

HISTOLOGICAL STUDIES OF SENSORY NERVES IN THE SIGMOID AND RECTUM

by

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I INTRODUCTION

The existence of sensitivity in the rectum has already been proved by many authors. According to R. ZIMMERMANN, who reported on rectal sensitivity, the rectum is sensitive to thermal and electric stimulation, and especially to changes in its internal pressure, which controls defecation. CH. KIMURA, Assit. Prof. of our clinic, demonstrated sensitivity throughout the whole alimentary canal using acetylcholine and mechanical stimulation. He also determined, on the basis of his physiological experiments, which of the vagal, thoracolumbar and sacral nerves had dominant innervation on each organ.

A. OTSU observed many sensory nerve endings in the sigmoid of a patient with congenital megacolon, and J. JABONERO also reported on the sensory nerve endings in the rectum.

Thus, the sensitivity of the rectum and sigmoid has already been proved physiologically, but the morphological characteristics of the sensory nerve endings there have not yet been studied in full detail.

As the sigmoid and rectum are, of course, innervated by autonomic nerves, sensory nerve endings there must be strictly distinguished from them. Prof. H. SETO, on the basis of P. STOEHR's theory of the "autonomic terminal-reticulum", maintained that the thick nerves with free terminations were considered to be sensory nerves, and that they could be easily differentiated from the peripheral structure of the autonomic nerves, which form a closed reticulated structure, i. e. the "autonomic terminal reticulum". He reported many sensory nerve endings (SETO) in the esophagus, stomach, duodenum, anus, genitourinary tract, perivascular region of the abdominal aorta, and pancreas.

According to A. Orsu, who found sensory nerve endings in the stomach, jejunum and colon, they were myelinated nerve fibers even near the mucous membrane, and they never had interposed neurons on the way.

In the present study, the sensory nerve endings in the human and dog sigmoid and rectum were investigated histologically from the standpoint of SETO's theory, and systematic observations of their sensory innervation were made.

According to J. N. LANGLEY'S neuron theory, the characteristics of the sensory nerve are as follows: (1) In general, sensory nerves are myelinated nerve fibers, (2) they do not have relay neurons until their terminals, and (3) visceral sensory nerves are commonly derived from the dorsal roots of the spinal cord.

Therefore, these points were confirmed in the sensory nerve endings demonstrated in this study.

II MATERIALS AND METHODS

Fresh specimens, taken from human sigmoid and rectum without inflammatory changes or neoplasmas, were used. They were fixed in 10% neutral formol solution for $3 \sim 4$ weeks, and then cut in $30 \sim 40\mu$ slices with the freezing microtome. Preparations were kept in 10% neutral formol solution again for at least 6 months before staining.

Dogs were used as experimental animals. Section of the dorsal roots of the spinal cord, section of their ventral roots, and vagotomy were performed. Rhizotomy was performed at points distal to their ganglia, and vagotomy was performed in the thorax on both ventral and dorsal branches.

SETO'S modification of BIELSCHOWSKY'S silver impregnating method (SETO'S Method) was used for staining the axiscylinders. EHRLICH'S acid haematoxyl'ne method was used for staining the myelin sheath.

SETO'S Method

The specimens, which have been cut with the freezing method and kept in neutral formol solution, are

- 1, washed with distilled water for a few minutes,
- 2, put into 20% silver nitrate solution, being protected from light, for $24 \sim 48$ hours,
- 3, washed in distilled water for $20 \sim 30$ seconds,
- 4, put into 20% neutral formol solution, This solution must be made by diluting the mother neutral formol only with running water, and placed in 4~5 plates. The specimens are transferred to these plates one by one until the white precipitation disappears.
- 5, washed with running water for $30 \sim 50$ seconds,
- 6, placed on filter paper to blot up the water.

- 7, immersed in warm ammoniacal silver solution for about 10 minutes,
- 8, washed with distilled water twice,
- 9, placed in $0.05 \sim 0.1\%$ gold chloride solution for $3 \sim 4$ hours,
- 10, placed in 20% sodium thiosulfate solution until the specimens are colored reddish brown,
- 11, washed in distilled water,
- 12, dehydrated and mounted.

