

A Histological Study of the Distribution of the III Cervical Sensory Nerve and Its Relationship to the Craniofacial Pain

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INTRODUCTION

It has been clinically evident that headache and facial pain are one of the commonst complaint of patients in the general medicine and much of interest has been published about the functional correlation of the upper cervical nerves with headache. Among the upper cervical nerves attention has been accumulated to the great occipital nerve, which consists of the fibers mainly from the first cervical root, as great occipital trigeminal syndrome, while this nerve had appeared to receive scant attention until Mason's report.¹⁸⁾

In 1953 Mason¹⁸⁾ reported that the great auricular neurotomy or block of this nerve with alcohol was carried out in 56 cases of tic douloureux and in about a half pain was successfully relieved. From this observation it seems that a pain in the face may be mediated to the cortex through the great auricular nerve. Furthermore he described as follows; "it appears that sensory fibers from the cervical plexus are carried into the trigeminal area with the facial nerve."

In 1954 Campbell and Lloid⁵⁾ reported that no effect was observed in the several cases of true trigeminal neuralgia by the Mason's operation. The same results were reported by Penman et al.²⁰⁾ and Aoki et al.,¹²⁾ Campbell et al.,⁵⁾ whereas the dramatic relief of pain was resulted by this procedure in the case of atypical facial neuralgia.

In our clinic, the great auricular neurotomy or block of this nerve with local anaesthetic has been carried out in various types of headache, complained in temporal and/or periauricular region; such as post-traumatic headache, atypical facial neuralgia, migraine etc., As a result, in about 80 per cent of these cases a pain was relieved successfully. From these observations it is supposed that the sensory overlap may exist over the trigeminal and the great auricular nerve.

Recently two cases of the glossopharyngeal neuralgia were treated in our clinic by means of the great auricular nerve block.³⁾ Pain was releaved completely and no recurrence has ocured for the 6 and 4 years following the treatment. From this clinical observation, such assumption is made that the sensory overlap

between the glossopharyngeal and third cervical nerve may exist not only trigeminal but also glossopharyngeal nerve. But from the anatomical point of view, the distribution of the great auricular nerve has not yet been clearly. Hence, an attempt was made to elucidate these problems in this study, that there is the peripheral sensory overlap between the upper cervical nerve, especially the third, and the fifth and ninth cranial nerves.

On the other hand, autonomic nerves are distributed in the face and head, while the peripheral structures of the autonomic nerve have not been known definitely, and many different findings have been reported concerning them. Stöhr Jr.²³⁾ has concluded that "the autonomic nerves from a fine, closed and reticulated structure in the periphery without distinction between the sympathetic and parasympathetic systems and they never terminate as free endings." Seto²⁴⁾ insists that the nerve which terminate freely in the periphery without forming the fine, closed and reticulated structure are sensory nerve, and these sensory nerve can be easily differentiated from the autonomic nerve by their thickness.

In order to study the histological correlation between the cervical and cranial nerves, tracing of the degenerated nerve fibers was carried out in the skin and hypodermic layer of the face, head, cervical region, and in the mucous membrane or submucous layer of the oral cavity and pharynx following neurotomy of the upper cervical sensory roots, and an attempt was made to confirm them as sensory nerve fibers according to the criteria by Seto.

MATERIALS AND METHODS

Eleven healthy adult dogs, both sexes, were used as experimental animals. The degenerated nerve fibers in the trigeminal area and the mucous membrane of the oral cavity and pharynx were sought after the neurotomy of the posterior roots of the third cervical nerve performing in the paravertebral region. All dogs were operated under general anesthesia with the intravenous injection of thiopental sodium. When the degeneration was fully developed, some of the nerve fibers became unstainable. Therefore the specimens taken between the 5 to 7 days after operation were the most suitable ones for tracing the degenerated nerve fibers. Hence, the animals were sacrificed on the 5 to 7 days postoperatively and the skin of the face and head, and mucous membrane of the oral cavity and pharynx were examined. Immediately after excision the specimens were fixed in 10 % neutral formalin solution. After the fixation for 3 months or more, the specimens were frozen sliced in thickness of 30-40 microns and stained by Birshowsky's method modified by SUZUKI²⁵⁾ (Table 1.), and Ehrlich's acid hematoxylin method, which was used the observation of the myelin sheath.

