ARRANGEMENT AND TERMINATIONS OF NERVES IN THE ŒSOPHAGUS OF MAMMALIA.

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With Plate XXVI.

Since but little work has been done on the innervation of the œsophagus, it seemed to me that it might be both interesting and profitable to determine, by means of the *intra-vitam* methylene blue method, the arrangement and terminations of the nerves in this part of the digestive tract, to verify the results already gained by other methods and, so far as practicable, to compare the innervation of the œsophagus with that of other parts of the alimentary canal.

In pursuance of these purposes, I have confined my investigations to the esophagus of the cat and rabbit and have used only the intra-vitam methylene blue method. In most cases, I injected into the thoracic aorta, proximal to the arch, a 1% solution of methylene blue in normal salt solution, the quantity varying with the size of the animal and the special purpose to When necessary, the carotids at the level of the thyroid cartilage and the aorta just above the diaphragm were ligated before the injection was made. After a time varying according to whether the staining of the motor or of the sensory apparatus was especially desired, the esophagus was removed and the mucosa with the muscularis mucosæ and the submucosa was separated from the underlying muscular coats. When the nerves seemed sufficiently stained, the tissue was fixed, either in a saturated solution of ammonium picrate, as recommended by Dogiel (9), or, after fixation for a few minutes in the ammonium picrate solution, was removed to the 10% solution of ammonium molybdate (Bethe (3)), in which it was allowed to remain for about twelve hours. The tissues fixed by the former method were cleared and mounted in equal parts of glycerine and the ammonium picrate solution; those fixed by the latter method were washed, dehydrated, cleared in xylol and either mounted at once in balsam or embedded in paraffin and sectioned, some transversely to the surface and others tangentially. The second method of fixation was used especially to avoid the maceration of the epithelium, which, after the continued action of the ammonium picrate, was often so excessive as to leave but little epithelium and hence but few of the terminations of the nerves in the epithelium.

Arrangements and Terminations of the Nerves in the muscular coats. Between the circular and longitudinal muscular layers, the nerve trunks, which, after ramifying in the outer connective tissue sheath, have penetrated the longitudinal muscular layer. form a coarse meshed plexus, at the nodal points of which numerous nerve cells forming larger or smaller ganglia are In the esophagus of the rabbit and in the upper part of the œsophagus of the cat, where striated muscle constitutes the muscular coats, the ganglia are much smaller and less frequent and contain relatively few nerve cells. The nerve cells comprising these ganglia vary in size and shape. Most of them are multipolar cells, each having a round or oval nucleus, a distinct nucleolus, a granular and pigmented protoplasm, with many dendritic processes and one neuraxis. The dendritic processes are usually short and thick and break up into a large number of branches which extend between the cells of the ganglion, forming a more or less intricate network, in the meshes of which the nerve cells are sometimes enclosed. In the latter case, we have an appearance like the "nidos pericellulares" described by Ramón y Cajal (4-7) for the ganglia of Auerbach's plexus of the intestinal canal, which Dogiel (11) has shown to be the result of an accidental enclosure of the cell, to be always extra-capsular, and of less physiologic importance than was assigned to them by Cajal Occasionally, as described by Dogiel for the cells of the ganglia of Auerbach's plexus of the intestine, one of the dendrites of these cells may be longer than the others and even extend through a nerve trunk to another gan-The neuraxis of this kind of cell is long and extends out into one of the nerve trunks leading from the ganglion, usually as a non-medullated (Remak's) fiber; it may often be traced, with no or very little branching, till it leaves the nerve trunk and enters into the formation of the intra-muscular plexuses, surrounding and supplying the non-striped muscles of the muscular coat and to some extent also of the muscularis mu-Although it has been shown by Kölliker (27 and 28), Dogiel (10) and others that the neuraxes of sympathetic neurones may possess a thin medullary sheath, it has seemed to me that most, at least, of the neuraxes of the neurones whose cell bodies constitute the ganglia of the intermuscular plexus of the œsophagus, were non-medullated throughout their course. This observation corroborates one made by Huber (20), who says that he believes that the neuraxes of the cells of the peripheral ganglia,—those of the heart, salivary glands, intestine, bladder, etc.—are non-medullated throughout. ings of these neuraxes are as described for the nerve endings in non-striated muscle of other parts of the body, the terminal branch dividing into two or three short twigs which end in an enlargement on the non-striated muscle cell (Huber and DeWitt While the arrangement of the muscular plexus is usually so complicated that it is impossible to trace a single neuraxis from the cell body where it originates to its termination on a muscle cell, yet I have occasionally seen a fiber which had a shorter course. In these cases, the fiber could, without difficulty, be traced from the cell body, leaving the ganglion, often without forming part of a nerve trunk, but passing independently to a muscle fiber in the vicinity of the ganglion. most of the neuraxes of the sympathetic cells of the intermuscular plexus of the œsophagus end on the non-striated muscle cells of the muscular walls of the œsophagus, I have at times, as I believed, been able to trace certain neuraxes to the walls of the blood vessels, where they helped to form the vascular plexus of vaso-motor nerves. ... s this observation, however,

