A HISTOLOGICAL STUDY ON THE AFFERENT INNERVATION OF THE LYMPHGLAND

by

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Contents

1. INTRODUCTION

Abdominal pain in the ileocecal region suggests, first of all, the sign of appendicitis.

However, the author experienced some cases of lymphadenitis in the ileocecal region, who were erroneously diagnosed as appendicitis due to the simulating abdominal pain.

This experience suggested to the author that the ileocecal lymphglands can evoke abdominal pain. Moreover, REILY (1930) found that the injection of some chemical agents into the mesenteric lymphglands caused segmentary pathologic changes in the intestine.

REILY considered this phenomenon might be due to the irritation of the autonomic nerves in the intestine originating from the lymphglands.

This phenomenon described by Reily also aroused the author's interest in this study.

SHEEHAN (1933) discovered the Vater-Paccinian corpuscles in the mesenteric lymphglands of the cat. In his opinion these corpuscles together with the myelinated nerves in the mesenteric lymphglands may cause abdominal pain.

Concerning the sensory nerves of the lymphglands there are some reports by TOLDT (1888), (1949), SUNDERPLASMANN (1951) and SAKURAOKA (1954).

ITO (1943) described two nerve plexuses in lymphglands, one in the hilum and another in the capsule. He found nerves running along the blood vessels and spreading to the parenchyma of the lymphgland in the form of fine networks.

SETO (1949) held the opinion the abdominal pain of tuberculous peritonitis or appendicitis may be caused partially by the mesenteric lymphglands stimulated by the inflammatory substances passing through them.

As for the autonomic nerves in the lymphglands SUNDERPLASMANN and RÖPER (1951) found terminal reticula (STÖHR) in the secondary follicles of the lymphglands.

The author hypothesized that the ileocecal lymphgland might be under the sensory innervation of the vagus nerve and spinal nerves arising from the thoracolumbar segments of the spinal cord.

The author, therefore, first studied the morphology of the sensory nerves as well as their endings and then conducted degeneration experiments to determine the sites of the roots of the sensory nerves in the ileocecal lymphglands by means of the vagotomy or posterior rhizotomy. The author did supplementary study on the nervous elements in the axillary and popliteal lymphglands.

II. MATERIALS AND METHODS

The materials used in this study were the lymphglands of human beings and dogs. The author used only fresh specimens taken from lymphglands which had been resected operatively. After fixation for 3-5 weeks in 10% neutral formol solution, the specimens were frozen, sliced in thickness of 30-40μ, fixed again in 10% neutral formol solution for 2 to 6 months, and then stained.

The axis-cylinders were stained with SETO's or SUZUKI's or the JABONERO's-SETO's modification of BILSCHOWSKY's silver impregnating method, while the myelin sheaths were stained with EHRLICH's acid hematoxylin.

Adult dogs were used as experimental animals. Operations were carried out under general anesthesia with the injection of isomytalsodium, and thoracotomy was performed under positive pressure breathing.

Considering the results of various experiments performed by many investigators from the anatomical or physiological standpoint, it can be assumed that most of the afferent nerves of the ileocecal lymphglands are derived from the thoracolumbar and vagal nerves.

Therefore, the spinal nerves and the vagus were sectioned at various points in the study in order to determine the course of the afferent nerves. Operations were carried out on the ventral or the dorsal roots of the spinal cord distal to the spinal ganglia, and on the vagus nerve.

Secondary degeneration of nerve fibers in the ileocecal lymphglands was observed mainly by EHRLICH's method.

Degenerated myelinated nerve fibers were pursued peripherally up to the point where autonomic nerves cells could no longer be found.

The author studied secondary degeneration of peripheral nerves 5~7 days after section of the roots of the spinal cord.

Operations were performed as follows.

1) Section of dorsal roots on both sides (T 3-T 4)
2) Section of dorsal roots on both sides (T 5-T 6)

3) Section of dorsal roots on both sides (T 7-T 9)
4) Section of dorsal roots on both sides (T 10-12)
5) Section of dorsal roots on both sides (T 13-L 1)
6) Section of dorsal roots on both sides (L 2-L 1)
7) Section of dorsal roots on the right side (T 5-T 8)
8) Section of dorsal roots on the right side (T 9-L 1)
9) Section of dorsal roots on the right side (L 2-L 4)
10) Section of ventral roots on the right side (T 5-T 8)
11) Section of ventral roots on the right side (T 9-L 1)
12) Section of ventral roots on the right side (L 2-14)

Vagotomies were performed as follows:

13) Cervical vagotomy on the right side at a point distal to the ganglion nodosum.

14) Cervical vagotomy on the left side at a point distal to the ganglion nodosum.

15) Bilateral vagotomy in the thorax.

III. NORMAL HISTOLOGY OF THE NERVES IN THE ILEOCECAL, AXILLARY AND POPLITEAL LYMPHGLANDS

1) Studies of the ileocecal lymphglands

The author found myelinated nerve fibers forming nerve bundles with non-myelinated fibers, entering the lymphglands at the hilum, either accompanied by vessels or alone (Fig. 1. 2. 3. 4). They ran through the medullary substance and medullary cord, entered the trabeculae (Fig. 5. 6. 7. 8. 16) and were distributed to the secondary follicles (Fig. 9-11).

These myelinated fibers consisted mostly of small and medium sized nerve fibers (less than 4-6μ in diameter), but a few large fibers were found among them.

In the capsule of the lymphgland the author found some large myelinated nerve fibers running into the trabeculae (Fig. 12).

As peripheral structures of the autonomic nerves, nerve networks in the plasmodia were found only at the hilum near the blood vessels (Fig. 13-15). The myelinated nerve fibers ended in free simple or arborized terminations soon after losing the myeline sheath (Fig. 17, 18). These terminal structures were clearly distinguishable from the nerve networks of the autonomic nerves.

The author considers that these myelinated nerves are sensory in nature. This assumption was later studied more closely by degeneration experiments.

Vater-Paccinian corpuscles, which have been described by SHEEHAN and by SAKURAOKA in the lymphglands, were not found in the author's study. Nerve cells did not exist in the lymphglands just like the previous reports.

2) Studies of the axillary lymphglands

The axillary lymphglands removed from the patients suffering from cancer of breast were studied.

In the hilum myelinated fibers were found along the blood vessels just as in the ileocecal lymphglands. (Fig. 19, 20)

In the capsule, the author found a special sensory nerve ending, which had a complicated glomerular appearance with many fine "Endöse" in it (Fig. 21-23).

The same sensory end-structure was also found in the trabeculae (Fig. 27) which, though it had a less complicated glomerular appearance, extended in a wide area of the trabeculae (Fig. 28, 29, 30).

Nerve syncytia of the autonomic nerves were seen in the medullary substance in the hilum (Fig. 24).

Myelinated nerve fibers and their endings, which were supposed sensory, were found in this case mainly in the capsule (Fig. 25, 26), but some of them entered the trabeculae.

