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Impaired Blood Circulation in the Gastric tube Utilized for Esophageal Reconstruction as a Sequel to Vagotomy, with Special Reference to Sympathectomy as a Countermeasure

by

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Received for Publication Nov. 10, 1965

INTRODUCTION

In the reconstructive surgery of the esophagus the KIRSCHNER-NAKAYAMA type of gastric tube is being widely used nowadays. Especially, the antethoracic esophagogastrostomy is found to be a relatively simple procedure, in which, however, suture disruption at the anastomosed region is not infrequent. The incidence of such anastomotic leakage is reported to be 0-6.8% in the intrathoracic anastomosis and to be 50-100% in the antethoracic anastomosis. To clarify the cause of this serious postoperative complication various studies have been undertaken by POSTLETHWAIT and others, and the impaired blood supply in the tip of the lifted gastric tube seems to be the most responsible factor ^{1) 32) 44) 53)}. Especially, in the KIRSCHNER-NAKAYAMA type of gastric tube the decrease in blood circulation due to the division of the gastric blood vessels on the left side as well as that of esophagogastric continuity should not be underestimated. In addition, the influence of bilateral vagotomy should also be taken into account. In the present study, the alteration of blood flow in the tip of the KIRSCHNER-NAKAYAMA type of gastric tube following bilateral vagotomy is investigated and the countermeasures are discussed. Relative mechanical strength of suture line in the esophagogastrostomy in this type of gastric tube is also experimentally studied.

Chapter I. Investigation on the disturbance of blood circulation in the tip of the KIRSCHNER-NAKAYAMA type of gastric tube

1. Methods

- (1) Experimental animals: Adult mongrel dogs weighing about 10 kg were used.
- (2) Operative procedure: The dogs were kept fasting 12 to 24 hours prior to surgery and anesthetized by intravenous Nembutal injection in a dose of 25 mg/kg. During surgery air way was secured by an intratracheal intubation and oxygenated by closed circuit anesthesia machine. Following laparotomy a pedunculated gastric tube was mobilized according to the procedure of KIRSCHNER-NAKAYAMA ^{25) 37)} and the stump was closed. Before the division of the stomach a point on the gastric wall about 1 cm distal to the line of division was marked by a silk thread to check the furthestmost region of the tube

(tip 1) and then another point lying about 2 cm further to the pyloric side was similarly marked (tip 2). The following measurements were made on both of these two points.

(3) Preparation of ^{32}P labelled erythrocytes suspended in physiologic saline solution; This was made according to the standard procedure of circulating blood volume measurement²¹⁾³²⁾⁴⁷⁾. Twenty ml of blood samples were taken from the femoral vein of the experimental dogs. Following the addition of 1 ml of 10% sodium citrate solution and 15 ml of physiologic saline solution, the samples were centrifuged for 10 minutes 2000 rounds per minutes. The sedimented blood cell clump was rinsed three times and suspended in the ^{32}P orthophosphate saline solution. The mixture was incubated for 2 hours at 37°C . Then the solution was centrifuged and rinsed again in repetition of the foregoing procedure and finally 20 ml of ^{32}P labelled erythrocyte suspension was prepared.

(4) Measurement of blood flow at the tip of the KIRSCHNER-NAKAYAMA type of gastric tube in each stage of its construction. Twenty to 30 ml of ^{32}P labelled erythrocytes suspension was injected into the femoral vein of the dogs. Utilizing the Shimazu Geiger-Müller counter devised to measure a circular point about 2 mm in diameter, radioactivity ratio was measured on the two points previously marked at the tip of the gastric tube. For each measurement radioactivity was determined on a point of the jejunum about 20 cm distal to the ligament of TREITZ to correct the decay of relative radioactivity of circulating red blood cells during the period of measurement. During determination, bleeding from the neighbouring structures was completely controlled and also it was attempted to exclude the influence from the remote organ. Considering MAJIMA's curve showing decrease of radioactivity of the circulating blood in the course of time following injection of ^{32}P labelled erythrocytes³²⁾, bilateral vagotomy was begun in this study about 10 minutes after injection of ^{32}P labelled erythrocytes suspension where the abruptly elevated radioactivity of the blood fell to a fairly stable level. All procedures and determinations were completed within 10 minutes, respectively, and we tried to terminate each experiment within about 50 minutes after the start.

II. Results

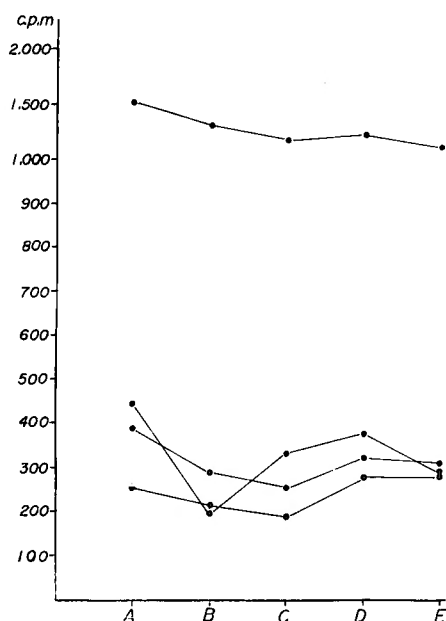
Blood circulation in the tip of the KIRSCHNER-NAKAYAMA type of gastric tube at various stages of its construction was determined by measuring radioactivity ratio in the following order; 1) before treatment, 2) following performance of bilateral vagotomy, 3) following division of the gastric blood vessels on the left side, 4) following division of the gastric continuity and 5) division of the hepatogastric, hepatoduodenal and gastrocolic ligaments as well as division of arches of blood vessels on the greater and lesser curvatures. It was found that blood circulation expressed in radioactivity ratio fell most markedly following bilateral vagotomy in all 4 cases, the mean fall being 26.4%. This was followed by the division of the gastric blood vessels on the left side, the mean decrement being 23.1%. At the division of the gastric continuity, the mean fall was only 10% (Table 1, Fig. 1).

III. Short summary

Utilizing ^{32}P labelled erythrocytes suspension the factors involved in the disturbance of

Tab. 1 Changes of blood circulation at the tip of the KIRSCHNER-NAKAYAMA type of gastric tube with the progress of operative procedures (c. p. m.).

Dog No.		1	2	3	4	Rate of decrease (%)
Treatment						
(1)	Before treatment	262	381	423	1504	
(2)	Performance of bilateral vagotomy	208	298	200	1275	26.4
(3)	Division of the gastric blood vessels on the left side additionally	196	269	341	1229	23.1
(4)	Division of the gastric continuity additionally	274	311	383	1249	10.0
(5)	Division of the hepatogastric, hepatoduodenal and gastrocolic ligaments and ligation of arches of blood vessels on the greater and lesser curvatures, additionally	275	302	300	1081	18.0

**Fig. 1** Changes of blood circulation at the tip of the KIRSCHNER-NAKAYAMA type of gastric tube with the progress of operative procedures. A: Before treatment B: Performance of bilateral vagotomy C: Division of the gastric blood vessels on the left side additionally D: Division of the gastric continuity additionally E: Division of the hepatogastric, hepatoduodenal and gastrocolic ligaments, and ligation of arches of blood vessels on the greater and lesser curvatures, additionally

circulation in the tip of the KIRSCHNER-NAKAYAMA type of gastric tube were analyzed. It was found that among various procedures in the construction of this gastric tube the bilateral vagotomy reduces blood circulation most markedly. This observation well agrees with that of AKAKURA who found in the local clearance study of the gastric fundus that the bilateral vagotomy by transthoracic approach significantly reduces the blood flow in the fundus¹⁾. These observations suggest that reduced blood flow in the tip of the gastric tube as the result of vagotomy is significantly involved in the occurrence of anastomosis disruption in the esophagogastrostomic region. In the present study the bilateral vagotomy was performed by the abdominal approach¹²⁾, but some difficulties were encountered, since in the dog the cardia lies in high and posterior region of the abdominal cavity and the costal arch is strongly curved.

