CHANGES PRODUCED IN THE SUPERIOR CERVICAL AND CAELIAC SYMPATHETIC GANGLIA BY IRRITATION OF THE PALATE IN GUINEA PIGS

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(Received for publication September 20, 1963)

INTRODUCTION

There are many difficulties to elucidate the mechanism of the reactions with which humans defend against and adapt themselves to external stimulation because of its complexity and exquisiteness.

On this complicated problem, the stability of internal environment of human body had been formerly suggested by Bernard⁽²⁾ and the "Homeostasis" had been introduced by Cannon in 1929 and lately the general adaptation syndrome was reported by Selye in 1936.^(15, 16) They evaluated in their theories the importance of automatic adjustment of habitual functions. In 1934, Reilly⁽¹⁴⁾ had reported the non-specific syndrome caused by hyperirritation of external causes on the vegetative nervous system and moreover Laborit⁽⁹⁾ had described the reacting system following the aggression in human body.

However, it is also an obvious fact that this defensive and adaptive reaction has its own limitation and the stronger the external stimuli become, the easier the individuals lead themselves to destruction. Many kinds of shock following hemorrhage, anaphylaxis and trauma have ever been studied, but these shocks reveals very different figure from those encountered at the oto-rhino-laryngological surgery.

Being mentioned by Stolze⁽¹⁹⁾, the head and neck connecting the brain with the trunk has a plenty of vessels and is regarded as an important portion of body. Suzuki and his co-workers⁽²¹⁾ made observations on the fact that the frequency of a sudden death associated with surgical procedures upon the tonsil and/or its surrounding region or the neck is higher than upon the other regions of body. And from the results of statistical analysis and pathological study on shock cases, they has confirmed that hyperirritation or abnormal stimulation on

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vegetative nervous system is responsible for the cause of death and the unstability of this system also predispose to it. Based on this concept, Suzuki, Iida, and Fukazawa⁽²²⁾ had extended the application of the Speransky's technique⁽¹⁷⁾ to his experiment and observed in detail the shock occurred by the injections of croton oil into the submucous tissue of the palate and the subcutaneous tissue of the abdomen of guinea pigs. On the contrary, they demonstrated that the interruption of this shock was arisen from the use of chlorpromazine. Therefore the view has been assumed by the authors that the characteristic of palate and the stimulation on the periphery of vegetative nervous system, which mentioned already by Reilly, might play a role as a cause of the shock. On the basis of our concept that the stimulation of croton oil injected into the palate may be transmitted to the superior cervical ganglia distributing to this region and thereafter may produce some pathological changes in the visceral organs via the vegetative nervous system, the pathohistological investigation of the superior cervical ganglia, the caeliac sympathetic ganglia, the visceral organs of guinea pigs after the repeated injections of croton oil into the palate of these animals for various length of time was performed.

EXPERIMENTAL METHODS

The materials used in this study were healthy adult guinea pigs ranging in weight from 250 g to 350 g without concerning of their sex, and were divided into 4 groups.

In the 1st group 0.1 cc of croton oil was injected into the palate. As the same as the report of Suzuki, Iida and Fukazawa⁽²²⁾, one third of animals died within 2 hours after injection. Dead cases were examined immediately after death. Others were stunned and sacrificed after 3 hours of injection.

The animals of the 2nd, 3rd, and 4th group were injected 0.1 cc of croton oil diluted to one tenth with olive oil. In the 2nd group the animals were injected

Table 1
Experimental Method

	Croton oil				Period of the observation
	Dose of one time	Frequency	Interval	total dosis	
First group	0.1 cc	once		0.1 cc	2~3 hrs.
Second group	0.01 cc	twice	2 days	0.02 cc	5 days
Third group	0.01 cc	3 times	3 days	0.03 cc	10 days
Fourth group	0.01 cc	4 times	4 days	0.04 cc	20 days

twice with two days' interval and observed for 5 days, in the 3rd group three times with three days' interval for 10 days, and in the 4th group four times with four days' interval for 20 days.

The technique was shown in table 1.

