M. Sc. Experimental Surgery

AN EXPERIMENTAL STUDY FOR EVALUATION OF SURGICAL PROCEDURES IN THE TREATMENT OF CORONARY ARTERY INSUFFICIENCY

Biresh C. Mahanti, M.D.

Research Assistant, Department of Experimental Surgery

Demonstrator in Anatomy, McGill University, Montreal.

Session - 1957 - 1958

Thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of Master of Science.

August, 1958. McGill University.

PREFACE

The experimental work presented in this thesis is enhanced in interest by the lively controversy surrounding the surgical procedures for coronary insufficiency. Literature has been filled with different types of operations carried out in the experimental laboratories and the results of clinical trials of many such procedures within the last twenty-eight years.

It was in an attempt to answer one of the questions, i.e., which one of the presently practiced operations gives better protection in coronary insufficiency, was undertaken in July, 1957, in the Department of Experimental Surgery of McGill University and the Radiology Department of Royal Victoria Hospital.

The author wishes to express his gratitude to Dr. Arthur Vineberg for his many suggestions and tireless co-operation which has made this research possible. The year was extremely interesting and a beneficial one.

I wish to take this opportunity to thank Dr. D. R. Webster, Director of the Experimental Surgical Laboratories, for his interest, co-operation throughout the year.

I would like to express my thanks to Dr. F. Granger and Dr. R. Fraser of the Department of Radiology, and Dr. A.C. Guha of the Department of Pathology for their valued assist-

ance and for the many hours of their time they so kindly set aside for this problem.

For the considerable technical assistance and most of the radiography, thanks are due to Mr. Albert Nagy and members of his staff.

Many thanks are due to Mr. Harold Colletta for most of the photography, and Miss I. Shepchensky for microscopic sections.

In addition, I would like to thank Mrs. I. Becker for her careful preparation of this manuscript.

Finally I would like to thank Drs. Dobell, Murphy, Gutelius, Freedman, Constantine and all the other of my associates during the past year for their fine fellowship and friendly interest.

B. C. Mahanti, M. D.

Montreal, August, 1958.

TABLE OF CONTENTS

TABLE OF ILLUSTRATIONS

INDEX OF TABLES

CHAPTER I

INTRODUCTION

During the past thirty years the report concerning coronary heart disease have increased almost geometrically. We are still far from solving the problems of this serious disease as is evidenced by the continuous flood of papers.

The greatest advance has been on the diagnostic front of myocardial infarction and its allied picture of coronary insufficiency. Practically all the schools of the world have contributed in the clinical study. The names of Parkinson, Bedford in England, Barnes, Whitten, Woolfirth, Wood, White, Levine, Wright, Levy, Master in the U.S.A. are closely associated with this work.

It is estimated that four to eight million people in the United States are afflicted with some form of heart disease. Deaths per annum from this cause is more than twice those due to cancer. Metropolitan Life figures show a death rate of 78.2 per 100,000 population. The incidence is higher in males than females.

It is difficult to get the accurate figure from the incidence of coronary disease from the figures for heart disease in general as there is much overlap. It is reported the incidence of coronary involvement is from 22 to 54 percent depending on clinical or necropsy diagnosis (Master - 1942, J. Mt.Sinai Hospital).

The poor prognosis of coronary artery insufficiency has been emphasized by Parker and his associates in the Journal of the American Medical Association in 1946, where they reported a series of more than three thousand cases with angina pectoris, none of whom survived more than five years.

In another series, Katz and his associates reported 25 percent of their patients dead in two months, 50 percent in one year, and 75 percent in three years (Arch. Int. Med., 84:1949).

Medicine has had little to offer to those who are struck with coronary artery disease. Obviously, in light of the severity of the disease, intensive efforts to develop a technique for the revascularization of the ischaemic heart were tried in different centers. Now it is possible to augment the deficient coronary circulation

by several surgical procedures, none of which is widely accepted.

The present study will attempt experimentally to evaluate the few surgical procedures proposed for the treatment of coronary artery disease using animals with coronary insufficiency mechanically induced by casein plastic called Ameroid.

CHAPTER II

ANATOMICAL CONSIDERATION

A. Arterial Blood Supply of Myocardium:-

Brief review of the coronary arterial system will be described as there has not been any contribution besides what is known (85, 91, 98, 99, 178, 180, 105). Myocardium is supplied by two coronary arteries, the right and the left. The left arises from the left anterior sinus of valsalva and about two millimeters from its osteum divides under cover of the left auricular appendage into left circumflex and anterior descending branch. The anterior descending branch which is more important runs downwards in the interventricular groove passing around the apex and appears in the posterior interventricular furrow in its lower third. Numerous branches run to both sides throughout its course. The septal branch arises near its origin or from the main trunk close to its bifurcation. The septal branch supplies the anterior third of the interventricular septum anastomosing with terminal branches of the septal portion of the posterior descending branch of right coronary artery (99). In our experimental animals this branch arises from main trunk or either of its bifurcations at their origin (30). Reference will be made re-

garding them in our experiments. The circumflex branch appears lateral to auricular appendage, runs in the atrio-ventricular groove to the left ending in the posterior descending branch. It supplies the musculature of the upper portion of the right ventricle. One of the common variations, is the separate origin of circumflex and anterior descending branch from the aorta.

The right coronary artery arises just below the right anterior cusp of the aortic valve and travels to the right emerging between the root of the pulmonary artery and aorta. It descends in the right atrio-ventricular sulcus where it descends vertically about two thirds of the way. On the posterior surface it gives several branches on its course to telae adiposae, right auricle and right ventricle. A small constant branch crosses the root of the pulmonary artery and anastomoses with a similar branch of left coronary artery. There are more than three branches which descend on the surface of the right ventricle, the largest and lateral branch runs over the posterior surface of the right ventricle to reach the interventricular sulcus. The terminal part arborizes into posterior descending branch along the interventricular sulcus to supply the lower third of the posterior surface of ventricle. Deeper branch of the terminal part supply

the posterior part of interventricular septum. So right coronary artery supplies the entire right ventricle except the left third of anterior wall, posterior third of the interventricular septum and the inferior right half of the posterior wall of the left ventricle.

The branches of the main coronary arteries descend superficially in the general direction of the apex and these give myocardial branches running at right angles up to endocardium where they change their course to make a rich arteriolar anastomosis. This vascular bed surrounds the muscle bundles arborizing into capillaries which surround the individual fibres as a plexus (169, 182, 219, 218). The lymph channels arise from the boundaries of these capillary plexuses, from where they drain into a subepicardial network of lymphatics. At the venous ends, the capillaries converge to form a small venule which may drain into larger vein draining into coronary sinus or occasionally drain directly into the chamber of the heart. Human hearts are divided into three common variations as classified by Schlesinger by injection studies. In group 1- fifty per cent are right coronary artery prodominance; group II - has a balance circulation between two arteries; group III - with left coronary artery perponderance. Group III is im-

portant since coronary arterial insufficiency is mostly due to pathology in the left coronary branches. Group II is least affected (179, 178).

B. Coronary Venous System:- (85, 91, 98, 99, 95)

The venous drainage of the myocardium is carried out by two systems. 1. Superficial and 2. Deep.

1. Superficial or subepicardial system closely follow the distribution of coronary arteries and empties in a short but wide venous trunk lying in the lower part of the atrio-ventricular groove between the left atrium and left ventricle which is covered superficially by some muscular fibres of the atrium. This is called coronary sinus which empties in the lower and posterior part of the right atrium between the opening of the inferior vena cava and right atrio-ventricular orifice. In the right heart the small venous branches merge to form the anterior cardiac veins, a lesser of the superficial venous system. They end directly in the right atrium.

1. A deeper system of vein which communicates directly with the heart chambers.

Tributaries of coronary sinus -1, great 2.middle and small cardiac veins. The anterior portion of the vent-

ricle is drained by great cardiac vein which begins at the apex of the heart and runs beside the anterior descending branch of the coronary artery and then follows the circumflex branch in auriculo-ventricular sulcus around the left border of the heart. It empties into coronary sinus while in the sulcus.

The middle cardiac vein also starts at the apex of the heart and runs backwards in the inferior interventricular groove and ends in the coronary sinus. It receives branches from both ventricles. The small cardiac veins run along the lower border of the heart and join middle cardiac vein just before it empties into coronary sinus. It is to be noted that the coronary venous system is deprived of any valves and the rudimentary condition of the valve which in lower animals guards the opening of coronary sinus.

C. Communications of the Coronary System:-

There are three types of communications with the coronary arteries: 1) intercoronary, 2) extracardiac, 3) direct communication with chambers of the heart. Present day surgical procedures for coronary artery insufficiency are based on extensive anatomic and physiologic study of these three types of communications with coronary arteries.

There is no longer any controversy that anastomoses

exist between the branches of an individual coronary artery as well as between branches from both arteries (114, 166, 165, 179, 219). Gross (1921) in his excellent monograph has shown the existence of many intercoronary anastomoses and they increase with age (99). They are mostly marked at the junctional area supplied by both arteries. The luminal diameter of 20 to 350 micra and length ranging from 1 or 2 cm to 4-5 cm are found in human hearts. These are two types, called homocoronary or intercoronary. The homocoronary communications are found everywhere except in the immediate subepicardial layers. Intercoronary anastomoses are formed in the areas supplied by both coronaries. These are corkscrew in shape. These homocoronary and intercoronaries are significantly increased in coronary obstruction (41). While in normal human hearts it does not appear to play any role in supplying blood to myocardium. Its response depends on the pressure differential and relative myocardial ischaemia. By back flow technique it has been shown that gradual occlusion of a vessel is followed by increase of 1 cc to 30 cc per minute within a period of 30 days. Although these communications are very small, they are capable of allowing some blood into myocardium. These type of collateral circulation which is formed in

various pathologic syndrome can be interpreted as the result of hypertrophic evolution of the collateral vessels existing in every human heart. (Blumgart 1940) In normal human heart intercoronary anastomoses larger than 40 micra in diameter are not found and anastomotic communication less than 40 micra are of little significance. Age has no relation and it develops after gradual coronary occlusion when and where it is needed. Blumgart believes these vessels will not protect against infarction although they will allow some blood into the area and some benefits (30, 48).

Printzmetal found the largest intercoronary artery communication range from 70-80 micra by injection of graduated glass spheres and radio active cells (166). In their view, the diameter of intercoronaries does not appear to increase with age.

D. Extra Cardiac Communication:- (141)

In 1880 Langer showed anastomoses between the coronary arteries and of the pericardium through which communication exist with branches of internal mammary artery. He also showed connections between the coronary and bronchial artery by means of vasa vasorum of the pulmonary artery. 1803 Van Haller described the extracardiac anastomoses in the

form of potential and actual communication with the surrounding structures, corroborated in 1880 by Langer (216).

Hudson by injection studies deomonstrated communications between the auricular and coronary branches to the pericardial fat, with pericardiacophenic, anterior mediastinal branches of internal mammary artery and bronchial artery. These anastomosis take place around the root of the 1) aorta, 2) pulmonary artery and veins, 3) around the ostia of the sup and inferior venacava, and 4) intervascular pericardial reflection. This anatomic evidence has been made use for revascularisation procedures by many groups and our series of experiments with findings will be described later (114, 48, 147, 102).

Direct Communications with the Chambers of the Heart (220, 39, 36).

Vieussens in 1706 first discovered the Thebesian system and was reported in 1708 by Thebesius whose name they bear. By injection and digestion study two types of communication were found between coronary arteries and chambers of the heart.

1) Arterioluminal (2 to 1 mm diameter) starting as an arteriole but loses its arteriolar structure before opening into

lumen of the heart.

2.) Arteriosinusoidal - These are more numerous and they loose their arteriolar structure much deeper in the myocardium breaking up into large irregular channels lying between the muscle bundles and at times between individual muscle fibres. These are also called "myocardial sinusoids" playing a role in the nourishment of the heart. These are 50 to 250 micra in diameter and anastomose freely with one another. Thebesian veins are more numerous in the right ventricle than in the left (86, 222, 219).

These above facts were also used in attempts to revascularize by Vineberg and Goldman. Recently Massimo successfully tapped the left ventricle with polyethylene T tubes in supplying blood to the left ventricular myocardium on animals (145).

E. Lymphatics of the Heart (173, 161, 66)

There has been much less work towards the anatomy and physiology of the cardiac lymphatics. In 1653 Rudbeck first described the lymphatic vessels of the heart followed by Aagaaro in 1924 and Patek in 1939.

In dogs subepicardial lymphatics consist of capillaries and drainage vessels which form a continuous plexus covering the whole of each ventricle. The large capillaries receive afferents

from the myocardial plexus and converge to form drainage vessels which generally accompany the blood vessels. These drainage vessels at last unite to form a single trunk which drains the entire heart. This trunk leaves the heart by passing on to the anterior surface of the pulmonary artery. Drinker and others also maintain this view but recently Allison and Sabiston showed multiple lymphatic channels in the mediastinum by injection studies (6).

Myocardium possesses lymphatic capillaries three times the diameter of myocardial blood capillaries. There are no collecting trunks in the myocardium and most of them pass directly into the subepicardial capillaries. Few only may empty into the small subepicardial drainage vessels.

Subendocardial and endocardial lymphatic plexuses are mainly capillaries lying in a single plane parallel to the surface of the endocardium. They communicate with myocardial plexus by means of short capillaries which pass directly into the myocardium. There are no lymphatics in atrioventricular valves.

The normal flow of lymph from the heart is explained by the pressure produced during systole and diastole. During diastole lymph is driven from subendocardial lymphatics to myocardial plexus and during systole the lymph from the myo-

cardial plexus forces into the subepicardial lymphatics. Towards the end of the diastole the pressure of the dilated heart against the pericardium probably drives the blood from the subepicardial lymphatics into the main lymphatic trunk. There are many problems of interest in cardiac lymphatics with reference to coronary arterial insufficiency and the absortion of fluid in pericarditis, but very little work has been done with regard to them. There is a possibility the lymphatics of heart might play a role in different surgical procedures for coronary artery insufficiency.

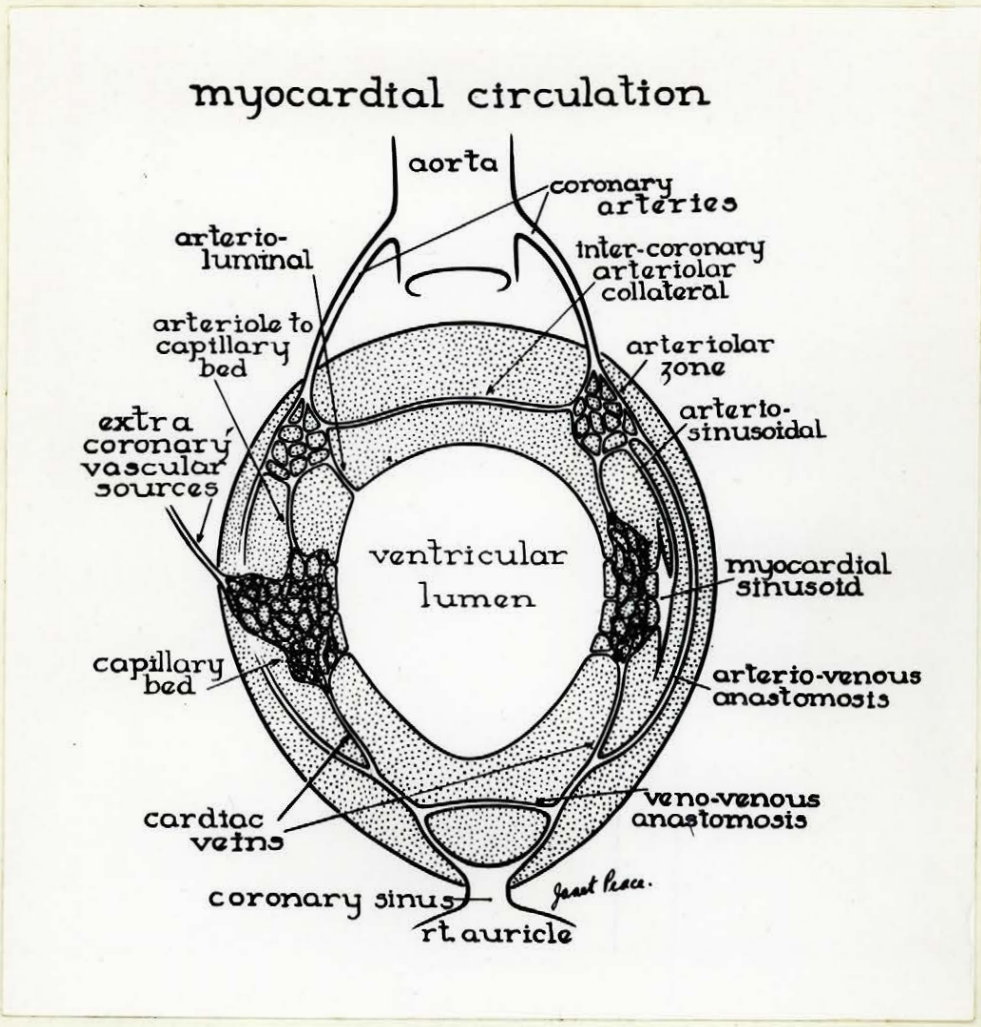

PLATE NO. 1

Diagram showing relationship of coronary arterial and venous circulation with the myocardial sinusoids and ventricular lumen.

CHAPTER III

PHYSIOLOGY OF THE CORONARY CIRCULATION

Main blood supply to the myocardium is by both right and left coronary arteries. Blood entering the coronary arteries have a possible exit through the following routes:

1) Extracardiac anastomosis.

2) By way of coronary sinus and anterior cardiac veins.

3) Through arterio luminal and arterio sinusoidal vessels into the chambers of the heart. (34)

There is a great difference of opinion regarding their importance in normal conditions but these different systems can develop extensively to serve the nutrition of myocardium when the lumen of the coronary vessel is gradually reduced. Our experiments make it questionable, however, whether they can compensate sufficiently to maintain normal action within the gradual occlusive period by our method.

A. Coronary Circulation

The circulation in the coronary system is very rapid as it takes eight seconds for a R.B.C. to pass through completely in its shortest course (34). Under normal conditions, four to five percent of total cardiac output goes

to the coronaries. The output of a normal human heart at rest is between three to four and a half litres per minute and thirty-seven litres during severe exercise. The average human heart consumes 250 cc. of oxygen per minute during strenuous exercise when the coronary circulation has increased three-fold reaching up to two litres per minute (112, 34).

The fraction of total cardiac output passing through the coronary arteries varies inversely with total output; the proportion is about five per cent, which may rise to nine percent in low output (91).

Besides the coronary vessels, the heart can obtain some metabolites from the sinusoidal vessels, lymphatics and the extracoronary anastomosis around the base of the heart (163).

By various methods of flow study, it has been found that the coronary blood flow is about 50 to 75 cc. per minute per gram of muscle. (91, 74, 94, 69, 70) In dogs the left coronary distributes about 80 percent of the total coronary blood and the right only 20 percent (3, 4). On a percentage basis anterior descending 30 percent and circumflex about 50 percent. Further, 70 percent of blood distributed by left coronary artery and 40 percent of that distributed by the right coronary artery return via the coronary sinus (89,225). This was also confirmed by Gregg (4, 95).