was made only in surface preparations, where it is possible to mistake a fiber passing over or under a vessel for one ending upon it, I am unwilling to make this statement positively until after further investigation.

Besides the neurones which have just been described and which may be regarded as motor sympathetic neurones both on account of their resemblance to the cells described as motor neurones in other sympathetic ganglia by Dogiel (10-12), Huber (20-21) and others, and from the fact that their neuraxes have been traced to their terminations on non-striated muscle cells, we find other cells in the ganglia of the œsophageal intermuscular plexus. These are usually spindle-shaped, with round or oval nucleus and granular protoplasm; from each extremity extends a single slender process, difficult to differentiate into neuraxis and dendrite and both forming parts of nerve trunks. The cells may be multipolar, with one neuraxis and several long slender dendritic processes, many of which extend into the nerve trunks leading from the ganglion. These cells stain more readily in methylene blue than do the motor cells; they are often situated near the periphery of the ganglion and are sometimes found embedded in a nerve trunk at some distance from any ganglion. While the processes of these cells enter the nerve trunks and may often be traced for some distance in them. I have never been able to trace them to their termination. They, however, correspond exactly to the cells described by Dogiel (12) as type II or sensory cells and found by him in both the central and peripheral sympathetic ganglia. ing to Dogiel, the single neuraxis of one of these cells passes in the nerve trunk, either as a non-medullated fiber or surrounded by a thin medullary sheath, to some other ganglion in which it forms an intercellular network. It often sends collateral branches to several ganglia, before finally terminating as described about the motor sympathetic cells. Huber (20), having seen sympathetic fibers terminating on the dendrites of sympathetic cells, suggests the possibility that this is the manner of termination of the neuraxes of the sensory sympathetic neurones. Other neuraxes of sensory sympathetic neurones, or their collaterals, according to Dogiel, pass through the rami communicantes, to the spinal ganglia and end, as described by Aronson (1) and Cajal (7) in pericellular plexuses about the spinal ganglion cells. The dendrites of these type II cells are described as long, slender and branching, difficult to distinguish from neuraxes and, according to Dogiel (12), they may be traced, either through the nerve trunks or in an independent course through the circular muscular coat, into the submucosa and mucosa. He, basing his assumption on the work of Sakussef (37), who believed he could trace these dendrites, in the intestine of the fish, through a subepithelial plexus into the epithelium, says: "Es ist möglich dass die Endverzweigungen dieser Fortsätze in den inneren Organen ebensolche sensible Apparate bilden, wie die sensiblen Fasern des Cerebro-spinalsystems in der Haut, etc." This would, if verified, form a complete apparatus for peripheral sympathetic reflexes.

In the periphery of these ganglia and along the nerve trunks, as well as in the mucosa and submucosa, are seen many branched cells, with long, slender, nerve like processes, which stain readily in methylene blue and in some respects resemble nerve cells. These seem to correspond to the cells described by Ramón y Cajal (4, 5) as nerve cells, which Dogiel (11) has demonstrated in the adventitia of arteries, in the sheaths of nerves and ganglia and in the connective tissue between the bundles of smooth muscle fibers. While their processes often resemble the processes of nerve cells and may even seem at times to be in communication with nerve fibers, these seem to be cells of connective tissue origin rather than nerve cells.

Many of the cell bodies of the sympathetic neurones of type I of the intermuscular plexus of the œsophagus' are surrounded by pericellular end-baskets, the telodendria of small medullated fibers, found in the nerve trunks and sending collateral branches to several ganglia before finally terminating. In any ganglion, one or two or three of these fine fibers may be seen, which often lose their medullary sheaths some time before terminating; they often branch several times in the ganglion, so that a single fiber may influence, through its collateral

branches, several cells in a single ganglion, as well as several ganglia. At its termination, each terminal branch breaks up into varicose twigs, which surround the type I cells in an end-basket which has been shown to be within the capsule of the cell. Similar end-baskets have been found, surrounding sympathetic cells in both central and peripheral ganglia in all parts of the body. As shown by Dogiel, Huber and others, they are the telodendria of white rami fibers or preganglionic fibers and are always intra-capsular. While these pericellular baskets have been found by Huber (21) in the ganglia of the cesophagus as well as in those of the intestine, he states that he believes that not all the cells of these ganglia are thus connected to the cerebro-spinal system, since the number of baskets found has been relatively small.

