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EXPERIMENTAL STUDIES ON THE SURGICAL TREATMENT FOR CORONARY INSUFFICIENCY

—THE MODIFIED CARDIOPNEUMONOPEXY UTILIZING THE CONGESTIVE LUNG—

by

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INTRODUCTION

Since it was concluded that anginal attack was caused by the deficiency of oxygen supply to the myocardium, some medical treatments have been generally performed for coronary insufficiency. These treatments, however, are nothing but symptomatic therapeutics, and it is natural that the studies of the surgical treatment have been attempted to improve the insufficient coronary circulation radically. In these surgical trials, both the blocking of the sympathetic nervous system (JONESCO) and the thyroidectomy (BLUMGART) were significant from the historical point of view, but these belonged after all to the conservative symptomatic therapy. On the other hand, BECK and his co-workers^{9,45)} have begun the studies of the surgical treatment to improve positively insufficient coronary circulations by means of direct procedure, that is, by "revascularization". Hence, various operative procedures have been devised during this quarter century:

A) Revascularization of the ischemic myocardium by newly established vascular communications between the heart and the surrounding tissues as follows:

- 1) mediastinal fat pad (BECK⁹⁾,
- 2) omentum (O'SHAUGHNESSY⁵⁰⁾,
- 3) pulmonary lobe (LEZIUS³⁷⁾, CARTER¹⁷⁾, HARKEN³¹⁾, BLOOMER¹⁶⁾, GARAMELLA²⁶⁾, PRUDDEN⁵¹⁾ and KOWNACKI³⁵⁾,
- 4) pericardium (with aseptic irritant) (THOMPSON¹²⁾, SCHILDT⁵³⁾ and STANTON⁵⁸⁾, and
- 5) several pedicle grafts, for example, minor pectoral muscle (BECK¹⁰⁾, jejunum (KEY³⁴⁾ and BARONOFKY⁶⁾, intercostal muscle (THAL⁶¹⁾, skin graft (WEDEL⁷⁵⁾ and MORAN⁴⁴⁾, gastric wall (DRAGSTEDT, Jr.²⁰⁾, etc.

B) Introduction of blood stream into the ischemic myocardium

- 1) by internal mammary artery implantation (VINEBERG^{69,70)} and LITVAK³⁹⁾,
- 2) by subclavian artery implantation (FUQUAY²⁵⁾, and
- 3) from the left ventricular cavity (GOLDMAN²⁸⁾ and MASSIMO⁴¹⁾.

C) Restoration of coronary circulation by means of direct procedures to the coronary system as follows:

- 1) ligation of the coronary sinus or great cardiac vein (GROSS³⁰⁾, FAUTEUX²¹⁾,

SIDERYS⁵⁵) and BAKST⁵¹),

- 2) arterialization of the coronary sinus (BECK¹²),
- 3) endarterectomy, resection and anastomosis of the coronary artery (ABSOLON¹¹),
- 4) anastomosis between the coronary and the systemic artery (JULIAN³³) and Moore⁴³), and
- 5) pericoronary sympathetic denervation (FAUTEUX²²).

D) Combinations of some of procedures described above (BECK¹¹) and FAUTEUX²³).

E) For myocardial infarction several procedures were devised as follows:

- 1) resection of the fibrotic cicatrix of myocardium (FORCHER²¹), and
- 2) cardiostathorrhaphy using the pericardium (ALLEN²).

F) Furthermore, bilateral mammary artery ligation (FIESCHI), although one of indirect methods, has been recently revived by BATESATTI⁷.

Among these various methods, those which have been adopted clinically and considered to be effective in general are the operations of THOMPSON^{63, 64, 65, 66, 19}), BECK I.^{14, 15}), HARKEN³¹), O'SHAUGHNESSY⁵⁰) and VINEBERG^{72, 73}).

In Japan, some studies and clinical experiences of these operations have been reported occasionally by several investigators^{52, 49, 47, 75, 3, 67, 46}), and yet the solution of this problem seems to be promised in future.

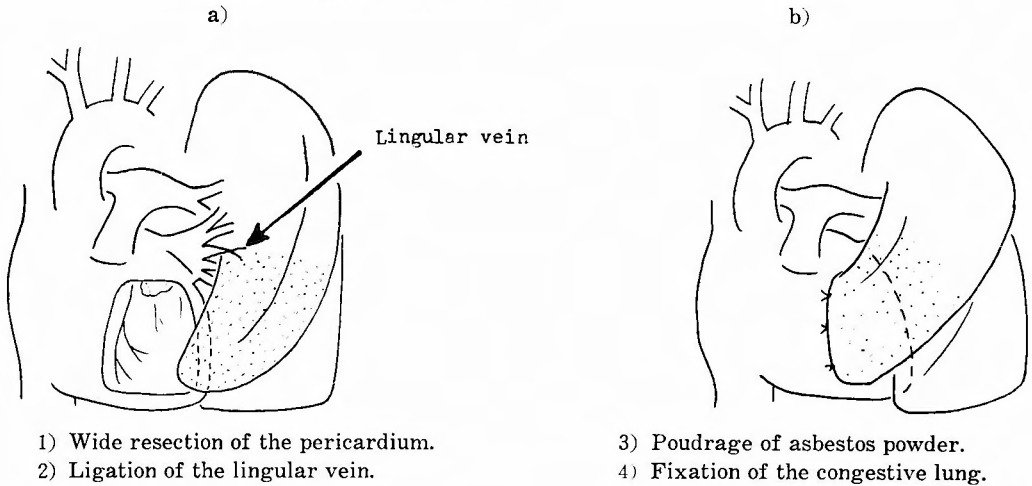
ASADA and the present author¹¹), in 1955, for the first time in Japan, performed the cardiopericardiopexy with asbestos powder for 3 patients suffering from severe anginal attacks, and hitherto, we have operated 7 cases. In consequence of these clinical experiences, we arrived at the idea that in the surgical treatment of the coronary artery disease, it was necessary to manipulate the heart with minimal operative intervention and introduce possibly the greatest deal of blood into the ischemic myocardium from outside. Therefore, using a pulmonary lobe, which is located nearest by the heart and has plenty of blood and vascular beds, we established a new operative procedure, which we have named the modified cardiopneumonopexy utilizing the congestive lung (ASADA-TAKEUCHI). This report describes the experimental studies on the beneficial effect of this new operative procedure undertaken in dogs.

OPERATIVE PROCEDURES

The mongrel dogs, 10~15 Kg in weight, were anesthetized with intravenous administration of thiopental sodium (per kilo 20 mg), and the left thoracotomy was carried out in the fourth intercostal space under endotracheal artificial respiration. The phrenic nerve was dissected and pulled aside, and the pericardium was resected widely to expose the anterior surface of the left ventricle. The middle lobe branches of the left pulmonary veins, corresponding to the lingular vein in human beings, were dissected at the hilum and ligated completely. As soon as these veins were ligated, the colour of the middle lobe changed into red, indicating the occurrence of congestion in the lobe. Then, the lung was reinflated sufficiently by higher endotracheal pressure, and the poudrage of asbestos powder (about 0.07g) was performed with a finger between the surface of the myocardium and the medial surface of the middle lobe. The top of the middle lobe was introduced into the pericardial sac and sutured

to the opened pericardial edges at several points by using a catgut or silk thread in order that the medial surface of the middle lobe might be in close contact with the anterior surface of the left ventricle (Fig. 1).

Fig. 1 Operative procedure of the modified cardiopneumonopexy utilizing the congestive lung (ASADA-TAKUCHI).