Table 1.

Suzuki's methode

The specimen has been cut with the freezing method as kept 10 % neutral formalin solution,

1. directly put into 20 % silver nitrate solution, being protected from light for 1 hour.
 2. Washed in distilled water for 2-3 seconds.
 3. Put into ammonical silver solution for about 10 minutes the specimen is colored light brawn.
 4. Directly placed in 10 % potassium sodium tartarate solution 15-20 seconds.
 5. Washed with distilled water for 5 minutes or more.
 6. Placed in 0.05-0.1 % gold chloride solution.
 7. Placed in 20 % sodium thiosulfate solution until the specimens are colored reddish brown.
 8. Washed in distilled water for about five minutes.
 9. Dehydrated with xylene solution and mounted.
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RESULTS

In agreement with Seto, the sensory nerves in the skin of the face or head were so thick and waves that were clearly distinguished from the autonomic nerve fibers which appeared to be thin and smooth.

In the untreated control animal these sensory nerve fibers were traced to the epitherium and terminated either in sharp free ending or in ramifying termination. These thick fibers ended in ramifying termination around the hair folliculus in the subcutaneous tissue, but no entrance into the sweat or sebaceous glands was observed.

Many myelinated nerve fibers were found in the cutaneous and subcutaneous tissues. The course and distribution of these myelinated nerve corresponded to the sensory nerve which were found by Seto using the silver impregnation method.

Summarizing above results, in control animals, thick nerve fibers were found in the skin of the face or head. They branched off smaller fibers in the subcutaneous tissue and terminated as free endings at the epitherium.

Now the degenerated nerve fibers were sought in the skin of the face and head after the neurotomy of the third cervical nerve. Consequently the degenerated nerve fibers were found in the epitherium and in the corium of the face (Fig. 1. 2. 3. 4.). Few degenerated nerve fibers were observed around the hairfolliculi or sweat and sebaceous glands (Fig. 5. 6.). Neither a termination with complicated structure nor a specific endapparatus could be observed.

Furthermore, no degenerated nerve fibers were found anywhere over the wall of blood vessels (Fig. 7. 7'). In other words, the cervical sensory nerve from the third roots would not distribute to the blood vessels in these region. The nerve fibers observing over the blood vessels consisted of very small fibers and formed abundant networks or running parallel with the vessels. From these character, these fibers were regarded as the autonomic nerves.

The course of the facial nerve which communicated with third cervical nerve in the mandibular or infraauricular region was traced. The investigation was made about the area of this anastomosis, which has been generally accepted, for the purpose of confirmation of the Mason's description that sensory fibers from the cervical plexuses are carried into the trigeminal area with the facial nerve. In the experimental animals treated by third cervical neurotomy, no degenerated fibers were observed in any branches of the facial nerve. However, beside the trunk of the facial nerve running below the stylomastoid foramen degenerated nerve fibers were observed (Fig. 8, 8'). Therefore, these intact nerve bundles were thought to be the facial nerve, whereas the degenerated nerve bundles were identified to be the cervical nerve. These two nerves were accompanied with each other in short distance, then separated gradually. In more distal many intact nerve fibers were observed among the degenerated ones in the subcutaneous layer of the buccal area (Fig. 9). The facial nerve and the third cervical nerve were communicated macroscopically in the infraauricular region, however no anastomosis were found microscopically. In other words, these two nerve fibers run in the separate nerve sheath respectively, and finally they separated each other in the peripheral part running towards the skin or mucous membrane or the muscle structure individually.

In summary, the third cervical nerve reached to the third division and a part of the second division of the trigeminal area as well as the retro-auricular, temporal and occipital region as shown in Figure 14.

