THE EXPERIMENTAL STUDIES ON SURGICAL TREATMENT OF ISCHEMIC HEART DISEASE*

Tomoyoshi Ishihara

1st Department of Surgery, Nagoya University School of Medicine
(Director: Associate Prof. Itsuro Fukukei)

ABSTRACT

Internal mammary artery implantation proposed by Vineberg is now in common use, and its effect on ischemic heart disease has been proved experimentally and clinically by many investigators.

Some problems concerning the procedure, however, have not yet been clarified thoroughly.

In order to elucidate these problems, the Vineberg procedure was experimentally evaluated and compared with three different methods to provide a new blood supply to the ischemic myocardium from a systemic artery.

The structure of vessels pertaining to myocardial revascularization was investigated by means of microangiography, histology and plastic casting method.

Results were analyzed and concluded, as follows:

(1) Though the Vineberg procedure showed a high patency rate, it had some restrictions in length or flow rate of the implant.

(2) Blood supply to the ischemic myocardium from the epicardial side using pericardial patch showed poor result due to technical difficulties and frequent thrombotic obstructions.

(3) No patency was obtained in the silicon rubber tube grafting method. Improvement in material and shape of the prosthesis should make the clinical application safe and easy.

(4) The patency rate in the autogenous vein grafting method was excellent. Any portion of the myocardium was enabled to be covered with this method by preparing a required length of graft. Development of implanted vein-coronary artery anastomosis in this group was as good as in internal mammary artery implantation.

INTRODUCTION

Recently, in Japan, as in other countries, deaths from ischemic heart disease have been increasing. Among many acquired heart diseases, ischemic heart disease...
disease has been considered to be very important together with valvular heart disease.

In spite of much effort directed continuously to surgical intervention in ischemic heart disease for over one half of a century, satisfactory results have not yet been obtained.

Various methods that have been proposed for establishment of blood supply to the ischemic myocardium may be categorized into four basic approaches, which are 1) production of a new arterial blood supply, 2) production of venous stasis or reversal of coronary circulation, 3) indirect methods to improve myocardial circulation, and 4) direct surgical attack on the coronary arteries.

Concerning the production of a new arterial blood supply, Beck first reported on epicardiectomy and cardiomyopexy using the pectoral major muscle, in 1935, though extracoronary anastomosis between the heart and pericardium had been reported in 1932 by Hudson and Moritz and their coworkers.

An artificial induction of sterile pericarditis by injection of chemical substances or foreign bodies such as Dakin's solution (chlorinated soda), carbon sand, talc (magnesium silicate), and so on, into the pericardial cavity belongs to this category, and has been utilized clinically.

Extracoronary anastomosis between the heart and other organs, other than the pericardium, has been carried out experimentally and clinically. The omentum, lung, jejunum and spleen were selected as the source of the blood supply to the ischemic myocardium. Omentopexy has occasionally been combined with other techniques for myocardial revascularization up to date.

Transplantation of an arterial vessel directly into the myocardium was first performed by Vineberg in 1946, using the internal mammary artery with a patency rate of between 50 and 73%. Thereafter, many reports concerning this technique have been published by Vineberg and his associates.

Modifications and variations of the original Vineberg procedure have also been presented by many authors.

The subclavian artery or the splenic artery has been substituted for the internal mammary artery. The blood supply to the ischemic myocardium even from the left ventricle has also been attempted.

Smith and others reported two successful clinical cases with prosthetic graft instead of the internal mammary artery.

Concerning the production of venous stasis or reversal of coronary circulation, Robertson attempted to nourish the myocardium with venous back flow by experimental ligation of the cardiac vein in 1934. The effect of venous stasis on the coronary system was investigated by Beck and Mako in 1941.

Beck proposed sinus aortic anastomosis with vein graft in 1948. He designed the Beck I operation in 1954, and the two-stage Beck II operation
during the period of between 1955 and 1957\(^ {57} - {60} \).

Actually, however, the Beck I procedure has been used more frequently, because of the Beck II procedure being technically more tedious and requiring two procedures.

