscle-fibers were not altered from their normal. He further states: "The intrafusal fibers seem in regard to their nutrition to be largely independent of both the afferent and the efferent nerves of the muscle, if one may judge by absence of obvious degeneration in them for five months after total enervation." On the other hand, Kerschner finds, as previously quoted, that the intrafusal fibers possess a motorial ending. He states: "Der motorische Nervenfaden (oder mehrere solcher) welcher gesondert oder mit den sensiblen Fasern eintritt, läuft eine Strecke weit mit dem Muskelbündel parallel und endet in ziemlicher Entfernung vom sensiblen Endapparate mit kleinen motorischen Endgeweihen." In a number of instances, we were able to find what we have interpreted as motorial endings on the intrafusal fibers; *m. e.* in Fig. 37 and 39, show such endings. More often, have we found medullated nerve fibers, smaller than the spindle-nerves, accompanying them to the spindle, but usually they could not be traced to the endings. These may have been motor fibers. We are inclined therefore to agree with Kerschner, that some of the intrafusal fibers at least have a motorial ending. The ones we have found, were, so far as we now remember, always distal to the sensory ending—the ending of the spindle-nerve.

We may further mention that we have, now and then, in rare cases, found sympathetic nerve-fibers in the capsule of the muscle-spindles. These are shown in Figs. 38 and 39, *s. n.* They are, no doubt, vaso-motor fibers of the spindle vessels, as such fibers are now and then seen in muscle-spindles double stained in methylene blue and alum carmine or cochineal, where they are in the immediate vicinity of vessels, or in a vessel wall. This may be seen in Fig. 34, *s. n.*

In closing this account, we may briefly refer to the probable function of these muscle-spindles. What we may have to say on this point has been implied in the preceding pages in discussing the endings of the spindle-nerves. Our observations have been entirely histological. That the muscle-spindle is a sensorial end-organ, situated in voluntary muscular tissue, there seems to us to be no doubt. The general structure of the spindle-organs, their rich nerve supply, and the distinctive ending of the spindle-nerves, would alone, it seems to us, warrant such a conclusion; this seems to us fully substantiated in Sherrington's observations showing that the spindle-nerves are spinal root ganglion nerves.

It has been suggested by Kerschner and Sihler, no doubt on *a priori* grounds, that the spindle-organs may have to do with the muscle sense. Sherrington has shown that under a large aponeurosis, belonging to the distal portion of the vastus medialis, spindle-organs are numerous. He states: "If this aponeurosis be thoroughly separated, however carefully, I have always found the 'knee-jerk' irrevocably lost from the muscle."

A study of the structure of the spindle-organs (we refer here more particularly to their capsule, peri-axial lymph space, etc.) and their resemblance in these respects to other sensorial end-organs—Pacinian and Herbst corpuscles—causes us to agree with Sherrington when he states: "That the stimulus to which these organs are especially adapted is mechanical in quality."

ADDENDUM. Since the completion of the manuscript for the foregoing contribution there have appeared a number of articles on the subject of the muscle-spindle. These may here receive brief mention. The first to be considered is one by Batten. His observations pertain largely to muscle-spindles found in man. The material was hardened in Müller's and Marchi's fluids and stained in hematoxylin and eosin and after Pal's and Sihler's methods. He has this to say of the ending of the spindle-nerves:

"The nerve-fibers terminate in various ways; as a rule, the large fiber which enters the equatorial region passes directly to the muscle-fiber, and seems to lose itself in the nuclei of the muscle-fiber above described; some fine fibers pass between the muscle-fibers and terminate in such an organ as is figured in (Fig. 7); others seem to have a spiral form. Others again form a fine plexus beneath or in the sheath of the spindle." In Fig. 7, which is reproduced from a photograph, the ending is only imperfectly shown, it would seem however to resemble the flower-like ending of Ruffini. From this figure, as also from Batten's description of the nerve-endings, we are led to believe that the endings seen by him show only partially stained nerve-endings, the methods used by him being therefore not so reliable as the gold chloride method, much less the methylene-blue method for staining the ultimate endings of the spindle-nerves.

The latter part of Batten's paper deals with the behavior of the muscle-spindle in certain pathological conditions: infantile paralysis, tabes, myopathy (Leyden's form), progressive muscular atrophy, peripheral neurites, injury to the brachial plexus, after section of the sciatic in cats.

Batten shows that "in infantile paralysis the spindle remains absolutely normal, although the surrounding tissue undergoes complete atrophy. In tabes, he shows that certain changes take place in the termination of the nerve, the general structure of the spindle remaining normal. In progressive muscular atrophy the spindle remains unaltered, and the same is probably true with regard to peripheral neurites. Section or atrophy of the nerve trunk leads to atrophy of the muscle-fibers within the spindle, though it is probable that it takes a considerable length of time for changes to take place in the muscle-fiber within the spindle."

