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## A HISTOLOGICAL STUDY ON THE INNERVATION OF THE PARATHYROID GLAND

by

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### 1. INTRODUCTION

The parathyroid glands are small globular or elliptical tissues of endocrine organs situated on both side of the thyroid gland. It is as small as a rice or a red bean, and weighs generally 0.2-0.5 gr. From the author's experience its color is often yellowish brown when it is fresh, though in the text book its color is described as dark brown.

The hormone, secreted from the parathyroid gland, was first extracted by COLLIP in 1925, and it was called Parathyrin, but the chemical quality was left unclarified for some years. TWEEDY (1930) and W. G. ALLERDYCE (1931) confirmed the existence of this hormone, but its pure crystallisation has not yet been succeeded. However, the relation of the hormone to the calcium metabolism was confirmed. According to KRAMER's report, the concentration of serum calcium of the parathyroprival animals clearly decreased, and the decreasing calcium was colloidal, while small molecular and super filterable calcium does not decrease so much. On the other hand, the parathyroprival animals show "Tetania parathyropriva" as deficiency symptom. BRYAN reported the existence of Alkalosis in such cases, but it is uncertain whether tetany and alkalosis are both due to hypocalcemia or not. CRILE, SNELL, HOAG et RIVKIN, and JOHNSON applied this hormone in clinical study, and at present, physical, chemical and biological quality of this hormone is clear to some degree.

The author does not know any reports on the innervation of the parathyroid gland, especially, the nerve structure in it.

Histological studies of nerve structures in endocrine are only reported by SUNDER-PLASMANN (1935, 1939) on Thyroid gland, STÖHR (1935), SUNDER-PLASMANN (1935) and SATO (1952) on Suprarenal gland, HAGEN (1951, 1952), KNOCH (1953) and SETO (1954) on Pituitary gland.

According to them, the histological characteristics of the nerve endings in various organs consists of fine fibers formed like a fishing-net with nervous protoplasm, and in whole form a closed net system. On the other hand, the nerve endings in the endocrine organs are composed of considerably thick fibers which do not

branch off fine fibers, and the thickness of this fiber varies considerably and shows an irregular arrangement. Under a close examination of the nerve ending, any net work structure was not found, and these reporters described that these nerve endings showed almost simple arborizations. But the above mentioned description of the nerve endings in the endocrine glands are only confined to the achievement of endocrine other than the parathyroid gland, they are able to be seen mainly in suprarenal gland and anterior lobe of the hypophysis.

The author does not yet know any report of the nerve ending of the parathyroid gland. From the above mentioned facts, the author imagined the existence of the same pattern of innervation in the parathyroid gland.

Hence the author tried to solve following questions.

1) Does the simple arborization exist in the parathyroid gland and control the parathyroid gland just like on the other endocrine organs?

2) Does the net work nerve ending—"Terminalreticulum"—exist in the parathyroid gland?

3) Does such a nerve ending not exist entirely in the parathyroid gland?

The present report is intended to clarify the existence of innervation and then to study the nerve structure if nerve fibers exist in the parathyroid gland.

## 2. MATERIALS AND METHODS

### 1) Obtainment of materials

Parathyroid gland are described in the textbook to be situated behind the thyroid gland as a pair, but from the author's experience the situation of the parathyroid gland depends on individual differences, especially the lower pair sometimes exists on the portion far from the thyroid gland. And the differentiation of the parathyroid gland from the surrounding tissues is sometimes very difficult. Especially, the differentiation of the parathyroid gland from the lymphatic tissue and the subcutaneous fat tissue is more difficult. In the case, when the distinction is difficult, the author tried to obtain a wide-area of the material containing the thyroid gland or the surrounding tissue, and the whole material fixed as described in the following chapter, the parathyroid gland distinguished by histological observation.

All the materials were obtained from the pathologic anatomic corpses which did not show any abnormal secretion of the parathyroid gland at the pathologic division, Kyoto University Medical School and Utano National Sanatorium.

### 2) Management of materials

All the materials for investigation fixed in 10% neutral formol solution as soon as possible after resection and were kept there over 6 monthes. As the differentiation of the parathyroid gland and the surrounding tissue was sometimes very difficult with macroscopical observation, the fixed specimens often included the surrounding tissue. Some of them were considerable large in size. The author distinguished the parathyroid gland histologically by EHRlich's Hämatoxylin-Eosin method, and studied the only confirmed parathyroid gland.

### 3) Method

Specimens, fixed in neutral formol solution, were sliced with the freezing microtome into frozen sections and paraffin sections of 20-30 $\mu$  thick in accordance with the method of impregnation. Impregnation with frozen section is, from the authors view, better than paraffin section when SETO's modification of BIELSCHOWSKY's method is employed.

The author employed mainly the following method;

- A) SETO's modification of BIELSCHOWSKY's silver impregnation method.
- B) SUGAMO's myelin sheath staining.
- C) EHRLICH's hämatoxylin-eosin staining.

EHRLICH's method was employed on a few specimen in order to confirm the parathyroid gland (Fig. 1, 2, 3 and 4.).

In the histological study of the peripheral nervous system the most difficulties are the technique of the impregnation and its unstability. For the purpose to make clear the terminal structure and the meaning of the nervous system, it is necessary to stain the nerve fiber and other tissue under its control at the same time. Bearing this in their mind, many neurologists have made effort in the improvement of the impregnating technique. Up to date many methods of impregnating the nervous system have been reported. However, the author believes the BIELSCHOWSKY's method reported after the CAJAL's method has approached the ideal impregnating method, and among many modifications of the BIELSCHOWSKY's method the SETO's modification is the most simplified and convenient, also superior in impregnation.

### 3. RESULT

The parathyroid gland, observed histologically, is a parenchymatous organ covered with thin tunic involucre, this tunic involucre intrude into the center of the parathyroid gland and form a septum. The septum divides the parathyroid gland into many small segments, and the blood vessels run towards the center along these septums.

In order to confirm the parathyroid gland the author observed the chief-, granular-, water-clear-, and oxyphilic cells in these specimens.

#### 1) Course of nerve fiber entering the parathyroid gland

Observing the course of nerve fiber entering the parathyroid gland, the author revealed two ways.

A) Nerve fiber proceeds into the parenchyma after running along the tunic involucre independent from the blood vessels.

B) Nerve fiber proceeds into the parenchyma after running along the blood vessels in the septum.

In the later case there are these two ways,

a) Nerve fiber ramified to the parenchyma from the relatively large blood vessels.

b) Nerve fiber ramified to the parenchyma after running along the wall of the capillary blood vessel.

The author describe these cases in present study.

A) Nerve fibers which enter the parathyroid gland directly from the tunic involucre.

A thick myelinated nerve fiber running along the tunic involucre abruptly changes its course and proceeds into the parenchyma passing through its surface obliquely or in right angle (Fig. 5 and 6).

Among many specimens of him the author was able to observe the nerve fibers taking such a course only in a few cases. Only a few nerve fiber may be considered to enter the parenchyma directly from the tunic involucre.

Nerve fiber near the tunic involucre, in the surrounding tissue of the parathyroid gland, may be considered to be those fibers (Fig. 7, 8, 9, and 10).

B) Nerve fibers which enter the parathyroid gland along the wall of the blood vessels.

The majority of the nerve fibers may be considered to proceed into the parathyroid gland along the wall of the blood vessels, because these cases are observed frequently. The parathyroid gland, have many blood vessels especially capillaries compared with the other organs. Observing the wall of the blood vessel or its surrounding portions, the author could observe the nerve fiber in most cases (Fig. 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, and 23).

After proceeding along the blood vessels into the inner part of the parathyroid gland, these nerve fibers ramify in the parenchyma (Fig. 14, 15 and 19). When capillaries branch off from the relatively thick blood vessel, nerve fibers may be seen running along the capillaries into the parenchymatous tissue (Fig. 14, 15, 17, 19 and 35). In either cases, when the nerve fiber ramifies it lost the myelin sheath, and in many cases nodulous expansions were observed there.