Sympathicotomy (gangliectomy), as the first trial of indirect surgical technique, was reported by Francois-Frank\(^ {61} \) in 1899. Later, many modifications and variations\(^ {62} - {63} \) have also been attempted. Resection of the preaortic plexus\(^ {64} - {65} \), total thyroid ablation\(^ {66} \), and ligation of the internal mammary artery\(^ {67} \) have been reported. Recently, stimulation of the carotid sinus nerves has been mentioned\(^ {68} \).

The direct anastomosis of the coronary artery, as the first trial of direct surgical approach to coronary artery disease, was performed by Murray and coworkers in 1953\(^ {69} \).

Experimental endarterectomy was reported by May in 1957\(^ {70} \), and its clinical application was achieved by Bailey and others in 1957\(^ {71} \).

Thereafter, numerous modifications of endarterectomy or direct anastomosis of the coronary arteries, and their clinical use have been reported\(^ {72} - {79} \). Direct surgical attack on the coronary artery, however, is applicable to limited cases, of which the coronary artery should be patent distal to the obstruction. Therefore, development in the direct method does not seem to reduce the necessity of revascularization by implantation of the internal mammary artery.

Though internal mammary artery implantation is now clinically in common use\(^ {35} \), less attention had been paid to the original Vineberg procedure until 1962, when the patency of the implant was proved by Sones and others\(^ {90} \) with coronary angiography.

Since then, the beneficial effect of internal mammary artery implantation on ischemic heart disease has gradually been clarified by many investigators from various aspects\(^ {91} - {110} \). Nevertheless, some problems remain in this procedure to be solved.

First, according to Vineberg\(^ {26} - {111} - {112} \), the blood from the implanted internal mammary artery once enters the sinusoid of the myocardium, then, flows through the arterio-sinusoidal vessels and into the arterioli. At the present time, however, there are some objections to his theory, and a final conclusion, as at what level of the vascular system and how the anastomosis develops, has not been obtained.

Secondly, many patients with ischemic heart disease are arteriosclerotic, and the internal mammary artery shows changes of arteriosclerosis most likely. In such instances, the implantation is not always possible.

Thirdly, the ischemic region of the myocardium may extend over the territory of two or three main coronary arteries\(^ {113} - {114} \), as seen in many cases, and the Vineberg procedure can not cover such a wide ischemic area even with the double implantation.
Finally, the dissected internal mammary artery may be long enough to reach the ischemic area situated in the anterior wall or some portion of the lateral wall, but not long enough to reach the posterior wall or the diaphragmatic surface of the heart.

In order to solve the abovementioned problems, this series of experimental studies was projected. The structure of vessels pertaining to myocardial revascularization from the implant was investigated by means of microangiography, histology and plastic casting method. Internal mammary artery implantation was selected as the control.

Three new methods of blood supply to the ischemic myocardium from a systemic artery were proposed and evaluated respectively.

**MATERIALS AND METHODS**

Adult healthy mongrel dogs of either sex weighing between 10 and 22 kg were used. After intravenous administration of 20 to 25 mg/kg body weight of Isozol, Sodium 5-allyl-5 (1-methyl butyl)-2-thiobarbiturate, the animal was intubated with a cuffed endotracheal tube, and connected to the Bird respirator. Intermittent positive pressure ventilation was carried out at a pressure of 15 cm H$_2$O with air mixed, oxygen concentration in inhalant being approximately 60%.

The left chest was opened through the fifth rib bed. The pericardium was incised longitudinally, and the heart was exposed. In order to produce an ischemic area in the myocardium, the anterior descending artery was ligated distally to the origin of the septal branch. Ligation of several interventricular branches may be added to confirm the creation of the ischemic area. Then, the animals were divided into four groups according to the experimental methods, in which development of communication between a systemic artery and the coronary arterial system across the ischemic area of the myocardium was evaluated.

1) **Group 1—Internal mammary artery implantation group**

As control, the left internal mammary artery implantation was carried out according to the Vineberg-Sewell's method.

Dissection of the internal mammary artery was combined with associated vein and adjacent tissue from the 2nd intercostal space to the 6th.

Redundant tissue was trimmed away from the portion of the artery to be implanted. Two or 3 intercostal arteries near to the distal end of the pedicle were opened. After confirming the blood running out through the stumps of the intercostal arteries, a myocardial tunnel was made adjacent to the ischemic area with a specially devised instrument (Fig. 1).