B. Coronary Circulation in Different Phases of Cardiac Cycle.

In 1689 Scaramucci enunciated that the arteries supplying the myocardium are filled during diastole and emptied during systole by muscular contraction (177). But Anrup and others proved the above hypothesis by showing experimentally greatly decreased coronary inflow or complete stoppage during systole and increase during diastole (1, 69, 91). But a slight retrograde flow from deep to superficial cardiac vessels is still found in vigorous contraction (1, 2).

Measurement of coronary flow by Green and Gregg showed that a definite forward flow occurs at all times throughout the cycle although it is reduced during systole (87, 93). Coronary artery pressure never reaches as high as aortic pressure (226). By constant pressure flow meter at low perfusion pressure Gregg showed that the potential inflow is reduced from the aorta during isometric contraction and early ejection by forcing back blood from the deep lying compressed vessels into large proximal arteries (91). These proximal vessels distend with rise of aortic pressure reaching its maximum at the end of systole and slightly after due to inertia of the moving column of blood. The myocardial vessels are released rapidly during isometric

relaxation and early diastole causing a greater inflow. When the aortic pressure falls, the total rate of inflow drops below the intramural flow because of the slow reduction of expansion of the superficial coronary vessels. Both the effects are minimal at the end of diastole. Wiggers also arrived at the same conclusion (89, 221)(151).

C. Venous Drainage.

Through Coronary Sinus - This is the major venous drainage system of the left coronary artery and sixty percent of the total circulation is delivered through this way (146). The outflow varies in changing aortic pressure and with elevation of right ventricular pressure. Gregg, however, does not believe that in increased right ventricular pressure the thebesian vessels drain into coronary sinus instead of into the right ventricular cavity as in normal physiological condition. Most of the venous drainage from the right heart is through the anterior cardiac vein into the right auricle. (91, 201, 95)

The outflow of coronary sinus occurs during the ventricular ejection phase and very slightly during the latter half of auricular systole. This is produced by mechanical squeezing of the vessels by myocardium. After the ventricular ejection the flow falls markedly due to emptying. Role of coronary sinus constriction in coronary insufficiency is later discussed in our experiments. (80,90,18).

With the heart beating in sity, acute obstruction of coronary sinus produces congestion of left ventricle but not right ventricle of atrium. Although the pressure in the coronary sinus may be equal to aortic systolic, still the flow in the major coronary artery branches is not reduced to any significant effect. Pressure in the right atrium is approximately 0-8 mm. Hg., in coronary sinus it is 0-5 mm. Hg, whereas in great cardiac vein it is 10-15 mm. Hg.

Even with the ligation of the coronary sinus the peripheral venous pressure returns to normal within thirty days. So increased right atrial pressure is not likely to influence the coronary inflow (201).

Through Anterior Cardiac Veins - (90, 94, 120).

About 50 to 92 percent of right coronary artery inflow drains into the right atrium through anterior cardiac vein (91). Only a smaller amount of the left coronary is drained by this way. Anatomically it drains the region supplied by right coronary artery. The drainage of most of right coronary artery through the thebesian venous system is questionable on account of non-physiological experimental procedures. Katz found a considerable right ventricular thebesian drainage, which is an important element in coronary drainage (120).

Luminal Vessels.

It has been shown that coronary vessels communicate with atrial and ventricular chambers by thebesian and luminal vessels (218, 219, 220, 192). In spite of much experimental work, there is nothing sufficiently conclusive about the function of these vessels in relation to their direction, extent of blood flow, and the functional value in myocardial ischaemia due to critical objection to the pitfalls of experimental methods (91). But many people believe that this system drains about 40 percent of venous blood. (8)

D. Regulation of Coronary Flow.

A very brief review of regulation of coronary flow will be described as there is still much confusion existing regarding the dominant controlling mechanism among the research workers (91, ,32, 74).

Important factors regulating the circulation of coronary arterial system is both physical and chemical. The flow varies directly with the size of the vascular bed and the pressure, but it varies inversely with resistance, the back pressure at the end of the system and viscosity of blood. Resistance of the vascular bed is found mostly in arterioles or vessels of one millimeter or smaller diameter, which can alter only by passive compression, active vasomotor changes

and pressure within the vessel (91).

By using various methods Gregg (91) could not find any relationship between aortic pressure and coronary flow in the beating heart in situ although other investigators were able to vary systolic and diastolic pressure with mean aortic pressure as a factor determining the coronary flow. Clinically these factors are independent. Anrup and his associates were able to vary systolic and diastolic pressures widely without affecting the coronary flow provided the mean pressure remained constant. So the mean aortic pressure is seen to be main controlling agent of the coronary blood flow (2, 3). The most important factors in changes in flow are:

1) the pressure relationship between coronary artery and vein;
2) various cardiac reflexes;
3) change in cardiac output;
4) cardiac rate, blood metabolites and ions (91, 94, 116).

The elasticity of large coronary arteries are an important factor in considering the relation of aortic pressure to coronary flow. This elasticity would allow the arteries to function as reservoir which is lost in atherosclerosis. Consequently there will be a smaller flow at the same pressure, so rise of blood pressure in arteriosclerosis or aortic insufficiency is of some value for blood supply to the myocardium (91).

E. Innervation of Coronaries.

The intrinsic smooth muscle of the coronary vessels may contract and relax by the action of cardiac nerves altering the coronary flow accordingly. The inhibitor and constrictor fibres are predominant in the vagus while dilator and activator fibres are in the sympathetic nerves. It is very difficult to establish the separate effect of nervous influences upon the myocardium and coronary vessels because of the intimate physiological function of these structures (39, 41).

Important vasomotor reflexes adapt the coronary flow to increase work of the heart. Such reflexes originate in the heart and great vessels producing coronary dilatation. This has been thought due to vagus inhibition. Anrup and Segal proved this by vagotomy then stellate ganglionectomy. They thought their experiments demonstrated vasoconstrictor fibres to the coronary in vagus and vasodilator in sympathetic (4).

F. Oxygen Lack and Carbon Dioxide Excess.

There is increase of flow in anoxia due to decreased coronary resistance (226, 91). The flow increases up to 200 percent and an oxygen saturation below the 20 percent level produces maximum dilatation. High carbon dioxide and lactic acid

levels do not produce the dilatory effect in the presence of normal oxygen concentration. In most of the anginal cases this factor probably plays a role in increasing the blood supply by accumulation of metabolites. (91)

CHAPTER IV

P A T H O L O G Y

Narrowing of the coronary arteries is mainly due to arteriosclerosis. This may be localized to the coronary arterial system or a generalized process involving all of the arteries of the body in approximately equal degree. Coronary occlusion, myocardial infarction, angina pectoris and acute coronary insufficiency are all essentially manifestations of the same underlying process of arteriosclerosis involving the coronary arteries. It is the latter group which is amenable to surgical treatment and better clinical result. Coronary arteriosclerosis is essentially an occlusive process of the large and medium sized coronary arteries due to progressive subintimal thickening and is invariably limited to the visible epicardial coronary vessels. The small branches without muscle coats are generally spared (180a). Thus there are possibilities for the development of an adequate collateral blood supply through these smaller branches (63, 75).

Subintimal thickening may progress to another stage when plaques of subintimal deposition of cholesterol or of actual ulceration predisposing to thrombus formation with complete obliteration of the lumen may occur. At the same

time, the media adjoining the cholesterol deposit may undergo degeneration (126).

Macroscopically the internal structure may be seriously deranged or it may be greatly thickened and hard. Microscopically the changes are limited chiefly to the subintimal and intimal layers where any combination of necrosis, haemorrhage, ulceration, calcification or connective tissue proliferation may be seen. Medial sclerosis also may involve these vessels and reduce or obliterate their lumina (175).

The anterior descending branch of the left coronary artery is the most involved due to sclerotic changes. It occurs in the proximal three centimeters. The site of the resulting infarct is in the anterior wall of the left ventricle and the anterior inferior part of the interventricular septum (179).

The most common complication is mural thrombus rather than pericarditis which explains the fact that the infarction occurs more markedly towards the endocardial surface (118). The sclerotic process also decreases as one travels distally down the artery.

It has been found that the patients suffering primarily from angina showed complete blockage of at least one major artery. The more prolonged cases showed diffuse myocardial

fibrosis. After infarction has occurred there can be little change in the size of the infarcted area even by the introduction of a quantity of oxygenated blood from an extra cardiac source. The ischaemic fringe area where the blood supply has not been compromised completely can be improved by this type of procedure, and angina ameliorated. The development of collateral circulation between the various segments of the coronary arterial system is unpredictable due to the marked variation in the vascular pattern in different individuals. Moreover, this newly developed collateral circulation cannot significantly increase the total amount of blood available for myocardial metabolism and nutrition if there is diminution of coronary supply in appreciable amount.

When there is acute occlusion which follows suddenly after gradual decrease of the lumen of an artery, the ischaemia may promote the development of sufficient collaterals to avoid infarction entirely, as has been seen in some human specimens (53, 76).

The presence of a moderate degree of ischaemia does play an important role in the promotion of an anastomosis; this has been shown in human and animal experiments using arterial implants. This is probably on the basis of pressure difference in the myocardial zone in need of more blood (65).

CHAPTER V

I. Principle underlying the different surgical procedures practiced at present.

A. Beck I Operation

B. Internal Mammary Implantation

C. Bilateral Internal Mammary Ligation

D. Cardiopneumopexy

E. Synthetic Tube Implantation from the Aorta into the Left Ventricular Myocardium.

II. Brief review of operations undergone in experimental or clinical trial.

A. Beck II

B. Muscle, Omental, Jejunal, Graft

C. Cardiostrathorrhaphy

D. Thebesian Vessels supplying nutrition to the Myocardium.

E. Direct Coronary Artery Suture Anastomosis

F. Endarterectomy

CHAPTER V

I. Principle underlying the different surgical procedures practiced at present.

A. Beck I Operation.

This operation consists of the following components:

1) The mechanical abrasion of the epicardium and the inner surface of the fibrous pericardium with a specially designed burr.
2) Application of an inflammatory agent like .2 gm. of powdered asbestos to the surface of the heart.
3) Partial ligation of the coronary sinus near its ostium into the right auricle by 3 mm.
4) Application of tissue graft, i.e., the abraded pericardium and vascular mediastinal fat to the surface of the heart.

Above steps of operation have been developed by Dr. Beck after years of experiments on thousands of dogs (13, 14, 17, 21, 23, 25, 24, 27, 28).

The first step of mechanical abrasion produces mild inflammatory reaction which leads to the growth of intercoronary arterial communications and removes the barrier for extra myocardial anastomosis. Stanton and Beck in 1941 demonstrated that this produces an effective stimulus

to the development of intercoronary channels (191, 12, 31). They reduced the mortality from 70 to 38 percent by this one step of operation. Beck also showed that there is objective evidence of extracardiac circulation when the epicardium is removed (13).

Powdered asbestos acts as an inflammatory agent and stimulates intercoronary anastomosis (13). Beck and group showed .2 gm. of asbestos powder produced a more favourable reaction. But Thomson still uses talcum powder and states it to be the perfect irritant. He is still continuing the operation of cardiopericardiopexy as he advocates it to be much safer procedure with a satisfactory result (198, 199, 153, 67).

Grafting of the mediastinal fat pad is for the possible growth of extra coronary communication from the branches of internal mammary supplying the mediastinum and pericardial fat pad. This was suggested by Moritz and Hudson by demonstrating anastomotic vascular channels in adhesions between the heart and pericardium. It was later confirmed by Tichy and Moritz (141, 14).

In 1934 Robertson in his attempt to ligate in stages the main venous channels and arteries of the heart, observed much haemorrhage when adhesions were separated

and the underlying heart became cyanotic. He concluded that the "myocardial nutrition distinctly depends upon vessels contained in the adhesions." There was no controlled statistical data as regards this conclusion based on his opinion.

Partial ligation of coronary sinus provides for greater extraction of oxygen from blood in the capillary bed and stimulation of intercoronary communication. Ligation of coronary sinus as a treatment for coronary artery insufficiency was first done by Gross in 1935 and he showed that there was no infarction or reduction in the size of the infarct when the left anterior descending branch was ligated. There was also an increase in the nutrition of the myocardium one week after the experimental procedure. In 1937 they also reported that the occasional disappearance of anginal pain during an attack of right sided heart failure was due to an increased tension in the coronary sinus and possible back flow through it (37, 100, 101, 171, 172, 82). This was corroborated by Ungerleider by showing that it was possible to ppen sufficient number of collaterals by raising venous pressure to prevent infarction following coronary artery ligation (202). Beck and Mako reported the reduction of frequency and size of infarction when the sinus

was occluded for more than six days. Fauteux in 1939 and 1940, Ripstein in 1948 carried out a series of great cardiac vein ligation and reported that this operation had a protective effect against coronary artery insufficiency. They had seventy percent benefit and one of the Fauteux's patient who died after two and a half years showed great increase vascularity (77, 78, 80,81, 168).

Eckstein in his series of experiments showed that when the coronary sinus pressure is elevated from 30 mm. Hg. to 90 mm. Hg., the back flow is increased from 6 to 11.6 cc. per minute and the blood was reduced to contain but 3.2 volumes of oxygen per 100 cc. which is the proof of its capillary passage and provides substantial evidence that blood flowing through myocardial capillaries does give up oxygen. Baily also states that simple ligation of coronary sinus may be considered as a total revascularization procedure although a lesser degree of intercoronary overdevelopment is obtained by this (71, 49). This step has been added to the internal mammary implant with the hope to increase the percentage of benefit to the patients.

The Beck I operation prevents the mechanism death which is the main cause in ninety percent of cases. This is due to electrical instability and noncoordinated mechanism of heart beat as a result of oxygen differential in the muscle at the periphery of the anoxic zone. When the heart is uniformly anoxic, it exhibits electrical stability and there is no difference in resting electric potential to produce spontaneous ventricular fibrillation. But when a small area of the myocardium becomes ischaemic it sends out impulses which destroy the normal mechanism due to different electrical potential. The myocardium becomes convulsive and goes to fibrillation. In severe exercise probably the same thing happens that destroys the co-ordinated beat. This ischaemic zone is called the "Trigger Zone" by Beck (26, 22, 24, 32, 28).

A small quantity of blood as even 1 to 5 cc. per minute can reduce the irritability and prevent firing, preserve the viability of myocardium. In Beck I operation this criteria is fulfilled by development of intercoronary asastomosis as the importance of the procedure is the uniformity of distribution of available blood and not the total amount of coronary artery inflow. Leighninger reported by back flow studies that in Beck I operation it is

much higher in comparison to the Thomson and Vineberg operation (127). As early as three weeks post-operative the collateral bed can be shown by injection studies and the anastomosis between cardiac and extra dardiac vascular beds are functional by that time. This is questioned in our experimental procedure of gradual myocardial ischaemia (32, 28). Beck reported his good result in 170 cases, with 8 percent mortality.

B. Left Internal Mammary Artery Implantation and Coronary Sinus Constriction.

In 1946 Dr. Vineberg reported on the study of the left internal mammary implant into the left ventricular myocardium. In this laboratory during this last eleven years, several hundred experiments on dogs have proved the following facts:

1) When internal mammary artery is placed in the left ventricular myocardium it grows arteriolar branches which anastomoses with the arteriolar branches of the left coronary artery.
2) Blood flow is in the direction of ischaemic myocardium sufficient to protect the heart. Blood could be perfused under constant pressure equal to the mean aortic pressure into the coronary vascular system

through the implanted internal mammary artery at the rate of 45 cc. per minute.

3) Mortality is reduced after anterior descending branch of the left coronary artery is ligated.

4) It has been also shown that the percentage of anastomoses has also increased from forty-six to eighty-nine percent for implants in normal to ischaemic heart (44, 150, 65, 154).

After several refinements in technique, the operative procedure is as follows: It consists of freeing the left internal mammary artery from the chest wall by ligating and transecting the branches up to sixth interspace. The internal mammary is divided between two ligatures distal to sixth interspace. The proximal free end of the artery is pulled into a tunnel made in the wall of the left ventricle. Before it is drawn into the tunnel the sixth intercostal and other branches are cut so that blood escapes freely through it from the artery into surrounding myocardial tunnel. Following this mediastinal, diaphragmatic and phrenic fat pad are reflected and placed in direct contact with the left ventricular myocardium without interfering with the implant.

By this procedure the blood readhes the myocardium immediately and within three to four weeks through

arteriolar anastomosis. These anastomotic branches have all the histologic characteristics of vessels.

In performance of this implant procedure there are certain generalized items of technique which were not followed by other workers who could not reproduce Dr. Vineberg's result. These have been mentioned by him repeatedly and will be mentioned here briefly:

1) The dissection on the internal mammary artery from the chest wall should be performed with extreme gentleness.
2) No instrument or clamps of any kind should be used upon the artery.
3) There should be no angulation of the artery as it enters the tunnel.
4) There should be an effort made to have the artery under the same amount of tension in its new site, as it was under its original position on the chest wall.
5) Myocardial tunnel should not be over one inch in length and should be placed in the middle third of the thickness of the left ventricular myocardium (54A).

The concept on which this procedure is efficacious is simple and based on the present day anatomical and pathological studies of coronary artery disease. The arteriosclerotic lesions of the coronary artery are most commonly

found in the superficial epicardial vessels at its origin or within the first few millimeters. It occurs only in a smaller percentage in the deeper myocardial vessels which have an extremely well marked spongelike vascular network. Implantation of the left internal mammary artery in this rich spongelike vascular network when arteriolar anastomosis occurs supplies blood to the area beyond the site of obstruction. These anastomotic channels take about five months to develop fully to counteract the reverse trigger zone of Beck (65).

Criticism of immediate and delayed thrombus formation, disappearance of anastomotic channels after six weeks, intimal proliferation in larger percentage by Glen, Baily and group have been rejected due to the failure of following the steps and precautions of operation as described above (46, 84, 142). Buller showed large arteriolar anastomotic branches after eighteen to twenty-five months on dogs' hearts by digestion cast. In eighteen month old human hearts, the internal mammary artery has been found patent with large arteriolar anastomotic branches and no intimal proliferation. Sabiston and Blalock reported 92 percent patency and 82 percent anastomosis when left common carotid artery with branches were implanted into the left ventricular myocardium. But in man

unfortunately there is no other artery of greater diameter than internal mammary which is available inside the thorax to be sacrificed. Implantation of homografts in this laboratory and others have already reported the high incidence of thrombosis (174, 180B, 82).

Bellman reported an excellent study on anastomosis of Vineberg implant by microangiography and concluded that the branching is confined to the distal third of the implant and the cut branches or scalloped openings in the implant are not related in any way to the branching, which they postulate to be from vasavasorum, which is questionable. Extracardiac branches of the implant never communicate with coronary arteries (51). Very few people besides Dr. Walker have given a clinical trial for proper evaluation. Vineberg and Walker series of 107 cases operated until today report seventy-eight percent cure after the procedure.

Coronary sinus constriction to 3 mm. diameter has been included to evaluate if the improvement could be increased beyond seventy-six percent by the addition of this step to implantation. The technique and steps of the operation are the same as described in Beck I. The rationality of its application is the same as Beck I operation, i.e., 1) greater extraction of oxygen from blood in the capillary bed; 2) stim-

ulation of intercoronary communication, which does not interfere with development of anastomotic channels from the implant.