The determination of blood circulation by means of ³²P labelled erythrocytes has been used since HEVESY mainly in the measurement of circulating blood volume. Since this method is essentially to measure the volume of blood corpuscular elements the experimental errors may not be small when there is hemorrhage or severe blood stasis^{9) 10)}. In comparison with other methods^{15) 29) 36)},

however, this method enables us to determine the blood circulation under physiological conditions and to demonstrate the results numerically. In the present study the gastric tube was made according to the original method of KIRSCHNER-NAKAYAMA. However, because

of a somewhat different arterial distribution in the canine stomach³⁾⁷⁾⁸⁾⁴⁾, the gastric tube was somewhat reduced in length, by which, even in the latter period of the experiment there was no apparent congestion at the tip of the gastric tube. BALLINGER reported that bilateral vagotomy significantly reduced the superior mesenteric blood flow⁵⁾. Then as in this experiment, the control radioactivity measured on the jejunum may not be absolutely correct, and the real effect of bilateral vagotomy may be greater than what was measured in this study.

Chapter II. The countermeasures against the impaired blood flow in the tip of the KIRSCHNER-NAKAYAMA type of gastric tube, especially the significance of sympathectomy

1. The objectives of the study

The blood supply to the KIRSCHNER-NAKAYAMA type of gastric tube is provided by the right gastric and right gastroepiploic arteries. In this gastric tube, the nerve fibers, mainly of sympathetic origin, in the neighbouring tissues of these arteries are preserved, whereas the vagal nerves are divided on both sides (Fig. 2).

In the foregoing chapter it has been clarified that the division of the bilateral vagal nerves has more decreasing effect on the blood flow than the division of the gastric vessels on the left side or that of esophago-gastric continuity. It may be then believed that the impaired blood circulation in the tip of the gastric tube is induced by the predominant sympathetic innervation on the arteries supplying blood to the gastric tube. In the present study, an attempt to relieve the sympathetic predominance and therefore to improve the blood circulation in the tip of gastric tube have been done by means of a thoracic sympathicoganglionectomy or periarterial sympathectomy on the arteries supplying the gastric tube.

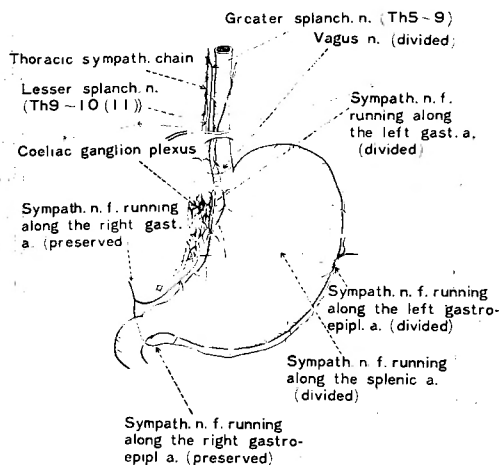


Fig. 2 Innervation of the KIRSCHNER-NAKAYAMA type of gastric tube.

2. Methods

A. Thoracic sympathicoganglionectomy on the right side

(1) Operative procedures; In experimental dogs the KIRSCHNER-NAKAYAMA type of gastric tube was constructed through an abdominal approach. Then right thoracotomy was done under oxygen insufflation by a closed circuit anesthesia apparatus. The right 5th to 10th thoracic sympathetic ganglia were dissected and removed. Especially, the 5th to 9th ganglia, from which the greater splanchnic nerves branch, were carefully removed. In the dog the lesser splanchnic nerves were considerably fine and the ganglia were also relatively small. During operation about 300 ml of 5% glucose solution were infused by

drip because the surgical invasion was extensive.

(2) The measurement of blood circulation

a) Preparation and method of infusion of ^{32}P labelled erythrocytes suspension

As in the method described in the foregoing chapter, radioactivity ratios were determined on the two points of the gastric tube tip pre- and postoperatively. As this operation may affect the blood flow in the abdominal organs, a point on the inferior surface of the tongue was preferred to get the control radioactivity.

b) Polarographic determination⁶⁾

On the tip 1 the alteration of oxygen partial pressures before and after operation were determined utilizing the polarograph (produced by Yanagimoto Works) with a Clark's open tip type platinum electrode (made by Yellow-Springs Co.). During the measurement, minute volume of oxygen insufflation was maintained on a constant level.

B. Periarterial sympathectomy of the common hepatic artery

(1) Operative method

1) In the dogs the KIRSCHNER-NAKAYAMA type of gastric tube was constructed in a typical manner, and periarterial sympathectomy was done along the common hepatic artery. At this procedure the periarterial tissues are adequately infiltrated by 4% Xylocain to avoid the angiospasm by mechanical stimulations. This procedure may also be helpful to avoid the transitory postoperative contraction of the blood vessels due to stimulated vasoconstrictor in the periarterial sympathectomy⁴⁸⁾. Then, periarterial sympathetic nerve fibers together with the adventitia were removed for about 3 cm distance on the common hepatic artery distal to the origin of the splenic artery. The periarterial sympathetic fibers of the common hepatic artery were commonly thick, some being about 1 mm in diameter, and could be easily identified.

2) In patients with cancer of the cardia, the KIRSCHNER-NAKAYAMA type of gastric tube was made and then periarterial sympathetic fibers were removed along the common hepatic artery.

(2) Measurement of the blood circulation

1) Measurement by ^{32}P labelled erythrocytes suspension

For dogs this method was employed.

2) Measurement of the blood flow by means of an electromagnetic flowmeter¹⁸⁾³³⁾

In clinical cases, an electromagnetic flowmeter (made by Medicon) was utilized to determine the blood flow in the gastroduodenal artery before and after the sympathectomy. The right gastroepiploic artery was too fine in diameter to measure the blood flow.

C. Periarterial sympathectomy of the right gastric and right gastroepiploic arteries

(1) Operative procedures

In the dogs, the KIRSCHNER-NAKAYAMA type of gastric tube was made. Then the periarterial tissues of the right gastric and right gastroepiploic arteries were infiltrated with local anesthetics and sympathetic fibers were resected. Near the pyloric ring the right gastroepiploic artery was bluntly dissected from the neighbouring tissues and the artery was exposed. The nerve fibers running close to the adventitia varied in size from cotton thread to hair thick, and were carefully removed so as not to injure the artery. Removal of the adventitia was further performed following application of Xylocain to the artery

wall. Then a similar procedure was done on the right gastric artery near the pyloric ring. The periarterial sympathectomy was then completed. In addition, the hepatogastric, hepatoduodenal and gastrocolic ligament were divided extensively to the right side in order to avoid damage to the main arteries lying in these ligaments (Fig. 3).

(2) Measurement of blood circulation

Utilizing ^{32}P labelled erythrocytes suspension, the radioactivity ratio was determined on the two points of the gastric tube pre- and postoperatively.

3. Results

A. The influence of thoracic sympathicoganglionectomy (Th 5-10) on the right side

i) The blood circulation as revealed by ^{32}P labelled erythrocytes was significantly altered after the operation, that is, the blood flow increased in all cases except one. The mean blood flow increase expressed in radioactivity ratio was 83.1% in tip 1 and 14.9% in tip 2 (Table 2, Fig. 4). ii) In polarographic study the partial oxygen pressure increased 54.5% in the mean in tip 1. This study was performed at the room temperature in 19.5°C and the temperature of the gastric serous membrane was kept in 27°C under a constant oxygen insufflation (Fig. 5).

Tab. 2 Effects of the right thoracic sympathectomy (Th 5~10) on blood circulation at the tip of the KIRSCHNER-NAKAYAMA type of gastric tube, measured with ^{32}P labelled erythrocytes (c. p. m.).