Then, the bleeding artery was inserted into the tunnel and the tip of the implant was fixed at the exit of the tunnel.
2) **Group 2—Pericardial patch group**

In this group, blood supply to the ischemic area from a systemic artery was provided from the epicardial side. An elliptical autogenous pericardial patch, 3 by 4 cm in size, was applied with running over-and-over suture to cover the ischemic area, in which several longitudinal incisions, as shallow as 3 mm to reach the myocardium, had been made with a surgical knife.

After being dissected free as far as the bifurcation of the brachial artery, the left subclavian artery was ligated and cut. An anastomosis was made between the artery and the aforementioned pericardial patch in the end-to-side fashion, so that the blood through the subclavian artery flowed into the cavity between the pericardial patch and the epicardium underneath, then, into the myocardium through the epicardial incisions. In cases in which the dissected subclavian artery was not long enough to reach the pericardial patch directly, an autogenous vein graft intervened. The whole procedure was carried out under beating heart (Fig. 2).

3) **Group 3—Silicon rubber tube grafting group**

Blood supply to the ischemic myocardium from a systemic artery was made according to the Vineberg's principle, but a soft silicon rubber tube was substituted for the internal mammary artery. A soft silicon rubber tube, 1.5 mm
in inner diameter and 7 to 8 cm long, having 3 to 4 side holes, 0.5 to 1.0 mm in diameter, at the tip area over 3 cm, was prepared in advance. The silicon rubber tube had a square Tetolon® cloth, 1 by 1 cm in size, at 5 cm from the tip, and a crimped knitted Tetolon® graft, DeBakey type, 4 mm in inner diameter and 10 to 15 mm long, at the proximal end. The square Tetolon® cloth was for fixation of the whole prosthesis in place and hemostasis at the entrance of the myocardial tunnel, whereas the Tetolon® arterial graft was for easiness of suturing the prosthesis to a systemic artery (Fig. 3).

The left subclavian artery was dissected free as far as 2.5 cm from its origin, ligated and cut. An end-to-end anastomosis, using a gentle bulldog clamp on the subclavian artery, was carried out between the aortic end of the divided artery and the Tetolon® arterial graft of the prosthesis. With the blood running through side holes, the silicon rubber tube of the prosthesis was inserted into a myocardial tunnel made with a specially devised instrument, as described before.

The tip of the tube was fixed to the epicardium at the exit of the tunnel, and the aforementioned square Tetolon® cloth was sutured to the epicardium at the entrance (Fig. 4).

4) Group 4—Autogenous vein grafting group

A vein graft was used for blood supply to the ischemic area from a systemic artery according to the Vineberg’s principle.29,31,39

Before the thoracotomy, the femoral vein was dissected free as long as possible. All branches were ligated and cut. The left subclavian artery was dissected free as far as the bifurcation of the brachial artery and divided. Then, the already dissected femoral vein was ligated and removed.
After the vein had been irrigated by heparinized normal saline, an end-to-end anastomosis was performed between the distal end of the vein and the aortic end of the divided subclavian artery. The other end of the vein graft was ligated. Previously ligated branches of the vein were reopened, where the vein graft was to be placed in the myocardial tunnel. Additional one or two small side holes were made, if necessary. Insertion and fixation of the graft into the myocardial tunnel were carried out with the same manner as described above (Fig. 5).

At the entrance of the tunnel, the epicardium was resected as wide as 2 mm to prevent possible postoperative constriction of the graft due to epicardial adhesion.

Methods for evaluation of experimental results

During the period of 7 days to 3 months postoperatively, the heart was removed from the animal under general anesthesia with intravenous Isozol®, including the subclavian artery in Groups 2, 3 and 4, and the internal mammary artery as proximally as possible in Group 1. In each specimen, patency of the implant, development of vessels and implant-coronary anastomosis were examined by means of 1) postmortem angiography and microangiography, 2) histology, and 3) plastic casting method.

(1) Postmortem angiography and microangiography

As soon as feasible after examination of the gross appearance on the removed heart, angiography was performed by the following method.

A small polyethylene catheter was inserted into the implanted vessel or silicon rubber tube and fixed. Through the catheter, heparinized normal saline was perfused to wash out the blood from the capillaries and the veins.