III SENSORY NERVE ENDINGS IN THE SIGMOID AND RECTUM

In all layers of human and dog sigmoid and rectum, the "autonomic terminalreticulum" was found in abundance. (Fig. 1.) In the muscular layer, winding thick nerve fibers, easily distinguishable from relatively thin autonomic nerves, are observed. Between the longitudinal and circular muscles, many myenteric plexuses were found, in which several thick and winding nerve fibers were observed. These nerves resembled those in the muscular layer, but no connection could be observed between these nerves and the nerve cells in the myenteric plexus. (Fig. 2 and 3.)

These nerve fibers were traced to the mucous membrane and entered the muscularis mucosae alone or with thin autonomic nerve fibers: and they terminate either in sharp free endings or in ramifying terminations after arborizing into two branches. (Fig. 4, 5 and 6.)

In the lamina propria mucosae, these thick nerves ended in arborized terminations around or between the glands, but they never entered the glands themselves. We may call these nerves sensory nerve endings (SETO) in agreement with SETO's opinion. (Fig. 7, 8, 9 and 10.)

Myelinated nerve fibers were found in all layers of the sigmoid and rectum, and they were most numerous in the lower portion of the rectum. The course and distribution of these myelinated nerve fibers were similar to those of the thick nerves mentioned above. That is, myelinated nerve fibers could be traced not only in the muscular, submucous and mucous layer, but also beside the glands. (Fig. 11, 12 and 13.)

In short, sensory nerve endings (SETO) were traced as far as the mucous membrane, without connecting with nerve cells in the myenteric plexus, and they had myelinated nerve fibers even near their terminals.

(1) Sensory Nerve Endings in the Sigmoid

In the specimens taken from normal sigmoids, wavy thick nerve fibers were observed running from the submucous to the mucous layer. In the mucous membrane, they were traced towards the bases of the glands with or without arborization and they terminated in simple nonarborized or simple arborized endings. (Fig. 14 and 15.) These were considered to be sensory nerve endings (SETO). In these specimens, myelinated nerve fibers were also observed in the submucous and mucous layer, and some of them were found between the glands.

In the sigmoid of a patient with congenital megacolon, very interesting findings were recognized. In the stenosed portion of the sigmoid, no nerve cells were seen

in the myenteric plexus, whereas those in the dilated portion showed an almost normal appearance. Abnormally thick and reticulated nerve fibers were observed forming abundant nerve networks in the mucous membrane of the dilated sigmoid, but their appearance was quite different from that of the "autonomic terminalreticulum", which consisted of very thin nerve fibers. Sensory nerve endings (SETO) were found in this dilated sigmoid, and they branch near the base of the glands to terminate in free ending arborizations. (Fig. 16 and 17.)

(2) Sensory Nerve Endings in the Rectum

Sensory nerve endings (SETO) with almost the same structure as those in the sigmoid were found in the rectum also. They terminated in the mucous membrane as sharp and simple endings or in terminal arborizations. (Fig. 18, 19, 20 and 21.) In the lower portion of the rectum sensory nerve endings (SETO) were more numerous than in its upper portion, and they had a more complicated appearance; i. e. they were traced around the glands showing many arborizations which reached to the adjoining glands, but finally these rami ended also in terminal arborizations. (Fig. 22, 23 and 24.)

In the Morganian zone of the rectum, sensory nerve endings were markedly increased in number, and there were numerous complex endings. Nerve bundles consisting of several thick nerve fibers were traced around the glands showing arborizations, and these arborized nerve ran through the interglandular tissues repeating arborizations, but these nerves had free-ending terminations without forming any specific end-apparti. (Fig. 25 and 26.)

In the rectum close to the anus, sensory nerve endings were very numerous and many thick nerve fibers were observed in nerve bundles with wavy, winding, tangled and looped appearances. In addition, nerve fibers could be traced from the subcutaneous layer to the basal membrane of the cutis. In the mucocutaneous junction of the anus, complicated tangled glomerular endings were found close to the basal membrane of the cutis. These endings may be in the category of genital nerve endings (SETO). (Fig. 27, 28, 29 and 30.)

Myelinated nerve fibers were found in all layers of the sigmoid and rectum, and they were more númerous in the rectum, especially in its lower portion, than in the sigmoid. They were recognized in the mucous membrane beside the glands sometimes with arborizations. Myelinated nerve fibers also had a complicated appearance in the lower portion of the rectum. Therefore it was certain that these myelinated nerve fibers were identical with sensory nerve endings (SETO), which were recognized by the silver stain, and it might be concluded that sensory nerve endings (SETO) consisted of myelinated nerve fibers even in the mucous membrane. (Fig. 31 and 32.)

