A CONTRIBUTION TO THE STUDY OF THE PERIPHERAL INNERVATION OF THE UTERUS.

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Thesis presented for the degree of

Doctor of Science

by

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C O N T E N T S

I. Introduction.

The present investigation was undertaken to throw some light upon the nature of the peripheral nervous mechanism of the uterus. The nervous mechanism of the uterus may be divided into a central and a peripheral part. This peripheral part may be further studied in its extrinsic and intrinsic mechanism.

A. Central Part.

Our knowledge of the nature and mode of action of the nervous mechanism of the uterus is far from complete. Valentin,[142] Brachet,[14] Budge[17] showed that a centre influencing uterine movements existed in the lumbar region. Langley and Anderson[83,86] traced the fibres destined for the uterus and vagina, by way of the splanchnic nerves in the region of the 4th, 5th and 6th lumbar ganglia to the inferior mesenteric ganglia (where some nerve fibres usually form cell-stations) and down the aortic plexus into one or other of the hypogastric nerves, to the more peripheral nerve cells.

Although Langley and Anderson[83,86] demonstrated that the hypogastric plexus (from which fibres pass to the rectum, internal genital organs and bladder) receives branches from the 3rd and 4th sacral nerves, Dale and Laidlaw[26] failed to show any connection between the pelvic nerve and the uterine musculature.[42] Gaskell, weighing up the evidence therefore did

not agree with Basch (6) and Fellner (36), who maintained that motor fibres from the pelvic nerve went to the uterine muscle; but considered that both the motor and inhibitory fibres for the musculature of the uterus arose from nerve cells belonging to the lumbar outflow.

B. Peripheral Part.

It is with the peripheral part of the nervous mechanism of the uterus that the present investigation is concerned.

1. Extrinsic Part.

Peripheral Cell Stations.

The position and relations of the peripheral cell stations and their morphology are imperfectly known. Langley and Anderson (85) described in the cat groups of ganglionic cells in the hypogastric nerve near the cervix, and in the rabbit, similar cell stations at the dorso-lateral border of the vagina. From these they found a ganglionated plexus stretched along the vagina.

So far the arrangement of these in the guineapig, rat, mouse and human subject have not been investigated. In the Transactions of the Royal Society of Edinburgh (38), the following findings of mine as to the distribution of the branches of the hypogastric nerves and the position of the groups of nerve cells on their course are published.

GUINEAPIG.

In the guineapig information was gained from (a) dissections and from (b) the microscopical study of serial transverse sections. By dissection the aortic, inferior mesenteric nerve plexuses and hypogastric nerves were displayed (fig.1). The connections of the hypogastric nerves with the second and third sacral nerves were shown (fig.2). Histological examination confirmed the fact that these strands contain nerve-fibres.

(b) Attempts were made to locate microscopically in the adult guineapig the position of the peripheral nerve-cells on the branches of the hypogastric plexus mentioned by Holste (60) as being in the connective tissue at the level of the cervix. It was found impracticable to prepare serial sections of a block large enough to include the relatively large uterus and sufficient of the broad ligament to include the cervical ganglion. For the reconstructions (fig.3, 4, 5 and 6), therefore, a female foetal guineapig of about 60 days' development was used. The vertebral column and pelvic bones were dissected out, and the pelvic contents embedded in paraffin. Complete serial transverse sections of the genital tract were then prepared, each 10 microns thick. The 2410 transverse sections were numbered from the vagina proximally.

A few sections were stained with haematoxylin and eosin, and the remainder were prepared by a modification of the

methyl-green-pyronin method used by Hynntschak.(171) With this special stain the best results were obtained when the staining in methyl-green-pyronin was continued between two and three hours at 37°C. No better results were obtained by increasing the proportion of pyronin from 0.3 per cent to 0.6 per cent. The sections were very rapidly dehydrated in acetone and absolute alcohol and cleared in xylol. This stain gives the protoplasm of nerve cells a very bright red granular appearance, which is conspicuous beside the faintly stained wall of the uterus. Each cell contains a light blue nucleus with a red-violet nucleolus.

Nerve fibres stain less deeply than do the smooth muscle-fibres of the uterus, bladder and rectum, and the cells forming the coats of the capillary vessels. Bundles of nerve fibres in cross section appear almost unstained and of a glistening appearance.

By means of reconstructions by the graphical and by glass-plate methods the distribution of the branches of the hypogastric nerves and the position of groups of nerve-cells on their course are demonstrated.

Results.

On the hypogastric nerve (fig.3) ganglionic cells are scattered, but are most numerous on that part distal to the level of the junction of the horns. From this latter

part (fig.4) arise the ganglionated branches supplying the uterus, rectum and bladder. No ganglionic cells are found on those parts of their course opposite that part of the uterus proximal to the level of the junction of the horns. The cervical ganglion is not circumscribed and at this stage of development lies close to the uterine artery lateral to the wall of the cervix.

The course of the nerves and arteries cannot be perfectly reproduced from a glass-plate and reconstruction, as in any reproduction; they are foreshortened, and to some extent projected on to the topmost of the series of sections (figs.3, 4, 5). Fig.6 shows by a graphical reconstruction the nerves and arteries passing to the uterus, cervix and vagina. As in the other drawings, the nerve tissue is indicated by very coarse stippling and the position of nerve-cells is indicated by the presence of a small triangle. This diagram demonstrates the widening out of the uterus indicated by the radial shading in fig.4.

RAT.

As in the guineapig, two methods of investigation were used, (a) dissection, (b) the microscopical study of serial sections.

(a) The dissection of the inferior mesenteric plexus and the hypogastric nerves is shown in fig.7.

(b) In the rat, serial longitudinal sections of the genital tract were prepared and stained as described in the guineapig. A reconstruction (figure 8) shows that in the adult rat a large cervical ganglion is present surrounding one of the main branches of the uterine artery and lying within 0.2 mm. (in this rat) from the lateral wall of the cervix.

In a new born rat the circumscribed collection of nerve cells is embedded near the surface of the connective tissue of the cervix (see fig . 9) The nerve cells are multipolar. The greatest diameter of the body of the cell averages .04mm. in length. The nucleus is excentric, oval in shape and measures .02mm.

Besides this large ganglion, scattered groups of cells occur on those portions of the branches of the hypogastric plexus opposite the vagina and the part of the uterus distal to the separation of the two horns.

MOUSE.

No dissection of the hypogastric nerves was made in the mouse, because in a mouse about one week old the sympathetic nerves to the uterus could be traced from the inferior mesenteric ganglia, in a series of transverse sections.

The complete series of 684 sections of about 10μ thickness are numbered from the vaginal end proximally and stained as in the guineapig and rat. From the aortic plexus, lying first anterior to the inferior vena cava and then anterior to the aorta, a ganglionated nerve plexus passes to the intestine along with the tortuous inferior mesenteric artery. Just distal to the bifurcation of the aorta the aortic plexus divides into the hypogastric nerves, which pass downwards and forwards on either side of the rectum. The hypogastric nerve begins to divide to form the hypogastric plexus 1 cm. below the level at which the horns unite, i.e. at the same level at which the cavities of the horn fuse to form one. These branches have nerve cells on their course; but these are restricted to those parts distal to a level about 0.5 cm. below the fusion of the cavities of the horns. The nerve-cells are especially numerous lateral to the vaginal fornix. Here the plexus intertwines with the vaginal branches of the uterine artery, and sends divisions anterior and posterior to the vaginal fornix (fig.10).

The anterior ganglionated strand passes mainly to the bladder, but ganglionated branches also pass to the adjacent vaginal wall. On the branches of the anterior division ganglionic cells cease to be numerous distal to the upper end of the urethra.

The posterior ganglionated division gives off branches accompanying the arteries running down the postero-lateral surface of the vagina. A distinct cervical ganglion is not seen in the mouse; instead there is a ganglionated plexus lying within .02 cm. of the vaginal fornix.

HUMAN SUBJECT.

Körner (75) as early as 1863, and Polle (107) in 1865, were reported by Labhardt (82) to have discovered in the human subject ganglionic cells in the connective tissue around the upper half of the vagina and the cervix. Lee (90), Frankenhäuser (40), Hashimoto (49) and Jung (65) all described a large cervical ganglion lateral to the uterus in the human subject. Jastreboff (63) described the cervical ganglion as consisting of a posterior and an anterior part from which most of the nerves arise. Pissemski (106) and Koch (72) were the first to find numerous ganglia scattered along the branches of the hypogastric plexus at both sides of the cervix. Dahl (24) confirmed this describing single, multi-polar nerve cells on the course of the nerve bundles of the plexus of Frankenhäuser and larger collections at their points of division. The larger ganglia he reported to be subdivided by connective tissue to form collections of nerve cells varying in number. Cordier (23) described two lateral ganglia and one posterior small ganglion. Mabuchi (97) recently described two lateral, two ventral and a dorsal ganglion at the level of the cervix.

The following work of mine on the cervical ganglion in the human subject was published in the Journal of Anatomy (37).

It was considered that valuable information on this subject might be obtained, if the position of the groups of nerve cells was found in a foetus of about 4 months, when the internal

genital organs are sufficiently small to permit a complete series of sections being made. Only in a specimen from a young foetus, can sufficient of the broad ligament be included in the sections to permit the localisation of these ganglia.

The specimen was obtained from a patient who died somewhat suddenly from Hyperemesis Gravidarum. The autopsy was carried out less than 12 hours after death. The contents of the pelvis were removed intact. The uterus was then opened, and the foetus extracted. The foetus looked quite fresh, no signs of maceration being evident. From vertex to breech it measured 15 cm. The pelvic bones and lower part of the vertebral column were dissected out carefully, and without damage to the contents of the foetal pelvis. The peritoneal cavity was then opened from in front, and the foetus divided across a short distance proximal to the internal genital organs. Unnecessary portions of the anterior abdominal wall and of the muscles of the back were then removed, leaving as complete a block as possible of the organs within the lower abdomen and pelvis. This block was fixed in Kaiserling's formalin solution, and a complete series of 2872 paraffin sections each 10 microns thick was prepared. These are numbered from the cranial extremity backwards.

With the exception of a few reserved for special stain-

ing methods, the sections were stained with haematoxylin and eosin. Microscopically the preservation is good.

While the unsectioned block was in xylol, the vessels and other structures showed up so beautifully that a freehand drawing was made of the upper part of the specimen at this stage (fig.11). The block includes the rectum posteriorly, the bladder anteriorly (portions only of the ureter being distinct on either side), and between these the genital organs. The ovaries are shaped like bay leaves, lying with their long axes horizontal. They lie proximal to and immediately above the Fallopian tubes. They extend from just within the up-turned lateral end of the tube to a short distance medial to the opening of the tube into that portion of the uterus which will form the future body. The anterior surface, as indicated in the drawing, is not smooth, but shows a horizontal groove, from which side branches run as shallow sulci towards the proximal and distal borders. The tube on either side passes out from the uterus to terminate in a curve around the lateral extremity of the ovary. In its course it is thrown into small rounded curves encountered in all planes. Relative to its length, the duct is narrower than is the adult Fallopian tube.

The drawing shows that the utero-vaginal tube consists of a long cylindrical portion a little narrower than the

rectum surmounted by a short broader part which widens out proximally, and which laterally is continued into the tubes. On the cranial extremity of the upper portion a shallow medial sulcus is seen, but no evidence of the presence of a sulcus is found on the anterior surface. There is no indication on the external surface whether the line of demarcation between the distal narrow and the proximal wide portion corresponds to the dividing line between the future body and the cervix, or between the cervix and the vagina.

The blood vessels show up particularly well. On the right-hand side, the loose tissue in which they lie had been slightly damaged during the manipulations of the block, and as a result the proximal portions of the vessels were displaced outwards. For this reason, their course is not shown in the drawing.

To show the stage of development the genital tract has reached a detailed description of the genital tract including the remnants of the Wolffian System and junctional tubules is given before describing the distribution of the branches of the hypogastric nerve to it.

The Internal Genital Organs of a Female Foetus of 15 cm.Length.

A flat reconstruction of the genital tract (fig.12) shows its outline, the lumen being indicated by a dotted line. Remnants of Gärtner's ducts, in those parts of their course near

the utero-vaginal canal and to the tubal portion of the uterus, e seen. The tubes are long and narrow, and show the multiple rves already mentioned, but naturally only those apparent in ie plane. The free end of the tube has a fimbriated extremity. s opening faces posteriorly. From the margins of the opening rands of connective tissue are continued laterally in the edge the mesosalpinx and also towards the ovary. At the other end, ie tubes enlarge to form the tubal portion of the body of the terus. In the reconstruction, the sulcus on the cranial extremity the uterus at this stage of development is 0.4 mm. deep.

There is no median septum in the cavity. The formation of single roughly symmetrical uterine cavity has kept pace with the ion of the tubes to form the tubal portion of the body of the terus. The unpaired portion of the generative tract is at this tage divisible into three portions. (1) The most proximal part s somewhat triangular in form, its base forming the future fundus f the uterus. (2) A cylindrical portion with thicker walls and narrower cavity. (3) A long portion narrower in its proximal han in its distal half and possessing a relatively thin wall. he opening of this portion into the uro-genital sinus is still losed by a solid mass of tissue. No sharp line of demarcation s present between these three portions. In length their cavities easure approximately 1.4 mm., 2.8 mm., and 5.6 mm. respectively. Diagrams illustrating the contour of a section from each of these

to the utero-vaginal canal and to the tubal portion of the uterus, are seen. The tubes are long and narrow, and show the multiple curves already mentioned, but naturally only those apparent in one plane. The free end of the tube has a fimbriated extremity. Its opening faces posteriorly. From the margins of the opening strands of connective tissue are continued laterally in the edge of the mesosalpinx and also towards the ovary. At the other end, the tubes enlarge to form the tubal portion of the body of the uterus. In the reconstruction, the sulcus on the cranial extremity of the uterus at this stage of development is 0.4 mm. deep.

There is no median septum in the cavity. The formation of a single roughly symmetrical uterine cavity has kept pace with the union of the tubes to form the tubal portion of the body of the uterus. The unpaired portion of the generative tract is at this stage divisible into three portions. (1) The most proximal part is somewhat triangular in form, its base forming the future fundus of the uterus. (2) A cylindrical portion with thicker walls and a narrower cavity. (3) A long portion narrower in its proximal than in its distal half and possessing a relatively thin wall. The opening of this portion into the uro-genital sinus is still closed by a solid mass of tissue. No sharp line of demarcation is present between these three portions. In length their cavities measure approximately 1.4 mm., 2.8 mm., and 5.6 mm. respectively. Diagrams illustrating the contour of a section from each of these

three portions are seen in fig.13. The region of the transition between the triangular proximal portion and the remainder is marked externally by the entrance of the ducts of Gärtner into the uterine substance. This is therefore probably the dividing line between that portion of the uterine mucous membrane developed from the uterine portion of the tubes and that developed from the utero-vaginal canal. These three portions are taken to correspond with the body of the uterus, cervix and vagina respectively, and later, histological evidence in support of this is given.

The Fallopian Tubes. From the reconstruction the tubes differ somewhat in measurement. That on the right is 1.12 cm. in length and varies in breadth from 0.02 to 0.08 cm.; the fimbriated extremity makes up 0.14 cm. of its length. The corresponding measurements on the left are 0.92 cm., 0.02 to 0.04 cm. and 0.14 cm. Both tubes pass outwards until opposite the lateral extremity of the ovary they curve upwards and finally terminate by a distinct inclination backwards, thus ending behind the ovary. Each tube possesses a canal patent throughout its entire length. The lining epithelium consists of cells whose protoplasm stains deeply. The nuclei are oval, intensely stained and large relative to the size of the cells. In places the epithelium is in the form of a single layer which is definitely columnar in parts. In places no epithelium is

recognisable because the walls of the tube are almost in apposition; but a potential lumen is always apparent.

The lumen in its simplest form in cross-section has the appearance of a four-rayed star. In this specimen the two ventral and the two dorsal folds producing this formation are not (as described by Felix in Keibel and Mall (169) in a 50 mm. head-foot length embryo) due almost entirely to difference in height of epithelium, but at this stage are formed of embryonic connective tissue. Towards the outer end of the tube, besides these primary folds, there are secondary ones varying in size and shape.

Regarding the remainder of the wall of the tube, the two coats are distinct which Felix (169) describes in a foetus of 80 mm. trunk length. In my specimen, however, they are approximately equal in thickness. Muscle fibres in the adult sense cannot be recognised. Both coats are well vascularised. The inner has irregularly arranged cells with faintly stained protoplasm and oval deeply stained nuclei. The spindle cells of the outer coat form circular layers. The two coats become ill-defined as they are traced towards the outer end of the tube. The inner coat I regard as the forerunner of the stroma of the mucosa and the outer band as destined to form the muscular layer. This is in agreement with Felix (169) and, in the case of

(164)
the outer band, with Bryce, who, however, makes no statement as to the fate of the inner coat.

The tissue of the entire tube is not sharply demarcated from that of the broad ligament. In the boundary zone between run the main vessels of supply to the tube. Near this, the layers, recognisable as serous and subserous by Felix, cannot be made out.

Caudal to the mesovarium the common urogenital mesentery passes forwards and distally to fuse with the connective tissue surrounding the inner end of the tube. Its point of attachment is about 2 mm. lateral to the median sulcus on the cranial aspect of the body of the uterus. The future body will therefore come to include the inner 1 mm. of the present Fallopian tube.

The Body of the Uterus. Regarding that part of the uterus proximal to the level at which the ducts of Gärtner enter, we find that the anterior and posterior walls are relatively thick. The walls are formed by a continuation of the two coats already described in the wall of the tube. At this level they become widely separated by a third zone which makes up a considerable thickness of the wall. In this, densely packed clusters of cells are found. The nuclei of the cells of this zone are directed for the most part at right angles to the cavity of

the uterus. Into this zone strands of cells turn inwards from the outer circular zone. The presence of these strands suggests that this middle zone represents part of the muscular coat of the fully formed uterus. No sharp demarcation exists between these three portions of the uterine wall. No fully formed smooth muscle bundles are present, but the nearest approach to this is found in the circular zone. Nagel (178) found smooth muscle arranged in bundles in embryos of 15-22 cm. length. This muscle appeared first under the peritoneal coat.

The cavity enclosed by these walls forms in transverse section a narrow wavy slit as the anterior and posterior uterine walls are for the most part in apposition. The epithelial lining is similar to that in the tube, although again it is absent in places.

The Cervix. This part, besides being marked off by the relative uniformity of the width of its cavity and by the width of its lateral walls (fig.13 B), differs from the body in some details. This portion, instead of forming an oval in transverse section, is almost circular. The arrangement of the cells of the middle layer of the wall is more irregular than in the body. The increase in depth of the wall of this part is due to an increase in the outer two layers of the wall, i.e. in those layers which will go to form the muscular

coat of the cervix.

The epithelium lining the cervix is similar in appearance to that present in the tube and body of the uterus, and here also at certain levels is absent. In the middle line into the upper part of the cervical canal there is a longitudinal bulging of the anterior wall. Opposite this prominence there is a longitudinal groove in the posterior wall. This prominence represents possibly the first commencement of the arbor vitae. No evidence is found in this specimen of the secondary folds of mucous membrane, which are described by Felix (169) as arising from the base of depressions in the wall of the cervix in embryos of about 150 mm. The lower end of the cavity of the cervix forms a narrow transverse slit.

The Vagina. Distal to this portion having a narrow slit-like lumen, there is a sudden widening of the genital canal, and a thinning of the walls (fig. 14C). This foetus resembles those described by both Van Eckeren (161) and Mihalkovicz (177). These observers considered that this dilatation was the first sign of division into vagina and uterus. Van Eckeren (161) described it as occurring in the second half of the fourth month. Mihalkovicz (177) found a slight dilatation below the position of the external os, even in an embryo 14 cm. long. On the other hand, Nagel (178) described the first beginning of formation of the portio as an ingrowth of the cubical epithelium into

the hind wall. He found this in an embryo of 12 cm. length, but in one of 14-15 cm. trunk length it did not occur. This is an example of the variation in time at which the portio develops. Other observers bring evidence in support of this variation. (165) Dohrn described the anterior lip in embryos of 15-16 weeks as a half-moon-shaped prominence on the anterior wall of the genital tract. (183) Tourneux and Legay described embryos of 12.5 and 16 cm. trunk length in which the portio is present, whereas in one of 20 cm. trunk length he found only the anterior lip. (170) Geibel found the formation of the posterior fornix occurring only in the 6th month, no anterior fornix even then being present.

Just as in the more proximal portions of the genital tract, in this specimen the cavity is lined by epithelium, but at various levels it is absent. The epithelium is stratified and non-vesicular. The nuclei of the cells are oval and small relative to the size of the cell and are rich in chromatin. It may now be noted that the character of the epithelium has been of no value in locating the exact limits of the different regions of the tract.

The structure of the remainder of the wall of the vagina differs from that of the uterus. At the junction of the cervix and vagina the circular layer described in the cervix becomes very thin. Traced distally it soon disappears as a distinct

layer. Otherwise the wall is formed of cells arranged irregularly, although the majority of them run longitudinally, especially in its proximal portion. About 2 mm. from the distal end of the vagina, the urethra becomes intimately associated with the anterior wall, so that the one mass of tissue appears to embrace both structures. The vagina tapers down to end in a short solid portion. Gland-like projections of the epithelium of the urogenital sinus pass into this. This distal solid portion of the vagina, for the length of about 1 mm., is enveloped in a band of tissue, like that of the wall of the urethra. The cells of this tissue stain more deeply with eosin than do those of the wall of the vagina.

That portion of the wall intervening between the distal end of the vagina and the cavity of the urethra is made up of interwoven bundles of cells. In the distal 2 mm. of this are embedded branching tubules communicating with the urethral canal and lined by epithelium similar to its epithelium. These tubules I regard as representing the prostate gland in the male, which agrees with the finding of Evatt (168) from the examination of a 3½ months old female foetus, and of Keibel (172) who found the openings of these glands similarly situated. On the other hand, Evatt (168) quotes Gustav Pallin (180) as having found their ducts opening neither into the urethra nor into the vagina, but exactly at the boundary between the two. Around these tubules,

in my specimen, spindle-shaped cells are arranged concentrically. In the antero-lateral wall of the urethra only one tubule is seen and it does not penetrate far into the wall of the urethra. The wall of the urethra is thickly beset with minute venous spaces, especially in its antero-lateral aspect.

The Remnants of the Wolffian System and Junctional Tubules.

A. In the mesosalpinx, hilum of the ovary, and common urogenital mesentery, there is on either side a number of tubular structures. They lie proximal to the horizontal part of the tube and posterior to the ovary.

The majority of the tubules are clustered together to form the epoöphoron which lies lateral to the mesovarium. Opposite and medial to the mesovarium, scattered tubules are found. The tubules are sinuous in their course. Each is cylindrical, lined with a single layer of cubical epithelium placed upon a basement membrane. The nuclei are large and deeply stained. The epithelial tube is surrounded by a condensation of primitive connective tissue cells. There is an inner coat longitudinal in arrangement and an outer ill-defined coat of circularly arranged cells. One of the more lateral of the tubules is distinguished by its larger lumen and by its thicker connective tissue wall. This is

the remnant of the Wolffian duct. It runs more or less parallel to the lateral portion of the Fallopian tube. No muscle cells are seen either in the walls of the Wolffian tubules or of the duct.

Two other types of tubules are found:

(a) The first is a group of tubules lined by cubical epithelial cells with deeply stained nuclei. Each is surrounded by a very thin connective tissue coat, the cells of which are arranged circularly. The tubules differ from those of the epoöphoron in having no well-defined longitudinal connective tissue coat. They lie medial and posterior to the ovarian artery in the common urogenital mesentery where it is reflected on to the posterior abdominal wall just lateral to the ureter. In this specimen they are better developed on the right than on the left side. One of the tubules is distended with epithelial débris, its contents staining deeply with eosin. The distended part is 0.12 mm. in length. Some of these tubules are replaced by solid cords of cells. No blood vessels are seen in these cell-clusters. The difference between this connective tissue wall and that of the tubules of the epoöphoron may result from a difference in their stage of retrogression. Whether these more medial tubules represent paroöphoron cannot be judged from the study of an isolated specimen. Duthie (167) failed to demonstrate the paroöphoron in all 20

specimens examined. Felix (169) quotes Waldeyer (184) as having described it in a position cranial to the medial pole of the ovary and Rielander (182) in older foetuses and children caudal to the lateral half of the ovary. In my specimen these tubules lie cranial to the hilum of the ovary.

(b) The second type occurs in the region of the ovarian fimbria. Each tube ends blindly and has a cavity irregular in outline. Three are present on the right side, one being in the hilum of the ovary and the other two nearer the tube. The one on the left side lies in an isolated projection from the posterior surface of the ovarian fimbria. No connection can be made out between them and the Wolffian duct and tubules. Each is lined with low cuboidal epithelial cells and is surrounded by a very thin condensation of connective tissue cells arranged circularly.

No smooth muscle fibres are seen in their walls. Duthie (167) describes similar spaces in a human foetus of the 8th month. They probably correspond to the rete or junctional tubules of Allen. (162) If they are rete or junctional tubules, the tissue in which they lie must be ovarian or hilum tissue which has made its way up the ovarian fimbria. Keith (174) and Doran describe the ovarian tissue as running some way up

the ovarian fimbria in a human foetus of the 8th month and in the new-born child. The facts that no connection can be made between any of them and the lateral end of the Wolffian duct and that their walls differ markedly from that of the Wolffian duct are against their being remnants of the pronephric duct.

B. Within and near the lower portion of the genital tract are remnants of Gärtner's duct. (176) Meyer found such remnants of Gärtner's duct in the uterus in all specimens at the stage of 2-3 months' development, but only in 28.5 per cent. of specimens aged 4-6 months. On both sides (fig.12) portions of Gärtner's duct are seen. On neither side can a connection be traced between these and the other remains of the Wolffian system in the lateral parts of the mesosalpinx. At their proximal end both appear as an ill-defined condensation of the connective tissue of the broad ligament. The duct on the right side begins at section 880 and can be traced down to section 1235. It lies about 0.4mm lateral to the wall of the uterus, surrounded by tortuous veins and just posterior to one of the branches of the uterine artery. Passing distally, it approaches the uterine wall. As it does so, its tissues become differentiated into an outer condensed and an inner loose zone. About 1 mm. from its commencement this central loose zone is replaced by

the cavity of the duct, which is lined by a layer of deeply staining cubical epithelium. The cells of the outer condensed zone are arranged concentrically. Peripheral to this latter zone, no distinct layer of longitudinally arranged cells, such as was found by Meyer (176), can be made out in this specimen. The duct becomes closely applied to, and eventually enters the wall of the genital tract, where the thin lateral wall of the future body thickens out to form the wall of the future cervix. As the duct is traced distally within the wall, its lumen enlarges antero-posteriorly and the epithelial lining assumes a columnar form. Its condensed band of connective tissue remains distinct from the tissue surrounding it, not only because of the concentric arrangement of its cells, but also because of their smaller size. As it passes down the cervical wall its cells become less regular in arrangement, so that it is less sharply marked off from the surrounding tissues. It passes gradually more deeply into the wall, until near its termination it lies completely within the circular layer and bulging the deeper layers inwards. It ceases to be recognised about 0.04 mm. above the proximal end of the future vagina. This remnant in this part of its course is 3.5 mm. long.

On the left side the duct is much shorter. It appears first in section 862, lying in close apposition to the

uterine artery about 3 mm. lateral to the wall of the uterus. As in the case of the right duct, no connection with the other vestigial structures in the broad ligament is established. As it is traced distally, it has the form of a poorly demarcated collection of cells with deeply stained rounded nuclei. A concentric arrangement of cells is only seen (fig.13A) opposite the minute epithelial lined cavity 0.02 mm. long. The duct cannot be traced beyond section 968, where it merges with the wall of the utero-vaginal canal. The left portion of the duct of Gärtner thus measures only 1 mm. in this part of its course.

On neither side is there any trace of Gärtner's duct in the walls of the proximal half of the vagina. In the distal half on the right side two portions of the duct are found, the proximal one, 0.1 mm. in length, possessing a lumen lined by columnar cells, and the distal, 0.04 mm. in length, having only a solid epithelial core. Both are placed in the antero-lateral wall of the vagina, but their position in the length of the vagina is represented in fig.13. Between these two portions traces of the wall of the duct can be seen. On the left side the three portions, 0.04, 0.03, 0.02 mm. in length respectively, each possess a lumen lined by epithelium. On neither side are any remnants found at the distal extremity of the wall of the vagina, and no communication is established

between the portions of the duct present and the glands opening dorsally from the urethra (cf. Kocks (175) and Böhm (163)). In this specimen, just as in those described by Rieder (181) and by Dohrn (166), the duct of Gärtner has been retained more upon the right side than upon the left.

Sympathetic Nerve Distribution. Of this specimen a graphical reconstruction (fig.14) has been made to show the branches of the hypogastric nerve to the uterus and the position of the groups of ganglionic cells on these branches. The series of sections extended to the inferior mesenteric ganglia, from which bundles of nerve fibres pass to the intestine along with the inferior mesenteric artery. A median plexus of nerve fibres runs distally anterior to the aorta. The last-named (fig.14) divides about 2 mm. distal to the fundus of the uterus, to form the hypogastric nerves, along the course of which ganglionic nerve cells are scattered. They are most numerous opposite the cervix in those parts from which the branches supplying the uterus and tubes arise. The hypogastric nerves lie about 0.2 mm. lateral to the wall of the uterus.

On the course of the most proximal of the branches of the hypogastric nerve is a mass of ganglionic cells. This branch passes upwards and anteriorly, giving off a transverse branch

to the cervix. Continuing its course it divides into two branches which run to the cervix at the level of the future internal os. From these transverse branches bundles of nerve fibres run upwards, to supply the upper part of the body of the uterus and the tubes. From the more lateral of these divisions a small branch is given off which passes into the hilum of the ovary. The original two branches, running to the uterus at the level of the internal os, communicated with the more distal branches of the main hypogastric nerve by lateral communicating unions in the broad ligament, which lie within 0.1 mm. from the wall of the cervix. The more lateral of these two lies behind the other.

Coming back now to the first branch of the hypogastric nerve mentioned above, about 0.5 mm. distal to it a second ganglionated branch runs transversely towards the cervix, and, as described, communicates with the branches already distributed to the uterus. This particular nerve shows two branches, one of which terminated at the middle of the cervix, and the other at the internal os. Another main branch is given off the hypogastric about 0.6 mm. distal to and communicating with this second branch. This branch comes off below the level of the peritoneal reflexion posteriorly. It supplies the lower part of the cervix, and sends a large branch laterally anterior to the ureter. This latter subdivision has

ganglionic cells upon its course and distributes branches to the bladder. Further distally two other branches of the hypogastric, supplying the lower end of the cervix, can be traced to the wall of the cervix. Excluding the first branch of the hypogastric, the communicating branches of which have been described, the remaining branches communicate with one another in an irregular manner.

It was found impossible to trace out the more distal branches supplying the vagina, as they are in such intimate association with the branches both to the rectum and to the urethra and bladder. The connections between the hypogastric plexus and the spinal nerves were necessarily destroyed during the removal of the vertebral column. In this specimen, therefore, the ganglionic cells are not confined to form a single cervical ganglion, but are scattered along the divisions of the hypogastric plexus in the region of the cervix. The scattered nature of Frankenhauser's cervical ganglion has since been confirmed by Naiditsch (154) in the adult human uterus.

Besides the groups of nerve cells on the branches of the hypogastric plexus opposite the cervix, ganglia are found in the human uterus close to the myometrium and in the superficial layers of the muscle. In Fig.15 a group of nerve cells

is seen in a section of the myometrium from which the utero-vesical reflexion of peritoneum has been stripped off in performing hysterectomy. Such groups of nerve cells I have found only on the course of the nerve bundles in the region of the cervix below the level of the reflexion of the peritoneum on to the bladder anteriorly and on to the rectum posteriorly.

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(2) INTRINSIC PART.

Intra-uterine Nerves.