Then, a thin solution of the Schlesinger mass was injected into the implants through the catheter under controlled pressure by hand. The pressure varied from 150 to 200 mmHg, but never exceeded this range. After complete filling of the material in the specimen, ligatures were placed on the open vessels and angiography was carried out.

A regular X-ray unit was used, with exposure conditions as follows; 40 kV and 100 mA at 100 cm distance with an intensifying screen. The exposure time was 1/15 second.

The specimen was then fixed in 10% buffered formalin solution. After 7
to 10 days' fixation, the specimen was sliced 3 to 4 mm thick at the center of the region. These slices were ranged on a X-ray film, and rentogenography was made with Sakura Konilitho contact film. An industrial X-ray unit (Softex EMB-type) was used, with exposure conditions as follows; 24 kV, 2.5 mA at 37.5 cm distance, with an average exposure of 8 minutes. These angiograms were observed with the naked eye.

(2) Histology

In cases in which the implant was patent, postmortem angiography and microangiography were followed by histological examination.

Tissue blocks were cut from the adovementioned slices according to the findings of angiography and buried in paraffin to prepare sections. Hematoxylin and eosin staining was employed.

(3) Plastic casting method

Survivors of longer than 3 weeks and having internal mammary implant or autogenous vein graft were subjected to the plastic casting method with Formula III of Eguchi and Daito.117

With this method, a stereographical observation for development of systemic coronary anastomoses and collaterals including their vascular structure was achieved satisfactorily in detail.118

Methyl meta-acrylate was used for all injections. Monomer of methyl meta-acrylate was mixed with benzoyl peroxide (C₆H₅CO-CO-COC₆H₅), as a catalyst, and dibutyl phthalate (C₆H₄(COOC₄H₉)₂), as a plasticizer, and heated to make a sticky mesopolymer.

After dimethyl anilin (C₆H₄N(CH₃)₂) was added, as a polymerization accelerator, the mesopolymer was injected under controlled manual pressure into the coronary arteries and the implant. Plastic polymer was stained in different colors according to the vessel system injected, so that blood supply to the myocardium from each system could be identified clearly. Also, the plastic cast can be cut in pieces to investigate in more detail the structure of vessels from the implant and development of anastomoses and to measure the diameter of these vessels.

RESULTS

Animals expired within one week postoperatively were excluded from this series, as the causes of death were thought to be technical failure in surgery and postoperative bleeding and pulmonary complications.

1) Group 1

Of the 11 long term survivors, 8 had a patent implant, the patency rate being 73%.

Microangiographical findings revealed a few fine vessels dividing from the implant. After giving off several branches, these vessels were connected to
the branches of the adjacent coronary artery (Fig. 6). Thus, the opaque material transferred from the implant to the coronary system.

Red colored plastic polymer injected into the implanted internal mammary artery spread over the apex to the diaphragmatic surface of the heart, and the development of the collateral circulation was clarified (Fig. 7). The implanted internal mammary artery branched into 3 to 4 very fine vessels, 200 to 500 μ in diameter, towards the ventricular cavity. Each vessel showed several branchings more peripherally to form fine networks mutually and entered the coronary artery system (Fig. 8).

According to plastic cast findings, even the finest branches showed regular vascular structures. The presence of sinusoids, as has been indicated by Vineberg, was not proved.

In addition, histological findings revealed that contrast material adjacent to the implant was not seen extravascularly among the muscle fibers, but in vascular structures, unless an extremely high injecting pressure was applied.
FIG. 7. Plastic casting model of the internal mammary artery implantation group: plastic polymer stained in different colors according to the system injected; blue, the right coronary artery, yellow, the left coronary artery, and red, implant. Note red dye at the apex among yellow dye.

FIG. 8. Plastic casting model, same as in Fig. 7, indicating the tip of the implanted internal mammary artery in detail. The left coronary artery system has been removed. Note mode of connection between the implant and the original coronary system.
2) Group 2

Six animals from long term survivors were sacrificed; 2 cases after 2 weeks, 2 after one month and 2 after 3 months.

There were no patent anastomoses observed. In both animals sacrificed 3 months after surgery, the pericardial patch was adherent to the epicardium underneath to develop scar tissue. Myocardial incisions were also scarred.

In one case that died after 24 hours due to respiratory insufficiency, there were clots in the lumen under the pericardial patch together with blood partially fluid. Histologically, the clots were noted to proceed into the myocardium through the incisions (Fig. 9).