C. Bilateral Internal Mammary Ligation

Direct communication between extracardiac branches of coronary arteries and the pericardial branches of the internal mammary artery has been shown to exist around the root of the aorta, pulmonary artery and vein, round the ostia of the superior and inferior venacava and intervascular pericardial reflexions. Widespread anastomosis between the auricular and coronary branches to the pericardial fat with pericardiophrenic of internal mammary by injection of India ink and bismuth oxychloride under positive pressure of 220 mm. for five minutes was shown by Hudson and Moritz in 1952 (114).

In 1939 Fieschi also described vascular channels form the internal mammary artery through its pericardiophrenic branch into a few periaortic and peripulmonary arterial rami. It was his hypothesis that the coronary arterial circulation might be favourably influenced by creating hypertension and directing an increased amount of blood to the pericardiophrenic to ppen anastomotic channels with coronary arteries.

In 1955 Battezati injected methylene blue and India ink into the internal mammary artery in the second interspace and found an excellent vascular network within the parietal pericardium and on occasions the dye was seen in the vascular rami of the myocardium and epicardial fat. Similar was the finding in dogs. They also reported clinical improvement on human patients by this procedure. (40A, 79A) Griffin and Glover also found slight increase in blood flow to the myocardium in their experiments, but they find objective evidence lagging behind the observed clinical improvement (102, 103).

This operation is simple and done under local anaesthesia. The internal mammary is exposed in the second intercostal space and divided between ligatures.

In my experiment the subclavian and all its branches, except the internal mammary, has been ligated to have the maximum of the hypertensive effect as suggested by Dr. Blalock. The results are reported later as studied by Schlesinger and India ink injection study.

Series E. Cardiopneumonopexy

Lezius in Germany first described the operation of using a lung graft for revascularization of the myocardium. His method of cardiopneumopexy consisted of painting acriflavin solution to the myocardium and lower middle lobe of the left lung and to suture them together. This was carried out on eighteen dogs, out of which two died of open pneumothorax (139, 131).

Carter, Gall and Wadsworth in 1949 thought this operation to be simple and practical for coronary insufficiency. In their series of experiments on fifty-four animals there was ninety percent mortality on control dogs after ligation of anterior descending branch, but one hundred percent survival after cardiopneumopexy. They found filling of the superficial vessels in the myocardium by injection of ten percent suspension of India ink in blood. In thirty days there was early organized reaction with formation of small thin-walled blood vessels. In forty-five days there were newly formed blood vessels, and in sixty days there was complete replacement of the epicardium by numerous blood vessel invasion (55). But there are several criticisms of the operation regarding the direction and volume of blood flow and degree of oxygenation which

is not known. Wigger has shown that the direction of flow in a given area is proportional to the pressure differential in that area, and regarding oxygen saturation it has been shown that oxygen tension of pulmonary artery venous blood is high enough to nourish a starving myocardium (55).

Many authors, however, believe that the main benefit of this procedure is from the formation of intercoronary anastomosis.

Smith has modified the operation by applying phenol and powdered asbestos into the myocardium at the site of the graft. He also found a higher percentage of protection by the above procedure and recently he has performed the operations on human hearts with coronary insufficiency (189).

Bloomer and associates have tried to alter the pressure relationship by ligating the pulmonary artery supply to the living segment employed in revascularisation. They have demonstrated well expanded collateral arterial circulation at the end of two and a half months and in almost all the animals there was a plexus of vessels each exceeding a diameter of 50 micron diameter after six months. No data on the experimental effectiveness of this method in the prevention of infarction and mortality consequent to experimental coronary insufficiency was published. These

experiments were done on normal animal hearts (48, 49, 119, 122).

There was also retrograde injection of pulmonary artery from periphery. In these animals there were intercoronary collaterals as early as fifteen weeks in fifty percent of cases.

The principle is based on the following facts:
1) By ligating pulmonary artery it induces the Bronchial collateral circulation.
2) Bronchial artery as a branch of the aorta has a higher pressure than pulmonary to compensate the pressure differential in the myocardium. It arises from first to fourth aortic intercostal arteries from each side. Pulmonary arterial pressure is approximately two millimeters of mercury which can not revascularize an area with a perfusion pressure of at least sixty millimeters of mercury higher.

The Author found this to be a more rational operation among all the modifications of cardiopneumopexy. On a series of ten animals with vaselinized ameroid constrictors this operation was carried out to test its efficacy.

Recently Prudden published on experimental re-

sults of another modification of cardiopneumopexy. He made a direct end to end subclavian left lower lobe pulmonary artery anastomosis to produce a high pressure cardiopneumopexy on eighteen animals. Although they had less complication in the grafted lung in contrast to other types of lung graft, there was no vascular communications between the coronary and lobar circulatory network due to a connective tissue filled barrier between the interface of the onlay and the myocardium. But his mortality was only twenty-one percent in operated animals after anterior descending branch ligation (165A).

Garmella and his associates reported about a modified form of cardiopneumopexy employing pulmonary segmental resection. Mortality was only 25.9 percent in contrast to fifty-five percent in control series, but it did not reduce the severity of myocardial infarcts. Complications like atelectasis, haemorrhage, and fluids in the chest were definite disadvantages by this method (104).

SERIES E

Synthetic graft implantation from aorta into left ventricular myocardium.

Smith and his associates reported on the nylon prosthetic graft implantation for myocardial revascularization on twenty-one dogs and two human patients. Anastomosis was proved on animals by injecting Diodrast and fluorescein into the graft which reappeared in the coronary circulation and later in other parts of the body. On x-ray there was pooling of Diodrast at the end of the implant. His two clinical cases also improved after such a procedure. There is no objective evidence of anastomosis and he has postulated that communication occurs with myocardial venous system (187).

This prompted the author to try prosthetic graft implantation in our ameroid treated dogs with coronary insufficiency as the Smith and group experiments were done on the normal hearts. Instead of using a nylon tube, polyvinyl sponge called Ivalon, made into tubes, was chosen. for the purpose due to the following advantages over cloth grafts:

1. The absence of inside seam

2. The blood tight characteristics of the material.
3. Easy accomplishment of suture anastomosis.
4. Wide use of polyvinyl sponge inside the heart without untoward effect (149, 191 A).

BRIEF REVIEW OF OPERATIONS UNDERGONE IN EXPERIMENTAL AND CLINICAL TRIAL

A. BECK II OPERATION

After many modifications, Beck devised his operation for myocardial revascularization by arterialization of coronary sinus in two stages. At first a jugular vein graft is put in between the aorta and coronary sinus (16, 19, 20, 28). Subsequently after three weeks the coronary sinus is constricted by a ligature. This was modified later by Baily into a one stage operation by direct anastomoses of the aorta to the coronary sinus. In the beginning the results were very encouraging as the grafts remained patent in 92 percent of animals.

All physiologic studies like pressure flow, and oxygen content revealed that the graft could maintain arterial pressure distal to an occlusion and that the blood had actually passed through the capillaries. Later study by Eckstein and Leighninger revealed that the graft perfuses the coronary bed for about five weeks and then loses functional contact with it. This is because of obliterative venous changes in response to the heightened pressure. Any improved blood supply after five weeks

were shown to be due to the formation of intercoronary anastomosis. Thus the coronary capillary bed is perfused with oxygenated blood from the aorta through the graft for the first five weeks only (43, 45, 47, 72).

Moir and Pritchard studied a group of patients with coronary artery disease in whom the Beck II procedure was done. They reported no circulatory abornormality among those in whom the graft was thrombosed. However, those patients with patent graft demonstrated haemodynamic changes of an arteriovenous fistula like greater blood volume, decreased effective systemic flow, decreased peripheral resistance and increased cardial output leading to cardiac failure (144).

B1 MUSCLE GRAFT

In 1935 Claude Beck reported that it is possible to protect dog's heart with coronary ligation after grafting a flap of the left pectoralis muscle to the myocardium.

He reported in the same year on one case which showed improvement after the muscle graft. Later the procedure was modified to use a smaller part of the muscle. In addition, powdered beef bone was used to produce inflammatory adhesions. In 1943 they reported on the follow-up of

thirty-seven cases, of which 62.2 percent survived the operation. At the time of the report fourteen were living. This operation was abandoned by Beck and group as other better operations were devised. (10, 11, 14).

2. OMENTAL GRAFT

In 1936 and 1937, O'Shaughnessy first reported the use of omentum as a source of fresh blood for the coronary system. Evidence of anastomosis between the vessels of the omentum and the heart was found in experimental animals. The same author also reported twelve patients on whom the operation was performed, out of which eight were survivors with signs of improvement (156, 157).

This was modified by other authors to extrapleural omentopexy instead of intrapleural (Lancet, 239, 36:1940). But the operation fell into disuse because of the high mortality rate due to the abdominothoracic approach and introduction of simpler operations (60).

3. JEJUNAL GRAFT

Baronofsky and his associates reported that after a loop of jejunum was placed on the left ventricular myocardium of dogs, the survival after anterior descending occ-

lusion was 75 percent in comparison to 35 percent in the control group. The mechanism of this protection was not clearly defined. (42)

C. CARDIOSTATHORRHAPHY

Allen in 1951 reported another surgical procedure for the treatment of coronary occlusion on the basis of improving the function of that ventricle which had been rendered less efficient by having had a portion of its wall thrown out of function. In experimental animals they have been able to splint and stabilize the ischaemic area by using sutures made from strips of pericardium or strips of fascia which were woven through the area of the myocardium. Their experience on twenty-one animals proved it to be of benefit to the hearts with coronary occlusion (7).

D. THEBESIAN VESSELS SUPPLYING NUTRITION TO THE MYOCARDIUM

Anatomical and physiological basis for the Thebesian vessels as a source of myocardial nutrition has already been discussed. Vineberg reported in the Canadian Medical Association Journal in 1953 his experimental attempt to create artificial Thebesian canals to revascularize the heart. The method followed was to implant an open arterial homograft from the ventricular cavity in-

to the wall of the ventricle. In only one animal was there slight evidence of anastomosis and a patent opening into the ventricular cavity. Massimo and Boffi reported implanting a polyethylene T. tube, the vertical branch of which is directly connected with the left ventricular cavity while the horizontal branch was embedded in the myocardium. This was performed on thirty-two dogs with no mortality. They feel the blood is transported to the coronary circulation and a continuous flow of blood is established under sufficient pressure (145).

E. DIRECT CORONARY ARTERY SUTURE ANASTOMOSIS

The feasibility of coronary artery suture anastomosis was demonstrated in 1940 by Gordon Murray. Recently Thal and his associates reported a technique of direct anastomosis of the internal mammary artery to the circumflex coronary artery in which oxygenated blood was shunted through the anastomosis in seventeen animals. Seven out of these seventeen had patent anastomosis after a two-to-six month period. No demonstration of long term survival with widely patent anastomosis has hitherto been accomplished due to high incidence of thrombosis in small blood vessel anastomosis which is shown to be greater within the range of an internal diameter of two to three mm. (195).

F. ENDARTERECTOMY

Julian and his associates reported in Annals of Surgery (136, 459:1952), that the peripheral arteries can be incised widely and under direct vision, a sufficient thickness of the hyperplastic intimal and medial wall can be curetted out.

Baily and Ray after animal experiments reported two successful human cases coronary endarterectomy in J.A.M.A. 164, 641-6, 1957. As the branches of the coronary artery in its subepicardial course does not reduce its lumen rapidly, the curette could be easily introduced from the distal portion towards the blockage for curettage without much difficulty. The two human cases reported had blockage of the lateral branch of the left circumflex artery. A tubular cast of about seven mm. long was removed and pulsation revived in both the arteries.

This procedure is an experimental one and there is no long term follow up. Bleeding from the endarterectomy site was a common immediate post-operative complication.

CHAPTER VI

THE EXPERIMENTAL PROBLEM

In large proportion of the experiments performed to solve the problem of coronary insufficiency surgically have been done on a normal heart followed by ligation of one or more of the branches of left coronary artery after days or weeks to test the efficacy of the operation. Some of the operations have also been transferred to human patients with encouraging result, though not widely accepted. The main criticism of this type being super vascularization rather than revascularization.

The ameroid plastic in a stainless steel jacket as devised by Litvak in this laboratory showed that the rate of closure of the ameroid was fairly constant and reasonably predictable in vivo to produce coronary insufficiency. These ameroids in this experiment were treated with vaseline to delay the rate of closure. As this device was very satisfactory for the purpose of producing coronary insufficiency, a series of experiments to test the efficacy of different surgical procedures practiced at present, on the ameroid treated heart of dogs, was planned. It is well known that none of the

surgical procedures have wide acceptance and moreover literature on this subject of different operations for the treatment of coronary artery disease appear to be very variable.

Experimentally the following operations were carried out on ten dogs in each series with ameroid constrictors.

1) Ameroid constrictors for control.

2) Beck I operation.

3) Internal Mammary ligation.

4) Internal mammary implantation with constriction of coronary sinus.

5) Cardiopneumopexy.

6) Cardio-aortic Ivalon tube implant.

First - studies were performed in all of these instances on the survival of these animals in comparison to control series.

Secondly - study of intercoronary anastomosis and the extracoronary vascular supply to the myocardium by Schlesinger injection and x-ray.

Thirdly - Study on coronary and extracoronary angiography in operated animals for visualisation of extra cardiac blood supply to the myocardium.

Fourthly - sections through the ameroid constrictors and

the left ventricular myocardium for microscopic study of amount of closure of the arteries and infarctions respectively were done.

For the purpose of coronary and extracoronary angiography in situ in the living anaesthetised animals, the assistance of Dr. F. Grainger and Dr. R. Fraser of the Department of Radiology, Royal Victoria Hospital, was utilized.

CHAPTER VII

A. Brief Review of Coronary Insufficiency in Experimental Animals.

Many methods have been used previously for producing infarcts in animals' heart but most articles in the literature give inadequate statistics regarding early, late mortality, and extent of infarction. The most popular method to test the efficiency of an operative procedure is to ligate one or more of the main branches of the left coronary artery following in days or weeks after the operative procedure on normal heart. The main criticism of this being a procedure of supervascularization rather than revascularization. Significant doubt also has arisen concerning the applicability of mortality rate to every experimental trial. Hann and Beck report a consistent operative mortality of approximately 70% in their control animals which is questioned by others (109).

The problem of producing coronary insufficiency in dogs has been a difficult one. Since the eighteenth century, several methods have been tried in order to effect gradual occlusion of blood vessels by both extra and intraluminally. Screw, gadgets, spring as a compression device have been tried before without good results (121). The major disadvantage being infection invading the artificial sinus from

outside, haemorrhage due to infection, compression atrophy and intravascular thrombosis. (129)

Methods of internally obstructing arteries like fascial plugs, short tubes, springs and thin wire with or without use of coagulating currents have been tried but they are most unsatisfactory as they produce rapid thrombosis plus danger of embolism and finally recanalisation in some instances which may or may not be desired. Recently small segments of polyethylene tube have been inserted into the arterial lumina with the same type of poor result. (181)

Injection of irritant solutions like iodine, silvernitrate, acriflavin, silicon particles and the sclerosants like sodium morrhuate into the tunica adventitia to produce mild to marked fibroplasia with resultant narrowing of the vascular lumen have been tried without much success.(135)

Besides cellophane, polyethylene, dicetylphosphate have been used by various groups as Abbott in 1949, Shapiroff, 1950, to produce fibrotic reaction around the arteries leading to diminution of lumen of the vessel. This was also experimented by Litvack in our laboratory and he found a variable amount of fibrotic reaction in the tunica adventitia of these arteries. None of the other vascular tunics were involved in this reaction and at no time was the free flow of blood impeded in any of the arteries. (129)

B. Technique of Ameroid Casein Plastic in Producing Coronary Insufficiency

Berman in 1954 used casein plastic material encased in a rigid shell which could occlude vessels in the dog in a predictable time. Casein is derived from skim milk as Rennet Casein. It is coloured white for the experimental purpose and is obtained from American Plastic Corporation of Bainbridge, New York, in form of round bars. It is fairly tough and strong. Its two most important factors are its hygroscopic nature and its curing in formaldehyde. The combination of these two factors produce gradual obliteration of the lumen of any blood vessels.

Litvack used these casein plastics called ameroids in stainless steel housing for producing coronary artery insufficiency with much success. Following is the size of ameroid jacket in inducing coronary insufficiency in the experimental animal:-

Ameroid inside diameter	3 m.m.
Ameroid outside diameter	6 m.m.
Total outside diameter	8 m.m.
Length	5 m.m.
Slot in Ameroid	.5 m.m.
Slot in Stainless Steel jacket	1.0 m.m.

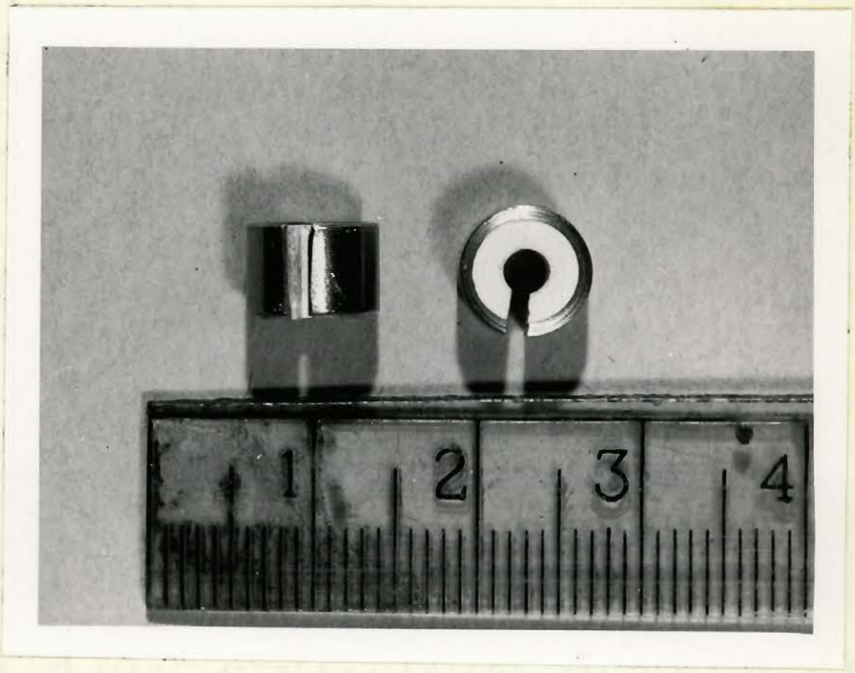

PLATE NO. 2

Photograph of ameroid constrictors used to produce coronary artery insufficiency. Note ameroid casein plastic with slot to fit over artery and encased in steel jacket. Absorption by casein plastic is controlled by coating ameroid surface with vaseline.

By using the above size ameroids without any treatment around the anterior descending and circumflex branch of the left coronary artery on twelve dogs the survival days ranged from four to twenty-six days. These twelve-animals were studied by E.K.G. which revealed gradually increasing myocardial ischaemia, injury and derangement in the excitability and conductivity.

Microscopic examination of all sleeve encased coronary artery segments revealed that none of the lumina were completely occluded. The final luminal diameter is estimated at 1/10th to 1/8th of normal. Tunica adventitia was thinner and coarser blending with tunica media after fifteen days. Tunica media showed changes of gradual thickening with few inflammatory cells. The heavy smooth muscle fibres seemed to lose their identity early and revert to a fibrocollagenous appearance.