The question of the character of the ganglia of Auerbach's plexus in the intestine has been discussed by Langley and Anderson (33), Kölliker, Huber, and others and, in spite of the apparent failure of Langley's physiologic experiments, the conclusion seems indisputable that these ganglia, as well as the ganglia of the œsophagus which are analogous to them, are sympathetic, since they correspond histologically in every respect to other sympathetic ganglia and like them are connected to the cerebro-spinal system by white rami fibers which terminate in pericellular, intracapsular end-baskets about the cells of the ganglia.

The nerve trunks of the intermuscular plexus of the cesophagus contain the white rami or preganglionic fibers, the non-medullated neuraxes of the sympathetic motor cells and the neuraxes and dendrites of the sympathetic sensory cells already mentioned; in addition to these, they contain non-medullated nerves, the neuraxes of sympathetic cells, whose cell bodies are situated either in the ganglia of the cesophagus or in more distant ganglia, the fibers forming a perivascular plexus and terminating on the smooth muscle fibers of the vessel walls; besides these, we find larger medullated nerves, which pass through the ganglia without making connection with any of the cells and pass into the submucosa and mucosa to end as will be

described later. Such large medullated nerves have been found in all parts of the sympathetic system and are generally recognized as cerebro-spinal sensory fibers. Kölliker (28) says that the sensory fibers of the sympathetic system are larger or smaller medullated fibers originating from the spinal ganglia and conveying the scanty sensory impressions which emanate from the several organs. In the upper and middle thirds of the æsophagus of the cat and in the whole æsophagus of the dog and rabbit and other animals which have striated muscle in the muscular coat throughout the whole æsophagus, other medullated nerves are found in the nerve trunks, which form no connection with the sympathetic ganglion cells, but, sooner or later, leave the nerve trunk to terminate on the striated muscle in an end-plate which is exactly like the end-plate found in voluntary muscle in all parts of the body.

The origin of these various nerves has been investigated by Howell and Huber (22), Langley (31), Kronecker and Lüscher (29), Kreidel (30) and others. Howell and Huber, while investigating the physiology of the communicating branch between the superior and inferior laryngeal nerves, determined that this was a sensory branch of the superior laryngeal nerve and carried sensory fibers from the trachea and œsophagus. Kronecker and Lüscher decided, as the result of their experiments, that the inferior or recurrent laryngeal nerve brought the motor fibers to the cervical and upper thoracic portions of the esophagus. Langley found that the motor innervation of the whole esophagus and of the cardiac end of the stomach is from the vagus nerves, which also carry inhibitory fibers to the cardiac and adjacent regions of the œsophagus. Kreidel, however, has carried out a number of experiments to determine from which root arise the nerves supplying the œsophagus and decided that, while the vagus nerves carry the fibers to their place of distribution, they arise, not from the vagus root, but from the glossopharyngeal. By comparing the results of these workers, we may arrive at the conclusion that all the nerve fibers-motor, sensory, vaso-motor and preganglionic-found in the nerve trunks of the intermuscular plexus of the œsophagus, except the neuraxes and dendrites of the nerve cells found in the œsophageal ganglia, arise from the vagus nerves.

Pl. XXVI, Fig. 1 represents, drawn under low magnification, a surface view of a portion of the intermuscular plexus of the lower part of the esophagus of a cat. In it we get a general view of the plexus and ganglia and, to some extent, see the two kinds of nerve cells and various kinds of nerve fibers constituting the nerve trunks. This, however, is better shown in Pl. XXVI, Fig. 2, A, which represents a portion of the same figure drawn under higher magnification. In this figure, the motor and sensory cells are plainly distinguished, with their neuraxes and dendrites extending out into the nerve trunks or breaking up in the ganglion. Other non-medullated fibers may be seen passing through the ganglion, the neuraxes of cells of some other ganglion on the way to their destination. large medullated fibers pass through the ganglion without making connection with any of its cells; these are sensory fibers, the dendrites of spinal ganglion cells. We may also distinguish two smaller medullated fibers, which lose their medullary sheaths near the center of the ganglion and send non-medullated fibers to several cells, about which they form pericellular networks. This relation of the white rami fibers to the ganglion and the formation of the end-baskets may be better seen, however, in B of the same figure, which represents a surface preparation of a ganglion from the intermuscular plexus of a rabbit, in which the cells with their processes were very imperfectly stained, but the white rami fibers with their telodendria were very clearly brought out. Occasionally in this preparation, only the peripheral zone of the cell is stained the central part and nucleus and the processes being completely unstained.