#### 2) Nerve fiber in the parenchyma of the parathyroid gland

A nerve fiber proceeded into the parenchyma from the wall of the blood vessel took an undulated course (Fig. 7, 8, 9, 10, 14, 15, 19, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38 and 39). However, the author did not observe any nerve fiber which entered the parenchymatous cells. More detailed observation showed that a nerve fiber, though it looked as a single fiber, was actually composed of many fine nerve fibrilles forming a bundle and its ramification was complicated (Fig. 16, 18, 41, 42, 43, 44 and 45).

Observing these nerve fibers towards its peripheral portions and nerve endings, some terminated in simple free endings but many others ramificated into very fine fibers, and these fine fibers crossed one another and looked like a network (Fig. 46, 47, 48, 49, 50, 51, 52, 53, 54, and 55).

Though these fine fibers presented a network-like appearance, they were quite different from the so-called "Terminal reticulum", and they did not anastomose each other (Fig. 56, 57, 58, 59 and 60). Interstitial cells were observed frequently.

The author did not observe any particular nerve endings in the parathyroid gland except above mentioned.

#### 4. DISCUSSION

According to the author's study, the nerve fibers in the parathyroid gland proceeds along the wall of the arterial blood vessel and enter into the parathyroid gland as a comparatively thick myelinated nerve fiber, which ramifies into fine myelinated nerve fibers near its peripheral portion, and switch over to the nerve endings. It rarely terminates in simple free ending but in most cases it further ramifies gradually into finer nonmyelinated fibers, and many of them cross one another and present a network-like appearance. It is an important fact that though the nerve fibers seem to end in myelinated free endings actually in many cases they ramifies further into fine nonmyelinated fibers and show the network appearance by detailed observation. With this fact, the author consider that these nerves ramify help either to enlarge the area of the innervation or to increase the sensibility for stimulation.

SETO described, in his writings, that he was doubtful on the existence of sensory nerve endings in the endocrine for the reason of no report in the past, but, from the results of the recent studies sensory nerve endings seem to exist also in some of the endocrine organs. In fact, SETO revealed the sensory nerve endings in the suprarenal gland and the anterior lobe of the hypophysis.

In his study on the parathyroid gland, the author revealed the existence of the nerve endings. Some of them may be sensory in nature, the physiological significance of these nerve endings are not yet uncertain. Probably they may serve as the route of reflex in the functional control of the internal secretion.

## 5. SUMMARY AND CONCLUSION

Employing SETO's modification of BIELSCHOWSKY's silver impregnation method, SUGAMO's myelin sheath staining and EHRLICH's hämatoxylin-eosin staining, the author studied the nerve endings in human parathyroid gland and obtained the following conclusion.

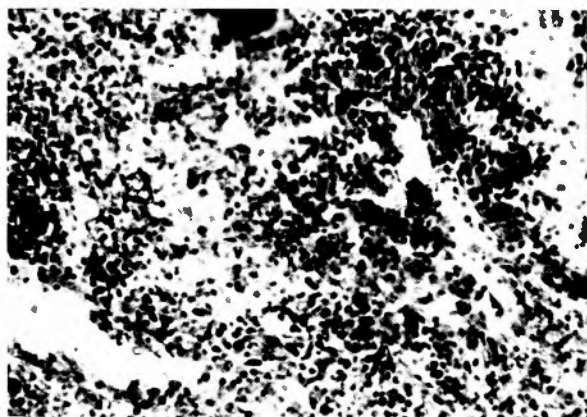
1. The author studied and revealed the nerve fibers and its endings in human parathyroid gland.
2. The nerve and its endings in human parathyroid gland are generally revealed in considerable number, especially, on the wall of the blood vessels, capillary and its surrounding tissues.
3. The structure of the nerve endings in human parathyroid gland show a few so-called free endings but most of them ramified into nonmyelinated fine fibers. These fine fibers never form so-called "Terminal reticulum", but present network-like appearance in crossing each other.
4. Physiological significance of the nerve fiber in human parathyroid gland is yet unknown.
5. The author does not reveal the vagal innervation.

I am greatly indebted to Assist. Prof. Dr. Ch. KIMURA of our clinic for his constant help during the course of this study.

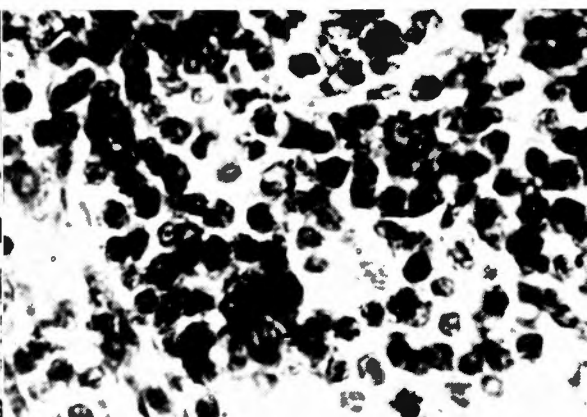
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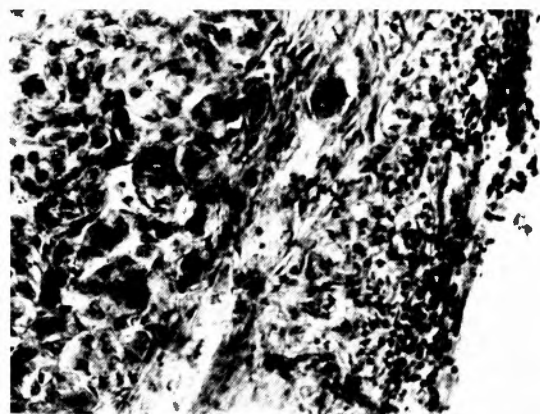
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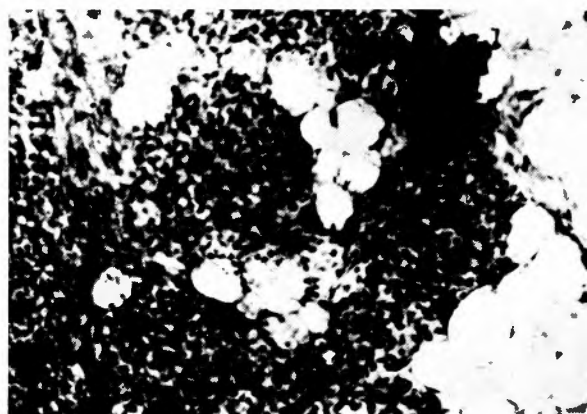
**Fig. 1** The parenchyma cells of human parathyroid gland. (H&E staining)  $\times 400$



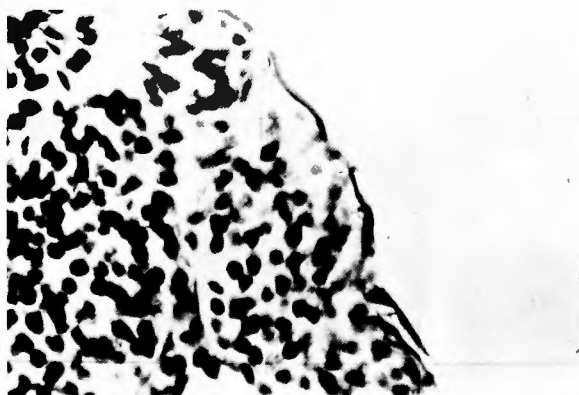
**Fig. 2** The parenchyma cells, showing the chief- and granular cells, of human parathyroid gland. (The same staining)  $\times 1500$