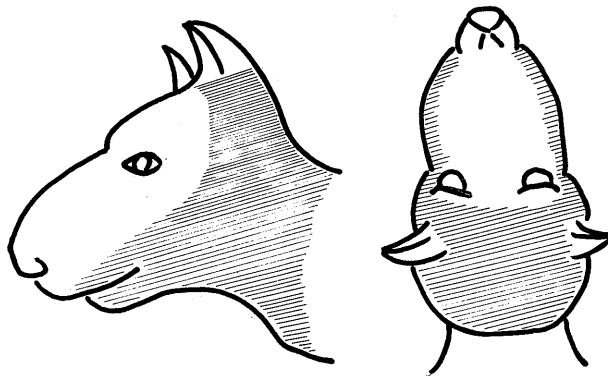


Fig. 14. The shaded area shows the distribution of the cervical nerve III

On the other hand, visceral distribution of the third cervical nerve was examined in the wall of the mouth, pharynx, tonsils, tongue and nasal cavity. Fixation and staining of the specimen was carried out in the same manner as in the skin.

The degenerated nerve fibers were found both in the submucous structure and

the mucous membrane. In submucous layer winding thick sensory nerve fibers were distinguished easily from relatively thin autonomic nerves. Tracing these thick nerve fibers to the mucous membrane, they entered the muscularis mucosa, then terminated at the epithelial layer as a sharp tips of the free ending or the ramifying termination (Fig. 10, 11); i. e. special nerve ending was not found in these tissues.

The myelinated degenerated fibers were demonstrated in the mucous membrane of the mouth or pharynx by Ehrlich's myelin sheath staining corresponding with the course of these nerve (Fig. 12, 13).

On the basis of above mentioned results it was evidenced that the third cervical nerve was widely distributed on the face, head and pharynx. In the oropharyngeal region, the branches of this nerve supplied some of the nasopharyngeal region and all over the pharynx lying between the level of the hard palate and the piriform fossa. Furthermore it distributed in the buccal mucosa (Fig. 15). The degenerated fibers were observed more frequently in the posterior and lateral wall of the pharynx than the other region. But no degenerative nerve fibers were found in the tonsils, tongue, palates, uvula, and nasal cavity.

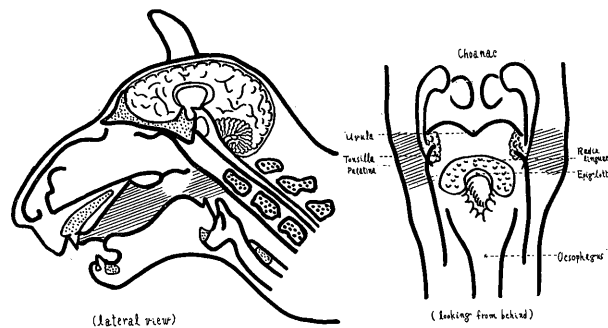


Fig. 15. The shaded area shows the distribution of the cervical nerve III in the pharynx and the mouth of the dog.

DISCUSSION

It appears that there are close relationship between upper cervical nerve (C III) and cranial nerve (V, IX); namely peripheral overlapping and other central connection. As to the later it is the relationship between the upper cervical sensory roots and descending tract of the trigeminal nerve.^{11) 15) 26)}

Now the purpose of this study is confined to an investigation of peripheral overlapping between upper cervical nerve (C III) and cranial nerve (V, IX). As a result, the degenerated nerve fibers, terminated as free ending, were found in the area of the third and a part of the second division of the trigeminal nerve,

retroauricular region, temporal region, mucous membrane of oral cavity and pharynx after the severing of the third cervical nerve.