Sensory nerves, demonstrated above, were quite different from the "Schlaengende Territorien (STOEHR)".

IV SYSTEMATIC OBSERVATIONS OF THE SENSORY INNERVATION OF THE SIGMOID AND RECTUM Vagotomy and posterior rhizotomy of the thoracolumbal and sacral portion of the spinal cord, were performed to decide the origin of these sensory nerve endings. Posterior rhizotomy was performed on both sides at points distal to the spinal ganglia, and the vagotomy was performed in the thorax on both its ventral and dorsal branches. The sigmoid and rectum were resected $5 \sim 8$ days after the operation. Degeneration of the nerve fibers in these specimens was examined mainly with EHRLICH's stain, but SETO'S Method was also used to confirm that these degenerated nerves were identical with sensory nerve endings (SETO).

Experiment 1. Vagotomy

Experiment 2. Posterior rhizotomy (Th. 13-L. 4 and L. 5-L. 7.)

Experiment 3. Anterior rhizotomy (Th. 13-L. 4 and L. 5-L. 7.)

Experiment 4. Anterior rhizotomy (S. 1. - S. 3.)

In the specimens taken after Experiment $1 \sim 4$, no degeneration of the nerve fibers was recognized.

Experiment 5. Posterior rhizotomy (S. 1--S. 2 and S. 3--Coc. 1.)

In the specimens taken after Experiment 5, degeneration of many myelinated nerve fibers was seen. Degenerated myelin sheaths showed marked swellings at places, and they were broken into beadlike appearance sometimes containing degene-These degenerated nerve fibers were found not only in the subrating glanules. mucous and muscular layer, but also in the mucous membrane or close to the glands. But a few myelinated nerve fibers with no appearance of degeneration could be observed in the lamina muscularis mucosae or submucosa. (Fig. 33, 34, 35 and 36.) It was proved by the observation with the silver stain that the degeneration of the myelin sheath was always accompanied by that of the axiscylinder. (Fig. 37 Degenerated nerve fibers were fewer in the upper part of the rectum and 38.) and in the sigmoid than in the rectum near the anus. But even in the upper sigmoid, which was $70 \sim 80$ cm away from the anus, a few degenerated nerve fibers were recognized. Degenerated nerve fibers were recognized more frequently after the posterior rhizotomy of S. 1. ~ S. 2. than after that of S. 3. ~ Coc.1. In all experiments, no degenerative findings were observed in the "autonomic terminalreticulum".

V DISCUSSION

In the present study, many sensory nerve endings (SETO) are demonstrated in agreement with the opinion of Prof. H. SETO, who maintained that the thick nerves with free terminations are sensory nerves. Sensory nerve endings (SETO) in the sigmoid and rectum are recognized in the more peripheral layer beyond the nerve plexus of the intestinal wall, and no connection is observed between these sensory nerves and nerve cells. Besides these sensory nerve, the "autonomic terminalreticulum" is, of course, definite. According to the results of my experiments, these nerves are myelinated even in the peripheral layer, and they terminate freely without neurons interposed in their course from the dorsal roots of the sacral cord to their terminals. These findings are in accordance with the general characteristics

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of the sensory nerve, deduced from LANGLEY'S neuron theory. Therefore, it is almost certain that the sensory nerve endings, demonstrated in this study, are visceral sensory nerves. Such sensory nerve endings, are quite different from the so-called "Schlaengende Territorien" or "Geschlaengerte Plasmastraenge" (STOEHR), because they are always nerve fibers themselves and look like neither "Leitplasmodium (leading plasmodium)" nor the terminal network.

Myelinated nerve fibers are more numerous in the lower portion of the rectum than its upper portion and in the sigmoid, and the sensory nerve endings also show the same distribution as that of myelinated nerve fibers. In the lower portion of the rectum, especially in the Morganian zone, the sensory nerve endings are complicated. It may be assumed from these findings, that the rectum is most sensitive in its lower portion.