Although intra-uterine nerves have been described by (71) Kilian, (20) Chroback, (104) Landowsky and Owsganikoff, (104) Rasumowsky, (109) Bordé, (13) Schenk, (120) Stoehr, (135) Herlitzka, (56) Patenko, (105) our knowledge of their morphology is very slight.

One point on which there is still a difference of opinion is as to whether within the uterine substance medullated nerve fibres occur and if so how far they penetrate the wall before loosing their myelin sheath.

Kilian (71), Herlitzka (56), Labhardt (82), Mabuchi (97) and Dahl (25) found both medullated and non-medullated nerve fibres.

According to Kilian (71) the medullated fibres do not pass far into the uterine substance in the non-pregnant animal before loosing their sheath. In the cervix of the pregnant animal Kilian (71) and Remak (113) considered that the fibres retain their myelin sheath.

Labhardt (82) and Dahl (24) agreed with Kilian (71) as they only saw medullated fibres within the thick nerve bundles.

Herlitzka (56) and Hoogkamer (61) however found their medullated fibres not only running in bundles but also singly, Hoogkamer (61) describing the loss of the sheath, as occurring near the end arborisations in the mucous membrane. Patenko (105) and Keiffer (70) however failed to find medullated nerve fibres within the uterine substance.

Controversy exists also with regard to the course of the nerves within the uterus. All agree that the larger nerve bundles and to a less extent the smaller nerve bundles and single nerve fibres have an undulating course throughout the uterine muscle. Difference of opinion is shown as to the degrees to which the course of the nerves follows that of the blood vessels. Kalischer (67), Keiffer (70), Kölliker (74) described the nerve bundles and even the finest nerve fibres as following the course of the blood vessels.

Labhardt (82), Dahl (25), Mabuchi (97) and Stöhr (135) although agreeing that the nerves are most numerous near the blood vessels, showed that the narrower nerve bundles rather follow the course of the muscle fasciculi running parallel with them and that the finest non-medullated nerve bundles run mostly parallel to the individual muscle fibres.

Little is known as to the mode of ending of the non-medullated nerve fibres within the uterus.

Rasumowski (109), Bordé (13), Kalischer (67), Herlitzka (56), Labhardt (82) were unable to demonstrate nerve endings in the muscle cells.

Gawronsky (44), Köstlin (76) and Mabuchi (97) described the fine non-medullated fibres as ending in knobs. Dahl (24) found treelike endings with small buttons at the tips of the branches.

Hoogkamer (61) reported the nerve fibres as ending near the muscle cell but never intra-cellularly. Stöhr (135) stated that the nerve

fibres end in a small fibrillar network within the muscle cell.

No satisfactory reproductions of these endings in relation to the muscle cells are, however, published in the available literature.

In the mucous membrane Patenko (105) was the first to describe around the glands a meshwork of non-medullated nerve fibres from which fibres go to the glandular epithelium. Clivio, (21) Hoogkamer, (61) Gawronsky, (44) Köstlin, (76) Herlitzka, (56) Keiffer (70) and Acconci (1) all took the network found by them in the mucous membrane to be nervous in origin. Although Labhardt, (82) Mabuchi, (97) Dahl (24) and Stöhr (135) were able to trace non-medullated fibres, either as single fibres or finest bundles, up to the mucous membrane they were unable to see any within the mucous membrane. So far I also have been unable to demonstrate nerve fibres within the mucous membrane.

Intra-uterine Nerve Cells.

The most interesting question with regard to the intrinsic innervation of the uterus is as to the presence of nerve cells within the uterine substance.

Clinical and experimental evidence shows that the uterus can act independently of the central nervous system. Simpson (126) working on the pig was the first to show that spontaneous birth could occur after destruction of the lumbar and dorsal regions of the cord. Riemann (116) in the same year confirmed this observation in a cat, after destruction of the cord from the third dorsal vertebra downwards. A few years later Goltz (46) observed that conception, placentation, and spontaneous birth could occur in a dog after section of the cord at the level of the first lumbar segment. In dogs after the nerves to the uterus were cut and time allowed for their degeneration Kabierski (66) and Heidenhain (66) and Masius (98) observed normal birth occurring.

Rein (111) at about the same time showed that the removal of the cervical ganglia in addition to section of the nerves to the uterus did not prevent a dog from giving birth to a litter. Kurdinowsky (80) found that birth occurred from a rabbit's uterus even after its extirpation late in pregnancy.

The successful completion of parturition thus depends on the functioning of the intrinsic nerve mechanism of the

uterus or of the muscle cells themselves or of both. In a paper published in the Transactions of the Royal Society of Edinburgh,(38) I recorded a series of experiments upon the rat and guineapig comparing the action of the uterine horns connected and not connected with the cervical ganglion. The absence of any effect on removal of the ganglion and the absence of any difference in the response of the uterus with and without the ganglion to various chemical substances seem to indicate that the ganglion does not exercise a direct influence in controlling the tone and movements of the excised uterus.

Later I described in the Journal of Obstetrics and Gynaecology of the British Empire(39) a series of pharmacological experiments, which indicate that in or upon the uterine wall there is some arrangement for the control of tone and movement probably distributed at three levels:- (a) a proximal (b) an intermediate, and (c) a peripheral. In spite therefore of the record of the repeated failures of former workers one is very unwilling to believe that in this all-important intrinsic nerve mechanism no nerve cells exist.

The following authors agree that no nerve cells are to be found in the uterine muscle - Remak,(113) Kilian,(71) Körner,(75) Luschka,(96) Polle,(107) Röhrig,(117) Kalischer,(67) Clivio,(21) Köstlin,(76) Herlitzka,(56) Kölliker,(74) Bruckner and Mezinescu,(16) Ogata,(101) Labhardt,(82) Mabuchi,(97) Dahl,(25) Sobotta,(127) and Stöhr.(135)

As early as 1864 Spiegelberg,(129) and a few years later Lindgren(94) found cells in the muscle and mucosa of the uterus which they took to be small nerve cells. Krause(77) described

microscopic round or oval ganglia on the smaller nerve bundles. (I have been unable to consult the original communications to examine any reproductions given of these nerve cells.) (44) Gawronsky described cells scattered through the muscle of the uterus of the guineapig, mouse, sheep and dog. Their form he reported to vary very much. Sometimes they were elongated in form and from their ends the processes arose. These processes then divided up into numerous finer processes.

Sometimes they were multipolar cells with numerous processes of varying calibre passing out from all sides of the cell. Such cells he found interpolated on the nerves before they reached the mucous membrane. Some of the processes of these cells entered the mucous membrane and were seen to end freely in the epithelium as knobs.

No Camera Lucida Reproductions or photographs are however given of these interesting cells.

Köstlin (76) described cells in the uterine muscle of the rabbit, guineapig, calf and sheep, calling them "Sternzellen", "Gabelzellen" and "Fadenzellen", but regarding them as not nervous in nature as no connection could be seen between them and the nerve fibres. (128) Again using the Golgi method Spampani reported that in the nerve network there were polygonal formations present which resembled nerve cells of the central

nervous system.

On the principal nerves ploughing all parts of the uterus Keiffer found small ganglia, cylindrical, fusiform, spherical or oval in shape. In these ganglia the cells were either round and small or larger and round with a more globular nucleus or less circular cells sending out prolongations in one or more directions (some of which were continuous with an axis cylinder).

Besides these ganglia he found isolated nerve cells and groups of nerve cells especially in the angular spaces - limited by several bundles of muscle.

(140)
La Torre described but gave no illustrations of nerve cells in the subperitoneal tissue and in other muscle layers of dogs.

(82)
Labhardt found no cells connected with nerve fibres. He took the elongated cells, with one or two more or less elongated but - relative to nerve fibres - short and thick processes, as muscle cells. His illustrations would lead one to agree that the cells in question are of the nature of connective tissue.

(161)
Hoogkamer using Supra-vital methylene blue method found three kinds of cells which he accepts as nerve cells.

(1) Small bipolar nerve cells on the course of the smallest nerves throughout the uterus. Their two processes run in the long axis of the nerve; they are never gathered together to form ganglia; they stain violet and have a large nucleus and

a scanty amount of protoplasm. These bipolar cells he found both in the human uterus and in that of lower animals. From this description and his Fig.5 I judge that the cells correspond to the cells taken by me to be cells of Schwann.

(2) Large, round, often unipolar, cells in the course of the larger bundles. These cells are always gathered together to form larger or smaller ganglia surrounded by a connective tissue capsule. They occur in the subperitoneal muscle. Each has a large vesicular nucleus and rarely two such nuclei are present. The ganglia are egg-shaped, spindle-shaped or circular, and less frequently elongated when lying in the course of a nerve running between the muscle layers. These ganglia resemble those occurring in the Broad Ligament and such ganglia contain from five to sixty nerve cells.

In these ganglia he also found the third type of nerve cell.

(3) The multipolar nerve cell with processes ten to twenty times as long as the cells. These cells occur in smaller groups especially around the smaller blood vessels and in the mucous membrane; and the larger groups, with longer processes around the larger vessels and irregular groups, are met with near the peritoneal surface. In the photographs of these cells no connections are shown with nerve fibres, the photographs of both these types of cells being indistinct.

The cells described by Rasumowski[109] in the mucous membrane and by Bruckner and Mezinescu[16] in the mucous membrane appear to be histiocytes rather than nerve cells.

Technique.

In this investigation I have succeeded in demonstrating intrauterine nerves by use of the following three methods:

(1) A Gold impregnation method as modified by Gairns, laboratory assistant in the Institute of Physiology, Glasgow University.

(2) the Gros modification of the Bielschowsky method; kindly demonstrated to me in Professor Boeke's laboratory at Utrecht;

(3) The intra-vitam methylene blue method.

Because of the well recognized fickleness of all methods of staining nerve tissue it might be well to describe in detail the exact method used.

I. Gold Impregnation Method of Gairns.

(a) Small portions of fresh tissue not exceeding 2mms. by 5 mms. by 4 mms. were allowed to remain in a solution composed of 3 parts of filtered fresh lemon juice and 1 part of Formic acid for 10 minutes in absolute darkness.

(b) The tissue was quickly but gently dried between sheets of blotting paper.

(c) Then it was passed into a 1 per cent Gold chloride solution and kept there for 12 minutes in absolute darkness.

(d) The tissue was then quickly dried as above.

(e) Then it was left for 24 hours in the darkness at room temperature (60° Fahrenheit) in 25 per cent Formic acid, and thereafter stored in glycerine.

and thereafter stored in glycerine.

I found it of importance to observe the following rules. (1) to keep the tissue in absolute darkness while in all the solutions:

(2) to use only enough fluid to cover the tissues;

(3) to make up all the solutions in distilled water;

(4) to use perfectly clean bottles and non-metallic or waxed forceps.

II. Gros Modification of Bielschowsky's Method.

(a) The tissue was fixed in 10 per cent neutralised Formalin for 24 hours. This fixative was prepared by adding to 10 parts of the 40 per cent Formaldehyde and 90 parts of water an excess of Magnesium Carbonate and filtering off the sediment.

(b) Frozen sections were prepared and received into glass-distilled water. A section was lifted with a glass rod into

(c) a 20 per cent silver nitrate solution and kept there in the dark for 3-5 minutes,

(d) Then it was passed through a series of glass vessels containing 20 per cent Formalin. Whenever white clouds appeared around the section it was at once removed with a glass rod and placed in the next vessel of 20 per cent Formalin. Ten changes were usually needed before the clouds ceased to form.

(e) A solution had been freshly prepared by adding 25 per cent Liq. Ammon. Caust, drop by drop to 10 cc. of a 20 per cent

silver nitrate solution until the brown precipitate which formed had again disappeared.

The section was placed in half a watchglassful of this solution to which had been added 2 drops of Liquor. Ammon. Caust. 25 per cent. Staining in this was controlled under the microscope.

(The structures stained depends on the amount of Liq. Ammon. Caust. 25 per cent added/and on the length of time the section is kept in the solution.)

(f) The section was washed for 1 minute in a solution composed of 2 parts of Liq. Ammon. Caust. 25 per cent and 8 parts of glass distilled water.

(g) Then it was washed in glass distilled water to which a few drops of acetic acid had been added.

(h) Then it was washed in Gold chloride solution 1/10 per cent until the colour changed to violet,

(i) and fixed in 5 per cent sodium hyposulphite for 1 minute.

(k) Then it was washed in glass distilled water for 15 minutes.

(L) Counterstained with carmalum for 2 minutes and mounted in laevulose.

III. Intra-Vitam Methylene Blue Method.

(a) The animal was killed with coal gas and then 150 ccs. of normal saline solution at 37°C. were injected into the

abdominal aorta under pressure.

(b) This was followed by the injection of 3 per cent Ehrlichs Methylene Blue Grüblers in saline under pressure.

(c) The uterus was removed from the body after 10-15 minutes.

(d) Small portions of the tissue were then exposed to the air for about 40 minutes on glass wool at 37°C. keeping them moist with 1/15 per cent methylene blue in saline and controlling length of the exposure under the microscope.

(e) The tissue was fixed in Ammonium Molybdate 8 per cent - prepared with glass distilled water - in the refrigerator for 12-15 hours. (No better results were obtained by adding a drop of 1 per cent osmic acid to this solution).

(f) It was washed for 2 hours in running water and in some instances frozen sections were prepared.

(g) The tissue was then dehydrated as quickly as possible in 90 per cent and afterwards in absolute alcohol.

(h) It was stored in Benzyl Benzoate or cleared in xylol and mounted in Canada Balsam. In the case of the human uterus the first step was of course omitted. The best results were obtained when it was placed immediately on removal into 1/10 per cent methylene blue at 37°C. and kept there for about 1 hour, an attempt being made to inject the methylene blue solution into the uterine vessels. Thin superficial portions were then cut

off and carried through as in (d) to (h) in the above description. The lower animals used were the cat, mouse, guineapig, rat, and rabbit. All three methods described I found extremely uncertain. The best results were obtained in the lower animals when the intra-vitam methylene blue was used.

The following other methods and various modifications of them were tried but with less success on account of the fact that the connective tissue was partially impregnated in addition to certain of the nerve elements - Donaggio's (31) Pyridine method, Cajals' (90) method, Guyer's (48) method, Golgi's (90) method, Ranson's (108) Silver Pyridine (119) method, Sand's method, Faworski's (35) method, Da Fano's (34) method, Agduhr's (3) method.

NERVE BUNDLES.

The coarse nerve bundles enter the uterus accompanying the arteries. Often, but not always, one sees thick nerve stems following the blood vessels. As the nerve bundles subdivide they adhere less and less to the course of the blood vessels. (Fig. 16). The narrower nerve bundles rather follow the course of the muscle fasciculi running parallel with them. (Fig. 17). The finest non-medullated nerve bundles run mostly parallel to the individual muscle cells.

The nerve bundles have an undulating course throughout the uterine muscle. (Fig. 20). Within the coarser bundles the individual nerve fibres run in a tortuous fashion, and the bundle may appear straighter in its course than does a fine nerve bundle - in which each curve of the individual constituent nerve fibres is more apparent. Each nerve bundle is connected up with neighbouring nerve bundles by a constant interchange of their component nerve fibres. Such interchanges are seen in (Fig.18&28). The nerve bundles as a rule divide in a dichotomous fashion to form a plexus. The individual fibre does not reach its destination by the shortest route but only after many circuitous passages within a number of nerve bundles.

The arrangement of nerve bundles in the plexus is not regular and symmetrical as in Auerbach's and Meissner's plexus. Interlacing and crossing of fibres and bundles occur as well as network formation.

On the course of the bundles which are composed of a few nerve fibres, spindle-shaped thickenings of the bundles occur. At these thickenings a wide separation of the individual nerve fibres is present with an intertwining of the constituent fibres.

Such a spindle-shaped enlargement of a nerve bundle running parallel to the mucous membrane of the horn of a cat is shown in (Fig. 22). Such a widening of the fine nerve bundle occurs sometimes twice on a relatively short stretch of nerve bundle. Even on the finest nerves such thickenings occur even upon the course of what appears to be a single nerve fibre.

Varicosities.

On the course of the individual nerve fibres varicosities are seen. These in some cases, when highly magnified, are seen to consist of a separation of very fine fibrils to form a circular or oval swelling on the coarse of the nerve fibres. These nerve fibrils are often so fine and the degrees of separation so slight that under a high magnification they appear as deeply stained beads on the course of the fibres. The presence of such varicosities on the nerve fibres with methylene blue staining is characteristic of non-medullated nerve fibres. The size of these varicosities varies on the individual fibres composing the nerve bundles. (Fig. 25). On any one nerve fibre variations in the size of the varicosities occur. The

size of the varicosity does not vary with the thickness of the nerve bundle. In some cases the nerve fibre is so fine as to be imperceptible, and yet the course of the fibre can be picked out by following the course mapped out by the varicosities.

At times varicosities of astonishing size are seen (Fig. 22). These varicosities may possibly be artefacts. They appear, however, to be localized separations of tightly packed nerve fibrils.

Nemiloff (100) has described varicosities composed of a mass of fibrils having a spiral course, separating from one another in the middle and following together at their ends in the nerve fibres of Raja clavata, of Carcinus maenas, and of the cat.

Tsunoda and Kasahara (141) 1928 (141) observed varicosities on the finest nerves of the heart and called them „Endnetzen."

The syncitium of the nerve bundle is almost homogeneous in appearance and shows very little affinity for methylene blue (although more than the muscle and fibrous tissue).

Nerve Endings.

The mode of ending of the nerve fibres within the muscle is still unknown.

In the mouse, guineapig, cat, rabbit and human subject I have seen nerve fibres ending in knobs and also some ending sharply as described by Labhardt (82). Smooth muscle cells are

seen enclosed in a net of very fine nerve fibres wound round the cell. I have been unable to demonstrate any terminal intracellular network.

This is in agreement so far as it goes with the observations on the motor endings in relation to smooth muscle cells in other situations. Löwit (95), Retzius (114), Müller (99), Kölliker (74), Dogiel (30), Huber and de Witt (144), Agababow (2), Boeke (11), Lawrentjew (89), Leontowitsch (92), Stöhr (134) agreed that the motor fibres, after forming complicated plexuses between the smooth muscle fibres, eventually terminate in close relationship to the muscle cells themselves, either on the surface of the cell or actually in its substance.

Agababow (2) found that the smooth muscle cells in the human eye-muscles are enclosed in a net of very fine nerve fibres winding round the cell. By the Golgi and intra-vitam methylene blue methods he failed to find any fibres which penetrated into the substance of the muscle cell. In the uterine smooth muscle I have been unable to demonstrate the finer fibrillae which Boeke (11) has shown branching off from this network in the ciliary muscle and penetrating into the substance of the muscle cell. Recently Boeke (12) has shown that one of the terminal fibrillae lies in close proximity to the nucleus, in some cases even indenting it. Lawrentjew (89), working on the musculature of the cat's stomach, and Hill (58) on that of the intestine also describe terminal intracellular nerve fibrillae.

My observations although compatible with the conclusion come to by Boeke (12), Lawrentjew (89), Leontowitsch (92) and Stöhr (133,135), that the non-medullated nerve fibres form a system of anastomosing strands forming a syncitium, do not add any further evidence in favour of this conclusion.

I have been unable to demonstrate any nerves in the mucosa, or to trace the medullated nerve fibres far into the depth of the uterine muscle.

Turning now to the important question as to cells found in connection with these nerve fibres, there follow (I) a description of the three types of nuclei found on the course of the varicose nerve bundles. The boundary of their cell bodies, if such exists, has not been demonstrated. The nuclei appear to belong to a plasmodium, the cytoplasm of which stains more deeply near the individual nuclei. (II) a description of the other cells which show a greater affinity for the methylene blue than do the surrounding connective tissue cells.

I. Nuclei on the Course of Nerve Bundles.

(a) On the course of the nerve bundle nuclei are seen at intervals (Fig.19 and 20). The most common nucleus lies in almost homogeneous protoplasm which shows only a slight affinity for the methylene blue stain. The protoplasm is traversed by the varicose nerve fibres and is continued along the nerve bundles

for a variable distance when it ceases to be identifiable from the cytoplasm in which the nerve fibre is embedded. (Fig.29) With methylene blue the nucleus stains a pinkish purple colour, is oval, symmetrical and regular in outline. The chromatin is finely divided. No nucleolus is seen. The nucleus measures on an average 13μ by 5μ. The longer axis usually lies along the course of the nerve fibres. No lobulation of the nucleus is seen except in (Fig. 39). Such a nucleus is seen at the point of division of nerve bundles. (Fig. 29a). They occur on the course of nerve bundles. Two are shown on a nerve bundle running parallel to the serous surface of the horn. (Fig. 38).

In (Fig. 40) such a nucleus is seen at the point of inter-communication of the nerve fibres of two nerve bundles. The syncitium surrounding the nerve fibres in each of the bundles widens out to form an oblong mass in the centre of which lies the nucleus. The nerve fibres are seen coursing round the nucleus. The appearances in my sections point to the nerve fibres being embedded in a syncitium with only a slight affinity for methylene blue compared with the nerve fibres themselves. In the course of this syncitium at intervals nuclei, such as are described and figured, are encountered. These nuclei resemble the nuclei taken by many authors to be the nuclei of Schwann.

In the cytoplasm surrounding these nuclei I have been unable to demonstrate the granules described by Reich (110) in the cytoplasm surrounding the nuclei of Schwann. These granules he depicts as especially numerous in the perinuclear zone of cytoplasm. They were often arranged like the sheaths of an onion and they were well shown with thionin or methylene blue. Spielmeyer (130) considered that their presence is a characteristic of the normal cells of Schwann of the peripheral nerve fibres.

(b) The second type of nucleus encountered on the course of the nerve bundle is more elongated, lobulated in outline and containing less finely divided chromatin. This nucleus stains of bluer purple-colour and no nucleolus is discernable. (Fig. 29b).. The nuclei are directed with their long axis parallel to the course of the fibres.

The nucleus measures on an average 20 μ by 2 μ. This type of nuclei has not been seen at the point of division of a nerve bundle, nor at a point where fibres from one bundle interconnect with those of another. The amount of surrounding cytoplasm demonstrated is less than that surrounding the broader, more symmetrical nuclei. The nerve fibres appear to lie in close contact with the nuclei and for a short distance one or more may lie directly on the nuclear membrane. Often several fibres come into relationship with the same nucleus especially where the fibres are crossing one another. I have been unable

to satisfy myself that the nerve fibres actually run in a groove on the surface of the nuclear membrane.

The difference between these two types of nuclei is not explainable as due to foreshortening or viewing of the same type of nucleus from two different points of view. As the sections are fairly thick it is relatively infrequent that the section passes through a nucleus on the nerve bundle.

The nature or function of these nuclei on the course of the nerve bundles is not known. Nuclei resembling these two types of nuclei are figured by various workers and designated nuclei of Schwann. Stöhr (135) figures nuclei resembling those of type I in his Figures 8, 9, and 12 as occurring in nerve bundles and on very fine nerve fibres in the terminal nerve plexus of the bladder.

The nuclei of Schwann encountered on the capillaries of the heart in man and figured by Stöhr (135), with the exception of one kidney-shaped nucleus, resemble those of type II. See his Figures 6, 7, 8, 9, 10 and 11.

Around these nuclei which Stöhr called nuclei of Schwann he was unable to demonstrate any cell body. He reported that he had never seen any trace of neurolemma around the nerve fibre and believed that in relation to the nerve fibres of fine calibre there are only nuclei and not cells.

Gruemhagen (47) has however described a fine mass of granulated protoplasm surrounding his nuclei of Schwann. He described the cytoplasm as having a number of fine processes growing out from where the cytoplasm is thickest and connecting up with the processes of neighbouring cells in a plasmodium.

More recently E. Müller (99), Lawrentjew (88), van Esveld (32), Leontowitsch (92), Riegele (115) got impregnations of the nerve plexus in smooth muscle which pointed to these nuclei occurring at intervals on the protoplasmic strands in which the nerve fibres are embedded.

The third type of nucleus occasionally seen in the course of the varicose nerve bundles or of a nerve fibre , stains of a dark blue colour. These nuclei vary in size from 7 μ to 12 μ by 5 μ. They may be irregular in shape or oval and regular in shape. No nucleolus is seen. Near one such nucleus the more deeply stained cytoplasm can be traced 43 μ along the course of the nerve fibre.

II. Cells apart from Nerve Bundles.

Apart from the varicose nerve fibres and their associated nuclei certain cells show a greater affinity for the methylene blue than do the surrounding connective tissue cells. These cells can be subdivided into those A. appearing to form a plexus of cells and B. those scattered throughout the tissues at some distance from one another.

(A) In sections of the myometrium parallel to the serous coat, in longitudinal sections at right angles to the serous coat and in transverse sections out at right angles to the serous coat large cells with numerous processes some of which anastomose to form a plexus are seen. (Fig. 52). In such a plexus of cells four types can be distinguished.

(1) Multipolar cells containing an oval nucleus staining a faint blue colour, with a distinct nucleolus.

(2) Multipolar cells containing an oval nucleus staining a faint blue colour but showing no nucleolus.

(3) Multipolar cell having an oval nucleus staining of dark pinkish purple colour in which a nucleolus is seen.

(4) Multipolar cell with a similar nucleus apart from the fact that in it no nucleolus is seen. A more detailed description of each of these types of cells follows.

(I) These multipolar cells resemble small sympathetic nerve cells. The size of the cytoplasm varies between 13 μ and 38 μ by from 5 μ to 20 μ. The average size of the cell bodies is 18 μ by 12 μ (Fig. 51). In the cytoplasm granules staining an intense bright blue colour are seen. Some of these granules appear to be joined together by very fine fibrils staining more intensely than the surrounding cytoplasm with methylene blue (Fig. 48). Such joined up beading is seen in the cell body, in some of the processes, and sometimes across the surface of the nucleus. The fibrils tend to run parallel with one another

when seen in the processes or as they enter the cell body. No such regular arrangement of the fibrils has been observed in the cell body. In some cells a connexion can be traced between a varicose nerve fibre and one of the processes. The number of processes varies between two and seven. The average number of processes seen is four. The processes vary in calibre, they are distributed around the cell (Fig. 49) or all at one end. Branching of the processes is seen.

The nucleus is oval in shape, its surface is regular showing no lobulation. The chromatin scaffolding is fine and difficult to recognise. Blue granules gathered into clusters are seen in certain of the nuclei (Fig. 48).

In none of the cells is more than one nucleus seen. The nucleus is usually excentrically placed (Fig. 48). The nucleolus is often centrally placed but sometimes it is excentric in position.

The size of the nucleus varies from 13 μ to 19 μ by from 5 μ to 13 μ . The average size of the nuclei measured is 15 μ by 8 μ.

(II) These cells are similar in structure to those of Type (I) except that in the nucleus no nucleolus is seen. They are less numerous than those of Type (I). The size of the cell body of those measured varies from 13 μ to 33 μ by from 7 μ to 11 μ.

The average size of the cell body is 9 μ by 24 μ. The number of processes varies between 4 and 6 the average number

being five. In one cell the connexion of a process with a varicose nerve fibre can be traced (Fig. 43).

Another cell appears to be connected by a process with a cell of the 3rd type - viz. one with a dull pink purple nucleus containing a nucleolus (Fig. 49). Intensely coloured blue granules joined by very fine blue fibrils are seen in the cytoplasm. The nucleus is usually oval in shape. Only in one such is a nucleus pointed at one end seen. The chromatin scaffolding is fine and difficult to recognise (Fig. 43). The size of the nucleus in the cells measured varies from 10 μ to 22 μ by from 6 μ to 9 μ.

The average size of the nucleus is 15 μ by 7 μ. In none of the cells of this type is more than one nucleus seen.

(III) The third type of multipolar cell is slightly more numerous than is the second type but less numerous than the first and fourth types.

The size of the cell body varies from 15 μ to 40 μ by from 8 μ to 20 μ in the case of those measured. The average size is 25 μ by 13 μ.

The processes vary in number from one to seven. The average number of processes is four. Branching of the processes is seen (Fig. 41). In one cell the process divides up into brush-like terminations (Fig. 47).

In the protoplasm dark blue granules are seen, sometimes gathered into clusters. In some cells there is a zone around the nucleus in which there are fewer granules than in the peripheral protoplasm. In some cells the granules appear to be arranged in the form of striae.

Intensely stained bright blue granules are also seen in certain of the processes. Sometimes these are seen in the cell bodies, even over the surface of the nuclei. In some cells these bright blue granules appear to be joined up by very fine blue fibrils (Fig. 45). A parallel distribution of these fibrils is sometimes seen (Fig. 41). The nucleus stains of a dull pinkish blue colour. The nucleus is roughly oval in shape. Although sometimes regular in outline occasionally distinct notching is present. Usually the nucleus is asymmetrical in form. The nucleus is usually excentric in position (Fig. 49). Its nucleolus is centrally placed. The size of the nuclei measured varies from 7μ to 22μ by from 5μ to 10μ, the average size being 3μ by 8μ.

A connexion is shown between its cytoplasm and a varicose nerve fibre in (Fig. 41). No cells of this type are seen containing more than one nucleus or nucleolus. The chromatin does not show the characteristic chromatic reticulum with small granules placed peripherally seen in smooth muscle cells.

(IV) The fourth type of multipolar cell is the most numerous of those picked out by the methylene blue staining.

Its cell body varies in size from 17μ to 104μ by from 2μ to 16μ. The average size of those measured is 38μ by 9μ. The processes vary in calibre. They are sometimes distributed around the cell but more frequently are more numerous at one or other or both ends of the cell.

The processes passing out from the cell vary in number from 3 to 9. The average number of processes is five per cell. On an average the number of processes per cell is greater than in the other types of multipolar cells forming a plexus. The processes are longer in average length than those of the other types. One process can be traced 75μ from the edge of the nucleus. Branching of the processes is seen. In the cytoplasm dark blue granules are seen. These are fewer in number around the nucleus. In some of the cells of this type clustering of these granules is present. There is no accummulation of these granules at the poles of the nucleus such as often is seen in smooth muscle cells. Intensely stained granules of a bright blue colour and joined by fine fibrils are not seen in all the cells but are distinctly seen in some cell bodies and their processes (Fig. 43). In the cytoplasm of one cell which appears to be connected with a nerve bundle no such joined up beads can

be seen. In one cell (Fig. 50) joined up beading is seen crossing over the surface of the nucleus. The nucleus stains as in type (III) of a dull pinkish purple colour with methylene blue.

The nuclei are of an oval shape and in cross section they are almost circular (Fig. 51). Although sometimes they are regular in outline and symmetrical in form a few are pointed at one end and many are lobulated. The size of nuclei varies from 7μ to 25μ by from 3μ to 17μ. The average size of the nucleus is 13μ by 5μ.

The chromatin appears to be finely divided in some but less so in others. The distribution of the chromatin is not that characteristic of smooth muscle cells. Several nuclei or several nucleoli are not seen in any of the cells of this type.

I have been unable to demonstrate these plexus forming cells in the mucous membrane, but Gawronsky's (44) and Köstlin's (76) description of cell formations shown up by the Golgi method in the mucous membrane may indicate that similar plexus forming cells are present in the mucous membrane.

II.

(B) Scattered throughout the tissues at some distance from one another are cells which show a greater affinity for the methylene blue stain than do the surrounding connective tissue

cells (Fig. 52). These cells are considered not to be nervous in nature but to be individual connective tissue cells which have been shown up by the methylene blue. They can be differentiated into two types according to the staining reaction of their nuclei. The variety in size and shape of the nucleus and of the cytoplasm in number and distribution of the processes is so great in each group that it may be that this difference in the staining affinity of the nucleus is however a matter of no importance.

These two types of connective tissue cells are:

(1) Those having a dark blue staining nucleus (Fig. 57).

(2) Those having a dark purple staining nucleus.

(1) The size of the cell body is in many cases small relative to the size of the nucleus. The cytoplasm of some cells is elongated and shows branching at one end. The number of processes varies from one to four. In these processes bright blue granules are sometimes seen (Fig. 57). In some instances a connection can be traced either between the cell body or a process and a varicose nerve fibre or nerve bundle (Fig. 53). The nuclei vary in size from 5μ to 18μ in length by from 1μ to 8μ in breadth. The average size of the nuclei is 11μ by 4μ.