The author could not pursue these myelinated nerve fibers to the secondary follicles.

Most of the myelinted fibers in this case were small sized and only a few were large or middle sized. Nerve cells were not found in the lymphglands.

Compared with the ileocecal lymphglands, myelinated nerves were more abundant in the hilum, the capsule and the trabeculae, but only a few were found in the parenchyma in the axillary lymphglands.

3) Studies of popliteal lymphglands.

Most of the materials were from patients undergoing amputation, but some were taken from dogs.

The results were almost the same as in the axillary lymphglands.

Fig. 36 shows large myelinated nerves in the hilum.

Fig. 37 presents a myelinated nerve in the trabeculae coming from the capsule.

Fig. 31～35 show sensory terminations: terminal expansions or "Endöse" in which the fine network is clearly seen.

In general, the popliteal lymphglands had fewer myelinated nerve fibers, and they were found only in the hilum, the capsule and the medullary substance (Fig. 36).

The autonomic nerve syncytia were also found in the hilum and the medullary substance, except the secondary follicles. No nerve cell was observed.

IV. THE SITES OF THE ROOTS OF THE SENSORY NERVES IN THE ILEOCECAL LYMPHGLANDS

Using adult dogs as experimental animals, operations were performed as follows : laminectomy was performed under general anesthesia with sodium isomytal. The spinal canal was openend, and the dorsal and ventral roots were separated carefully from each other and only the ventral or the dorsal roots were cut at a point distal to their ganglia on both sides or on one side.

The ileocecal lymphglands were removed mostly 5～7 days after rhizotomy.

Vagus nerves were cut on one side in the neck distal to the ganglion nodosum or on both sides in the thorax under positive pressure breathing. Specimens were taken out more than 6～7 days after vagotomy, and stained by Ehrlich's haematoxylin method.

(1) Section of the dorsal roots on both sides (T 3-T 4)

No degenerated nerve fiber was found in the ileocecal lymphglands.

(2) Section of the dorsal roots on both sides (T 5-T 6)

No degenerated nerve fiber was found in the ileocecal lymphglands.

(3) Section of the dorsal roots on both sides (T 7-T 9)

A few degenerated myelinated nerve fibers were found in the ileocecal lymphgland trabeculae (Fig. 39).

(4) Section of the dorsal roots on both sides (T 10-T 12)

Most of the degenerated fibers were found in the ileocecal lymphglands. Degeneration was most marked in the hilum and the trabeculae and almsot all the myelinated fibers were involved, including large, medium and small myelinated fibers. In the medullary substance near the blood vessels, a small number of degenerated fibers was observed (Fig. 40, 41, 42). But the author could not pursue the degenerated fibers as far as the secnodary follicles.

(5) Setion of both sides (T 13-L 1)

Many degenerated fibers were found in the cases of the sections (T 10-T 12 and T 7-9). They were especially in the medullary substance (Fig. 43).

(6) Section of the dorsal roots on both sides (L 2-L 4)

No degenerated nerve fiber was found in the ileocecal lymphglands.

(7) Section of the dorsal roots on the right side (T 5-T 8)

A few degenerated myelinated nerve fibers were found in the trabeculae and medullary substance of ileocecal lymphglands (Fig. 44).

(8) Section of the dorsal roots on the right side (T 9-L 1)

As in the case of bilateral posterior rhizotomy, granular degeneration was marked. Secondary degeneration was found not only in the trabeculae but also in the medullary substance around the blood vessels (Fig. 45, 46).

(9) Section of the dorsal roots on the right side (L 2-L 4).

No degenerated nerve fiber was found in the ileocecal lymphglands.

(10) Section of the ventral roots on the right side (T 5-T 8)

(11) Section of the ventral roots on the right side (T 9-L 1)

(12) Section of the ventral roots on the right side (L 2-L 4)

In no case were degenerated nerve fibers found in the ileocecal lymphglands.

(13) Cervical vagotomy on the right side at a point distal to the ganglion nodosum

(14) Cervical vagotomy on the left side at a point distal to the ganglion nodosum

(15) Bilateral vagotomy in the thorax

In no case were degnerated nerve fibers discovered in any portion of the ileocecal lymphglands.

V. DISCUSSION

The most common form of sensory endings in these lymphglands were free endings. However, in the axillary and popliteal lymphglands, typical forms of sensory ending such as glomerular endings with terminal expansions and "Endöse" were observed by the author.

As above mentioned, the nerve endings exhibit the various final structures. Therefore, it is not certain that whether the free endings are true endings or only apparent ones.

Ito reported that a very small number of myelinated fibers are observed in lymphglands. They exist only in the nerve bundle of the hilum and in the capsule as a few small and medium sized fibers, but on entering the parenchyma they lose their myelin sheaths and are distributed as non-myelinated fibers.

In his study, the author found myelinated fibers in the hilum, the capsule, the trabeculae, and the medullary cord as far as the secondary follicles.

Degeneration experiments after posterior rhizotomy and after vagotomy were performed by the author.

The author could pursue secondary degenergation of the myeline sheath in the ileocecal lymphglands through the hilum, the capsule, the trabeculae, to the medullary cord.

In the silver impregnation preparations, degenerated axis cylinders were found in the trabeculae of the ileocecal lymphglands as a linear distribution of granules in the thick nerve bundles.

In the specimens obtained 5～7 days after the section of nerve roots, the number of degenerated axis cylinders was far less than those of degenerated myelin sheaths.

This is a matter of course, since the axis-cylinders degenerate earlier than the myelin sheaths.

Thus, it was confirmed that myelinated fibers are present in the ileocecal lymphglands and are still myelinated near their endings and they pass through the posterior roots of the spinal cord.

These nerve fibers have, therefore, been determined as sensory in nature. The same can be said for other lymphglands.

These degeneration experiments showed that the sensory innervation of the ileocecal lymphglands of the dog covers 7 segments of the spinal cord. i. e. from T 7-L 1, especially from T 10-T 12.

The number of degenerated myelinated fibers after unilateral posterior rhizotomy on the right side seemed fewer than when rhizotomy was carried out on both sides.

This fact suggests that the ileocecal lymphglands are under bilateral sensory innervation of the spinal cord. Sensory innervation of the ileocecal lymphgland by nerve fibers passing through the anterior roots or the vagus nerve was not proved.

Therfore, the author concludes that the ileocecal lymphglands receive most of their sensory nerves from the thoraco-lumbar segments of the spinal cord, while they have little or no vagal sensory supply.

The author described, in this study, myelinated sensory nerves in the lymphglands, but did not study non-myelinated sensory fibers, because he cannot find a proper method to prove them.

VI. SUMMARY AND CONCLUSIONS

Using BIELSHOWSKY's silver impregnation method modified by SETO, SUZUKI or JABONERO, and EHRLICH's hematoxylin myelin sheath stain, the author studied the afferent nerves in the ileocecal, axillary and popliteal lymphglands. In addition, he examined the sites of their roots by degeneration experiments following section of nerve roots.