Arrangement and terminations of Nerves in the Submucosa and Mucosa. In the submucosa of the esophagus, smaller nerve trunks form a finer meshed plexus analogous to Meissner's plexus of the stomach and intestine. These nerve trunks contain medullated and non-medullated nerves, many of them originating from the intermuscular plexus. Few ganglia have been found by me, however, in this submucous plexus of the

œsophagus. In the course of the nerve trunks and occasionally at the nodal points of the plexus, single usually bipolar, but occasionally multipolar nerve cells are found, which, according to Dogiel's (12) definition, are sensory sympathetic cells. the lower part of the œsophagus, I have occasionally seen small ganglia containing from four to eight cells, some of which were surrounded by the telodendria of white rami fibers. These ganglia, when present, show the two types of nerve cells with their processes found in the ganglia of the intermuscular plexus; they present also the large medullated sensory fibers and fine non-medullated sympathetic fibers passing through the ganglion on the way to their termination. Such a ganglion is represented in Pl. XXVI, Fig. 4. This ganglion was found in the lower part of the œsophagus of a cat and presents four large cells, of which one is surrounded by the end-basket of white rami fibers, the others showing the long, fine, dendritic processes characteristic of sensory cells. The form of plexus found in the greater part of the œsophagus is represented in Pl. XXVI, Fig. 3, showing the interwoven nerve trunks with here and there a While I have never been able to trace a few, isolated cells. fiber of the submucous plexus from its origin in a cell to its termination, it has seemed to me probable that most, if not all, of the type I cells found in this plexus are secretory cells, whose neuraxes terminate on the gland cells. Typical œsophageal glands are found in the submucosa only in that part of the œsophagus in which ganglia are seen. Both medullated and non-medullated fibers follow the course of the gland ducts, the former terminating, as in the salivary glands (Arnstein (2) and Huber (23)), in free endings on the epithelial cells of the duct, while the latter form a plexus about the acinus, from which branches may be traced to their endings in slight enlargements on the gland cells. I have found no ganglion cells in direct connection with any of these glands.

The blood vessels of the submucosa, as well as those of other parts of the œsophagus, are, like the vessels of other parts of the body (Dogiel (13), Schemetkin (38) and Huber (24)) supplied with medullated sensory fibers, which end in telodendria

in and around the adventitia, and non-medullated sympathetic, vaso-motor fibers, which form a plexus in the adventitia and end on the non-striped muscle of the media.

Non-medullated nerves, the neuraxes of neurones, the cell bodies of which are found in the ganglia of the intermuscular plexus of the œsophagus, pass through the nerve trunks of that plexus, penetrate the circular muscular layer, help to form the nerve trunks of Meissner's plexus and finally, leaving this plexus, break up into an intra-muscular plexus in the muscularis mucosæ, from which fine fibers are given off which end on the muscle cells as on non-striped muscle in other parts of the body. The general arrangement of this intra-muscular plexus and its relation to the submucous plexus is shown in Pl. XXVI, Fig. 3, which represents, sketched under low magnification, a portion of the muscularis mucosæ with the submucosa over it.

The large, medullated, sensory fibers, found in the nerve trunks of both the intermuscular and the submucous plexus, pass through the muscularis mucosæ and form, with frequent branching, a finer meshed plexus in the deeper parts of the mucosa. From this plexus branches, still medullated, are given off, which pass, repeatedly dividing at the nodes of Ranvier, toward the epithelium. Under the epithelium, these nerve fibers lose their medullary sheaths and form a fine meshed sub-epithelial plexus, whose fibers extend for considerable distances under the epithelium. Before losing their medullary sheaths, many of the medullated fibers give off at the nodes of Ranvier non-medullated fibers, which also pass up toward the epithelium and assist in the formation of the sub-epithelial plexus. From this plexus, as well as from non-medullated fibers which come up directly from the mucosa and seem to take no part in the formation of the plexus, fine, varicose nerves pass up into the epithelium, wind between the epithelial cells, occasionally giving off longer or shorter branches, which terminate in varicosities of different forms and sizes; the terminal fibers also finally end in ball-like thickenings on or between the epithelial cells, either near the surface or at a greater depth.