No nucleolus is present. A few nuclei are oval in shape; most show some irregularity of shape, some being notched, others pear-shaped, others narrow and curved. Some but not all the

nuclei appear to be centrally placed, but the excentric position at least in some cases is explained by the foreshortening of irregularly placed cells in thick sections.

(2) The cytoplasm of these connective tissue cells is scanty in amount, in some cells it is spindle-shaped. Bright blue granules are seen in some cells. A connexion between the cell body and a varicose nerve fibre has been traced. (fig.54).

The number of processes varies between 3 and 6.

The dark purple nuclei vary in size between 7 μ and 16 μ in length by between 3 μ and 6 μ in breadth. The average size of these nuclei also is 11 μ by 4 μ.

A few nuclei are oval in shape, others are curved, lobulated or pear-shaped (Fig. 59). No nucleolus is seen. Some but not all the nuclei appear to be centrally placed.

Discussion.

The nature of the plexus forming cells has to be considered. The question to be settled is whether these plexus forming cells are (1) the so-called interstitial cells described in the gastro-intestinal tract. (2) Connective tissue cells. (3) Sympathetic nerve cells.

One has also to consider whether either of the types of nuclei scattered along the nerve bundles are the nuclei of the much discussed interstitial cells of the intestine.

A short summary of work done on these interstitial cells follows.

Findings of Previous Workers.

Cajal (19) in 1889 and 1893 and in his book Histologie du système nerveux 1911 using Golgi preparations of the gastro-intestinal canal of the frog and various mammals discovered spindle-shaped, three-cornered, or star-shaped elements to which he gave the name of "neurones sympathiques interstitiels." He described these interstitial cells as having a small cell body and long anastomosing processes forming a narrow meshed plexus, and as occurring around the ganglia and nerve bundles of Auerbach's plexus, near the blood vessels, in the mucosa and submucosa and in the muscle coats. He considered that the axis cylinders of the plexus running at right angles and parallel to the muscle coats - the "plexus musculaire profond" and of the finer plexus - the "plexus terminalou interstitiel" were composed of the axis cylinders of the ganglionic cells of Auerbach's plexus and of the interstitial cells.

He concluded thus "Il result de cette déscription qu'il existe dans les muscles lissés deux sortes d'arborisations nerveuses; les principales qui proviennent des grandes cellules ganglionnaires du plexus d'Auerbach et sont au même temps les plus nombreuses, et les accessoires qui émanent des cellules interstitielles."

He and his pupil La Villa (143) described a neuro-fibrillar network within the cells. These neurofibrillae may correspond to the varicose nerve fibres of the uterine plexus.

Dogiel (29) 1895 using methylene blue found in the intestine cells which he considered were the same as the interstitial cells of Cajal. He considered they were connective tissue cells, which formed a perivascular network and had no connexion (Beziehung) with the ganglia or nerve bundles. Later 1901 he (30) described similar "sternförmige Zellen" in the subcutaneous tissue and the central tendon of the diaphragm. These cells he was satisfied were connective tissue in nature. I have not been able to consult his paper and cannot judge whether these cells resemble any of the plexus forming cells described in the present paper.

Erik Müller (99) chiefly using the Bielschowsky method demonstrated that in Selachian embryo (Squalus acanthias) the nerve plexus formed a true net in which the neurofibrillae ran from one cell to another. The pictures he got resembled those found by Apathy (5) in the intestine of Pontobdella. The nuclei in this embryonic nerve plexus appear to bear the same relationship to the neurofibrillae as the described nuclei do to the nerve fibres in the nerve bundles of the uterine wall.

M. Heidenhain (50) and Huber (62) and Kuntz (79) described similar nuclei along the nerve bundles which they considered were

connective tissue in nature. M. Heidenhain (50) did not agree with Held (51,53) that the fibres were embedded in a protoplasmic strand but each in a nucleated sheath. He described "Fasern mit einheitlicher kernhaltiger Scheide, deren fibrillärer Inhalt sich aus mehreren Ursprungszellen ableitet."

Johnson (64) figured a network of cells shown up with methylene blue in the myenteric plexus of the dog. These cells, the nuclei of which measure .013 by .005 mm. in his figure (Fig.3) he regarded as interstitial cells and considered they looked very much like connective tissue, pointing out the contrast in size, shape and character of branches between them and the ganglionic cells. He pointed out that the syncitial network although it occupied the intermuscular space in company with the myenteric plexus extended beyond the limits of this space, between the muscle bundles. Cole (22) demonstrated anastomosing cells in the myenteric plexus of the frog using methylene blue and considered these were interstitial cells and were of connective tissue nature. He argued from the absence of a hyaline zone around the nucleus, and of Nissl substance, and from their 'brittle' appearance that they were not true nerve cells. He says "The fact that these cells are to be found in all layers of the digestive tube instead of being localised in the region of the myenteric plexus, is further evidence that they are not of a nervous nature."

(22)
Cole, on interstitial cells, continued: "In the muscular coats their processes are interwoven between and around the muscle cells, strongly suggesting that they function as supporting elements. They were invariably found where special stains demonstrate connective tissue to be abundant and infrequently elsewhere. On the basis of histological demonstration, therefore, the conclusion seems warranted that these cells are connective tissue elements."

(43)
Gasser described interstitial cells in the small intestine which stains more intensely with methylene blue and have thicker processes than the nerve cells of Auerbach's plexus and do not stain as far as he could see with methyl-green-pyronin. These cells he did not figure and he considered that the question as to their nature must be regarded as still open.

(88,89)
Lawrentjew worked at this question using the gastro-intestinal canal of the cat and staining it with methylene blue and by the Gros method. He concluded that the rich network of neurofibrillar bundles in the intestinal wall was made up of branching strands of protoplasm which connected up with one another and which contained within them round or oval deeply staining nuclei and bundles of neurofibrillae. These nuclei corresponded in size and position to the broader of the two types of nuclei seen on the course of the nerve bundles within the uterus.

These nuclei and the protoplasmic strands in which the neurofibrillae run he considered were the same as the

interstitial cells described by earlier workers. He says: „Die Nervenfäden gehen um den kern von der einen oder von beiden Seiten herum und verzweigen sich dann nach allen Seiten unter einem weit stumpfen Winkel, indem sie aber stets innerhalb des feinen Protoplasmafortsatzes bleiben, und sobald sie eine bestimmte glatte Muskelfaser erreichen, bilden sie in derselben eine motorische Endigung. Ist das Protoplasma und einen solcher Kern genügend intensiv imprägniert, so hat das ganze Gebilde das Aussehen einer spindelförmigen oder dreieckigen Zelle mit feinen langen nach verschiedenen Richtungen verlaufenden Fortsätzen, d.h. wir haben eine typische interstitielle Zelle Cajals oder Dogiels vor uns."

Hill (58) did not make a special study of the "interstitial cells of Cajal" but found them forming "an interlacing system in the meshes of the fibro-cellular plexus." In her figures 18 and 19 no neurofibrillae are seen within their protoplasm, their processes do not join up with those of other cells but their nuclei seem to correspond in size and structure with the nuclei found on the course of the nerve bundles of the intestine by Lawrentjew. On the course of the nerve bundles figured by

Hill in which the nerve fibres are beautifully demonstrated no such nuclei are shown up.

It may be that where the interlacing system of interstitial cells are shown up the protoplasm and nuclei of the so-called Lemnoblasts of Held have picked up the methylene blue and the neurofibrillae have not, whereas where the neurofibrillae are so very distinct the nuclei and protoplasm have not taken up the stain.

(135)
Stöhr (1928) demonstrated similar nuclei on the course of the bundles of nerve fibres in the bladder wall and on capillaries by Bielschowsky's method, but called them nuclei of Schwann, although he has failed to demonstrate the presence of any cell body belonging to these nuclei; nor any trace of a neurilemma.

(32)
Van Esveld compared the plexus of interstitial cells demonstrated by him in Auerbach's plexus with methylene blue and once with silver by the method of Gros with a plexus of connective tissue cells in which the anastomosing processes are shorter and more numerous (Fig.18). He succeeded in demonstrating a nervous syncitium in the ureter of the pig using the Gros method on the course of which were nuclei similar to those demonstrated by me using methylene blue on the course of the nerve fibre bundles in the uterus. see his figures 19&20

(115)
Riegele showed that in the spleen the peripheral nerve fibres run partly in nucleated protoplasmic strands and partly in the cytoplasm of cells of the reticulum. He also (156)
showed that in the liver the nerve fibres traverse the cytoplasm of Von Kupffer's cells, see his figure (Abb.11).

(137)
Terni a short time ago described cells in the thymus which he named "piccola cellula simpatica interstiziale." These cells resemble connective tissue cells described by Tello. Their cell bodies are about .007 mm. in width and their nuclei between .002 and .003 mm (his figures 26 to 38).

(146)
Akkeringa recently has described in the conjunctiva a syncitial pathway in which the non-medullated nerve fibres run and considered that its nuclei are identical with those of the lemnoblasts or interstitial cells. He made out a connection between this protoplasmic pathway and phagocytic cells.

(29)
From a comparison of the reproductions of Dogiel (Taf. 33. Abb.21); Cajal (19) (Abb.573, S.925); La Villa (143) (Abb.572, S.924); O.Schultze (122) (Fig.15; Taf.4, Abb.12; Taf.5, Abb.24); Lapinsky (87) (Taf.29, Abb.4); Hoffmann (59) (Taf.21, Fig.10 and 13); A.Bethe (7) (Taf.12, Abb.7 and 8); E. Muller (99) (Taf.18a, Abb.58 and 60); Paul Schultz (124) (Taf.4, Abb.34; Taf.7, Abb.38); Tiegs (138)

(Fig.1 and 2); Lawrentjew (89) (Fig.5, 6, 9); Van Esveld (32) (Fig.15, 16,19); Riegele (115) (Fig.5); Kolossow and Sabussow (151) (Abb.18 and 19) one is led to conclude that imperfect staining or impregnation with stain, of the protoplasmic strand, its nuclei or the contained nerve fibres might well give rise to the formations variously named by the many authors. The fact that they have used different methods, however, renders it impossible to decide whether their descriptions and figures refer to the same elements.

Let us turn now to a consideration of the nature of the nuclei found on the course of the nerve bundles of the myometrium.

These nuclei correspond with those already demonstrated in the ureter (32), intestine (89), skin (92) and spleen (115). They also correspond with the nuclei of Schwann found by Stöhr (134) on the terminal nerve plexus of the human bladder and seminal vesicle, and by Leontowitsch (152) on the nerve bundles of the blood vessels. It must remain to some extent a matter of conjecture whether these nuclei correspond to the nuclei of the interstitial cells - described by the other workers - in which the connection with the non-myelinated nerve bundles is not shown satisfactorily. The argument is not valid that, because the interstitial cells

contrast in size, shape, in thickness of their processes, in absence of a hyaline zone around the nucleus from ganglionic cells, they are not of neural origin.

The occurrence of nuclei at intervals in the course of the nerve bundles does not prove that these nuclei are of nervous nature. These nuclei may be the nuclei of a supporting plasmodium, or of individual cells of connective tissue nature.

The embryological work of Apáthy (147) on the intestine of Pontobdella, of O.Schultze (122) on Amphibian Larvae, of Graham Kerr on Lepidosiren, of E. Müller (99) on Selachian Embryos, and of Boeke and Heringa (55) is a valuable beginning to the work of determining their nature.

Graham Kerr (185) showed in Lepidosiren that a spinal nerve develops in a non-nucleated protoplasmic bridge connecting the myotome to the spinal cord. This was confirmed in the case of the motor trunks of Elasmobranchs by Paton, (155) in the case of the olfactory nerve of various vertebrates by Elliot Smith, (160) and by Dohrn (149) in the trochlear nerve in Selachian embryos.

Graham Kerr (185) showed that in Lepidosiren the sheath cells are coarse and heavily yolk-laden mesenchymatous cells which collect round and it may be migrate into the, at first non-

cellular, nerve trunk.

Disagreeing with Balfour (148), Apáthy (147), O.Schultze (159), Held (150) concluded that the Schwann cells are glial cells which wander peripherally after the neurofibrillae have developed. In the small-celled highly specialized vertebrates it has been impossible up to now to get a convincing proof of the origin of these cells on the nerve bundles in smooth muscle.

Let us turn to a consideration of the nature of the plexus-forming cells. The plexus-forming cells found by me in the myometrium are not the same cells as these described on the course of the nerve bundles through which the nerve fibres can be traced. These plexus-forming cells cannot be explained as being stained portions of the nucleated protoplasmic strands in which the varicose nerve fibres are shewn up imperfectly or not at all. Their nuclei differ in size, staining reaction, and structure from one another and from the nuclei on the course of the nerve bundles. If the view of Lawrentjew (89) be true, that the nuclei and their protoplasm distinctly shewn up on the course of the nerve bundles are the same as the so-called interstitial cells of earlier workers, then these plexus-forming cells found by me in the uterine muscle are not merely interstitial cells.

The cells, especially those with a vesicular clear blue

oval nucleus with a distinct nucleolus and having their chromatin in a fine state of division, resemble sympathetic nerve cells much more than they do connective tissue cells. Their nucleus is always excentric in position, which contrasts with the usual central position of that of a connective tissue cell. Sobotta (127) points out that often sympathetic nerve cells, in contrast to cells of the cerebrospinal system, have two or even three nuclei. In all of my plexus forming cells the nucleus is single. Just as is seen in many sympathetic nerve cells stained with methylene blue, a zone of cytoplasm surrounding the nucleus shows less affinity for the stain than the more peripheral cytoplasm.

It is commonly said that the cell body of the sympathetic nerve cell is approximately circular in shape. Measurement however, of undoubted nerve cells, demonstrated by Stöhr (135) in the superior cervical ganglion and the bladder, show that this is not always so. The fact therefore that, although some of the cell bodies of the first type of plexus forming cells are circular in shape, others are oval, is not against their being of nervous nature. These cells which show very fine fibrils intertwining within their cell body, but arranging themselves parallel to one another in the processes, resemble sympathetic nerve cells. Amongst the features which my

plexus-forming cells have in common with sympathetic nerve cells, are the thinness of their processes and the variety they show as to number and as to distribution around the cell body.

No classification of the cell processes of these plexus-forming cells into dendrite-like processes in contrast to neurite-like processes is possible. In sympathetic nerve cells too a subdivision of the processes into neurites and dendrites is impossible. Branching of the processes of my plexus-forming cells is a more marked feature than it is in many of the sympathetic nerve cells demonstrated. Sobotta (127) reports however that branching of the processes of sympathetic nerve cells does occur.

Just as described in the sympathetic nerve cells, certain processes, either after a short or after a long course, appear to end in a thick knob of protoplasm having the structure of the cell body. It is just as impossible to demonstrate with certainty so-called free-endings of the processes of these plexus-forming cells, as it is in the case of sympathetic nerve cells. Where endings apparently occur, it probably is either a case of the process being cut off, or incompletely impregnated.

It is difficult to compare my plexus-forming cells with

the third type of ganglion cell described by Hoogkamer (61) as the reproduction of his photographs is indistinct.

The fact that a connexion can be established between one of the plexus-forming cells and a nerve fibre, does not prove that they are nervous in nature. Such a nerve fibre may be ending in the cell under consideration. I have been unable to trace a nerve fibre throughout and beyond such a cell. The failure to do so may however be proved by later work to be due to imperfect staining of the fibre. The fact that individual fibrils cannot be traced throughout the cell cannot be taken as proof that the cell is not nervous in nature.

The question as to whether the nuclei on the course of the nerve bundles or the plexus-forming cells are of neural origin or of mesodermal origin can only be settled by an extensive embryological study of the innervation of smooth muscle in lower animals and in man, preferably using more reliable staining techniques than those at present known.

Summary.

(1) In the rat, guineapig, mouse and human subject the sympathetic nerve-fibres supplying the uterus and vagina pass down the hypogastric nerves to the level of the cervix and then pass to the tubes, uterus, cervix and upper portion of the vagina by several branches. These branches are intimately associated with branches of the uterine artery.

(2) Nerve-cells are scattered along the hypogastric nerves and are specially numerous on the course of the hypogastric plexus opposite the cervix. On each side they form a ganglion, the cervical ganglion, which is largest and most circumscribed in the rat and least so in the mouse.

(3) In a female human foetus of 15 cm. length nerve cells are scattered along the hypogastric nerves and occur on each of their main branches on that part of their course opposite to the cervix and vagina.

(4) Groups of nerve cells are found in the adult human uterus close to the myometrium and in the superficial layers of the muscle on the branches of the hypogastric plexus. These groups of nerve cells are only seen on the course of the nerve bundles in the region of the cervix below

the level of the reflexion of the peritoneum on to the bladder anteriorly and on to the rectum posteriorly.

(5) (a) A comparison of the action of the uterine horn of the rat and the guineapig connected with and that not connected with the cervical ganglion;

(b) the absence of any effect on removal of the ganglion - and -

(c) the absence of any difference in the response of the uterus with and without the ganglion to various chemical substances seem to indicate that the ganglion does not exercise a direct influence in controlling the tone and movements of the excised uterus. The point of origin of the impulse controlling the tone and movements of the uterus appears to lie within the uterine wall itself.

(6) A study of the action of drugs and their antagonisms indicates that in or upon the uterine wall there is some arrangement for the control of tone and movement probably distributed at three levels:- (a) a proximal, (b) an intermediate, and (c) a peripheral.

(7) Interlacing and crossing of the nerve fibres and nerve bundles with plexus formation occurs in the uterine muscle. The plexus is not regular and symmetrical.

(8) At intervals on the nerve bundles separation and intertwining of the constituent fibres occur producing a spindle-shaped enlargement of the bundle. Circular or oval swellings produced by the separation of fine fibrils are seen on the nerve fibres.

(9) Smooth muscle cells are wound round with a net of very fine nerve fibres, but no intracellular endings are found.

(10) No nerves are seen in the endometrium.

(11) Medullated nerve fibres have not been traced far into the depth of the uterine muscle.

(12) The non-medullated nerve fibres of a nerve bundle appear to run in a syncitium, the cytoplasm of which has only a slight affinity for methylene blue stain except near the nuclei.

(13) Three types of nuclei are found in the course of the nerve bundles.

(a) An oval nucleus measuring on an average .013 mm. by .005 mm., staining a pinkish purple colour with methylene blue, and having its chromatin finely divided. Lobulation of the nucleus is the exception.

(b) An elongated lobulated nucleus measuring on an average .02 mm. by .002 mm., staining of a bluer purple colour

with methylene blue and having its chromatin less finely divided.

(c) An irregularly shaped or oval neucleus measuring from .007 mm. to .012 mm. by .005 mm., staining of a dark blue colour with methylene blue. In each type of nucleus no nucleolus is seen.

(14) In the myometrium there are four types of plexus-forming cells which show a greater affinity for methylene blue than do the surrounding connective tissue cells.

(1) Multipolar cells, measuring on an average .018 mm. by .012 mm. containing an oval usually excentrically placed nucleus staining a faint blue colour. The average size of their nucleus is .014 mm. by .008 mm. and it contains a nucleolus.

(2) Multipolar cells - their cell bodies measuring on an average .024 mm. by .009 mm. Each contains an oval nucleus staining a faint blue colour, but containing no nucleolus and on an average measuring .015 mm. by .007 mm.

(3) Multipolar cells - the average size of the cell bodies of which is .025 mm. by .013 mm. Each contains a nucleus staining of a dull pinkish purple colour, the average size being .013 mm. by .008 mm. Their nuclei are usually asymmetrical and excentric in position with

a central nucleolus.

(4) Multipolar cells measuring on an average .038 mm. by .009 mm. with a nucleus similar to the above, except that in it no nucleolus is seen. The average size of the nuclei is .013 mm. by .005 mm.

(15) In some of the cells of each of the four types of multipolar plexus-forming cells -

(a) there are granules sometimes joined by very fine fibrils, staining more intensely than the surrounding cytoplasm with methylene blue;

(b) a connection can be traced between a varicose nerve fibre and one of the processes.

(16) In each of the types of multipolar cells branching of the processes is seen.

(17) In the various types of multipolar cells the number of the cell processes ranges between 2 and 9. The average number for each type of cell is either 4 or 5.

(18) In none of the multipolar plexus-forming cells is more than one nucleus seen.

Fig.1. Dissection of aortic, inferior mesenteric nerve plexuses, and hypogastric nerves, HN, in the guinea-pig.

B = bladder.
D = descending aorta.
HU = uterine horn.
IM = inferior mesenteric artery.
MS = middle sacral artery.
O = ovary.
OA = ovarian artery.
R = rectum.
RA = renal artery.
UA = uterine artery.
Ur = ureter.
V = vagina.
VA = vesical artery.

Fig.2. Dissection of hypogastric plexus in the guinea-pig.

B = bladder.
D = descending aorta.
HN = hypogastric nerve.
HU = uterine horn.
LA = lumbar artery.
LS = lumbo-sacral nerve trunk.
MS = middle sacral artery.
Ob = obturator nerve.
R = rectum.
S = vertebral sympathetic nerve trunk.
SI, SII, and SIII = first, second and third sacral nerves.
UA = uterine artery.
Ur = ureter.
V = vagina.

Fig.3. Foetal guinea-pig (60 days). Diagram of reconstruction (sections 1449-1595) as seen from the cranial aspect. Showing -

ci = common iliac artery.
ei = external iliac artery.
g△ = position of nerve-cells.
hn = hypogastric nerve.
hu = uterine horn.
ii = internal iliac artery.
iia = anterior division internal iliac artery.
r = rectum.
ra = artery to rectum.
ua = uterine artery.
un = uterine nerve.
ur = ureter.

Fig.4. Foetal guinea-pig (60 days). Diagram of reconstruction (sections 1252-1449) as seen from the cranial aspect. Showing -

b = bladder.
g△ = position of nerve cells.
hn = hypogastric nerve.
ii = internal iliac artery.
iia = anterior division internal iliac artery.
r = rectum.
ra = artery to rectum.
ru = nerve to rectum.
u = uterus.
un = uterine nerve.
ur = ureter.

Fig.5. Foetal guinea-pig (60 days). Diagram of reconstruction (sections 1032-1252) as seen from the cranial

aspect. Showing -

b = bladder.
bn = nerve to bladder.
g△ = position of nerve-cells.
r = rectum.
ra = artery to rectum.
rn = nerve to rectum.
umb = umbilical artery.
ur = ureter.
v = vagina.
va = vaginal artery.

Fig.6. Foetal guineapig (60 days). Graphical reconstruction of the nerve and arteries to the uterus and vagina (sections 1126-1745).

bn = nerve to bladder.
ci = common iliac artery.
ei = external iliac artery.
hn = hypogastric nerve.
iia = anterior division internal iliac artery.
g△ = position of nerve-cells.
ra = artery to rectum.
rn = nerve to rectum.
ua = uterine artery.
un = uterine nerve.
va = vaginal artery.

Fig.7. Dissection of aortic, inferior mesenteric nerve plexuses, and hypogastric nerves, HN, in the rat.

B = bladder
D = descending aorta.
CV = inferior vena cava.

HU = uterine horn.
IM = inferior mesenteric artery.
OA = ovarian artery.
R = intestine.
UA = uterine artery.
Ur = ureter.
V == vagina.
VA = vesical artery.

Fig.8. Diagram from the reconstruction (posterior view) of the pelvic organs in the adult rat showing -

C = cervix.
G△ = position of nerve-cells.
HU = uterine horn.
II = internal iliac artery.
UA = uterine artery.
Ur = ureter.
V = vagina.
VA = vesical artery.

Fig.9. Diagram of part of longitudinal section No.64 of the genital organs of a new-born rat to show the position - G△, of nerve-cells in relation to the cervix, C; uterus, U; and vagina, V.

Fig.10. Mouse. Diagram of reconstruction (sections 647-785) seen from caudal aspect. Showing -

B = bladder
C = cervix.
G△ = position of nerve-cells.
HN = hypogastric nerve.
R rectum
UA = Uterine artery.

UA = urethra.
Ur = ureter.
V = vagina.
VA = vesical artery.

Fig.11. Human foetus of 15 cm. length. Drawing of block of internal genital organs while in xylol.

b = bladder.
O = ovary.
r = rectum.
t = Fallopian tube.
u = ureter.
V = blood vessels.

Fig.12. Flat reconstruction of the genital tract of a human foetus of 15 cm. length.

Fig.13. Three transverse sections of the pelvic organs of a human foetus of 15 cm. length.

Fig.14. Flat reconstruction of the nerves from the serial sections of a human foetus of 15 cm. length.

ap = aortic plexus.
c = cervix.
d = Gartner's duct.
g = portion of nerve-cell.
hn = hypogastric nerve.
O = nerve to the ovary.
V = vagina.

Fig.15. Photograph of a group of nerve cells on a nerve bundle in the Human myometrium under the utero-vesical reflexion of peritoneum.

Fig.16. Nerve bundles in relation to vessels in the uterus of the kitten. Gold impregnation.

Fig.17. Plexus of nerve bundles in the uterus of the kitten in the region of the bifurcation. Gold impregnation.

Fig.18. Nerve plexus deep in the uterine muscle of the cat. The topmost nucleus seen in the plexus is an example of the first type of nucleus described as occurring on the nerve bundles. The cytoplasm of the nerve bundle stained faintly with methylene-blue.

Fig.19. Nerve plexus is shown in contrast to capillary plexus in the uterine horn of the kitten near the mucous membrane. Gold impregnation.

Fig.20. Undulating nerve bundles in the uterus of the cat. In each of the two bundles towards the right side there runs a thicker nerve fibre on which no varicosities are seen. The variation in size of the varicosities is noticeable. All the cells appearing in the field are shown in the reproduction. The connective tissue cells had dark blue nuclei without nucleoli. Their cytoplasm stained faintly and was granular. On the lowest cross branch of the plexus the nucleus, containing a nucleolus, stained a faint blue with methylene-blue.

Fig.21. Nerve bundles in the lower end of the uterus of the mouse. Gros.

Fig.22. A spindle-shaped enlargement of a nerve bundle in the uterus of a cat. Methylene-blue.

Fig.23. Nerve bundle in the uterus of the cat showing three sizes of varicosities. Methylene-blue.

Fig.24. In a non-medullated nerve bundle - which ran parallel to the endometrium - variety in the size of the varicosities is seen. Methylene-blue. Cat.

Fig.25. A fairly thick nerve bundle containing one coarse nerve fibre on which no varicosity is seen. No nuclei are seen on this nerve bundle. Variety in the fineness of the varicosities is seen equally in the main bundle and its branches. Methylene-blue.

Fig.26. A fine non-medullated nerve is seen accompanied by a relatively thick non-varicose nerve fibre. Methylene-blue. Cat.

Fig.27. Non-medullated nerve plexus near the serous surface of the uterus of the cat. Three types of nucleus are seen in the figure, (1) nuclei on the course of the nerve bundles which were stained purplish; (2) nuclei of connective tissue cells which stained dark blue; (3) faintly staining nuclei considered to belong to endothelial cells.
Methylene-blue.

Fig.28. An interchange of nerve fibrils is seen between the nerve bundles. All cells occurring in the field

are shown with the exception of one lying at a higher plane than the plexus. The connective tissue cells had dark blue nuclei in which no nucleoli were seen. Lobulation of their nuclei is seen. Methylene-blue. Cat.

Fig.29.(a) On the left side a nucleus of Type I is seen at a point of division of a nerve bundle.
(b) On the right side a nucleus of Type II is seen on a nerve bundle. Note the presence of a thick fibre above the nucleus.
Methylene-blue. Cat.

Fig.30. Non-medullated nerve bundles seen in a section of myometrium taken at right angles to the endometrium of a cat. Two types of nucleus are seen on them, the upper narrow one staining dark blue, and the lower oval one bluish with methylene-blue.

Fig.31. Distinct nerve cell on the course of a fine nerve bundle. The cytoplasm fades away up and down the nerve bundle. The nucleus stained dark blue and is lobulated. Methylene-blue. Cat.

Fig.32. Showing triangular formation of the cytoplasm of a nerve bundle at its point of division. The cytoplasm of the nerve bundle stained faintly blue with methylene-blue. Uterus. Cat.

Fig.33. Two nuclei of Schwann on a non-medullated nerve bundle running near the serous surface of the uterus of a cat. Methylene-blue.

Fig.34. Fine non-medullated nerve bundles in the uterus of the cat.
One is seen running under the serous surface (shown as a dotted line) and the other between the muscle-bundles.
Numerous nuclei of the second type are seen on the nerve bundles.
Methylene-blue.

Fig.35. An oval nucleus is seen at a point of intercommunication between two non-medullated nerve bundles in the uterus of the cat. The nucleus stained of a purplish colour with methylene-blue. Bundles A and B are also seen in Fig.(36).

Fig.36. Fine nerve bundles from the uterus of the cat. On the course of the bundles both types of nuclei are seen. Bundles A and B are also seen in Fig.(35).

Fig.37. An oval large nucleus with its chromatin in a fine state of division is seen within a mass of cytoplasm traversed by non-medullated nerve fibres. The nucleus stained blue with methylene-blue. Cat.

Fig.38. Two nuclei are seen on the course of a nerve bundle. The upper one is one of Type I, see Fig.(29), the lower one is larger, stained purple with methylene-blue, and lies in a triangular mass of cytoplasm continuous with the three nerve bundles. Cat.

Fig.39. On the course of a fine nerve bundle a nucleus resembling Type I is seen to be notched. Methylene-blue. Cat.

Fig.40. Nerve fibres are seen intertwining in a mass of of cytoplasm containing an oval nucleus which stained bluish with methylene-blue.

Fig.41. A plexus-forming cell of Type III shows distinct longitudinal striation of one process. Another process connects up with a varicose nerve bundle. A relatively non-granular zone surrounds the nucleus. Methylene-blue. Cat.

Fig.42. Towards the right side is a plexus-forming cell of Type II. A connection appears to exist between one process and the varicose nerve bundle. Bright blue granules were present in the cytoplasm. An oval dark pink nucleus was seen at the point of division of the nerve bundle. Methylene-blue. Cat.

Fig.43. A plexus-forming cell with some of the processes continued into varicose fibrils. Methylene-blue. Cat.

Fig.44. A plexus-forming cell of Type I in which blue granules on fine fibrils are seen. Methylene-blue, Cat.

Fig.45. One of the plexus-forming c ells of Type III. Fibrils are seen crossing over the nucleus and interlacing in the cytoplasm. Methylene-blue. Cat.

Fig.46. A cell of Type III in which one process is continued into a varicose nerve fibre running parallel to the serous surface of the uterus. Methylene-blue. Cat.

Fig.47. Multipolar cell of type III in the uterus of the cat showing fine branching of its processes. Methylene-blue.

Fig.48. One of the plexus-forming cells of Type I. One process is seen to be connected with a varicose nerve fibre. Bright blue granules joined up by fine fibrils were seen in the cytoplasm. Methylene-blue. Cat.

Cell-plexus in the uterine horn of the cat
Figures 49, 50, 51 show three adjacent fields.

Fig.49. Cells of Types I, II, and III are shown. A connection is seen between the processes of the topmost two cells, and with the cell on the left side. The central cell is one of Type I in which granules joined by fine fibrils were seen. Bright blue granules were also seen in the cytoplasm of the topmost two cells. Methylene-blue.

Fig.50. Cells of Types I, II and IV are shown. The second topmost cell on the right side is one of Type IV and in its cytoplasm granules, which were stained bright blue, are seen joined up by fine fibrils. Methylene-blue.

Fig.51. Cells of Types I, II and IV are shown. Methylene-blue.

Fig.52. Plexus of multipolar cells in the uterus of the cat. Cells of Types I and III are seen. Methylene-blue.

Fig.53. A connective tissue cell which had a dark blue nucleus is seen connected up with a nerve bundle. Methylene blue. Cat.

Fig.54. Three connective tissue cells are seen. Their nuclei stained purple with methylene-blue. The processes of one appear to be connected with the varicose nerve bundle. A cell resembling a sympathetic nerve cell is also seen. Cat.

Fig.55. A multipolar cell resembling those of Type III but showing notching of its nucleus is seen. The processes of this cell, of the plexus-forming cell of Type I below it, and of the elongated connective tissue cell merely overlap. Methylene-blue. Cat.