The results lead to the following conclusion.

1) Sensory nerves and their free endings were found in the ileocecal lymphglands of human beings and dogs.

2) In the axillary and popliteal lymphglands, the sensory nerves and their typical endings, such as glomerular endings with many terminal expansions and Endöse, were found in the capsule near the hilum and the trabeculae.

3) The ileocecal lymphglands receive most of their afferent nerves from many posterior roots on both sides of the spinal cord, i. e. between T 7-L 4, especially between T 9-L 1.

4) Vagal sensory innervation of the ileocecal lymphglands was not found by the author.

I am very grateful to our Assist.-Prof. Ch. KIMURA who gave me constant help and good suggestions throughout this work.

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和文抄録

リンパ節の知覚神経に関する組織学的研究

京都大学医学部外科学教室第2講座（指導　青柳安誠教授）

請　田　安　夫

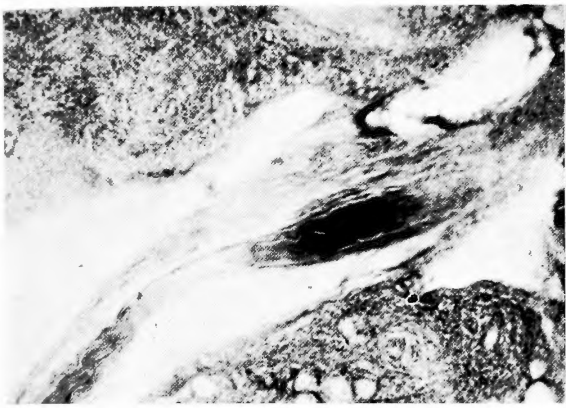
Bielschowsky 氏神経軸索鍍銀染色法の瀬戸氏変法，鈴木氏変法，Jabonero鍍銀染色法並びにEhrlich氏神経髄鞘染色法を用い人及び犬の廻盲部腋窩，膝膕の各リンパ節の知覚神経に就いて検討し，更に犬の神経幹切断による廻盲部リンパ節内の神経の二次的変性を追求して，次の結論を得た.

1）人及び犬の廻盲部リンパ節に有髄神経及び知覚神経が存在する.

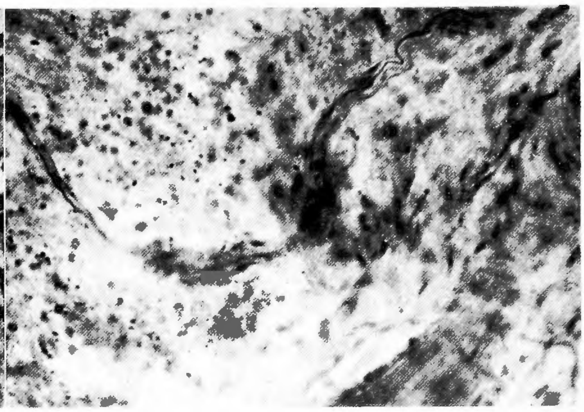
2）人の腋窩及び膝膕リンパ節の節門部被膜及び梁材に典型的耳状終末を見出した.

3）廻盲部リンパ節の求心性有髄神経の大半は同側の脊髄後根を通り Th_7-L_4 の間にあるが特に Th_9-L_1 を中心とする胸腰髄に入る.

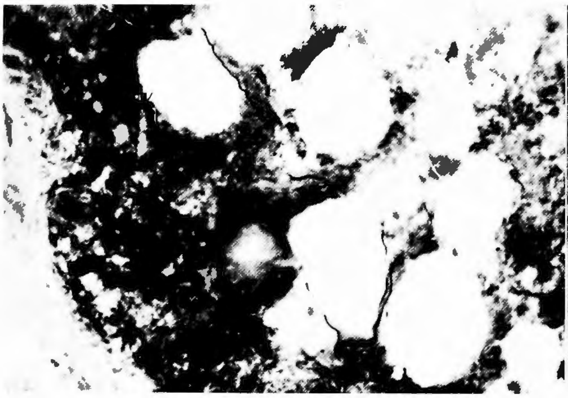
4）廻盲部リンパ節の迷走神経性求心性支配は証明し得ない.



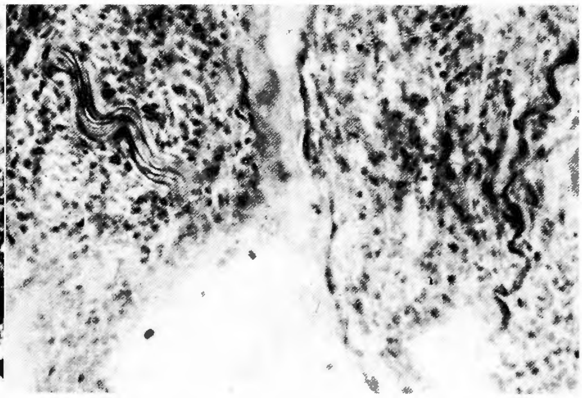
1) Nerve bundles in the hilum of an ileocecal lymphgland. ×200



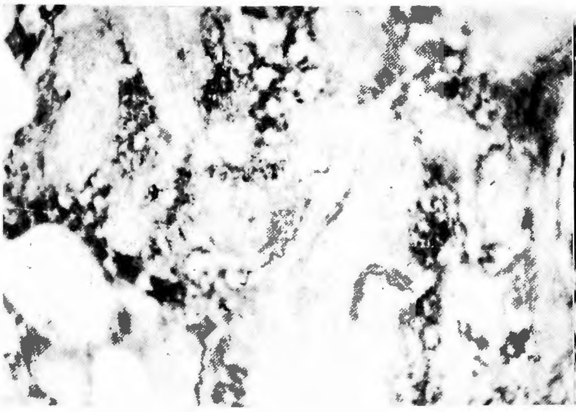
2) Myelinated nerve fibers around the blood vessels in the hilum of an ileocecal lymphgland. ×200



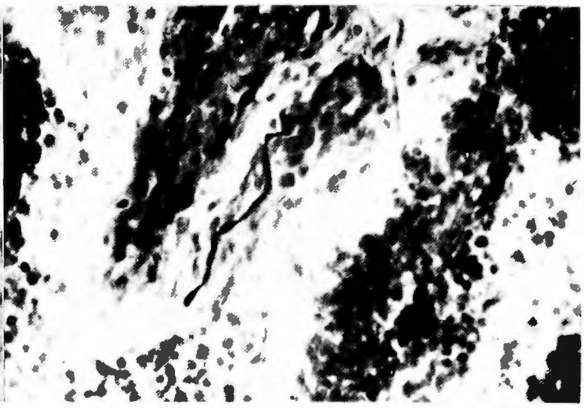
3) Afferent nerves in the hilum of an ileocecal lymphgland running in various directions. ×200