A well stained preparation of the œsophageal mucosa,

viewed from the surface, presents an intermingled and confused mass of nerves, medullated and non-medullated, with their telodendria, in which it is impossible to trace any single fiber through all its branchings to its terminations and so view in a connected and orderly way the relations of the several parts to each other. Occasionally however, a preparation may be obtained in which, in a given area, few or perhaps only one fiber is stained with the methylene blue and this one very perfectly In this case, we may observe over to its minutest branches. how large an area a single nerve is distributed. Pl. XXVI, Fig. 5, represents such a fiber with its terminal branching. As this is taken from a rather thick, tangential or somwhat oblique section of the mucosa, however, and not from a surface preparation, there is no doubt that many of the terminal branches with their telodendria have been removed and that the ending. if complete, would occupy a much larger area. This has been demonstrated in surface preparations, in some of which the medullated and non-medullated nerves have been traced through much more complicated branching and dividing than that shown in the figure. The end-branches of these nerves intertwine and overlap in such a way that a surface view of the mucosa with the surface of the epithelium in focus shows an almost uniform distribution of the telodendria in most of the epithelium.

When we compare the small number of the large, medulated, sensory fibers found in the nerve trunks of the esophageal plexuses with the large number of non-medulated nerves taking part in the free sensory ending in the epithelium, we are convinced that each nerve divides repeatedly and covers with its branches a relatively large area. Similar free sensory nerve endings have been found in the ducts of the salivary glands by Arnstein (2) and Huber (23), in the respiratory tract by Ploschko (35), Berkley (2a) and Smirnow (39), in the endo- and peri-cardium by Smirnow (40) and Dogiel (13) and in the bladder by Ehrlich (16), Cuccatti (8), Grünstein (19) and Huber (24). The latter has described and figured, from the mucosa of the urethra of a cat, a free sensory ending in which twenty medullated nerve fibers arising from a single nerve fiber could

be counted, each giving off numerous non-medullated branches with their divisions and telodendria; the whole ending was estimated to cover an area 1.4 mm. by 0.8 mm. As Gaskell (17), Edgeworth (15) and Langley (32) agree that the number of sensory fibers in the white rami is small, Huber believes that "this may be compensated for by the repeated division of those fibers and by the relatively large area covered by their branches." Both the terminal branches after losing their medullary sheaths and the collateral non-medullated branches given off from the medullated fibers at some node of Ranvier are beset with varicosities of different forms and sizes.

That the terminal and lateral arborizations surround the epithelial cells, ending on or between the cells in small varicose thickenings, sometimes on the surface cells and sometimes on the deeper ones, may be seen in Pl. XXVI, Fig. 7, taken from a cross section of the œsophageal mucosa of a young cat. the greater part of the œsophagus, these terminal arborizations seem to be quite evenly distributed and it has seemed to me probable that nearly all of the epithelial cells come in contact with one or more of the terminal nerve fibers. In the upper part of the œsophagus, however, near its junction with the pharynx, there are, in addition to these uniformly distributed telodendria, certain peculiar ball-like masses, consisting of the telodendria of several nerve fibers, whose branches are very short and soon become non-medullated. The non-medullated fibers soon break up into long, slender, varicose end branches, forming end-brushes which meet and intermingle with the endbrushes of other nerve fibers, making a dense and compact mass of terminal nerve fibers, which, on superficial examination, resembles a special sensory end-organ. Closer study, however, fails to reveal the presence of a connective tissue capsule and, in cross sections, we find that the ending is in the epithelium and does not differ from the end-arborizations in other parts of the mucosa except for the fact that here they are more closely crowded together, more richly branched and beset with larger and more abundant varicosities. Pl. XXVI, Fig. 6, represents the surface view of one of these end-oalls, which I have found

only in the pharyngo-œsophageal region, but which I have found there in considerable numbers. Two large medullated nerves are seen, which divide repeatedly into short medullated branches, these breaking up almost at once into terminal endbrushes, whose extremities meet and intermingle with those from the fiber at the opposite extremity of the mass of telodendria. Fig. 8 represents a cross section of a similar mass of endings, showing the fine sub-epithelial plexus and the rich branching of the terminal varicose fibers in the epithelium.