Weddell,²⁷⁾ using the biostain and the silver impregnation, reported that these ramifying nerve fibers terminated in the epitherium or subepithelial tissue, in quite agreement with the present results. Ranson²¹⁾ and Fulton¹²⁾ reported that sensory nerve endings on the skin are generally ramified and formed free endings rather than any specific shape. Furthermore, by Ranson,²¹⁾ it seemed certain that at least a part of the free nerve endings in the epidermis was pain receptors. In this study the free nerve endings found in the skin or mucous membrane of the dog undoubtedly reached at the epitherium or submucous membrane. Therefore pain impulse from the area of the third division and a part of the second division of the trigeminal nerve, retroauricular and temporal region should be conducted through the trigeminal and third cervical nerves simultaneously.

In the electrophysiological study, the peripheral nerve action potential was divided into four main groups from the oscillographic record; group A- β , group A- γ , group A- δ and unmyelinated or C fibers.

Group A- β fibers have the lowest threshold (0.05-0.3V) and the largest diameter (12-14 μ), with conduction velocities of 80 to 85 m/sec... Group A- γ fibers have the diameter varied from 9 to 12 with conduction velocity estimated at 50 to 55 m/sec... Stimulus threshold in usually is twice the voltage of the β threshold (0.1-0.8). The group A- δ threshold is two to three times higher than the γ -threshold (0.25-7.0), conduction velocity from 25 to 30 m/sec... Fiber diameter is 1 to 9 μ . The unmyelinated or C-fibers have diameters of 0.5 to 2 μ . and conduction velocity is 1 to 1.5 m/sec., Threshold for stimulation is as high as 9.0 to 18.0 V...

As Gasser¹³⁾ has pointed out, because of the different rates of conduction in large and small fibers, the times arrived at the spinal cord of a painful impulse are very different. And he has thought that there are two kinds of nerve fibers in the conduction of painful impulse; the first is myelinated nerve, the second unmyelinated. He designated the former A- δ fiber and the latter C-fiber.

Collins et al.⁴⁾ reported that nerve fibers which included no fibers smaller than A- δ fibers was never perceived as painful. In other words, no pain was perceived unless fibers smaller than the A- β group were stimulated. They also demonstrated that the pain can be elicited where small fibers are stimulated in repetitive fashion.

According to the measurement of diameter of the degenerative nerve fibers in this study, they were ranged from 2 to 5 μ ... Considering the pathological change in themselves such as vacuolation or swelling in consequence of necrosis original thickness of these fibers has to be smaller than the measured values. Therefore, it is assumed that these fibers belong to A- δ or C fibers and that they have some connection with the mediation of pain or activating the consciousness by means of appreciation of pain in craniofacial and oropharyngeal region.

More recently the sympathetic system has been suggested as a pathway of the pain sensation. Some authors⁵⁾⁹⁾¹⁴⁾¹⁵⁾ have paid attention to the role of cervical sympathetic system in the problem of pain in the head and face. Regarding as production and appreciation of pain, Campbell and Lloid⁵⁾ described as follows; "In approaching this problem were impressed by sympathetic factor; a large proportion of patients had associated with sympathetic symptoms and procedures which relieved the pain sometimes also relieved the manifestation of the sympathetic distribution."

Davis and Pallock⁹⁾ examined the role of the sympathetic nervous system in the production of pain in the head and neck. They showed that the sympathetic supply to the head and face consisted of postganglionic efferent fibers arising in the superior cervical ganglion and reaching their destination by way of vascular plexuses and together with other cervical nerves. They postulated that possible afferent pathways for pain perception were: (1) by posterior roots of the cervical nerve; (2) by antidromic impulses from this area; and (3) by the sensory cranial nerve. By section of these nerves, either singly or in conjunction, they found that the only way to present pain was to destroy all pathways in the posterior cervical roots and the sensory roots of the fifth cranial nerve. Their theory of the mechanisms of the production of pain was that the stimulation of the superior cervical ganglion produced effects by way of postganglionic fibers passing to structure innervated by these nerves. They suggested that nature of this effect was linked with the sympathetic innervation of the blood vessels and that a metabolite was liberated which in turn stimulated ordinary sensory nerve endings of the fifth nerve and cervical sensory nerves. Campbell and Lloid⁵⁾ further described that "we believe the Davis' theory is probably true, and that the metabolite is histamine." In the results of the present experiments, no degenerated nerve fibers were found around the vessels, after the section of the third cervical nerve in the paravertebral region. Therefore, it is thought that there is no connection between the third cervical nerve and the vascular system at this region. However, Davis' theory is applied in this case these become close relation between the cervical sensory nerve and the sympathetic system or vascular system.