Dog No.	Site of measurement	Before operation	After operation
1	Tip 1	403	946
	Tip 2	596	664
2	Tip 1	247	626
	Tip 2	363	565
3	Tip 1	520	780
	Tip 2	510	704
4	Tip 1	344	222
	Tip 2	499	268
Rate of increase	Tip 1		83.1%
	Tip 2		14.9%

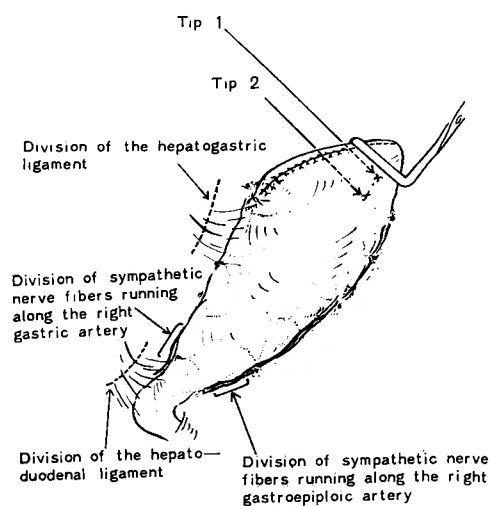


Fig. 3 Denervation of the sympathetic nerve fibers supplied to the KIRSCHNER-NAKAYAMA type of gastric tube.

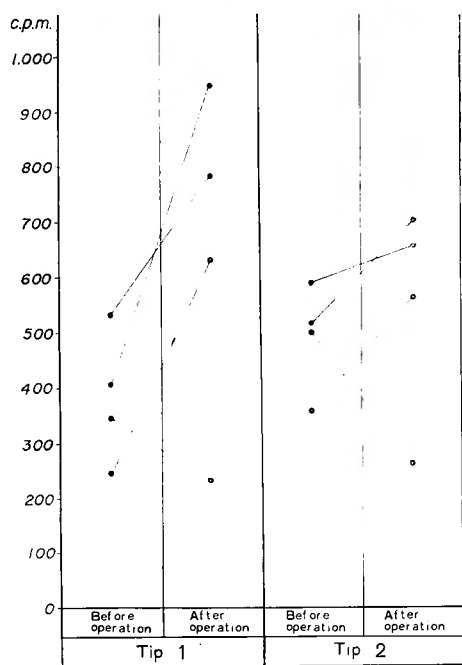


Fig. 4 Effects of the right thoracic sympathectomy (Th 5~10) on blood circulation at the tip of the KIRSCHNER-NAKAYAMA type of gastric tube, measured with ^{32}P labelled erythrocytes.

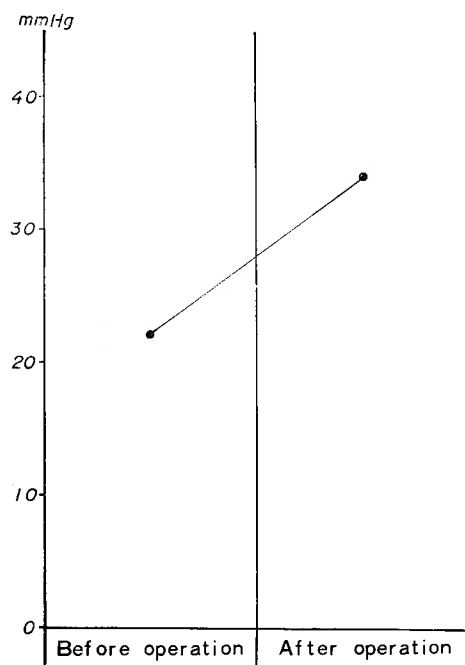


Fig. 5 Effects of the right thoracic sympathectomy (Th 5~10) on oxygen tension at the tip of the KIRSCHNER-NAKAYAMA type of gastric tube, measured with a polarograph.

B. The influence of periarterial sympathectomy of the common hepatic artery

i) Measurement by means of ^{32}P labelled erythrocytes suspension.

The surgery did not produce a definite beneficial effect, the blood flow being decreased by 10.8% in tip 1 and 10.4% at tip 2. (Table 3, Fig. 6).

ii) Determination by an electromagnetic flowmeter

The blood flow (ml/min) of the gastroduodenal artery somewhat decreased follow-

Tab. 3 Effects of the periarterial sympathectomy of the common hepatic artery on blood circulation at the tip of the KIRSCHNER-NAKAYAMA type of gastric tube, measured with ^{32}P labelled erythrocytes (c. p. m.).

Dog No.	Site of measurement	Before operation	After operation
1	Tip 1	882	869
	Tip 2	1038	997
2	Tip 1	698	507
	Tip 2	554	397
3	Tip 1	868	835
	Tip 2	870	879
Rate of increase	Tip 1		-10.8%
	Tip 2		-10.4%

ing the operation, the mean decrease being 10% immediately after the operation, 21%, 15 minutes after operation and 21%, 20 minutes postoperatively (Table 4, Fig. 7). This result supports the somewhat decreased blood flow as revealed by means of ³²P labelled erythrocytes suspension.

C. The influence of periarterial sympathectomy of the right gastric and right gastro-epiploic arteries

Following the surgery blood flow significantly increased in all 7 cases. The increment in radioactivity ratio was 42.7% in tip 1 and 31.2% in tip 2. The operation

proved to be quite effective in elevating the blood flow although it was a minor surgical intervention. In 2 cases the blood flow was determined 2 weeks after the surgery which revealed an increase by 9.5% as compared with preoperative level. The effect of surgery, although somewhat decreasing, was found to

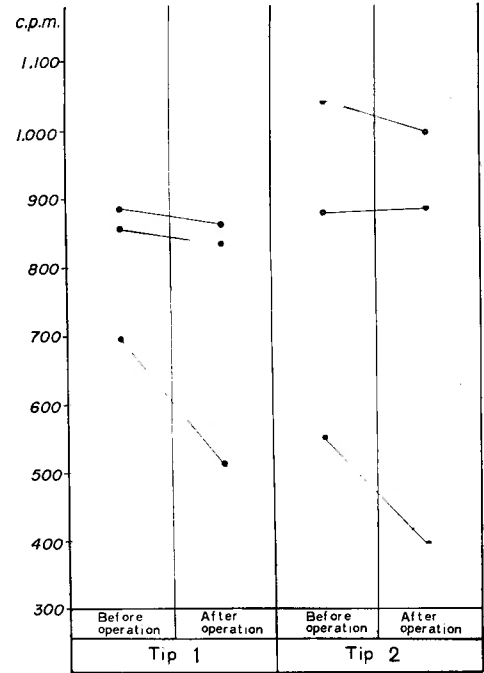


Fig. 6 Effects of the periarterial sympathectomy of the common hepatic artery on blood circulation at the tip of the KIRSCHNER-NAKAYAMA type of gastric tube, measured with ³²P labelled erythrocytes.

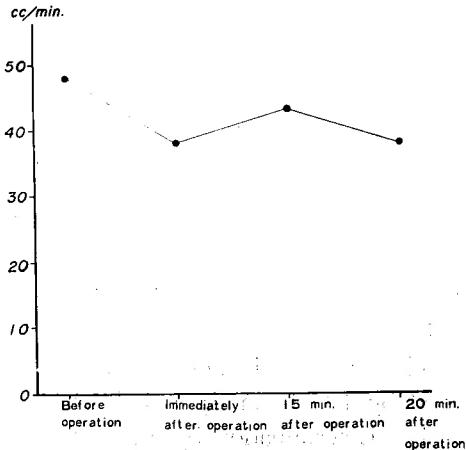


Fig. 7 Changes in blood flow through the gastroduodenal artery after the periarterial sympathectomy of the common hepatic artery, measured with a non-cannulating square-wave electromagnetic flowmeter.

Tab. 4 Changes in blood flow through the gastroduodenal artery after the periarterial sympathectomy of the common hepatic artery, measured with a non-cannulating square-wave electromagnetic flowmeter.

	Before operation	After operation		
		Immediately	15 min.	20 min.
Diameter of electromagnetic probe	5 mm	5 mm	5 mm	5 mm
Meter readings	1.0	0.8	0.9	0.8
Blood flow (cc/min.)	48	38	43	38

Tab. 5 Effects of the periarterial sympathectomy of the right gastric and right gastroepiploic arteries on blood circulation at the tip of the KIRSCHNER-NAKAYAMA type of gastric tube, measured with ³²P labelled erythrocytes (c. p. m.).