These findings correlated with the clinical course of the above animals suggests that total anatomical occlusion of these coronary arteries was not necessary for production of wide spread infarction of myocardium and significant alteration to the depolarization of conducting system (129). When these sleeves were coated with petrolatum it produced an almost linear rate of expansion by

the twentieth day which lagged behind the plain and glycerine coated sleeves of the same type. After twentieth day the luminal diameter gradually decreases. There is generally an initial burst of swelling over the first two weeks with coated and uncoated sleeves which is followed by slower rate of expansion.

This gradual occlusion of arteries by the ameroid plastic sleeve is accomplished by means of 1) Hygroscopic swelling of the plastic which mechanically narrows the vessel. 2) Fibroplastic reaction in the arterial walls. 3) Intraluminal thrombosis with organization and intimal hyperplasia.

For evaluating the efficacy of the different surgical procedures the above technique in a modified form was adopted for our experimental purpose (129). Following is the technique that was used in our series of experiments.

The ameroid sleeves as required for the day of operation were put inside a clean bottle with fresh white petrolatum (U.S.P.). The bottle is loosely covered and placed in a boiling water bowl for one hour, during which the sleeve absorbs and coats itself with melted petrolatum at a constant temperature of 94° Centigrade. After one

hour the sleeves are removed for use. The inside diameter of the ameroid after this type of treatment with petrolatum varies from .001 to .003 m.m. due to swelling. Each time new ameroids were treated on the day of operation.

PLATE NO. 3

Control Dog No. 119

Photomicrograph of section through anterior descending artery proximal to ameroid constriction. Note normal patency of the artery. Same is also in circumflex branch.

PLATE NO. 4

Dog No. 119

Photomicrograph of section through anterior descending branch within the ameroid. Note complete obstruction due to organized thrombus.

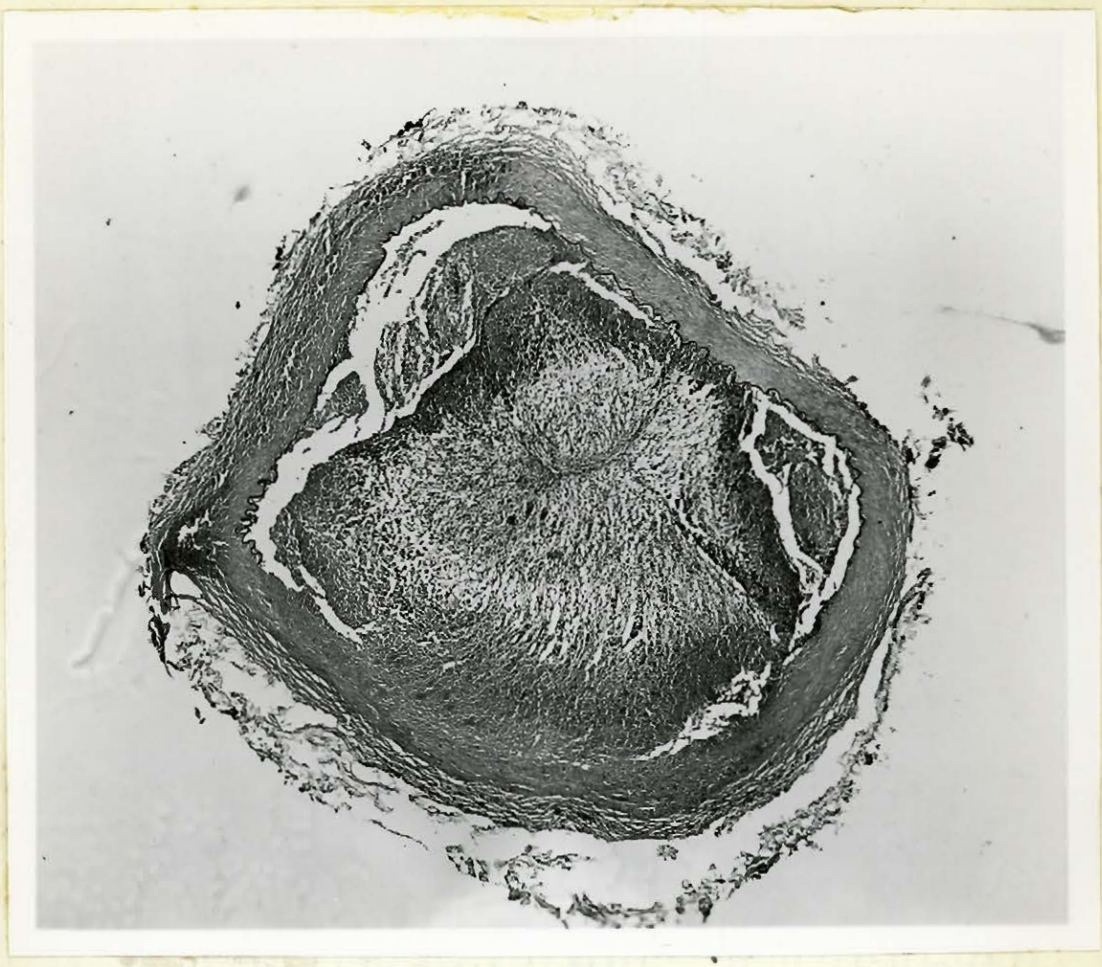

PLATE NO. 5

Control Dog No. 119

Photomicrograph of section through circumflex branch within the ameroid. Note 90 percent obstruction of the lumen.

PLATE NO. 6

Control Dog No. 119

Photomicrograph of section through anterior descending distal to ameroid constriction. Note normal arterial lumen. Similar is the section of the circumflex branch.

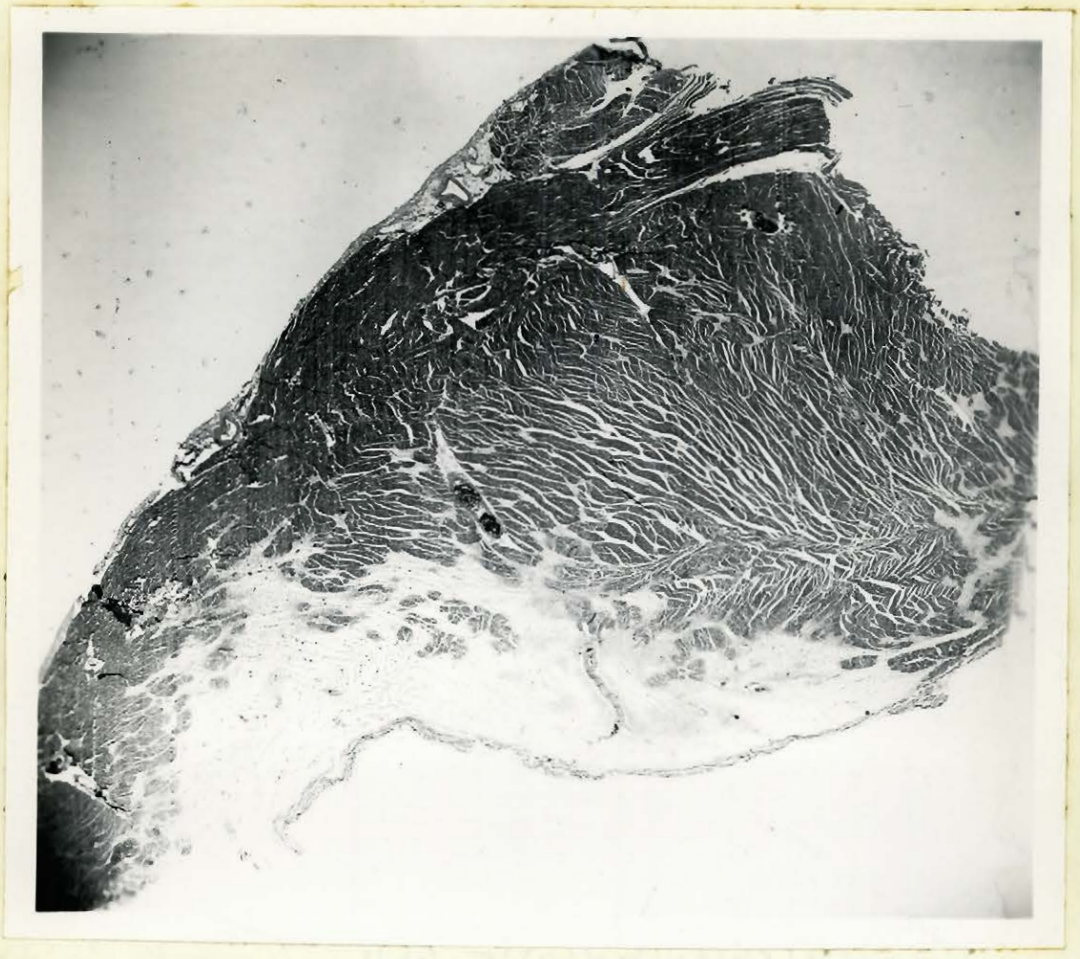

PLATE NO. 7

Dog No. 117

Microphotograph of section through the left ventricle, interventricular septum and right ventricle. Note the infarcted area involving the interventricular septum and left ventricular wall. (Innerside only)

CHAPTER VIII

MATERIALS AND METHOD

A. Experimental Animal

In most of the experimental work on cardiac revascularization, dogs have been chosen in this laboratory and all other placed. Moreover, the mongrel dogs were preferred as they have a) increased resistance to operative trauma and disease, b) ease of procuring, although difficulty was encountered several times during the year, c) comparison of result with previous workers in this field. In literature also there has been extensive writing about dogs' coronary circulation which has a close resemblance to common human type.

Mongrel dogs between 42 to 50 pounds were selected very specifically to have a uniform size of hearts with coronary arteries for production of coronary insufficiency by ameroid sleeves. Immediately after operation the dogs were kept in individual cages for 6 to 7 days after which they were sent to farm for boarding with close watch on their behaviour.

B. The operation

1. Anaesthesia - Standard anaesthesia of 1.V Nembutal (Abbott Laboratory) in a dose of one gram per five pounds of animal giving a third plane of anaesthesia for three hours

which was enough for any kind of procedure even with a lone operator.

2. Position - In all cases the animal was postured on the right side with left side uppermost. The four extremities were fastened to the upper and lower posts on the side of the operating table.

3. Intubation - The animals were intubated with rubber endotracheal tube having a balloon on the end to provide airtight communication with respirator. Positive pressure respiration with room air was maintained all time till the chest was closed and lung reinflated. A pump with large exchange volume was used for the purpose.

4. Sterilization - Proper sterile precautions as practiced in human operating room was practiced, like steam sterilization of instruments and drapes, surgical scrub with wearing of donned cap, mask, sterile gowns and gloves.

The animal's left chest and abdomen clipped, shaved and cleaned with soap and water followed by application of Tr Merthrolate Solution 1:1000 sol. Sterile drapes were applied after the left chest was prepared for sterility.

5. Incision - The animal was started on the positive pressure respirator and the incision was made between 3rd to 5th interspace depending on the procedure for proper exposure of the field of operation. After the skin was incised from the sternum anter-

iorly to the line of transverse processes of the vertebra posteriorly, the subcutaneous tissue and muscles were divided by Bovi cautery and bleeders electrocoagulated. Chest was then opened in the intercostal space required and a self retaining retractor placed to obtain the exposure. The respiration was then adjusted by the screw clamp on the side arm of the connection with endotracheal tube.

SERIES I. 10 Dogs (65, 129)

Operation for Control with Ameroid Sleeves

This is the control series of coronary artery insufficiency produced by vaselinized ameroid sleeves around the anterior descending and circumflex branch of the left coronary artery. All other procedures are to be compared with this series.

Left chest was opened through 4th interspace. The lung was retracted posteriorly and the pericardium incised longitudinally parallel to phrenic nerve anteriorly or posteriorly from its superior reflection on to the aorta to halfway between the base and apex of the left ventricle. No novocaine was used in the pericardial sac routinely to avoid ventricular fibrillation. Only on 3 to 4 occasions it was necessary when the heart rate went beyond 160 beats per minute with auricular fibrillation.

The posterior edge of the pericardium was retracted with self retaining sutures displaying the area between the aortic bulb and the left auriculoventricular junction through which the left coronary artery runs. The great cardiac vein turning into the coronary sinus and the branching of the left coronary artery to anterior descending and circumflex are seen in the area. The epicardium was dissected from these vessels and then by careful sharp and blunt dissection, the anterior descending and circumflex branches just beyond their origin were exposed with their branches and the origin of the septal branch identified. Elevating ligatures were passed under each vessel and the vessel was lifted up by gentle traction and a prepared ameroid was slipped around it using a Lahey cystic duct clamp. After this was completed the pericardium was closed with interrupted silk. Penicillin and Dihidro-streptomycin powder were sprinkled inside the pleural cavity and the thoracotomy was closed by interrupted heavy cotton pericostal suture, continuous 000 cotton in the muscle and continuous number thirty size wire in the skin. The lung was completely re-inflated through a rubber catheter which was removed after the closure of the chest. This operation could be completed in one hour by a lone operator. The above procedure was carried out routinely in the following

type of experiment to test their efficacy.

SERIES II. 11 Dogs

Beck I Operation (13, 22, 23, 25, 26)

The pericardium was incised longitudinally anterior to the phrenic nerve and retracted laterally by retaining suture. By slightly elevating and rotating the heart the coronary sinus near its ostium into the right auriole was visualized. By sharp and blunt dissection the coronary sinus was isolated from accompanying arterial branches. Atraumatic 000 black silk was passed around the sinus by reversing the needle and tied over a 3 m.m. Beck probe. Only in one instance the heart went into fibrillation after the coronary sinus constriction. So the constriction was removed and the heart immediately returned to its normal contraction. This animal was not included in the series.

Then epicardium and inner surface of fibrous pericardium were abraded by a Beck burr. Particular care was taken not to injure the coronary vessels running close to the epicardium. Fine powdered asbestos .2 gms was sprinkled over the surface of the heart. The pericardial opening was approximately loosely exposing a space for suturing of the vascular mediastinal fat pad. Chest was closed similarly as

described before.

Series III. 10 Dogs

Internal Mammary Implantation into Left Ventricular Myocardium and Constriction of Coronary Sinus (208, 210, 65, 206, 204)

The chest was opened in the third intercostal space and 4th costal cartilage divided for proper exposure. The subcostalis muscle was dissected exposing the left internal mammary artery which was freed from the chest wall by ligating and transecting the branches from the subclavian artery up to sixth interspace. Internal mammary was transected distal to sixth interspace and ligated doubly with medium cotton. The ligation on the end of the internal mammary is left long and is used at a later stage in the procedure. A suture of medium cotton is then placed in the apex of the heart near where the exit of the tunnel will be., and the artery lined up with it so as to ascertain the direction of the tunnel. It is important that there is no angulation of the implanted artery inside or outside the tunnel. A small nick is then made in the epicardium close to the apical suture and a crib artery forceps introduced. This forcep is then forced gently to make a tunnel of one inch in the proposed direction. The ligature on the end of the internal mammary artery is then drawn through the tunnel by the

orib forceps. Before it is drawn into the tunnel the sixth intercostal branch and other branches were cut so that blood escapes freely through it from the artery into the surrounding tunnel. No scalloping was done; only visible branches were divided. On the average the openings were from 2 to 4. The ligature on the end of the artery is then anchored to the apical suture. Haemorrhage from both ends of the tunnel often occurs but this is readily controlled by slight pressure. Only 00000 silk was used in ligature of internal mammary branches. Coronary sinus constriction was done as described in Beck I procedure previously.

These are some of the important steps in technique in implant procedure which are followed scrupulously:

No.1 - Gentle handling in dissection of the internal mammary to avoid haematoma or injury leading to early thrombosis.

No.2 - There should be no angulation or torsion of the artery inside or outside the tunnel.

No.3 - There should be an effort to have the artery under the same amount of tension in its new position as it was under its original position on the chest wall.

No.4 - The branches should be bleeding freely when the internal mammary is drawn into the tunnel as one of the beneficial effects is from washing out of any clots which might have

formed in the artery during the slight trauma of dissection.

It is interesting to note that there has never been any evidence of haematoma formation in any of the specimens studied before and whether the blood stops flowing due to compression of the myocardium or whether it is actually being carried away by any of the disrupted vessels from the dissection of the tunnel has not yet been established.

SERIES IV. 10 Dogs

Internal Mammary Ligation (79a, 5, 103)

The chest was opened through fourth interspace and an ameroid sleeve placed around the anterior descending and circumflex branch. The left subclavian artery was identified and ligated by medium cotton distal to the internal mammary artery. All other branches of left subclavian were also similarly ligated individually. Left internal mammary was ligated and divided in the second interspace to increase pressure by diverting all the blood into pericardio-phrenic branch. The Pericardiophrenic branch was ligated at the apex of the heart near the diaphragm.

SERIES V. 10 Dogs

Cardio Aortic Ivalon Tube Graft

Ivalon tubes were prepared as per the method by Shumway in 1955. Thin sheets of two millimeter thickness Ivalon were sliced. These thin sheets were wrapped around a glass tube of 5 m.m. diameter. Approximately two layers were used to get the required thickness. External splinting was done by strongly wrapping around the Ivalon, Cheese cloth in many layers with uniform pressure and it was placed in distilled water. Sterilization was done by boiling for twenty minutes. During this time besides the sterilization, the fusion of the Ivalon was achieved and it keeps its tubular shape. It is more impermeable and not too rigid to lose its elasticity. The proximal thoracic aorta was dissected and mobilized along its medial border. The site of anastomosis was then enclosed within a Beck clamp and a punch hole was made by scissors. Anastomosis with Ivalon tube was done by continuous 5.0 silk running suture. The Beck clamp was gradually released to seal the anastomotic site and to check the free flow of blood through the Ivalon tube. The segment of the tube for implantation into the left ventricular myocardium was scalloped for bleeding and drawn through the tunnel as described before for implant procedure. On the average the tunnels are between 3/4 to 1 inch in length. The distal end of the tube is anchored at the end of the tunnel without ligating it completely. Pulsation could be felt after gradual release of the clamp in the aorta.

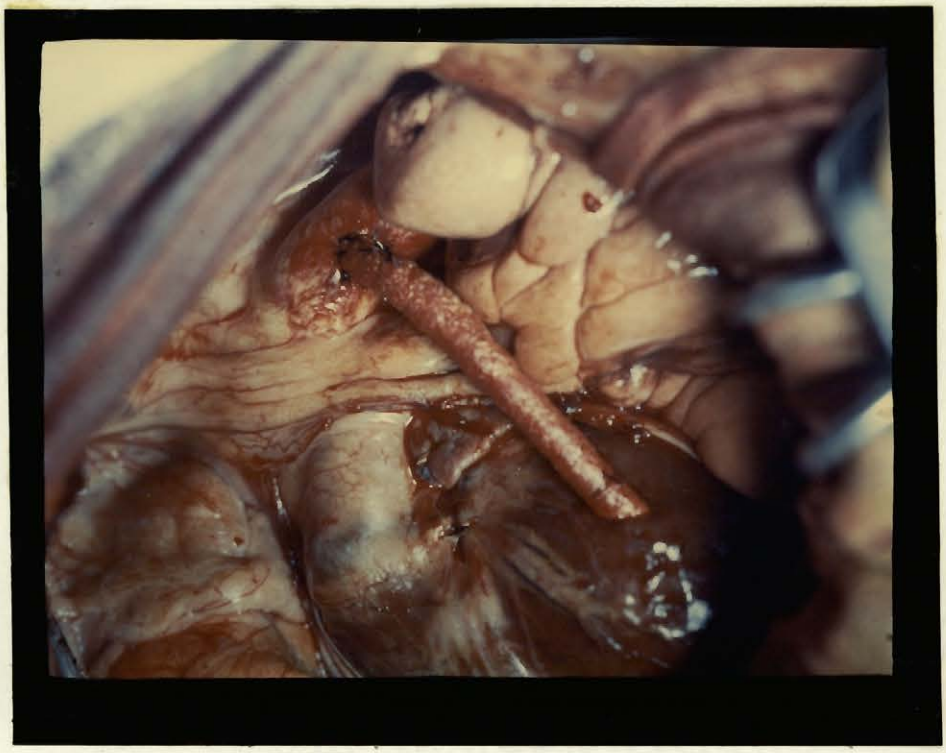

PLATE NO.8

Dog No. 119

Photograph of the heart, aorta, and Ivalon tube from the aorta to left ventricular myocardium. Note: 1.) pericardiophrenic artery with phrenic nerve; 2.) capillaries over the pulmonary artery continuous with pericardiophrenic; 3.) Ameroids around the anterior descending. Another ameroid under the left auricular appendage.