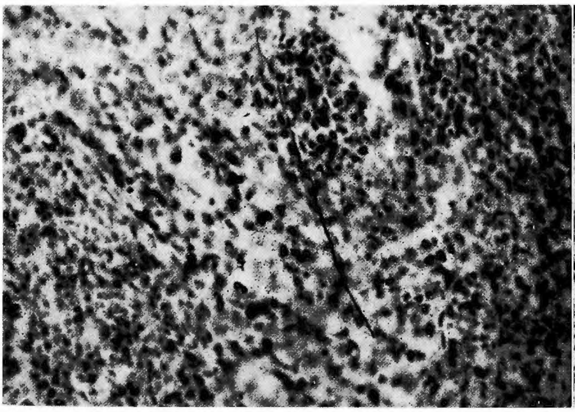
4) Nerve bundles and myelinated nerve fibers in the hilum of an ileocecal lymphgland. ×200



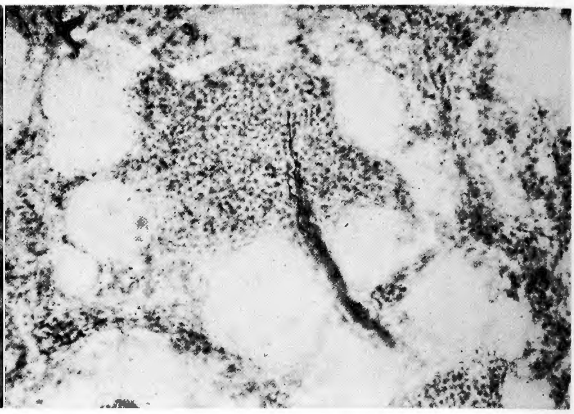
5) Myelinated nerve fibers in the medullary cord of an ileocecal lymphgland. ×200



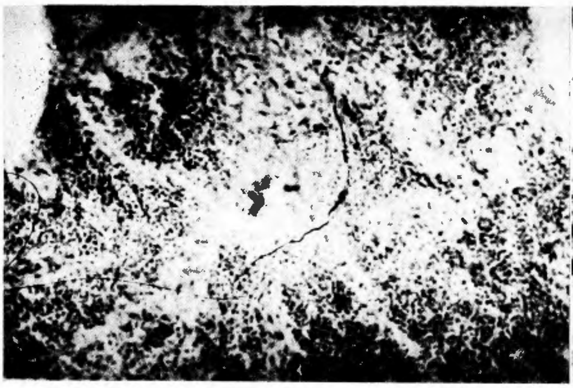
6) Myelinated nerve fibers in the medullary substance of an ileocecal lymphgland. ×200



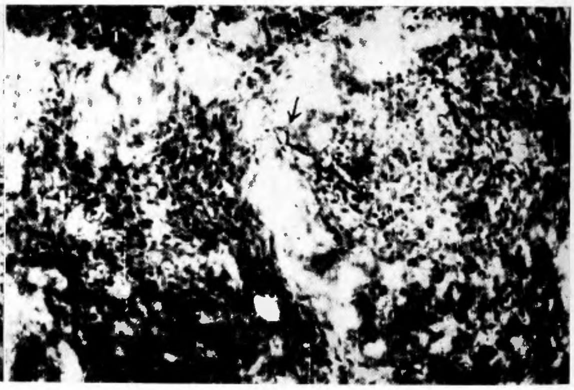
7) A sensory nerve in an ileocecal lymphgland which enter the medullary band from the trabeculae and ending in free ending in the medullary band. ×400



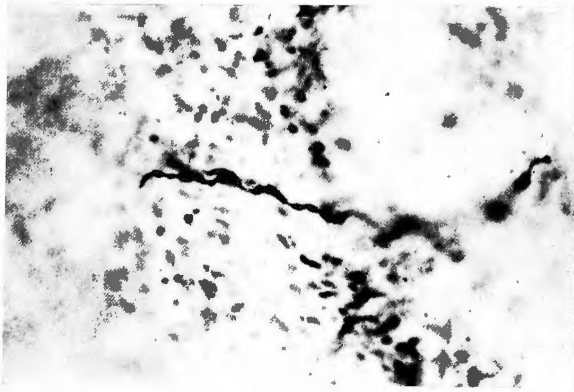
8) A nerve bundle entering the medullary band from the trabeculae in an ileocecal lymphgland. ×200



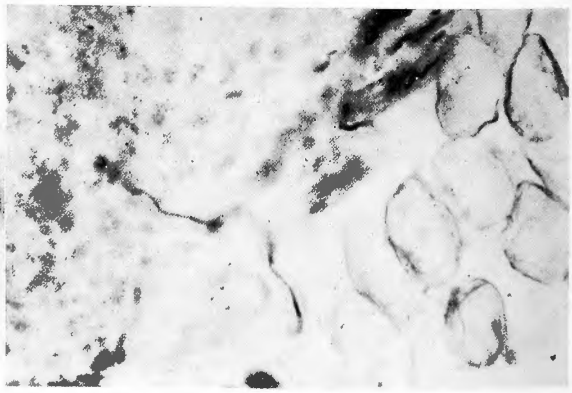
9) Sensory nerve ending around the secondary follicles of an ileocecal lymphgland. ×200



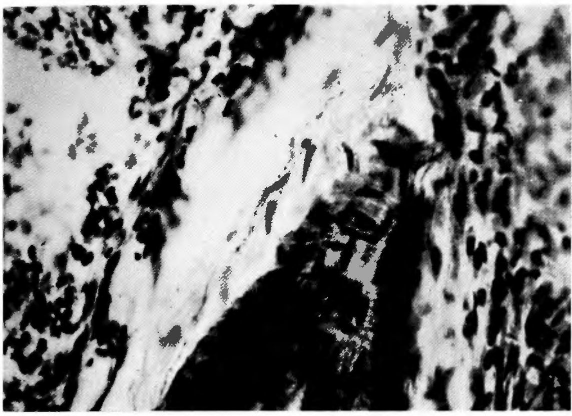
10) Sensory nerve ending entering a secondary follicle. ×200



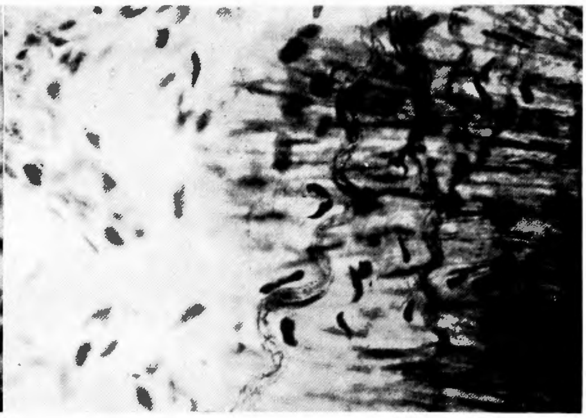
11) Sensory nerve ending entering a secondary follicle. Same as Fig. 10 enlarged 900 times