Dog No.	Site of measurement	Before operation	After operation	2 weeks postoperatively
1	Tip 1	305	359	
	Tip 2	229	314	
2	Tip 1	403	663	552
	Tip 2	502	590	
3	Tip 1	125	280	
	Tip 2	204	219	
4	Tip 1	681	714	
	Tip 2	732	999	
5	Tip 1	1536	2109	
	Tip 2	1272	2000	
6	Tip 1	1273	1657	1398
	Tip 2	1438	1798	
7	Tip 1	754	902	
	Tip 2	688	990	
Rate of increase	Tip 1		42.7%	9.5%
	Tip 2		31.2%	

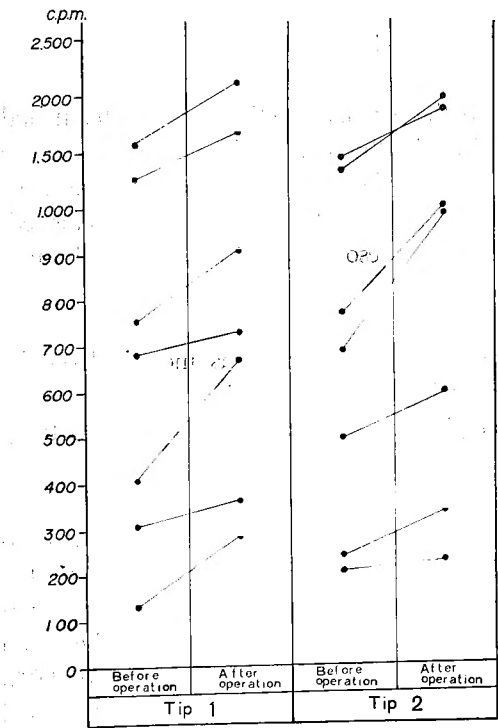


Fig. 8 Effects of the periarterial sympathectomy of the right gastric and right gastroepiploic arteries on blood circulation at the tip of the KIRSCHNER-NAKAYAMA type of gastric tube, measured with ³²P labelled erythrocytes.

be still maintained at a late postoperative period (Table 5, Fig. 8).

4. Short summary

In the previous chapter, the most significant factor that is involved in the production of blood circulation disturbance in the tip of the KIRSCHNER-NAKAYAMA type of gastric tube was evidenced to result from the bilateral vagotomy. Based on this finding an effective treatment was sought for the purpose of blocking off the preserved sympathetic nerve. As for results, it has been found that sympathectomy on various regions can produce significant increase of blood flow with a limited exception.

Thoracic sympathicoganglionectomy was performed on Th5 to Th10 on the right side only. When the active autoregulated vasomotion is present, the blood flow in the gastrointestinal tract should be maintained stable irrespective of the varying systemic arterial pressure. However, such autoregulation has not been found to occur in the gastric

vascular bed¹⁹⁾, therefore, thoracic sympathicoganglionectomy may not be simply practised, since this may produce a severe fall in the blood pressure in elder patients with esophageal cancer or may have some unfavorable effect on the functions of the visceral organs⁴¹⁾. The periarterial sympathectomy of the right gastric and right gastroepiploic arteries has been found to be easy to perform and to produce a significantly good result. Strictly speaking, the surgery, as viewed from the histology of the vascular innervation, can not completely remove all the sympathetic nerve fibers supplied to the stomach²²⁾²⁶⁾. However, actually the experiment has obtained good results to justify the surgery.

The periarterial sympathectomy of the common hepatic artery could not produce an expected effect, rather the blood flow was slightly reduced by this procedure. The cause of this observation may deserve closer attention.

In short, among the various procedures of sympathectomy, the periarterial sympathectomy of the right gastric and right gastroepiploic arteries by which selective removal of the sympathetic fibers to the KIRSCHNER-NAKAYAMA type of gastric tube is possible, has been found to be the procedure of choice as seen from its technical easiness, extent of the surgical intervention and the effect on blood flow.

Chapter III. The effect of the periarterial sympathectomy of the left gastroepiploic artery in the HEIMLICH-GAVRILIU type of gastric tube

(I) Methods

(1) Experimental animals

Adult mongrel dogs weighing about 10 kg were used.

(2) Operative procedure

The gastric tube was constructed according to the original method of HEIMLICH and the following procedures were additionally made¹⁴⁾. At the root of the left gastroepiploic artery that supplies the gastric tube, the artery was anesthetized for about 3 cm distance by locally injecting 4% Xylocain. The periarterial sympathetic fibers were removed. Then bilateral vagotomy was performed at the region of esophagogastric junction through the abdominal approach.

(3) Determination of blood circulation

Utilizing ³²P labelled erythrocytes suspension, blood circulation was measured on the two points at the tip of the gastric tube at the following time period; i) before treatment, ii) periarterial sympathectomy of the left gastroepiploic artery and iii) bilateral vagotomy additionally performed.

(II) Results

The periarterial sympathectomy of the left gastroepiploic artery produced in 2 of 3 cases slight increase of blood flow in both tip 1 and tip 2. In the remaining case the blood flow was elevated in tip 2 but fell in tip 1. When the bilateral vagotomy was additionally performed, all cases showed significant decrease in the blood flow. The mean increase of blood flow following sympathectomy expressed in radioactivity ratio was 2.0% in tip 1 and 27% in tip 2. When bilateral vagotomy was added, the blood flow decreased in the mean by 18.7% in tip 1 and 20.2% in tip 2. In one case first bilateral vagotomy, then sympathectomy was performed, by which the increase of blood flow was 24.4% in

Tab. 6 Effects of the periarterial sympathectomy of the left gastroepiploic artery and bilateral vagotomy on blood circulation at the tip of the HEIMLICH-GAVRILIU type of gastric tube, measured with ³²P labelled erythrocytes (c. p. m.).

Dog No.	Site of measurement	Performance of bilateral vagotomy	Before treatment	Performance of periarterial sympathectomy of left gastroepiploic artery	Performance of bilateral vagotomy additionally
1	Tip 1		281	304	252
	Tip 2		275	292	248
2	Tip 1		301	288	212
	Tip 2		244	363	202
3	Tip 1		345	351	289
	Tip 2		438	552	291
Rate of increase	Tip 1			2.0%	18.7%
	Tip 2			27.0%	20.2%
4	Tip 1	369		457	
	Tip 2	502		634	

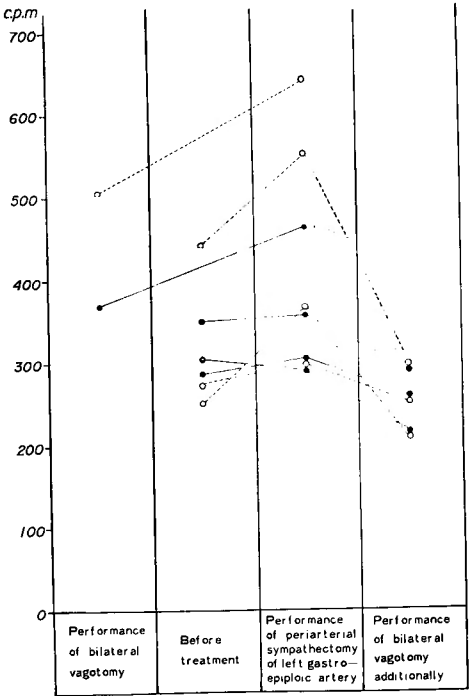


Fig. 9 Effects of the periarterial sympathectomy of the left gastroepiploic artery and bilateral vagotomy on blood circulation at the tip of the HEIMLICH-GAVRILIU type of gastric tube, measured with ³²P labelled erythrocytes.

tip 1 and 26.3% in tip 2 (Table 6, Fig. 9).

(III) Short summary

As seen in Fig. 10, the vascular supply to the HEIMLICH-GAVRILIU type of gastric tube is provided by the left gastroepiploic artery and some additional intramural vasculatures from the proximal half of the stomach. As for the

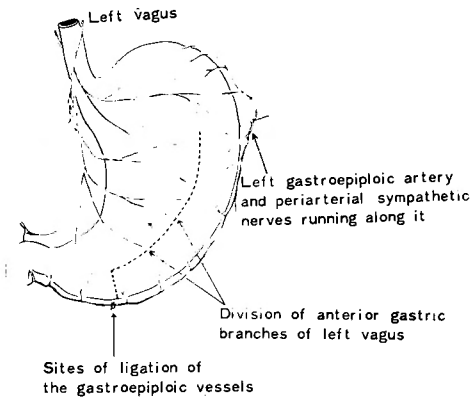


Fig. 10 Arterial supply, venous drainage and innervation of the HEIMLICH-GAVRILIU type of gastric tube.

nervous system, the sympathetic fibers running along the left gastroepiploic artery are left intact, whereas in the vagal nerve, the anterior gastric fibers from the left vagal branch and the posterior gastric fibers from the right vagus are considerably but variously damaged depending on the length of the constructed gastric tube. It is believed that, like in the KIRSCHNER-NAKAYAMA type of gastric tube, but probably in a lesser degree, the sympathetic nervous tone may predominate also in this type of gastric tube.