C. I POST-MORTEM - EXAMINATION

Within twelve hours after the death of each dog a routine gross autopsy was done. At this time the heart was removed en mass with extravascular blood supply as per operation performed. The specimen is then refrigerated in physiologic saline to allow for relaxation of muscular spasm.

II. Injection Method

After trying different injection media for visualization of coronary arterial system to serve our experimental project, Schlesinger solution was found to be best. It has several advantages: it is radio-opaque, its ease of microscopic study after injection, and the constant size of the particles (40 micra). Besides it is sufficiently fluid to permit easy injection when heated and rapidly sets to a solid of gelatin consistency as it cools. The hearts were removed from the deep freeze and dissected of the left anterior descending and circumflex branch enclosed within the ameroid sleeve for pathological section before defreezing so that the exact relation of the intraluminal changes to arterial diameter could be measured microscopically. Then the hearts were warmed to 44 degrees C. and the divided anterior descending circumflex and right coronary artery were cannulated with polyethylene tubing of comparable size. Cannulation of extra-

coronary vessels like internal mammary and pulmonary artery where possible, was similarly done before the coronaries, to evaluate the myocardial filling supply. Each heart was then positioned in the physiologic saline bath to warm up to 44 degrees C. Injection of each cannulation by Schlesinger mass was completed as outlined in the original article with slight modifications of method and apparatus. Schlesinger solution was injected under a pressure of 130 mm. mercury and was consistently agitated in a boiling water bath in order to maintain its homogenity and liquid state. The heart was suspended in the normal saline bath at 44 degrees Centigrade during the injection to keep the Schlesinger solution liquid allowing free passage through the coronary and extracoronary vessels. After completion of injection, pressure was maintained and the cannulas clamped to prevent backflow of the Schlesinger solution. The heart was disconnected from the apparatus, removed from the saline bath and dipped in cold tap water to produce solidification of the Schlesinger solution in the arteries. X-rays were then taken of the injected heart to observe the extent of filling of the myocardium in case of extracoronary vessels and intercoronaries in case of coronary vessels. Schlesinger solution is radio-opaque due to the presence of lead acetate.

The hearts were then preserved in ten percent formaldehyde solution and after seventy-two hours, sections were taken from the suspicious areas of ischaemia and infarction in the myocardium.

CHAPTER IX

CORONARY ARTERIOGRAM

Its application for visualization of extracardial vessels used in myocardial revascularization

It is not always possible to diagnose coronary artery disease until one or two days after an attack. There is no reliable clinical method to localise the obstructing site in the coronary arterial tree. In recent years more and more medical people are being gradually convinced that it is not only a medical but a surgical problem as well. For sound surgical treatment a very precise knowledge of the anatomic location and distribution of pathology in the coronary tree is essential. Coronary arteriogram helps in solving the above problem. In this experimental work, besides visualizing the extent of obstruction in the left coronary artery, an attempt has been made to evaluate the arterial supply to the myocardium from the extracardiac vessels by cannulating them in vivo.

In recent years investigative work on animals followed by clinical application at a few centers of coronary arteriogram has been done. However it has not been accepted as a routine procedure due to several complications which may occur during and after the injection study.

Di Guglielmo reported 192 arteriograms on children

done under general anaesthesia during retrograde aortography for congenital heart disease (108). Canon visualized localised obstruction in the coronary arterial tree by angiography on animals and in no instances there was any secondary clotting distal to the point of obstruction (56). Radio-opaque solutions four to ten times the relative volume commonly used in human angiography did not appear to irritate the heart, other than transient E.C.G. changes. This was not done by multiple exposure method.

As regards the contrast media for coronary arteriography various radio-opaque substances like Urokon, Hypaque, Miokon, Renografin, have been tested. OHheinrich and group in their study found 50% Hypaque and 50% Miokon suitable for coronary angiography. They believe a comparatively small amount of contrast media during the specific fractional period of the cardiac cycle can produce the desired visualization of coronary arterial tree (111).

Thal and group have used 76% Renografin without any untoward results on twenty human patients by cannulating the left brachial artery with Lehman cardiac catheter under local anaesthesia. Preoperatively the patients were given 50 mgms. of dramamine and 25 mgms. of phenargen half an hour before an atropine sulphate 1/100 gr ten minutes before

cannulation by intravenous route (194). During the angiography in all experimental animals, fluctuation of blood pressure and arrythmias are produced. When the radio-opaque substances are injected directly into the coronary arterial bed it produces transient changes in T wave and prolongation of diastolic interval. In rapid injection technique to avoid large amount of dye travelling into the cerebral circulation and producing convulsion, the carotid arteries on both sides of the neck are compressed during the injection. Thal and group did not have any cerebral complication following the above method.

In our experiments as the animals were ready to be sacrificed no precaution was taken to avoid these complications. Two of the six animals had convulsions during the injection from which they recovered. Rapid heart rate and arrythmias were also observed during our experiments.

EXPERIMENTAL METHOD

Our experiments for coronary and extracoronary angiography was done in the radiology department of the Royal Victoria Hospital with close co-operation of Dr. R. Fraser and Dr. F. Granger. The animals were anaesthetized with I.V. nembutal with a dose of one gram per five pounds weight to give a third plane anaesthesia for approximately two hours.

Cannulation was done in the Experimental Laboratory of the Donner Research Building and the animals were then transported to x-ray department.

Group I - Normal dog, 42 pounds in weight. Cannulation with No. 7 Lehman catheter was done through the left common carotid artery under sterile precautions. The catheter was then connected to a syringe full of heparinised glucose in normal saline to avoid clotting of the catheter.

Group II - This animal underwent the operation of vaselinised ameroid sleeves around the anterior descending and circumflex branch of the left coronary artery. Cannulation with No. 7 Lehman catheter was done through the left common carotid artery for visualization of coronary tree.

Group III - These animals had left internal mammary implantation and coronary sinus constriction on the average of six months duration. Cannulation was done through the left common carotid artery for coronary angiography and through the left brachial artery for extracoronary visualization.

Group IV - This animal survived more than five months with the Beck I Operation. Cannulation with six and seven French thin walled Lehman cardiac catheters was done through left common carotid artery for coronary angiography and through the left brachial artery for visualization of extracoronary vessels supplying the myocardium.

INJECTION DEVICES-

In our studies, the "Gidlund" high pressure injection syringe coupled with the rapid film changer was used. The injection syringe works with compressed air at a pressure between one to ten kilograms per square centimeter. In all our experiments eight kilograms per square centimeter of pressure was used. Immediately after injection which is between .5 to 1½ seconds, it automatically starts the exposure device in the rapid film. In all our series 70% Urokon was used from ten to twenty cc at a time with a pressure of eight kilogram per square centimeter.

Positioning and Exposure Factor -

The animals were first fluoroscoped for the positioning of the tip of catheter. Normally the tips of catheter were placed about five centimeter above the sinus of valsalva for coronary arteriogram. Several other authors have also mentioned that the coronary arteries may not be visualized if the tip is placed too far away from the sinus as there will be greater dilution; also when it is placed too close, it may not visualize one of the branches.

In our groups III and IV the catheter tip could be guided into the left internal mammary artery from the left subclavian without much difficulty. It was positioned near its

origin from the left subclavian for extracardiac angiography in the operated animals. It was not difficult to guide the tip as experience was gained with the procedure.

After fluoroscopy the animals were placed in a left posterior oblique position and films (size of 12 by 14 inches) were taken at 250 to 350 milliamperes on average, with 95 to 110 kilovolt at 1/30 to 1/60th of a second, with the speed of six per second. The injection material remains at body temperature automatically in the syringe. The speed in this machine can be lowered to one in ten seconds.

With the above technique a very satisfactory coronary and extracoronary angiogram was obtained.

CHAPTER X

A. SUMMARY OF PROTOCOL

Section I

Series A. Control - 10 Dogs, Weight between 43 to 50 pounds

In this series, vaseline treated ameroid sleeves were applied on the anterior descending and circumflex branch of the left coronary artery to produce coronary insufficiency. The survival rate and collateral circulation visualized by injection and x-ray studies will be compared with other procedures.

Dog No. 153 This animal underwent the procedure on December 13th, 1957, and died on the farm on Feb. 10th, 1957. Death came all of a sudden while fighting over food, when it fell down on the floor crying. This animal lived for forty-one days. Post-mortem examination revealed an adherent lingula of left lung. There was no gross manifestation of myocardial ischaemia. Schlesinger Injection study showed + + homocoronary and + intercoronary anastomosis. On microscopic examination the arteries were obstructed to 87% of their lumen by intimal hyperplasia.

Arteriogram on thirtieth day revealed filling of the radio-opaque dye in right coronary artery and very little filling of the anterior descending and none in the circumflex branch of left coronary artery. Septal branch was arising from the anterior descending.

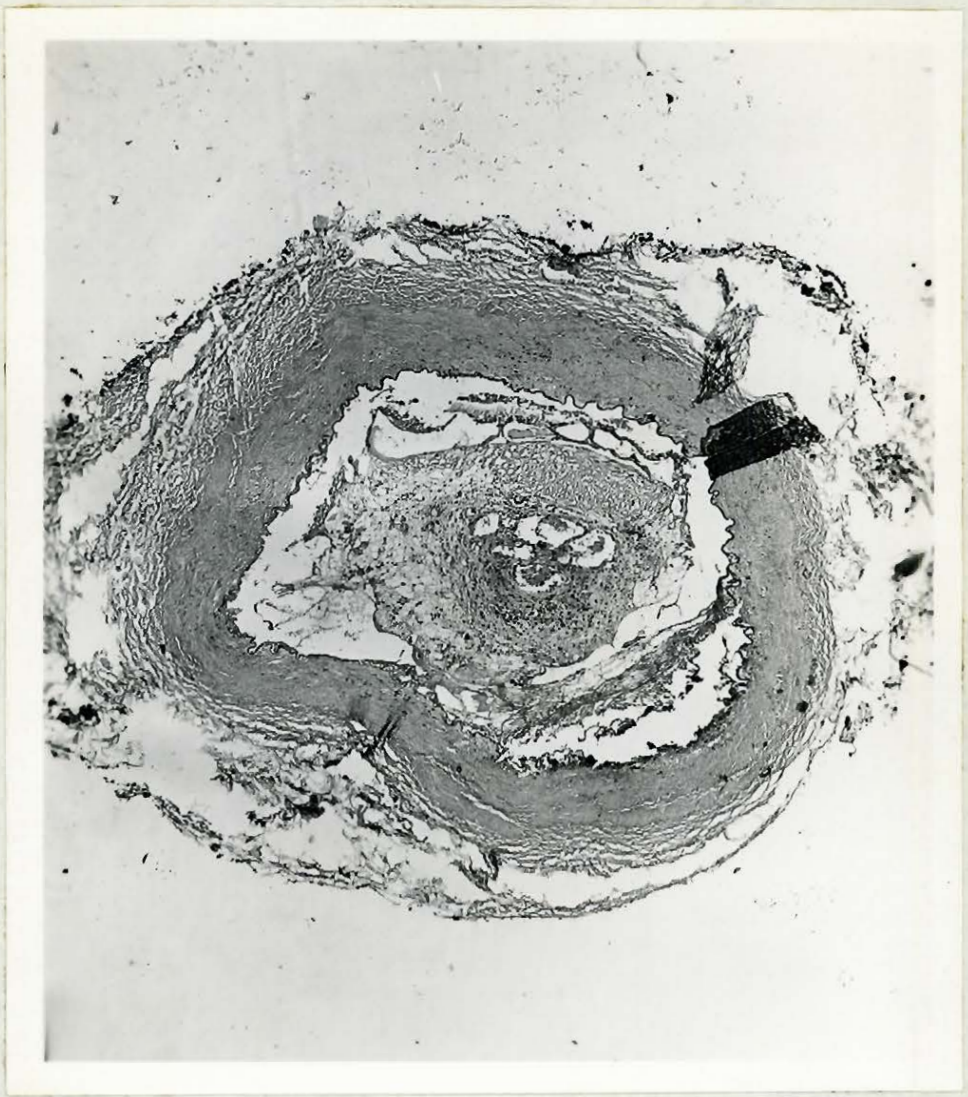

PLATE NO. 9

Dog No. 153 - Microscopic section through the anterior descending branch within the ameroid. Note the obstruction of the lumen and thickened media with chronic inflammatory cells.

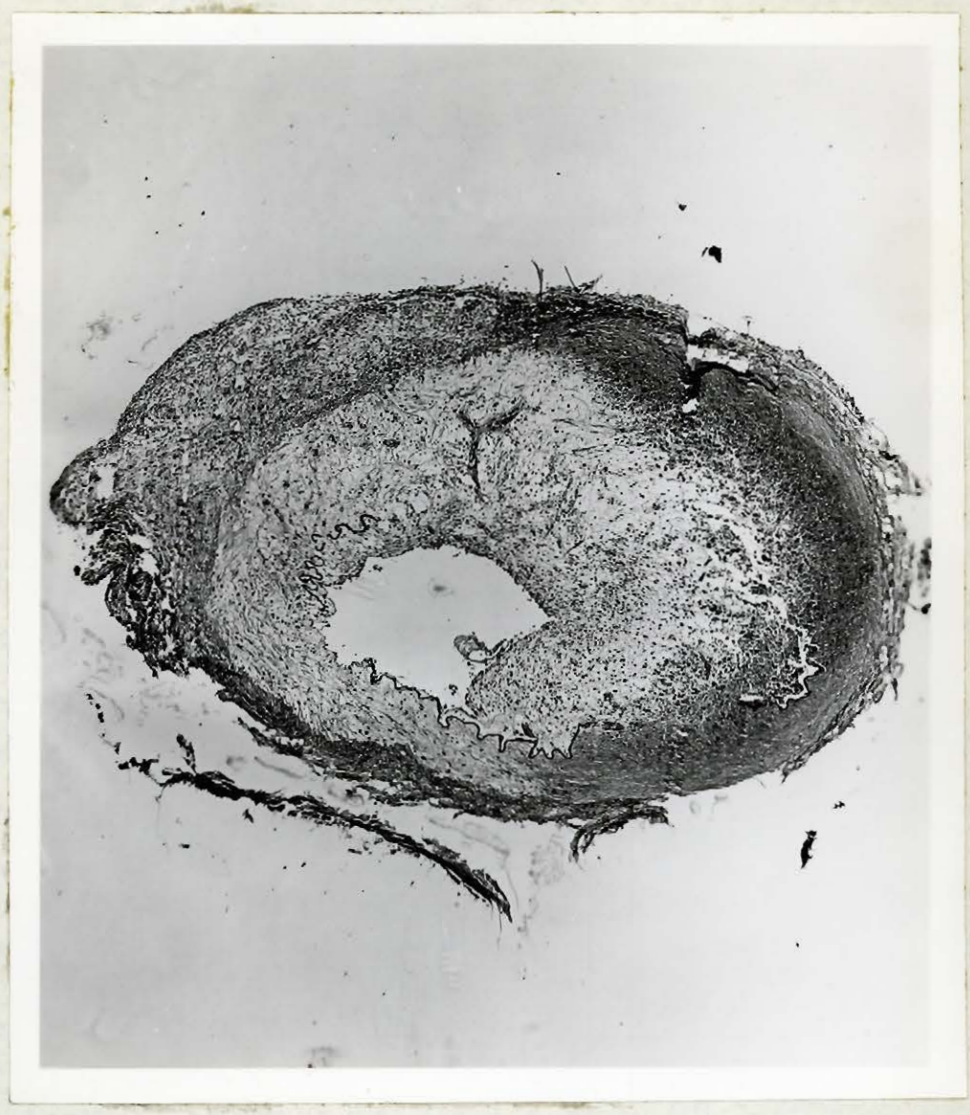

PLATE NO. 10

Dog No. 153 - Microscopic section through the circumflex branch showing the extent of obstruction of the lumen due to intimal proliferation.

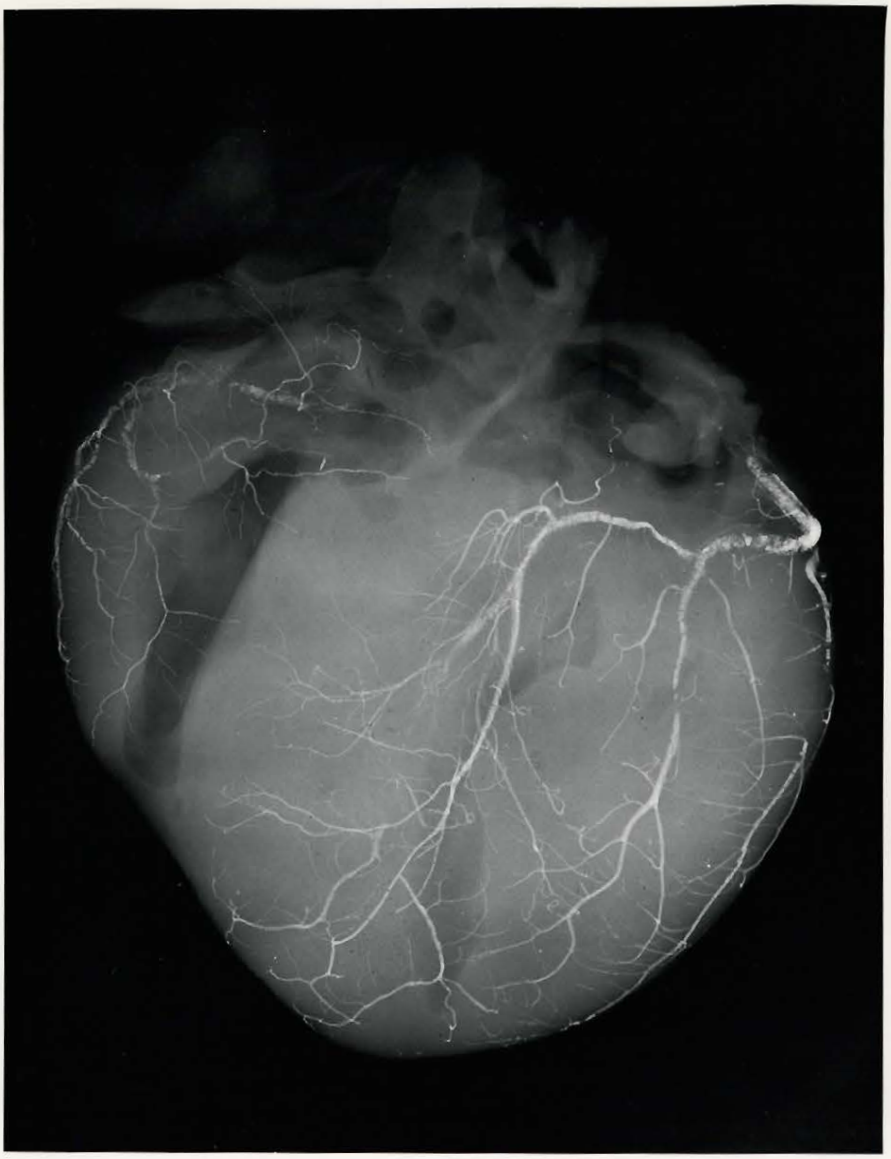

PLATE NO. 11

Dog No. 153 - Schlesinger injection study by x-ray for intercoronary anastomosis. This is an antero-posterior view.