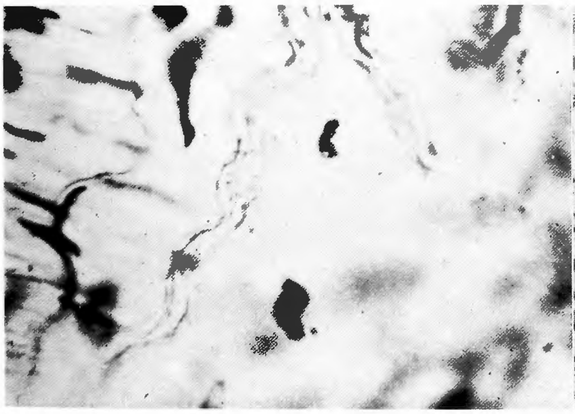
12) A large myelinated nerve in the capsule of an ileocecal lymphgland. ×400



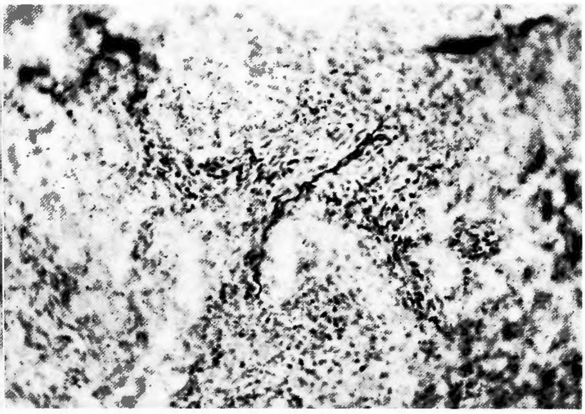
13) Autonomic nerve syncytium running along a blood vessel in the hilum of an ileocecal lymphglands. ×400



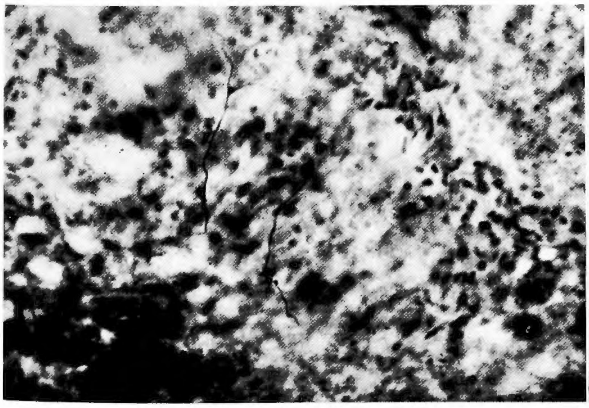
14) An autonomic nerve syncytium running along a blood vessel in the hilum of an ileocecal lymphglands. ×600



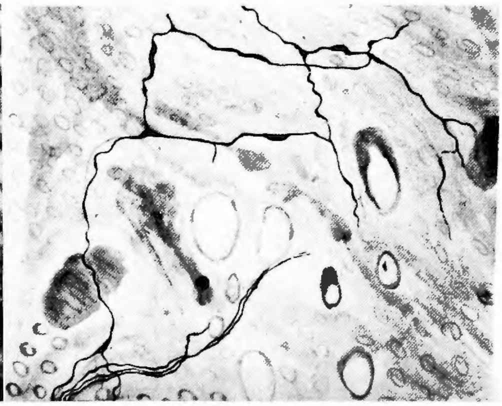
15) An autonomic nerve syncytium running along a blood vessel in the hilum of an ileocecal lymphgland. Same as Fig. 14 enlarged ×900.



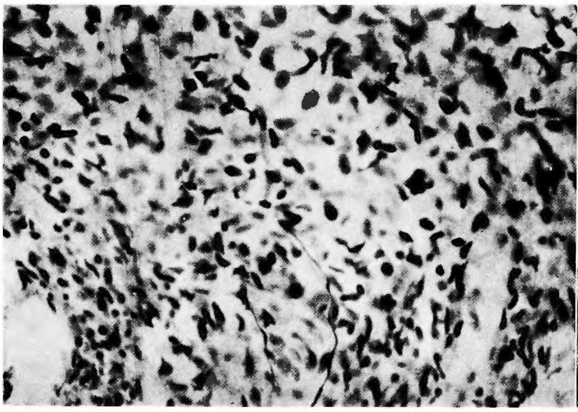
16) A free ending nerve fiber in the trabeculae of an ileocecal lymphgland. ×400



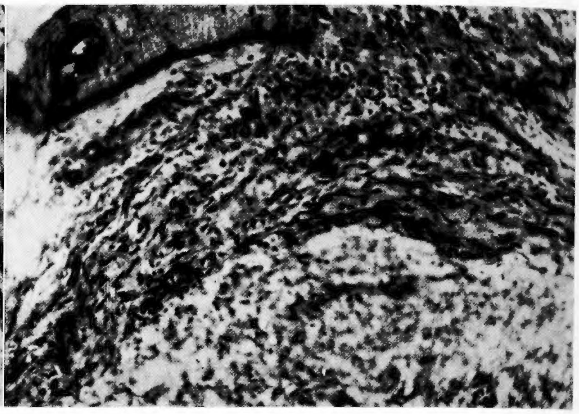
17) Nerve fiber (17) and terminal bifurcations with expansions. (Fig. 17 photo. Fig. 18 sketsh of Fig. 17)



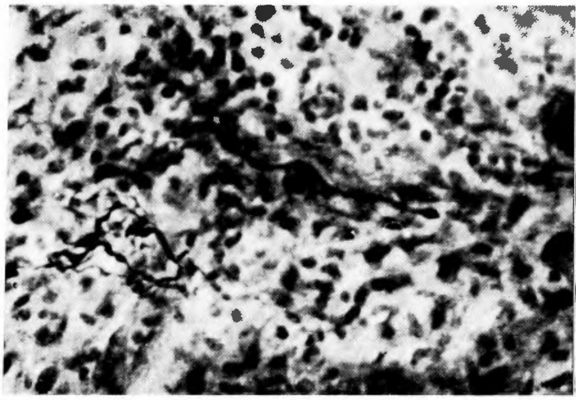
18) Nerve fiber (17) and terminal bifurcations with expansions. (Fig. 17 photo. Fig. 18 sketsh of Fig. 17)



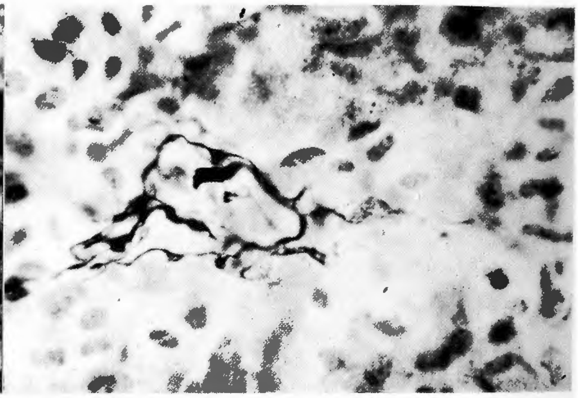
19) Sensory nerve in the capsule of an axillary lymphgland.