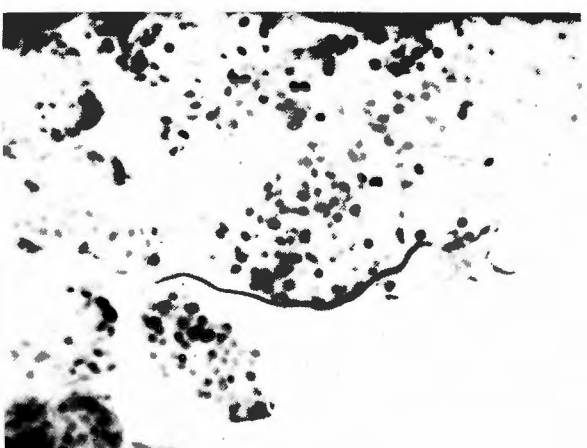
**Fig. 3** The parenchyma cells of human parathyroid gland. (The same staining)  $\times 400$



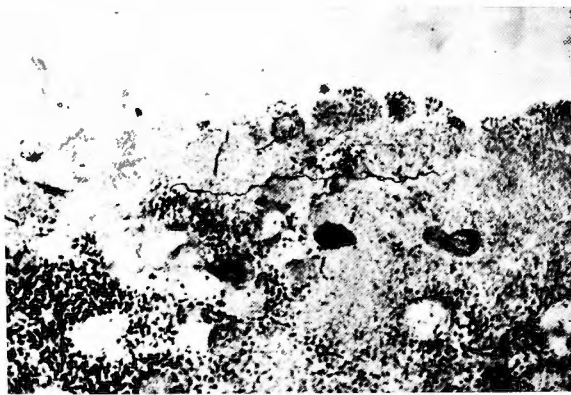
**Fig. 4** The parenchyma cells, showing the waterclear- and oxyphilic cells, of human parathyroid gland. (The same staining)  $\times 400$



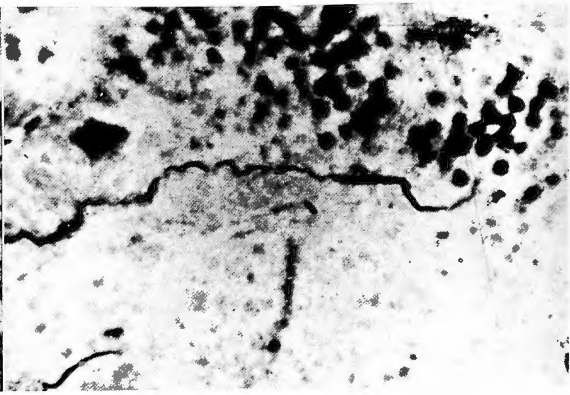
**Fig. 5** The nerve fiber running along the tunic involucre of human parathyroid gland. (Sero's modification of Bielschowsky's silver impregnation)  $\times 1000$



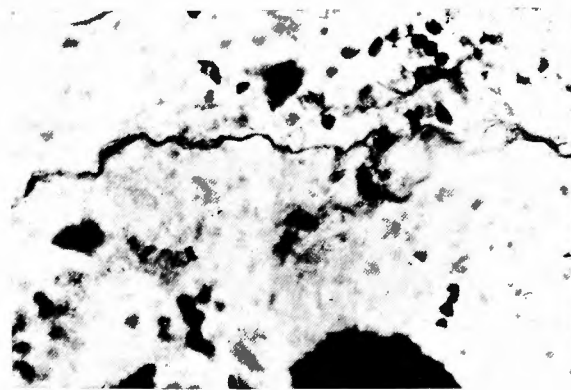
**Fig. 6** The nerve fiber proceeding into the parenchyma from the tunic involucre of human parathyroid gland. (The same impregnation)  $\times 400$



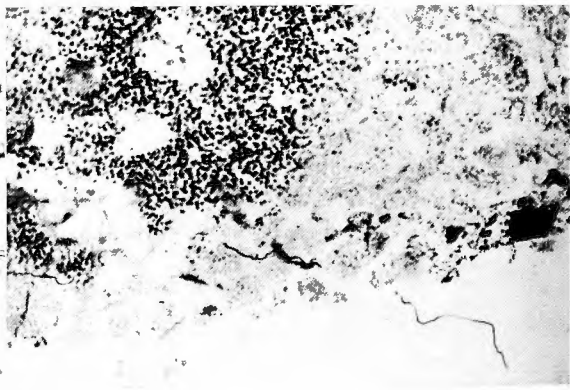
**Fig. 7** The nerve fiber near the tunic involucre, in the surrounding tissue of the parathyroid gland. (The same impregnation)  $\times 400$



**Fig. 8** Enlargement of Fig. 7. (The same impregnation)  $\times 1000$



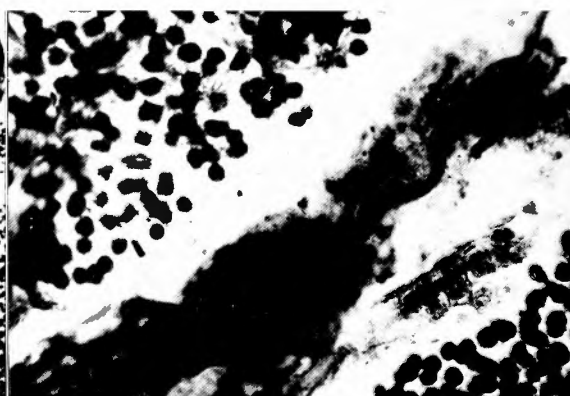
**Fig. 9** Enlargement of Fig. 7 (The same impregnation)  $\times 1000$



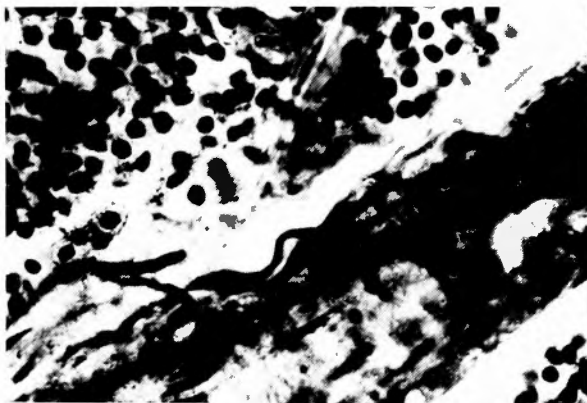
**Fig. 10** The nerve fiber near the tunic involucre, in the surrounding tissue of human parathyroid gland. (The same impregnation)  $\times 400$



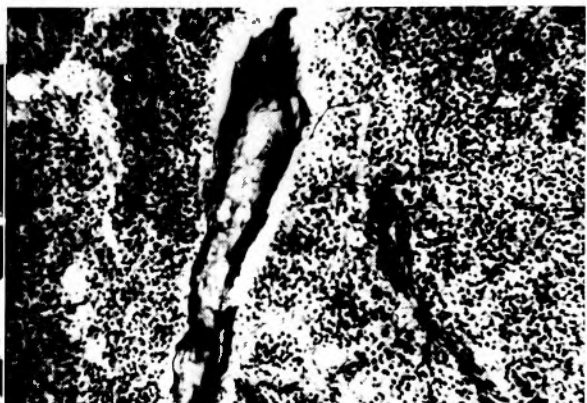
**Fig. 11** The nerve fiber proceeding into the parenchyma along the wall of the blood vessel of human parathyroid gland. (The same impregnation)  $\times 400$



**Fig. 12** Enlargement of Fig. 11. (The same impregnation)  $\times 1000$



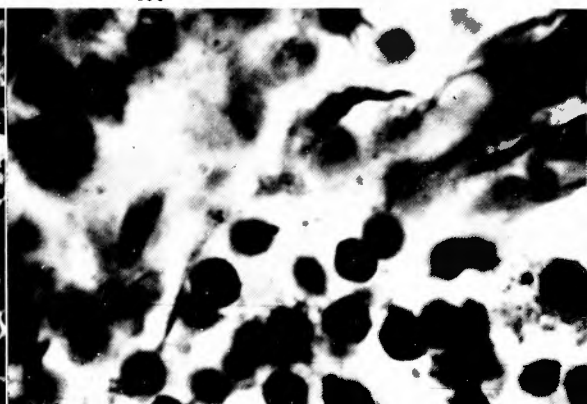
**Fig. 13** Enlargement of Fig 11.  
(The same impregnation)  $\times 1000$