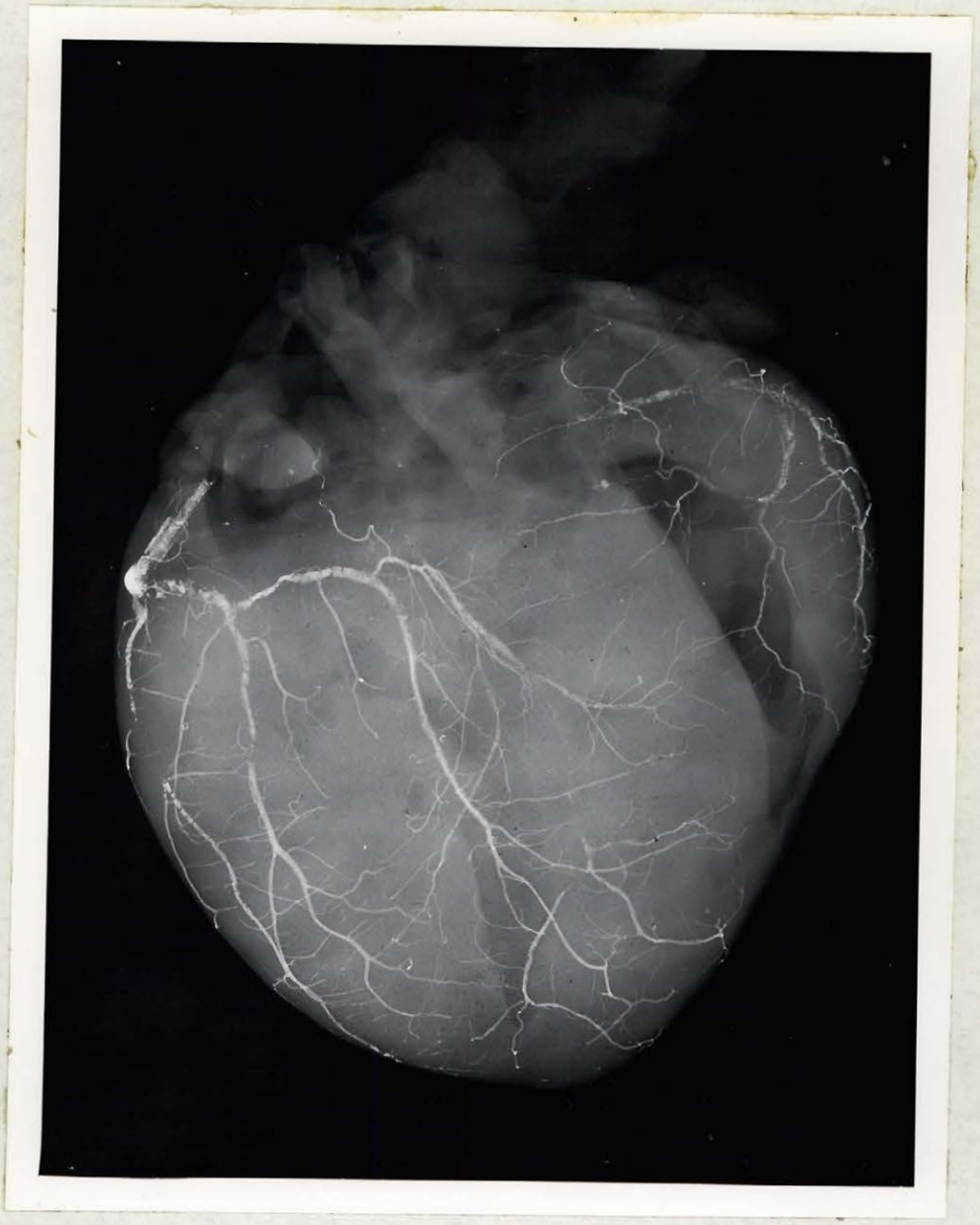

PLATE NO. 12

Dog No. 153 - X-ray study of intercoronary anastomosis by Schlesinger injection. Note only one intercoronary between right and left coronary artery. This is P.A. view.

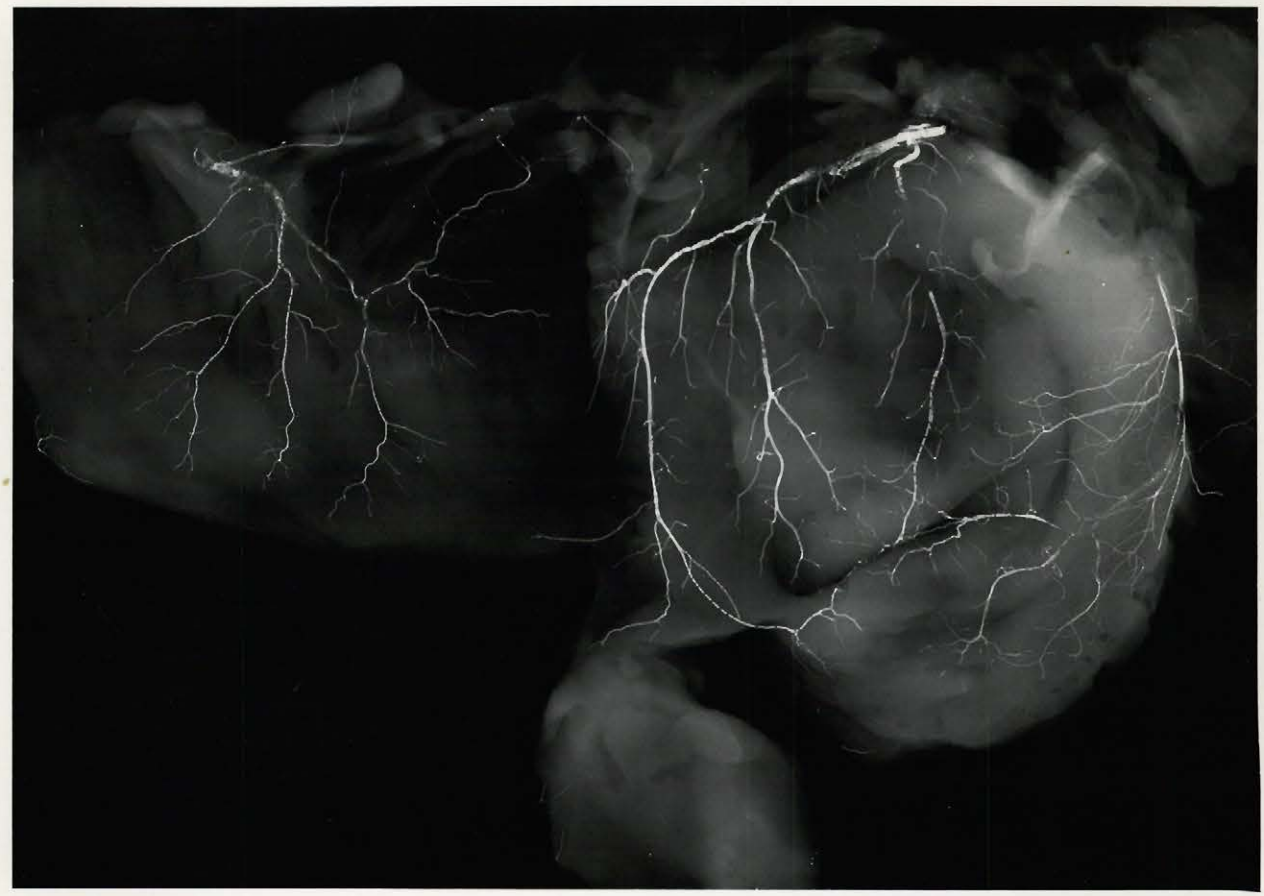

PLATE NO. 13

Dog No. 153 - X-ray study of an unrolled heart for intercoronary anastomosis. Note only ∕ intercoronary and more than one homocoronary anastomosis in left side of the photograph.

Dog No. 348 This animal underwent the same ameroid sleeve application on December 31st, 1957, and died on February 4th, surviving for thirty-five days. The animal was lethargic and lost weight in last week. Post-mortem examination revealed suspicious areas of infarction near the apex of the heart. Schlesinger Injection study showed, + homocoronary and + intercoronary anastomosis. Arteries were obstructed by 70% of their lumen on microscopic examination. The septal branch was arising from the bifurcation of the left coronary artery.

Dog No. 119 This animal underwent ameroid sleeve application on February 10th, 1958, and died on March 5th in the farm. The animal was quite active previous to death. It survived for 25 days. On post-mortem examination the upper lobe of lung was adherent to the heart. Schlesinger Injection study revealed + + homocoronary and + intercoronary anastomosis. Arteries were obstructed to 90% of their lumen on microscopic examination. The septal branch was arising from anterior descending branch.

Dog No. 373 This animal underwent a similar procedure on February 20th, 1958, and died March 20th, surviving for thirty days. It dropped dead while fighting with another dog.

Schlesinger Injection study revealed + homocoronary and + intercoronary anastomosis. Arteries were constricted to 75% by organized thrombus and there were areas of infarction at the apex confirmed by microscopic examination. The septal branch was arising from the left coronary artery at its bifurcation.

Dog No. 375 This animal underwent ameroid sleeve application on February 24th, 1958, and expired March 10th, 1958, surviving for sixteen days, dropping dead on the farm before the farmer. Left lung was adherent to the heart on post-mortem examination. Schlesinger Injection study reveals + + homocoronary and + intercoronary anastomosis. Arteries were obstructed 75% of their lumen. The septal branch came from the circumflex branch.

Dog No. 376 This animal underwent the same procedure on March 6th, 1958, and died on April 2nd, 1958, on the farm, surviving for 28 days. Post-mortem examination was negative for any gross pathology. Schlesinger Injection study revealed + homocoronary and + intercoronary anastomosis. Arteries were obstructed up to 80% of their lumen. The septal branch was arising from the anterior descending branch.

Dog No. 126 This animal underwent ameroid sleeve application on March 17th, 1958, and expired twenty-one days after on April 21st, 1958, on the farm. The dog died quite suddenly while playing. On post-mortem examination, left lung was

adherent and there was suspicious area of infarction near the apex. Schlesinger Injection study revealed + homocoronary and + intercoronary anastomosis. The arteries were obstructed 68% of their diameter. The septal branch arose from the anterior descending branch.

Dog No. 328 This animal underwent the same procedure on February 10th, 1958, and died on February 30th, after twenty days. On post-mortem examination the left lung was adherent to the heart and there was no suspicion of gross infarction. Schlessinger Injection study revealed + homocoronary and + intercoronary anastomosis. Arteries within the ameroid sleeve were obstructed up to 65% of their diameter. The septal branch arose from anterior descending branch.

Dog No. 372 This animal underwent the ameroid sleeve application on March 5th, 1958, and died on April 5th, after thirty days. On post-mortem examination left lung was adherent. Schlesinger Injection study was not satisfactory for evaluating collateral anastomosis. Arteries within the ameroid sleeve were obstructed by internal hyperplasia up to 72% of their lumen. The septal branch was arising from the anterior descending.

Dog No. 176 This animal underwent the same procedure as above on March 17th, 1958, and died on April 2nd, after seventeen days. Found dead by farmer in its cage. Schlesinger

injection study revealed + intercoronary + homocoronary anastomosis. Arteries within the ameroids were obstructed up to 87% of their diameter. Septal branch was arising from the left coronary at its bifurcation.

Series B. 10 dogs weighing between 44 to 52 pounds

Beck I Operation

In this series the animals underwent the vaselinized ameroid sleeve application around the anterior descending and circumflex branch of the left coronary artery as done in the control series. In addition, the Beck I operation was performed simultaneously to test the efficacy of the procedure.

Dog No. 313 This animal underwent Beck I operation on September 8th, 1957, and sacrificed on March 10th, 1958, after 190 days. Septal branch was arising from the left coronary artery at its bifurcation. Schlesinger injection study revealed + + + + intercoronary and + homocoronary anastomosis. Arteries within the ameroid sleeve were obstructed 85% of their diameter. Cannulation of the left internal mammary for arteriogram was done and there was no visualization of extracardiac blood supply to the myocardium. The animal was sacrificed after the arteriogram and there were widely dilated vessels in the mediastinal fat running towards the heart.

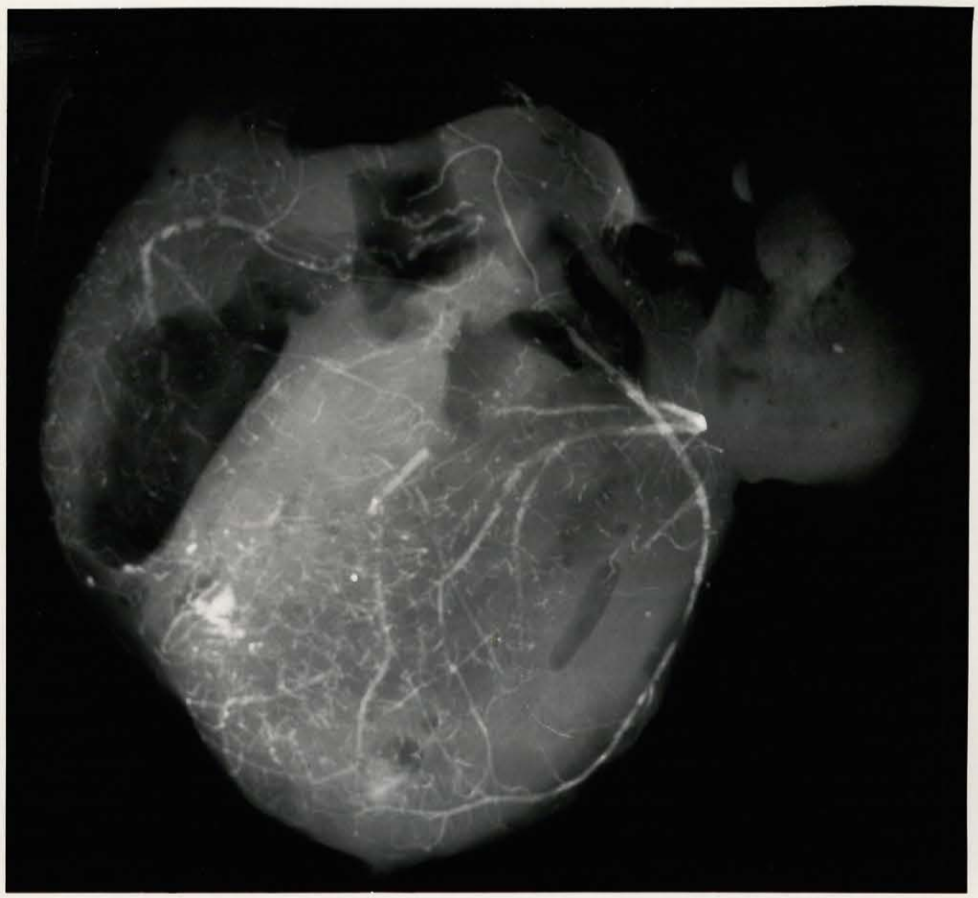

PLATE NO. 14

Dog No. 313 - X-ray study of intercoronary anastomosis by Schlesinger injection. Note large number of intercoronary anastomosis.

Dog No. 171 This animal underwent Beck I operation on Sept. 13th, 1957, and died on October 6th, 1957, after twenty-three days. It dropped dead while fighting over food. On post-mortem examination left upper lobe was adherent to the lung. Mediastinal vessels were dilated and enlarged. Schlesinger injection study revealed + homocoronary and no intercoronary anastomosis. Arteries within the ameroid were obstructed up to 82.5% of their lumen. Septal branch was arising from the anterior descending.

Dog No. 314 This animal underwent Beck I operation on September 16th, and died on December 14th, 1957, after eighty-eight days. Septal branch was arising from the anterior descending. On post-mortem examination lingula was adherent to the heart. Schlesinger injection study revealed + homocoronary and + + intercoronary anastomosis. Arteries within the ameroid were obstructed 80% of their lumen.

Dog No. 116 This animal underwent Beck I operation on September 17th, 1957, and died on October 18th, after thirty days. This dog also had a sudden death while playing. Septal branch was arising from the anterior descending. On post-mortem examination lingula was found to be adherent to

the heart. Schlesinger injection study revealed -/- homocoronary and -/- intercoronary anastomosis. Arteries within the ameroids were found to be obstructed 85% of their lumen.

Dog No. 303 this animal similarly underwent Beck I operation on September 18th and died on October 6th, 1957, after eighteen days. It dropped dead crying before the farmer. Post-mortem examination revealed adherent left upper lobe. Schlesinger injection study showed / homocoronary and / intercoronary anastomosis. Arteries were obstructed by 65% of their lumen by intimal proliferation. Septal branch was arising from the circumflex and the ameroid was placed proximal to septal branch in this case.

Dog No. 145 This animal underwent Beck I operation on September 18th, 1957, and died on October 6th, after eighteen days. This dog died on the farm similar to the above animal. Septal branch was arising from the left coronary artery at its bifurcation. Schlesinger injection study revealed / homocoronary and no intercoronary anastomosis. Arteries within the ameroids were obstructed to 70% of their lumen.

Dog No. 307 This animal underwent Beck I operation on September 19th, 1957, and died on October 12th, 1957. It

survived for only twenty-three days. On post-mortem examination the lingula was adherent to the heart. Schlesinger injection study revealed + intercoronary and + homocoronary anastomosis. Arteries within the ameroid were obstructed 92.5% of their lumen by organised thrombus. Septal branch in this case was arising from anterior descending branch.

Dog No. 94 This animal underwent Beck I operation on September 23rd and died on October 9th, 1957, sixteen days later. Septal branch was arising from the left coronary artery at its bifurcation. On post-mortem examination the upper lobe was found to be adherent and mediastinal vessels were larger and dilated. Schlesinger injection study revealed + intercoronary and + homocoronary. Arteries were obstructed 90% of their lumen, within the ameroids.

Dog No. 141 This animal underwent Beck I operation on September 27th, 1957, and died suddenly on the farm on October 19th, after twenty-two days. Septal branch was arising from the anterior descending. Schlesinger injection study revealed + intercoronary and + homocoronary anastomosis. Arteries within the ameroids were obstructed 85% of its lumen by organized thrombus.

Dog No. 136 This animal underwent Beck I operation on December 27th, 1957, and died on January 16th, 1958, after nineteen days. Septal branch was arising from the anterior descending branch. On Schlesinger injection homocoronary or intercoronaries could not be estimated well due to unsatisfactory injection. Arteries within the ameroid were obstructed up to 75% of its lumen.