The superior cervical ganglia, the caeliac ganglia, lung, liver, kidney, adrenal glands, and the palate were removed to be examined. These specimens were transferred for fixation to 10% formalin or absolute alcohol. Thereafter they were stained by hematoxylineosin, Asan-Mallory's method, Nissls' method, or P.A.S. method.

RESULTS

I. *Palate*

1. Normal findings

According to Ohno⁽¹²⁾, authers' collaborator, histological findings are different on each of anterior, middle and posterior portion of the palate of guinea pig.

Quotation from his report is as follow:

Surface of the palate consists of the keratinized squamous epithelium, and connective tissue of corium are partially well developed, generally papillae are well developed, and the network of vessels is abundantly formed. In corium there are roots of hairs and accessory glands of the skin. In connective tissue, formed the corium, elastic fibers and collagen fibers and silverphilic fibers, and the network of elastic fibers surrounding the hair follicle are found. In subcutaneous tissue rough or dense connective tissue, and striated muscle fibers are much found. Subcutaneous fatty tissue of the posterior portion is more abundant than the anterior. Between corium and subcutaneous tissue, and subpapillary tissue fine nets of the much vessels are formed.

2. Changes due to croton oil injection

In histological findings, 2 or 3 hours after injection of croton oil, any changes are not found in the epithelium. Arrangement of connective tissue is rough in corium, and the diffuse edema at injection place is widely noted and continuously found in subcutaneous tissue. Some muscular fibers are torn, and their striae are disordered. In general, edematous tissue is infiltrated with small round cells, and capillaries are congested with blood. But granular cells reveals no changes and excretory duct is filled with no secretion.

The 2nd, 3rd and 4th group, 5-20 days after injection of croton oil, showed various findings of ulcer formation, epithelium where croton oil was injected is almost desquamated and rest of them shows such serious changes as followed. Nuclei are destroyed, intracellular space are disappeared and many vacuolization,

partial necrosis are noted within cytoplasm, and around of them infiltration of small cell is found. Surface of the ulceration covered with the small cells is widely destroyed and shows distinct necrosis. Under the ulceration the fatty tissue, revealed in general little changes, is necrotic only in adjacent portion to the ulceration and is replaced by infiltration of cells. Bundle of striated muscle fibers is found bordered on this fatty tissue, and shows not extremely alternations but roughness. Muscle fibers adjacent to the surface of the ulceration are distinctly discontinued and severely degenerated and partially necrotized. Infiltrated cells are almost small round cells but large neutrophilic cells are also found. Ulceration is extensive to the subcutaneous tissue. In subcutaneous tissue edema is remarkable in several portions. The lumen of the vessels is markedly congested with blood. The connective tissue covered the surface of the ulceration is proliferated in some portions. In cases of cicatrical formation, epithelium, especially keratinized layer, is remarkably thick and desquamation is also distinct. Epithelial cells are irregular in shape and large in size and lose their own shapes in proportion to near the upper layer of epithelium. Generally, wandering cells is found a little in epithelium.

Basal cells are almost arranged accurately. In corium the development of the connective tissue is prosperous and premature, fibroblasts are found, and cicatrization is found in some portions. Generally, vascularization is poor and congestion is scanty. Endothelium of vessels is remarkably thick and diffuse infiltration of the small cells is noted.

In the groups to which stimulation is added for long term, ulceration or the cicatrix is found separately or parallel, but in the 2nd group ulceration is marked, and in the 3rd and the 4th group ulceration and cicatrical formation are both found.

II. *Findings of Normal Ganglion Cells*

Findings of normal superior cervical sympathetic ganglion cells are as follows.

Almost all cells are shaped round or oval and protoplasm is stained by eosin. At the margin of protoplasm there is a band of basophilic stained substance and ganglion cells has 1-3 nuclei as usual, but most of them are binuclear. Among these ganglia there are deeply stained cells whose protoplasm and nuclei show atrophic change. By Nissl's staining, granules are found at marginal portion of the cell in a large number, and form so called a marginal chromatophilic band, but they are not found at the boundary of the nuclei. At the space between a marginal chromatophilic band and center of cell fine granules thickly arranged, or scattered accumulation of gross granules or lack of chromatophilic band or

concentration of the Nissl's body, or lack of the Nissl's body which can not be distinguished from chromatolysis are noted in each specimen. Nuclei covered by the nucleous membrane includes one to three nuclei and their containing structure makes a network.