In comparison of the effect of periarterial sympathectomy of the arteries supplying the gastric tube in these two types, it is found that the increment of blood flow in the HEIMLICH-GAVRILIU type of gastric tube is lower by 40.7% in tip 1 and 11% in tip 2 than in the KIRSCHNER-NAKAYAMA type of gastric tube. In addition, an observation made in one case deserves some attention in that the periarterial sympathectomy of the left gastroepiploic artery performed immediately after bilateral vagotomy produced far better elevation of blood flow as compared with this procedure without the previous performance of bilateral vagotomy.

Chapter IV. The changes in the relative mechanical strength of the suture line in the esophagogastrostomy in the KIRSCHNER-NAKAYAMA type of gastric tube with note on the effect of vitamine E

Vitamine E⁽¹⁾⁽⁵⁵⁾ reportedly dilates capillaries, increases rapidly the collateral blood flow, promoting the peripheral circulation. It may also dissolve fresh blood coagula and reduce oxygen requirement of the tissues. The administration of this vitamine produces an effect like an oxygen tent. With these characteristics of vitamine E in mind, the following experiments were performed.

(I) Methods

(1) Animals

Adult mongrel dogs weighing 10 to 15 kg were used. Although the importance of age, nutrition, hydration and other factors in healing was recognized, no selection of dogs was made. The dogs had been on the usual kennel diet for a period of at least three weeks and fasted 24 hours prior to the operation.

(2) Operative procedures

Utilizing the KIRSCHNER-NAKAYAMA type of gastric tube, esophagogastrostomy was made between the distal esophagus and the stomach through the abdominal approach. All the animals received 200 mg of terramycin intraperitoneally postoperatively. They received also every day 60×10^4 units of water soluble penicillin intramuscularly and 200 ml of polytamin subcutaneously. Each ampoule of vitamine E containing 100 mg of alpha-Tocopherol acetate in aqueous solution was intramuscularly injected in the thigh on the day of operation and the following day. On the 4th and 7th postoperative days the anastomosed region was excised between 10 cm oral to the anastomosis in the distal esophagus and in the pyloric part anally to measure the mechanical strength of the anastomosis. Control animals did not receive vitamine E. To produce identically conditioned esophagogastric anastomoses, the sutures of the anastomoses were made with JIS No. 4 silk of identical fabrics and the interrupted through and through, and outer LEMBERT sutures were made in an identical fashion.

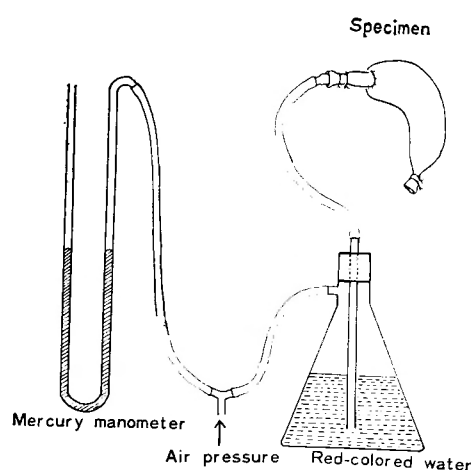


Fig. 11 Method of determining pressure necessary to cause leakage or disruption at the esophagogastrostomic region.

(3) Determination of the mechanical strength

According to the report of POSTLETHWAIT⁴⁴ the following apparatus (Fig. 11) was utilized. By introduction of air from the rubber balloon, the colored water fills the lumen of the specimen. By elevating pressure further, the mercurial pressure at the first occurrence of a leak from the suture line was recorded. Also the pressure at which the leak takes place from many points in the suture line was determined.

(II) Results

In only one specimen taken on the 7th postoperative day, the pressure at the time of leakage from the anastomotic circumference was 252 mmHg, which was about 4.1% higher than the mean pressure in the groups without vitamine E administration. Except this one case, there was no significant difference between the two groups. Between the specimens taken on the 4th and the 7th postoperative days the latter specimens showed higher mechanical strength regardless of the vitamine E administration. Thus the mean pressure at the time of leakage at one point was elevated by 48.4% in the group with vitamine E administration and 56.7% in the group without vitamine E as compared with the specimens taken on the 4th postoperative day. The mean increment in the pressure at the time of leakage at many points was 62.4% in the vitamine E group and 33.7% in the non-vitamine E group (Table 7, Fig. 12).

Tab. 7 Effects of postoperative vitamine E administration on the relative mechanical strength of suture line in the esophagogastrostomic region.

	Vit. E	Dog No.	Values of tensile strength (mmHg)	
			Leakage at one point	Leakage at many points
4th postoperative day	Administered	1	118	176
		2	102	141
		3	99	116
		Mean	106.3	144.3
	None	4	110	204
		5	105	158
		Mean	107.5	181.0
7th postoperative day	Administered	6	170	252
		7	152	233
		8	151	218
		Mean	157.7	234.3
	None	9	164	240
		10	173	244
		Mean	168.5	242.0

Comments on the histological pictures of the adrenal gland and hypophysis following vitamine E administration.

The first receptor of the action of vitamine E lies in the hypophysis and administration of large amounts of this vitamine promotes the hypophyseal adrenal functions. Histologically there is an increase of basophilic cells and increased staining, cell proliferation and hypertrophy in the adrenocortical zona fasciculata and increase of substances that are stained by Sudan III²⁰⁾.

In the present study, in order to ascertain whether administered vitamine E had actually developed a pharmacological effect, the hypophysis and bilateral adrenal glands were removed on the 4th postoperative day from the dogs in the vitamine E group previously described. The specimens were fixed in 10% formalin solution and stained by hematoxylin-eosin. In the adrenal gland the following findings were observed ; thickening of the connective tissues of the capsule (Photo 1), round cell infiltration in the capsule, swelling of the matrix cells in the zona glomerulosa (Photo 2) and dilated capillaries in the medulla (Photo 3). In the hypophysis, slightly increased chromophobe cells of the anterior lobe (Photo 4) and dilated sinus were noted but cellular infiltration was scarcely found.

(III) Short summary

Utilizing the KIRSCHNER-NAKAYAMA type of gastric tube anastomosis with the distal esophagus was performed in the abdominal cavity. The mechanical strength of the anastomosed portion was determined by an apparatus described previously.

In this experiment, vitamine E was administered expecting that it would reinforce the anastomosis through its promoting effect on the peripheral circulation, elevate oxygen consumption in the varying tissues and accelerate granulation. However, with the 2 day doses postoperatively mechanical strength of the suture line on the 4th postoperative day was not increased and on the 7th postoperative day it was slightly increased. POSTLETH-WAIT reported that the mechanical strength of the esophagogastrostomy is most significantly decreased on the 4th postoperative day and thence up to the 7th postoperative day, wound healing is quite rapidly accelerated⁴⁴⁾. In clinical cases also, suture disruption occurs frequently at this period, since up to the 4th postoperative day the nutritional state of the patient is reduced and the influence of the bilateral vagotomy lasts. In this respect, in the present study vitamine E administration was done expecting it to reinforce the

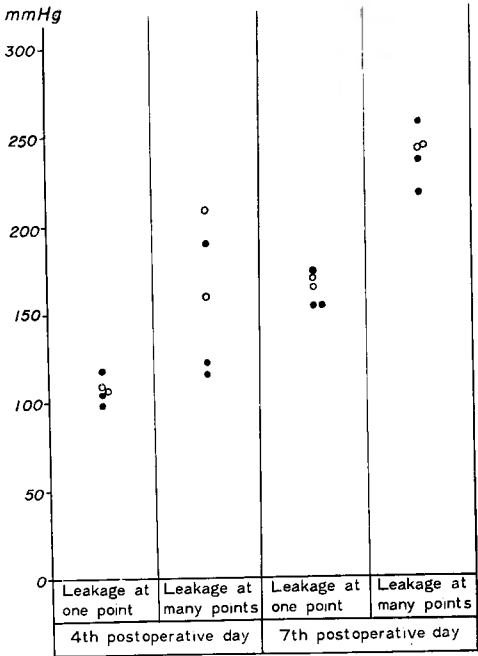


Fig. 12 Effects of postoperative vitamine E administration on the relative mechanical strength of suture line in the esophagogastrostomic region.
● Group with vit. E administration for 2 postoperative days.
○ Group without vit. E administration.

mechanical strength of the anastomosis on the 4th postoperative day but the results were contrary to expectation.