The nerves ending in the mucosa of the frog's œsophagus have been stained in gold chloride by Goniaew (18), working under Arnstein's direction, and in chrome silver by Smirnow (41). Both describe the formation of plexuses of medullated fibers in the deeper parts of the mucosa and of non-medullated fibers just under the epithelium, from which varicose fibers were traced into the epithelium. The nerve fibers in the epithelium, according to Smirnow, run either straight or in a more or less winding course, between the epithelial cells, divide several times, and, as fine, varicose fibers, surround the ciliated, as well as the goblet cells which line the œsophageal mucosa of the frog, ending free on both kinds of cells, either in points or in knob-like thickenings. The goblet cells have an especially rich nerve supply and are here regarded as unicellular glands.

Malischeff (34) has recently investigated the nerve endings in the œsophagus of the bird, but I have not had access to his report of the results of his investigations.

Retzius (36), with the chrome silver method, demonstrated nerves entering the epithelium of the æsophageal mucosa of the cat. These nerves branched freely in the epithelium and ended between the epithelial cells. He says, however, that the nerves in the æsophageal mucosa are by no means so numerous as in that of the pharynx and larynx and end much nearer the basement membrane. While some of the terminal fibers in my preparations end on the deeper cells of the epithelial layer, many may be traced, as seen in Pl. XXVI, Fig. 7, to the flattened cells near the surface, on which they may be seen to end.

In summarizing the results of my investigations, it may be

said that the œsophagus receives its motor and secretory innervation through sympathetic neurones the cell bodies of which are situated in the ganglia in the intermuscular (Auerbach's) and the submucous (Meissner's) plexuses, the neuraxes of which terminate on the non-striped muscle of the muscular coat and of the muscularis mucosæ and on the gland cells of the submucosa in those portions of the œsophagus in which glands are found. These sympathetic neurones are, in part at least, connected to the cerebro-spinal system by white rami or preganglionic fibers, which terminate in intracapsular end-baskets surrounding the cell bodies. In so far as the muscular wall of the œsophagus consists of striated muscle, it receives its motor innervation through medullated fibers, the neuraxes of motor neurones, the cell bodies of which are situated in the anterior horn of the spinal cord, and which terminate in motor endplates as in voluntary, striated muscle in other parts of the body. The esophagus receives its sensory innervation through the dendrites of spinal ganglion cells which terminate in free sensory endings in the adventitia of the blood vessel walls and in the epithelial lining of the mucosa and of the gland ducts. There are in addition sympathetic neurones, the cell bodies of which are situated in the ganglia of the œsophageal plexuses and along their nerve trunks, the neuraxes of which are believed to terminate in other sympathetic ganglia or in the spinal ganglia, while the mode of termination of the dendrites has not yet been determined; these are the so-called sensory sympathetic neurones which may be concerned in the establishment of peripheral sympathetic reflexes.

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LITERATURE CONSULTED.

- 1. Aronson. Beiträge zur Kenntniss der centralen und peripheren Nervenendigungen, Inaug. Diss., Berlin, 1886.
- 2. Arnstein. Zur Morphologie der sekretorischen Nervenendapparaten. Anat. Anzeiger. Vol. X, 1895.
- 2a. BERKLEY. The Intrinsic Pulmonary Nerves in Mammalia. Report in Neurol. II, Johns Hopkins Hosp. Reports, 1894.
- 3. BETHE. Eine neue Methode der Methylenblaufixation. Anat. Anzeiger. Vol. XII, No. 18.
- RAMON Y CAJAL. Los ganglios y plexos nerviosos del intestino de los mamiferos. Madrid. 1893.
- 5. RAMON Y CAJAL. Sur les ganglions et plexus nerveux de l'intestin. Comptes rendus hebdomadaires des séances de la société de biologie. 1893-94. p. 217.
- 6. RAMON Y CAJAL. Estrutura del gran simpático de los mamiferos. Ergebnisse der Anat. und Entwickl. Vol. II, 1892.
- RAMON Y CAJAL. Estrutura y conexiones de los ganglios simpaticos.
 Pequeñas contribuciones al conocimento del sistemo nervioso. Barcelona. 1891.
- 8. CUCCATTI. Nouvelles observations au sujet de la distribution et de la terminaison des fibres nerveuses dans la vessie urinaire de quelques amphibies, reptiles et mammifères. Reviewed in Arch. Ital. de Biologie Vol XI, 1889.
- 9. DOGIEL. Ein Beitrag zur Farbenfixirung von mit Methylenblau tingirten Präparaten. Zeitschr. f. wissensch. Mikroskopie. Bd VIII, 1891.
- 10. DOGIEL. Zur Frage über den feineren Bau des sympath. Nervensystems bei den Säugetieren. Arch. f. mik. Anat. Vol. XLVI, 1895.
- 11. DOGIEL. Zur Frage über die Ganglien der Darmgeflechte bei den Säugetieren, Anat. Anzeiger, Vol. X, 1895.
- 12. DOGIEL. Zwei Arten sympath. Nervenzellen. Anat. Anzeiger, Vol. XI, 1895-6.
- 13. DOGIEL. Die sensiblen Nervenendigungen im Herzen und in den Blutgefassen der Säugetiere. Arch. f. mik. Anat. und Entwickl. LII, 1898.
- 14. DOGIEL. Ueber den Bau der Ganglien in den Geflechten des Darmes und der Gallenblase des Menschen und der Säugetiere. Arch. f. Anat. und Phys. Anat. Abt. 1899.
- 15. EDGEWORTH On a Large-fibred Sensory Supply of the Thoracic and Abdominal Viscera. The Journal of Physiology, Vol. XIII, 1802.
- Abdominal Viscera. The Journal of Physiology, Vol. XIII, 1892.