Recently the possibility of other pathways of pain sensation than the trigeminal nerve from the face or head was emphasized. Davis,¹⁰⁾ in experimental work in cats, suggested that the seventh cranial nerve may subserve pain and offered clinical evidence in favour of this hypothesis. On the other hand, Carmichael et al.⁶⁾ reported that no evidence was obtained that impulses subserving pain in the face and orbita follow any pathway other than in the fifth nerve. Furthermore in 1953 Mason¹⁸⁾ reported that the third cervical nerve is purely sensory and these fibers are carried into the trigeminal area with the facial nerve. But from the present experimental result it was clear that although the communication

between these two nerves was demonstrated macroscopically, there was no microscopical intermingling of these fibers. In addition the cervical nerve was distributed into the skin and its appendage in the trigeminal area. Above findings were incompatible with Mason's and Carmichael's opinion.

Cushing⁷⁾ described an interesting condition, which he called "painful tic convulsiv"; violent pain in the eye and face was accompanied by unilateral facial spasm. This pain was unrelieved by removal of the trigeminal ganglion, but was subsided when the facial nerve was cut down, thought not complete because the patient still complained of pain in his jaw. Such observation suggests that the residual pain following the treatment is mediated by fibers other than either the trigeminal or the facial nerve. The operation carried out by Cushing was interruption of the two pathways of the pain sensation, therefore, it seemed that the third pathway of the pain impulse remained intact. Namely, in my opinion, the pain remaining in the jaw may be reached at the cerebral cortex via ascending pathway resting to the cervical sensory nerve.

Much of interest have been paid to the functional correlation between the cranial nerves and the upper cervical nerves in the headache and facial pain.¹⁾
8)16)19)

From these literatures it appears that the trigeminal does not totally innervate as wide area as has been assumed. It is certain that the upper cervical nerves entered in wider area than previously assumed. In short, the pain impulses which arised in the so-called trigeminal area of the head and face should be conducted through those pathways first trigeminal nerve, second sensory fiber of the facial nerve, third upper cervical nerves and fourth autonomic nerve.

As mentioned above, in our clinic, two cases of glossopharyngeal neuralgia were treated successfully by the great auricular block by anesthesia and neurotomy of this nerve.³⁾

On the other hand, the etiology of the glossopharyngeal neuralgia was not clarified, but the cause of pain in pharyngeal type may be in peripheral stimulation, since its pain was relieved by topical anesthesia of the pharynx. If this assumption may be accepted, then some of the impulses may pass via the glossopharyngeal and great auricular nerve simultaneously, both of which distribution in identical area. Hence an explanation of the clinical effect of the great auricular nerve block on glossopharyngeal neuralgia was safely done on the anatomical basis.

In this experiment, the degeneration of nerve fibers was observed in the pharynx, particularly in the posterior and lateral wall, following the severing of the third cervical nerve. At that site the degeneration of the nerve fibers was not observed frequently in myelinated fibers, but also unmyelinated one in submucous layer. Such findings suggests the evidence of sensory overlap over the peripheral innervation between the ninth cranial and third cervical nerve, and is unable to

be accounted for by the general concept having so far been believed that the sensation of the pharynx is innervated by merely the glossopharyngeal nerve.