Before the closure of the thorax, a silk thread was looped loosely around the dissected anterior descending branch of the left coronary artery at the point of 0.5 cm distal from its origin, and both ends of this nonligated thread were led into the chest wall through the intercostal space and kept in the muscle. In order to evaluate the effect of this operation, the anterior descending branch was ligated by using this silk thread 1 month later under rethoracotomy. This thread proved to be very useful as a guidance to avoid the excessive damage of tissues and the bleeding which were apt to be provoked by exposing the required artery, and as an indicator whether the ligation was carried out at the correct point or not. The technic of this operation was, as mentioned above, very simple, and all its procedure finished within 30~40 minutes including the dissection of the anterior descending branch.

PRELIMINARY STUDIES

Before the establishment of this operative technic, some problems were investigated as preliminary studies.

1) Ligation of the lingular vein

It is supposed that, when the unilateral pulmonary veins are ligated, not only the ipsilateral lung but also the whole systemic circulation will be severely affected⁶⁰. But, on the occasion of the middle lobe vein ligation in a dog, corresponding to the lingular vein ligation in human beings, does any influence happen?

a) In the performance of the middle lobe vein ligation, the left lung had to be pushed aside for exposing the pulmonary hilum. At the moment, abnormal taller P wave was found in E. C. G. tracing of all the animals. But this was only temporarily observed, and soon after the ligation of the vein and inflation of the lung,

it used to disappear completely.

b) The pulmonary arterial pressure was measured by puncture at its main stem, but it showed no change before and after the vein ligation. It was indicated, therefore, that the whole pulmonary circulation was scarcely influenced by the middle lobe vein ligation.

c) As described above, the colour of the middle lobe changed into red as soon as its vein was ligated, and the blood congestion and the bleeding in this pulmonary lobe were observed macroscopically and histologically in several postoperative days. The animals were sluggish in the duration and expectorated some sputa, but by penicillin injection, 600,000 units a day, they became quite well within several days.

d) Oki, a member of our laboratory, by investigating the animals successively after the pulmonary vein ligation, proved that remarkable adhesions were produced between the lobe and the surrounding organs — mediastinum, parietal pleura and other lobes of the lung, that the engorgement and the bleeding in the lobe disappeared within 1 month in consequence of the remarkable development of the collateral vessels in the tissues of these adhesions, and that although the visceral pleura of the lobe was thickened and white in colour, the lung parenchyma itself recovered almost completely to the normal structure (Fig. 2)⁴⁸⁾.

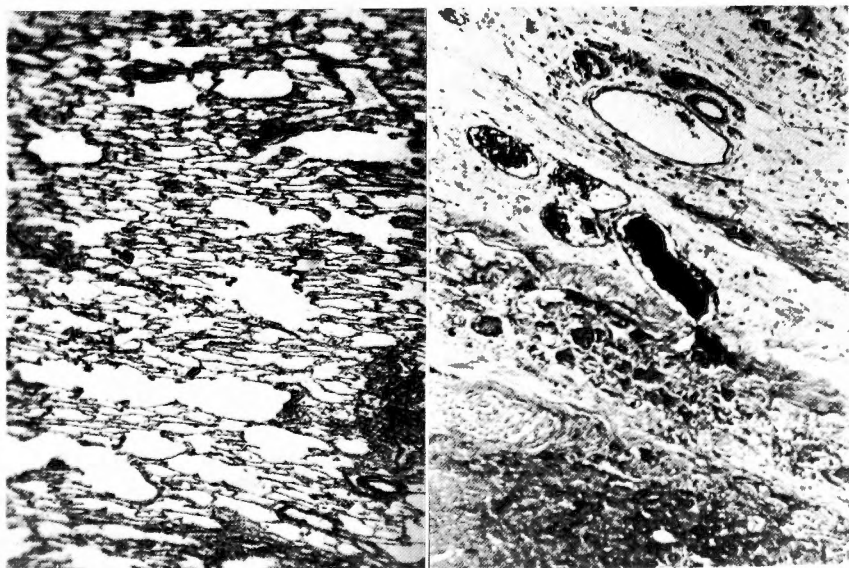


Fig. 2 The lung parenchyma recovered almost completely to the normal structure within 1 month after the pulmonary vein ligation. ($\times 50$, hematoxylin and eosin stain.)

Fig. 3 The granulomatous adhesions with newly developed vascular communications were seen between the pericardium and the myocardium 4 weeks after asbestos poudrage. ($\times 50$, hematoxylin and eosin stain.)

For these reasons, it was suggested that any harmful effect did not supervene by the middle lobe vein ligation.

Selection of the aseptic irritant

Hitherto, for the purpose of producing granulomatous adhesions between the myocardial surface and the surrounding organs which induce the collateral blood flow from the extracoronary blood source into the ischemic myocardium, many kinds of aseptic irritants have been applied. After a great many investigations, talcum powder (THOMPSON⁶²) and asbestos powder (SHILDT⁵³) and STANTON⁵⁸) have been commended as the representative, while some investigators emphasized that the layer of the epicardium could be a barrier against vascular communications between the myocardium and the surrounding tissues, and they commended to use the corrosive agents, such as 95% phenol³¹), 5% tripaflavin³⁸) and others to destroy the barrier.

In these preliminary studies, by applying these aseptic irritants and corrosive agents on the cardiac surface of dogs, it was cleared after all that asbestos powder was more effective than talcum powder in producing the granuloma and many new collateral vessels, that several corrosive agents, such as phenol, had such a violent destructive effect against protein that the E. C. G. pattern revealed evident ST elevation as these agents were applied, and that as they formed cicatrix later, which was scanty of blood vessels and was accompanied by the degeneration of the superficial myocardium, these agents could not be expected to bring out favourable effects.

In using asbestos powder, it was the most effective manipulation to apply a little quantity of it with the finger tip as evenly as possible, and a long-term observation for 2 years proved that there was no tendency to produce cicatricial shrinkage (Fig. 3).

Based upon the results of these preliminary studies, the technic of the modified cardiopneumonopexy was established.

EXPERIMENTAL METHODS AND RESULTS

For the purpose of experimental evaluation of the effects of many operations for coronary insufficiency, various critical methods have been attempted as follows:

a) physiological methods:

- 1) mortality study of the ligation of a major branch of the coronary artery,
- 2) investigation of the E. C. G. findings following the ligation of a major branch of the coronary artery,
- 3) study by the MAUTZ-GREGG backflow method⁴⁹), and
- 4) demonstration of new collateral vessels by injection of dyes or radiopaque masses on living animals.

b) morphological methods:

- 1) demonstration of new collateral vessels by injection of dyes or radiopaque masses at autopsy,
- 2) estimation of the degree of the infarction after the ligation of a major branch of the coronary artery, and
- 3) macroscopic investigation of new collateral formation by the plastic resin cast, etc.

In the present study, several methods were selected as follows.

A) Physiological studies

1) Studies on the mortality rate of the anterior descending branch ligation

The modified cardiopneumonopexy was performed previously, and after a decided interval the ligation of the anterior descending branch of the left coronary artery was carried out, and then it was determined whether the consequent coronary insufficiency or cardiac death was protected by the foregone operation or not. The site of the coronary artery ligation was decided about 0.5 cm distal from the origin of the anterior descending branch, because, if the septal branch which supplied blood to the interventricular septum was ligated together, the mortality rate would increase remarkably, and because the septal branch was in most cases originated more proximally than that site. On postmortem examinations, it was strictly confirmed that the septal branch was never ligated in any cases.

The interval between the protective operation and the ligation of the coronary artery was decided to be about 1 month, because it was proved histologically that more than 2 weeks were necessary for developing new collateral vessels in the granulation tissue.