Caeliac ganglion cells are much the same as the superior cervical ganglions, but irregularity of shape or atrophy or sclerosis of cells are more abundantly observed.

III. *Changes of the Ganglion Cells*

1. General findings

Finding of the ganglion cells recognized in this experiment are as follows:

a) Swelling: Enlarged cell body occupying the intracellular space and protoplasma stained lightly with eosin, and roughness of cytoplasmic structure and swelling of nuclei are existing.

b) Atrophy: There are general or concentrating atrophy of ganglion cells and deeply stained cell body and irregularity of their shape. Nuclei shaped flat oval or amorphous are stained deeply. This atrophy is observed at the central portion of cell fixed by alcohol, and is the more remarkable at the experimental group in comparison with the contrast group.

c) Vacuolization: Vacuolization is occurred with destruction of cells at many cases. Vacuoles are various in size and number at various portion such as peripheral, central, local or diffuse. There is an existence of many large vacuoles occupying protoplasma of the cells.

d) Destruction: At the beginning, cytoplasm is rough and makes network but the changes progress further more, destruction of protoplasma is in central portion or in peripheral portion. In the latter case cellular membrane is broken and becomes granular. In the marked cases protoplasma almost disappear with trace and nuclei are disappeared in some cases. At alcoholic fixation peripheral cells infused rapidly are destroyed a little in the contrast group.

e) Changes of the Nissl's granules: Arrangement of the Nissl's granules are disordered, and some of them are stained deeply. Following this, destruction of the chromatin, chromatolysis, is found at the all portion of cell, and granules of these portions are lost or assembled and stained very dark. Local or central chromatolysis are oftenly found.

f) Changes of the nucleus: Normal nucleus shapes round or oval but in the experimental cases nucleus swelled mostly combining with cellular swelling, and it shows atrophy or deeply stained. The form is irregular and the margin is concave or convex, cellular membrane is destroyed at the same cases. Material of nucleus lose its network and assume it at one portion, or disappear. Some

Table 2
Findings of the Sympathetic Ganglion Cells of the First Group

Guinea pig	Ganglion	Swelling	Atrophy	Vacuoliza- tion	Destruc- tion	Chroma- tolysis	Changing of nucleus
19	GCS*	—	+	+	—		—
20	GCS	—	—	+	+		—
21	GCS	—	+	+	—		—
	G. Cael.**	—	—	+	+		—
22	GCS	—	—	+	+		—
	G. Cael.	—	—	+	+		—
26	G. Cael.	—	+	—	+		—
27	GCS	—	—	+	+		—
28	GCS	—	—	+	+		—
	G. Cael.	—	—	+	+		—
29	GCS	—	+	—	—		—
30	GCS	—	—	+	+		—
31	GCS	—	+	—	+		+
32	GCS	—	+	+	+		—
33	GCS	—	+	—	—		—
34	GCS	—	+	+	—		—
35	GCS	—	+	+	—		—
43	GCS	—	+	+	+	+	—
44	GCS	—	—	+	—	+	—
48	GCS	—	—	+	—	+	—
49	GCS	—	—	+	—	+	—
50	GCS	—	—	—	—	—	—

* GCS=Ganglion cervicalis superior.

** G. Cael.=Ganglion caeliaca.

Table 3
Findings of the Sympathetic Ganglion Cells of the Second Group

Guinea pig	Ganglion	Swelling	Atrophy	Vacuoliza- tion	Destruc- tion	Chroma- tolysis	Changing of nucleus
401	GCS	+	+	+	+	+	+
	G. Cael.	—	+	+	+	+	+
402	GCS	—	+	+	+		+
	G. Cael.	—	—	—	+	+	—
411	GCS	—	+	+	+	+	+
	G. Cael.	+	+	+	+		+
413	GCS	+	+	+	+	+	+
	G. Cael.	+	—	+	+		+
416	GCS	+	+	+	—	+	—
	G. Cael.	—	—	—	+	—	—
419	GCS	—	+	+	+	+	+
	G. Cael.	—	—	+	+		+
420	GCS	—	+	+	+	+	+
	G. Cael.	+	+	+	+	+	+
421	GCS	—	+	—	—	+	+
	G. Cael.	—	+	+	+	+	+
423	GCS	—	+	+	+	+	+
	G. Cael.	+	+	+	+		+
425	GCS	—	+	+	+	+	+
	G. Cael.	+	—	+	+		+