Fig.56. A connective tissue cell containing a tortuous nucleus which stained dark blue with methylene-blue. Cat.

Fig.57. A connective tissue cell is seen which had a dark blue curved nucleus. Blue granules were seen in some of the processes. Methylene-blue. Cat.

Fig.58. Connective tissue cells having relatively short blunt processes. Methylene-blue. Cat.

Fig.59. On the bundle of non-medullated nerve fibres both Types of nucleus are seen. Numerous connective tissue cells are seen towards the right side. Their nuclei stained dark blue with methylene-blue. Cat.

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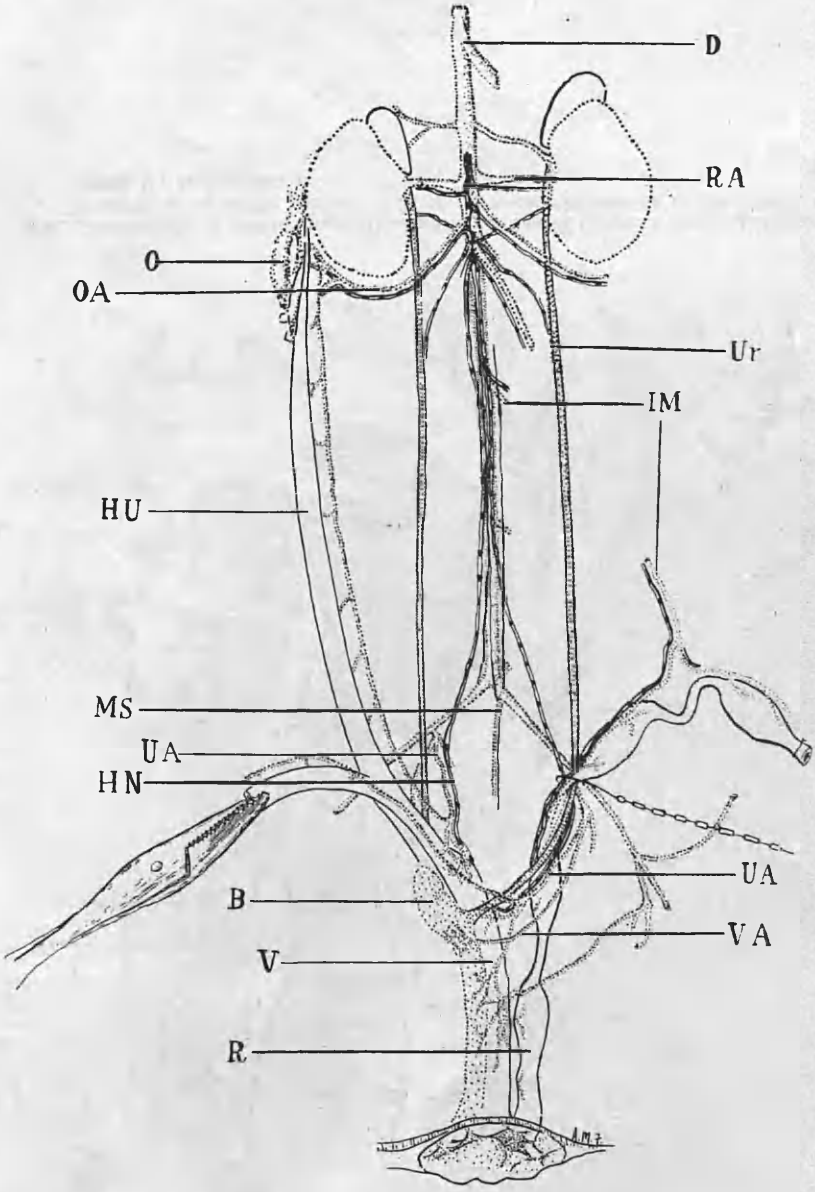


FIG. 1.—Dissection of aortic, inferior mesenteric nerve plexuses, and hypogastric nerves, HN, in the guinea-pig. B, bladder; D, descending aorta; HU, uterine horn; IM, inferior mesenteric artery; MS, middle sacral artery; O, ovary; OA, ovarian artery; R, rectum; RA, renal artery; UA, uterine artery; Ur, ureter; V, vagina; VA, vesical artery.

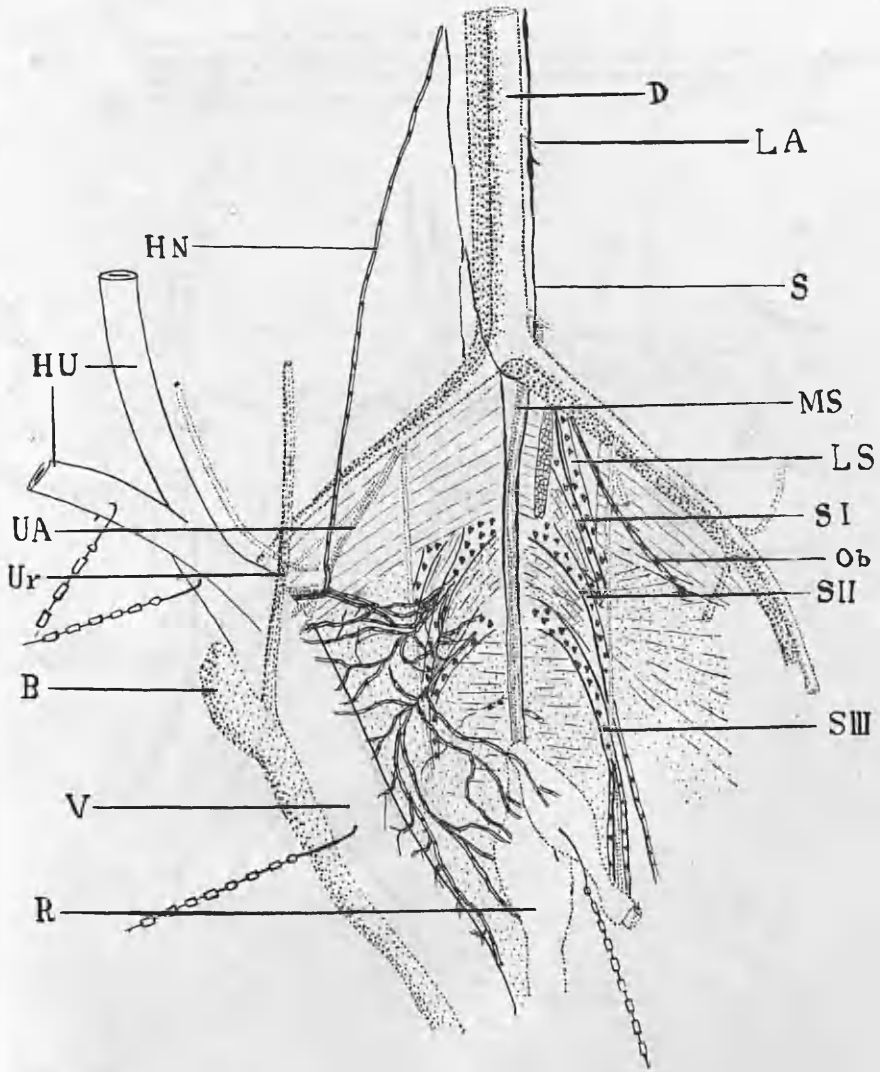


FIG. 2.—Dissection of hypogastric plexus in the guinea-pig. B, bladder; D, descending aorta; HN, hypogastric nerve; HU, uterine horn; LA, lumbar artery; LS, lumbo-sacral nerve trunk; MS, middle sacral artery; Ob, obturator nerve; R, rectum; S, vertebral sympathetic nerve trunk; SI, SII, and SIII, first, second, and third sacral nerves; UA, uterine artery; Ur, ureter; V, vagina.

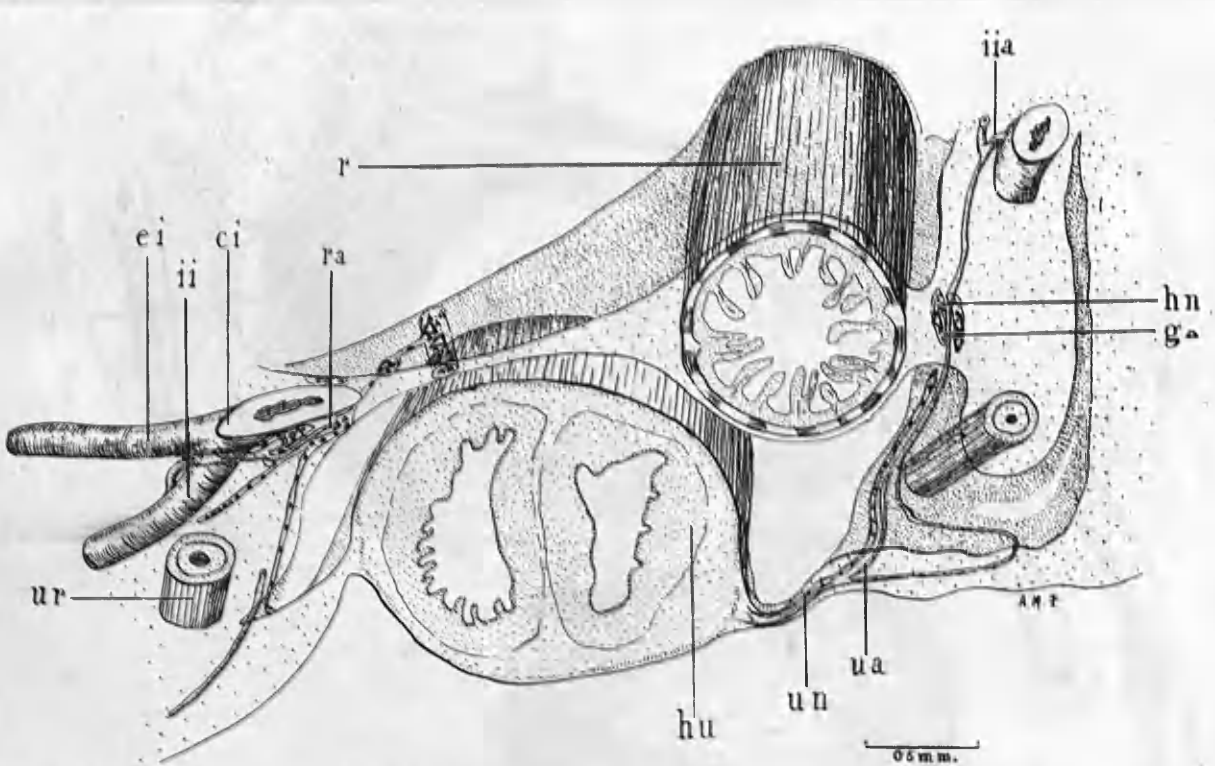


FIG. 3.—Fœtal guinea-pig (60 days). Diagram of reconstruction (sections 1449–1595) as seen from the cranial aspect. Showing *ci*, common iliac artery; *ei*, external iliac artery; *gΔ*, position of nerve-cells; *hn*, hypogastric nerve; *hu*, uterine horn; *ii*, internal iliac artery; *iia*, anterior division internal iliac artery; *r*, rectum; *ra*, artery to rectum; *ua*, uterine artery; *un*, uterine nerve; and *ur*, ureter.

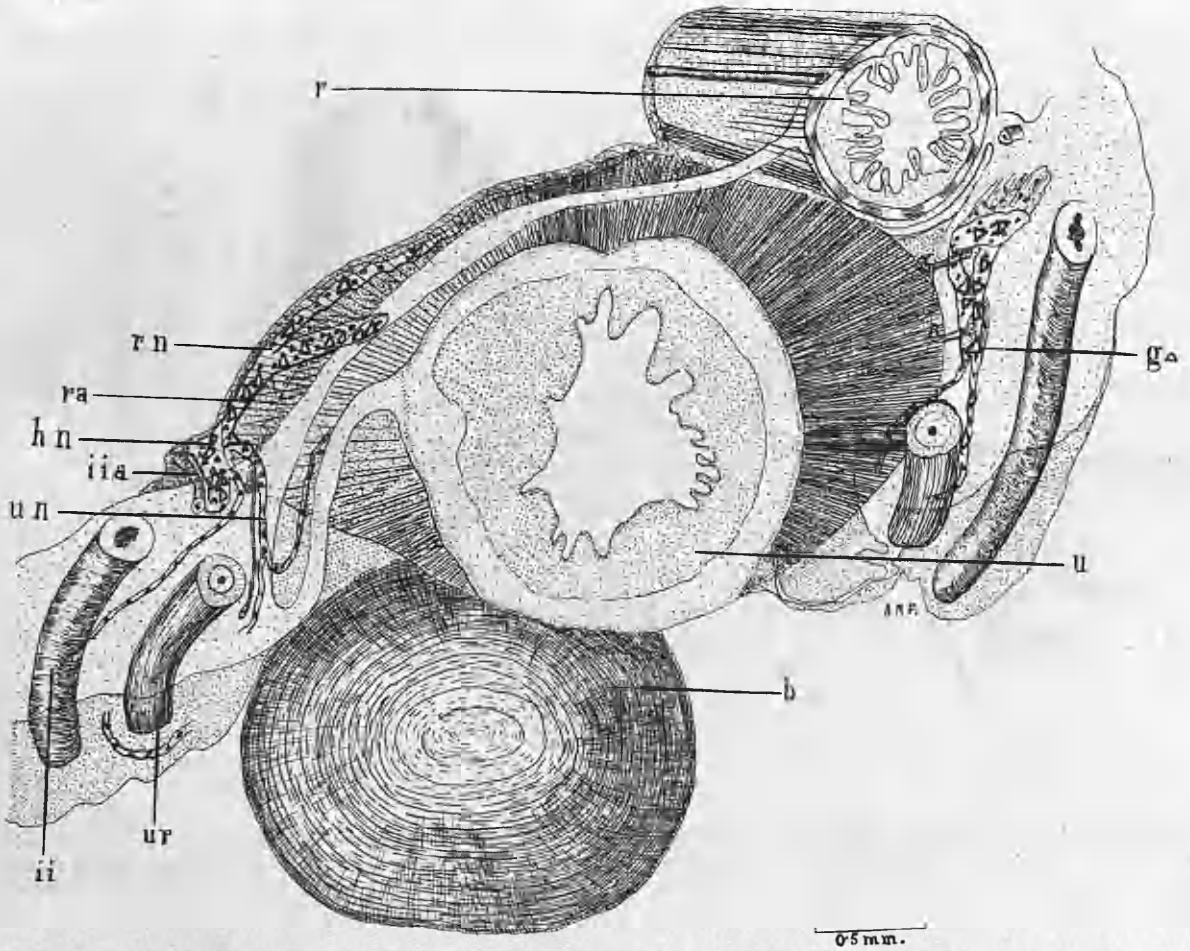


FIG. 4.—Fœtal guinea-pig (60 days). Diagram of reconstruction (sections 1252–1449) as seen from the cranial aspect. Showing *b*, bladder, *g*Δ position of nerve-cells; *hn*, hypogastric nerve; *ii*, internal iliac artery; *iia*, anterior division internal iliac artery; *r*, rectum; *ra*, artery to rectum; *rn*, nerve to rectum; *u*, uterus; *un*, uterine nerve; and *ur*, ureter.

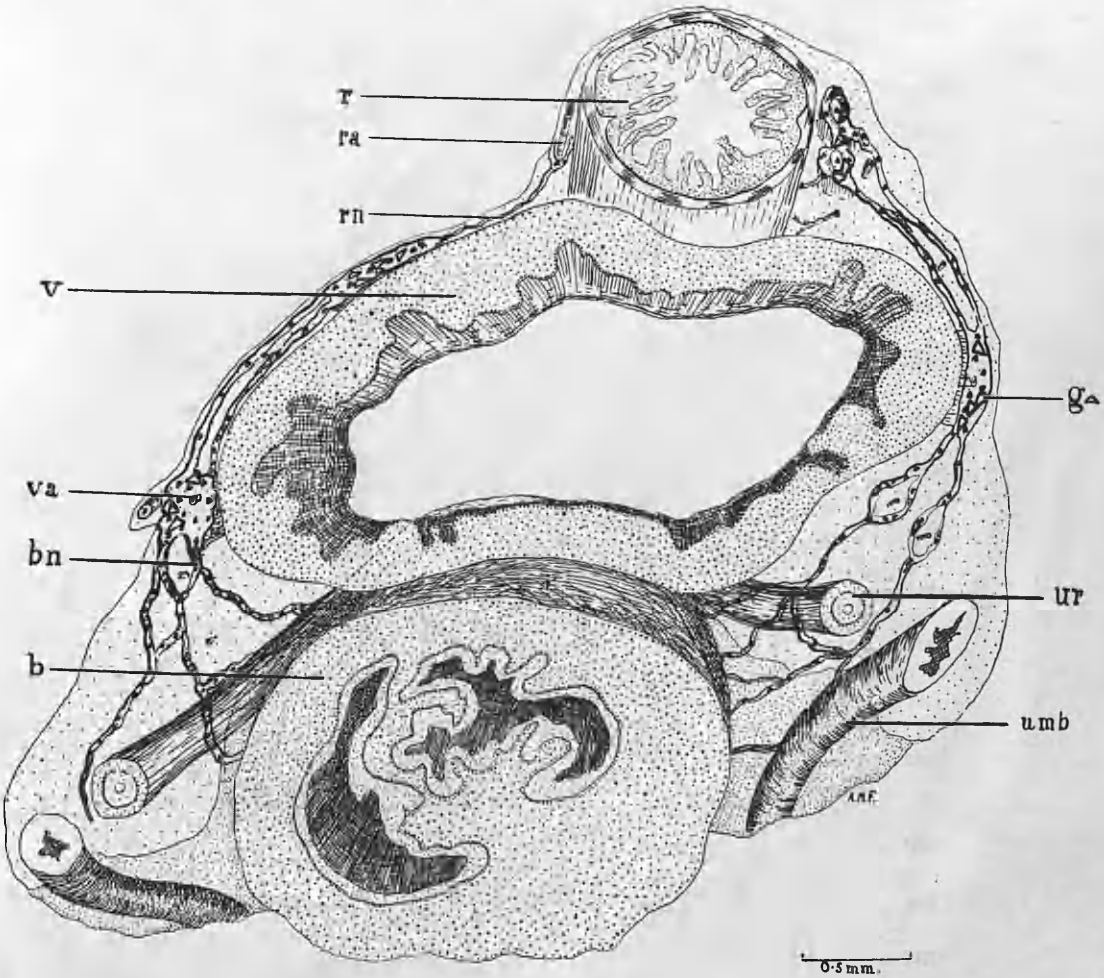


FIG. 5.—Fœtal guinea-pig (60 days). Diagram of reconstruction (sections 1032–1252) as seen from the cranial aspect. Showing *b*, bladder; *bn*, nerve to bladder; *g*Δ, position of nerve-cells; *r*, rectum; *ra*, artery to rectum; *rn*, nerve to rectum; *umb*, umbilical artery; *ur*, ureter; *v*, vagina; and *va*, vaginal artery.

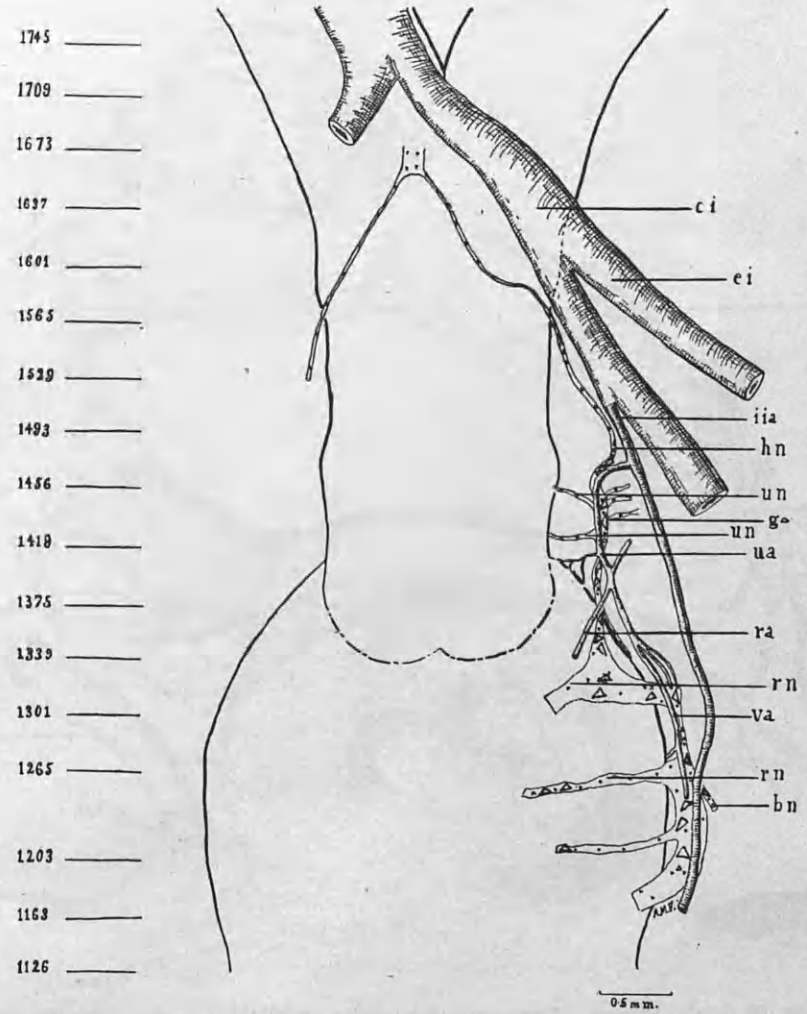


FIG. 61.—Fœtal guinea-pig (60 days). Graphical reconstruction of the nerves and arteries to the uterus and vagina (sections 1126–1745). *bn*, nerve to bladder; *ci*, common iliac artery; *ei*, external iliac artery; *hn*, hypogastric nerve; *iia*, anterior division internal iliac artery; *g*Δ, position of nerve-cells; *ra*, artery to rectum; *rn*, nerve to rectum; *ua*, uterine artery; *un*, uterine nerve; and *va*, vaginal artery.

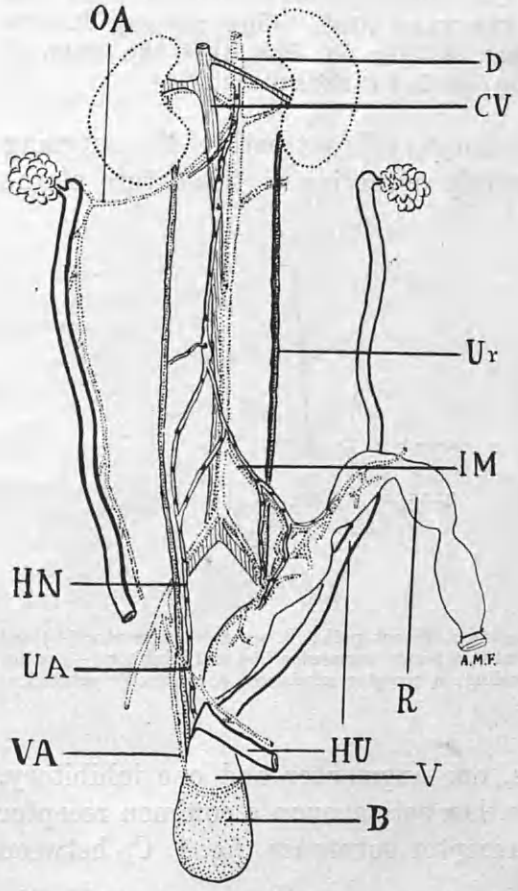


FIG. 7.—Dissection of aortic, inferior mesenteric nerve plexuses, and hypogastric nerves, HN, in the rat. B, bladder; D, descending aorta; CV, inferior vena cava; HU, uterine horn; IM, inferior mesenteric artery; OA, ovarian artery; R, intestine; UA, uterine artery; Ur, ureter; V, vagina; VA, vesical artery.

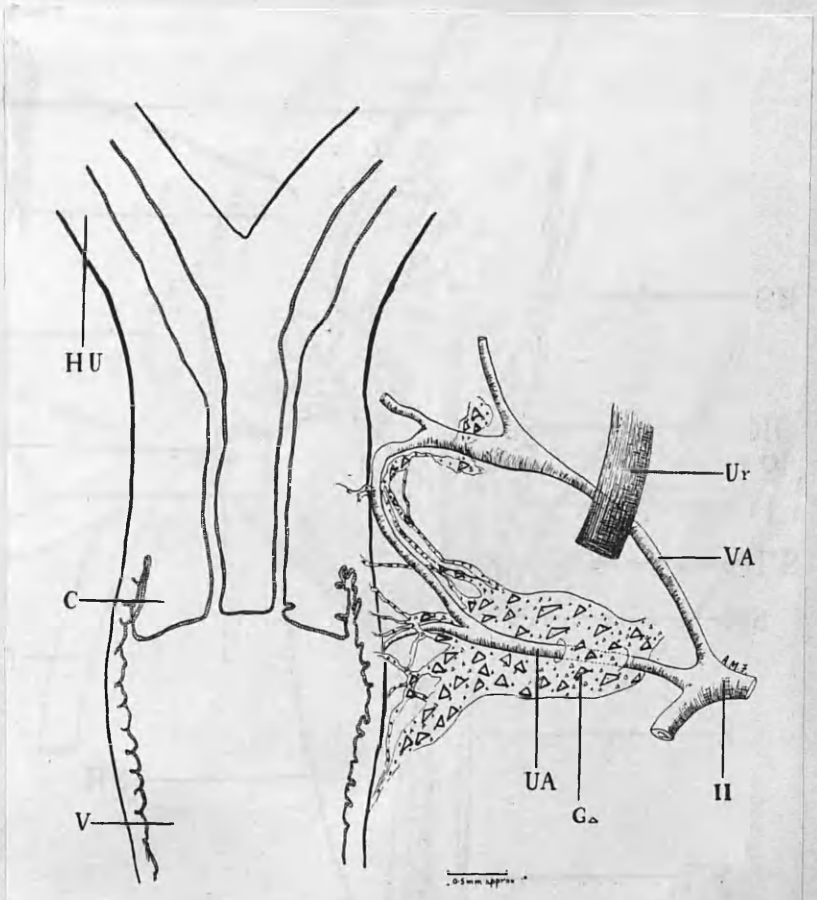


FIG. 8.—Diagram from the reconstruction (posterior view) of the pelvic organs in the adult rat showing C, cervix; GΔ, position of nerve-cells; HU, uterine horn; II, internal iliac artery; UA, uterine artery; Ur, ureter; V, vagina; and VA, vesical artery.

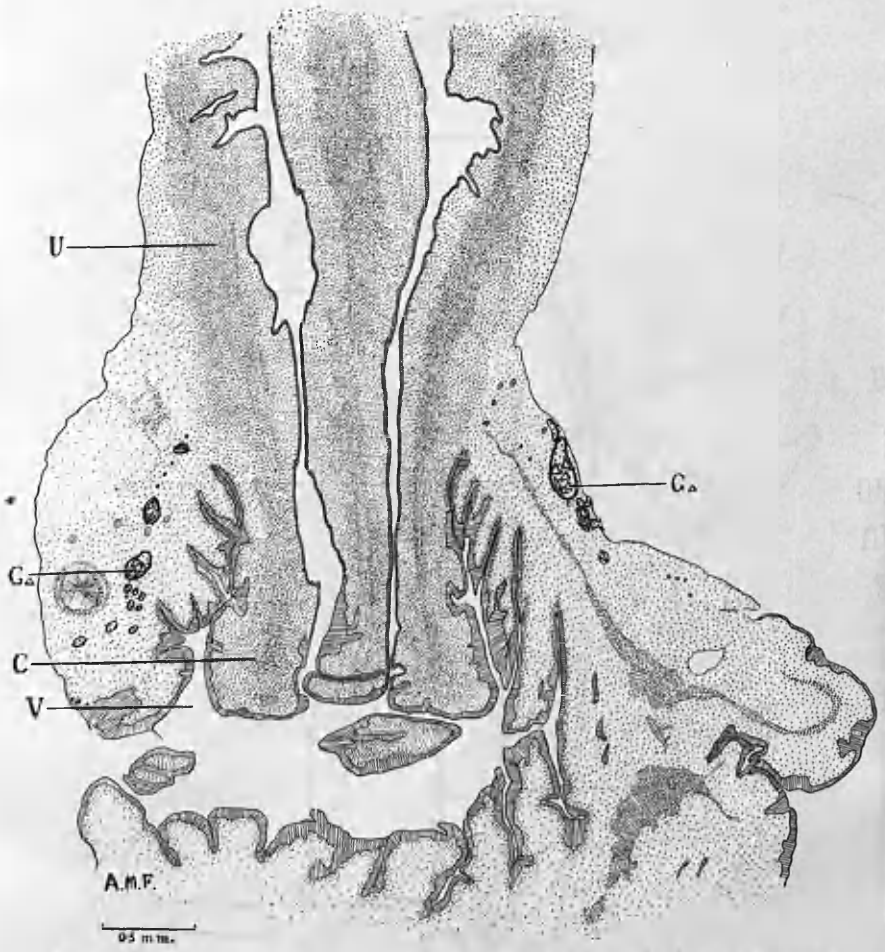


FIG. 9.—Diagram of part of longitudinal section No. 64 of the genital organs of a newborn rat to show the position, GΔ, of nerve-cells in relation to the cervix, C; uterus, U; and vagina, V.

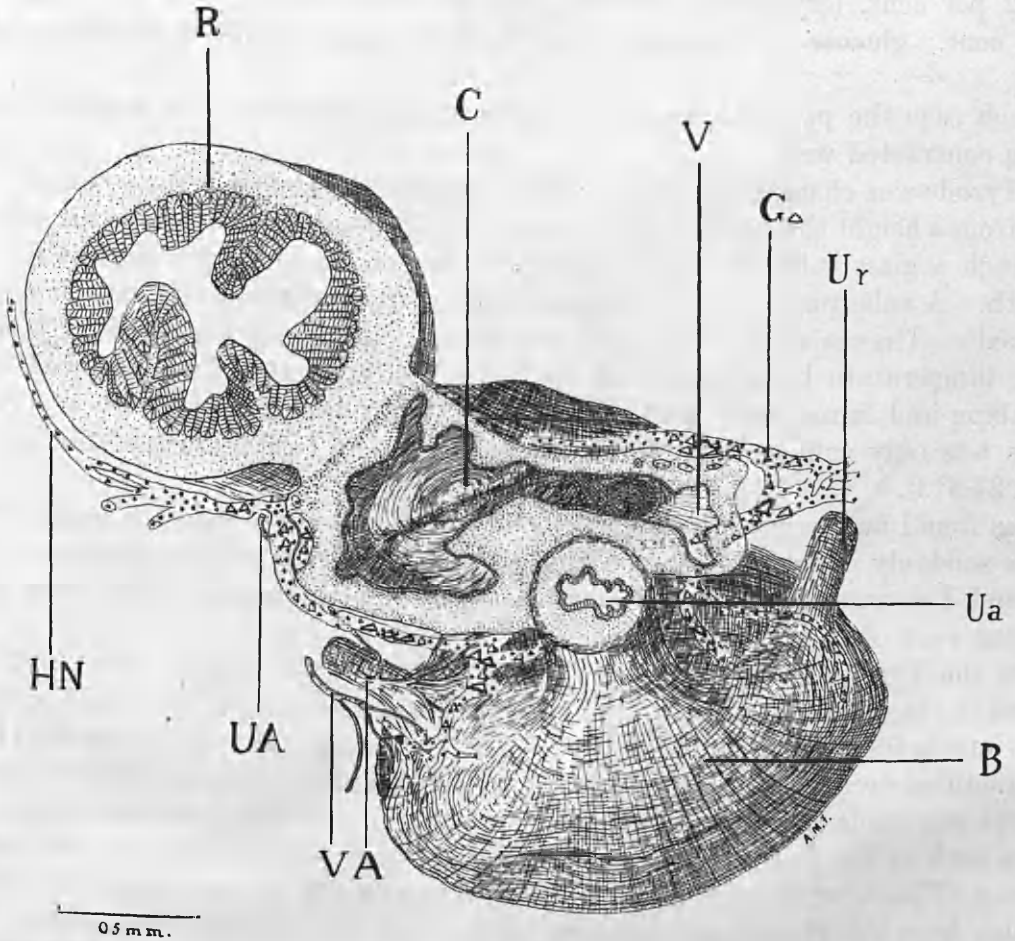


FIG. 10.—Mouse. Diagram of reconstruction (sections 647–785) seen from caudal aspect. Showing B, bladder; C, cervix; GΔ, position of nerve-cells; HN, hypogastric nerve; R, rectum; UA, uterine artery; Ua, urethra; Ur, ureter; V, vagina; and VA, vesical artery.