 16. EHRLICH. Ueber die Methylenblau-reaction der lebenden Nervensubstanz. Deutsche Med. Wochenschr. 1886.
- 17. GASKELL. On the Structure, Distribution and Function of the Nerves which Innervate the Visceral and Vascular Systems. Journal of Physiology. Vol. VII.
- 18. GONIAEW. Die Nervenendigungen in der Speiseröhre des Frosches. Mitgetheilt von Prof. Arnstein. Arch. f. mik. Anat. Bd. XI, 1875, p. 487.
- 19. GRUENSTEIN. Zur Innervation der Harnblase. Arch. f. mik. Anat. und Entwicklungsgeschichte. Vol. LV, 1899.

- 20. HUBER. A Contribution on the Minute Anatomy of the Sympathetic Ganglia of the Different Classes of Vertebrates. Journal of Morphology. Vol. XVI, 1899.
- 21. HUBER. Four Lectures on the Sympathetic System. Journal of Comp. Neurology, Vol. VII, 1897.
- 22. HOWELL and HUBER. Physiology of the Communicating Branch of the Superior Laryngeal Nerve. Journal of Physiology, Vol. XII, 1891, p. 5.
- 23. HUBER. Observations on the Innervation of the Sublingual and Submaxillary Glands. Journal of Experimental Medicine. Vol. I, 1896.
- 24. Huber. Observations on Sensory Nerve-fibers in Visceral Nerves and on their Modes of Terminating. Journal of Comp. Neurology. Vol. X, 1900.
 - 25. HUBER. The Spinal Ganglia of Amphibia. Anat. Anzeiger. Vol. XII.
- 26. HUBER and DEWITT. A Contribution on the Motor Nerve endings and on the Nerve endings in the Muscle Spindle. Journal of Comp. Neurology, Vol. VII, 1898.
- 27. KÖLLIKER. Ueber die feinere Anatomie und die physiologische Bedeutung des sympathischen Nervensystems. Gesellschaft Deutscher Naturforscher und Aerzte. Verhandlungen. 1894. Allgemeiner Theil.
- 28. Kölliker. Handbuch der Gewebelehre des Menschen. Vol. II, p. 858, 1896.
- 29. KRONECKER and LUESCHER. Innervation de l'oesophage. Arch. Ital. de Biologie. Vol. XXVI, 1896-7, p. 308.
- 30. KREIDEL. Die Wurzelfasern der motorischen Nerven des Oesophagus. Arch. f. d. gesammt. Physiologie. LIX, 1895.
- 31. LANGLEY. On Inhibitory Fibers in the Vagus for the Stomach and End of the Esophagus. Journal of Physiology. Vol. 23, 1898-9.
- 32. LANGLEY. On the larger Medullated Fibers of the Sympathetic System Journal of Physiology, Vol. 13, 1892.
- 33. LANGLEY and ANDERSON. The Peripheral Ganglia. Journal of Physiology, Vol 19, 1895-6, p. 131.
- 34 Malischeff. Nerve Endings in Esophagus of Bird. Bull. Imp. Soc. of Naturalists. Moscow, 1897.
- 35. PLOSCHKO. Die Nervenendigungen und Ganglien der Respirationsorgane. Anat. Anzeiger. Vol. XIII, 1897.
 - 36. RETZIUS. Biologische Untersuchungen. Neue Folge, Vol. IV, 1892.
- 37. SAKUSSEF. Comptes rendus des séances de la Société Impériale des Naturalistes de St. Petersburg. 16 December, 1895. Cited by Dogiel.
 - 38. SCHEMETKIN. Cited by Huber.
- 39. SMIRNOW. Ueber Nervenendknäuel in der Froschlunge. Anat. Anzeiger. Vol. III, 1888.
- 40. SMIRNOW Ueber die sensiblen Nervenendigungen im Herzen bei Amphibien und Säugetieren. Anat. Anzeiger. Vol. X, 1895.
- 41 SMIRNOW. Ueber die Nervenendigungen im Œsophagus des Frosches. Internat. Monatsschr. f. Anatomie und Physiologie. Vol. X, 1893.