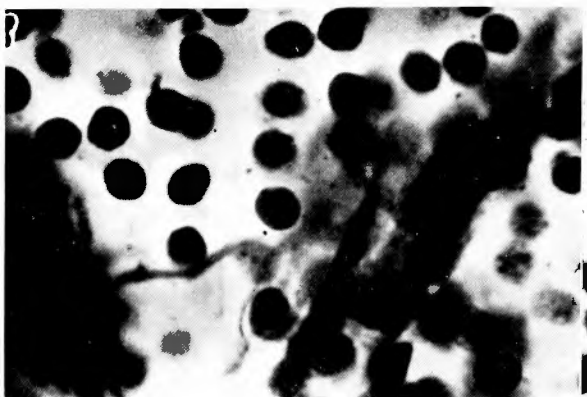
**Fig. 14** After proceeding along the blood vessel, enter the parenchymatous tissue along the capillary blood vessel in human parathyroid gland. (The same impregnation)  $\times 400$



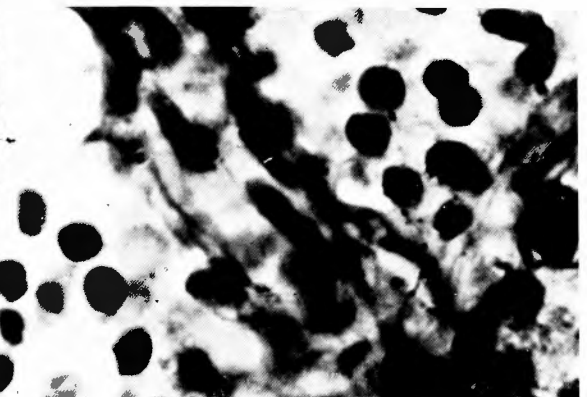
**Fig. 15** Enlargement of Fig. 14.  
(The same impregnation)  $\times 1000$



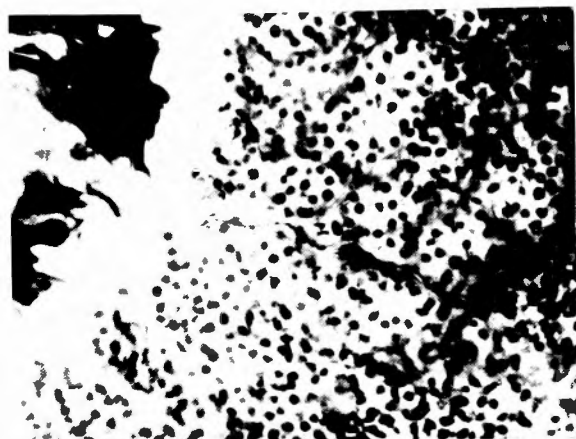
**Fig. 16** A nerve fiber proceeding into the parenchyma from the wall of the capillary of human parathyroid gland. This picture shows SCHWANN'S nucleus.  
(The same impregnation)  $\times 1500$



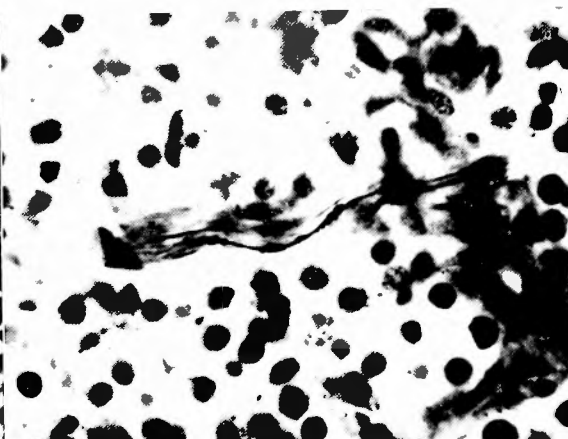
**Fig. 17** A nerve fiber after proceeding along the blood vessel on the left side ramifies to the right side capillary in human parathyroid gland. (The same impregnation)  $\times 1500$



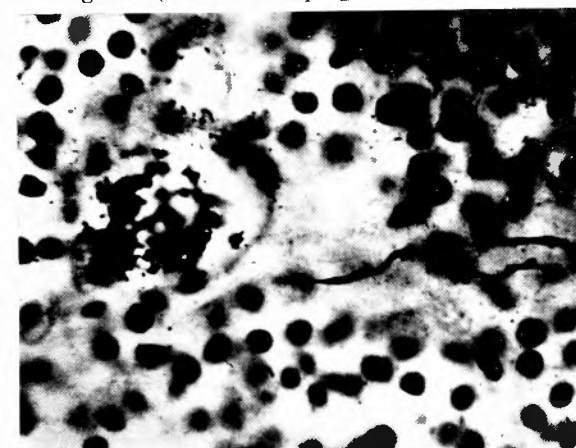
**Fig. 18** A nerve fiber proceeding along the capillary in human parathyroid gland.  
(The same impregnation)  $\times 1500$



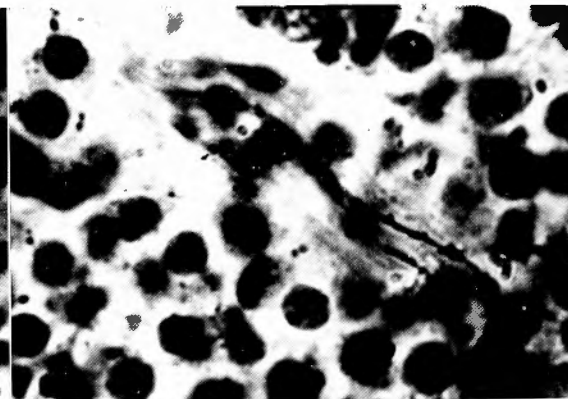
**Fig. 19** After leaving the wall of the blood vessel, the nerve fiber runs between the parenchyma cells of human parathyroid gland. (The same impregnation)  $\times 400$



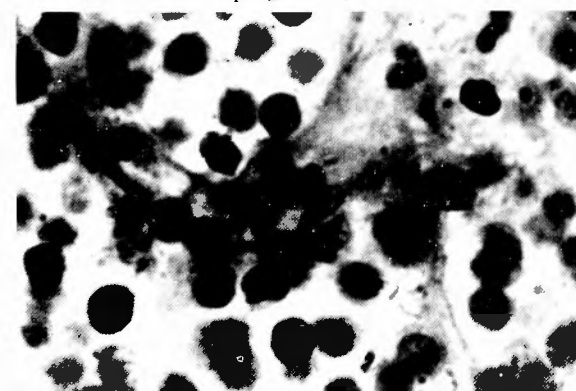
**Fig. 20** A nerve fiber running along the wall of the capillary in human parathyroid gland. (The same impregnation)  $\times 1000$



**Fig. 21** After leaving the wall of the capillary a nerve fiber runs between the parenchyma cells in human parathyroid gland. (The same impregnation)  $\times 1000$



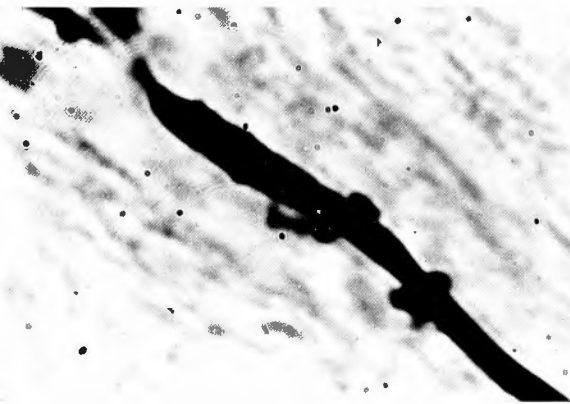
**Fig. 22** A nerve fiber proceeding along the wall of the capillary and ramifying two fine fibers in human parathyroid gland. (The same impregnation)  $\times 1500$