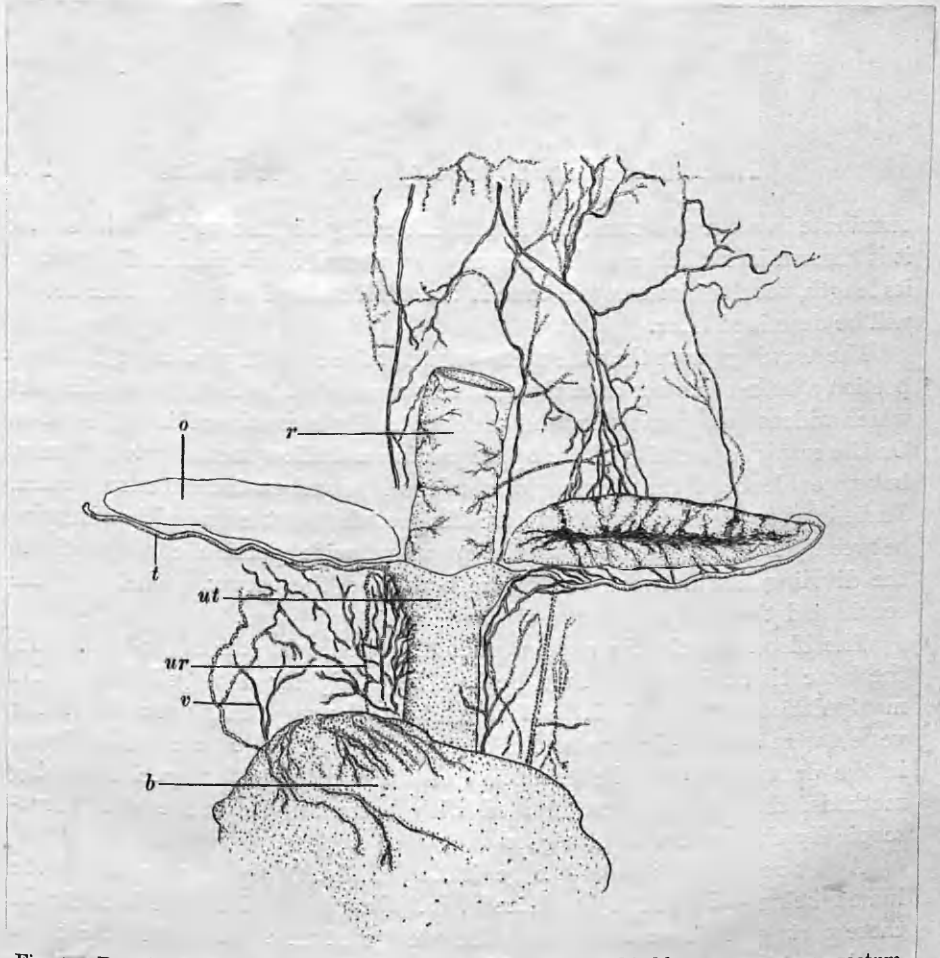


Fig. 11 Drawing of upper part of block while in xylol. *b* = bladder, *o* = ovary, *r* = rectum, *t* = Fallopian tube, *ur* = ureter, *ut* = uterus, *v* = blood vessels.

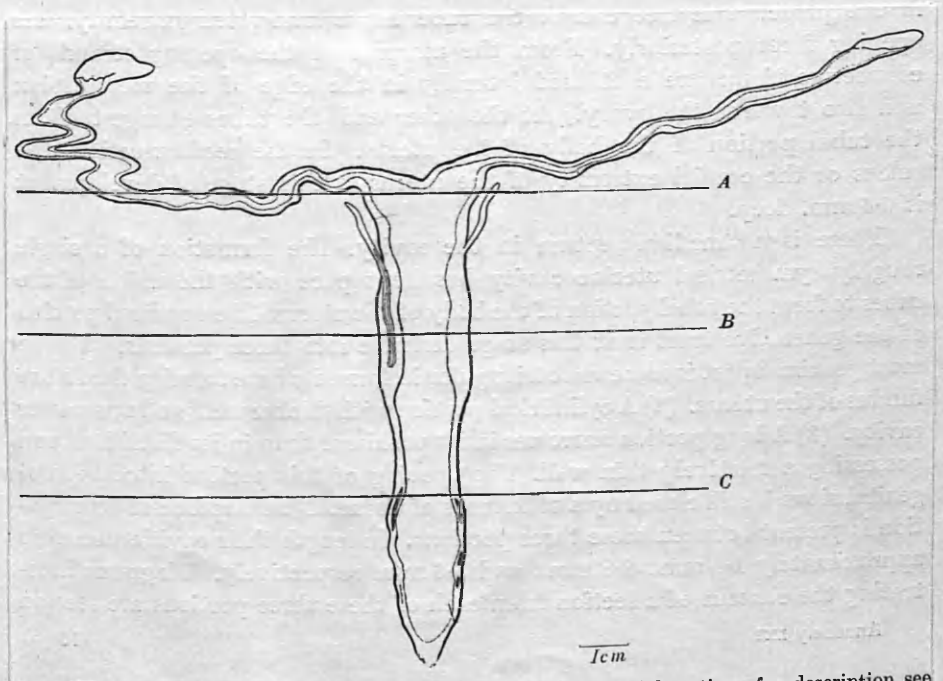


Fig. 12 Flat reconstructions of the genital tract from the serial section: for description see text. The levels from which Fig. 3 (*A*, *B*, *C*) are taken are indicated.

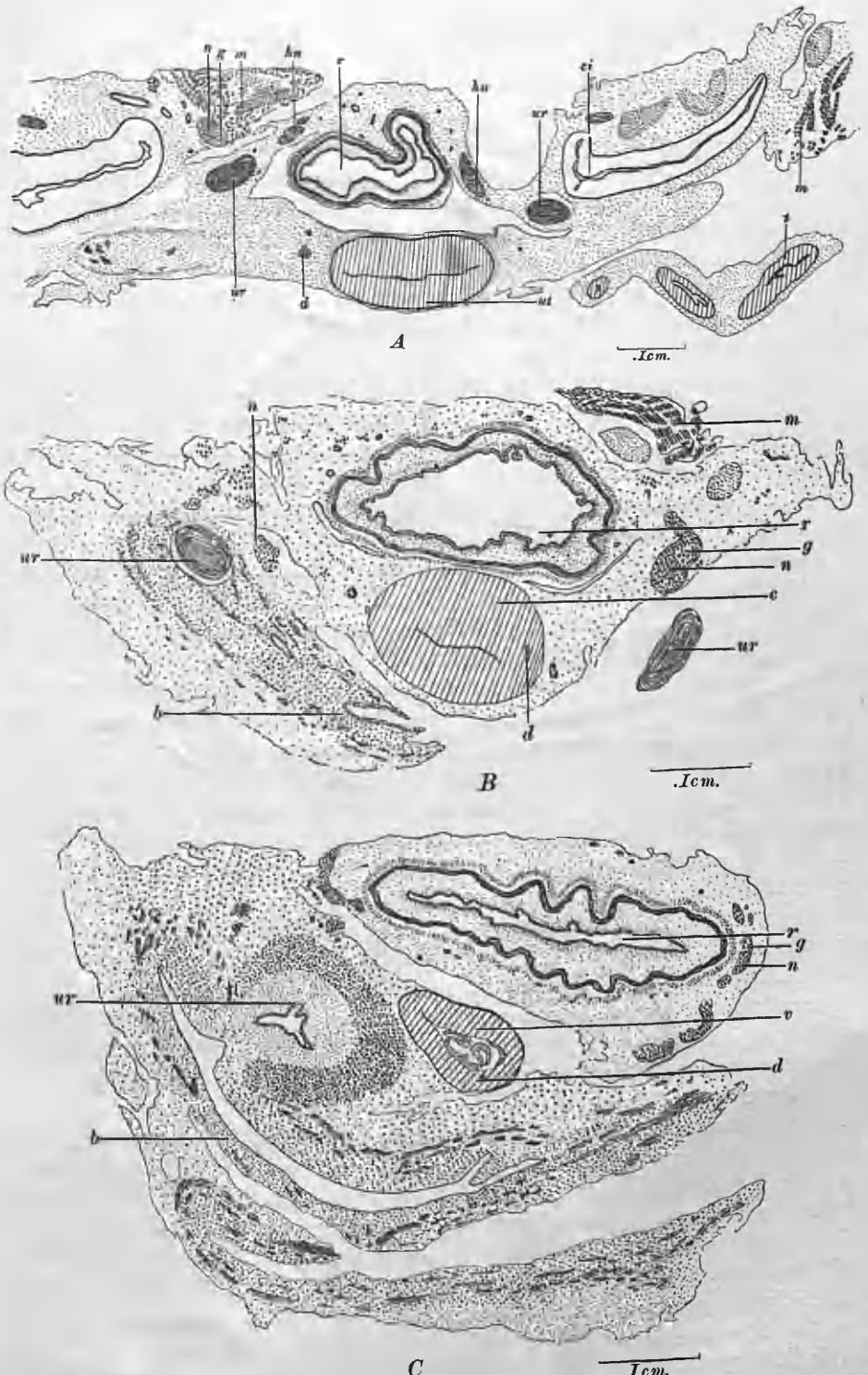


Fig. 13 *A*, transverse section no. 871: for level see fig. 2. *B*, transverse section no. 1159: for level see fig. 2. *C*, transverse section no. 1486: for level see fig. 2. *b* = bladder, *c* = cervix, *ci* = common iliac artery, *d* = Gärtner's duct, *g* = ganglionic nerve cell, *hn* = hypogastric nerve, *m* = striped muscle, *n* = nerve bundle, *r* = rectum, *t* = Fallopian tube, *ut* = body of uterus, *ur* = ureter, *v* = vagina.

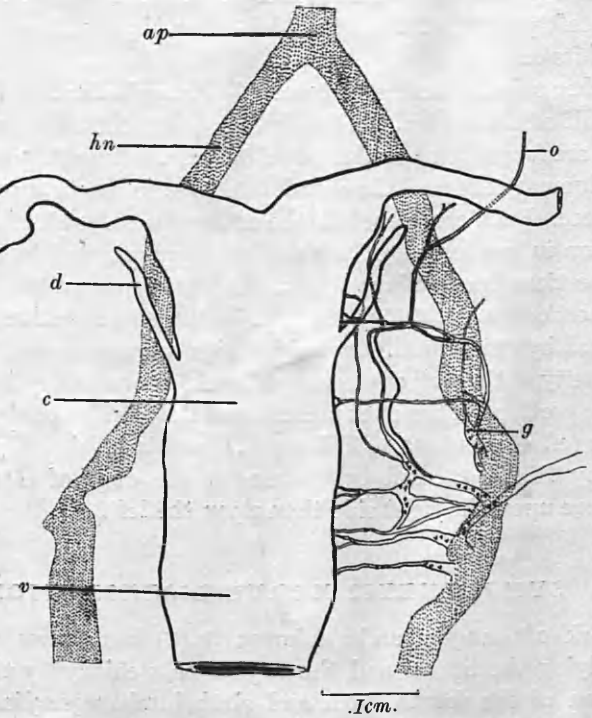


Fig. 14 Flat reconstruction of the nerves from the serial sections. *ap*=aortic plexus, *c*=cervix, *d*=Gärtner's duct, *g*=position of ganglionic nerve cell, *hn*=hypogastric nerve, *o*=nerve to the ovary, *v*=vagina.

FIGURE 15.

Photograph of a group of nerve cells on a nerve bundle in the Human myometrium under the utero-vesical reflexion of peritoneum.

J.T.Bell.

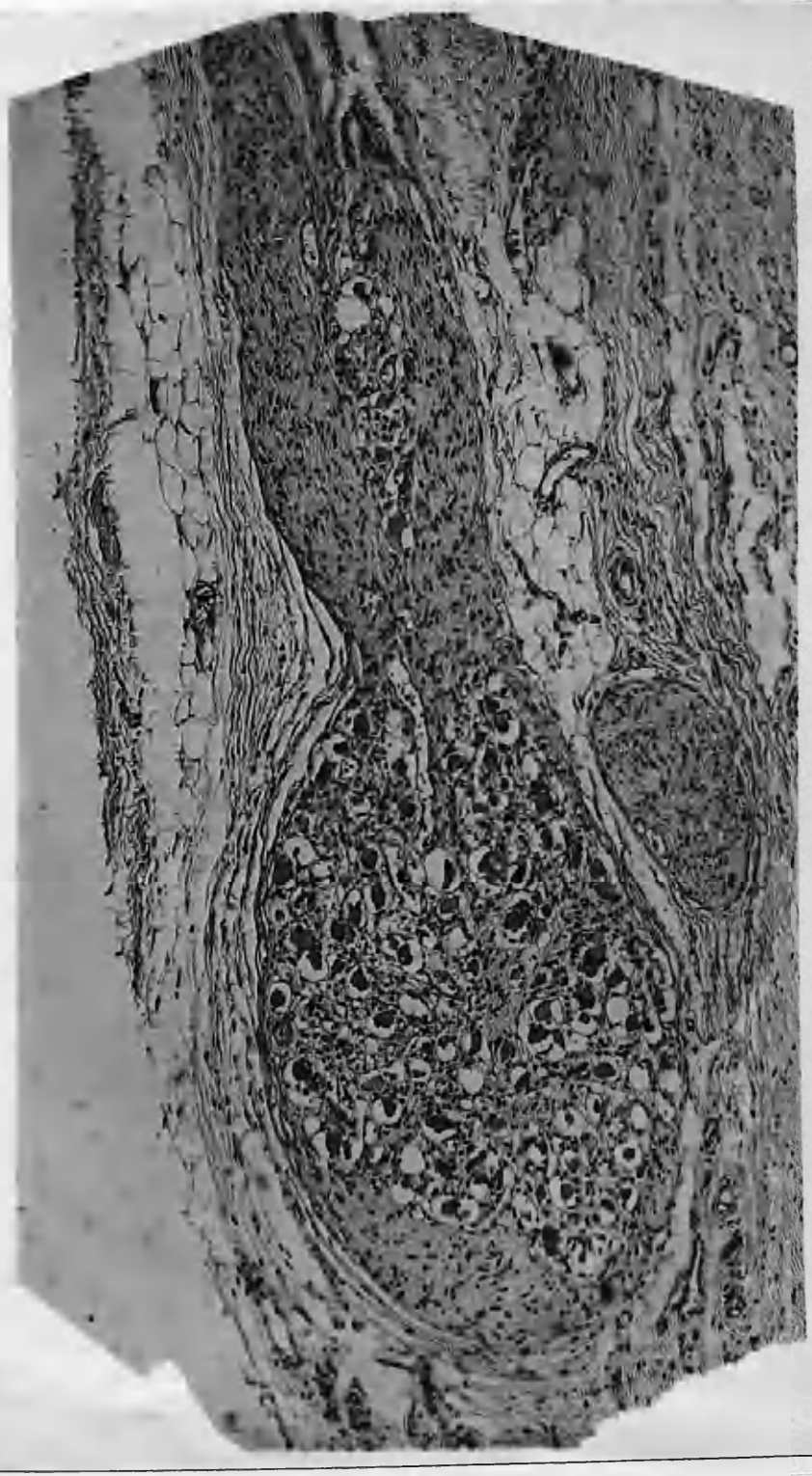


Fig.I5

FIGURE 16.

Nerve bundles in relation to vessels

in the uterus of the kitten.

Gold impregnation.

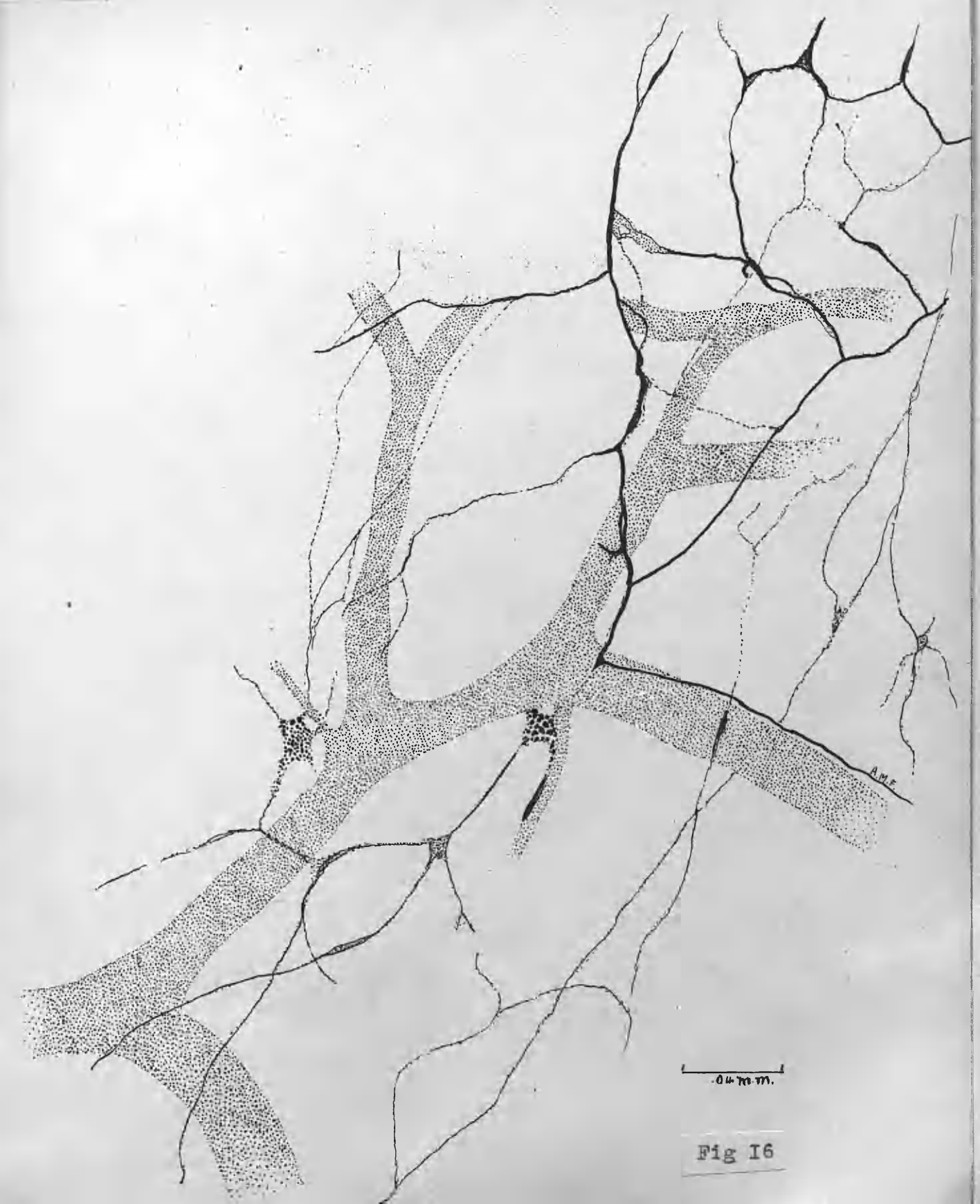


Fig I6

FIGURE 17.

Plexus of nerve bundles in the uterus of the kitten in the region of the bifurcation.

Gold impregnation.

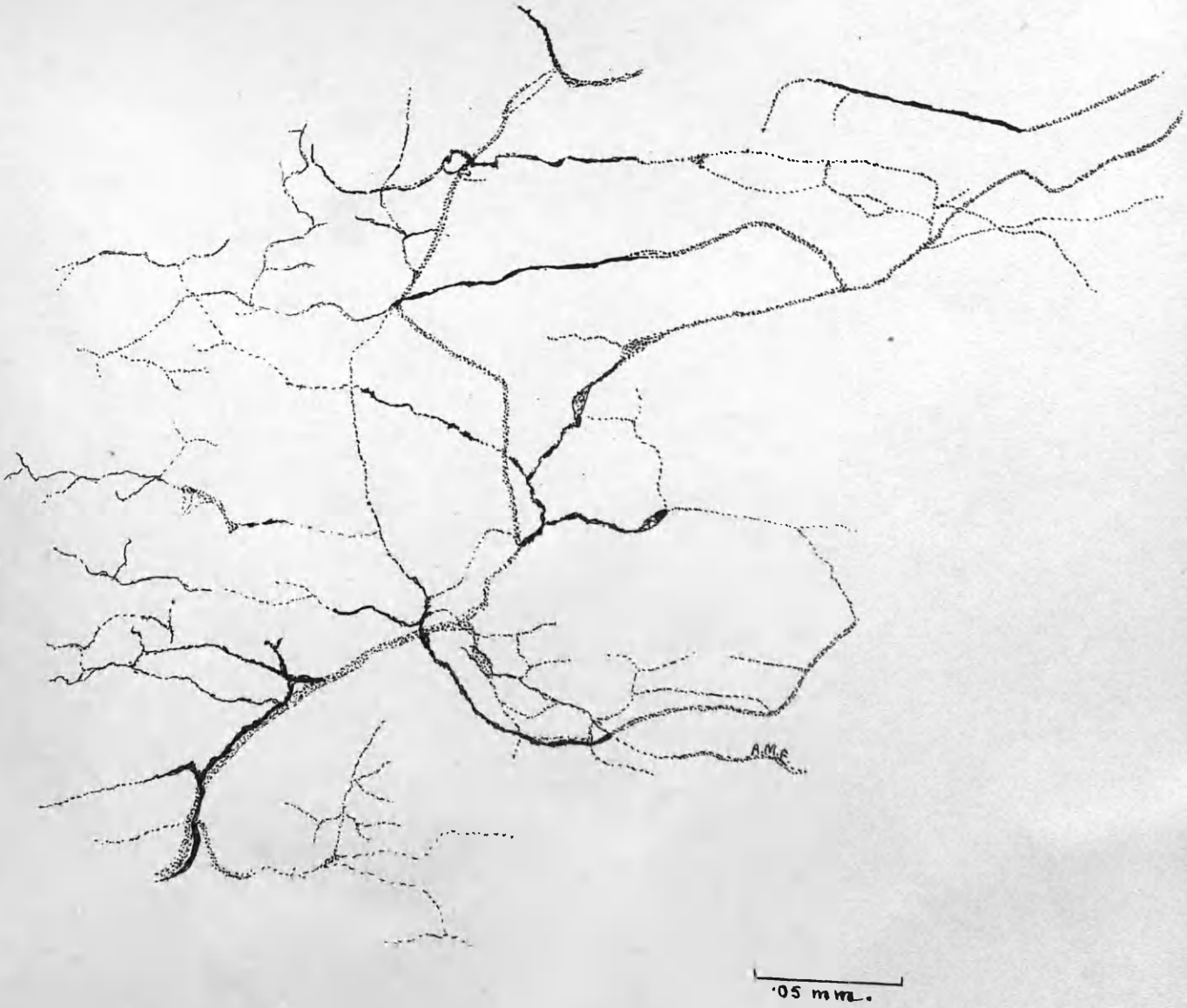


Fig.17

FIGURE 18.

Nerve plexus deep in the uterine muscle of the cat. The topmost nucleus seen in the plexus is an example of the first type of nucleus described as occurring on the nerve bundles. The cytoplasm of the nerve bundle stained faintly with methylene-blue.

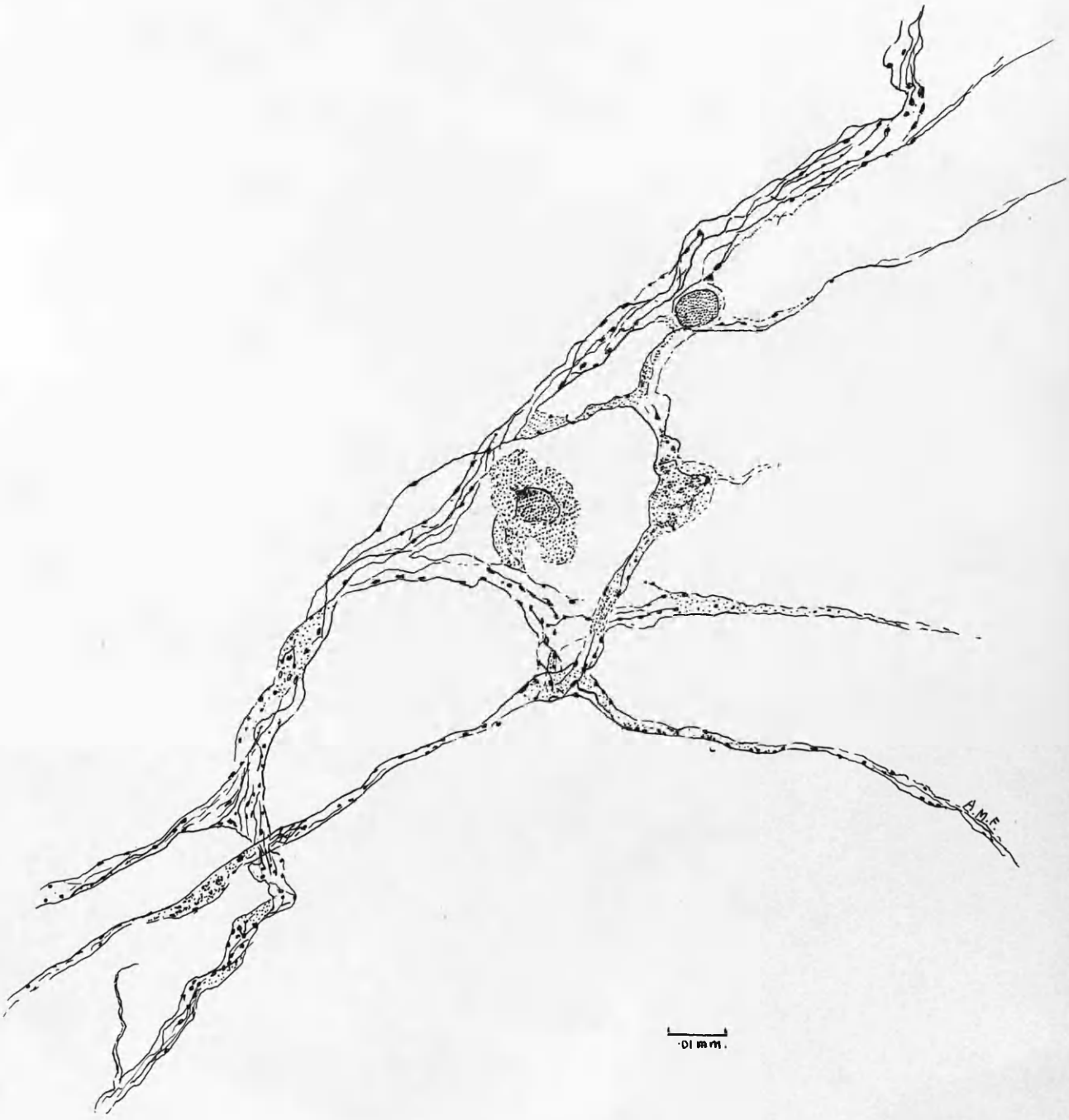


Fig.I8

FIGURE 19.

Nerve plexus is shown in contrast to capillary plexus in the uterine horn of the kitten near the mucous membrane.

Gold impregnation.

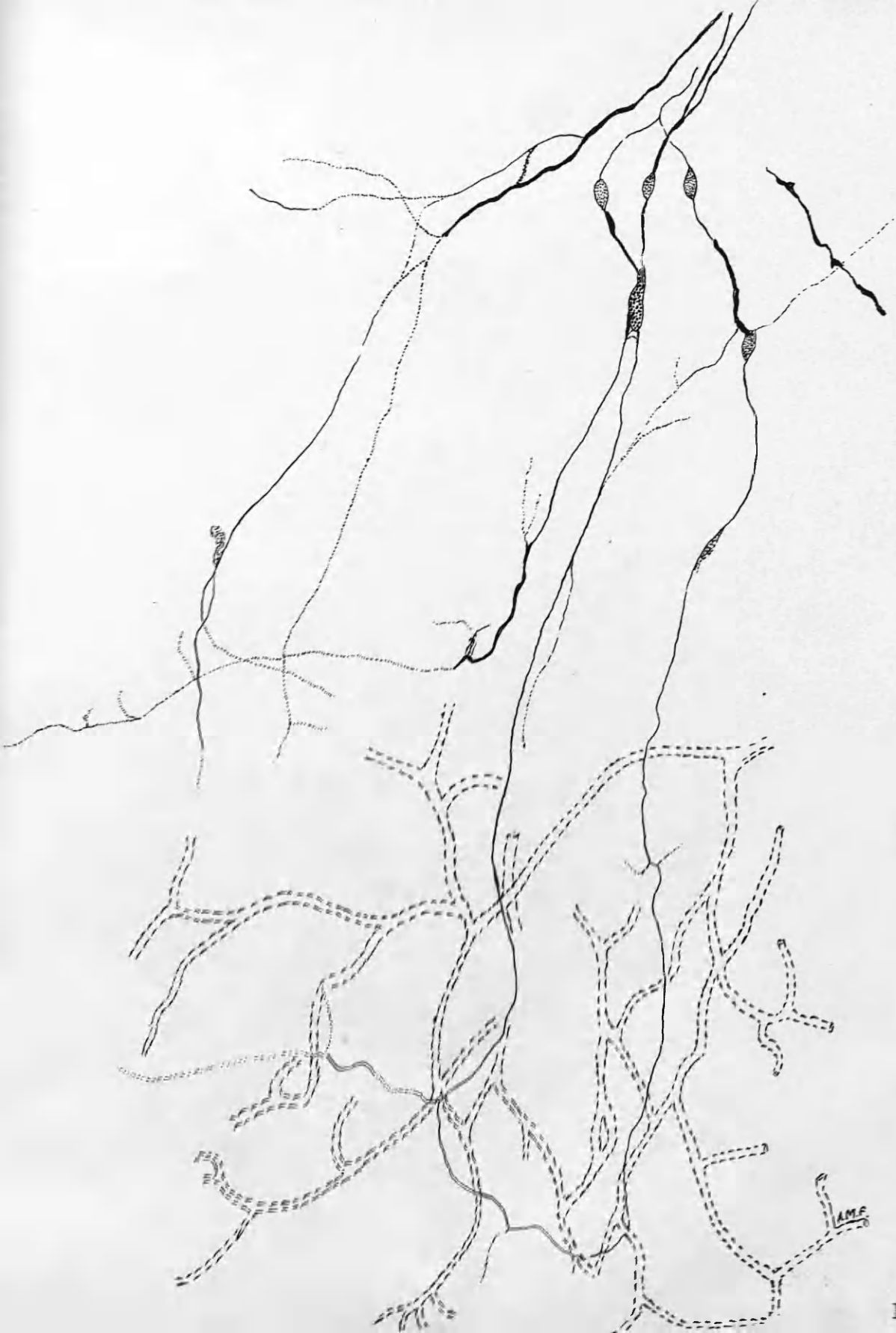


Fig.I9

FIGURE 20.

Undulating nerve bundles in the uterus of the cat, In each of the two bundles towards the right side there runs a thicker nerve fibre on which no varicosities are seen. The variation in size of the varicosities is noticeable.All the cells appearing in the field are shown in the reproduction. The connective tissue cells had dark blue nuclei without nucleoli. Their cytoplasm stained faintly and was granular.ON the lowest cross branch of the plexus the nucleuscontaining a nucleolus,stained a faint blue with methylene-blue.