Experimental results: a) control dogs:—In 23 normal dogs, the anterior descending branch was ligated, and 5 dogs died, consequently the mortality rate revealing 21.7%.

b) protected dogs:—In 15 protected dogs, the artery was ligated as in the control dogs. All the animals survived the ligation, and the mortality rate revealed 0%. However, 2 animals died 3 and 6 days later respectively by thoracic empyema, and the other 2 animals, which had been severely emaciated suffering from heavy diarrhoea with bloody stools before the second operation, stopped breathing at the onset of the intravenous anesthesia, and died 10 and 20 hours after the ligation respectively, falling into apnoea in spite of the remaining normal heart beats and normal E. C. G. findings.

2) Studies of the E. C. G. findings of the ligation of the anterior descending branch

E. C. G. tracings were carried out 4 times by standard leads and unipolar limb leads;—before the thoracotomy, before the ligation, after the ligation (5 min. later) and after the operation (about 1 hour later). In order to indicate the electropotential

Table 1 The E. C. G. findings by the anterior descending branch ligation in normal control dogs.

ST _r	T _r
in 13 dogs.....depressed	in 4 dogs.....unchanged in 5 dogs.....taller in 4 dogs.....biphasic
in 8 dogs.....elevated	in 6 dogs.....taller in 1 dog.....flattened in 1 dog.....inverted
in 4 dogs.....unchanged	in 4 dogs.....taller

In 11 out of the total 25 dogs premature beat was recognized.

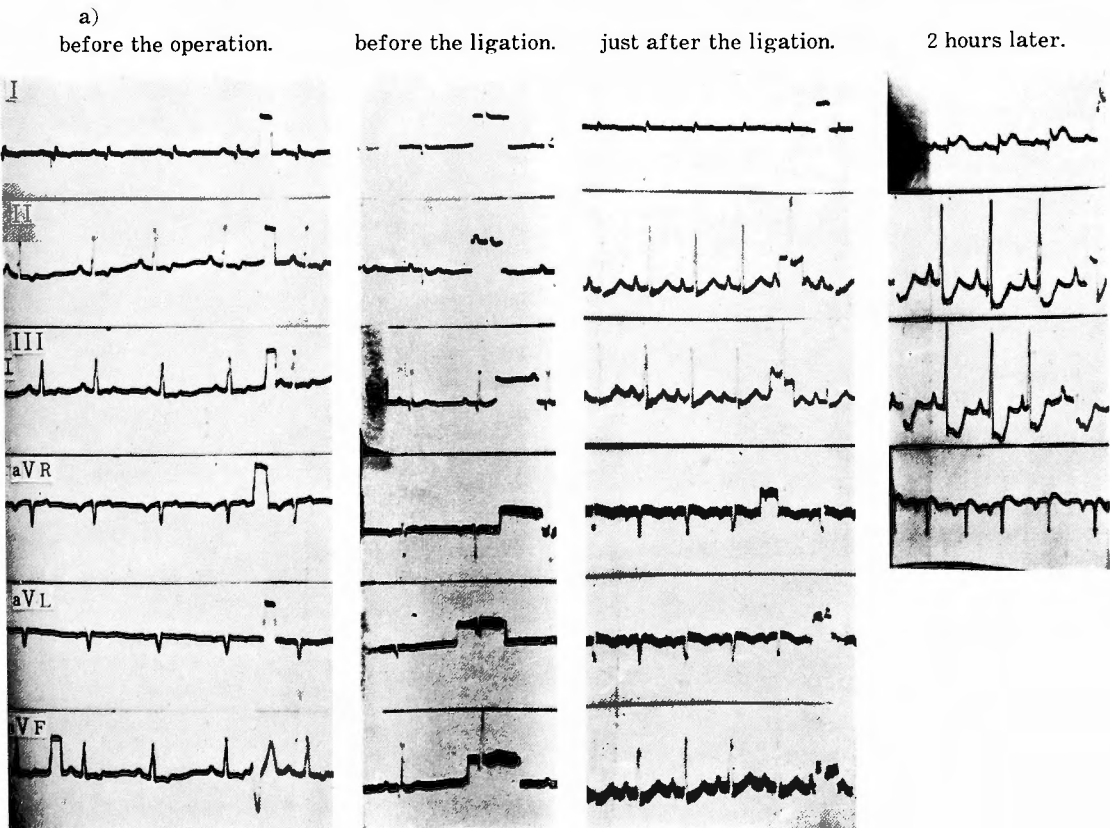
alteration in the anterior wall of the left ventricle, the findings of the lead II, especially ST segment and T wave were collected and evaluated.

Experimental results : a) control dogs: — Immediately after the anterior descending branch was ligated in normal dogs, remarkable changes on the E. C. G. pattern were seen in all the 25 dogs. Within 5 minutes after the ligation, depression of ST segment was seen in 13 cases, elevation of ST segment in 8 cases and taller T wave without abnormal ST segment in the other 4 cases (Table 1).

In 13 cases in which each ST segment was depressed, T wave became taller in 5 cases and became biphasic in 4 cases. In 8 cases in which each ST segment was elevated, T wave became taller in 6 cases, flattened in 1 case and inverted in 1 case. That is, T wave became taller by more than 0.03 millivolt in 15 out of 25 cases. Premature beat was seen in 11 cases (Fig. 4).

It was supposed that if the ligation had not been released these changes of ST segment and T wave would have developed to the typical curves of the myocardial damage. In 21 cases out of all the 25 dogs, however, the ligature was released after the observation for 5 minutes. And they were subjected to the protective operation which was performed 1 month later by the same silk thread at the same site.

Fig. 4 (a, b) The E. C. G. tracings on normal control dogs showing the typical myocardial ischemic pattern after the ligation of the anterior descending branch.



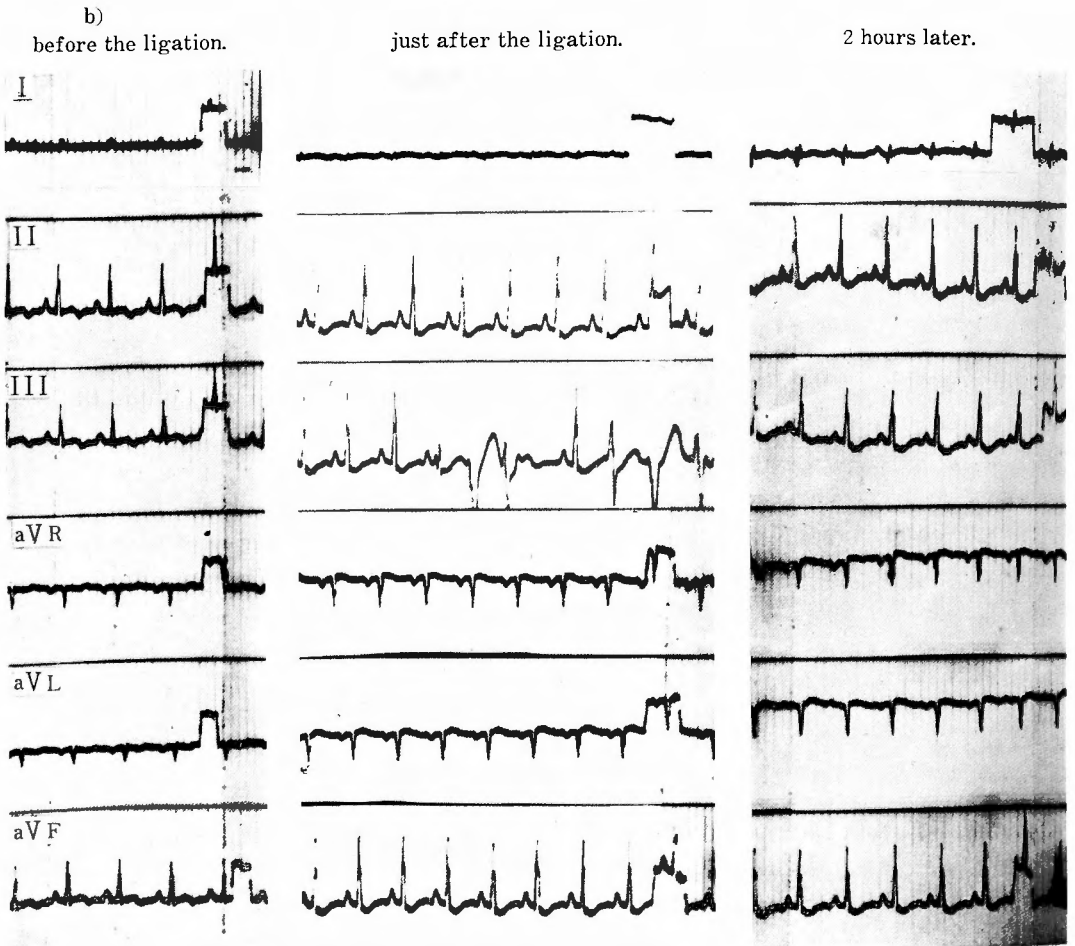


Table 2 The E. C. G. findings by the anterior descending branch ligation in protected dogs.