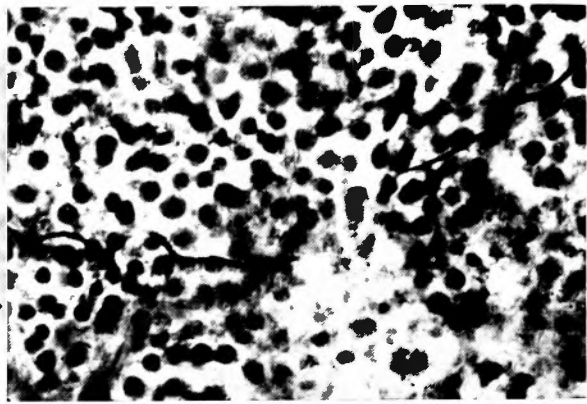
**Fig. 23** A nerve fiber proceeding the wall of the capillary in human parathyroid gland. (The same impregnation)  $\times 1500$



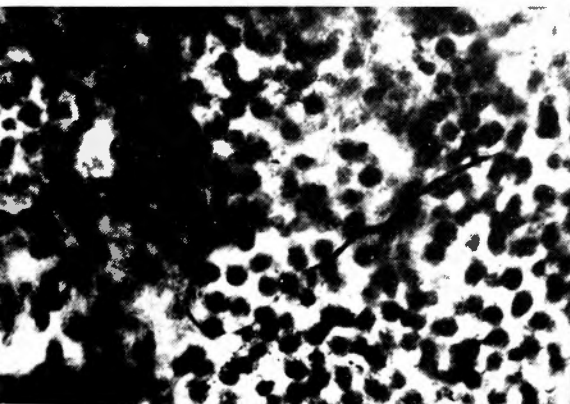
**Fig. 24** A thick myelinated nerve fiber, with nodular expansions, proceeds along the wall of the blood vessel in human parathyroid gland. (The same impregnation)  $\times 1500$



**Fig. 25** The same nerve fiber in Fig. 24.  
(The same impregnation)  $\times 1500$



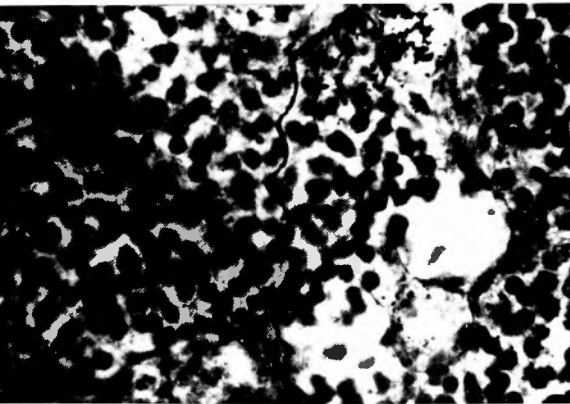
**Fig. 26** A relatively thick myelinated nerve fiber running between the parenchyma cells with undulated course in human parathyroid gland. (The same impregnation)  $\times 1000$



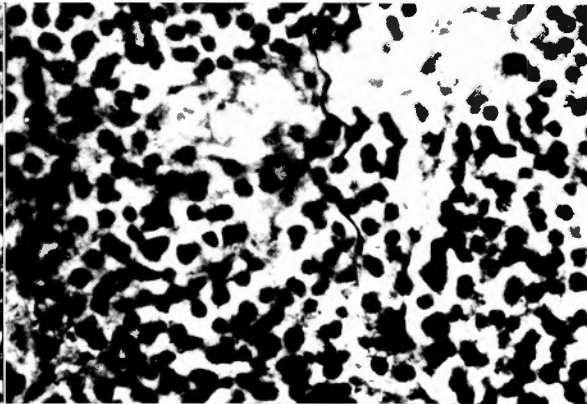
**Fig. 27** A relatively thick myelinated nerve fiber runs between the parenchyma cells with undulated course in human parathyroid gland. (The same impregnation)  $\times 1000$



**Fig. 28** The relatively long nerve fiber runs with undulated course in human parathyroid gland. (The same impregnation)  $\times 1000$



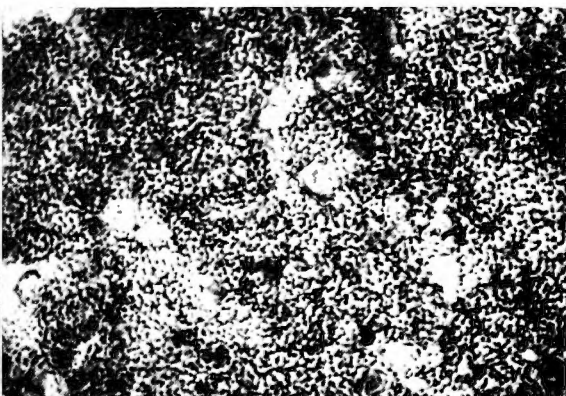
**Fig. 29** The peripheral portion of the same nerve fiber in Fig. 28 in human parathyroid gland. (The same impregnation)  $\times 1000$



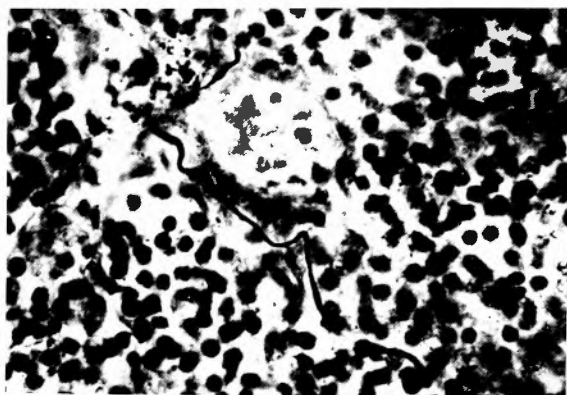
**Fig. 30** The peripheral portion of the same nerve fiber in Fig. 28 in human parathyroid gland. (The same impregnation)  $\times 1000$



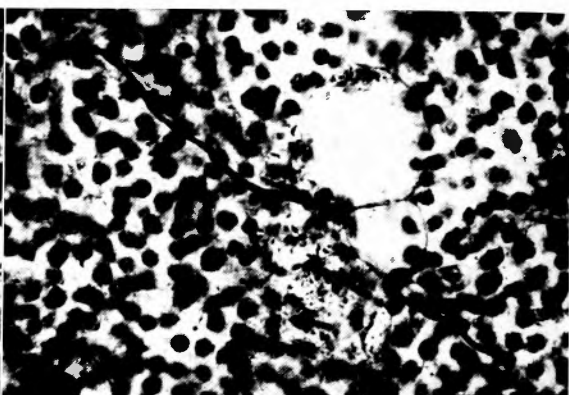
**Fig. 31** The relatively thick nerve fiber runs between the parenchyma cells with undulated course in human parathyroid gland. (The same impregnation)  $\times 1000$



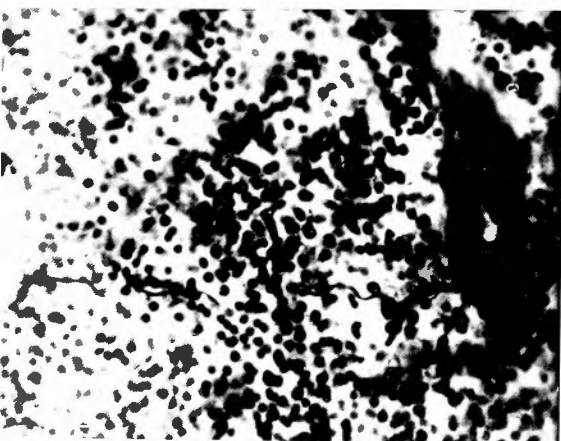
**Fig. 32** The relatively thick nerve fiber runs between the parenchyma cells with undulated course in human parathyroid gland. (The same impregnation)  $\times 400$