Histologically speaking, however, the changes on the 4th postoperative day as already described may suggest the action of vitamine E, although it was administered only during two days postoperatively. In most instances the first leakage following exertion of pressure occurred in the mid-portion of the anterior wall of the esophagogastric anastomosis regardless of the length of the postoperative period or vitamine E administration. This occurrence is easily understandable when one considers the blood circulation in the anastomosed region^{4) 36) 39)}.

DISCUSSION

Suture disruption is not infrequent following an esophageal reconstruction utilizing the KIRSCHNER-NAKAYAMA type of gastric tube. This complication occurs more often following antethoracic esophagogastrostomy¹⁷⁾. The local factors involved in the development of this suture insufficiency are the following; i) Decreased blood flow in the anastomosed portion, especially in the lifted gastric tube. ii) The esophagus lacks in the serosal coat to aid in immediate sealing of the suture line, and in mobility. The external longitudinal musculature holds sutures poorly, and the blood supply to the esophagus is meager compared with the remainder of the gastrointestinal tract. iii) Movement with respiration and with swallowing prevents the rest period so conducive to healing. iv) The protein of the esophageal mucosa is less resistant to the digestion by pepsin and trypsin^{1) 16) 32) 53)}. Among these factors the most important one is the necrosis in the tip of the lifted gastric tube due to the impaired blood circulation. In this condition, a kink, traction or compression of the nutritional blood vessels may also be contributing factors depending on the position of the lifted gastric tube. The most significant factors appears to be either the bilateral vagotomy, division of the gastric blood vessels on the left side or the severance of the esophagogastric continuity, those procedures being necessary to perform in constructing this type of gastric tube.

Utilizing ³²P AKAKURA et al. of Keio University made the local clearance study of the fundus of canine stomach and found that the local disturbance of blood circulation was slight following severance of the gastric blood vessels on the left side alone, but was significantly aggravated when bilateral vagotomy was additionally performed¹⁾. In the present study bilateral vagotomy was first performed and then the gastric blood vessels on the left side were divided. It has been found that bilateral vagotomy produces significant reduction in the blood flow but the additional division of the gastric blood vessels on the left side does not aggravate the decreased blood flow. This may be due to the summation of two contrary events, the interruption of the blood flow from the left gastric artery and others, the severance of the sympathetic fibers that are particularly rich along this artery. When the division of the gastric continuity is additionally performed, the decrease of the blood flow is relieved, which may be induced by the decrease of vascular bed to be supplied by unit blood vessel. In conclusion the most influential factor that is responsible for the development of impaired blood flow in the tip of the KIRSCHNER-NAKAYAMA type of gastric tube is found to be the bilateral vagotomy.

The autonomic nerve supply to the stomach is much complicated²³⁾³⁴⁾. Generally speaking, however, this may be grouped in the following way; Sympathetic system; the one starting from the celiac ganglion and terminating in the lesser curvature along the right and left gastric arteries trunks via the epigastric plexus and the other starting also from the celiac ganglion and terminating in the greater curvature along the gastroduodenal and splenic arteries and gastroepiploic arteries on both sides via the hypogastric plexus. Parasympathetic nerve; Bilateral vagal nerves entering the abdominal cavity through the esophageal hiatus and branching out on the anterior and posterior surfaces of the stomach. In making of the KIRSCHNER-NAKAYAMA type of gastric tube both trunks of the vagal nerve have to be divided, which subsequently produces predominant sympathetic nerve innervation in the gastric tube. Under this condition an inhibition of the motility of the gastric tube as well as the spasm of the right gastric and right gastroepiploic arteries supplying the gastric tube will occur. These conditions combined with adrenergic predominance of humoral factor in the postoperative period increase the blood flow disturbance in the tip of the gastric tube. The influence of bilateral vagotomy or selective vagotomy has been studied by BALLINGER, GRIFFITH, HARKINS, KRAFT and SEO⁵⁾¹²⁾¹³⁾²⁷⁾⁴⁹⁾. BALLINGER has pointed out that subphrenic total vagotomy in the dog decreased the superior mesenteric venous flow to $42 \pm 11.6\%$ of the normal flow⁵⁾. NYLANDER also indicated that in rats the blood flow of the gastric mucosa decreased following bilateral vagotomy³⁸⁾, and ARABEHETY et al. reported that blood flow of the gastric mucosa of the rat increased following sympathectomy²⁾. PETER et al. also evidenced that the blood flow in the canine stomach is decreased by 30.5% following bilateral vagotomy and celiac ganglionectomy increased the blood flow by 56.4%⁴²⁾.

Based on these observations it is easily understood that in the KIRSCHNER-NAKAYAMA type of gastric tube also, blood flow is decreased under the influence of sympathetic nerve predominance, which readily induces the blood circulation disturbance in the tip of the gastric tube.

As a countermeasure against this, the present author attempted selective sympathectomy, as described in the foregoing chapters. It has been found that periarterial sympathectomy of the right gastric and right gastroepiploic arteries significantly improves the blood flow, the mean increase being 42.7% in tip 1 and 31.2% in tip 2. LERICHE found that following periarterial sympathectomy of the femoral artery the artery remains rather spastic about 6 hours after the operation but thence, the blood flow is improved by dilating artery²⁴⁾³⁰⁾. This improved arterial flow is reported to last usually only 5 to 6 days postoperatively. In the present experiment improvement of the blood flow in the gastric tube was evidenced to occur immediately after the completion of the periarterial sympathectomy of the right gastric and right gastroepiploic arteries. This may be due to the foregoing bilateral vagotomy and elimination of the stimulus to the sympathetic nerve stump by injection of a local anesthetic agent. The sympathetic fibers innervate the arteries of an extremity only segmentally. The periarterial sympathectomy on the femoral artery causes a fall of sympathetic nervous tone in fingers and toes by blocking only a part of afferent arterial nerves of extremities, i. e. the vasodilatory result must be attributed to an indirect effect. In the internal organs, however, the sympathetic efferents as well

as afferents run along the arteries, so the denervation at the arterial root causes total blockage of them in the peripheral side, i. e. it may be far effective than the case of extremities. It was also evidenced that this improved blood flow was maintained even 2 weeks postoperatively to a considerable degree. The suture disruption of the esophago-gastrostomy usually occurs from 3 to 8 days postoperatively so that the sympathectomy can be employed also in clinical patients, since the duration of its effect sufficiently covers the dangerous period.

The thoracic sympathicoganglionectomy also was found to have a good effect on the blood flow. This procedure is, however, definitely a major one as compared with periarterial sympathectomy from the viewpoint of surgical intervention⁴¹). In older cancer patients, this might cause a negative effect by depressing systemic blood pressure. Periarterial sympathectomy of the common hepatic artery was found to have no good effect on the blood flow. Probably this arises from the anatomical situation of the two arteries branching out from the common hepatic artery, the gastroduodenal and proper hepatic arteries. In all seven experimental dogs examined, the angle of bifurcation between the common hepatic and proper hepatic arteries is obtuse and it is acute between the common hepatic and gastroduodenal arteries. It appears also that adventitia and media of the common hepatic and proper hepatic arteries are similar in appearance while those of common hepatic artery and gastroduodenal arteries are different. It follows then that when the blood flow is actually increased by periarterial sympathectomy and more blood is shunted to the proper hepatic artery, the blood flow in the gastroduodenal artery and subsequently in the tip of the gastric tube would not increase. The similar phenomenon appears in extremities after sympathectomy and it is called as lend and borrowing phenomenon. Further study is necessary to evaluate this problem.