Table 4
Findings of the Sympathetic Ganglion Cells of the Third Group

Guinea pig	Ganglion	Swelling	Atrophy	Vacuoliza- tion	Destruc- tion	Chroma- tolysis	Changings of nucleus
301	GCS G. Cael.	— +	+ —	+ +	+ +	+	+ +
305	GCS G. Cael.	++ ++	— —	+ +	+ +	+	+ +
308	GCS G. Cael.	++ ++	— —	+ +	+ +	+	+ +
313	GCS G. Cael.	— +	++ —	+ +	+ +	++	— +
317	GCS G. Cael.	— +	+ —	+ +	+ +	+ +	— —
320	GCS G. Cael.	+ +	+ —	— +	— +	+ +	— +
322	GCS G. Cael.	— +	++ —	+ +	++ ++	++ ++	+ +
324	GCS G. Cael.	— —	+ +	+ +	+ +	+ +	— +
331	GCS G. Cael.	+ +	+ +	+ +	+ +	+ +	+ +
334	GCS G. Cael.	— —	+ +	+ +	+ +	+ +	+ +

Table 5
Findings of the Sympathetic Ganglion Cells of the Fourth Group

Guinea pig	Ganglion	Swelling	Atrophy	Vacuoliza- tion	Destruc- tion	Chroma- tolysis	Changings of nucleus
101	GCS G. Cael.	++ —	++ ++	++ +	++ +		+ +
103	GCS G. Cael.	— —	++ ++	— +	++ +	+ +	— —
109	GCS G. Cael.	++ +	++ ++	+ +	+ +		+ —
113	GCS	—	++	++	++		++
115	G. Cael.	—	+	++	++		++
116	GCS G. Cael.	— +	++ ++	— +	+ +	++	+ +
117	GCS G. Cael.	+ +	++ ++	++ +	++ +	++	+ +
119	GCS G. Cael.	— —	++ ++	++ +	+ +	+	+ +
121	GCS G. Cael.	++ —	+ ++	++ +	++ +	++	++ +
122	GCS	—	++	+	++		+
123	GCS	—	++	++	+	++	+
124	GCS G. Cael.	+ —	++ +	++ +	++ +		+ +

nuclei are remarkably destroyed or leave its trace only and in a few cases nuclei are destroyed perfectly. At some cases dislocation of nuclei are remarkably found.

2. Findings of the sympathetic ganglion cells of each experimental group.

In 1st group there are little pathologic changes in the superior cervical and caeliac ganglion cells. In 2nd, 3rd and 4th group changes are found strongly. The most remarkable changes are shown in the 4th group and the next in the 3rd and the 2nd group. The findings of each group are shown in the table 2, 3, 4 and 5.

IV. *Microscopic Findings of the Visceral Organs*

1. Lung

Alveolar walls show various findings; normal, emphysema, or atelectasis, however in most cases, especially in the 1st and 4th group, edematous swelling is found. Congestion of capillary vessels is noted but bleeding in alveolus is seen in only one case of the 4th group. Infiltration of round cells in the interstitium fairly notable. Walls of the bronchus and bronchioles are thicken in all cases. In many cases material stained light red by eosin is found in bronchial cavity. There is no remarkable difference of pathological change between each group but in the 1st group the most notable changes are found.

2. Liver

Generally, congestion is obviously found especially in the central vein, Glissons' sheath and interlobular capillary. Atrophied liver cells are not commonly observed but degeneration and/or vacuolization of protoplasm are noted. Nuclei and star cells reveal no changes. Infiltration of round cells in interstitium is not noted. Difference between each group is not remarkable except the 1st group.