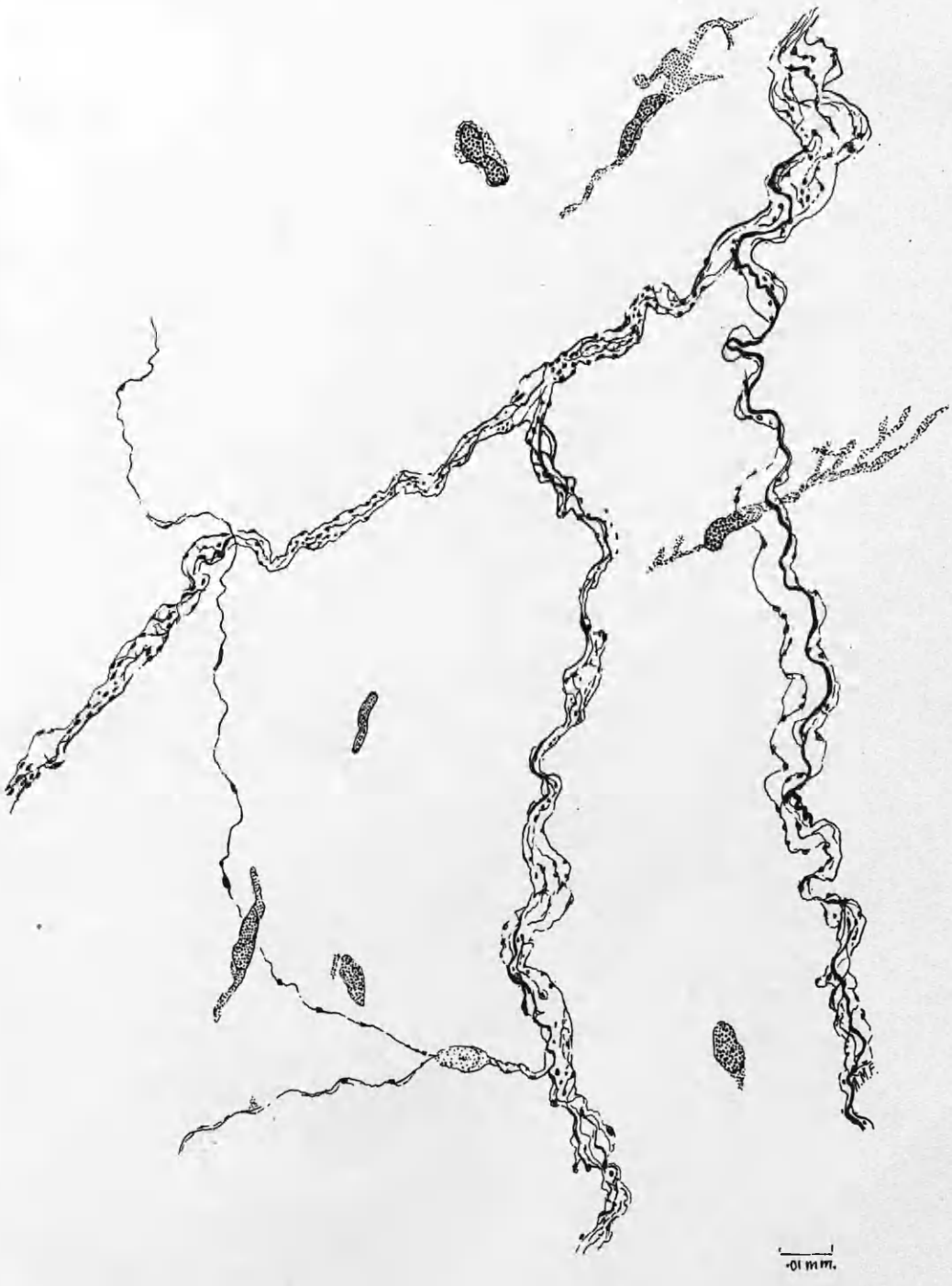


Fig.20

FIGURE 21.

Nerve bundles in the lower end of the uterus of the mouse.

Gros.

Fig.21

FIGURE 22.

A spindle shaped enlargement of a nerve bundle in the uterus of a cat.

Methylene-blue.

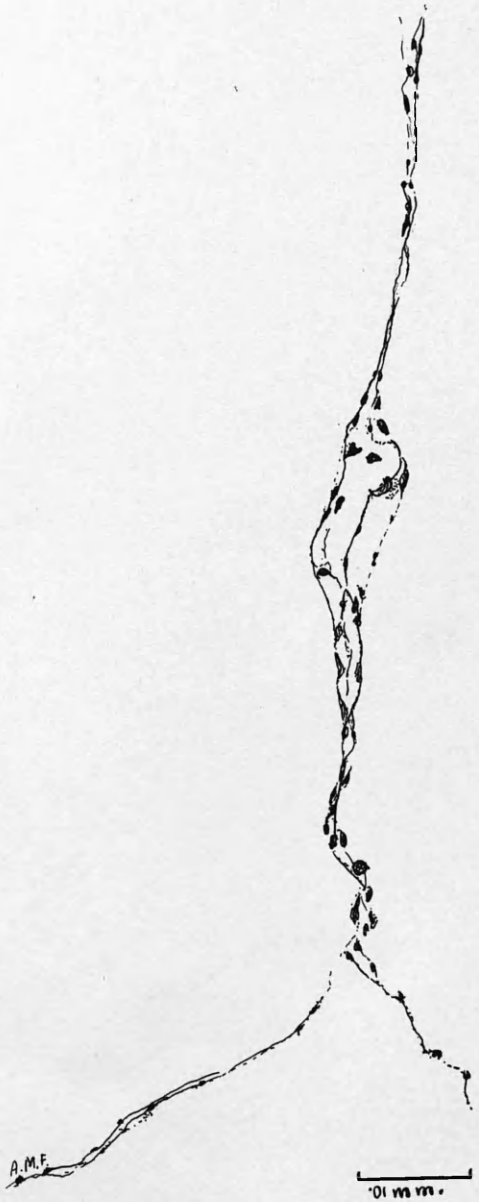


Fig.22

FIGURE 23.

Nerve bundle in the uterus of the cat showing three sizes of varicosities.

Methylene-blue.

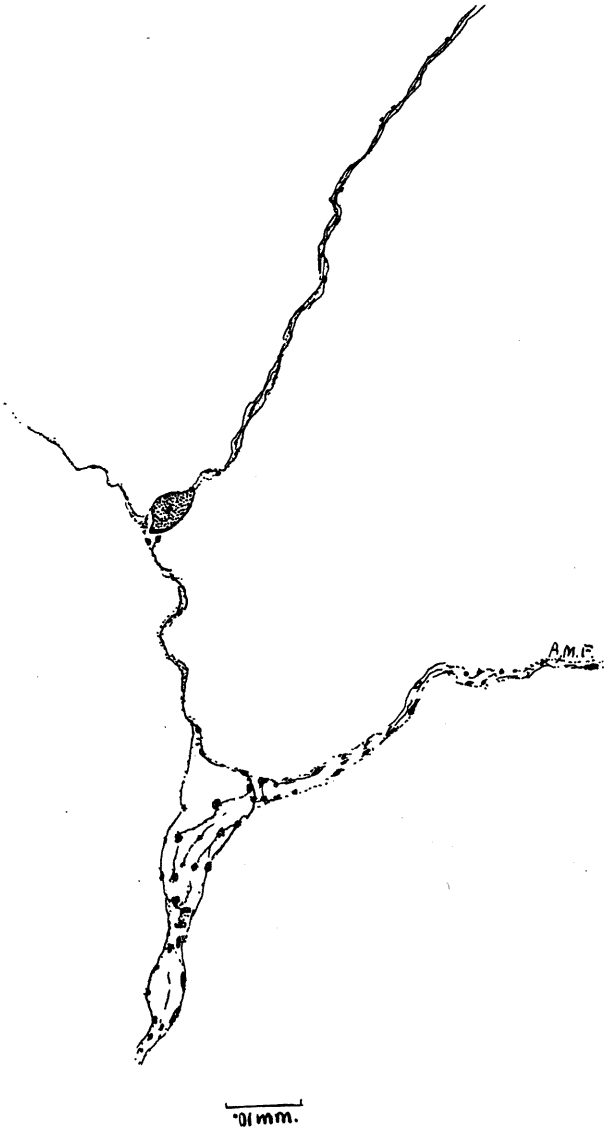


Fig. 23

FOGURE 24.

In a non-medullated nerve bundle--which ran parallel to the endometrium--variety in the size of the varicosities is seen.

Methylene-blue. Cat.

Fig. 24

FIGURE 25.

A fairly thick nerve bundle containing one coarse nerve fibre on which no varicosity is seen. No nuclei are seen on this nerve bundle. Variety in the fineness of the varicosities is seen equally in the main bundle and its branches.

Methylene-blue.

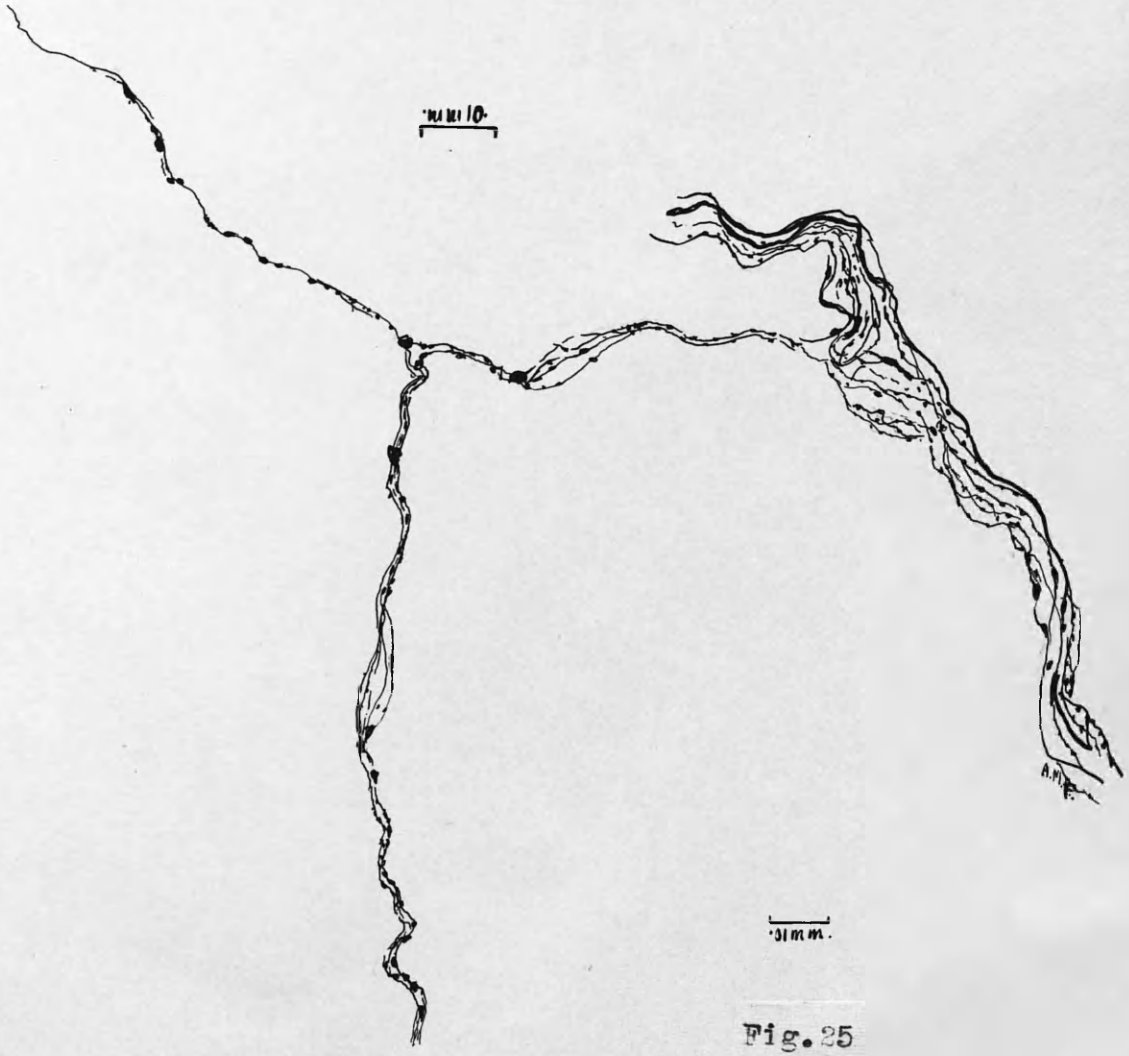


Fig. 25

FIGURE 26.

A fine non-medullated nerve is seen accompanied by a relatively thick non-varicose nerve fibre .

Methylene-blue.Cat.

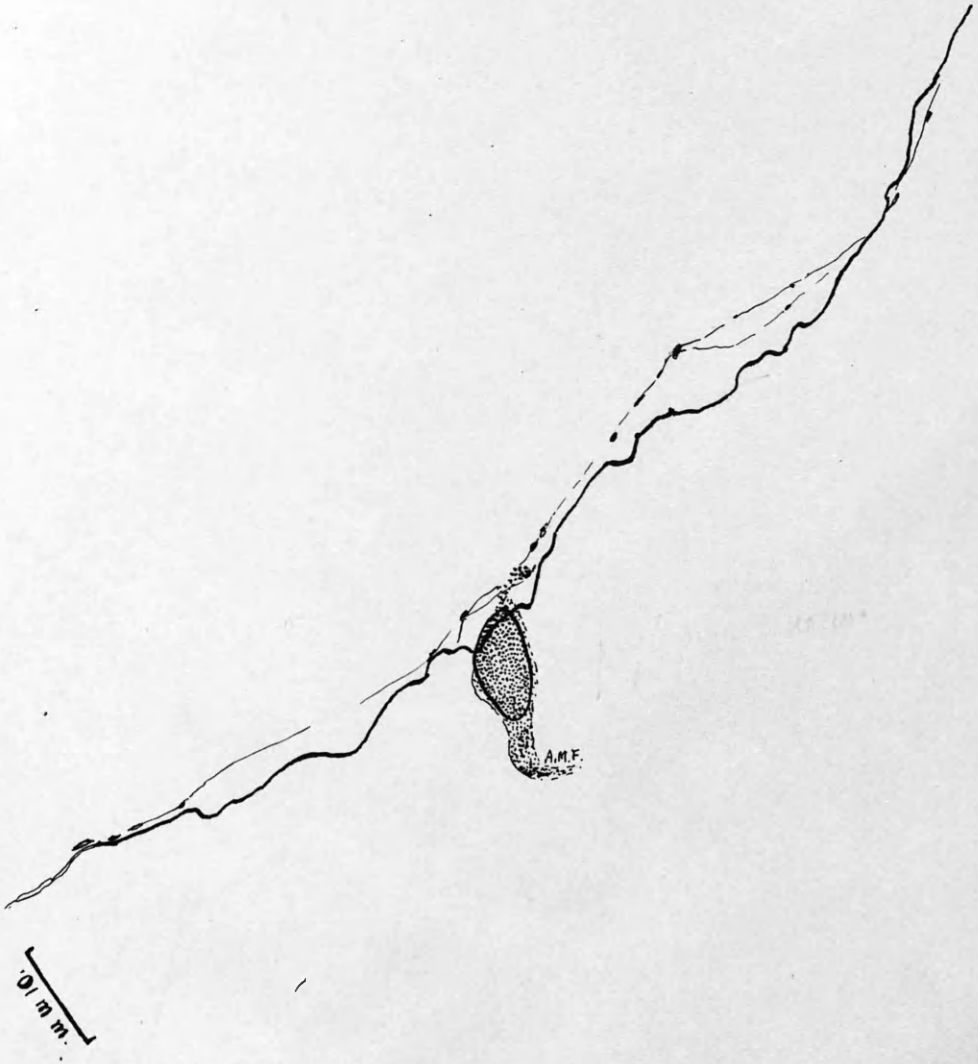


Fig.26

FIGURE 27.

Non medullated nerve plexus near the serous surface of the uterus of the cat.

Three types of nucleus are seen in the figure

(I) Nuclei on the course of the nerve bundles which were stained purplish,

(2) Nuclei of connective tissuecells which stained dark blue,

(3) Faintly staining nuclei considered to belong to endothelial cells.

Methylene-blue.

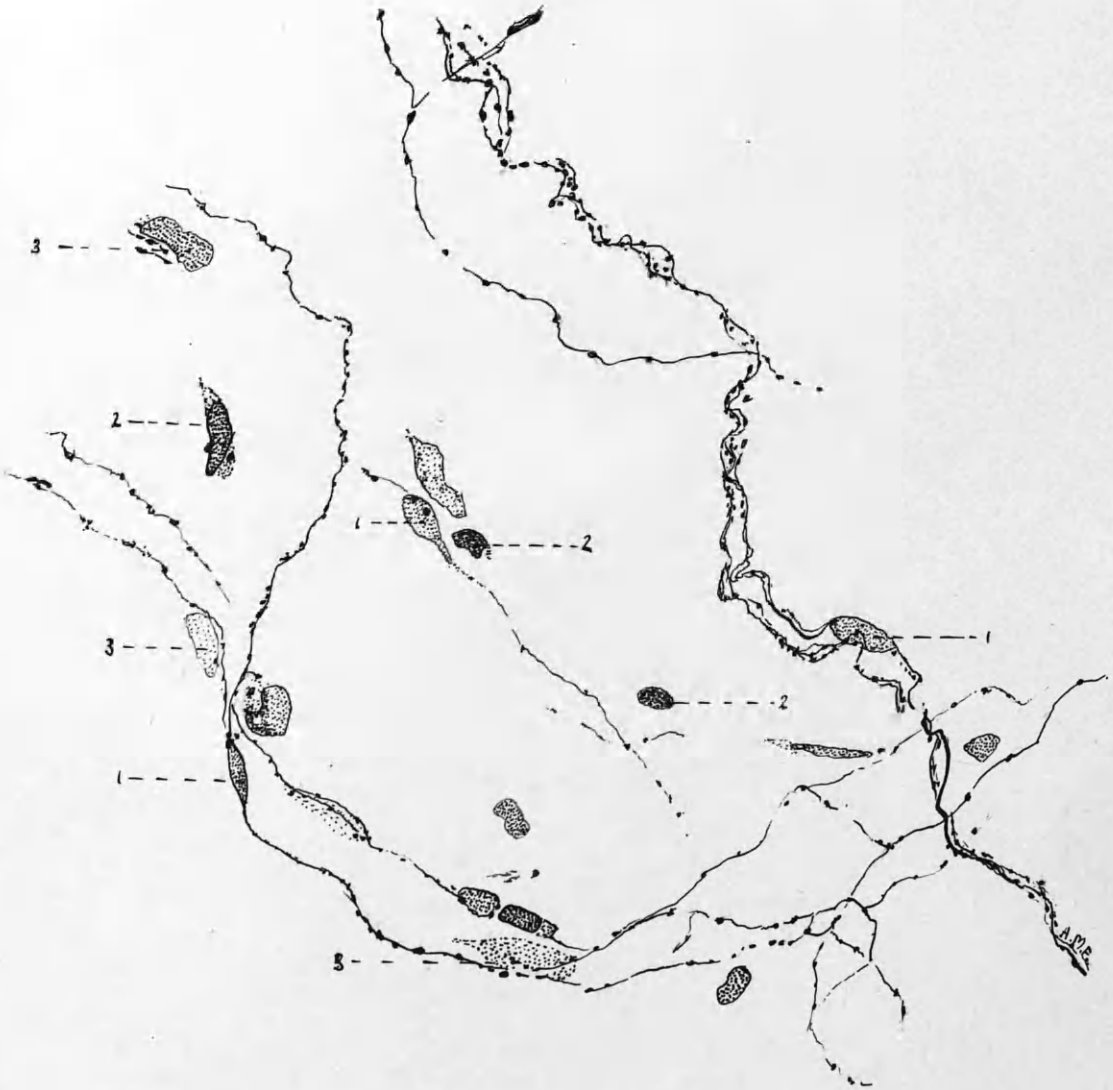


Fig.27

FIGURE 28.

An interchange of nerve fibrils is seen between the nerve bundles. All cells occurring in the field are shown with the exception of one lying at a higher plane than the plexus. The connective tissue cells had dark blue nuclei in which no nucleoli were seen. Lobulation of their nuclei is seen.

Methylene-blue Cat.

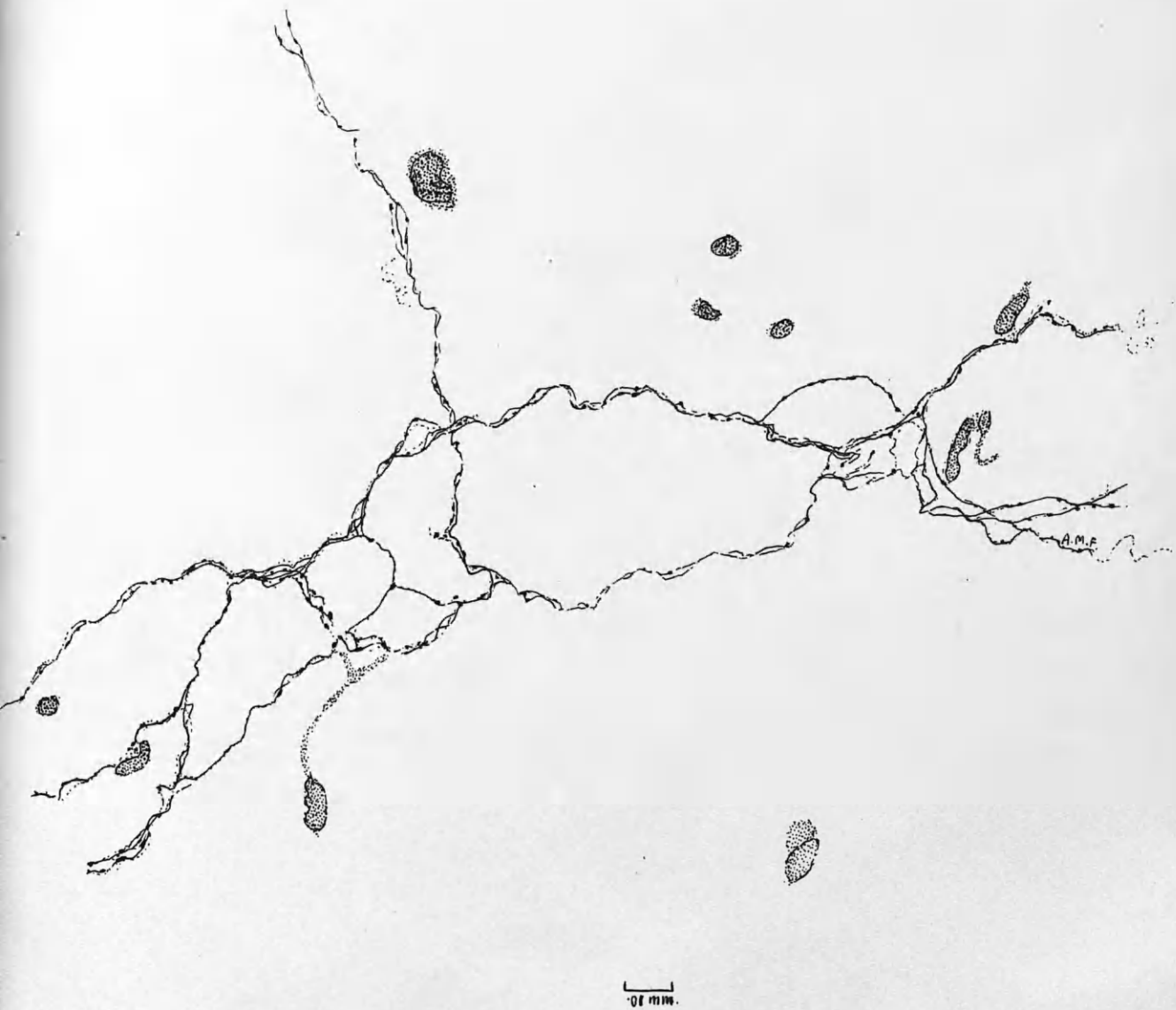


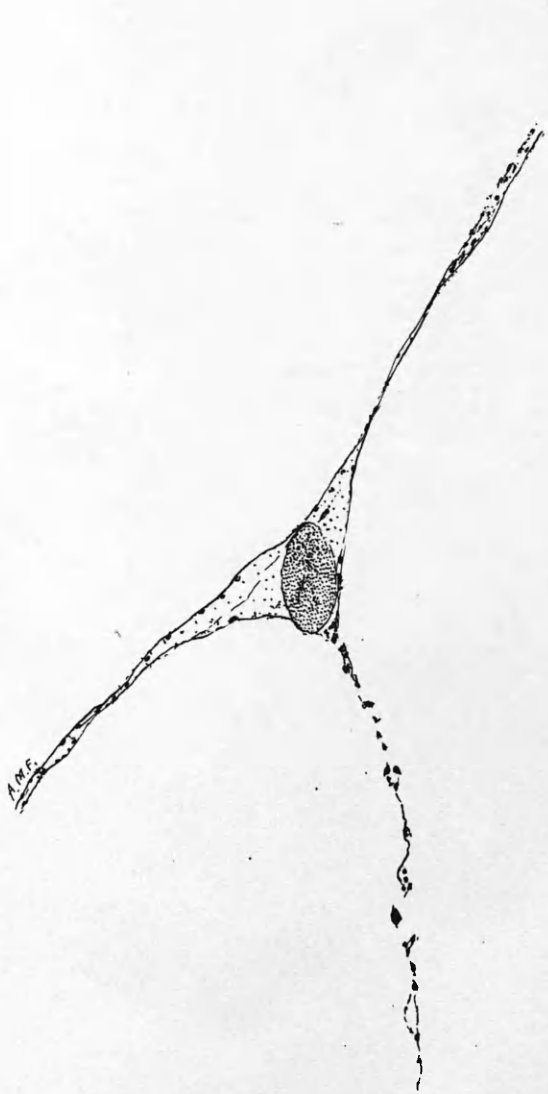
Fig.28

FIGURE 29..

(a) ON the left side a nucleus of Type I is seen at a point of division of a nerve bundle.

(b) On the right side a nucleus of Type II is seen on a nerve bundle. Note the presence of a thick fibre above the nucleus.

Methylene-blue, Cat.



.01 mm.

Fig.29a

Fig.29b

FIGURE 30.

Non-medullated nerve bundles seen in a section of myometrium taken at right angles to the endometrium of a cat. Two types of nucleus are seen on them, the upper narrow one staining dark blue, and the lower oval one bluish with methylene-blue.

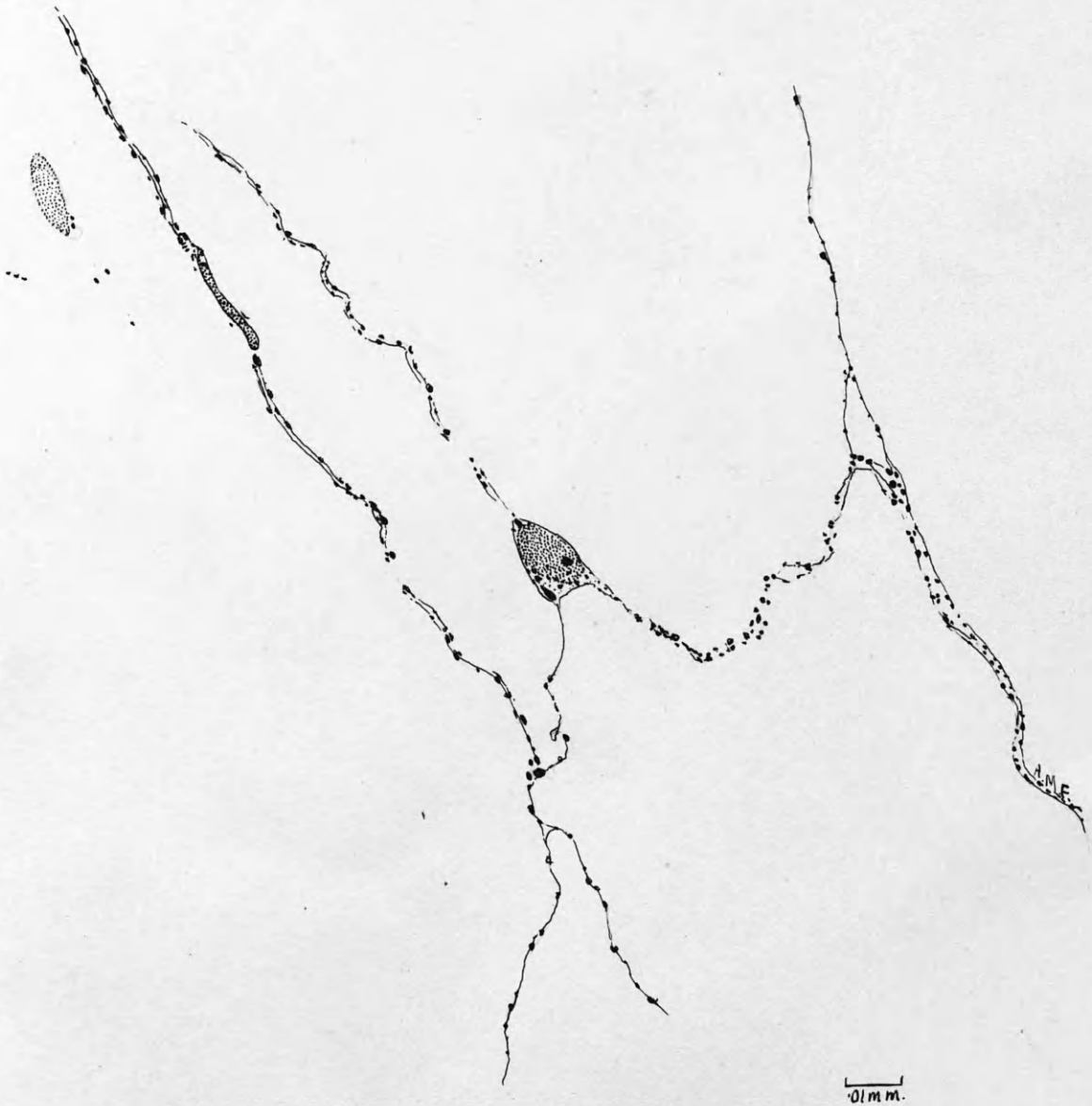


Fig.30

FIGURE 31.

Distinct nerve cell on the course of a fine nerve bundle. The cytoplasm fades away up and down the nerve bundle. The nucleus stained dark blue and is lobulated.

Methylene blue, Cat.

·01 m m.

Fig.3I

FIGURE 32.

Showing triangular formation of the cytoplasm of a nerve bundle at its point of division. The cytoplasm of the nerve bundle stained faintly blue with methylene-blue.

Uterus. Cat.