Spiller describes the muscle-spindle in a case of intense muscular dystrophy. The muscle-spindles were normal, also medullated "intra-muscular nerves." He gives no observations on the ending of the spindle-nerves.

Horsley, in a brief note accompanied with photographs, summarizes observations made on trans-sections of gastronenemii and solei of dogs and cats in which the sciatics were divided at periods varying from 3 days to 1 year before the animal was killed.

Horsely shows that although the muscle-spindle seems to undergo an apparent shrinkage from about the 17th day after the section of the nerve, this shrinkage is parallel to the general shrinkage which the atrophy of the muscle gradually undergoes as a whole, the intrafusal fibers being apparently unaltered in character.

In a case of pseudo-hypertrophic paralysis, in which the muscle-spindles were examined by Grünbaum, he finds "the muscle-spindles were for the most part unaffected, but in a few there was a diminution in size of an intrafusal fiber with a deposit of hyaline material around."

We wish finally to refer briefly, to that portion of Ruffini's recent note on the sensory endings in striated muscle, in which he summarizes his observations on the spindle-nerves. Ruffini has studied more particularly the muscle-spindles in the cat, and describes these three kinds of endings of the spindle-nerves:—primary, secondary, and plate-like.

Primary endings. The large nerve-fiber going to the spindle almost always divides into two or more secondary branches, each of which divides into tertiary branches after having passed through the capsule; each of these ends on the intrafusal muscle fiber. These tertiary branches lose their sheath of myelin, become broad, flat and ribbon like, and are either spirally wound about an intrafusal fiber or run along one side of it as a longitudinal band from which, from point to point and at varying intervals, 'troop-like terminal expansions' clasp the entire circumference of the fiber. To these the name of "annulo-spiral ribbon endings" is given.

Secondary form of ending. The parent nerve also divides into secondary branches but usually only after having penetrated the spindle. "The secondary branches soon break up into a number of varicose axis-cylinders, united by very delicate and short filaments. The varicosity of the nerve-fibrils is of various kinds, rounded, bifid, triangular, leaflet-like." This ending is called the "flower-wreath ending."

Plate-like ending. These vary greatly in size. Some are smaller than the end-plates, some equal to them in size some much larger; the last named are the most usual. They differ from the ordinary end-plate. "The terminal expansion of these plate-endings are attached to short and extremely delicate filaments, so that they form, as it were, chaplets, in which rounded axis-cylinders and cross-pieces of the finest delicacy succeed each other in turn."

These three forms of endings are not found in every spindle. Ruffini thus distinguishes three forms of spindles:

1. Spindles with complex nerve ending;
2. Spindles with simpler nerve ending;
3. Spindles with simplest nerve ending.

As to the first four of the five papers here briefly reviewed we wish to add only a few words of comment:

1. From the observations in pathological cases referred to in the above review, it would seem safe to venture the statement, that in such cases where the motor nerves or muscle fibers are primarily affected, the muscle-spindle is not altered in appearance so far as may be determined with the more ordinary histological methods.

2. Strangely as it may seem, after section of the nerve going to the muscle, the muscle-spindle does not materially alter its structural appearances, even after a considerable period of time has elapsed since the section of the nerve. This seems

the more inexplicable, since, as we have shown, the intrafusal fibers are supplied with a motorial ending. We have at the present time no observations to offer in explanation of this fact. So far as we are aware, no concerted effort has been made to ascertain the behavior of the spindle-nerves, and we refer here more especially to the ultimate ending of these nerves, after nerve-sections. This we hope to do in the near future, also to ascertain as to whether so complicated a nerve-ending is capable of regeneration.

As to the account of the ultimate endings of the spindle-nerves given by Ruffini in the note from which we have quoted, we would say,—that, so far as we can determine from the brief account given by him, he has not materially added to his former, and more fully reported observations, which in the preceding pages we have quoted; and further, that we believe our figures will show the various forms of ending mentioned by him, with the exception perhaps of the plate-like endings. Concerning these it is rather difficult, owing to the meager account given, to form a definite idea as to the kind of ending Ruffini had in mind when formulating his description.

A division of the muscle-spindles into the three forms given by Ruffini seems to us somewhat arbitrary. The configurations of the ultimate endings differ, yet these differences appear in every well-stained spindle. A division into simple and complex, or perhaps better compound, spindles—simple, with only one area of nerve distribution, compound, with two or more such areas—seems to us more justifiable.