![Diagram of pericardial patch, clots, and incised space](image)

Fig. 9. The clots noted to proceed into the myocardium through the incision beneath the pericardial patch. Hematoxylin and eosin stain. ×40.

These facts may suggest the presence of blood supply to the myocardium from the epicardial side postoperatively, though for a very short period of time.

3) Group 3

Six animals from long term survivors were sacrificed; one after one week,
2 after 2 weeks, 2 after one month and one after 3 months. All prostheses were obstructed. The sites of obstruction were the connection between silicon rubber tube and Tetolon® arterial graft in 2 cases, and anastomosis between Tetolon® arterial graft and the subclavian artery in 4 cases. In the silicon rubber tube there was sanguineous fluid in all cases.

In microangiograms from cases of early death, the Schlesinger mass was noted to proceed into the coronary system from the silicon rubber tube, which indicated the presence of temporary blood supply through the implant (Fig. 10).

Histologically, many newly developed vessels were observed in the myocardium around the implanted silicon rubber tube after 2 weeks (Fig. 11).

It was not clear whether these findings could be explained as the result of continuous blood supply to the myocardium from the silicon rubber tube. It may be due to tissue reaction to the foreign body implanted.

Fig. 10. Microangiogram of silicon rubber tube implantation: opaque material noted to proceed into the coronary system from the silicon rubber tube, of which section seen at the right bottom of the picture.
In the case sacrificed 3 months after surgery, in which obstruction of the prosthesis at the Tetolon® arterial graft was noted macroscopically, and no angiography was enabled, the silicon rubber tube contained old thrombi which showed histologically hyalinized degeneration partially together with red blood cells over a great extent (Fig. 12).

This fact indicated that the blood had flowed through the silicon rubber tube to produce collateral circulation, though no proof of the presence of anastomosis between the implant and the coronary system was obtained due to lack of angiography.

4) Group 4

Ten animals from long term survivors were sacrificed; 3 animals after 2 weeks, 2 after 1 month, 3 after 2 months and 2 after 3 months. There were 6 patent grafts, the patency rate being 60%.

In 3 cases in which angiography and microangiography were carried out, the opaque material was transferred from the implant to the coronary system,
and development of collateral circulation was proved (Fig. 13).

Small vessels containing opaque material, also, were noted around the implanted vein graft histologically (Fig. 14). In 3 cases, plastic polymer, different in color according to the vessel system, was injected into the right and left coronary arteries and the implanted vein graft.

Plastic polymer injected into the implanted vein, stained red, transferred to the coronary artery and vein, and distributed over the apex and the diaphragmatic surface of the heart. A part of the polymer was noted in the left ventricular cavity (Fig. 15).

It, therefore, is clear that blood supply through the implanted vein graft spread widely around the aforementioned areas.

A meticulous examination of the cast demonstrated that the implanted vein graft branched into one to 4 very fine vessels, the diameter of each being 200 to 500 µ (Fig. 16).
FIG. 13. Microangiogram of autogenous vein implantation: opaque material transferred from the vein graft to the coronary system, and many collaterals demonstrated.

In the case in which postoperative pyothorax had been treated with medications including antibiotics, round cell infiltration was noted in the myocardium around the implanted vein graft 3 months after surgery. This prominent inflammatory change seems to have blocked the vein graft during the period of postoperative 3 months (Fig. 17).

In another case sacrificed after 2 months, there was marked thickening of the media, making the venous cavity narrow and blocking the blood flow.

DISCUSSION

Internal mammary artery implantation group

Concerning the development of collateral circulation after internal mammary artery implantation (Vineberg procedure), Vineberg himself described that the blood from the implanted vessel entered once the sinusoid, then flowed into the arterio-sinusoidal vessel to reach the arterioli.

In our experiment, however, microangiography and plastic cast from
animals sacrificed early after implantation did not indicate the blood appearing extravascularly or intermuscularly, but intravascularly.

Vineberg pointed out that India ink injected into the implanted internal mammary artery was noted among the muscle bundles. The India ink, however, may appear intermuscularly due probably to high pressure injection.

In our cases, also, opaque material injection at high pressure resulted in intermuscular or extravascular appearance of the material, as demonstrated histologically and microangiographically.