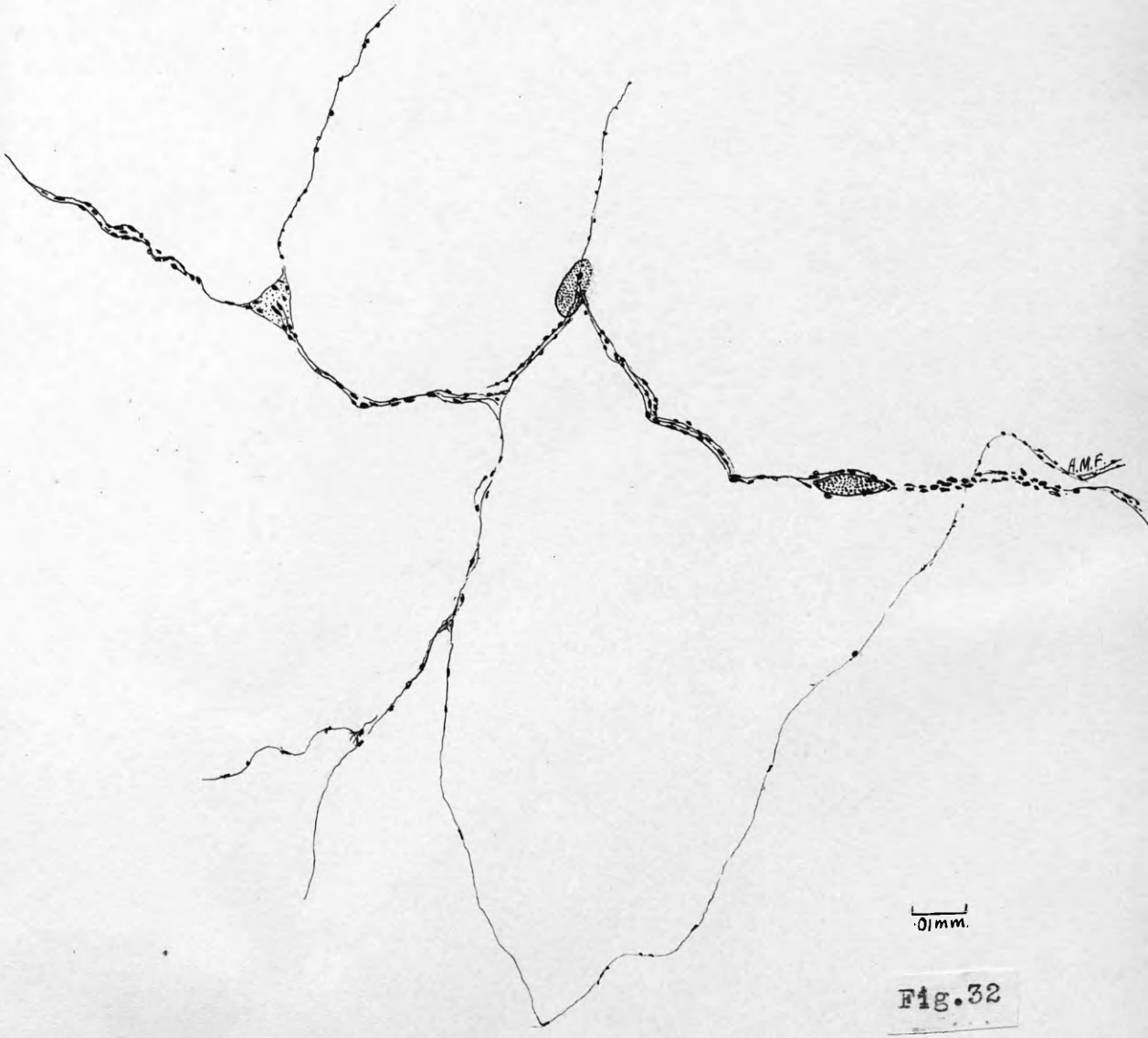


Fig.32

FIGURE 33.

Two nuclei of Schwann on a non-medullated nerve bundle running near the serous surface of the uterus of a cat.

Methylene-blue.

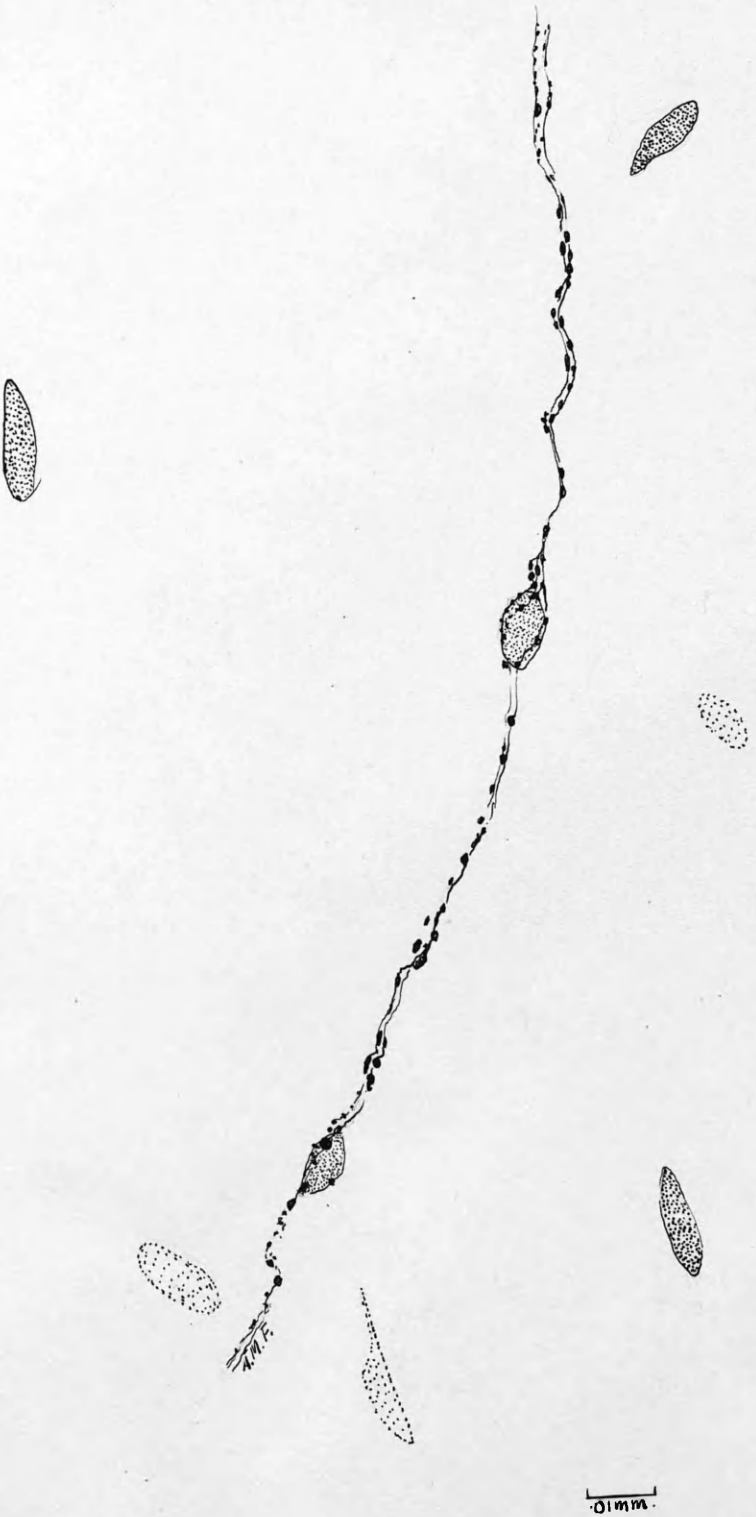


Fig.33

FIGURE 34

Fine-non-medullated nerve bundles in the uterus of the cat.

Oneis seen running under the serous surface (shown as a dotted line)and the other between the musclebundles.

Numerous nuclei of the second type are seen on the nerve bundles.

Methylene-blue.

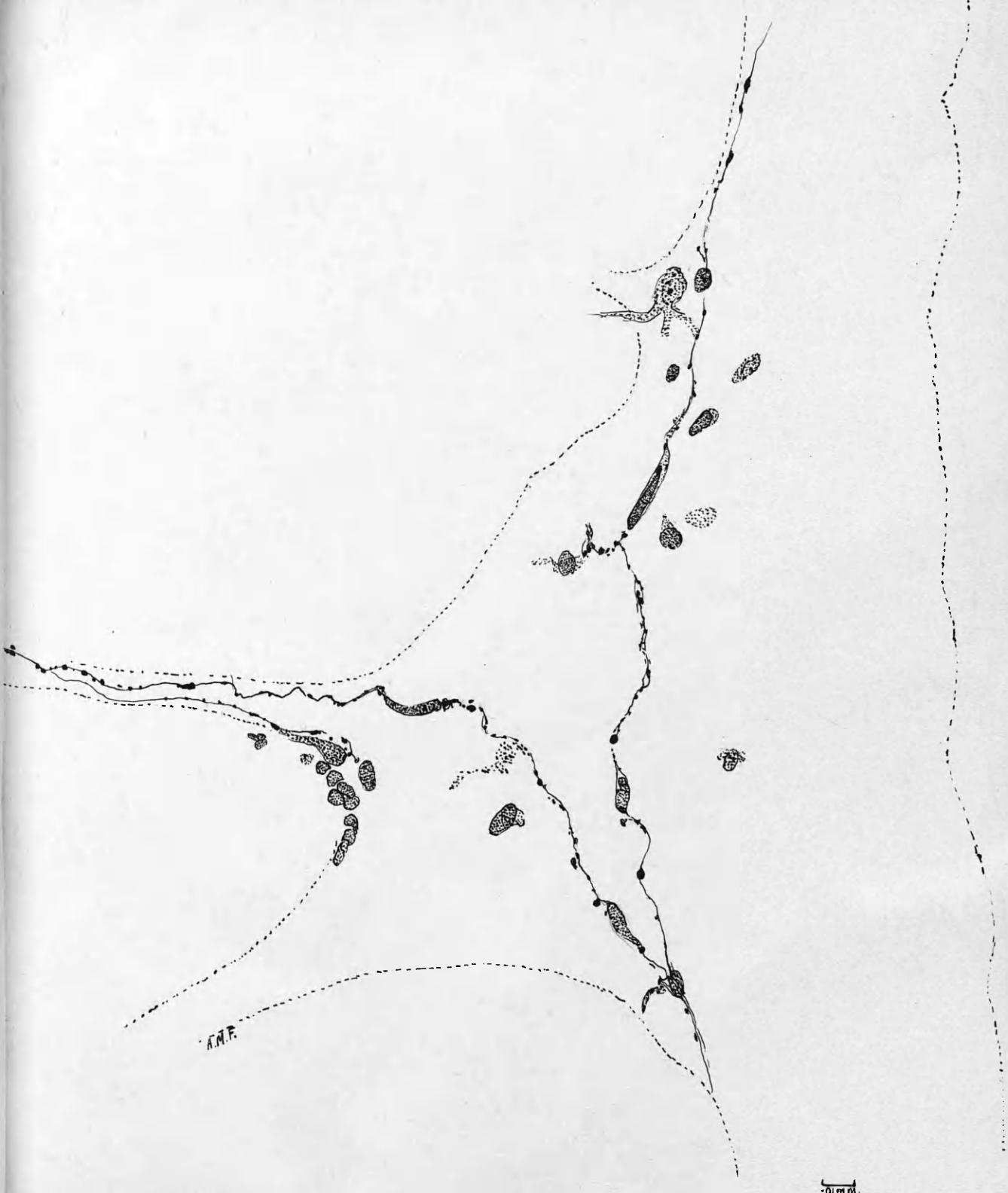


Fig.34

FIGURE 35.

An oval nucleus is seen at a point of intercommunication between two non-medullated nerve bundles in the uterus of the cat. The nucleus stained of a purplish colour with methylene-blue. Bundles A and B are also seen in Fig.(36).

Fig.35

FIGURE36.

FIGURE 36 .

Fine nerve bundles from the uterus of the cat. On the course of the bundles both types of nuclei are seen. Bundles A and B are also seen in FIG.(35).

Fig.36

FIGURE 37.

An oval large nucleus with its chromatin in a fine state of division is seen within a mass of cytoplasm traversed by non-medullated nerve fibres. The nucleus stained blue with methylene-blue.

Cat.

Fig.37

FIGURE 38.

Two nuclei are seen on the course of a nerve bundle. The upper one is one of Type I see Fig. 29; the lower one is larger, stained purple with methylene-blue, and lies in a triangular mass of cytoplasm continuous with the three nerve bundles.

Cat.

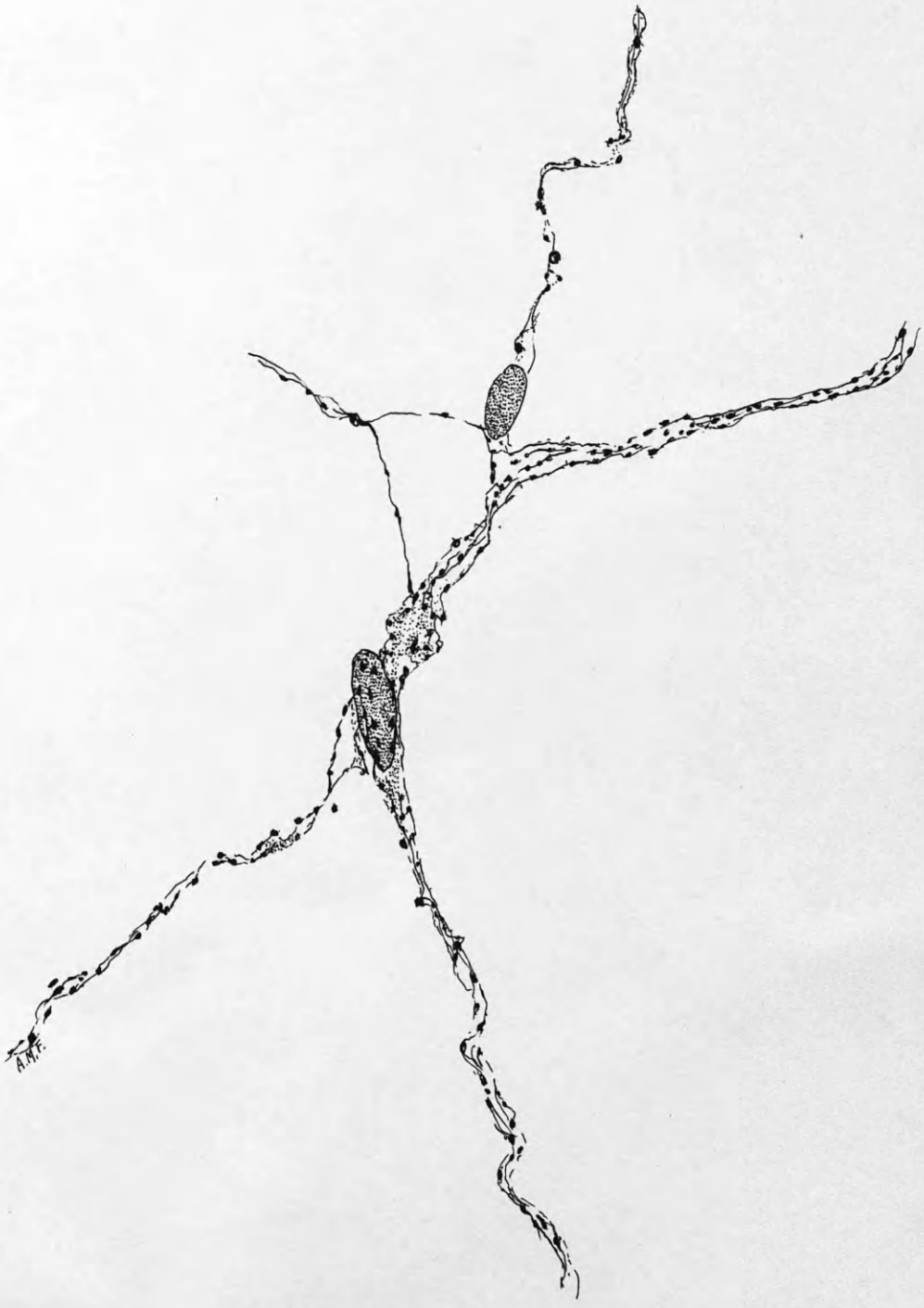


Fig.38

FIGURE 39.

On the course of a fine nerve bundle a nucleus resembling Type I is seen to be notched.

Methylene-blue

Cat.

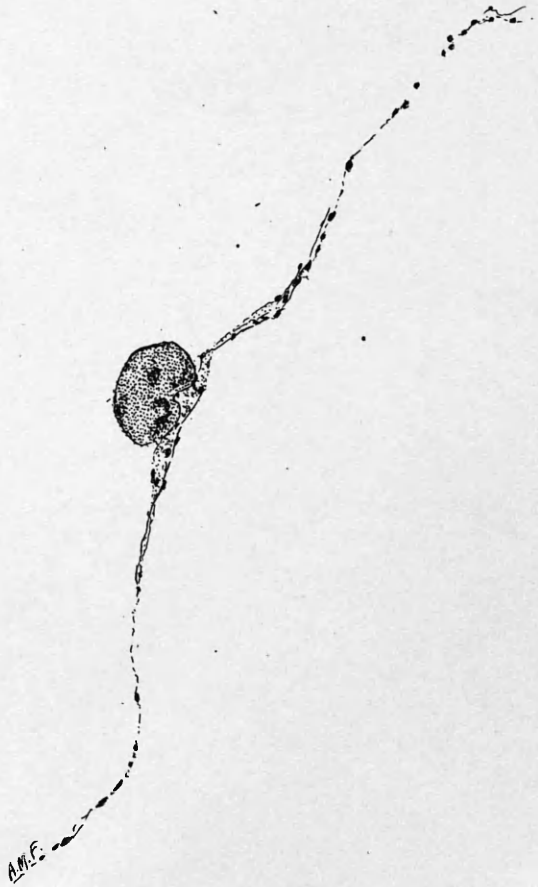


Fig.39

FIGURE 40.

Nerve fibres are seen intertwining in a mass of cytoplasm containing an oval nucleus which stained bluish with methylene-blue.

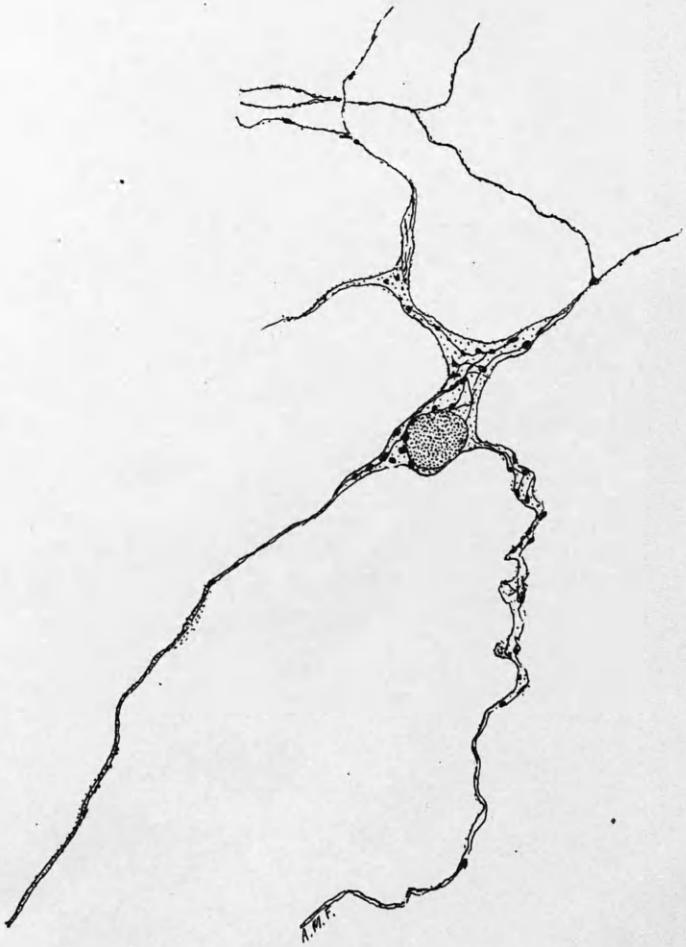


Fig.40

FIGURE 41.

A plexus-forming cell of Type III shows distinct longitudinal striation of one process. Another process connects up with a varicose nerve bundle. A relatively non-granular zone surrounds the nucleus.

Mrthylene-blue. Cat.

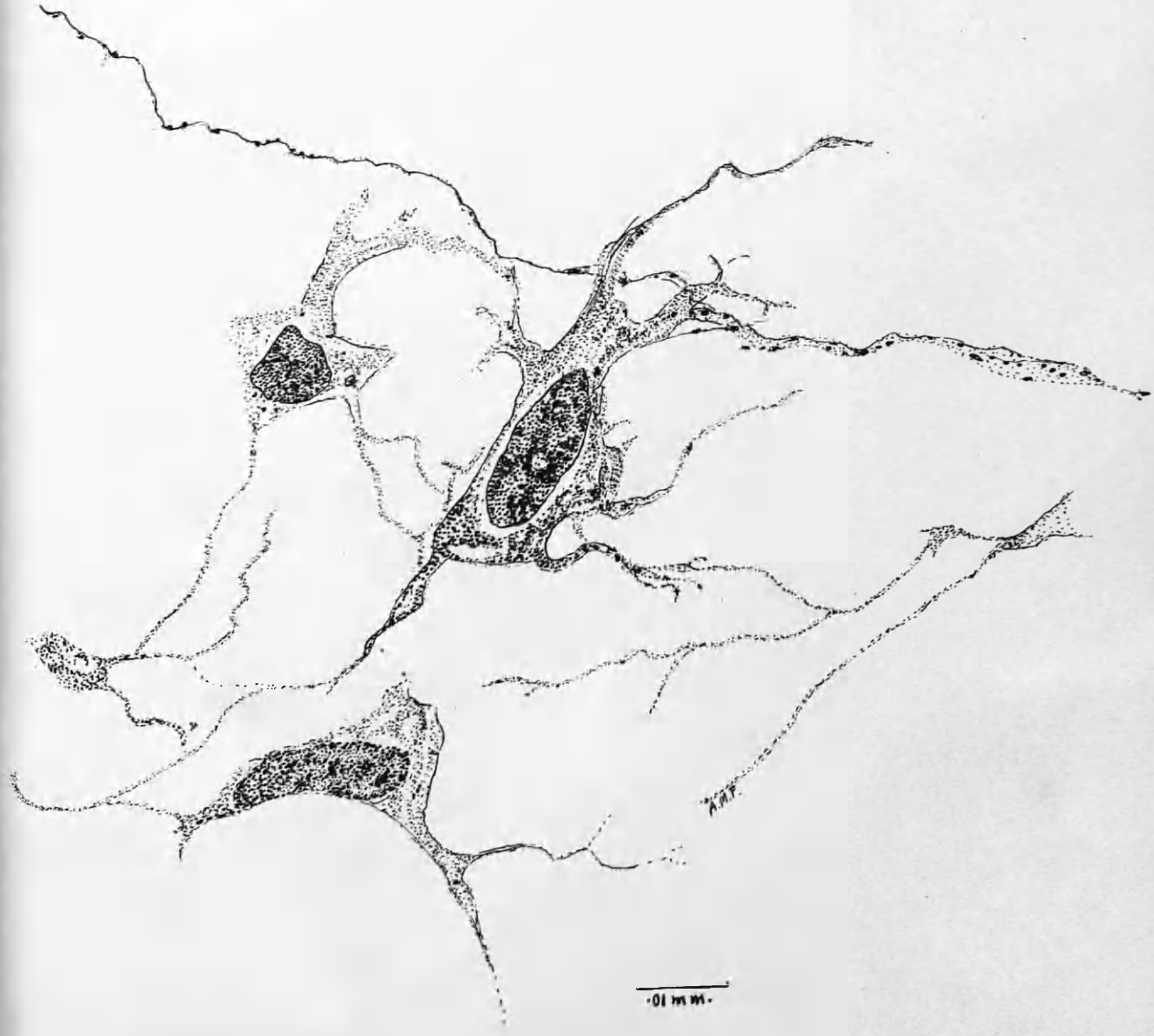


Fig.4I

FIGURE 42.

Towards the right side is a plexus-forming cell of Type II. A connection appears to exist between one process and the varicose nerve bundle. Bright blue granules were present in the cytoplasm. An oval dark pink nucleus was seen at the point of division of the nerve bundle.

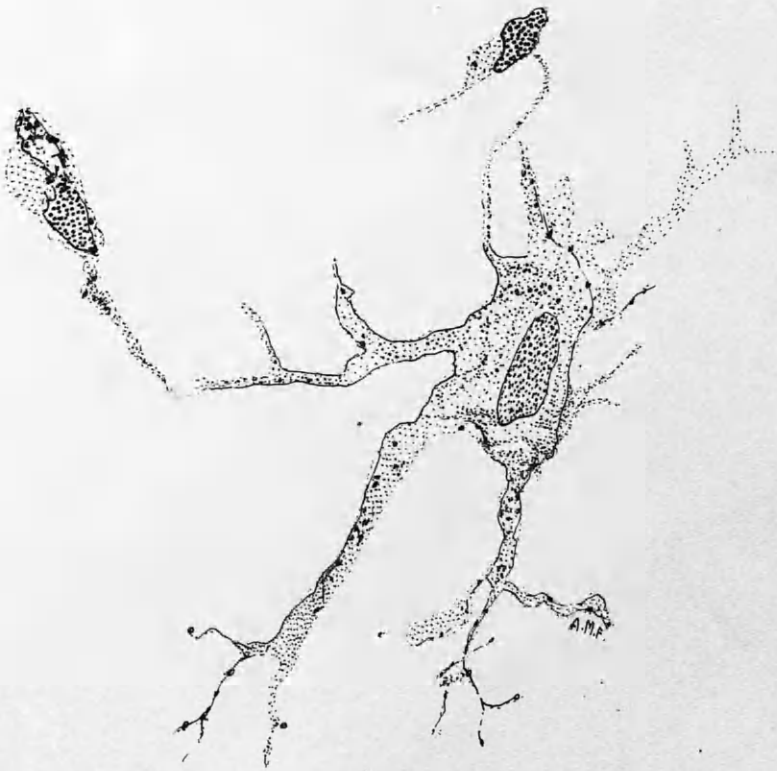
Methylene-blue. Cat.

Fig.42

FIGURE 43.

A plexus-forming cell with some of the processes continued into varicose fibrils.

Methylene-blue, Cat.



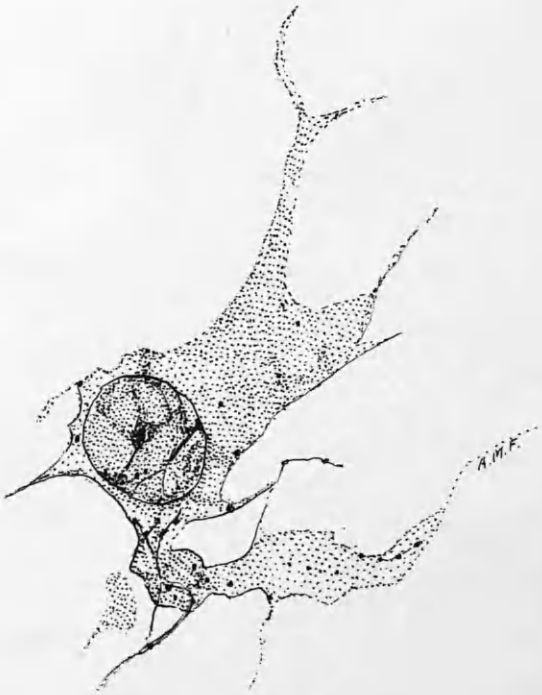
·01 mm.

Fig.43

FIGURE 44.

A plexus-forming cell of Type I in which blue granules on fine fibrils are seen.

Methylene-blue, Cat.



·01 m m·

Fig.44

FIGURE 45.

One of the plexus-forming cells of Type III. Fibrils are seen crossing over the nucleus and interlacing in the cytoplasm.

Methylene-blue. Cat.

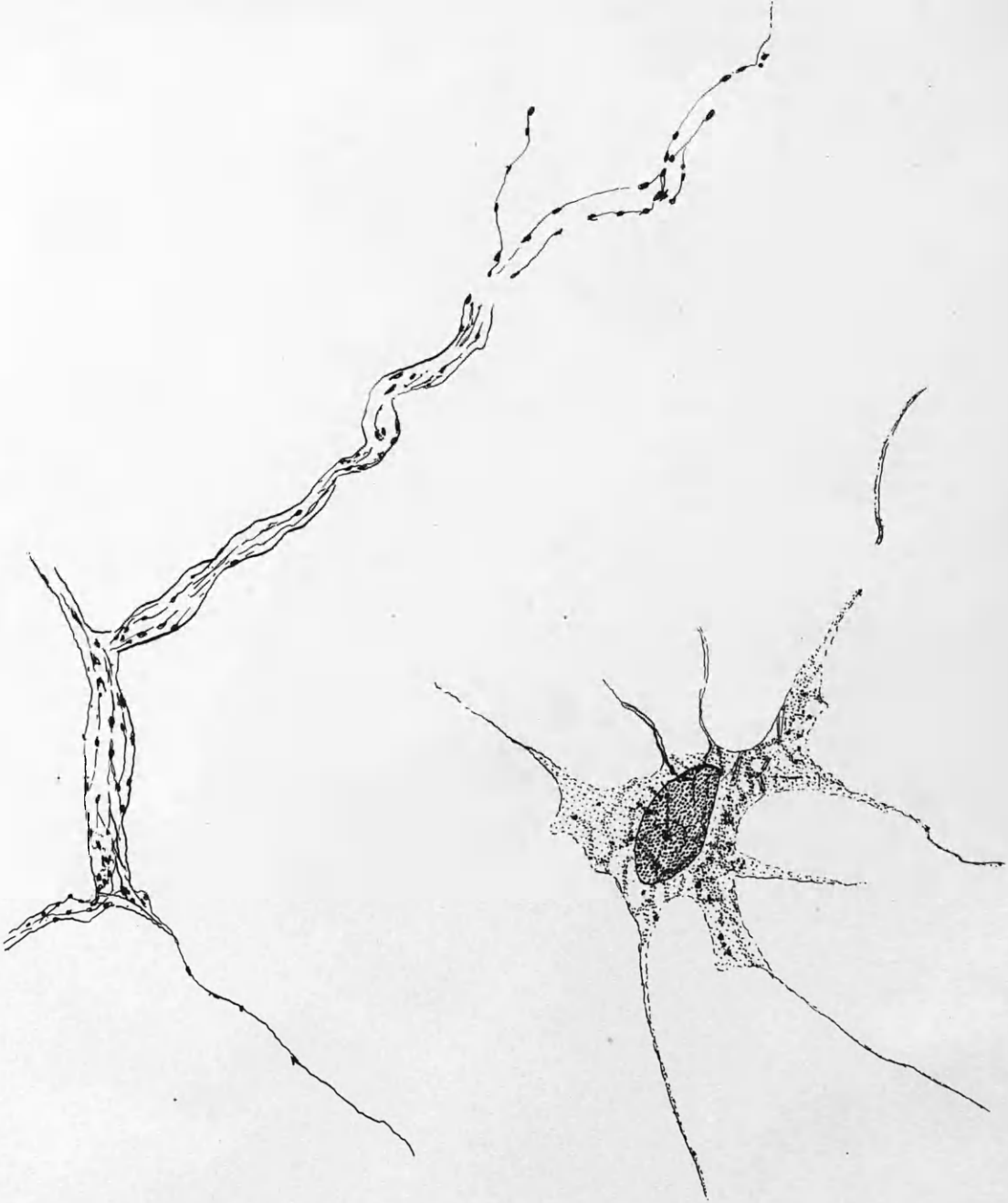
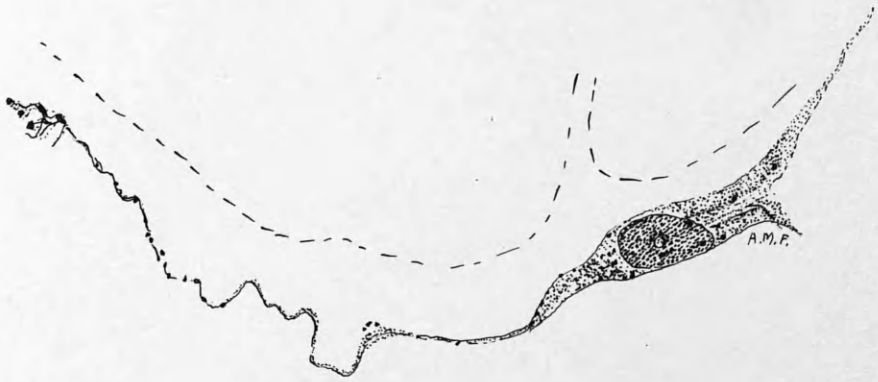


Fig.45

FIGURE 46.

A cell of TYPE III in which one process is continued into a varicose nerve fibre running parallel to the serous surface of the uterus.

Methylene-blue, Cat.



·01 mm.

Fig.46

FIGURE 47.

FIGURE 47.

Multipolar cell of type III in the uterus of the cat showing fine branching of its processes.

Methylene-blue.