ST _r		T _r	
in 1 dog	depressed	unchanged	
in 14 dogs	unchanged	in 2 dogs.....	taller
		in 2 dogs.....	flattened
		in 3 dogs.....	taller temporarily
		in 7 dogs.....	unchanged

b) protected dogs: — Only 5 out of 15 cases revealed abnormal findings in the E. C. G. follow-ups: ST segment was depressed only in 1 case, T wave became taller in 2 cases and flattened in 2 cases, and the degree of these changes was relatively slighter than in control dogs — within only 0.2 millivolt (Fig. 5). In 1 case premature beat was seen, but just temporarily. In the other 10 cases, abnormal findings were not found for more than 1 hour (Table 2).

B) Morphological studies

1) Studies of the collateral blood vessels in the adhesions between the lung

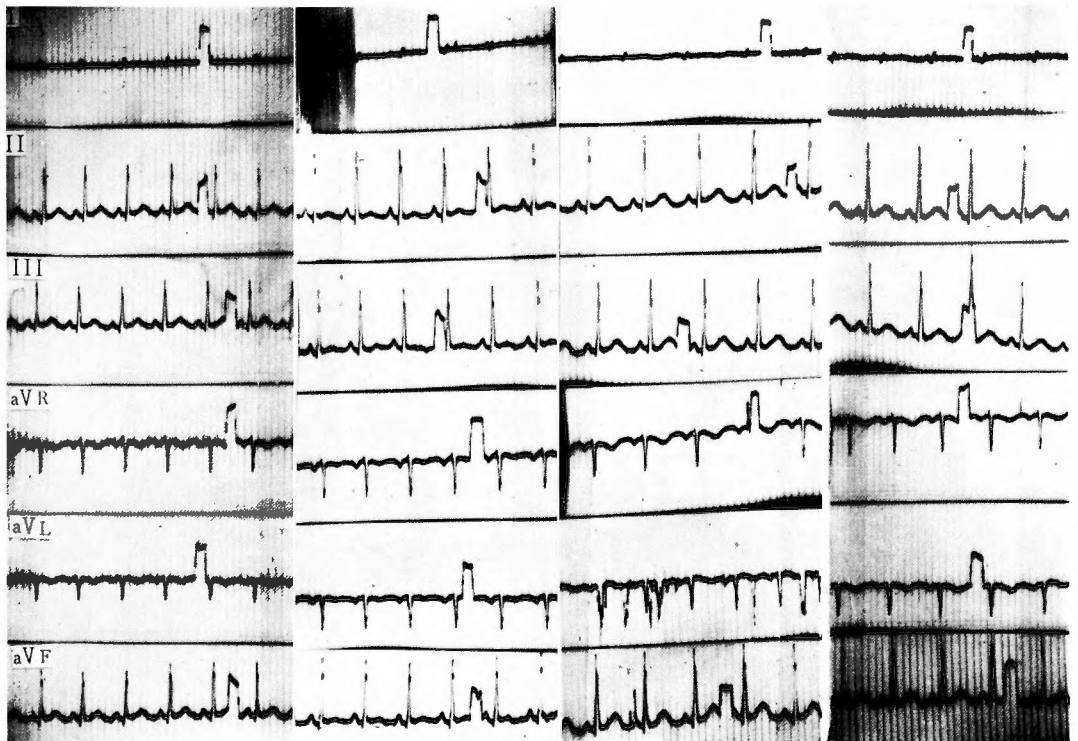
and the heart.

As the modified cardiopneumonopexy has been intended to endow the lung with the potential ability of collateral anastomosis formation by the ligation of the pulmonary vein, it seems most important to estimate the collateral anastomoses between the lung and the heart. The dog, which had survived the ligation of the anterior descending branch, was killed after 4 days in 1 group and after 2 or 5 months in another group. A dorsolateral thoracotomy was performed, the previously operated region being avoided, the middle lobe artery was dissected carefully not to destroy the cardiopulmonary adhesions and the pulmonary tissues, a quantity of 50~80 cc of india ink was injected slowly from the dissected pulmonary artery, and then the lung and the heart were removed en bloc. The specimen was cut sagittally at the forewall of the left ventricle, and the sections of the cardiopulmonary adhesions were investigated macro- and microscopically. The pressure of the india ink injection was not strictly provided, because any heavy resistance was not felt in the course of the injection.

Experimental results: a) Macroscopic findings:—In 10 dogs which were injected with india ink, close adhesions were clearly recognized between the middle lobe and the left ventricular wall. The former looked quite black and the latter was also coloured darkly by the infiltration of the india ink from the lung via adhesions,

Fig. 5 (a, b) The E. C. G. tracings on the protected dogs showing taller T wave after the ligation of the anterior descending branch.

a)
before the operation. before the ligation. just after the ligation. 1 hour later.