3. Kidney

Congestion is remarkable in general especially in the glomerulus and the renal tubules. Swelling or atrophy and, in a few case, destruction of glomerulus are found. Tubular epithelium swells in many cases but degeneration is also noted. There is cylindershaped material stained by eosin in tubular cavity in some cases, but bleeding and infiltration of round cells in the interstitium are not observed. Compared each group, congestion is noted in the 1st group at the most degree and the 4th group in the next degree. But distinct difference on other changes is not noted.

4. Adrenal gland

There are not so strong changes but slight congestion in the cortex and the marrow. No bleeding is seen in all cases. Degeneration of cells is obvious in the 1st group whose pathological findings are mostly distinct in each groups.

Table 8
Changes of the Kidneys

Group Guinea pig		1st group						2nd group			3rd group			4th group					
		19	20	22	26	29	41	401	402	411	301	305	308	101	103	109	115	116	119
Findings																			
Con- ges- tion	Glomerulus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
	Renal tubule	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	-
Hemorr- hage	Glomerulus	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Renal tubule	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Glomerulus	Destruction	-	+	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-
	Swelling	-	+	+	+	-	-	+	+	-	-	-	-	+	-	+	-	-	-
	Atrophy	+	+	+	-	+	-	-	+	-	-	-	-	-	+	+	-	+	-
Renal tubule	Degeneration of epithelium	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+
	Swelling of epithelium	+	+	+	+	+	+	+	+	-	+	-	-	-	+	-	+	+	+
	Atrophy of epithelium	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Abnormality in the lumen	+	+	+	-	+	+	-	-	+	+	-	+	+	-	-	-	-	-
Small round cells infiltratiaon in the interstitial tissue		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Table 9
Changes of the Adrenal Glands

Group Guinea pig		1st group						2nd group			3rd group			4th group					
		19	20	22	26	29	41	401	402	411	301	305	308	101	103	109	115	116	
Findings																			
Con- ges- tion	Cortex	+	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	-
	Medulla	+	+	-	+	+	+	-	-	-	+	-	+	-	+	-	+	-	-
Hemorr- hage	Cortex	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Medulla	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Vacuoli- zation	Cortex	+	+	+	-	-	+	+	+	+	-	+	+	+	+	+	-	+	+
	Medulla	-	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+
Changes in cortical cell	Protoplasm	+	+	+	+	+	+	+	+	+	-	+	-	-	+	-	+	+	+
	Nucleus	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Necrosis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

DISCUSSION

About the histological studies of the ganglions many reports have been done and microscopic findings have been pursued by Cajal, Müller, Stöhr⁽¹⁸⁾, Herzog⁽³⁾, Ohnuma⁽¹³⁾ and others. Ide, Moriya and Anraku said about the difference between normal and abnormal findings of the ganglions. Almost all the reports were of the humans or the rabbits, but of the guinea pigs were little. Atrophic sclerosis of cells or nuclei, often found in the ganglions, was revealed only by formalin fixation but alcohol fixation. Therefore Ohnuma said these changes were artificial products, but Abrikossoff and Mogilnizky recognized them pathologic findings. Authors found the above changes by alcohol fixation a little and more changes were found in experimental groups than contrast group. But the difference between them was slight, so it is infinite that these changes have pathologic meanings or not.

Müller said that in animals binuclear ganglions were most common and in guinea pig, according to Ohnuma, half was binuclear and half was mononuclear, but polynuclear was rare in comparison with human beings. Guye and Remark found trinuclear ganglions and Schwalbe said binuclear cells most often. This findings are same as the upper opinions. Vas⁽²⁸⁾ said that human ganglion cells had peripheral chromophilic band and perinuclear chromophilic band, but rabbit has only the former. Ide⁽⁵⁾ reported the same findings and supported Vas' opinion and authors found only the peripheral chromophilic band in guinea pig as same as rabbit. The changes of ganglions in authors' experiment are as follows.