The sensory nerve endings, demonstrated in the present study, consist of myelinated nerve fibers, and this finding coincides with A. Orsu's report, which maintained that the sensory nerve endings (SETO) had myelinated nerve fibers. Of course, it can be assumed that some of the visceral sensory nerves are non-myelinated nerve fibers, but systematic observation of them is very difficult and their existence has not been proved definitely. Sensory nerve endings are often observed near the glands, but they are traced, if examined in detail, only around or beneath the glands without entering the glands themselves, and these nerves are very few in comparison to the number of the glands. Therefore, it is inconceivable that these nerves innervate the glands directly.

M. CLARA believes that the sensory nerve endings have, in common, morphological characteristics which serve to extend their terminal surfaces. But G. WEDDEL maintains, on the basis of his physiological and histological study, that the sensory nerve endings is, in general, a free-ending arborization, and he does not emphasize the complicated structure of the sensory nerve ending. In his view, the same ending can, under certain conditions, give rise to different sensations.

The sensory nerve endings in the sigmoid and rectum are simple-branched endings or free-ending arborizations, and they never arborize into more than two branches. In the Morganian zone, complicated arborized endings are recognized, and many tangled glomerular endings are found near the anus. The endings in the sigmoid and upper portion of the rectum are more simpler than those in the lower portion of the rectum.

A. OTSU reported complicated glomerular endings in the sigmoid of a patient with congenital megacolon. But in my specimens taken from a patient with congenital megacolon, no complicated endings was found except some simple arborized endings. F. R. WHITEHOUSE reported that, nerve cells in the myenteric plexus disappeared or decreased in congenital megacolon, and this degeneration of the nerve plexus caused a disturbance of peristalsis in the stenosed portion of the colon, and the compensatory dilation of the upper portion of the colon. N. ISHIKAWA and T. TAKAYASU also maintained that congenital megacolon was due to the degeneration

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of the autonomic nervous system, which innervated the colon. In my specimens, the disappearance of nerve cells in the myenteric plexus was recognized in the stenosed portion. In the dilated portion, on the other hand, abnormally thick and reticulated nerve fibers were found, which resembled the so-called "Neurom (FEYRTER)" but were quite different from the "autonomic terminalreticulum". According to the study of J. BOEKE and J. JABONERO, the "autonomic terminalreticulum" consists mainly of sympathetic nerves. Considering these findings, it may be assumed that congenital megacolon is caused by the abnormal impulse of the sympathetic nervous system.

In experiments on dogs, no sensory nerve derived from the vagus or the ventral roots of the spinal cord, was proved to exist in the sigmoid and rectum. Sensory nerves, derived from the dorsal roots of the lumbal cord were not recognized either. But after posterior rhizotomy of the sacral cord, degeneration of both the myelin sheath and axis-cylinder was observed in the sigmoid and rectum. According to Y. NITTA, about 2/3 of the thin myelinated nerve fibers in the pelvic nerve are sensory nerves with their cell bodies in the dorsal root ganglia. S. OKINAKA maintained that many thin myelinated nerves are contained in the S.2. nerve; and he stated that most of them might be spinal parasympathetic afferents. In my experiments, degenerated nerve fibers were more frequently found after posterior rhizotomy of $S.1 \sim S.2$ than after that of $S.3 \sim Coc.1$. These findings are in accordance with S. OKINAKA's opinion, mentioned above. According to S. OKINAKA, both afferent and efferent nerves are derived from the lumbal cord. But in my experiments, no degenerated nerves were observed after rhizotomy of the thoracolumbal cord. Considering these results, it is certain that as far as afferent innervation is concerned, the sacral cord innervates the sigmoid and rectum more than does the thoracolumbal cord.

The sensory nerve endings demonstrated in this study are myelinated nerve fibers, derived from the dorsal roots of the sacral cord without relaying neurons on their way. Therefore, it can be concluded that these sensory nerve endings are definite enough to prove the sensitivity of the sigmoid and rectum.

VI SUMMARY

(1) Sensory nerve endings with simple arborized terminations or free-ending arborizations are found in the mucous membrane of the sigmoid and rectum of human beings and dogs.

(2) Sensory nerve endings are most numerous and complicated in the lower portion of the rectum.

(3) In the sigmoid and rectum, no specific sensory end-apparatus is found except some glomerular endings in the anal region.

(4) Abnormally thick and reticulated autonomic nerves are found in the mucous membrane of the dilated portion in congenital megacolon.