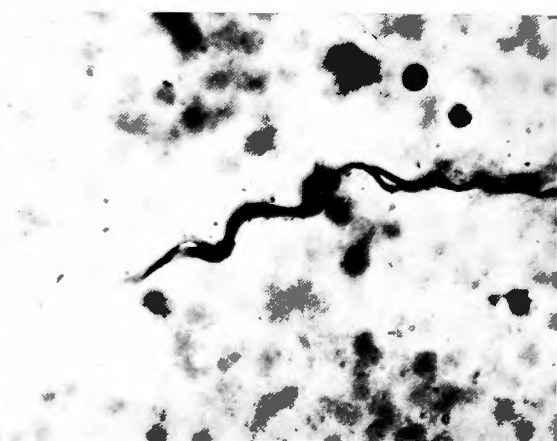
**Fig. 33** Enlargement of Fig. 32. (The same impregnation)  $\times 1000$



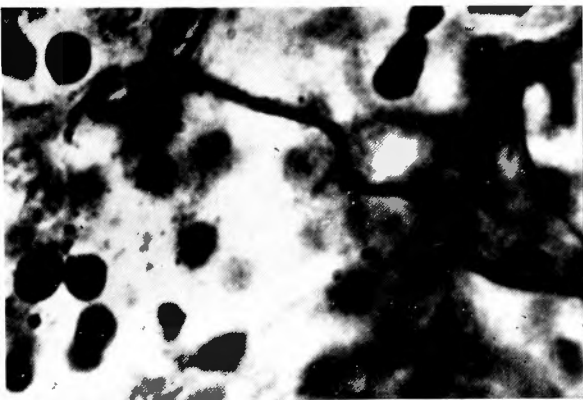
**Fig. 34** Enlargement of Fig. 32. (The same impregnation)  $\times 1000$



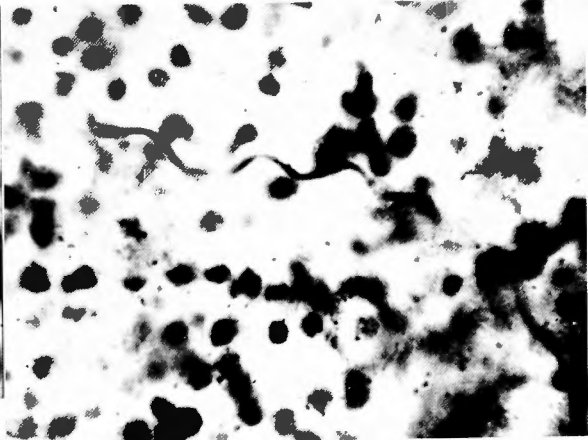
**Fig. 35** After proceeding along the wall of the blood vessel, ramifying and running between the parenchyma cells in human parathyroid gland. (The same impregnation)  $\times 400$



**Fig. 36** A nerve fiber runs between the parenchyma cells with undulated course and ramifies into many fine nerve fibers in human parathyroid gland. (The same impregnation)  $\times 1000$



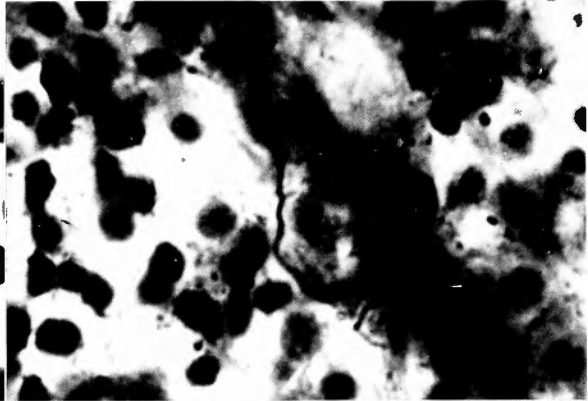
**Fig. 37** A nerve fiber runs between the parenchyma cells with undulated course in human parathyroid gland.  
(The same impregnation)  $\times 1000$



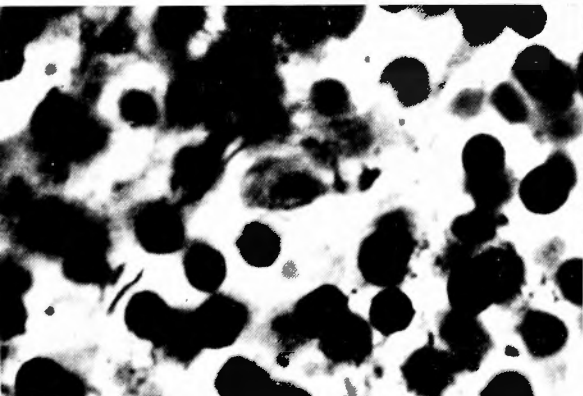
**Fig. 38** A nerve fiber runs between the parenchyma cells with undulated course in human parathyroid gland.  
(The same impregnation)  $\times 1000$



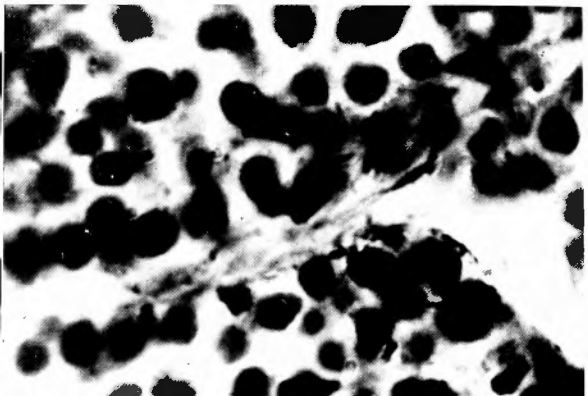
**Fig. 39** A nerve fiber runs between the parenchyma cells with undulated course in human parathyroid gland.  
(The same impregnation)  $\times 1000$



**Fig. 40** A nerve fiber runs between the parenchyma cells with undulated course in human parathyroid gland.  
(The same impregnation)  $\times 1000$



**Fig. 41** A nerve fiber runs between the parenchyma cells with undulated course and ramifies into many fine nerve fibers in human parathyroid gland.  
(The same impregnation)  $\times 1000$



**Fig. 42** A nerve fiber runs between the parenchyma cells with undulated course and ramifies the many fine nerve fibers in human parathyroid gland.  
(The same impregnation)  $\times 1000$

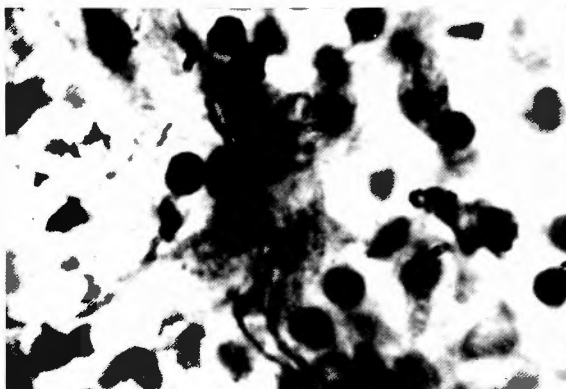


Fig. 43 A nerve fiber runs between the parenchyma cells with undulated course and ramifies the many fine nerve fibers in human parathyroid gland.  
(The same impregnation)  $\times 1000$

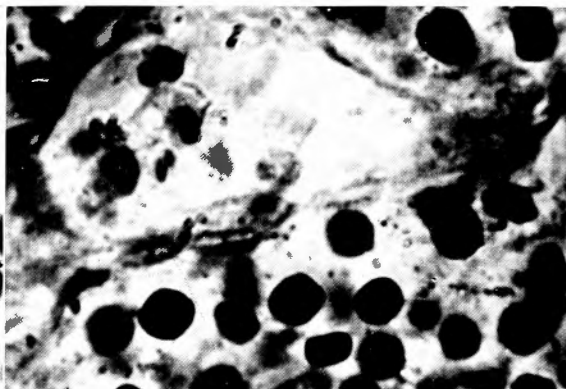


Fig. 44 A nerve fiber runs between the parenchyma cells with undulated course and ramifies the many fine nerve fibers in human parathyroid gland.  
(The same impregnation)  $\times 1000$