At the 1st group, 2-3 hours after injection of croton oil, ganglions showed swelling, atrophy, small vacuolization and chromatolysis, but these alternations have not much difference from the contrast group. The 2nd, 3rd and 4th groups which are stimulated for long time revealed more prominent swelling, atrophy, vacuolization and destruction of cells than the 1st group. Nuclei showed also pathological findings. Groups stimulated for long period showed more changes in proportion to the observed period, but the difference between 2nd and 3rd or 4th group were less remarkable than that between 1st and 2nd group. What is the reason from which these changes product?

Many literature have been reported of the changes of the sympathetic ganglions but most of them state the changes due to the sympathetic toxin or various sickness. Hedinger, Takakura and Ide⁽⁵⁾ investigated the changes of the vegetative nervous system of rabbits injected with adrenalin, and Takakura and Nakajima injected with pilocarpin, Ide cocain, Herzog and Takakura nicotin, Takakura reported the findings of ganglions in beri-beri, avitaminosis, and

Trousseau, Petor, Siemrling, Grienfield, Herzel, Möbius, Graupner, Ehrlich, Virchow, Horand, Aoyagi and Matsumura in Basedow's disease. Matsumura and Moriya demonstrated the changes of the superior cervical ganglions of animals given the thyroidal substance, and Fos, Ljubinoﬀ, van Gechuchter, Daddy and Lavastine, Abrikossoﬀ and Herzog⁽⁴⁾ in the infectious disease, and Anraku, Terplan, Wohlwill, Koide, Asami and Ohnuma in other various diseases and Vas described the changes of ganglion in the case of electrocution.

All of them observed atrophy, swelling, destruction, degeneration, chromatolysis, infiltration of cells and the changes of nuclei. The literature above mentioned stated about the changes of sympathetic nervous system caused by some drugs or illness.

The authors, in other point of view, researched that stimulation to the palate, which Suzuki, Iida and Fukazawa reported formerly, could make some changes on the sympathetic ganglions in the process giving effects to the whole body. Croton oil which is less absorbable and adequate to local stimulus was injected in the palate and subcutaneous tissue of the abdomen. The experiment of Suzuki, Iida and Fukazawa⁽²²⁾ with only 0.1 cc of croton oil injected to the palate revealed the shock syndrome and changes of the several organs. What mechanisms are connected with these changes?

It is very difficult to solve them and there are various opinions about them. However it is also very interest to study them in the standpoint of the Reilly's phenomenon. Reilly^(14, 29-32) demonstrated that the intestinal mucous membrane revealed a typhoid-like alternation after the caeliac ganglions were experimentally affected with the typhoid toxin, and stated that a stimulation on the vegetative nervous system caused this alternation. The authors regard the cervical sympatheticus as one of the course of conduction between the palate and other organs, and considered that the stimulus added to the palate is conducted to the superior cervical ganglion and further to the caeliac ganglion through the vegetative nervous fibers. In this point of view ganglions were investigated. Of course, there is intimate relation with the central brain. Mellet-Guy⁽¹⁰⁾ reported on the changes of the caeliac ganglion on a patient of pancreatitis and his experiment may support authers' opinion.

Since Reilly reported, the same investigations have been done. Marquezy, Ladet and Villarís researched the organs of animals stimulated with the diphtheria toxin. In Japan Suzuki, Iida and Fukazawa, mentioned above, and Sato reported the fluctuation of vitamin B₁ in the organs after vegetative irritation was added and Shiraishi *et al* reported the haemorrhagic change of the lung and adrenal gland, induced by cervical vegetative irritation and stated this