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DESCRIPTION OF FIGURES.

All figures were drawn under the 1-12 in. oil immersion, and No. I eyepiece (Leitz) with the aid of the camera lucida, giving them a magnification of about 900.

The colored figures are from tissues injected with methylene blue, fixed in ammonium molybdate, sectioned in paraffin and double stained in alum carmine or alum cochineal and mounted in balsam. The other figures are from methylene blue preparations, fixed in ammonium picrate, teased, cleared and mounted in a glycerine-picrate-solution. The latter figures are reduced as will be indicated later.

PLATE XIV. MOTOR NERVE-ENDINGS.

Figs. 1 to 11. Motor nerve ending in voluntary muscle of rabbit. Axis cylinder and ending stained blue; other structures, red.

s.—sarcolemma.

n. l.—neurolemma.

t. n.—telolemma nuclei.

Figs. 1 to 5. Surface view of muscle fiber and nerve ending.

Figs. 6 to 8. Longitudinal section of muscle fiber and motor ending.

Figs. 9 to 11. Cross-section of muscle fiber and nerve ending.

Figs. 12 to 14. Nerve ending in amphibian muscle—frog.

Fig. 12. Surface view of muscle fiber and nerve ending.

Figs. 13 to 14. Cross section of muscle fiber of frog and hypolemmal nerve fibers.

The lettering is here the same as in the previous figures.

Figs. 15 to 21. Ending of nerve fibers on cardiac muscle of the auricle of the cat's heart.

Figs. 15 to 20. Surface view of cardiac muscle cells with nerve endings of varying degrees of complexity.

Fig. 21. Cross section cardiac muscle cell with nerve ending.

Figs. 22 to 24. Ending of nerves in involuntary, smooth muscle from muscular wall of the intestine of a cat.

Figs. 22 to 23. Longitudinal section.

a.—axis cylinder terminating.

b.—termination.

n —nucleus of the cell.

Fig. 24. Cross section of involuntary muscle cell through the point where nerve fibril terminates.

PLATE XV. NERVE-ENDING IN MUSCLE-SPINDLES.

c.— capsule.

a. s.—axial sheath.

c. n.—connective tissue sheath, surrounding each intrafusal fiber; only here and there designated.

i. f.—intrafusal fiber.

p. a. s.—periaxial space.

s. n.—medullated spindle-nerve.

H. S.—Henle's sheath.

s. m.—striated muscle fiber from muscle, given to show the relative size of intrafusal and the other striated muscle fibers.

Sy. n.—sympathetic nerve fiber—vaso-motor fiber.

bl. v.—blood vessel.

Nerve fibers and endings blue, all other stuctures red.

Figs. 25 to 27. Muscle-spindles of amphibia.

Fig. 25. Longitudinal section of the distal portion of the muscle-spindle.

Fig. 26. Cross section of a muscle-spindle at the place of entrance of a spindle-nerve.

Fig. 27. Cross section of the distal portion of a muscle-spindle.

Figs. 28 to 30. Muscle-spindles of tortoise.

Fig. 28. Longitudinal section through equatorial region, showing entrance of spindle-nerve.

Fig. 29. Cross section of distal portion of muscle-spindle.

Fig. 30. Cross section of muscle-spindle through place of entrance of spindle-nerves.

Figs. 31, 32. Muscle-spindle of a bird.

Fig. 31. Longitudinal section of muscle-spindle of a dove, showing the ending of one of non-medullated terminal branches (*a*) of a spindle-nerve.

Fig. 32. Cross section of muscle-spindle of a dove.

PLATE XVI. MUSCLE-SPINDLE OF MAMMALIA.

Lettering the same as on plate XV.

Fig. 33. Longitudinal section of compound muscle-spindle from the intrinsic plantar muscle of the rabbit.

Fig. 34. Cross section of muscle from the intrinsic plantar muscle of a cat.

Fig. 35. The same.

PLATE XVII.

Fig. 36. Muscle-spindles from cutaneous pectoris muscle of frog. Reduced to one half.

Fig. 37. Muscle-spindle from back muscles of the snake. Reduced to one half.

m. e.—motorial ending; *m. e.* (*a*) is under the fiber and probably the ending is on another fiber.

Fig. 38. Muscle-spindle from intrinsic plantar muscles of a dog. Reduced to one half.

PLATE XVIII.

Fig. 39. Compound muscle-spindle fram the intrinsic plantar muscles of a dog, showing three areas of nerve distribution.

Sy. n.—Sympathetic nerve fibers—vaso-motor fibers.

m. e.—motorial endings.

Reduced three times.