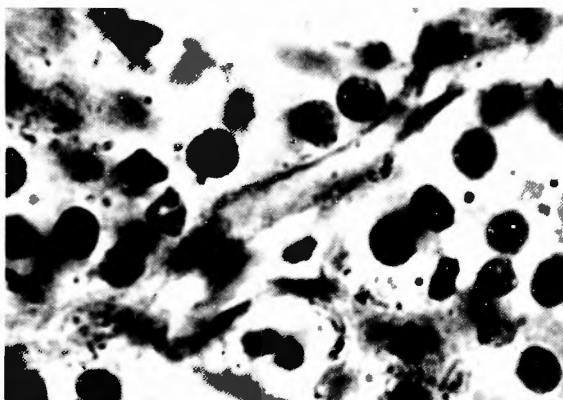


Fig. 45 A nerve fiber runs along the wall of the capillary ramifies the many fine nerve fibers in human parathyroid gland.  
(The same impregnation)  $\times 1000$

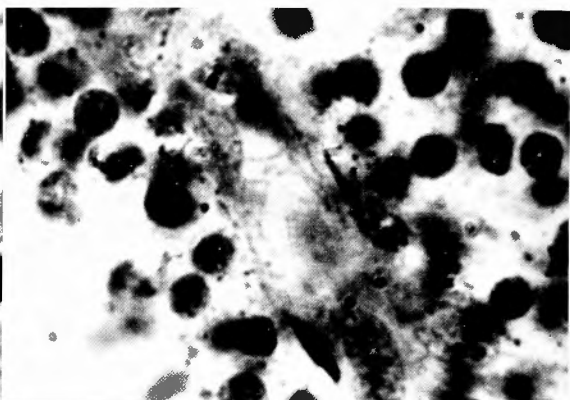


Fig. 46 After ramifying into many fine nerve fibrilles which cross one another and looked like a network in human parathyroid gland.  
(The same impregnation)  $\times 1000$

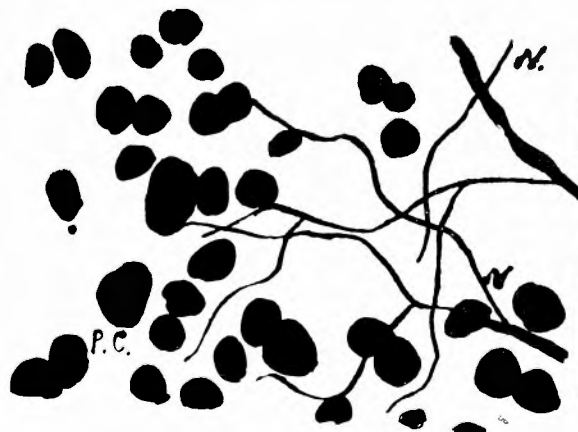


Fig. 47 Schema shows a network-like appearance in human parathyroid gland.  
P. C. Parenchyma Cell Nucleus  
N. Nerve Fibrilles

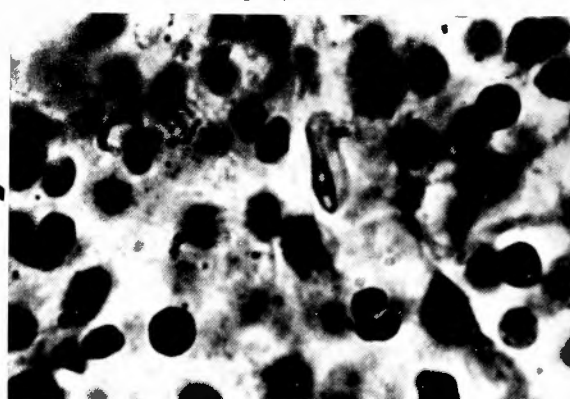
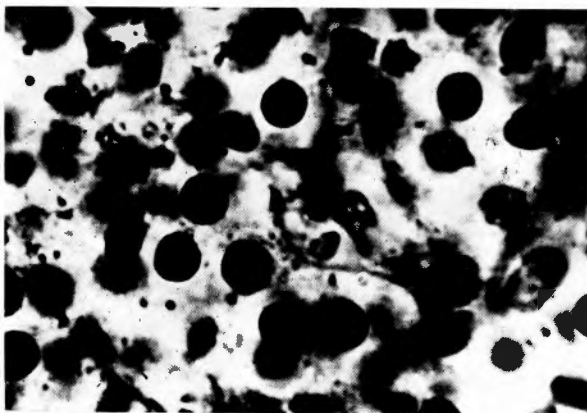
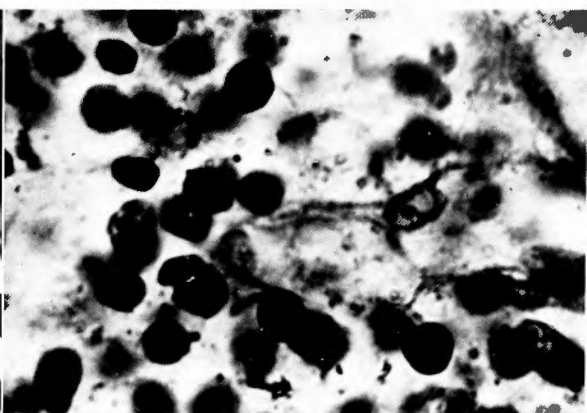


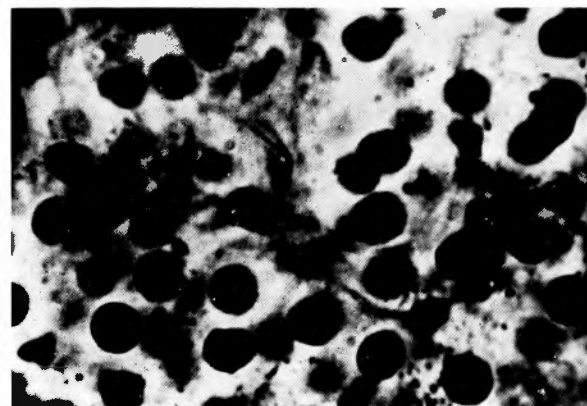
Fig. 48 After ramifies into many fine nerve fibrilles which cross one another and looked like a network in human parathyroid gland.  
(Sero's modification of Bielschowsky's silver impregnation)  $\times 1000$



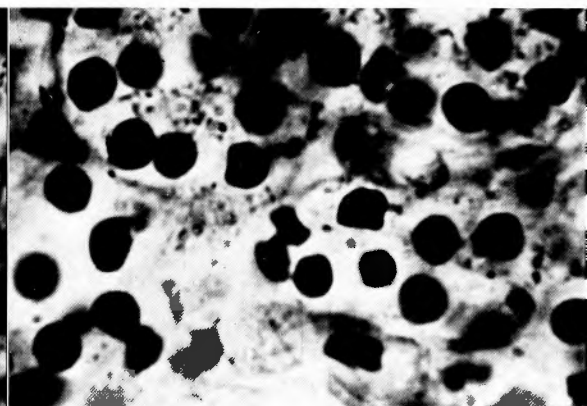
**Fig. 49** After ramifying into many fine nerve fibrilles which cross one another and looked like a network in human parathyroid gland. (The same impregnation)  $\times 1000$