(5) Sensory nerve endings demonstrated in the present study consist of myelinated nerve fibers. (6) Sensory nerve endings in the sigmoid and rectum are derived from the dorsal roots of the sacral cord without relaying neurons on their way.

(7) As for afferent innervation, the sacral cord innervate the sigmoid and rectum more dominantly than the thoracolumbar cord.

(8) The sensory nerve endings demonstrated in the present study are quite different from the so-called "Schlaengende Territorien (Stoehr)" or "Geschlaengerte Plasmastraenge (Stoehr)".

I am greatly indebted to Dr. HACHIRO SETO (Prof. of Tohoku University) for his kind advice and also to Dr. CHUJI KIMURA (Assist. Prof. of our Clinic) for his constant help during the course of this study.

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和文抄録

S字結腸及び直腸知覺神経の組織学的研究

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S字結腸及び直腸の標本(人間及び犬)及び先天性 巨大結腸症の標本に就て Bielschowsky氏神経鍍銀法 の瀬戸氏変法及び Ehrlich 氏神経髄鞘染色法を用い, 知覚神経終末の形態及び分布を検索し,更に系統的観 察を行う為犬を使用し迷走神経,脊髄前根(Th.13-L.4, L.5-L.-, S.1-S.3),脊髄後根(Th.13-L.4, L.5-L.-, S.1-S.2, S.3-Coc.1)を切断し,S字結腸及び直 腸内の末梢神経の二次変性を追求し,之等の結果より S字結腸及び直腸知覚神経に就て次の結論を得た.

1) 人間及び犬のS字結腸, 直腸の粘膜層に単純分 岐性樹枝状及び**遊離性知覚**神経終末(瀬戸)が発見さ れる.

2) 知覚神経終末は直腸下部に於て増加し形状も複 雑化する. 3) 肛門附近に糸毬状知覚神経終末を発見した外に はS字結腸及び直腸に特殊知覚神経終末を発見する事 が出来なかつた。

4) 先天性巨大結腸症の膨大部の粘膜層に異状に発 達せる自律神経線維網が発見された。

5) 上記の知覚神経終末は有髄性のものである.

6) S字結腸及び直腸の知覚神経は仙髄後根を通り 終末に到る迄神経元を交替しない。

7) S字結腸及び直腸に於ては仙髄後根性の知覚支 配が胸腰髄性のものより優勢である.

8) 上記の知覚神経は Ph. Stoehr, Jr. の言う "Schlaengende Territorien" や "Geschlaengerte Plasmastraenge" とは全く別個の神経線維である。

限局性小腸炎に於る腸筋層内神経叢:24例の回腸に於る神経細胞数に就いての研究

The Myenteric Plexus in Regional Enteritis : A Study of the Number of Ganglion Cells in the Ileum in 24 Cases D. R. Davis, M. B. Dockerty and C. W. Mayo.

(Surg. Gynec. & Obst., 101 : 208, 1955)

従来先天性巨大結腸には結腸筋層内神経細胞を欠如すると云われ、久噴門痉攣患者の噴門部神経細胞が減少していると云う報告もある.又之等の疾患と反対の性格を有すると考えられる慢性潰瘍性結腸炎の場合は逆に之等の神経細胞が正常の3倍も増加していると云われる.

限局性小腸炎は慢性潰瘍性結腸炎と同様な性格を有する疾患と考えられ,共に迷走神経切断術が良結果をもた らすようである.

著者等は之等の事から24例の限局性小腸炎の小腸と、対照として同数、同性、同年令の健常小腸との Myenteric Plexus の神経細胞数を計算した.

即ちホルマリン固定30日間.計算する小腸の部分は4ヵ所で、回盲部より口側, 夫々 5,13,24.40糎の部を選び,横断切片を作る.染色は Cresyl Violet. 8µ切片で神経細胞数を計算した.

その結果

1.)限局性小腸炎のそれは対照に比し約3倍増加している.然もこの事実は肉眼的に明かに侵されている部分のみならず,その近くの一見正常に見える小腸に於ても同様である.

2.) 若年の本患者のそれは老年の同患者のそれに比し,明かに少い.更に本疾患が長く存在したもの程その数 が多い.

3.) 之等の数は性別,炎症の範囲,腸閉塞の有無等とは関係がない.