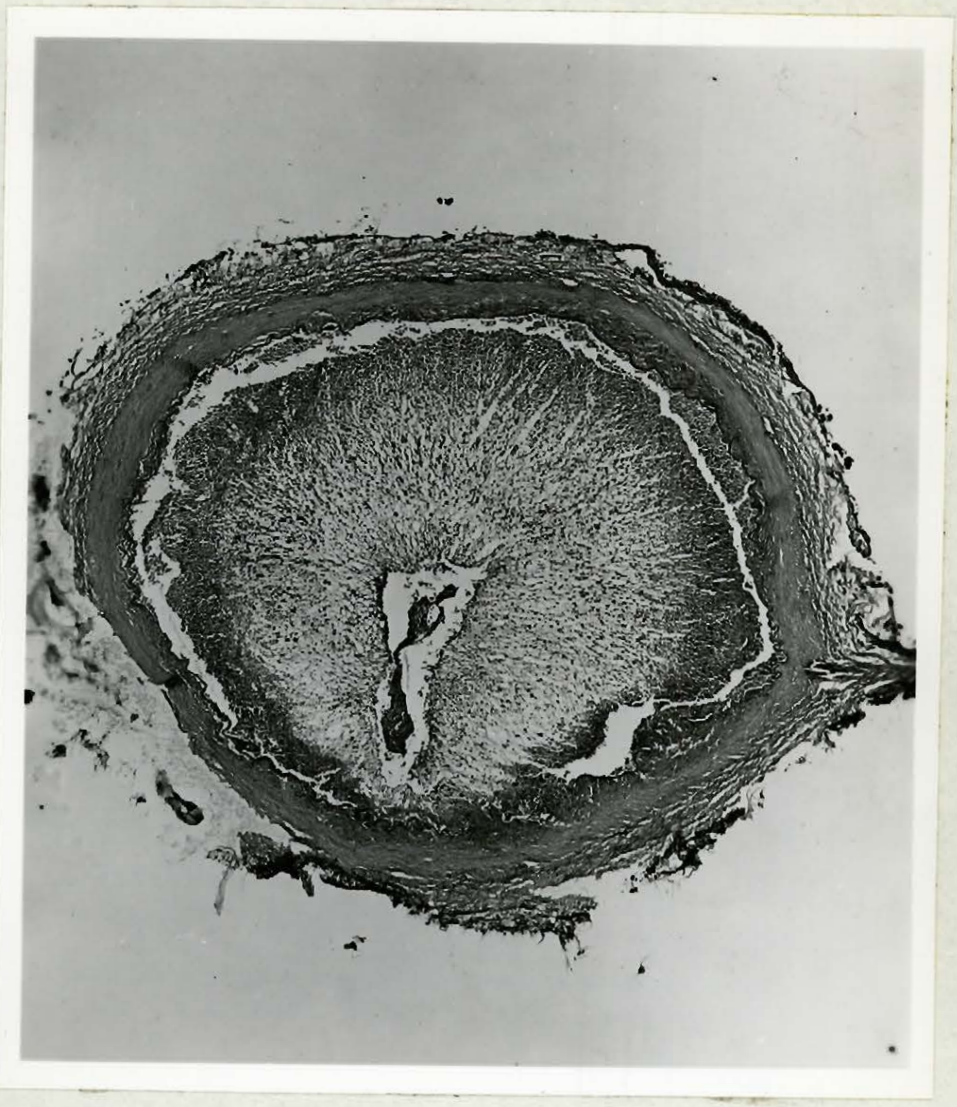

PLATE NO. 15

Dog No. 307 - Microscopic section through the anterior descending branch. Note the obstruction of its lumen by ninety percent due to an organized thrombus.

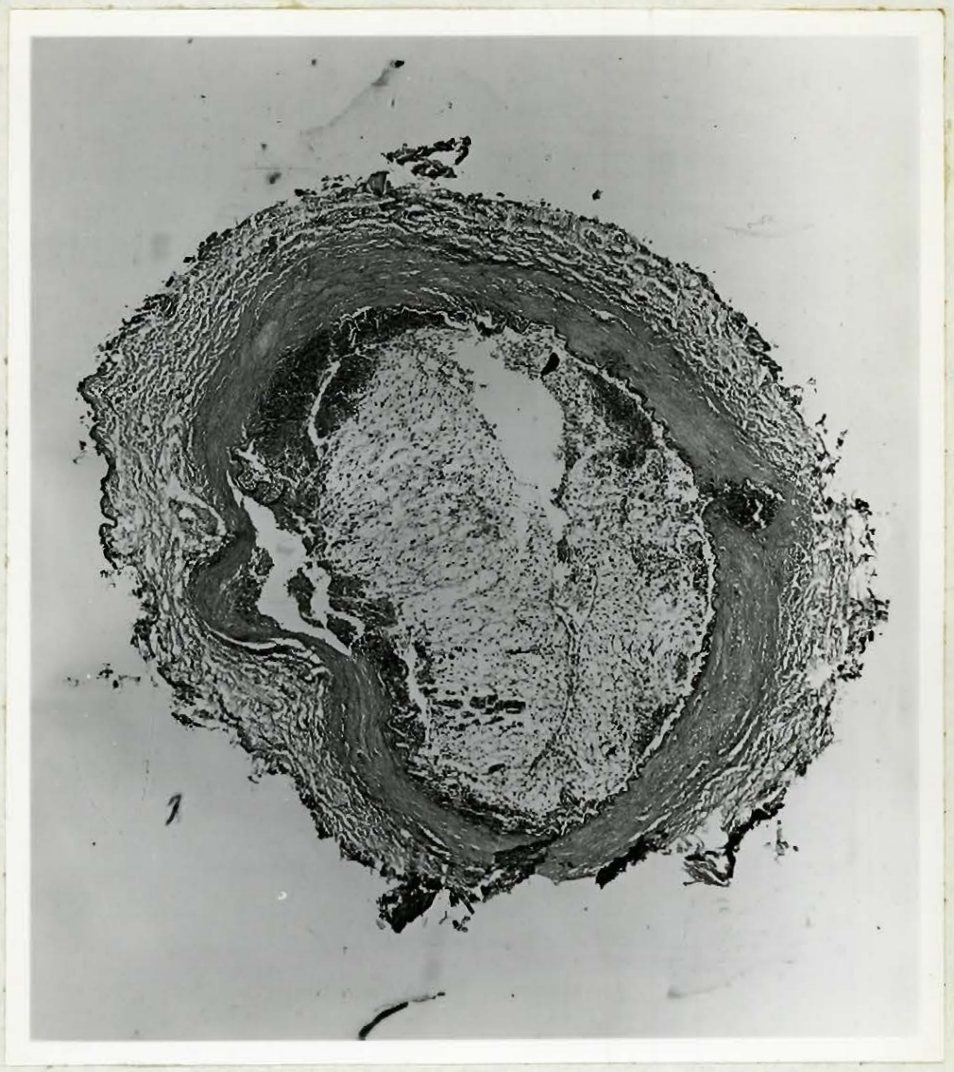

PLATE NO. 16

Dog No. 307 - Microscopic section through the circumflex branch. Note the obstruction of its lumen by organized thrombus.

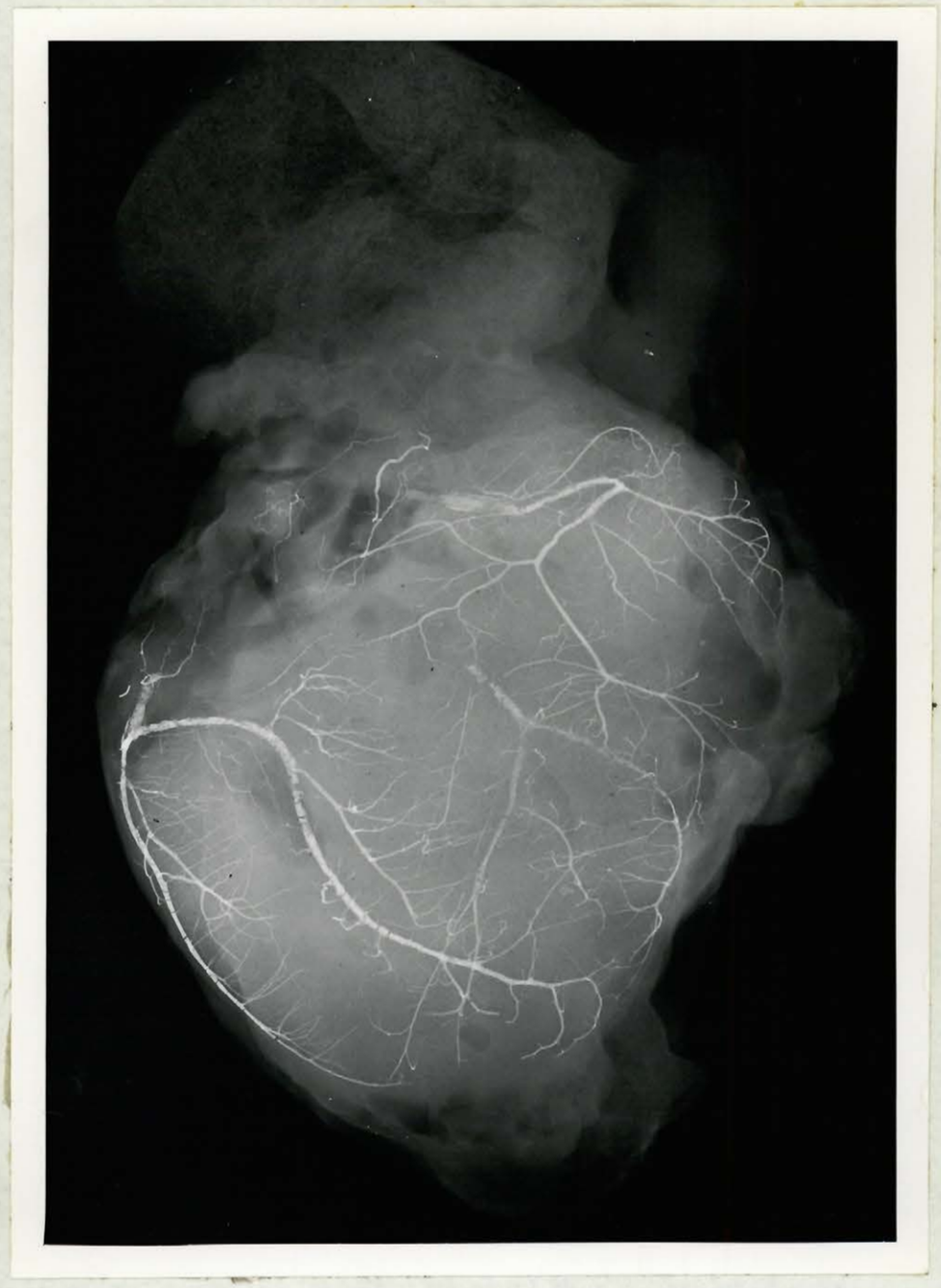

PLATE NO. 17

Dog No. 307 - X-ray study of intercoronary and homo-coronary by Schlesinger injection. P.A. view.

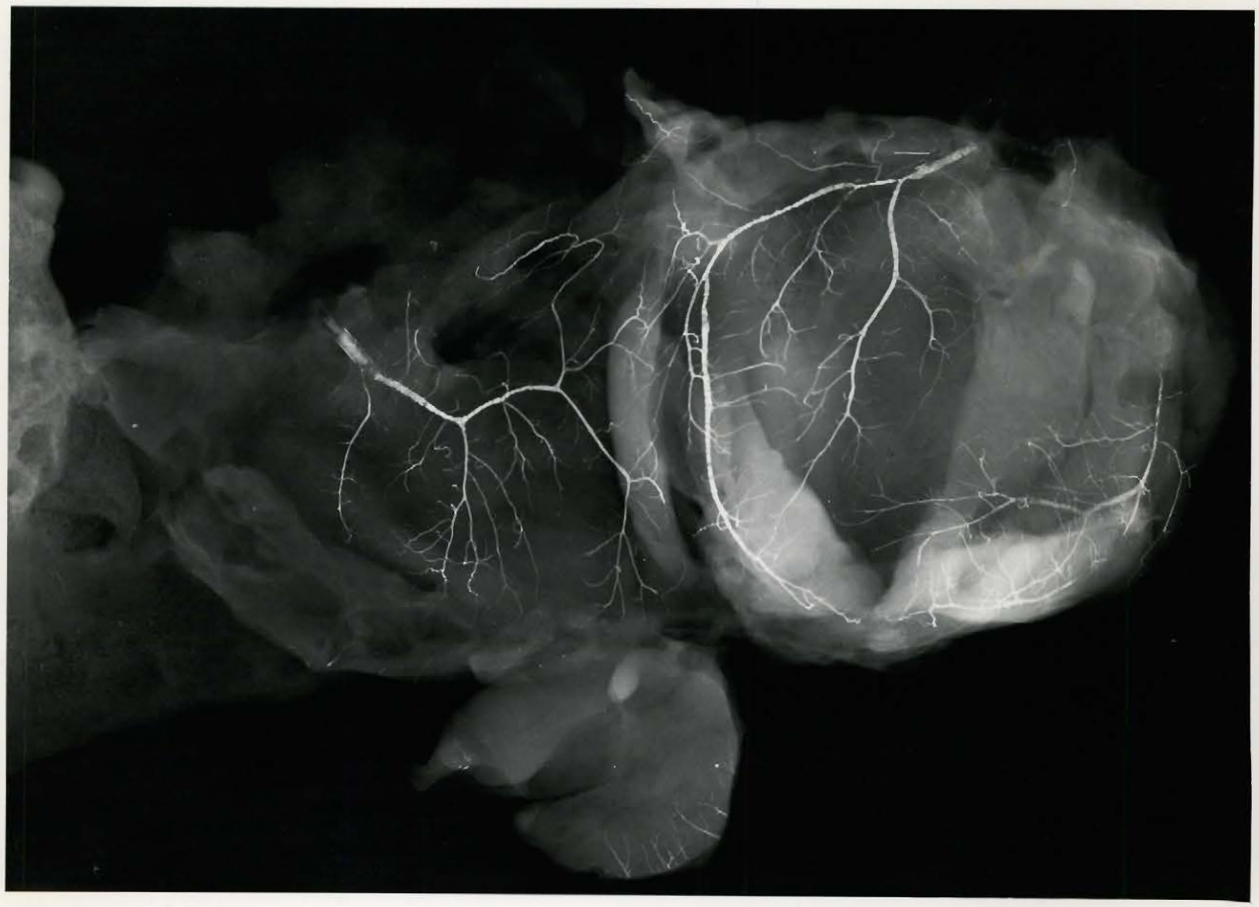

PLATE NO. 18

Dog No. 307 - X-ray study of an unrolled heart for intercoronary anastomosis. Note between circumflex branch and right coronary artery, the intercoronary connections.

SERIES C. 10 dogs weighing between 42 to 50 pounds

Internal mammary implantation into left ventricular myocardium and coronary sinus constriction up to 3 millimeters

In this series the animals are first prepared with vaselinised ameroids for producing coronary insufficiency, after which the bleeding left internal mammary artery was implanted in the left ventricular myocardium. In addition, the coronary sinus was constricted to give added benefit of collateral circulation.

Dog No. 13 This animal underwent the implant procedure with coronary sinus constriction on August 1st, 1957, and was sacrificed on April 16th, 1958, after surviving for two hundred and fifty-six days. The septal branch was arising from the anterior descending. On exploration of the left chest the internal mammary was soft and the left upper lobe was adherent to the artery and the heart. Methylene blue injected into the implanted artery revealed the patency of the artery with wide spread anastomosis. This was confirmed by Schlesinger injection study. Arteries within the ameroids were obstructed 85% of their lumen.

Dog No. 123 This animal underwent similar procedure on August 5th, 1957, and died on October 19th, 1957, after fifty-six days. On post-mortem examination artery was soft but slightly angulated due to fibrous adhesion to the chest wall.

Left lung was also adherent. Schlesinger injection study revealed open artery but no anastomosis. Septal branch was arising from the circumflex branch. Arteries within the ameroid were obstructed to 82.5% of their lumen.

Dog No. 168 This animal underwent internal mammary implantation and coronary sinus constriction on August 9th, 1957, and was sacrificed on April 25th after surviving for two hundred and thirty-six days. Arteriogram through left subclavian artery was unsuccessful. On exploration the artery was found to be soft and patent. Methylene blue easily flowed into the myocardium through excellent anastomotic channels confirmed by Schlesinger injection study. The septal branch was arising from the anterior descending branch. Arteries within the ameroid were obstructed up to 67.5% of their lumen by organized thrombus.

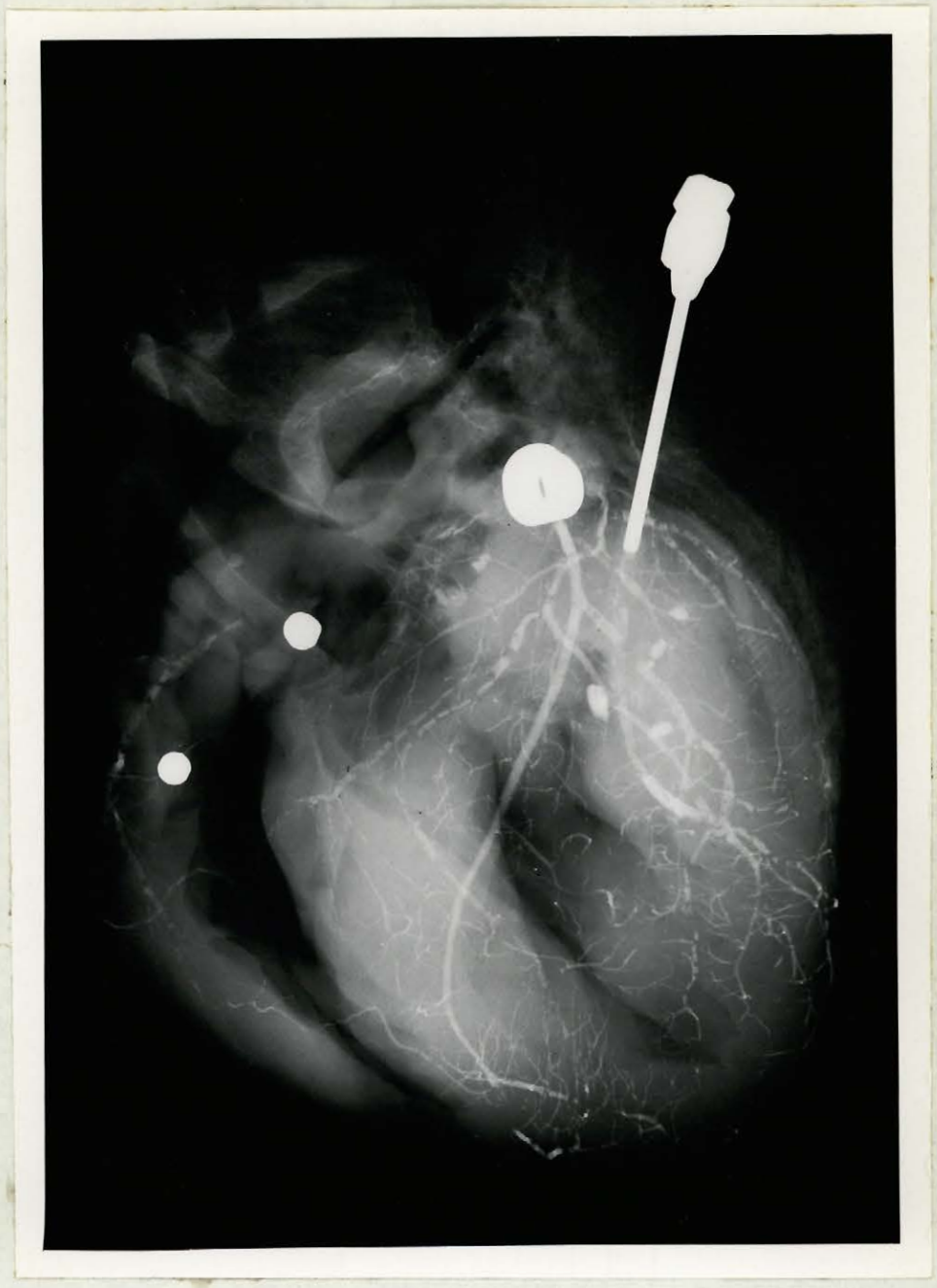

PLATE NO. 19

Dog No. 168 - X-ray study of myocardial filling by Schlesinger injection mass through the internal mammary implant. Note the injection mass in all the branches of the anterior descending and right coronary artery supplying the left and right ventricle respectively.