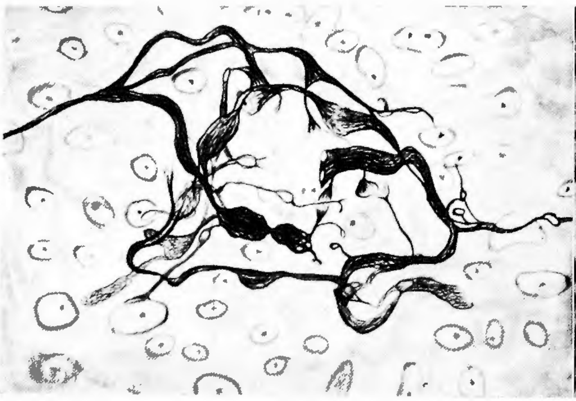
20) Abundant nerve fibers around blood-vessels in the capsule of an axillary lymphgland. × 200



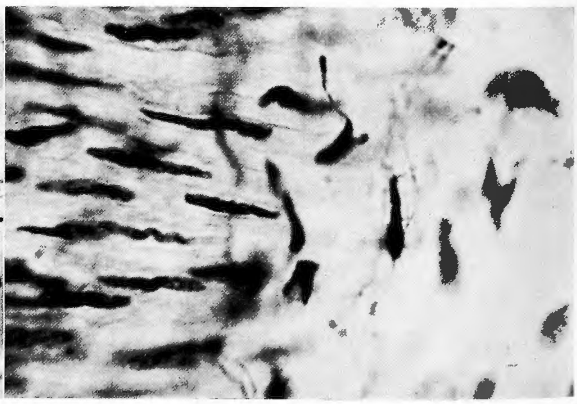
21) A myelinated nerve a receptor field of a senosry nerve ending which forms a glomerular structure with many expansions like "Endöse", in the capsule of an axillary lymphgland. ×400



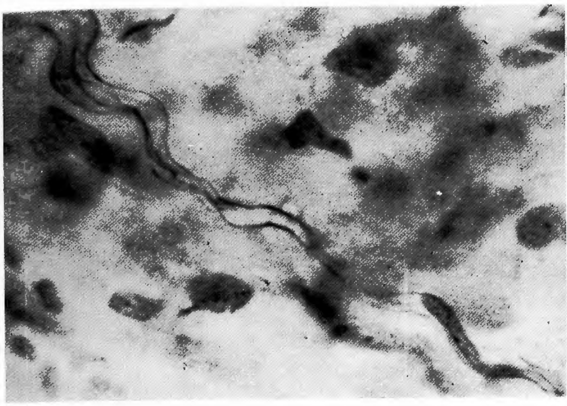
22) Same as Fig. 21 900 times enlarged.



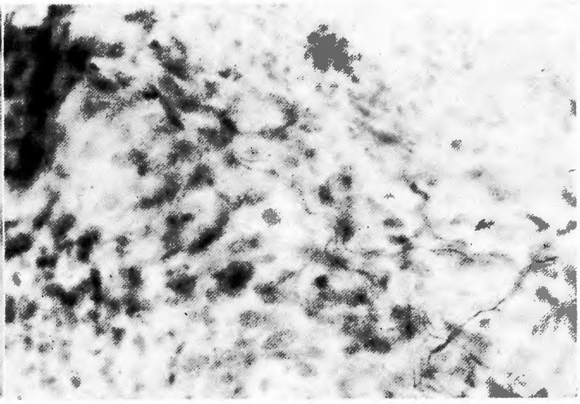
23) Sketch of Fig. 22.



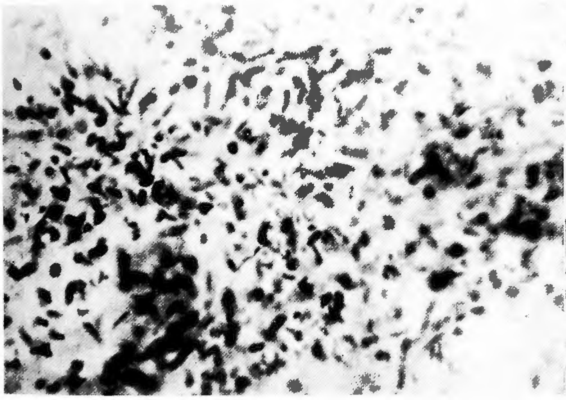
24) An autonomic nerve syncytium around the blood vessels in the hilum of an axillary lymphgland 900 times enlarged.



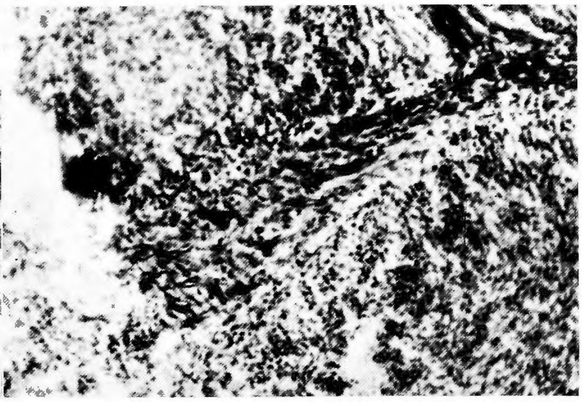
25) An autonomic nerve syncytium in the parenchyma of an axillary lymphgland 900 times enlarged.



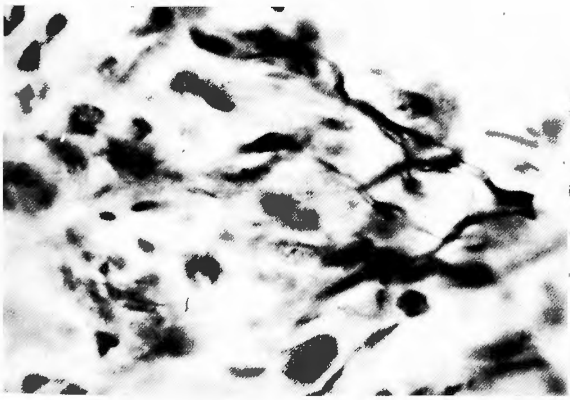
26) An autonomic nerve syncytium and a sensory nerve in the medullary substance of an axillary lymphgland. × 400



27) Sensory nerve ending in the trabeculae of an axillary lymphgland. × 200

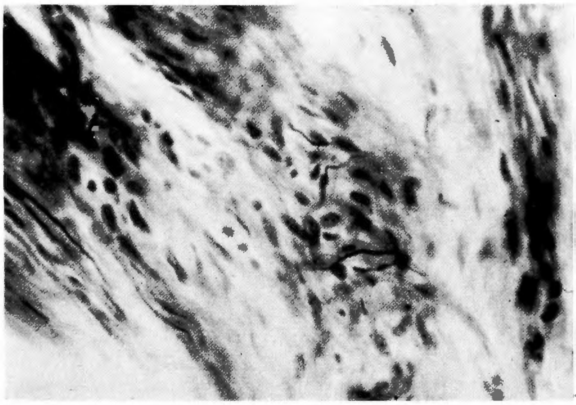


28) A glomerular sensory field with many terminal expansions and "Endöse" extending in a wide area of the trabeculae in an axillary lymphgland. × 200