phenomenon connected with the central nervous system. Tsuchiya⁽²⁷⁾ and Akiba⁽¹⁾ described that the Reilly's phenomenon was intimately related to the middle brain-hypophysis-adrenal gland system. Ito *et al* stated the change of organ was produced by stimulation of the cervical sympathetic nerve, caeliac cympathetic nerve, mesointestinal lymph nodes and pharyngeal mucous membrane with croton oil, alcohol and electro-stimulus. Ueyama described the findings of pancreas of animals whose cervical ganglions were stimulated with aloxan or oxin. Suzuki⁽²⁰⁾ and Takasaki⁽²⁶⁾ reported that the stimulation of the infraorbital nerve with croton oil produced changes of organs of guinea pigs and that by the administration of chlorpromazine these changes were inhibited. They stated that these changes were caused by the vegetative irritation conducted in the infraorbital nerve. Igarashi⁽⁶⁾ demonstrated that the toxin of nephritogenic hemolytic streptococcus applied to "Jugular Sac" was susceptible to histological changes of the kidney, and Suzuki and others⁽²⁴⁾ reported the abnormal findings of electrocardiogram assumed to be caused by vegetative irritation of the peritonsillar portion on the patient of peritonsillar abscess. The palate and pharynx where croton oil was experimentally injected were very sensitive positions for stimulus as reported by Suzuki, Iida, Fukazawa, and Nagamine, who described adrenal bleeding due to irritation of the diphtheria toxin at the palate, and Takeuchi stated the changes of organs due to injection of adrenalin to the pharynx. Stolze⁽¹⁹⁾ expressed in his writing "Das obere Kreuz" that the neck connected brain with body and included a rich of important vessels and nerves, and so it was the specific place in morphology.⁽²⁵⁾

Suzuki and Nagase⁽²³⁾ investigated the innervation of the human palatine tonsils. Miyabe⁽¹¹⁾ researched the innervation of the mucous membrane of palate in human, and Kurai⁽⁷⁾ did the innervation of the inferior nasal concha in human being. And they stated that the autonomic nervous fibers were found in large number and succeeded to stain the terminal network of fine vegetative nerves. Many causes are considered to make the changes in sympathetic ganglia, induced by irritation given at the palate. According to predecessor's works, these changes may be occurred by the intoxication of croton oil, but there are not so much difference in the changes of organs especially liver between shorter stimulated group and longer one, and degeneration of the liver cells and changes of the Kupffer's cells are not so remarkable. So it is confirmed that these changes caused by intoxication are denied.

Considered to this experiment, the stimulation which added to the peripheral portion of vegetative nerve should be conducted to the central brain by various routes and changes of the whole body should be occurred. The superior cervical

ganglion cell may be the one of the conducting way and the stimulation will be transmitted to the vegetative nervous system of the whole body through this central way viz. the superior cervical ganglion, so that the same changes are seen at the caeliac ganglion. And findings of the organs were chiefly of the circulatory system. So this fact may be illustrated that these changes are arisen from the vegetative irritation. Irritation should be conducted to the vegetative nerves which distributed around the peripheral vessels and elicited the congestion or bleeding. In the 1st group of animals on which stimulation continued only for 2-3 hours ganglion cells reveals no organic changes, but the visceral organs show the most notable changes; namely ganglion cells would be changed functionally in great deal, so that the constancy of their internal environment of body is broken and might progress to shock. The stimulus added for long period, the organic changes may be appeared.

In the 2nd, 3rd and 4th group diluted croton oil less than half of amount injected in the 1st group was injected, but changes above mentioned might be occurred after stimulus was continued for long time.

The early opinion that stimulation of the autonomic nervous conduction was only centrifugal was recently changed to that centripetal conduction was also present. It is proved by Okinaka *et al*⁽⁸⁾ that the superior cervical ganglia are connected with the nucleus of vagal nerve. Sympathetic nerve and parasympathetic nerve connected each other intimately, hypophysis-adrenal system which was demonstrated by Selye and the control of the central brain and other factors make a complicated mechanism under which human being protects and supports themselves. But shock symptom might be occurred following the failure to adjust them.

Suzuki *et al*⁽²¹⁾ assumed the reason of shock as follows:

- 1) Status thymicolymphaticus
- 2) Intoxication of local aneaesthetica
- 3) Postoperative autointoxication
- 4) Hyperirritation or abnormal stimulation of the vegetative nervous system
- 5) Others

And they pointed the 4th factor as the most important one, and considered clinically the reason of the so called novocain shock that occurred by plasty of the palate or tonsillectomy etc. most frequently in otorhinolaryngological operations may be vegetative hyperirritation, that is Reilly's phenomenon as mentioned by Suzuki and Nagase etc. Stimulation may be conducted to the central brain or peripheral nerves through the superior cervical ganglions as one of organs are

mainly found as a circulatory disturbance.