SUMMARY AND CONCLUSION

1. Peripheral distribution of the third cervical nerve was studied histologically after the neurotomy of this nerve on dogs. The degenerated nerve fibers were detected in the face, head, oral cavity and pharynx.
2. Sensory nerve with simple ramifying termination or free-ending were found in the skin and these appendage of dog's face.
3. Sensory nerve fibers demonstrated in the present study were consisted of myelinated nerve fibers, losing the myelin sheath in the extreme peripheral part.
4. Degenerated sensory nerve fibers were measured as 2-5 μ . in diameter. This size of sensory nerve fibers is equivalent to A- δ or C fiber which is thought to be the kind of nerve fibers conducting painful impulse.
5. Although communications between the facial nerve and the third cervical nerve existed macroscopically, there was no microscopical intermingling of their fibers.
6. The third cervical nerve fibers were distributed in the third division and a part of the second division of the trigeminal area as well as in the retroauricular, temporal and occipital region. These sensory nerve endings were usually found in the epithelial layer of the skin.
7. The degenerated nerve fibers were found in a part of the nasopharyngeal region ; i.e. the oral cavity and all of the posterior and lateral wall of the pharynx lying between the level of the hard palate and pyriform fossa. The sensory fibers ended in the epithelium and subepithelial layer of the pharynx.
8. Overlapping of the sensory innervation was proved between the cervical nerve (C III) and the cranial nerves (V, VII and IX) in the head, oral cavity and pharynx.

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Fig. 1. 2. Degenerated nerve fibers in the epitherium and subepithelial tissues of the skin of a dog face. Suzuki's method $\times 800$

Fig. 1. A sharp free ending

Fig. 2. Ramifying terminations

Fig. 3. 4. Degenerated myelinated nerve fivers in the subepithelial tissues. Ehrlich's method $\times 800$



Fig. 1.



Fig. 2.



Fig. 3.

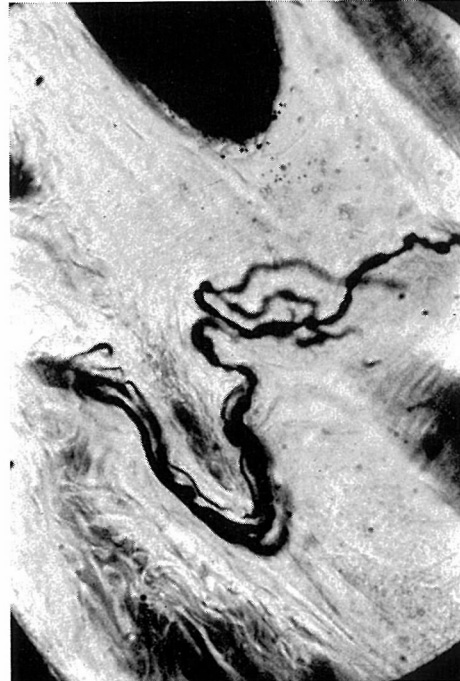


Fig. 4.

Fig. 5.6. Degenerated nerve fibers around the hair folliculus (Fig. 5.) or sweet gland (Fig. 6.)

Fig. 5. ×200

Fig. 6. ×800

Fig. 7.7'. No degenerated nerve fibers were found the wall of the blood vessels, which consisted of very small neve fibers and were observed as abundant network or running parallel with blood vessels. Suzuki's method.

Fig. 7. 200

Fig. 7'. The same preparation as Fig. 7. ×800

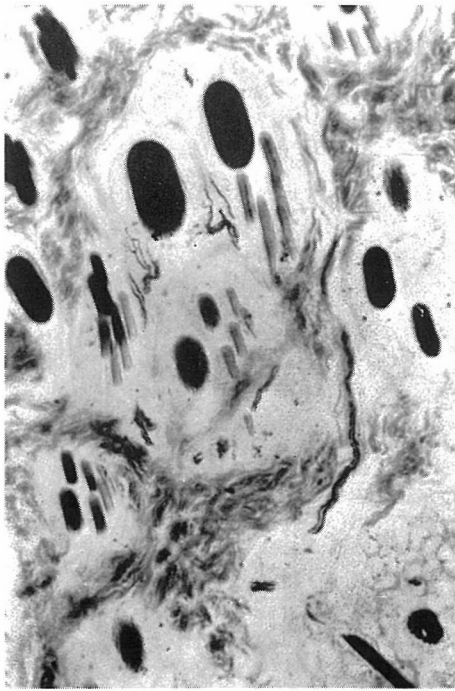


Fig. 5.