The plastic cast obtained from animals sacrificed 2 to 3 months after implantation showed that fine vessels, 200 to 500 μ in diameter, that originated from the implanted artery produced several branches to form fine networks, 20 to 50 μ in diameter.

This fact indicated clearly that collateral circulation from the implanted artery was established, as Bencosme stated, through channels having a vascular structure, the true arterioli.
FIG. 15. Plastic casting model of the autogenous vein grafting group: plastic polymer stained in different colors according to the system injected; blue, the right coronary artery, yellow, the left coronary artery, and red implant. Note red dye at the apex among yellow dye.

FIG. 16. Plastic casting model, same as in Fig. 15, indicating the tip of the implanted autogenous vein graft in detail. The left coronary artery system has been removed.
FIG. 17. Implanted vein graft seen in the middle of the picture. Around the graft, inflammatory changes noted. Hematoxylin and eosin stain. ×1.

It, however, was not able to make clear to what extent the vessel developed newly from the implanted artery and to what extent the vessel belonged to the original coronary arterioli.

Making of intramyocardial tunnel

Vineberg stated that cutting of intramyocardial fibers and binding perimysium strands may result in localized aneurysms, left ventricular failure, and hemorrhage from tunnel.

Considering these factors, a specially devised instrument was used for creation of tunnel in our experiment. On the other hand, Sewell and coworkers pointed out that better results could be expected if a penetrating muscular branch from a surface branch of a coronary artery was incised. This apparently offers an opportunity for the collateral channels to connect to the coronary system.

However, it is hard to believe that anastomoses develop at the site of muscular branches being cut, as Sewell stated. Anastomoses actually develop
not at the very site of the muscular branch being cut, but a little away from the implanted artery, as was seen in the plastic cast, in which the vascular structure can clearly be identified in detail.

**Pericardial patch group**

From the technical point of view, suture of the pericardial patch to the epicardium under a beating heart seems to be very difficult. As a matter of fact, many deaths were encountered in this group due to hemorrhage during surgery and postoperative period.

To overcome the technical difficulties, the procedure should be carried out in an arrested heart with the aid of cardio-pulmonary bypass.

Vineberg\(^{(24)}\) reported in his initial experiments that the internal mammary artery was implanted in a myocardial groove, not in a myocardial tunnel, and covered with a pleural strip.

Consequently, he failed to find anastomosis developed\(^{(122)}\). According to him, scarring tissue at the site of myocardial incision was responsible for the failure in development of anastomosis. Myocardial scarring was noticed in our long term survivors, in which the implant had been obstructed. Therefore, scarring tissue at the site of myocardial incision was thought to be one of the most important factors to decrease the patency rate in this group.

Takao and his coworkers\(^{(120)}\) described that thrombus formation at the junction of two vessels was accelerated by the turbulence which usually occurs as the blood flowed into a large vessel from a small one. In our cases, the blood stream through the subclavian artery emptied itself into the subpericardial cavity, a relatively wide space compared with the artery, and thrombus may easily be developed due to turbulence.

Considering the aforementioned facts, pericardial patch grafting method may not be beneficial to expect a high patency rate. This difficulty, however, may be overcome by using heparin during surgery and postoperatively to prevent early clot formation. The blood current through the subclavian artery and the pericardial patch graft can be maintained until the current is possibly interrupted by scarring tissue, by which time collaterals will be expected to develop.

This technique, therefore, should be considered to be effective for revascularization to some extent.

**Silicon rubber tube grafting group**

To obtain satisfactory results by this method, the property of implant prosthesis against thrombus formation should be considered to be essential rather than the surgical technique, in which no difficulties have actually been encountered.

Smith and others\(^{(51)}\) tested a tailor made nylon prosthetic vessel, similar to the now commercially available crimped knitted vessel of DeBakey type,
for this purpose, with success in two clinical cases. No long term results, however, have been reported, yet.

In the flow meter study\(^{93-95}\) of the implanted internal mammary artery, the maximum flow rate of around 30 ml/min has been reported by many investigators. The less the blood flow through a fine prosthetic tube, the higher the incidence of thrombus formation.

Therefore, in our experiments a silicon rubber tube was selected as an implanted material to reduce the incidence of thrombus formation as much as possible.