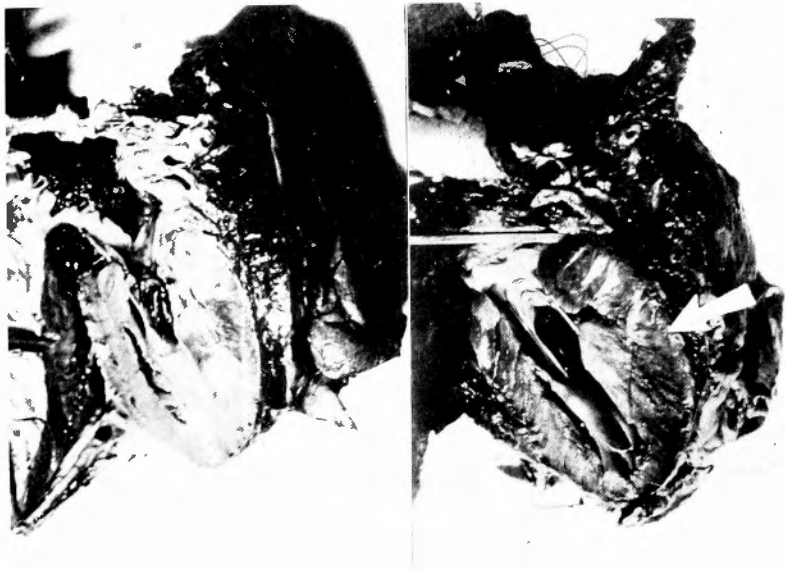
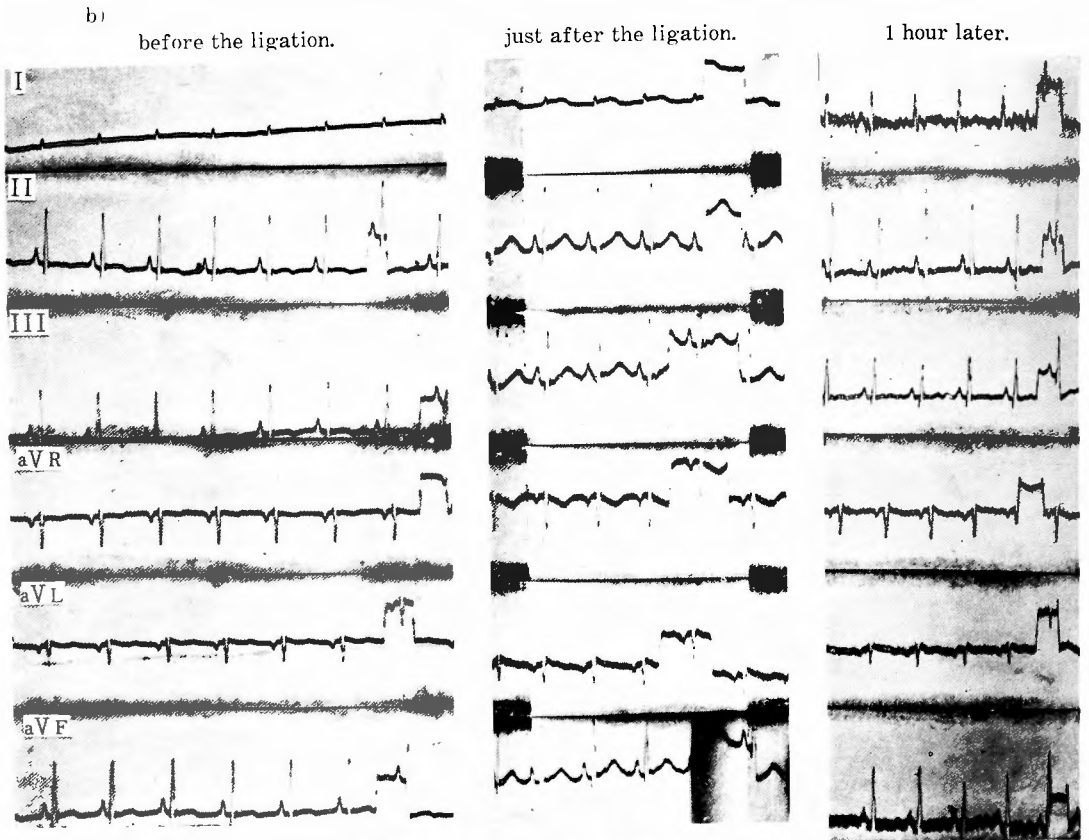


Fig. 6 (a, b) The specimens show the sections of the left ventricular wall and the adherent lung. As the arrows indicate, the myocardiums are coloured darkly by the infiltration of india ink.

into the deep myocardium. Especially in No. 61, 77 and 126, even papillary muscles were dyed distinctly by a sufficient amount of india ink infiltration (Fig. 6).

b) Microscopic findings:—In the cardiopulmonary adhesions, the endothelial layer of the pulmonary pleura and of the epicardium disappeared or fell into disorder, and the granulation tissues with plenty of newly produced abundant vessels were seen to be closely adherent both to the parenchyma of the lung and to the myocardium (Fig. 7). There were also found scattered crystals of asbestos, surrounded by macrophages and foreign-body giant cells in these granulation tissues. Newly produced



Fig. 7 The adhesion tissues between the lung and the myocardium with plenty of newly produced abundant vessels, including many particles of india ink which was injected from the pulmonary artery. ($\times 50$, hematoxylin and eosin stain.)



Fig. 8 The microphotograph shows the intramyocardial vessels filled with many particles of india ink. ($\times 50$, hematoxylin and eosin stain.)

vessels revealed winding and sometimes became over 60 microns in diameter, in which lumina particles of india ink existed densely. Furthermore, in the major branches of the subepicardial coronary arteries and in the intramural arteriovenous system, a great many particles of india ink were also found in all the animals (Fig. 8).

2) Investigation of the infarction caused by the ligation of the anterior descending branch.

As soon as the anterior descending branch was ligated, the myocardial area, which was supplied with blood by this branch, fell into ischemia, and caused by and by such retrograde course as myocardial degeneration, myocardial necrosis, granulation and scarformation. These morphological changes were evidently seen by eyes 10 ~ 14 days after the ligation. Therefore, the macroscopic studies of the infarction, especially in regard to its grade and width, were performed more than 1 month after the ligation, when the cicatricial shrinkage of the myocardium was considered to be almost over.

In this investigation, the animals were divided into 3 groups, the 1st group consisting of normal dogs as control, the 2nd group being the one on which had been carried out both protective operation and ligation of the anterior descending branch at the same time, and the 3rd group being that which had been operated 1 month before the ligation.

Experimental results: a) control dogs: — When the anterior descending branch was ligated, the myocardium which was supplied with blood by this branch changed colour immediately into the cyanotic ton, and the myocardial infarction was found at the postmortem examination after 2 ~ 28 weeks. Over the infarction, there were found fibrinous adhesions between the pericardium and the myocardium, which were easily dissected with a finger, and after the dissection grayish scar was seen in the

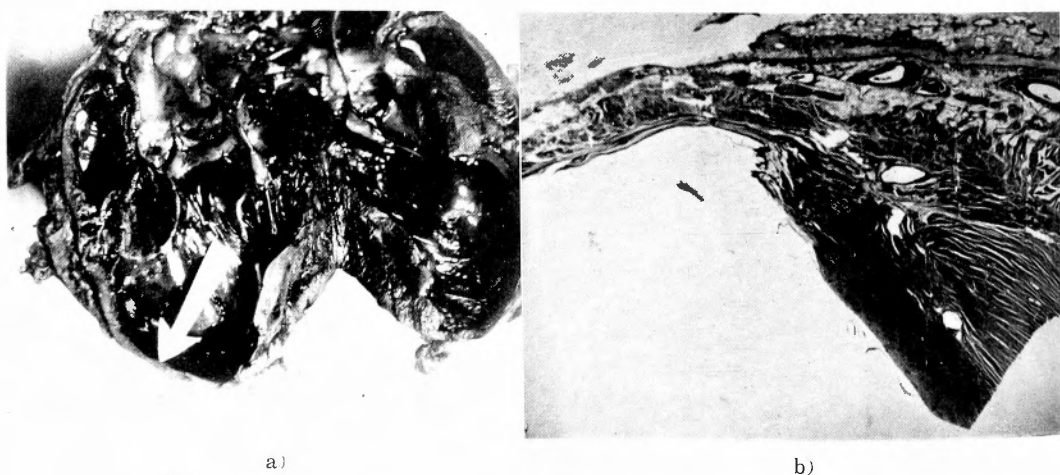


Fig. 9 (a) The complete transmural infarction, including the papillary muscles in a control dog, is indicated by the arrow. (b) The thickness of the scar is remarkably decreased. Notice the differences of thickness between the scar (left side) and the normal myocardium (right side). ($\times 8$, Heidenhain's azan stain.)

myocardium. This diamond-shaped infarction extended over both ventricular walls: one-fourth was on the right ventricle, and the other three-fourths was on the left ventricle. The sagittal section of the left ventricle demonstrated the complete transmural infarction including the papillary muscles in the anterior wall (Fig. 9). One month after the ligation, the thickness of the scar remarkably decreased to 0.2~0.3 cm from the normal thickness of the myocardium (0.7~1 cm), but within 2 weeks after the ligation, even the colour of the myocardium was white, and its thickness was kept more than 0.5 cm in almost all the animals. This infarction was seen in all the control dogs.

b) the second group:— Two out of the 10 dogs died within several hours after the operation. The other 8 dogs were sacrificed after 3 months, and all of them demonstrated the same damage of the myocardial wall as the control animals. Transmural infarction was also found histologically. There was no essential difference between the scar of the 1st group and that of the 2nd group.

c) protected dogs:— Five animals were sacrificed more than 1 month after the ligation. In all the animals, the adhesions between the heart and the lung were so closely completed that observation from outside was scarcely possible, but it was supposed by the palpation of the heart that the ventricular wall was keeping its normal thickness. Three of them, in fact, revealed the normal thickness of the myocardium by the macroscopic investigation of the section of the ventricular wall, and there was no change in the heart muscles histologically, neither proliferation of the stroma nor cicatrization of the myocardium (Fig. 10).

