De-Epicardialization: A Simple, Effective Surgical Treatment for Angina Pectoris

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Removal of the epicardium of the dog's heart with 95 per cent phenol permits anastomoses between pericardial vessels and the coronary arteries that are large enough to carry the Schlesinger mass (40 micra or larger). In 18 patients suffering from intractable angina pectoris an operation consisting of phenolization, instillation of talc and pneumonopexy has resulted in consistent relief of pain. The simplicity of the procedure exposes the patient to minimum risk of fresh thrombosis; its effectiveness justifies further trial.

CORONARY insufficiency on the basis of atherosclerosis, with or without pain, is a medical problem of first importance. Medical or surgical maneuvers designed to increase the blood supply to the human myocardium will require many years for conclusive evaluation. The alleviation of pain, however, is a more immediately attainable objective. If experimental work on laboratory animals yields a safe procedure that is likely to increase the myocardial blood supply and which on conservative clinical trial relieves pain, it is worthy of further application to patients in whom pain is a dominant factor. Such a procedure is presented here.

The accumulated work in this field over the past 40 years falls into distinct patterns. Conclusions can be drawn from these that greatly simplify new work. There have been three principal approaches to the problem. The first is lowering of the metabolic work load. This is now accomplished by chemical rather than surgical thyroideectomy. Although proponents of this therapy can point to improvement of their cases, a new disease state has been created and no favorable influence on blood supply to the myocardium can be anticipated. The second great field of surgical therapy for angina consists of the interruption of sensory nerve pathways. Pain can be relieved by this procedure, vasoconstriction may be reduced, and, in the combination of these effects, there may be "protection" against coronary occlusion. The third approach is directed at the creation of new vascular channels and has seemed most attractive to us.

BACKGROUND

In 1899, Francois Franck13 first proposed sympathectomy as a surgical treatment for angina pectoris. It was not until 1916, however, that Jonnesco17 of Bucharest actually operated on a patient with syphilitic aortitis and angina by this technic and obtained complete relief of pain. His operation consisted of bilateral extirpation of the cervical sympathetic chain and the removal of both first dorsal ganglia. Interruption of the sympathetic pain pathways has been practiced extensively throughout the intervening decades by Royle,23 White23 and others including ourselves.16 Although control of pain by this means is at times dramatic, it is not consistent. Furthermore, in our experience the late mortality of 50 per cent in a
two and one-half year period after operation suggests that the progress of the primary disease had not been significantly altered.

Therefore, our interest in recent years has been in those procedures which seek to create new vascular channels to supply the myocardium. The work of Beck's \cite{1-7, 24} is preeminent among the direct attempts to improve myocardial blood supply. His early efforts were directed toward the development of vascular adhesions as a source of extrinsic coronary collateral circulation. In 1935, he used a pectoralis major muscle graft as the proposed source of new vessels with bone dust applied as an irritant after mechanical abrasion of the epicardium. Similarly, O'Shaughnessy \cite{29} in 1936 used aleuronat paste as an irritating substance and omentum as the source of external collateral vascular supply. He presented similar experimental and clinical results. Lezius \cite{19} in 1937 suggested lung as the source of vascularization. Various modifications of these basic recommendations have been described. \cite{18} Outstanding among these has been the work of Thompson \cite{27} using tale or magnesium silicate. His clinical success has been impressive.

All of the above authors reported a strikingly similar mortality (about 70 per cent) from ligation of the anterior descending coronary artery in the unprotected dog. Fauteux \cite{12, 13} reaffirmed this and then reported a salvage rate of 75 per cent after ligating the great cardiac vein. He modified this operation \cite{14} in 1946 by combining pericoronary neurectomy and felt that this had further salutary protective effect.

Vineberg \cite{29-32} since 1946 has ingeniously employed the left internal mammary artery as a source of arterial blood for the ventricular myocardium. Again, his success in protecting animals from death after ligation of the anterior descending coronary artery has been remarkably similar to that of the technique just described. Vineberg has implanted the internal mammary artery in the wall of the left ventricle and is convinced from injected and cleared specimens that new vessels branch out and communicate with the existing coronary arterial tree. Although this behavior is unlike that seen in any other part of the body, Vineberg's subsequent demonstration that the dog heart can be supplied through these anastomoses alone is quite impressive. It is still true, however, that the transplanted vessel thromboses in a significant percentage of cases and that other workers have had difficulty in repeating this work. Nevertheless this ingenious concept has had experimental support and has relieved pain in humans.