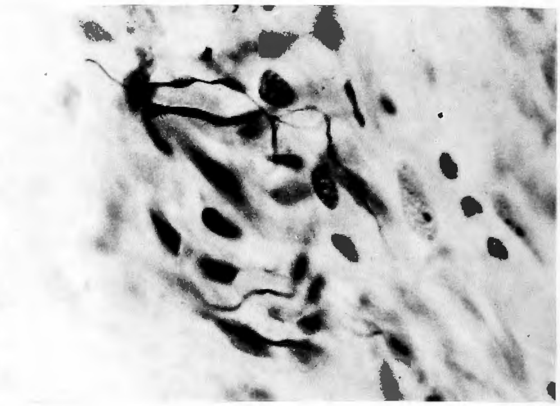


29) Figure of Fig. 28 enlarged 900 times.

30) Sketch of Fig. 29.

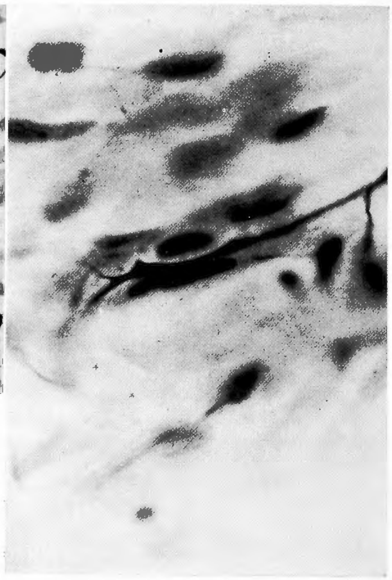


31) A human popliteal lymphgland.
A sensory field arising from a thick nerve fiber. The thick nerve fiber changes into fine fibrils with many ampulla like expansions and terminal divisions and forms glomerular appearance as a whole. ×400

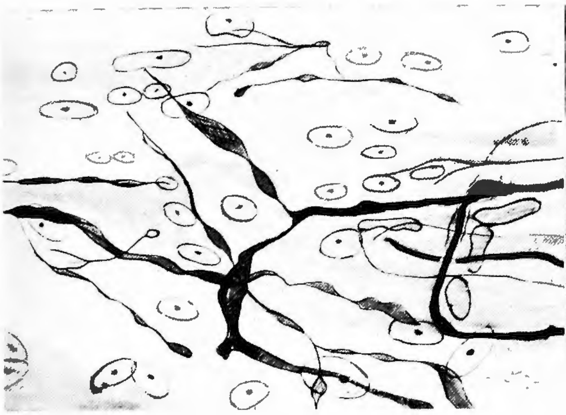


32) Fig. 31 enlarged 900 times.

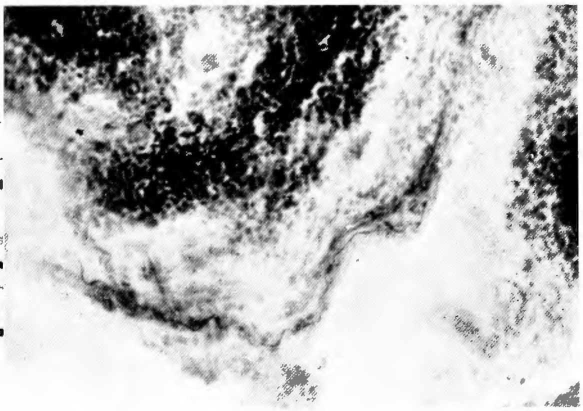
33) Sketch of Fig. 32.



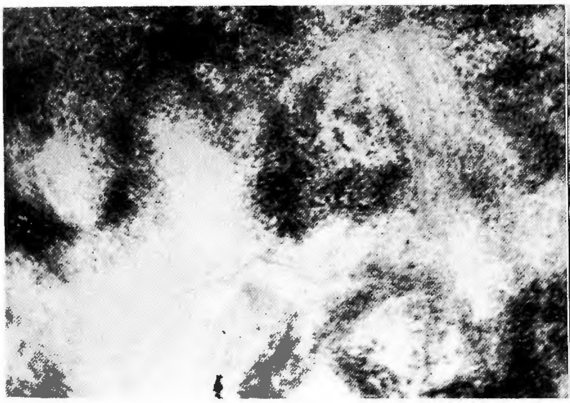
34) A human popliteal lymphgland.
A sensory field arising from a thick nerve fiber; a thick nerve arising from a thick nerve fiber; the thick nerve fiber changing into fine fibrils with many ampulla like expansions and terminal divisions and forming a glomerular appearance as a whole. 900 times enlarged.



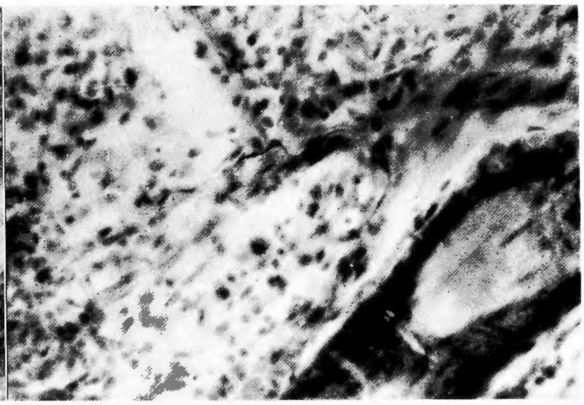
35) Sketch of Fig. 34



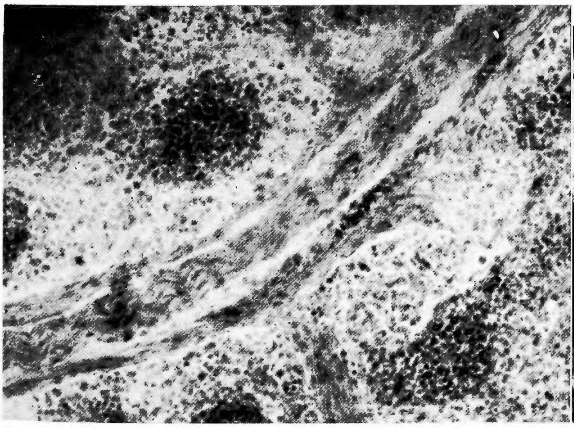
36) Sensory nerve fibers in the hilum of a popliteal lymphgland. × 200