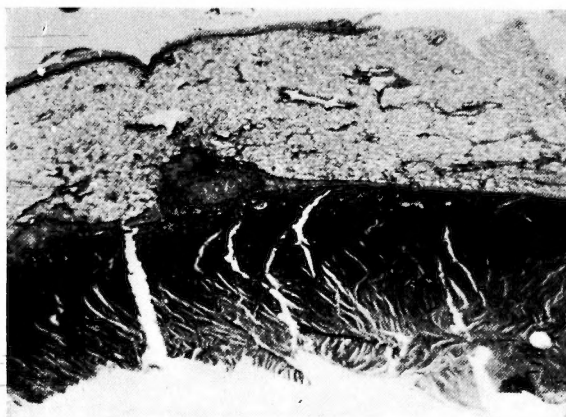


Fig. 10 This microphotograph shows the adherent lung (upper portion) and the myocardium (lower portion) whose anterior descending branch was ligated. There is neither proliferation of stroma nor cicatrization. ($\times 3$, hematoxylin and eosin stain.)

C) Studies on the mechanism of the protective effect

As regards the mechanism of the protective effect of various cardiopexies against the myocardial damage following the coronary artery ligation, it had been supposed previously that the extracoronary blood sources played the leading roles, from which the blood was considered to be transported to the ischemic myocardium through the newly produced collateral vessels²⁾. But recently, STANTON²⁸⁾ and GREGG²⁹⁾ reported

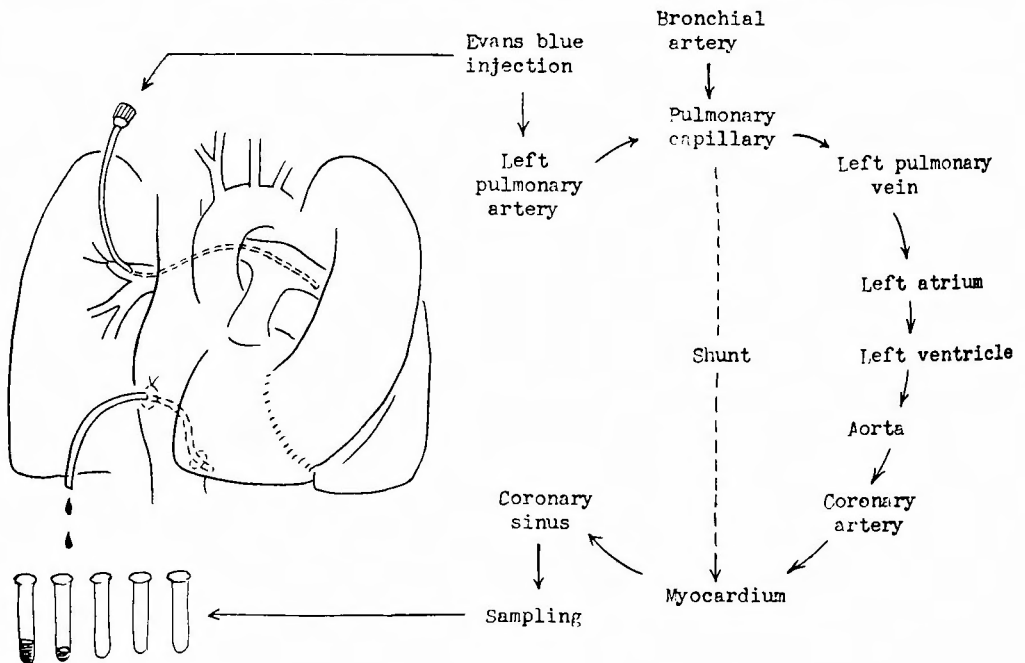
that it was not the extracoronary but the intercoronary collateral communications that prevented or relieved the occurrence of the myocardial damage.

As ASADA and the present author had devised the above-mentioned new operative modes with the object of increasing the extracoronary collateral communications, it was natural that a doubt was laid upon the opinion of the former investigators, and accordingly the following investigations were performed.

1) Investigation of the collateral blood flow from the lung to the myocardium : In order to determine whether the extracoronary collateral blood flow from the lung to the myocardium existed or not, the circulation time was measured under quite a physiological condition.

A transsternal bilateral thoracotomy was carried out, and the right upper pulmonary artery was dissected at its hilar portion. A polyethylen catheter was inserted from the proximal end of this artery beyond the bifurcation into the stem of the left pulmonary artery. On the other hand, by incising the pericardium at its right basal portion and exposing the right atrial wall and the coronary sinus, another polyethylen catheter was inserted into the coronary sinus through the right atrial wall. Then, 2.5 cc of 0.3% Evans blue solution was injected rapidly into the pulmonary artery through the first catheter, and immediately thereafter the coronary venous blood was collected through the second catheter by every second. The time that the dye firstly appeared in the coronary sinus — via the left pulmonary vein — left atrium — left ventricle — aorta — coronary artery — myocardium — and coronary vein — was obtained. If the collateral blood flow or shunt from the left lung to the myocardium existed, the circulation time had to be shortened by the short circuit of

Fig. 11 Demonstration of the extracoronary blood supply



the circulation course (Fig. 11).

Experimental results: a) control dogs — The circulation time in normal 5 dogs was 11, 13, 12, 12 and 11 seconds respectively, and 11.8 seconds on the average.

b) protected dogs with normal coronary circulation — In this group the modified cardiopneumonopexy was performed, but the coronary artery was not ligated. Two dogs demonstrated almost the same time as controls, that is, 11.5 seconds on the average.

c) protected dogs with the ligations of the anterior descending branch — In this group, the anterior descending branch was ligated 1 month after the protective operation. In 4 dogs the circulation time was 12, 7, 8 and 8 seconds respectively, that is, except for the first case, the circulating time was shortened by about one-third than in controls (Table 3).

Table 3 Circulation time from the left pulmonary artery to the coronary sinus.

a) control normal dogs	11, 13, 12, 12, 11 sec.
b) operated dogs (modified cardiopneumonopexy)	12, 11 sec.
c) ligated dogs (modified cardiopneumonopexy + coronary artery ligation)	12, 7, 8, 8 sec.

2) Studies on the intercoronary collateral communications: A plastic resin cast of the coronary vessels was made in order to examine whether the intercoronary collateral communications had been established or not. The heart was removed from the pleural cavity, and the blood was washed away with tepid water. Then, coloured meta-acrylate was injected with a catalyzer into the ascending aorta. After the resin cast became completely stiff, the heart was corroded away by the immersion of hydrochloric acid. After gentle washing, the plastic resin cast was investigated.