However, for the technical ease of suturing the silicon rubber tube to the subclavian artery, a Tetolon\(^{\circ}\) graft, 10 to 15 mm long, had to be attached at the proximal end of the tube.

Actually, thrombus formation was occasionally encountered in the vessel graft attached rather than in the silicon rubber tube, and further improvement should be mandatory in this regard.

Greenstein and Mannich\(^{121}\) used experimentally a Dacron graft of DeBakey type, 8 mm in inner diameter, and reported that no graft remained patent at a flow rate of below 28 ml/min.

In our experiment possible scarring tissue adjacent to the silicon rubber tube was seen histologically in cases sacrificed early after implantation.

This finding may be explained as a result of tissue reaction against a foreign body, and has to be solved in future if many new vessels developing in the possible scarring tissue contribute to revascularization.

An ideal implant prosthesis should be soft enough to collapse during cardiac systole and elastic enough to resume its original shape promptly during cardiac diastole.

Our silicon rubber tube may be somewhat hard in nature. If the implant prosthesis is as soft and elastic as the coronary artery, blood flow in the prosthesis may be to-and-fro, and such changes in the direction of blood flow may contribute to lessen the incidence of thrombus formation, as reported by Carlson and associates\(^{129}\).

Histological examination of one dog sacrificed 3 months after implantation revealed that the silicon rubber tube was filled with red blood cells, as the coronary vessels were (Fig. 12). These findings indicated the presence of a blood stream in the silicon rubber tube until the time of sacrifice, though the morphology of the vascular structure anastomosing with the coronary vascular system was obscure because of no angiographical examination being enabled due to thrombotic obstruction of the prosthesis at the site of the Tetolon\(^{\circ}\) graft.

Blesovsky\(^{34}\) reported the development of collateral anastomoses in one case, in which the implant had been blocked, and the mechanism of development of anastomoses in such a case should be investigated in future.
Autogenous vein grafting group

In our experiments, manual anastomosis was carried out between the subclavian artery and vein graft. The anastomosis may be simplified when a stapler or a tantalum ring is used.

The major saphenous vein seems to be adequate for clinical purpose. From the technical point of view, as in case of the internal mammary arterial implantation, twisting of the vein graft should carefully be avoided, as the vein is softer than the artery. The adventitia should be removed as much as possible from the vein, especially from the portion placed in the myocardial tunnel, if sufficient blood flow through the side holes is expected.

The flow rate through the implanted vessel was 2 to 5 ml/min initially and increased to 30 ml/min, maximum, after 6 weeks to 6 months. The initial poor rate of blood flow through the implant may cause thickening of the media, and the media, once proliferated, may not recover even after the increase in blood flow.

The femoral vein used experimentally as a graft seemed to be somewhat large in size, and such a large size of graft may actually not be necessary.

According to Leighninger and Julian, the instability of the heart, resulting from the inequality of blood distribution to the myocardium, can be improved by a small amount of additional arterial blood supply to the ischemic area. If so, a large vein graft should not be used as an implant at the expense of possible obstruction due to thickening of the media.

On the other hand, in dogs there seems to be much difficulty experimentally to obtain an adequate ischemic area, with demand great enough to accelerate collateral development, as there are abundant anastomoses in the coronary vascular system and the development of anastomoses after ligation of the anterior descending artery is easy and prompt.

Less blood demand by the ischemic area and less pressure difference between the implant and the coronary artery seem to result in narrowing the lumen of the implant due to proliferation of the media.

In clinical cases, however, ischemia is usually chronic with poor collateral anastomoses and more pressure gradient, and the flow rate through the implant is considered to be sufficient enough to keep the venous wall away from thickening. Therefore, the patency rate of the implant should be reasonable. Comparing the result from endarterectomy using a venous autograft patch with that using an arterial autograft patch, Ellis and Cooley indicated that arterial patch had an advantage over venous patch in the patency rate after surgery. The property of venous patch per se is thought to be responsible, to a certain extent, for the difference in results.

Concerning vein graft, Pifarre mentioned that because of the presence of valves pressure in the implant at the intramyocardial portion was higher than that at the extracardiac portion during the systolic phase and thus, an
increased pressure gradient was beneficial to the development of anastomoses.