1.)回腸全体を通じての神経細胞の分布は大体一様で、1ヵ所の神経細胞数が、同一個人の他の部の細胞数を 代表する事が出来る. (山 本)

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- Fig. 1. "Autonomic terminalreticulum" in the tunica muscularis mucosae of human rectum. B-S. × 1200
- Fig. 2. Sensory nerve fibers in the muscular layer of the rectum. B-S. \times 320
- Fig. 3. Sensory nerve fibers in the myenteric plexus of the rectum. B-S. \times 320
- Fig. 4. Sensory nerve endings in the lamina muscularis mucosae of the rectum. B-S

 $\times 320$

- Fig. 5. Drawing from the same preparation as Fig. 4.
- Fig. 6. Arborized sensory nerve endings in the tunica muscularis mucosae of the sigmoid (Drawing).
- Fig. 7. Sensory nerve endings in the mucous membrane of the rectum. B-S. × 320
- Fig. 8. Drawing from the same preparation as Fig. 7.

Figures

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membrane of the sigmoid. E. × 320 Fig. 14. Sensory nerve endings in the lamina mus cularis mucosae of the sigmoid. B-S. \times 320 Fig. 15. Sensory nerve endings in the lamina muscularis mucosae of the sigmoid. B-S. ×

- Abnormally thick and reticulated nerve Fig. 16. fibers forming network in the mucous membrane of the dilated portion of congenital megacooln. B-S. × 400
- Fig. 12. Myelinated nerve fibers in the mucous membrane of the rectum. E. × 320
 Fig. 13. Myelinated nerve fibers in the mucous

layer of the rectum. E. $\times 320$

Drawing from the same preparation as

Myelinated nerve fibers in the submucous

Fig. 10.

Fig. 11.

Fig. 9.

320

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Fig. 20. Sensory nerve endings in the mucous membrane of the rectum. B-S. × 320

Fig. 24. Drawing from the same preparation as F_{12}^{i} or

Figures

SENSORY NERVES IN THE SIGMOID AND RECTUM





- Fig. 25. Complicated sensory nerve endings in the mucous membrane of the human Morganian zone. B-S. ×400
- Fig. 26. Sensory nerve endings in the mucous membrane of the lower portion of the rectum of a dog. (This portion corresponds to the Morganian zone of the human rectum.) B-S ×400
- Fig. 27. Sensory nerve fibers in the subcutaneous tissue of human anus. B-S. × 320
- Fig. 28. Sensory nerve-endings entering in the subcutaneous layer and basal membrane of the cutis near the anus. B-S. × 320
- Fig. 29. A complicated glomerular sensory nerve ending in the subcutaneous tissue of the mucocutaneous junction of human anus. $B-S. \times 320$
- Fig. 30. Drawing from the same preparation as Fig. 29.



Fig. 31. Myelinated nerves in the mucous membrane of the rectum. E. ×320

Figures

- Fig. 32. Arborized myelinated nerve fibers in the mucous membrane of the lower portion of the rectum. E. × 320
- Fig. 33. Degeneration of myelinated nerve fibers in the submucous layer of the sigmoid of a dog with posterior rhizotomy (S.1.~S. 2.) E. ×320
- Fig. 34. Degeneration of myelinated nerve fibers in the submucous layer of the rectum of a dog with posterior rhizotomy (S. 3~ Coc. 1.) (non-degenerated nerves are also observed) E. $\times 320$
- Fig. 35. Degeneration of myelinated nerve fibers in the mucous membrane of the rectum of a dog with posterior rhizotomy (S.1 \sim

S.2.) E. × 320

- Fig. 36. Degeneration of myelinated nerve fibers in the lamina muscularis mucosae of the rectum of a dog with posterior rhizotomy (S.1.~S.2.) E. × 320
- Fig. 37. Degeneration of myelinated nerve fibers in the submucous layer of the rectum of a dog with posterior rhizotomy (S. $1 \sim S$. 2.) E. × 320
- Fig. 38. Degeneration of the axis-cylinders in the submucous layer of the rectum of a dog with posterior rhizotomy (S1~S.2.) B-S. ×640
- Notes : B-S....SETO'S Method (SETO'S modification of BIELSCHOWSKY'S silver impregnating method.) E....EHRLIGH's acid haematoxyline method.