In the HEIMLICH-GAVRILIU type of gastric tube⁴⁴), most of the gastric branches of the bilateral vagal nerves, especially the anterior gastric branches, are divided, although the extent of vagotomy may vary depending on the operative procedure and the length of constructed gastric tube. Therefore, even when both vagal trunks are left intact, blood flow will decrease as a result of the autonomic nerve imbalance.

As it appears, periarterial sympathectomy of the left gastroepiploic artery may be effective in order to improve blood flow in this type of gastric tube. Actually, blood flow increased by 2.0% in tip 1 and 27.6% in tip 2, in this experiment. This definitely minor increase in tip 1 as compared with that in the KIRSCHNER-NAKAYAMA type of gastric tube may be accounted for by the following factors; i) Different autonomic innervation in these two types of gastric tubes, ii) the difference in the number of arteries supplying the gastric tube, and iii) the peculiarity of anastomosis between the left and right gastroepiploic arteries in the dogs³). It has been clarified by histological and physiological studies that the vasomotion is controlled by the autonomic nerves. However, the distribution of the motor and sensory nerves to the blood vessels has not yet been completely clarified. It has been believed that nerve fibers run over or in the adventitia only. YAT MAN CHENG, KITAHABA and others of our laboratory have pointed out that they are present also in the media²⁸⁾⁵⁸). From the histological viewpoint, the periarterial sympathectomy as performed in the present study may not sever all the nerve fibers run-

ning in the arterial wall, but clinically this appears to be of minor significance. In 1950 SHAPIRO and others, based on a similar concept, recommended periarterial sympathectomy in the treatment of gastric dysfunctions following vagotomy⁵⁰⁾.

Nevertheless, the periarterial sympathectomy of the right gastric and right gastroploic arteries is found to be quite effective to improve the blood flow disturbance in the tip of the KIRSCHNER-NAKAYAMA type of gastric tube. This procedure appears to be worthy of clinical trial.

As has been shown in these experimental results the blood flow in the tip of both the KIRSCHNER-NAKAYAMA and the HEIMLICH-GAVRILIU types of gastric tube is seriously impaired by bilateral vagotomy. When the thoracic esophagus is removed together with the lesion, the vagal nerves on both sides must be necessarily severed. On the other hand, the influence of vagotomy on the motor and secretory functions of the KIRSCHNER-NAKAYAMA type of gastric tube disappears to a considerable degree 6 months postoperatively⁵¹⁾.

When defect of the esophagus is replaced by such gastric tubes but no additional small vessel anastomosis is performed to provide adequate blood supply to the tip of the gastric tubes, the result of one stage esophageal reconstruction, in which subtotal resection of the esophagus is combined with bilateral vagotomy, is naturally poorer than that for cicatricial esophageal stenosis or multi-stage and by-pass operations, in which the esophagus is not resected. Actually, we have had such experience with the HEIMLICH-GAVRILIU type of gastric tube.

Tocopherol acetate, the main ingredient of vitamine E, is reportedly known to have promoting effect on granulation and peripheral circulation. In the present study vitamine E was experimentally administered with the expectation of improving blood circulation in the esophagogastric anastomosis and to accelerate wound healing. It was found, however, that 2 day dosages of the vitamine postoperatively did not produce significant effect on the relative mechanical strength of the anastomotic region as compared with specimens without the vitamine administration. This was true with specimens examined both on the 4th and 7th postoperative days. Vitamine E is classified in the tocopherol group. The alpha tocopherol is the most active element and is known i) to be an active antioxidant, ii) to act on the hypophyseal-adrenal system and accelerate production of hypophyseal and adrenal hormones, iii) to be an important participant in the enzymatic system, and iv) to be related with nucleic acid metabolism and participate in the plasma protein synthesis¹¹⁾. Clinically, the vitamine alone seldom produces a definite effect, but in combination with amino acid mixture or other vitamins or hormones, it is often effective for amyotrophic disease, nervous and vascular diseases, and gynecologic or skin diseases⁵²⁾. In this experiment vitamine E was found to accelerate the healing of superficial skin wound but less effective for the healing of the esophagogastric anastomosis. This may arise mainly from two factors; for one thing the esophageal wall has poor vascular supply and for another the blood flow in the tip of the lifted gastric tube is poor. Attempts to improve blood circulation by means of periarterial sympathectomy of the arteries supplying the gastric tube may be also significant in this respect.

CONCLUSION

Factors involved in the development of blood circulation disturbance in the tip of the KIRSCHNER-NAKAYAMA type of gastric tube and of the HEIMLICH-GAVRILIU type of gastric tube for esophageal reconstruction are analyzed in experimental dogs. Also some counter-measures against it were studied.

1) In the occurrence of impaired blood circulation in the tip of the KIRSCHNER-NAKAYAMA type of gastric tube bilateral vagotomy plays a role more significant than the division of gastric blood vessels on the left side or the severance of the esophagogastric continuity. It reduced blood flow in the gastric tube by 26.4%.

2) To relieve the impaired blood circulation in the tip of the KIRSCHNER-NAKAYAMA type of gastric tube, severance of sympathetic nerve fibers innervating the gastric tube was attempted. Among various techniques, periarterial sympathectomy of the right gastric and right gastroepiploic arteries was found to be most effective, the blood flow being increased by 42.7% in tip 1 and 31.2% in tip 2. This technique may be performed on clinical patients.

3) Periarterial sympathectomy of the common hepatic artery has no improving effect on the impaired blood flow in the tip of the KIRSCHNER-NAKAYAMA type of gastric tube. The blood flow was reduced by 10.8% in tip 1 and 10.4% in tip 2.

4) Right thoracic sympathicoganglionectomy (Th 5-10) significantly raised blood flow in the tip of the KIRSCHNER-NAKAYAMA type of gastric tube, the increment being 83.1% in tip 1 and 14.9% in tip 2. However, employment of this technique in esophageal cancer patients may not be without difficulty.

5) Blood flow in the tip of the HEIMLICH-GAVRILIU type of gastric tube is raised by periarterial sympathectomy of the left gastroepiploic artery, the increase being 2.0% in tip 1 and 27.0% in tip 2. When bilateral vagotomy is additionally performed, the blood flow is reduced by 18.7% in tip 1 and 20.2% in tip 2.

6) Vitamine E is administered intramuscularly for 2 days postoperatively in dogs undergoing abdominal esophagogastronomy utilizing the KIRSCHNER-NAKAYAMA type of gastric tube. In 6 dogs, sacrificed on the 4th and 7th postoperative days vitamine E administration did not produce significant difference in relative mechanical strength of the anastomosis.

These observations indicate that, when the reconstruction of the esophagus is performed by utilizing the KIRSCHNER-NAKAYAMA type or the HEIMLICH-GAVRILIU type of gastric tubes, the blood flow in the tips of gastric tubes is significantly reduced by bilateral vagotomy. From this viewpoint, successful esophagogastric anastomosis appears to be more frequent following multi-stage or by-pass operation than one stage esophageal reconstruction in which the subtotal esophagectomy and bilateral vagotomy are performed at the same time. It is then recommended that, when reconstruction is made in one stage, interruption of sympathetic fibers remaining in the gastric tube had better be made combinedly.

The author wishes to express his deep gratitude to Prof. Dr. CHUJI KIMURA for his kind guidance, and to Dr. KOICHI ISHIGAMI, the instructor of our clinic, for many valuable suggestions and criticisms throughout this investigation.

An abstract of the present article was reported before the 7th meeting of the Kansai Section of the Japanese Association for Thoracic Surgery, Kyoto, June 26, 1964.

This investigation was supported by a Grant from the Fujiwara Memorial Foundation.