In 1948, Beck \cite{4} first reported arterialization of the cardiac veins by producing an arterial shunt from the aorta to the coronary sinus. In a second operation, he ligated the coronary sinus between its termination in the right atrium and the anastomosis in order to effect complete reversal of flow through the coronary veins. Once again, a survival rate of approximately 75 per cent of animals, following anterior descending coronary artery ligation, was reported as well as a reduction in the size of the infarct produced. In humans suffering from angina, pain has been relieved by this procedure as well. This ambitious effort appears to have several important defects. First, it involves two major operations, one for the anastomosis and a second for ligation of the coronary sinus. This is a strenuous program for patients suffering from coronary insufficiency. Second, a number of these anastomotic shunts thrombose. Finally, if the patient does survive both of the operations and his shunt does remain patent, it is possible that high venomuroluminal shunts may enlarge and carry the blood more or less directly from the aorta into the chamber of the ventricle without being distributed to the myocardium. Furthermore, there may exist an analogy with attempts at reversal of circulation in the leg of the dog. These have clearly demonstrated that the result is commonly the same as producing a high arteriovenous fistula with a reduction, rather than increase, in the distal capillary circulation. \cite{21} It must be conceded however, that pain is reportedly alleviated following such a procedure. Finally a serious late complication has been found by Beck's group. \cite{22} Postmortem studies have shown that atheromatous plaques have occluded the "arterialized
venous system” suggesting that these vessels may not be able to withstand the high arterial pressures.

Again, we see substantial protection by an experimental procedure and successful human trial presented by competent observers. Yet there remains the possibility that the mechanism by which success is achieved varies from that intended. By studying these efforts at myocardial revascularization, a fascinating recurrence of experimental and clinical findings is revealed. Over and over for the past 20 years, investigators have ligated the anterior descending coronary artery in dogs and have found that approximately 70 per cent of the normal, “unprotected” animals have died. With this base line, a wide variety of surgical procedures have been carried out on experimental animals to bring about “protection” against this fairly constant control mortality. The investigations have been associated with rather surprisingly uniform success. Not only has there been uniformity in the fact that each “protective operation” has been reported as successful by reliable investigators, but the incidence of that protection has remained the same. It is a remarkable fact that approximately 75 per cent of animals have survived ligation of the anterior descending coronary artery regardless of which of the diverse “protective” procedures was employed. Trial on humans suffering from angina has then been suggested and, generally speaking, the reports of human trial have been encouraging in terms of the relief of pain.

The inescapable conclusion that one derives from these reports is that most of the operations are successful in a substantial number of instances and possibly, for the most part, not for the reasons put forward. It is conceivable that intrinsic coronary collaterals, as opposed to an external collateral coronary supply, have been opened. The significant increase in coronary backflow reported by Beck, following a “sham operation” in which he went through all steps of his second method without permitting actual reversal of circulation to occur, supports this view.

A significant contribution in this field was that of Burchell who repeated many of these technics directed at the production of vascular adhesions. He reported that small channels sufficient to carry water-soluble dyes could be produced. However, the epicardium was found to constitute a barrier that prevented the penetration of vascular channels of substantial size. The lead acetate-agar injection mass of Schlesinger which will enter only vessels 40 miera or larger in diameter did not enter the vessels produced by any of the technics tested by Burchell.

**Experimental Data**

It is apparent from a review of the above efforts that much work remains to be done to clarify the nature of the protective effect shared by these various techniques. The importance of hemorrhage, prolonged periods of hypotension, anoxia, even anesthesia alone in relieving angina need to be scrutinized.

The work of Burchell, however, was convincing and prompted us to investigate methods of removing the epicardial barrier. At first, mechanical stripping was tried. While it is possible to remove the epicardium surgically from the normal dog’s heart, this method causes such myocardial irritability and is sufficiently time consuming that it seems undesirable for application to patients suffering from extensive arteriosclerosis. In human coronary insufficiency, it seems axiomatic that direct manipulation must be as gentle and as brief as possible. It is presumed that a long operation will, per se, increase the opportunities for fall in blood pressure and tachycardia that reduce coronary flow and increase the opportunity for coronary thrombosis. Direct surgical stripping of the epicardium appeared to have both disadvantages.