Fig. 6.

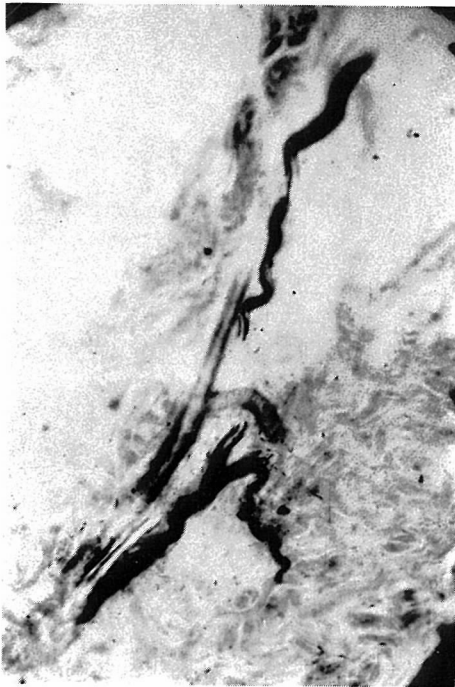


Fig. 7.

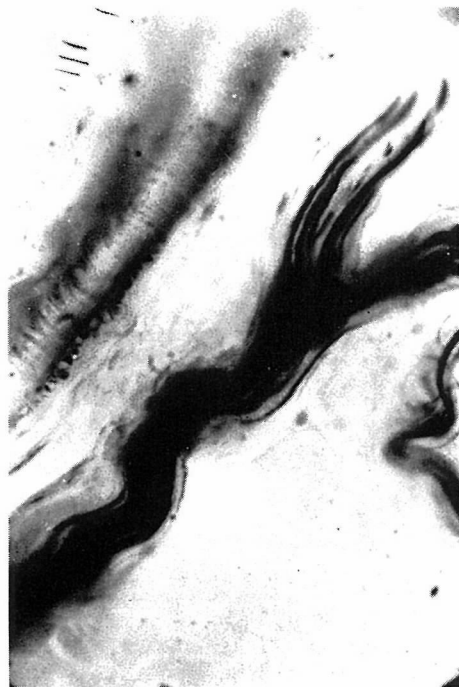


Fig. 7.

Fig. 8. 8'. Transverse section of a degenerated bundle from the cervical root (a), mostly containing intact facial nerve bundle (b) Bielschowsky's method

Fig. 8. ×200

Fig. 8'. The same preparation as Fig. 8. ×800

Fig. 9. More distal. transverse section of the facial nerve shown in fig. 8. in the subcutaneous layer of the buccal area. Many intact nerve fibers were observed among the degenerated nerve fibers.

Suzuki's method. ×200

↑ : Degenerated nerve bundle.

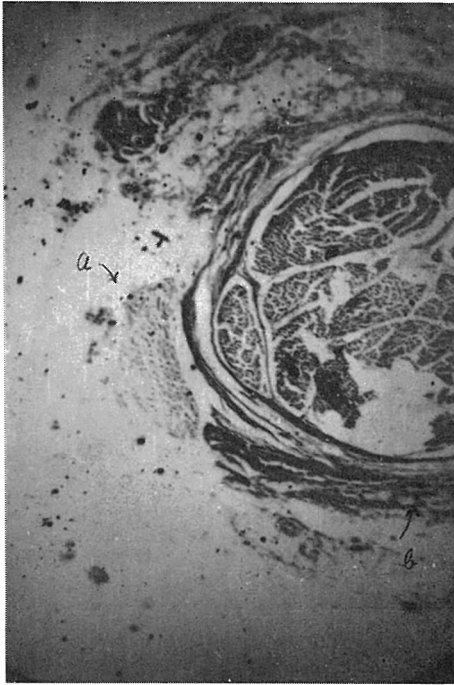


Fig. 8.