Experimental results: a) control dogs — The plastic resin was injected into the aorta after the ligation of the anterior descending branch. Three main arteries — the right coronary artery, the circumflex and the septal branch — were demonstrated

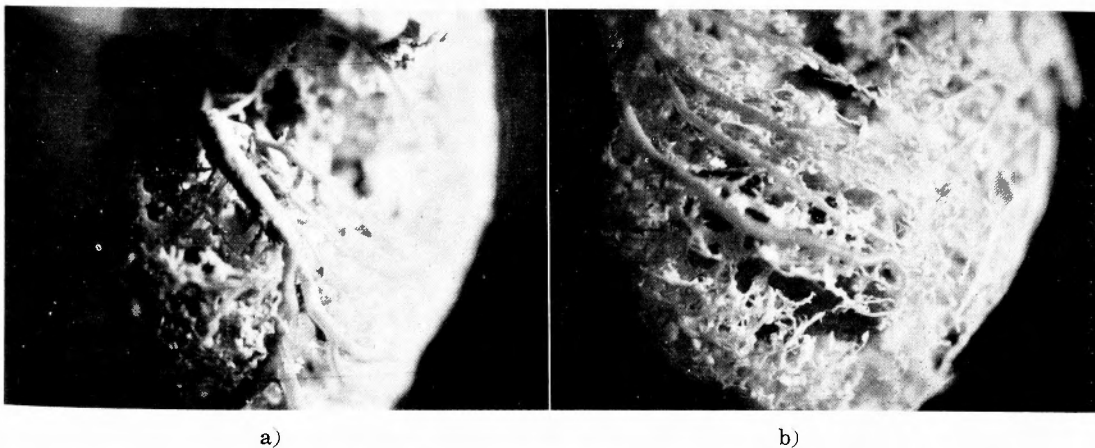


Fig. 12 (a) The resin cast shows the peripheral division of the anterior descending branch in spite of the definite interruption of its stem by the foregoing ligation. (b) The netted anastomoses are seen between the anterior descending branch (left side) and the circumflex branch (right side).

respectively, but the anterior descending branch was interrupted at the site of the ligation, showing its peripheral division completely defected.

b) protected dogs — Two dogs were injected with plastic resin after the intervals of 2 and 5 months after the ligation of the anterior descending branch. The cast demonstrated the peripheral division of the anterior descending branch, and many netted communications were observed at the apex between the anterior descending branch and the circumflex branch (especially at Ramus marginis obtusi) on the ventricular surface (Fig. 12). The diameter of these communications was as large as that of arterioles or praecapillaries. Furthermore, from the periphery of the anterior descending branch, a large number of fine twigs protruded to the profound myocardium at right angles, as were seen in the other non-ligated artery and branches.

Accordingly, it was supposed that intercoronary communications were established between the peripheral portion of the anterior descending branch and the other artery and branches, through which the plastic resin was injected retrogradely into the division of the interrupted branch.

DISCUSSION

Many investigators reported various mortality rates of the anterior descending branch ligation in dogs^{71,35,13,49,5,17,67,42,40} (Table 4). As indicated in table 4, they are

Table 4 The mortality rate of the anterior descending branch ligation.

VINEBERG } KOWNACKI }	80—90%
BECK	70%
OKUBO	68.5%
BAKST	60%
CARTER	48%
UCHIYAMA	31.8%
MC EACHERN	10%
MARCUS	0%

widely distributed from 80~90% to 0%. MARCUS reported that all the dogs that died were those in which the ligation was performed including the septal branch, and except for these dogs, the mortality rate became 0%⁴⁰. UCHIYAMA described that, if the pericardium remained opened for a long time after the ligation, the heart was apt to fall into ventricular fibrillation⁶⁷. CHARDACK et al., investigating the O₂ concentration of the gas respired at the time of the ligation, proved that the mortality of dogs which respired 100% O₂ was about 9%, that of those which respired the room air was 16% and that of those which respired 10% O₂ increased to 50%¹⁸. Therefore, in the present investigation, the conditions at the time of the ligation were established as follows: the site of the ligation was 0.5 cm distal from the origin of the anterior descending branch, the dog was made to respire the room air and the pericardium was closed within 30 sec. after the ligation. The mortality rate obtained under these conditions showed 21.7% in normal control dogs.

In the protected dogs, the branch was ligated with the same thread which had

been laid around it in the previous operation exactly at the above-mentioned site. And the modified cardiopneumonopexy demonstrated such a remarkable protective effect as the mortality rate being 0%. Less beneficial effects had been reported by many investigators except for SMITH's excellent results, who had performed his cardiopneumonopexy using asbestos and phenol^{56,57}, while HARKEN described that the mortality rate remained about 25% by any kind of protective operation³¹.

BAYLEY described in his E. C. G. study on the ligation of the anterior descending branch that the ischemic changes of T wave constituted the first stage in the E. C. G. evolution of myocardial infarction, that the inversion of T wave began within 20~25 sec. and that the T wave became taller 1~2 min. later with the deviation of RS-T junction⁸.

In the present study, 15 out of the 25 normal dogs, revealed taller T wave after the ligation. In the other 10 dogs, 4 dogs revealed biphasic T, 1 dog flattened T, 1 dog inverted T and 4 dogs no change. As the follow-ups were not carried out, it was not clear to which stage of the E. C. G. alteration of BAYLEY these findings belonged, but it seemed that the diversity in alterations of ST, T pattern was caused by individual differences in the course of the myocardial damage. In fact, two different courses could be followed from the same ligations. In the present study, changes of ST segments without those of T waves were seen in 4 cases, and changes of T waves without those of ST segments were found in 4 cases. HELLERSTEIN, also, reported in his study of intraventricular lead that the change of T wave was prior to those of ST segment in 7 cases and that to the contrary the change of ST segment was followed by that of T wave in 5 cases after the anterior descending branch ligation³².

In protected dogs, there was seen no or little change of ST, T pattern in almost any cases, and even in the positive cases the changes were slighter than in control dogs, and such a typical pattern of myocardial damage could never be demonstrated in any cases.

Consequently, it was considered that the coronary circulation was protected by the operation against the occurrence of coronary insufficiency by the ligation, and in fact, there happened no cardiac death in this group.

In 3 cases T wave became taller in a slight degree, but soon returned to the normal. These temporary changes were sharply contrasted to the findings in control dogs, which became more serious as the time passed. It seemed that in protected dogs the acute coronary ligation stimulated and activated the latent collateral blood flow which had been formed previously, and that consequently the E. C. G. changes disappeared in a little while.

In order to demonstrate the existence of the extracoronary collateral communications morphologically, many investigators injected various kinds of dye, india ink, radiopaque mass or plastic resin, etc. from the extracoronary blood sources, and GARAMELLA et al. injected air or physiological saline solution both into the aorta and into the pulmonary artery in order to demonstrate the reciprocal communications between the heart and the lung^{26,27}. In these functional experiments, injections were

performed so as to keep the physiological conditions; for example, CARTER injected india ink mixed with blood into the pulmonary artery under 40 mmHg pressure¹⁷⁾, LITVAK et al. established the injecting condition as 100 mmHg/10 cc/min.³⁹⁾ and SCHLESINGER also injected under a definite pressure⁵¹⁾.

However, it seems not to be quite physiological even if the strict conditions of the injecting pressure and dosage were decided, because the heart had been already extirpated and had no normal myocardial tension and vascular resistance. In the present study, therefore, the physiological and functional investigations were transferred to the other experiments in vivo, and here the injection of india ink was done under not strictly provided pressure.

Consequently, the india ink infiltrated into the myocardium enough to be observed macroscopically, widely spread into the papillary muscles, and SUZUKI, a member of our laboratory, demonstrated clearly that the amount of intramyocardial india ink in the dogs which had been operated by the modified cardiopneumonopexy was far more than that in the dogs which had undergone the cardiopneumonopexy by LEZICUS, HARKEN and CARTER's methods⁵²⁾. But the amount of these intramyocardial dyes was not necessarily proportional to the grade of the development of collateral communications, actually showing no close relationship between the grade of E. C. G. alterations and the amount of intramyocardial india ink.

In order to evaluate the degree of the myocardial infarction in consequence of the anterior descending branch ligation, GROSS measured simply the vertical and horizontal diameter of the infarction³⁰⁾, CARTER divided the infarction into 3 classes: severe (transmural), moderate (not transmural) and slight (only in apex or superficial)¹⁷⁾, and GOLDMAN and UCHIYAMA devised formulae for estimating it quantitatively^{28, 67)}. The form of the myocardial infarction, however, is so irregular and complicated in most cases that there are many discrepancies in the extent of the infarction between the epicardial and the endocardial side, and it seems very difficult and not so significant to investigate strictly the grade of the myocardial damage quantitatively.