Having abandoned direct surgical de-epicardialization, a variety of chemicals and irritating substances such as chlorine solutions, iodine solutions, trichloracetic acid, talc, bone dust, etc., were used. The reaction to these substances was either too violent at the time of application or too benign to destroy the epicardium. The fortunate combination of an agent that could destroy the epicardium and
yet not produce irritability during application
was found in 95 per cent phenol.

Thirty-one mongrel dogs were used in phenol
study. After opening the pericardium, the
surface of the left ventricle was painted with
95 per cent phenol on a cotton swab. Only the
left ventricle was so treated and, in order to
standardize the technic, only a single applica-
tion of material was employed. This resulted
routinely in a graying of the epicardial surface.
No alcohol was used to neutralize the phenol.
In 20 of these animals Gelfoam sponges were
placed over the phenolized area and the peri-
cardium loosely closed, while in 11 one of the
adjacent lobes of the lung was pulled in beneath
the pericardium and sutured in this position.
The results following these two slightly differ-
et modifications were essentially the same and
will therefore be considered together. In all
animals a strip of reactive cellophane was
wrapped loosely about the origin of the an-
terior descending coronary artery for the pur-
pose of producing fibrosis which would in turn
reduce the calibre of the vessel and create a
need for new blood supply in the area pheno-
lized. Histologic examination of all these
arteries at the time of sacrifice revealed a
failure to produce the desired narrowing of
the vessel and, therefore, no increased demand
for new blood supply can be assumed. Whatever
ingrowth of vessels was found may therefore
be considered to have occurred in the absence
of any ischemic stimulus.

After periods of time varying from 1 to 6
months after phenolization the surviving
animals were examined in one or more of the
following four ways:

(1) The chest was reopened and the ad-
hesions to the myocardium dissected off.
Both the myocardial and adhesions surfaces
were then examined for evidence of arterial
bleeding. In 100 per cent of animals studied
in this manner three or more months after
phenolization, significant arterial bleeding
was noted as contrasted with none in those
surviving less than three months.

(2) Survival after ligation of the anterior
descending coronary artery was found to be
91 per cent, (10 out of 11) after three months;
only one out of two survived before this time.

(3) Histologic examination of the hearts
after phenolization revealed that the epicar-
dium was selectively removed without damage
to the underlying myocardium (fig. 1). Vessels
of significant size could be found in the ad-
hesions by this method (fig. 2) and india ink
injected in these vessels revealed anastomoses
with vessels within the myocardium (fig. 3).

(4) The final indication of revasculariza-
tion came from injecting the agar-lead phos-
phate mass of Schlesinger through these new
vessels. This was accomplished via the coronary
system and demonstrated microscopic ar-
terioles in the adhesions. While this injection
of the adhesions establishes the fact that there

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**Fig. 1.** Dog heart three days after application
of 95 per cent phenol. Epicardium (above) is degenerating. Note lack of damage to cardiac muscle (below).

**Fig. 2.** Dog heart four months after phenolization.
Macroscopic vessels (central arrow) between surface
of heart and adhesions (right) are filled with Schle-
singer mass injected into coronary artery system.
are vessels large enough to take the Schlesinger mass, we are certainly not interested in how much blood can be supplied to the adhesions by the coronary arteries, but rather in how much can flow from the aorta directly into the myocardium through the adhesions. That this occurs is strongly suggested by isolating the mid-portion of the descending aorta with clamps and then injecting this segment with Schlesinger mass. The material found its way into the lungs and pericardium, thence into the myocardium through the adhesions as illustrated by roentgenograms of the myocardium after stripping away the investing structures (fig. 4).

As controls, three normal dogs that had not had the phenolization procedure had isolated aortic injection with the Schlesinger mass by an identical technique. The mass did not enter the coronary arteries. This would appear to eliminate the possibility of a false positive result in the experimental animals from previously existing collateral channels. No evidence
of phenol toxicity was found in any of the animals.

The uniform relief of anginal pain reported following the clinical trial of the many procedures proposed elsewhere in the past for the treatment of angina pectoris fortified our hope that this extremely simple technique would also relieve pain. The experimental evidence suggested that significant extrinsic collateral blood supply might be produced and ischemia be relieved. The simplicity of this operation undoubtedly assures less risk to the patient than the more extensive procedures previously proposed.* The operation is much simpler, even, than palliatives such as denervation (figs. 5, 6). It seemed justifiable to apply the operation to a selected group of patients suffering from intractable angina. The irritating effect of powdered asbestos or talc as proposed by Beck¹ and Thompson² seemed a desirable addition (fig. 7). Finally, the encouraging reports of Lezius suggested the application of the lingula of the lung to the denuded myocardium as a highly vascular source of new blood supply (fig. 8).