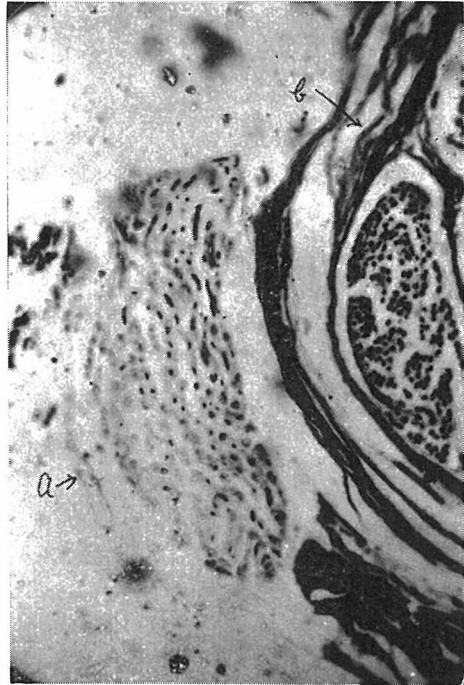


Fig. 8'.

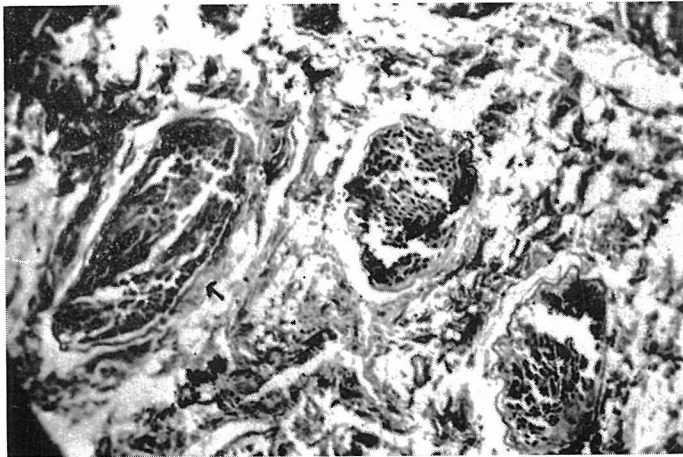


Fig. 9.

Fig. 10.11. A degenerated nerve fibers terminated in the epitherium layer of the pharyngeal wall as a sharp free ending.
Suzuki's method.

Fig. 10. The lateral pharyngeal wall ×200

Fig. 11. The posterior pharyngeal wall ×800

Fig. 12.13. Degenerated myelinated nerve fibers.
Ehrlich's method.

800

Fig. 12. in the mucous membrane of posterior pharyngeal wall.

Fig. 13. in the submucous membrane of posterior pharyngeal wall.



Fig. 10.



Fig. 11.



Fig. 12.

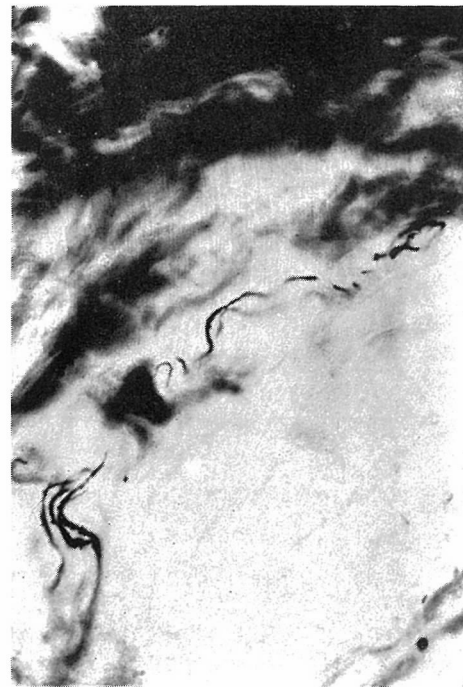


Fig. 13.