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和文抄録

食道再建用胃管に発生する血行障害の原因としての 迷走神経切断とその対策としての 交感神経遮断術について

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現在最も広く行なわれている Kirschner・中山式胃管による食道再建術は、術式としては比較的簡単であるが、術後屢々、胃管先端部に血行障害を発生し、そのために縫合不全を来すことが少なくない。著者はその血行障害の原因として、同胃管においては両側迷走神経が切断せられるにもかかわらず、右胃動脈や右胃大網動脈を屈繞する線維を主とした多数の交感神経が保存されることによつて、胃管の自律神経支配にアンバランスを招来することが重要な意味をもつものと考え、実験犬においてこれを分析検討した。さらにその対策を見出だそうとして、それら動脈周囲交感神経切除を初めとする種々の交感神経遮断術を実験犬に施行し、同胃管先端部における術前後の血行動態の変動を観察した。

また、Heimlich-Gavriliu 式胃管についても同様な考えのもとに、実験を行なつた。

さらに、Kirschner・中山式胃管を使用して食道胃吻合術を腹腔内において施行した実験犬について、Vit. E 剤の投与が吻合部抗張力にもたらす影響を実験検討した。以上について次の結果を得た。

1) Kirschner・中山式胃管先端部の血行障害を来す因子としては、左側胃血管系の切断や食道胃連続性の離断などに比べて、両側迷走神経切断が重要な意味をもっており、その施行によつて胃管の血行量は 26.4% の減少を示した。

2) この血行障害を改善する方法としては、右胃動脈・右胃大網動脈周囲交感神経を初めとする、胃管を支配する多数の残存交感神経を遮断する各種の術式中、右胃動脈および右胃大網動脈周囲交感神経切除術が最も効果的であり、胃管の最先端部で 42.7%、先端

部で 31.2% の血行量の増加を来し、とくに臨床例にも応用し得るものと考えられた。

3) 総肝動脈周囲交感神経切除術は、Kirschner・中山式胃管先端部の血行を改善する効果はなく、むしろ胃管の最先端部で 10.8%、先端部で 10.4% の血行量の減少を来した。

4) 右側胸部交感神経節 (Th 5~10) 切除術は、Kirschner・中山式胃管先端部の血行量を著しく増加せしめ、最先端部で 83.1%、先端部で 14.9% の血行量の増加を来した。

しかし、これを食道癌患者の手術の際に応用するには、若干の難点が予想される。

5) Heimlich-Gavriliu 式胃管先端部の血行量は、左胃大網動脈周囲交感神経切除術によつて、最先端部で 2.0%、先端部で 27.0% の増加を示し、さらに両側迷走神経切断を追加すると、最先端部で 18.7%、先端部で 20.2% の血行量の減少を示した。

6) Kirschner・中山式胃管使用による腹腔内食道胃吻合術において、術後、Vit. E 剤筋注投与を 2 日間行なつたが、術後 4 日目および 7 日目例の実験犬 6 例では、吻合部抗張力に関して有意な変化は認められなかつた。

以上の諸成績より考えると、Kirschner・中山式胃管や Heimlich-Gavriliu 式胃管を用いて食道再建術を行なう際には、両側迷走切による血行量の著減に留意すべきであり、したがつて食道亜全摘と両側迷走切を同時に行なう一次的手術は血行改善法を併施しない場合には好ましくない。強いて一次的手術を行なう必要のあるときは、上述の胃管に残存する交感神経を遮断する術式を併施することが望ましい。

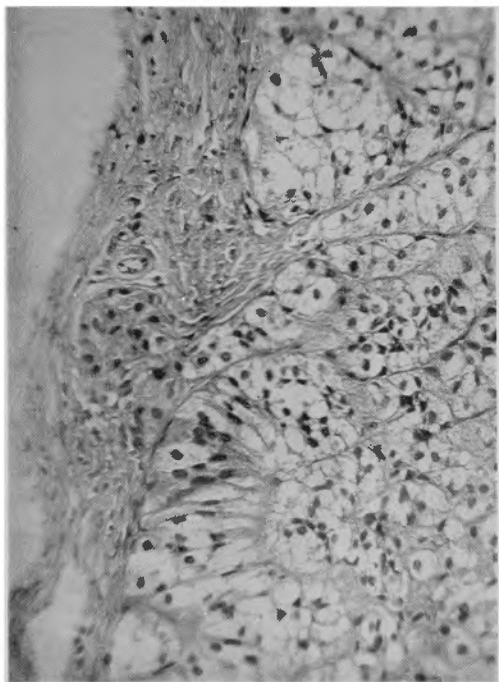


Photo. 1 Histological findings of the adrenal gland following vitamin E administration. Thickening of the connective tissues of the capsule was observed.

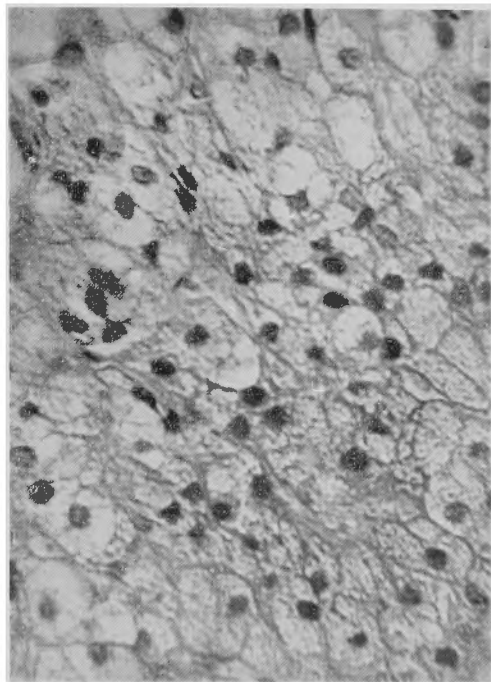


Photo. 2 Histological findings of the adrenal gland following vitamin E administration. Swelling of the matrix cells in the zona glomerulosa was observed.

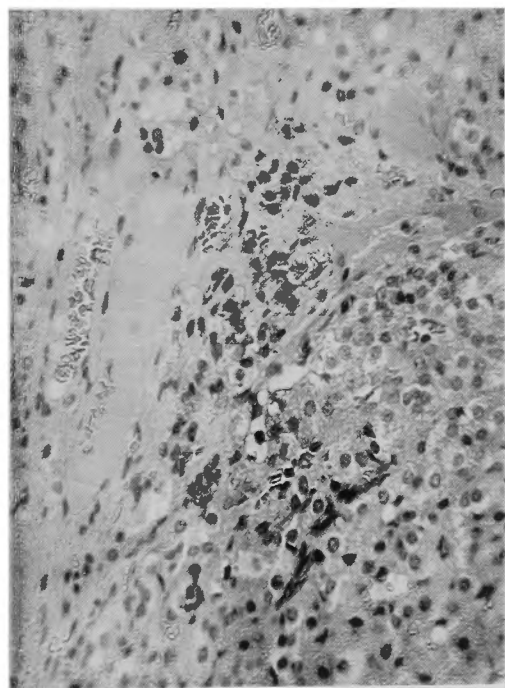


Photo. 3 Histological findings of the adrenal gland following vitamin E administration. Dilatation of the capillaries in the medulla was observed.

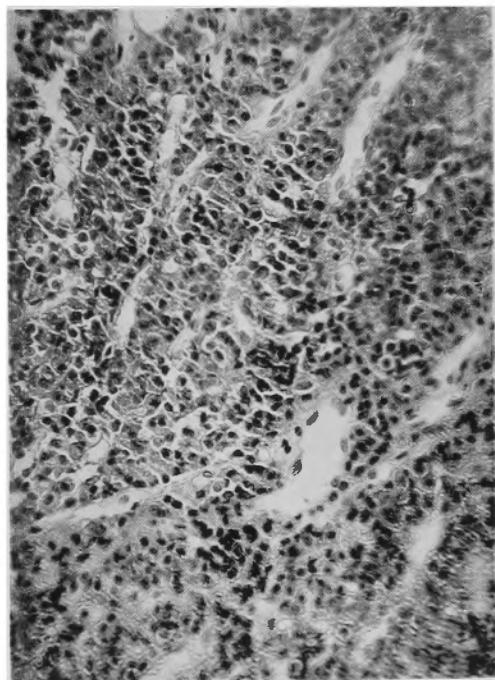


Photo. 4 Histological findings of the hypophysis following vitamin E administration. Chromophobe cells of the anterior lobe increased slightly.