**Clinical Application**

On Dec. 3, 1951, the first phenol de-epicardialization and pneumonopexy was performed on a 34 year old white Italian male (PBBH No. 9B755) who had had angina pectoris of severe degree for two years following an electrocardiographically-documented myocardial infarction. At the time of operation, he was having angina at bed rest. Following operation, there was a dramatic and immediate reduction in the amount of pain and almost complete disappearance within two weeks. During the next six months on restricted activity, there was occasional chest pain suggestive of angina but this was readily controlled by 2 or 3 nitroglycerine tablets a week. In less than a year, the pain had completely disappeared. The patient remains completely well except for occasional intermittent claudication which existed preoperatively and which is associated with extensive calcification of the arteries of the legs. He has been working full time for two years and has a daughter born 16 months after operation.

Seventeen additional patients have now had similar operations. All but four have had complete relief of pain; two had a recurrence of some angina about two months after operation but the pain is subsiding in one. Two patients in whom the operation has been less than completely successful have psychiatric problems that render evaluation of the real anginal residuum difficult.

In these 18 patients there have been no operative deaths. Two, however, have died within two months of the operation from fresh coronary occlusion although they had been completely relieved of pain. In both instances the patients, enjoying their first respite from pain in many months, were excessively active. The experimental work would suggest that

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* Total operating time in human cases has ranged from only 11 to 26 minutes.
this was before adequate collateral channels could have developed.

It is far too early to speculate about "revascularization" of the myocardium in the individuals operated on to date. However, the rather dramatic relief of pain and the simplicity of the surgery without surgical mortality suggests that it is a method worthy of continued trial.

A warning must be sounded concerning the obvious futility of attempting to improve the clinical condition of patients who have very extensive myocardial damage. It serves no useful purpose to bring a blood supply to scar. Contrariwise, no patients have been rejected from consideration for operation because of previous coronary occlusions. More than half of these patients had suffered previous myocardial infarction.

At the present time, this procedure is not being proposed for the treatment of coronary insufficiency, solely as a method of increasing coronary arterial blood flow when angina is not present. If, however, the patient has severe angina pectoris which is unresponsive to medical treatment, the operation is offered for the relief of this distressing symptom. There is reason to conclude from the experimental data and some of the longer follow-up results that a substantial improvement in coronary blood supply may also result. This experience would seem to justify the further application of this operation in human angina pectoris.

Conclusions

Some of the many surgical procedures that have been proposed for the treatment of angina pectoris have been reviewed. Most of these operations have had a remarkably similar protective effect on the survival of dogs following ligation of the anterior descending coronary artery, regardless of their nature or complexity.

The development of extrinsic collateral circulation appears to be blocked by the intact epicardium. Removal of this epicardial barrier with 95 per cent phenol has permitted the development of anastomoses with the coronary arterial tree that are large enough to carry the Schlesinger mass (40 micra or larger).

The operation of de-epicardialization, pou-

dragé and pneumonopexy can be carried out rapidly and simply without subjecting the patient to the hazards of a fresh coronary thrombosis inherent in the more complicated operations. In 18 persons suffering from intractable angina pectoris this operation has resulted in consistent relief of pain. Further trial of this simple, clinically effective technique seems justified.

Summario in Interlingua

Es revide alecune del numerose procedimenti chirurgic pro le tractamento de angina de pectore. Le majoritate de iste operationes ha habite remarcabilemente simile effectos protective super le supervivenitia de canes post ligation del descendent artery coronari anterior, e isto in despecto del facto que il se tracta de operationes de varie typos e de varie grades de complexitate.

Le disveloppamento de un extrinsec circulatio collateral es apparentemente blocate per le epicardio si isto es intacte. Le ablation de iste barriera epicardial per medio de phenol a 95 pro cento ha permitite le disveloppamento de anastomoses con le arbo del arteria coronari le quales es satis large pro portar le massa de Schlesinger (40 micra o plus).

Le operation de dis-epicardialization, impulveramento, e pneumonopexia pote esser effectuate simple- e rapidemente sin exponer le patiente al risco de un nove thrombose como es le caso in le plus complicate operationes. In 18 patietes qui suffreva de formas intractabile de angina de pectore, iste operation ha resultate in perdurante alleviation del dolor. Essayos additional de iste simple e clinicamente efficace technica es justificate.

REFERENCES

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