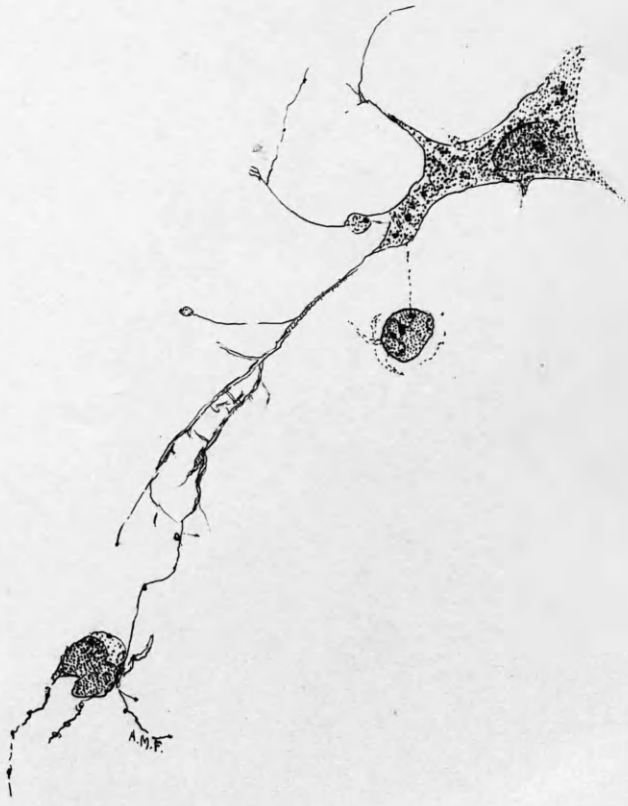


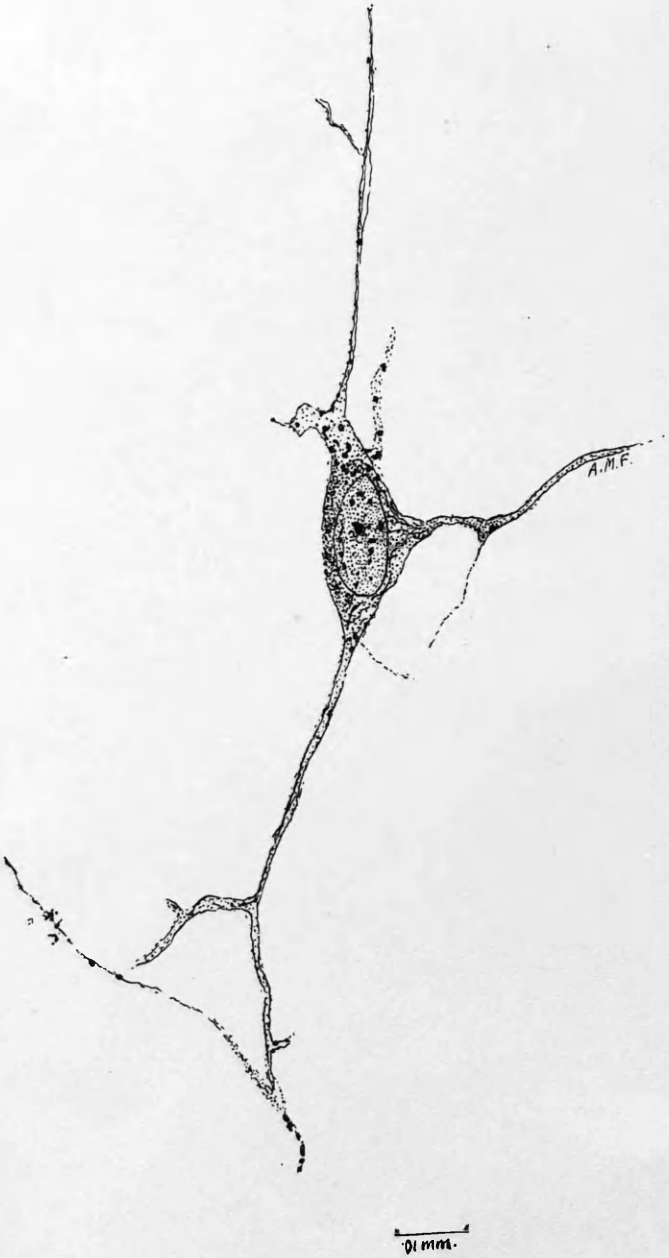
Fig.47

FIGURE 48.

One of the plexus-forming cells of Type I.

One process is seen to be connected with a varicose nerve fibre. Bright blue granules joined up by fine fibrils were seen in the cytoplasm.

Methylene-blue, Cat.



Fig,48

Cell-plexus in the uterine horn of the cat FIGURES 49, 50, 5I show three adjacent fields.

FIGURE 49.

Cells of TypeI, II, andIII are shown. A connection is seen between the processes of the topmost two cells, and with the cell on the left side. The central cell is one of Type I in which granules joined by fine fibrils were seen. Bright blue granules were also seen in the cytoplasm of the topmost two cells.

Methylene-blue.

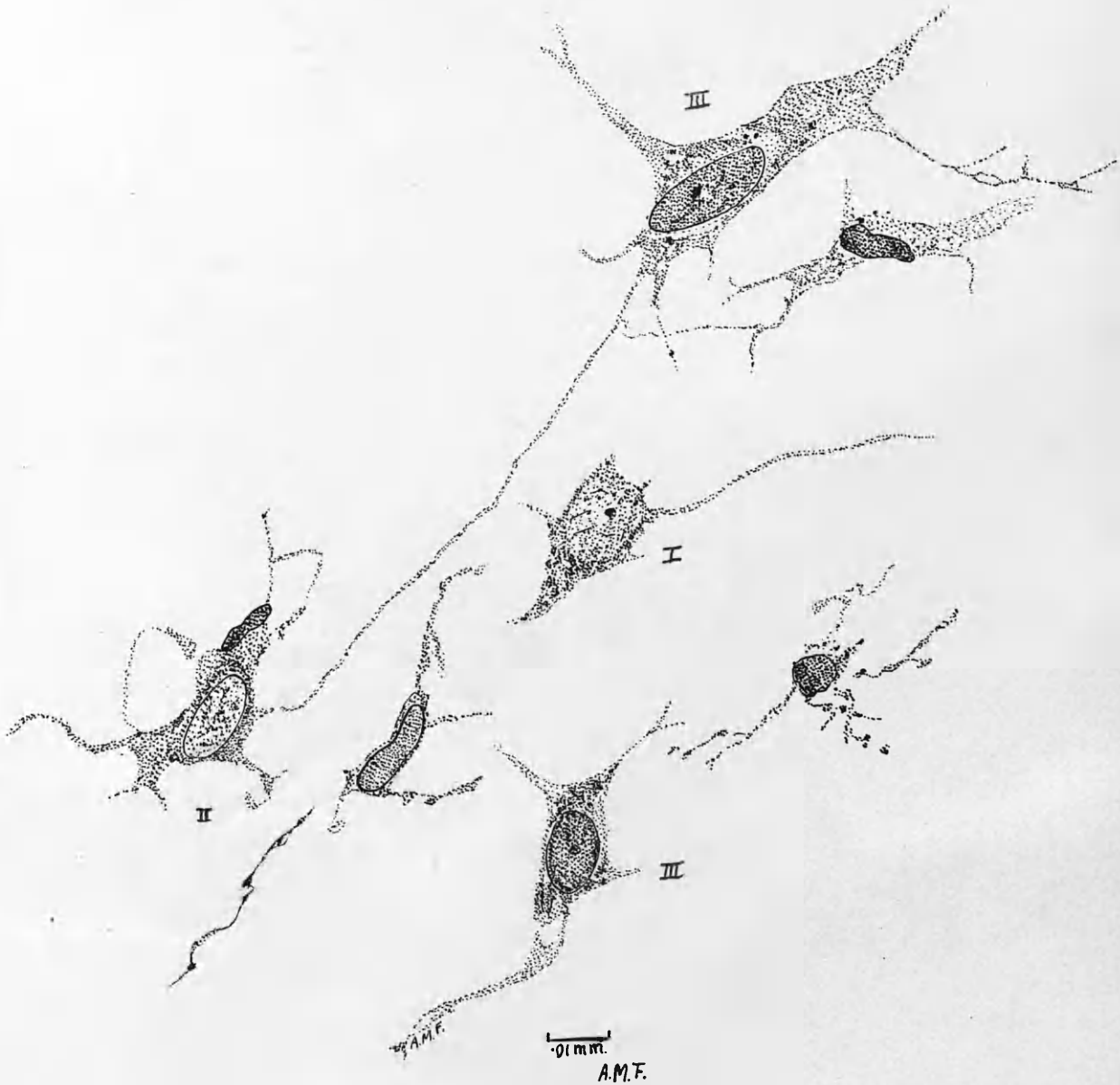


Fig.49

Cell-plexus in uterine horn of a cat.

FIGURES 49 50 5I show adjacent fields of the plexus.

FIGURE 50.

Cells of Type I,II and IV are shown. The second topmost cell on the right side is one of Type IV and in its cytoplasm granules,which were stained bright blue, are seen joined up by fine fibrils.

Methylene-blue.

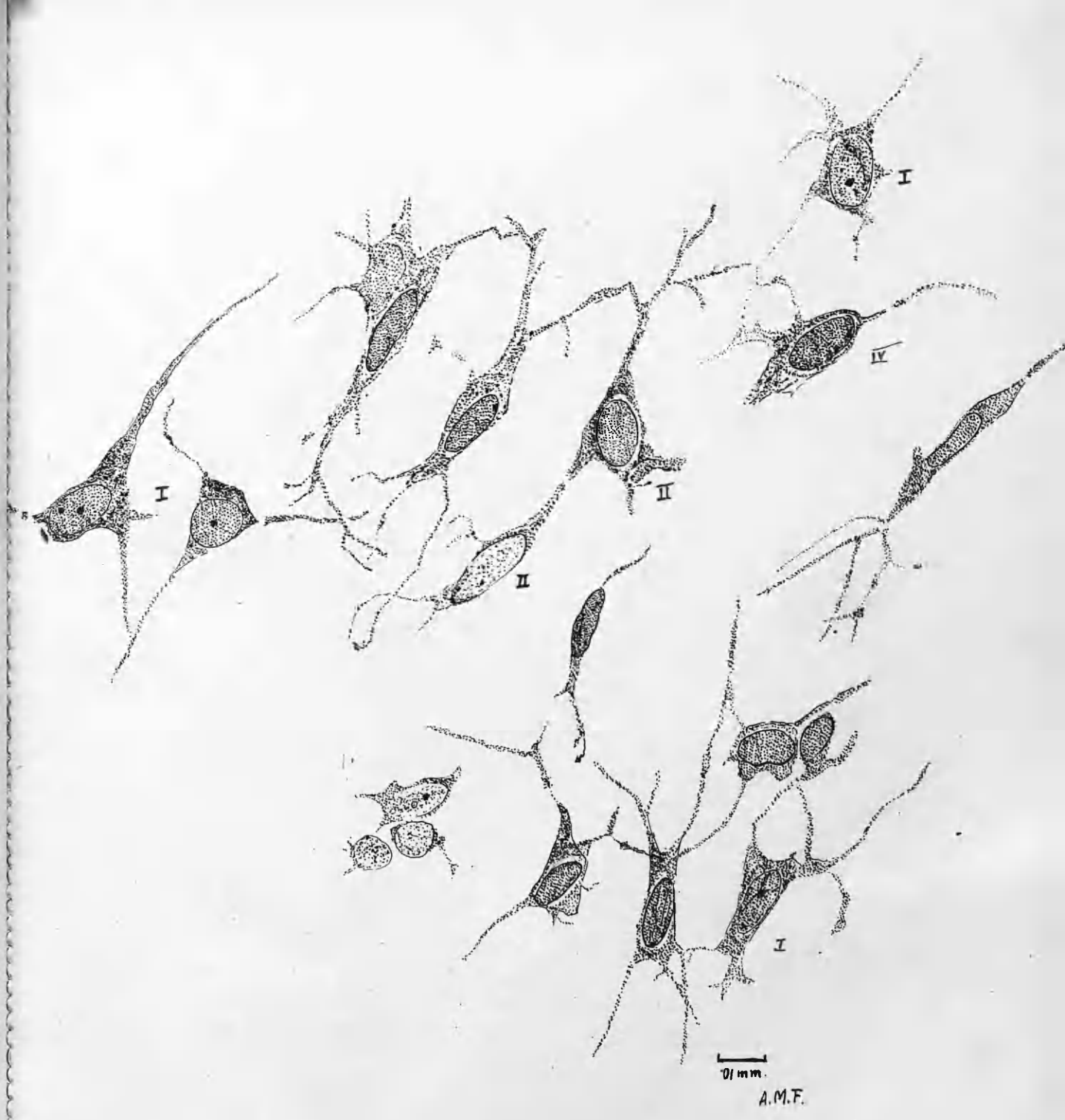


Fig.50

Cell-plexus in the uterine horn of a cat.

FIGURES 49 50 and 5I show three adjacent fields.

FIGURE 5I.

Cells of Type I, II, and IV are shown.

Methylene-blue.

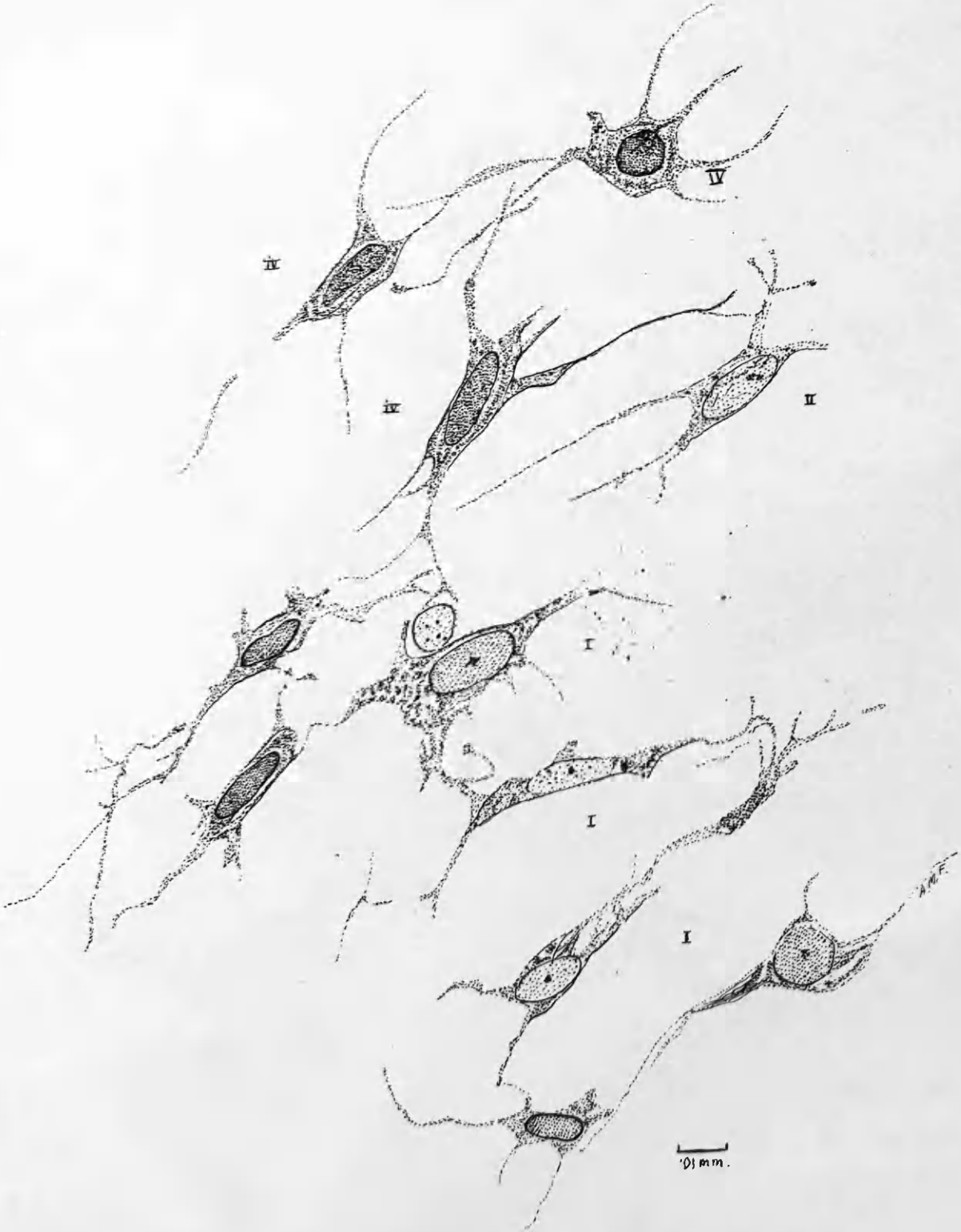


Fig.51

FIGURE 52.

Plexus of multipolar cells in the uterus of the cat. Cells of types I and III are seen.

Methylene-blue.

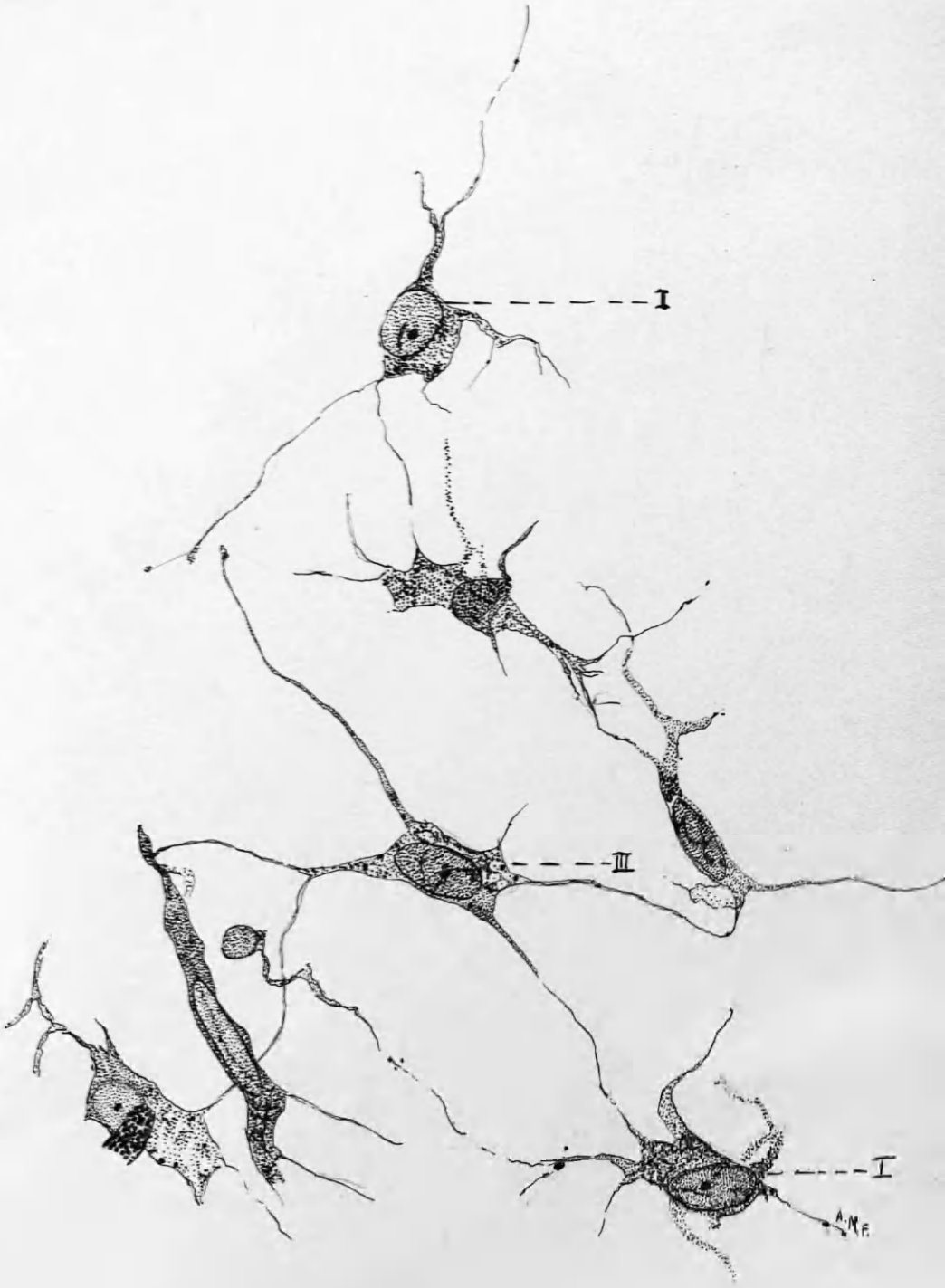
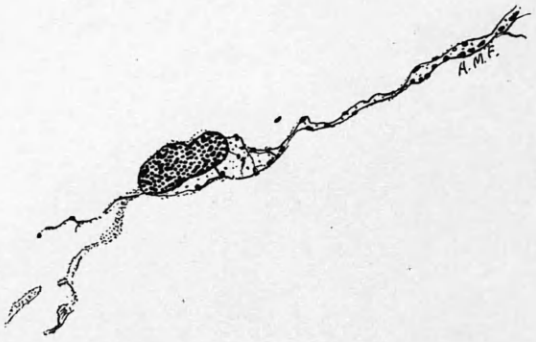


Fig.52

FIGURE 53.

A connective tissue cell which had a dark blue nucleus is seen connected up with a nerve bundle.

Methylene-blue, Cat.



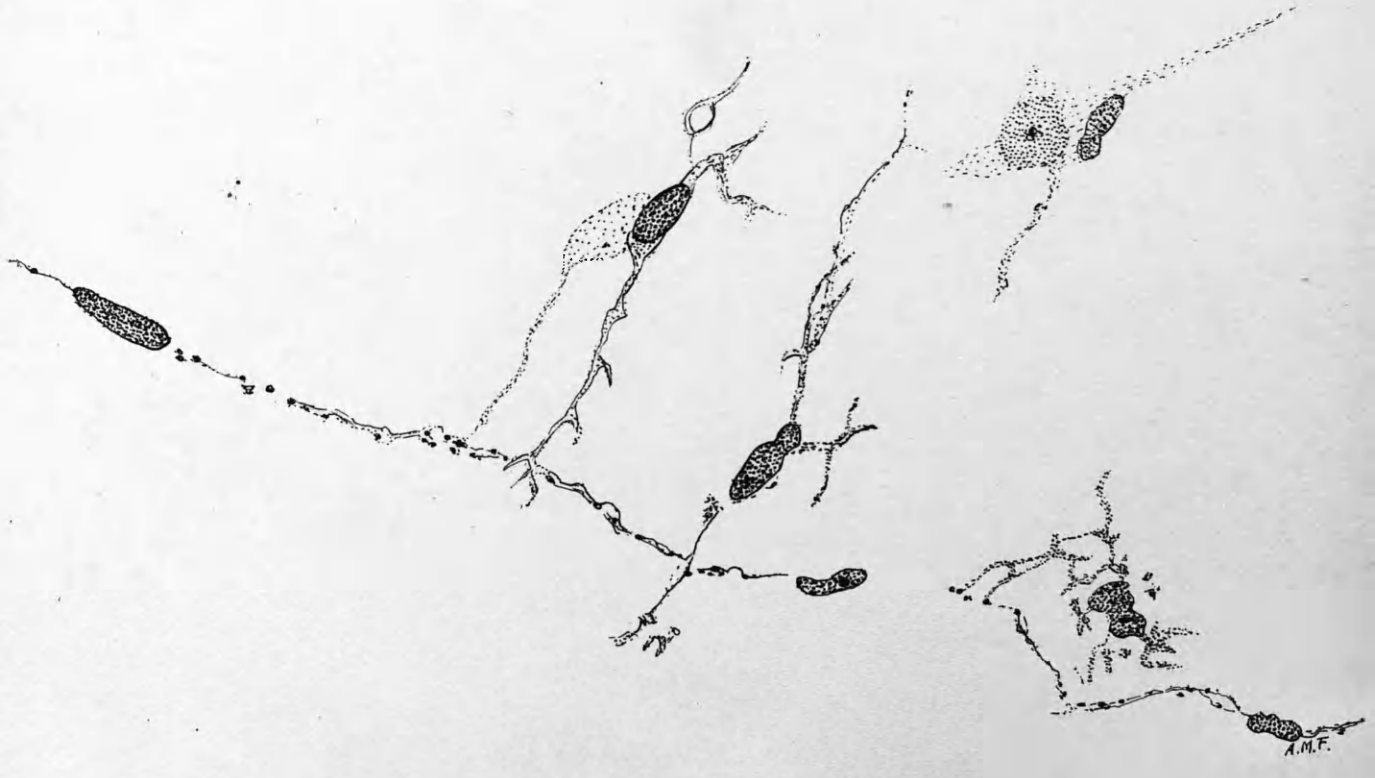
·01 mm.

Fig.53

FIGURE 54.

Three connective tissue cells are seen. Their nuclei stained purple with methylene-blue. The processes of one appear to be connected with the varicose nerve bundle. A cell resembling a synpathetic nerve cell is also seen.

Cat.



·01 mm.

Fig.54

FIGURE 55.

FIGURE 55.

A multipolar cell resembling those of type III but showing notching of its nucleus is seen. The processes of this cell, of the plexus-forming cell of type I, below it, and of the elongated connective tissue cell merely overlap.

Methylene-blue. Cat.

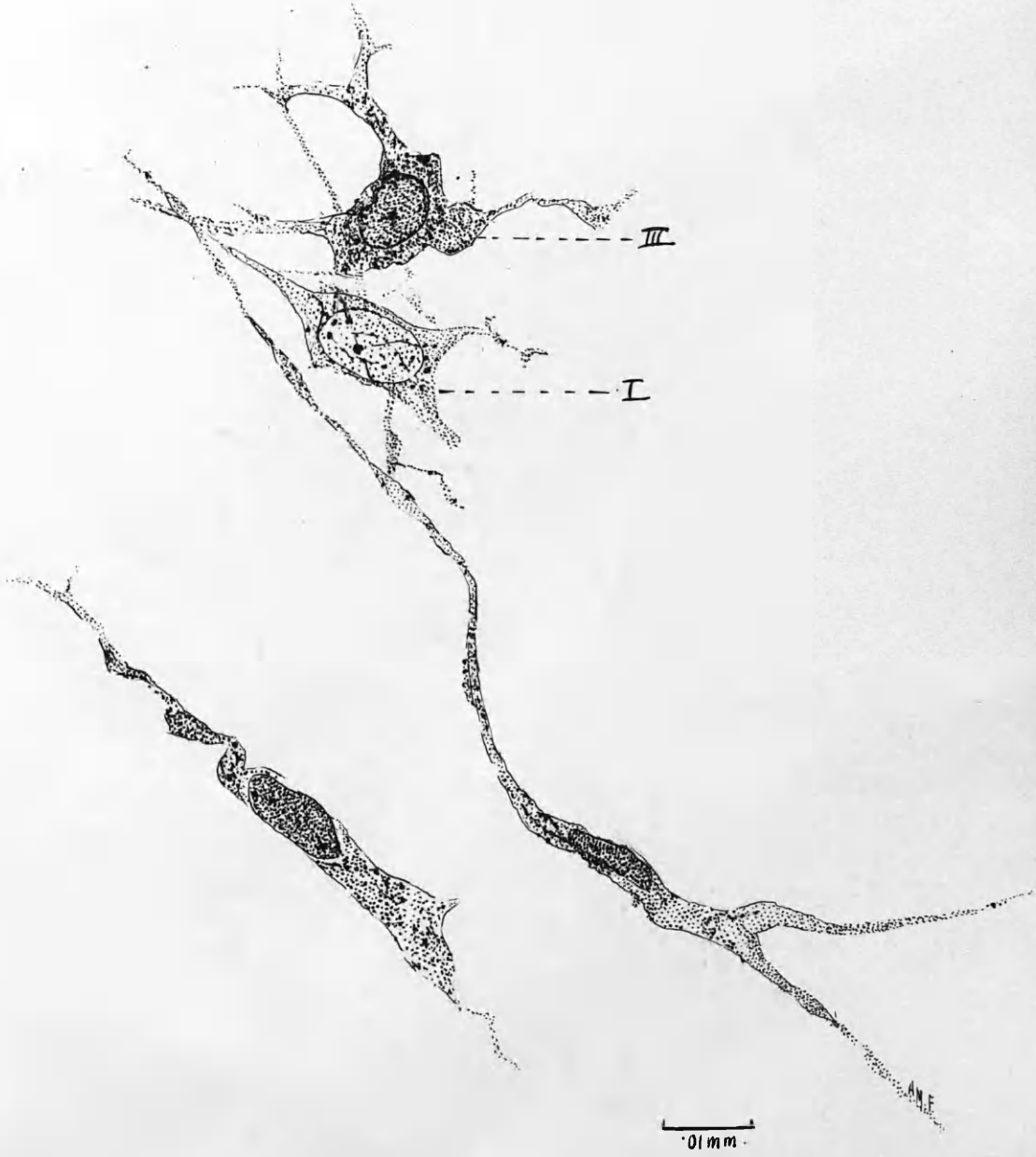


Fig.55

FIGURE 56.

A connective tissue cell containing a tortuous nucleus which stained dark blue with methylene-blue.

Cat.

.01 mm.

Fig.56

FIGURE 57.

A connective tissue cell is seen which had a dark blue curved nucleus. Blue granules were seen in some of the processes.

Methylene-blue, Cat.

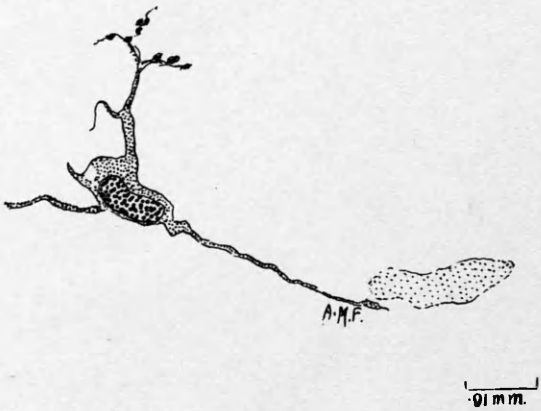
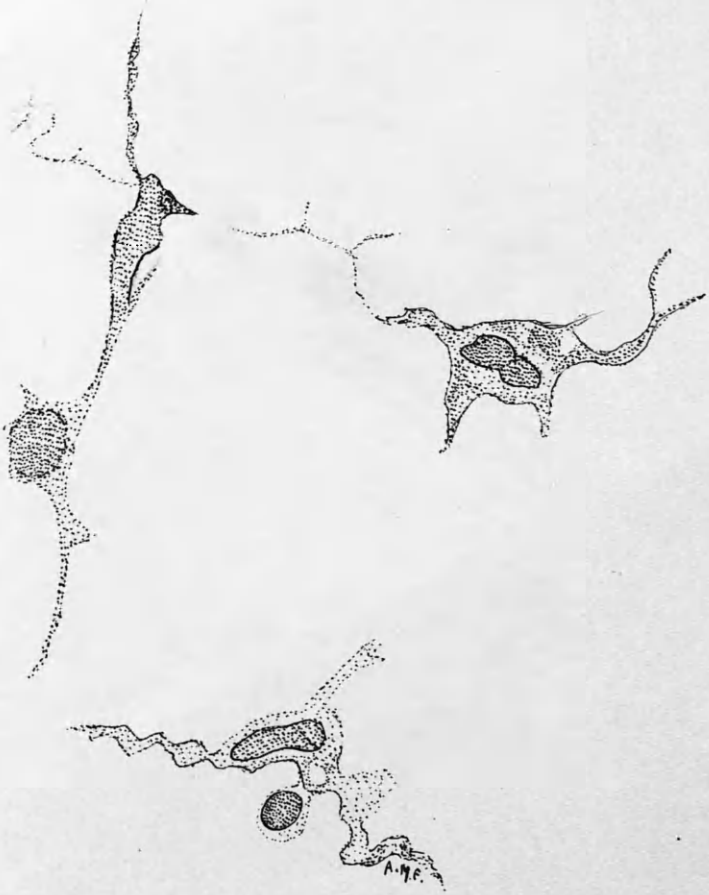


Fig.57

FIGURE 58.

Connective tissue cells having relatively short blunt processes.

Methylene-blue, Cat.



.01 mm.

Fig, 58

FIGURE 59.

On the bundle of nerve fibres both types of nucleus are seen. Numerous connective tissue cells are seen towards the right side. Their nuclei stained dark blue with methylene-blue.

Cat.

Fig.59