CONCLUSION

1) In guinea pig the palate was irritated with repeated injections of croton oil for various length of time and changes produced in the palate superior cervical and caeliac sympathetic ganglions and various organs were investigated histopathologically.

2) In the 1st group of animals to which croton oil was injected for a short period only edema of the palate was observed, whereas in the 2nd group to which injection was repeated for long period necrosis and/or cicatrical formation were remarkable.

3) The sympathetic ganglion cells showed little change in animals of the 1st group, while in the 2nd group they showed degenerative change mainly consisting of atrophy and swelling of cell, vacuolization or destruction of cytoplasm, chromatolysis, swelling, atrophy, deformation and destruction of nuclei. The longer the palate was exposed to irritation the higher was degree of changes. Change in the superior cervical and caeliac sympathetic ganglions were similar to each other.

4) In various organs changes due to circulatory disturbance such as congestion and hemorrhage as well as various degenerative changes were observed. These changes were more pronounced in the 1st group.

5) On the basis of these findings, authors explained that the shock symptom produced by irritation of the palate, as a manifestation of Reilly's phenomenon, and offered a postulation that the irritation to the palate was transmitted to the autonomic nervous system of whole body through the superior cervical ganglion working as one of the mediators of stimulus transmission.

ACKNOWLEDGEMENT

In closing we wish to express our thanks to Prof. Dr. Kobayashi, Chief of Department of Pathology, and Dr. Yamamura for their advice and encouragement. This article is released on April in 1959 at 36th Session of Oto-Rhino-Laryngology in Kanto District.

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EXPLANATION OF THE FIGURES

- Fig. 1. Lung. $\times 100$, Hematoxylin & Eosin staining.
Thickened alveolar wall, marked congestion and infiltration of round cells.
- Fig. 2. Liver. $\times 400$, H. & E. staining.
Remarkable congestion, vacuolar degeneration of hepatic cell.
- Fig. 3. Kidney. $\times 400$, H. & E. staining.
Atrophic change of glomerulus, congestion and hydrops of tubuli.
- Fig. 4. Adrenal gland. $\times 100$, H. & E. staining.
Congestion in vessels.
- Fig. 5. Palate in the 1st group. $\times 100$, H. & E. staining.
Edema in subcutaneous tissue without changes of epithelium.
- Fig. 6. Palate in the 2nd group. $\times 100$, H. & E. staining.
Desquamative necrosis of epithelium, fibrosis and infiltration of round cells in subcutaneous tissue.
- Fig. 7. Normal superior cervical ganglion. $\times 1000$, H. & E. staining.
- Fig. 8. The same as Fig. 7. $\times 1000$, Nissl's staining.
- Fig. 9. Sup. cervical ganglion in the 1st group. $\times 1000$, H. & E. staining.
Atrophic sclerosis of ganglion cell and small vacuolus.
- Fig. 10. The same as Fig. 9. $\times 1000$, Nissl's staining.
Slight chromatolysis and slight vacuolization.
- Fig. 11. Sup. cervical ganglion in the 2nd group. $\times 1000$, H. & E. staining.
Swelling and marginal destruction of cells on the central portion.
- Fig. 12. The same as Fig. 11. $\times 1000$, Nissl's staining.
Slight chromatolysis.
- Fig. 13. Sup. cervical ganglion in the 3rd group $\times 1000$, H. & E. staining.
Destruction of cytoplasm and slight change of nucleus.
- Fig. 14. Celiac ganglion in the 3rd group. $\times 1000$, Nissl's staining.
Moderate chromatolysis and remarkable vacuolization.
- Fig. 15. Celiac ganglion in the 4th group. $\times 1000$, H. & E. staining.
Excessive vacuolization and destruction of cytoplasm.
- Fig. 16. The same as Fig. 15. $\times 1000$, Nissl's staining.
Marked chromatolysis. Disappearance of Nissl's granules and small vacuoles in the two cells of central portion.

PLATE I

PLATE II

PLATE III

PLATE IV