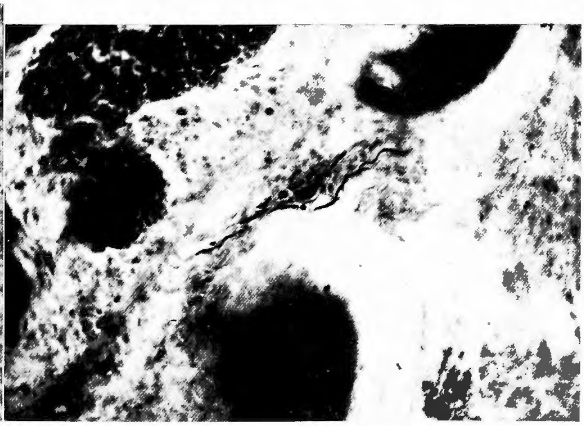
37) Sensory nerve fibers in the medullary substance of a popliteal lymphgland. × 200



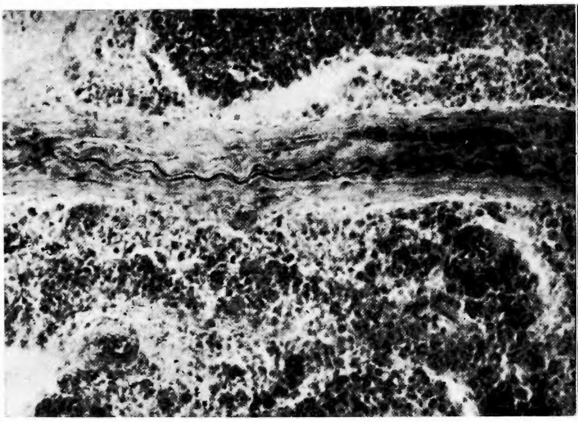
38) Sensory nerve fibers around the blood vessels in the hilum of a popliteal lymphgland. × 200



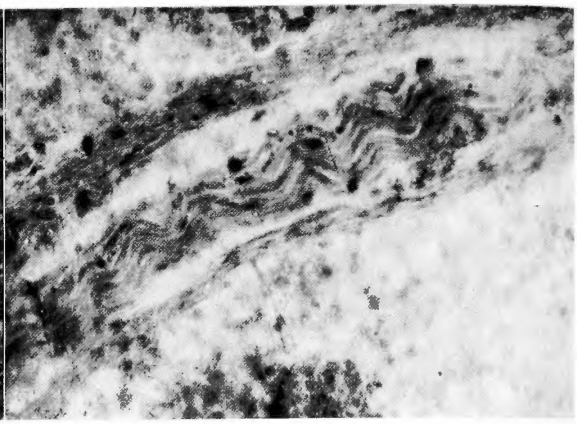
39) A degenerated nerve fiber in the trabeculae of an ileocecal lymphgland after bilateral post. rhiz. (T7-T9) ×200



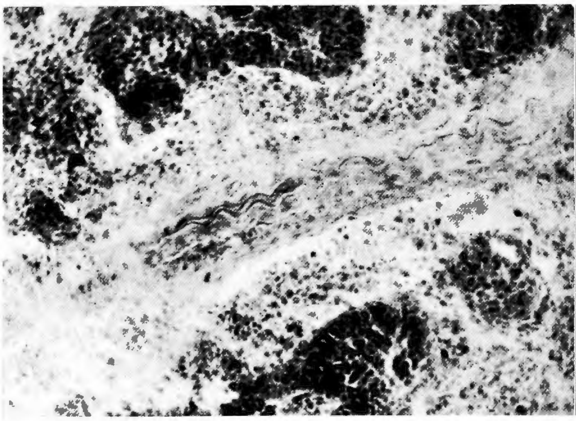
40) A markedly degenerated nerve fiber in the hilum of an ileocecal lymphgland after bilateral post.-rhiz. (T 10-T 12) × 200



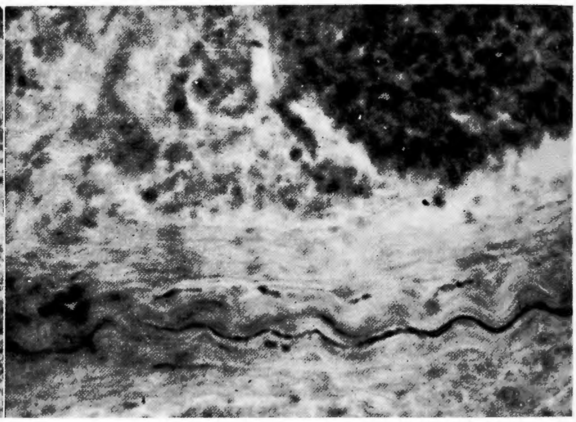
41) A degenerated nerve fiber in the trabeculae of an ileocecal lymphgland after bilateral post.-rhiz. (T 10-T 12) × 200



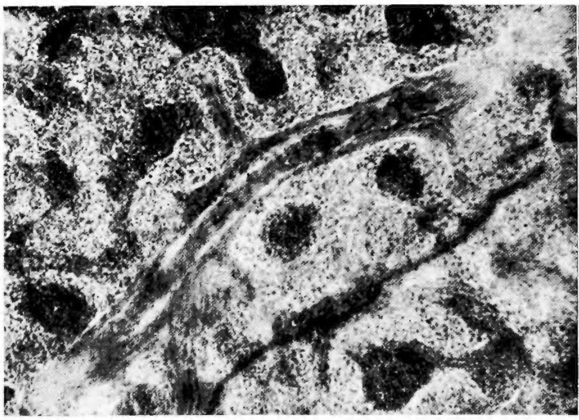
42) A degenerated nerve fiber in the trabeculae of an ileocecal lymphgland after bilateral post.-rhiz. (T 10-T 12)



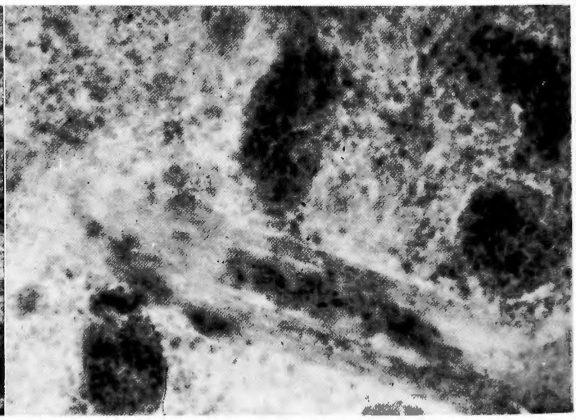
43) A few degenerated nerve fibers in the trabeculae of an ileocecal lymphgland (T13-L 1). × 400



44) A few degenerated nerve fibers in the trabeculae of an ileocecal lymphgland after right post.-rhiz. (T 5-T 8)



45) A markedly degenerated nerve fiber in the trabeculae of an ileocecal lymphgland after right post.-rhiz. on right side. (T 9-L 1) × 200



46) A markedly degenerated nerve fiber in the trabeculae of an ileocecal lymphgland after right post.-rhiz. (T 9-L 1) × 400