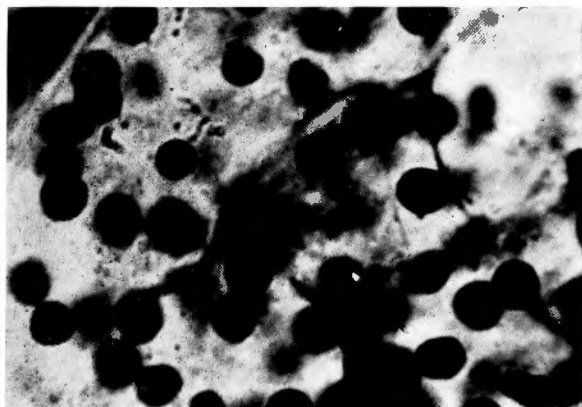
**Fig. 50** The nerve fibrilles cross one another and present a network-like appearance in human parathyroid gland. (The same impregnation)  $\times 1000$



**Fig. 51** The nerve fibrilles cross one another and present a network-like appearance in human parathyroid gland. (The same impregnation)  $\times 1000$



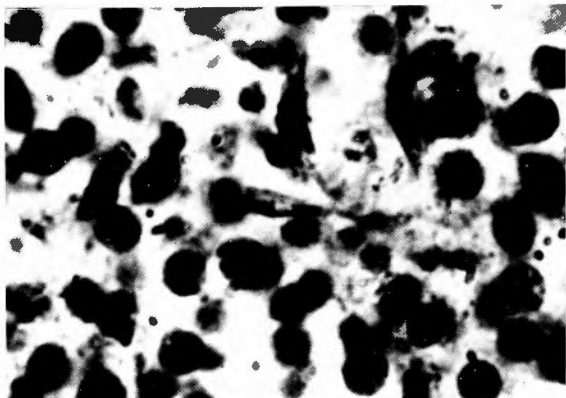
**Fig. 52** The nerve fibrilles cross one another and present a network-like appearance in human parathyroid gland. (The same impregnation)  $\times 1000$



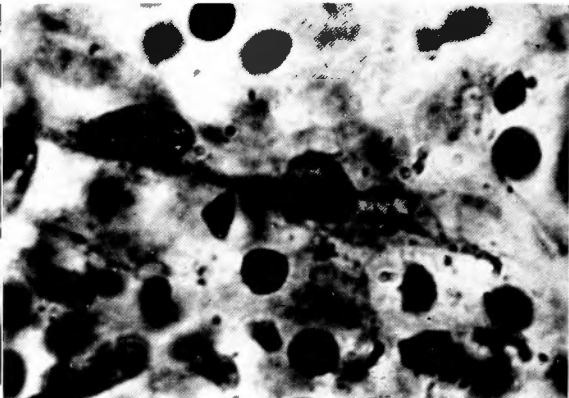
**Fig. 53** The nerve fibrilles cross one another and present a network-like appearance in human parathyroid gland. (The same impregnation)  $\times 1000$



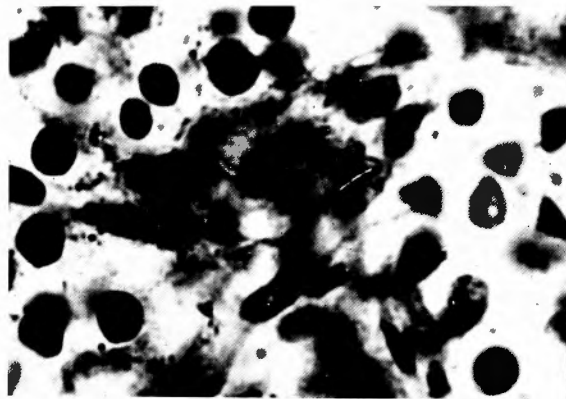
**Fig. 54** The nerve fibrilles cross one another and present a network-like appearance in human parathyroid gland. (The same impregnation)  $\times 1000$



**Fig. 55** The nerve fibrilles cross one another and present a network-like appearance in human parathyroid gland. (The same impregnation)  $\times 1000$



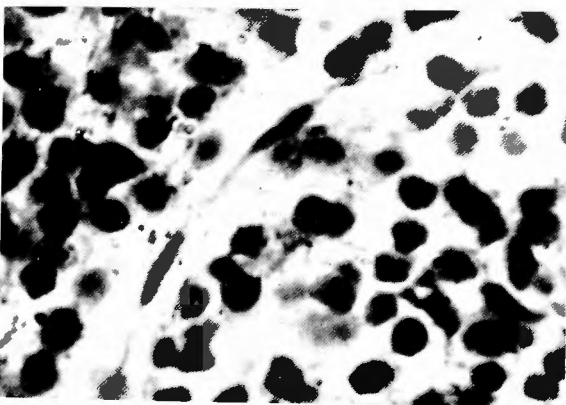
**Fig. 56** A nerve fiber runs between the parenchyma cells with the large spindle-shaped SCHWANN'S nucleus in human parathyroid gland. (The same impregnation)  $\times 1000$



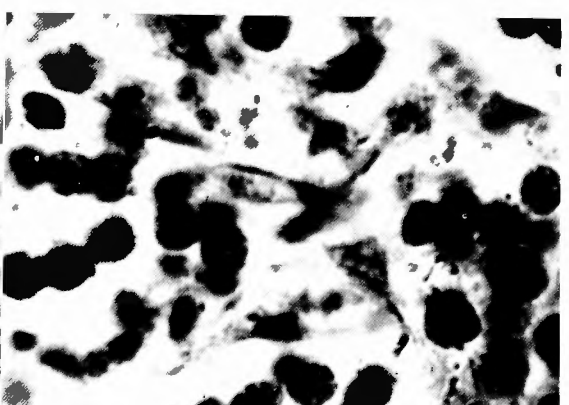
**Fig. 57** A nerve fiber runs between the parenchyma cells with the large spindle-shaped SCHWANN'S nucleus in human parathyroid gland. (The same impregnation)  $\times 1000$



**Fig. 58** A nerve fiber runs between the parenchyma cells with the large spindle-shaped SCHWANN'S nucleus in human parathyroid gland. (The same impregnation)  $\times 1000$



**Fig. 59** A nerve fiber runs along the septum with the large spindle-shaped SCHWANN'S nucleus in human parathyroid gland. (The same impregnation)  $\times 1000$



**Fig. 60** A nerve fiber runs between the parenchyma cells with the large spindle-shaped SCHWANN'S nucleus in human parathyroid gland. (The same impregnation)  $\times 1000$

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## 和 文 抄 録

# 上皮小体に於ける神経支配の組織学的研究

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国立宇多野療養所外科（所長 日下部周利博士）

杉 浦 慶 男

内分泌腺組織に於ける神経支配の研究は、その報告が極めて少なく、著者の知る範囲に於いては僅かに脳下垂体前葉、甲状腺、副腎等に関してあるのみである。しかして、それらの報告を要約すれば、内分泌腺組織に於ける神経終末部の構造は、内分泌腺組織以外の一般組織に於けるそれと異なり、網状構造を呈することなく比較的太い神経線維による非分岐性乃至は単純性分岐性の神経終末を形成していることであると云う。

ここに於て著者は、上皮小体に於ける神経支配は如何なる構造を有するかに興味を抱き、京都大学病理学教室及び国立宇多野療養所より得たる人の上皮小体に於ける神経支配の研究を Bielschowsky 氏神経軸索染色法瀬戸氏変法、巢鴨髄鞘染色法、Ehrlich 氏ヘマトキシリン、エオジン染色法等を適宜に使用して行つた結果、次の様な結論を得た。

1) 人の上皮小体に於ける神経及びその終末部を研究し、その存在を確認した。

2) 人の上皮小体に於ける神経及びその終末部は、上皮小体全野に於いて普遍的に発見されるが、特に血管、毛細血管壁及びその周囲に多く見られた。

3) 人の上皮小体に於ける神経終末部の形態は、所謂遊離性終末を呈することは比較的少なく、大部分は更に微細な多くの場合無髄性の線維に分岐している。そして、それらの微細な線維は所謂, Terminal Reticulum を形成することはないが、互いに交錯するので一見あたかも網状構造を呈しているかの様に見える事が多い。

4) 人の上皮小体に於ける神経線維の生理的意義については不明である。

5) 人の上皮小体には迷走神経性支配は証明し得なかつた。