Blesovsky and others attempted the retrograde internal mammary artery implantation into the posterior myocardium, and reported that this method was anatomically feasible. No successful results were obtained because of low pressure and less flow rate of the artery.

Recently, many techniques concerning direct coronary artery surgery have been reported. These techniques have their advantages and disadvantages.

First, they should be carried out with the aid of cardio-pulmonary bypass. Secondly, there are difficulties in anastomosis of coronary arteries at a very fine level, though technical improvement has been marked, and thrombus formation at the site is troublesome. Finally, there are some restrictions in actual application according to the location, length and number of coronary artery occlusion.

Swedland and colleagues reported that 32% of coronary patients were candidates for direct surgery and the remainder for palliative operation or inoperable. According to Szilagyi and associates, only 21% of coronary patients were operable.

Diethrich and coworkers reported that 23% of coronary patients have single vessel coronary arterial disease, whereas 77% have double or triple or quadruple vessel coronary arterial disease. He also mentioned that in 9% of them coronary disease was quadruple, including the right, anterior descending, circumflex and left main coronary arteries. These reports seem to indicate apparent anatomical restrictions in clinical application of direct coronary artery surgery.

It has been controversial that autogenous vein graft or internal mammary artery implantation can provide sufficient blood supply enough to improve signs and symptoms especially in advanced cases.

Hammond and Provan presented doubt on the effect of myocardial revascularization in coronary heart disease based on findings from their experimental study, and concluded that the survival rate and the survival time were not improved significantly by myocardial revascularization, such as by internal mammary artery implantation, epicardectomy, free omental graft and so on.

Leighninger, however, reported that the majority of deaths from coronary artery disease were due to unequal oxygenation of the myocardium resulting in electrical instability of the heart and a break in the coordinated mechanism of the heart beat. Therefore, a little additional blood to the myocardium beyond an occlusion can save life.

On the other hand, in order to increase the blood supply to the ischemic area, other than from extracardiac source, a new surgical approach has recently been advocated by Braunwald and associates. These workers have demonstrated that intermittent carotid sinus nerve stimulation can, by reducing sympathetic efferent stimuli, promote a drop in arterial pressure, a reduction
in heart rate, and a decrease in myocardial contractility—all factors conducive to reducing myocardial oxygen requirements and thus to the relief of angina pectoris. Lower coronary flow rate becomes adequate, therefore, both at rest and during various levels of physical exertion.

In future, the treatment of ischemic heart disease from a new standpoint should be evaluated in more detail, and compared with the method of revascularization from an extracardiac blood source.

**SUMMARY**

In order to investigate several problems concerning the Vineberg procedure, internal mammary artery implantation was experimentally evaluated and compared with three other different techniques to provide a new blood supply to the ischemic myocardium from a systemic artery, by means of microangiography, histology and a plastic casting method.

Results were analyzed and concluded, as follows:

1. The Vineberg procedure had anatomical restrictions, though it showed a high patency rate, as seen in many previous reports, and was easy technically. The length of the internal mammary artery available was not always long enough to reach any portion of the myocardium. The diameter of the artery was relatively small, and the blood flow rate possibly low.

   Concerning the mechanism of development of collateral anastomoses, the intramuscular sinusoid described by Vineberg failed to be identified, and anastomoses consisted of true arterioli having vascular structure.

2. Blood supply to the ischemic area from the epicardial side using a pericardial patch showed poor result due to technical difficulties and frequent thrombotic obstruction.

   This method, however, is still under study; and its clinical application should be possible after improvement of surgical technique.

3. No patency was obtained in the series of silicon rubber tube grafting method. Improvements in material and shape of the prosthesis should make clinical application safe and easy.

   In only one case in which the proximal portion of the prosthesis had been obstructed, the silicon rubber tube in the myocardial tunnel was filled with fresh red blood cells. The fact suggested this method to be applicable clinically, though the mechanism of collateral development was not thoroughly clear.

4. The patency rate in the autogenous vein grafting method was excellent, though somehow below that of the Vineberg procedure.

   Any portion of the myocardium was enabled to be covered with this method by preparing the required length of vein graft. The major saphenous vein seemed to be suitable for clinical purpose. Development of implanted vein-coronary artery anastomoses in this group was as good as in internal mammary
artery implantation.

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