As described above, the protective effect of this operation was so excellent that infarction could never be demonstrated. We cannot find any report which revealed so excellent a result as this operation, except for the study of SMITH describing no infarction formation after the ligation.

In the 10 dogs, which were subjected to the protective operation and the ligation at the same time, the mortality rate was quite similar to that of the control dogs, and myocardial infarctions were also demonstrated evidently as in the control dogs. It may be concluded from these facts that a certain duration of interval, at least 2~4 weeks, is necessary for the production of extracoronary communications by this operation to display their protective effect. However, as far as the development of the intercoronaries is concerned, the protective effect might be expectable earlier, because STANTON described that the intercoronaries developed within 1 week after the abrasion of the myocardial surface⁶¹⁾.

By measuring the circulation time from the left pulmonary artery to the

coronary sinus, it was cleared that the results of group II, which was subjected only to the protective operation, was similar to that of normal control dogs, contrary to group III, which was subjected to the protective operation and thereafter the anterior descending branch ligation. It is concluded, therefore, that even if the adhesions with new vascular communications between the heart and the lung were closely established, the blood flow from the lung to the heart through the adhesions could not happen so far as the coronary circulation was normally kept up, and that to the contrary, if once the coronary circulation was interrupted and myocardial ischemia occurred, the blood flow from the lung to the heart began distinctly. In only one excepted case, which was examined 2 and a half months after the ligation, the circulation time was similar to those of the control dogs, that is, the blood flow from the lung to the heart might scarcely exist, while in this case the intercoronary collateral communications were proved to be developed enough to prevent the myocardial damage. In performing this experiment, it is most important to carry it out in a short time and by minimal operative intervention, because, if the general circulatory dynamics changed, the circulating time might be easily influenced. In the present experiment, the influences on the general circulation were as little as in the experiments by WEDEL⁷⁴⁾ and VIDONE⁶⁸⁾, while in GARAMELLA's directional study, the operative intervention was so great that many cases fell into the ventricular fibrillation in the latter half of the experiments⁷⁷⁾.

As a functional and quantitative investigation for intercoronaries, LEIGHNINGER carried out the MAUTZ-GREGG backflow method³⁶⁾. However, the amounts of the backflow differed so greatly that a conclusion can only be drawn after a great many experiments. Furthermore, in the present study, as the lung had adhered to the mediastinal tissue closely and the ligation of the anterior descending branch had been added after 1 month, the preparation of the coronary branch was found to be very difficult with much bleeding and damage of the organs. In the present experiment this method was not adopted for these reasons.

The plastic resin cast, even though it has a fault that histological studies can not be performed at the same specimen, can reveal three dimensional correlations of the blood vessels, indicating clearly the course of the vessels and the relation of the anastomoses, while the other coronary angiogram performed by SCHLESINGER⁵⁴⁾ shows only a figure on a plane film.

By careful observations of the coronary resin casts, the intercoronary collaterals were seen enough developed by the protective operation, that is, the interrupted anterior descending branch was almost fully injected retrogradely through the peripheral intercoronaries. And the fact that many fine secondary branches were found in the deep myocardium, agreed with the fact that the myocardium had kept the normal thickness after the ligation of the anterior descending branch.

From these results of physiological and morphological experiments, it was concluded that the mechanism of the protective effect of this modified cardiopneumopexy consisted in the blood flow which came from both extracoronary blood sources and intercoronaries. These results were a little different from those of Beck and

his co-workers.

SUMMARY AND CONCLUSIONS

Experimental studies were performed in dogs on the modified cardiopneumonopexy utilizing the congestive lung, which was devised originally by ASADA and the present author, and the results were obtained as follows :

1) The mortality rate of the ligation of the anterior descending branch of the left coronary artery in protected dogs was 0%. It was very excellent, compared with 21.7% of the control dogs.

2) The E. C. G. changes caused by the ligation of the anterior descending branch in the protected dogs were very little, and those typical patterns of the myocardial damage could not be demonstrated which were usually seen in the control dogs.

3) Although distinct and widely spread transmural infarctions were always found in the ventricular wall in the control dogs by the ligation of the anterior descending branch, yet, to the contrary, in all the protected dogs the myocardium kept its normal thickness and no infarction was found microscopically.

4) In the lung whose pulmonary veins were ligated, severe pulmonary congestion occurred, but as the collateral vessels in the adhesions with the surrounding tissues developed, it recovered gradually and returned to the normal within 1 month. This pulmonary segment was conglutinated with the heart by using asbestos powder, and the close granulomatous adhesions were established between the heart and the lung with a great many new collateral vessels.

5) The studies of the mechanism of the beneficial effect of this operation made clear that the blood flow from lung to the heart was not proved unless there existed coronary insufficiency in the myocardium, and the value of the extracoronary collaterals was confirmed, while by the observation of the plastic resin cast of the coronary artery, the development of the intercoronary collaterals was also demonstrated even in the same myocardium.

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和文抄録

冠不全の外科的療法に関する実験的研究

——鬱血肺・心癒着術の効果について——

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冠不全に対する外科的療法としてすでに各種の術式が考案されているが、われわれは冠不全という疾患の性質上手術侵襲が小さいことが望ましく、しかも血液を外部から心筋内へ積極的に導入したいとの考えから、心臓に近く且つ血液に富む肺に注目して、Lezius, Carter 等の肺心癒着術に工夫を加えた術式、即ち予めその区域静脈を結紮して鬱血を生ぜしめた左肺舌状部を asbest 粉末を以て心表面に癒着させる方法——鬱血肺・心癒着術(麻田・武内)を創案したが、本手術の効果に関して犬による実験を行い、以下の如き結論をえた。

1) 本手術施行約1ヵ月後に左冠状動脈前下行枝を結紮しても、心臓死は認められず、即ち死亡率は0%で、対照正常犬の死亡率21.7%と比べ明かな好結果を示した。

2) 鬱血肺・心癒着犬の前下行枝結紮に際してみられる心電図の変化は極めて軽微で、全く変化を示さなかつた例が2/3を占め、正常犬の前下行枝結紮の際にみられるような著明な心筋障害曲線を示す例は殆どなかつた。

3) 正常犬では前下行枝結紮1ヵ月目には左心室前壁に明瞭且つ広範囲の transmural infarction が認

められたが、鬱血肺・心癒着犬では前下行枝を結紮しても心筋は正常の厚さに保たれ、組織学的にも癒着形成は見られなかつた。

4) 舌状部区域静脈(犬では左肺中葉静脈)が結紮されると、舌状部は一時的に著しい鬱血を来したが、間もなくこの肺区域が周囲組織と癒着を生じ其処に著明な副血行路が発達し、およそ1ヵ月後には肉眼的並びに組織学的には、正常の肺構造に恢復した。従つてこの鬱血肺区域を asbest 粉末を用いて心筋に接触せしめておくと、肺と心筋との間には多数の新生副血行路を有する緊密な肉芽性癒着が形成され、肺動脈から注入された墨汁はこの副血行路をへて多量に心筋内血管に滲透していくのが認められた。

5) 本手術が前下行枝結紮によつて生じる心筋障害を防禦する機序について検討を加え、心筋に循環障害が存するならば肺から心筋に向う血流が生ずるものであることを生存中色素灌流法により証明した。即ち extracoronary collateral の効果を確認したが、一方では合成樹脂注入によつて作成した冠血管系の鋳型標本の観察から、かゝる心筋に於ては intercoronary collaterals の発達も又或程度証明されることをも知つた。