DESCRIPTION OF FIGURES.

PLATE XXVI.

Fig. 1. Surface preparation of part of the intermuscular plexus of the cosophagus of a young cat. Stained in methylene blue and fixed in ammonium picrate. Sketched with the aid of the camera lucida under $\frac{2}{3}$ in. objective and 2 in. ocular. Reduced to $\frac{1}{3}$.

Fig. 2, A. Surface preparation of one of the ganglia from Fig. 1. Sketched under ½ in. objective and 2 in. ocular with the aid of the camera lucida. Reduced to ½. a.—sympathetic fiber passing through ganglion; s.s.—sensory cerebro-spinal fibers passing through ganglion; m.m.—sensory sympathetic cells; c.c.c.—motor sympathetic cells surrounded by end-baskets of white rami fibers; p.—preganglionic fiber.

Fig. 2, B. Surface preparation of ganglion from intermuscular plexus of rabbit. Stained in methylene blue, fixed in ammonium picrate. Cells imperfectly stained, but end-baskets of preganglionic fibers showing very distinctly. Drawn with the aid of the camera lucida, under 1/6 in. objective and 2 in. eyepiece. Lettering same as in A.

Fig 3. Surface preparation of submucosa and muscularis mucosæ of young cat. Stained in methylene blue and fixed in ammonium picrate Drawn with the aid of the camera lucida, under $\frac{2}{3}$ in objective, 2 in eye-piece. Reduced to $\frac{1}{3}$, p—intramuscular plexus; s.s.s.—sensory sympathetic nerve cells; t.—nerve trunk of submucous plexus; no type I cells are seen in this part of the plexus.

Fig. 4. Surface preparation of small ganglion from lower part of submucous plexus of esophagus of cat. Stained in methylene blue and fixed in ammonium picrate. Drawn with the aid of the camera lucida under 1/6 in. objective and 2 in. eye piece. Reduced to 1/5. c.—type I cell, surrounded by end-basket of preganglionic fiber; p.—preganglionic fiber; m.m.—sensory sympathetic cells; s.—sensory cerebro-spinal fiber passing through ganglion; a.—non-medullated sympathetic fiber passing through ganglion.

Fig. 5. Tangential section of part of the mucosa of a young cat. Stained in methylene blue and fixed in ammonium molybdate after prefixation for 15 minutes in ammonium picrate. Section about 80 μ in thickness. Drawn with the camera lucida, under $\frac{1}{16}$ in objective and 2 in eye-piece. Reduced to $\frac{1}{16}$. Shows the end branching of a large, medullated sensory nerve in the mucosa with the telodendria in the epithelium.

Fig. 6. Surface preparation of one of the end-balls in the upper part of the esophagus of a cat. Stained in methylene blue and fixed in ammonium picrate. Drawn with the aid of the camera lucida under 1/6 in. objective and 2 in. ocular. Reduced to 1/3. Shows medullated nerves, with short medullated and non-medullated branches and telodendria closely crowded together.

Fig. 7. Section through epithelium and part of mucosa of young cat. Stained in methylene blue, fixed for 15 minutes in ammonium picrate and afterwards for 12 hours in ammonium molybdate. Drawn with camera lucida, under I-12 in. oil immersion objective and 2 in. ocular. Reduced to ½. Shows medulated sensory fibers, subepithelial plexus, and terminal arborization in the epithelium.

Fig. 8. Section through end-ball similar to that in Fig. 6. Preparation prepared and sketched as in Fig. 7. Shows the rich terminal arborization in epithelium.