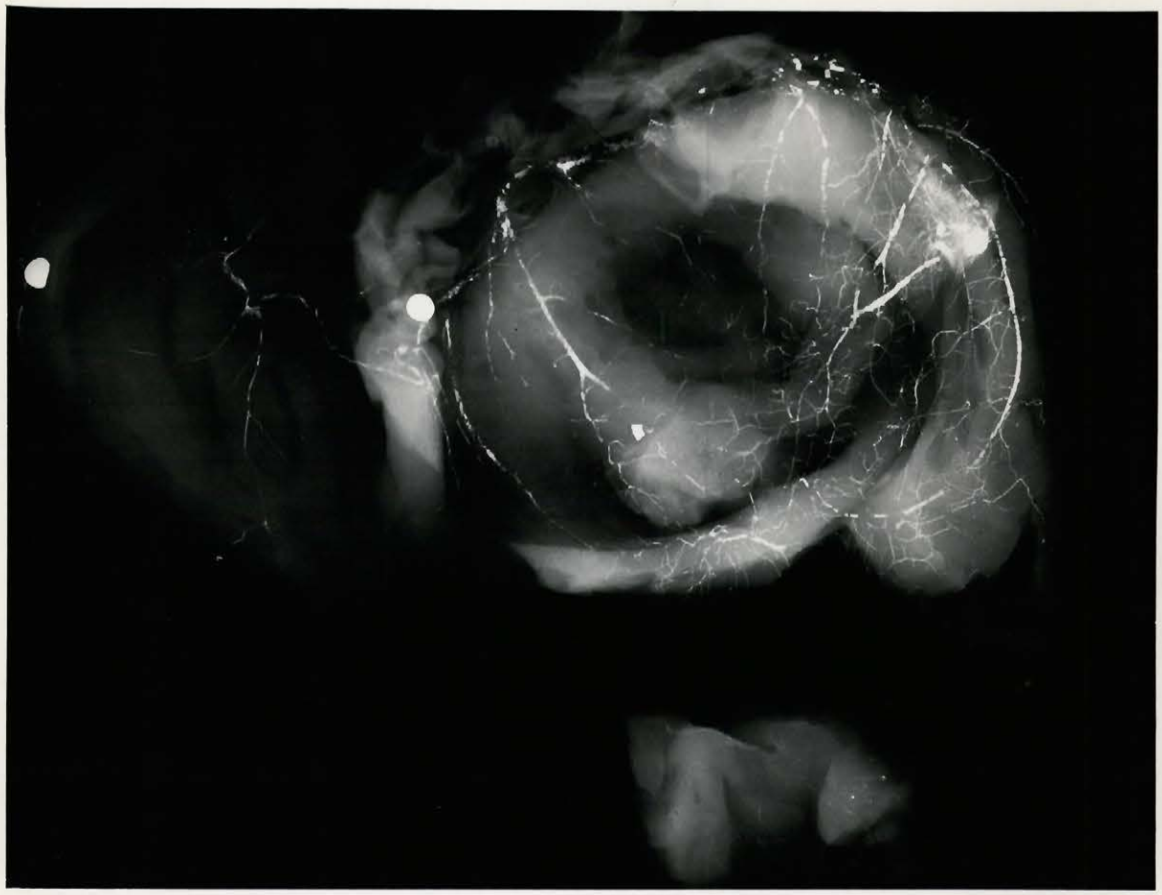

PLATE NO. 20

Dog No. 168 X-ray of an unrolled heart injected through the internal mammary implant. Note the filling of both coronary arteries. Anterior descending with its branches are filled more than others.

Dog No. 309 This animal underwent the implant procedure and coronary sinus constriction on July 29th, 1957, and was sacrificed on April 18th, 1958. Septal branch was arising from the anterior descending branch. On exploration of left chest the artery was found to be soft and straight with left upper lobe enclosing a segment of it. Methylene blue circulation through the myocardium revealing the potent artery with anastomosis. Later Schlesinger injection study confirmed the observation. Arteries within the ameroids were obstructed up to 75% of its lumen.

Dog No. 151 This animal underwent internal mammary implantation and coronary sinus constriction on August 30th, 1957, and was sacrificed after arteriogram on April 4th, 1958. It survived for two hundred and fourteen days. Septal branch was arising in this case from the left coronary artery at its bifurcation. Arteriogram through the implanted artery revealed the anastomosis with the coronary arteries by rapid film exposure. The dog died on the x-ray table at the end of arteriogram. On post-mortem examination left upper lobe was found to be adherent to the heart and the implanted artery was soft. There were many branches from the artery spreading over the adherent lung. Schlesinger injection study revealed open artery with excellent anastomosis. Arteries within the ameroids were obstructed by intimal hyperplasia up to 85% of its lumen.

PLATE NO. 21

Dog No. 151 Photograph of the specimen after injection through the left internal mammary at its origin. Note numerous extracardiac branches running over the adherent lung making a widespread anastomoses.

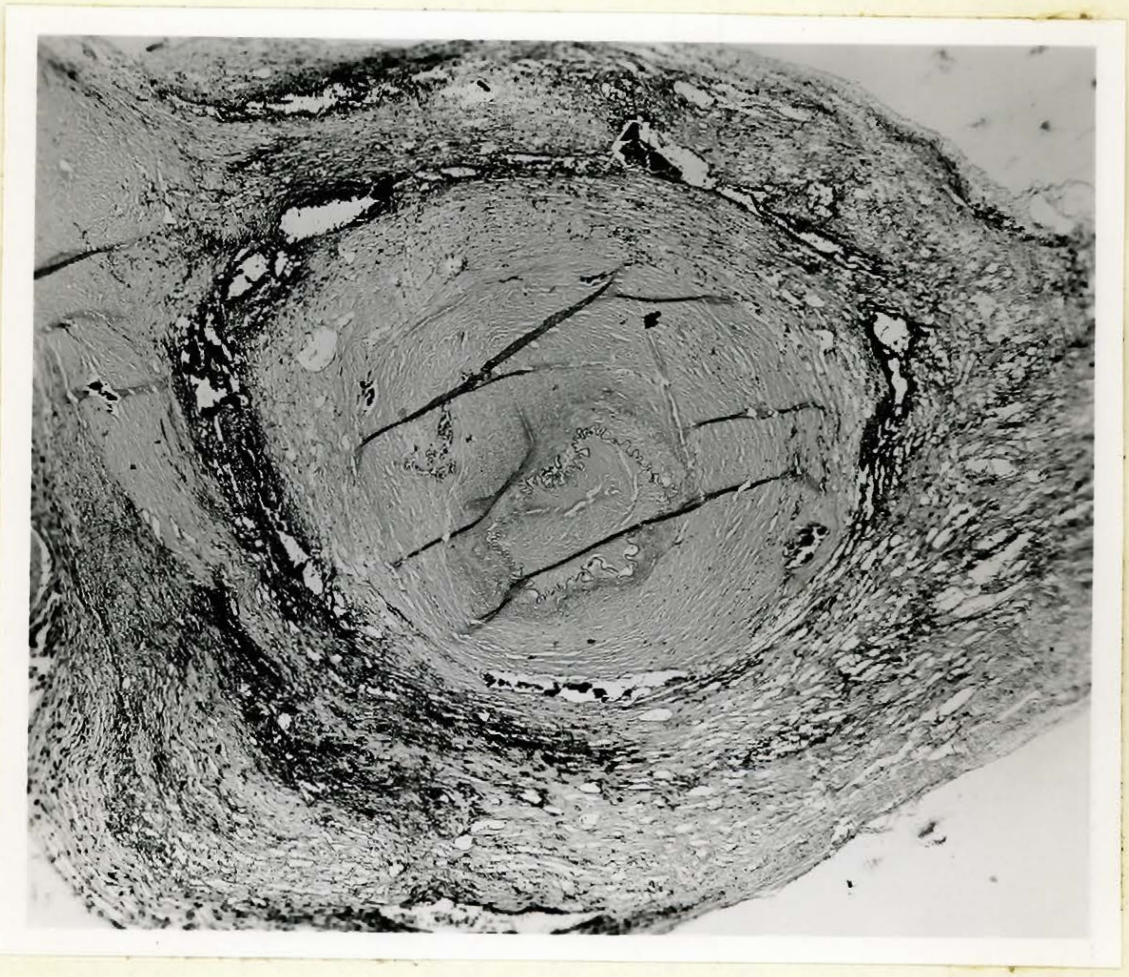

PLATE NO. 22

Dog No. 151 Microscopic section through the anterior descending branch within the ameroid constrictor. Note complete obstruction of the lumen by intimal proliferation.

PLATE NO. 23

Dog No. 151 Microscopic section through the circumflex branch within the ameroid. Note the obstruction due to intimal hyperplasia.

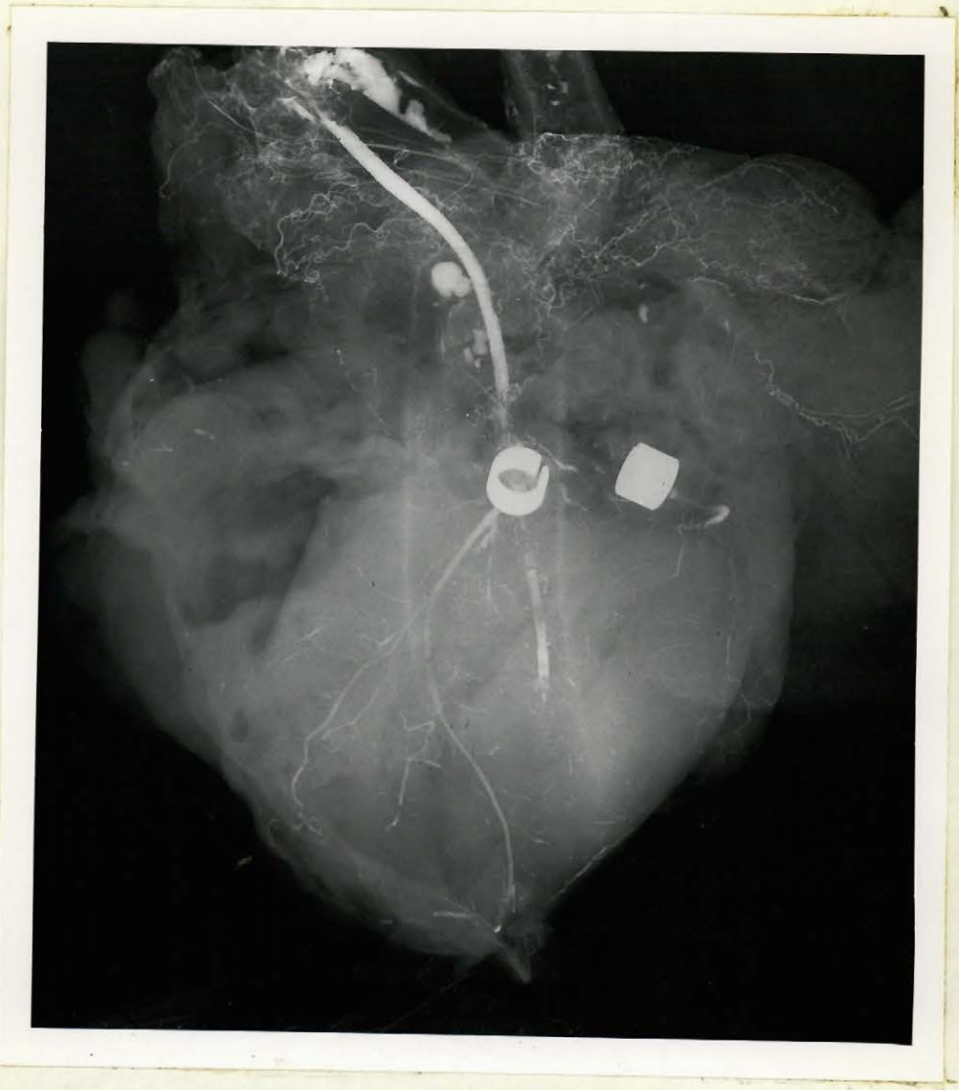

PLATE NO. 24

Dog No. 151 X-ray study of the left internal mammary implantation injected with Schlesinger mass. Note the filling of the anterior descending branch and other arterioles within the left ventricular wall. Note also the extracardiac branches.

Dog No. 175 This animal was operated on September 4th, 1957, in a similar manner and was sacrificed on April 8th, 1958. The septal branch was arising from the anterior descending branch. On exploration of the operated area a soft pulsating artery was found and methylene blue injection revealed open artery with circulating dye in the myocardium. Schlesinger injection study showed fair anastomosis. Arteries within the ameroids were obstructed by intimal hyperplasia up to 67.5% of its lumen.

Dog No. 17 This animal underwent the implantation and coronary sinus constriction operation on September 5th, 1957, and was sacrificed after one hundred and ninety-nine days on April 24th, 1958. The septal branch was arising from the anterior descending branch and on post-mortem examination the artery was soft but slightly angulated due to fibrous adhesions. On Schlesinger injection study the artery was patent with fair number of anastomoses. Arteries within the ameroids were obstructed 72.5% of its lumen.

Dog No. 301 This animal underwent a similar procedure on September 12th and was sacrificed on April 24th, 1958, surviving for two hundred and twenty-two days. At the time of sacrifice the artery was soft and pulsatile. Schlesinger injection study revealed patent artery with no anastomosis.

The artery within the ameroid was obstructed 60% of its lumen. The septal branch in this case was arising from the anterior descending branch.

Dog No. 319 This animal underwent implant and coronary sinus constriction operation on January 30th, 1958, and dropped dead on February 22nd, 1958. On post-mortem examination the implant was found to be thrombosed. Septal branch arose from the coronary artery at its bifurcation. Microscopic section of the artery was unsatisfactory for evaluating the amount of obstruction of the lumen.

Dog No. 145 This animal underwent a similar procedure on January 29th, 1958, and dropped dead on February 18th, 1958, after twenty days. On post-mortem examination the implant was thrombosed and left upper lobe was adherent. In this case plain catgut was used for ligating the internal mammary branches, which was not dissolved at the time post-mortem examination. The septal branch was arising in this case from the circumflex branch. The arteries within the ameroid were obstructed up to 95% of its lumen by intimal hyperplasia.

CARDIOPNEUMOPEXY

SERIES D

10 dogs weighing between 43 to 52 pounds

In this series the pulmonary artery to the lingula or upper lobe of the left lung was tied before grafting into phenolized myocardium of the left ventricle. All these animals also had a simultaneous application of vaselinized ameroid around the circumflex and anterior descending branch of the left coronary artery to produce coronary insufficiency.

Dog No. 25 This animal underwent the cardiopneumonopexy operation on October 9th, 1957, and was sacrificed on April 4th after extracoronary angiography. The animal survived for one hundred and seventy-five days. The septal branch was arising from the anterior descending branch. An arteriogram did not visualize the bronchial artery supplying the left ventricular myocardium. Schlesinger injection study of the coronary tree revealed + + + intercoronary anastomosis. No Schlesinger mass visualized in the adherent lung by retrograde injection. Microscopic study of the junctional area of the adherent lung and heart suggests of chronic inflammatory reaction with fibrosis. No vascular connections were visualized. The arteries within the ameroids were obstructed by 65% of its lumen by intimal hyperplasia.

Dog No. 329 This animal underwent cardiopneumopexy on October 3rd, 1957, and dropped dead on October 27th, after twenty-four

days. The septal branch arose from the anterior descending branch. Schlesinger mass injection through the cannulated pulmonary artery did not visualize the myocardial supply. Arteries within the ameroids were obstructed 100% of its lumen by thrombus formation.

Dog No. 120 This animal underwent cardiopneumonopexy operation on October 26th, 1957, and died on November 25th, 1957. The septal branch was arising from the left coronary artery at its bifurcation. The pulmonary artery of the lingula was cannulated and injected with Schlesinger mass. There was no visible injection mass in the left ventricular myocardium. Arteries within the ameroids were obstructed by 75% of its lumen by intimal hyperplasia.

Dog No. 135 This animal underwent cardiopneumopexy on September 27th, 1957, and died on October 8th, 1957, after twenty-two days. On post-mortem examination the lung was found to be separated from the heart. The septal branch was arising from the circumflex branch. Arteries within the ameroid were obstructed 60% of its lumen. No injection study was carried out.

Dog No. 358 This animal underwent cardiopneumopexy on October 10th, 1957, and died on November 13th, 1957, surviving for thirty-three days. On post-mortem examination the grafted lobe was found to have pneumonia, confirmed histologically. Septal branch was arising from the anterior descending branch. Arteries within the ameroid were obstructed 80% of its lumen. No injection study was done.

Dog No. 350 This animal underwent cardiopneumopexy on October 3rd, 1957, and died on October 24th, as many of our control animals. On post-mortem examination there was about 250 cc of old blood in the pleural cavity. Retrograde injection of the coronary tree by Schlesinger mass did not reveal any vascular connections between the lung and the heart. In this case the ameroid was proximal to the septal branch which arose from the anterior descending branch. Arteries within the ameroids were obstructed to 65% of its lumen.

Dog No. 94 This animal underwent cardiopneumopexy on December 4th, 1957, and was sacrificed on April 23rd, 1958, after one hundred and thirty-nine days. An arteriogram did not reveal injection of bronchial artery. Schlesinger injection of the coronary tree revealed + + + intercoronary anastomosis. The septal branch arose from the anterior descending branch. Arteries within the ameroids were obstructed 77.5% of its lumen.

Dog No. 106 This animal underwent cardiopneumopexy on January 3rd, 1958, and died on January 28th, after twenty-five days. On post-mortem examination the lung was found not to be well adherent to the heart. Schlesinger injection through the pulmonary artery did not show any vascular connections between the heart and the lung. Septal branch arose from the left coronary artery. Arteries within the ameroids were constricted 50% of its lumen.

Dog No. 126 This animal underwent cardiopneumopexy on January 16th, 1958, and died on January 30th, 1958. On post-mortem examination the adherent lobe was found to have pneumatic consolidation. Microscopic examination revealed no vascular connection but there were sign of inflammatory reaction in the muscle. The septal branch arose from the left coronary artery at its bifurcation. Arteries within the ameroid were obstructed 75% of its lumen.

In addition four other animals died of distemper and other lung complications which are not included in this series.

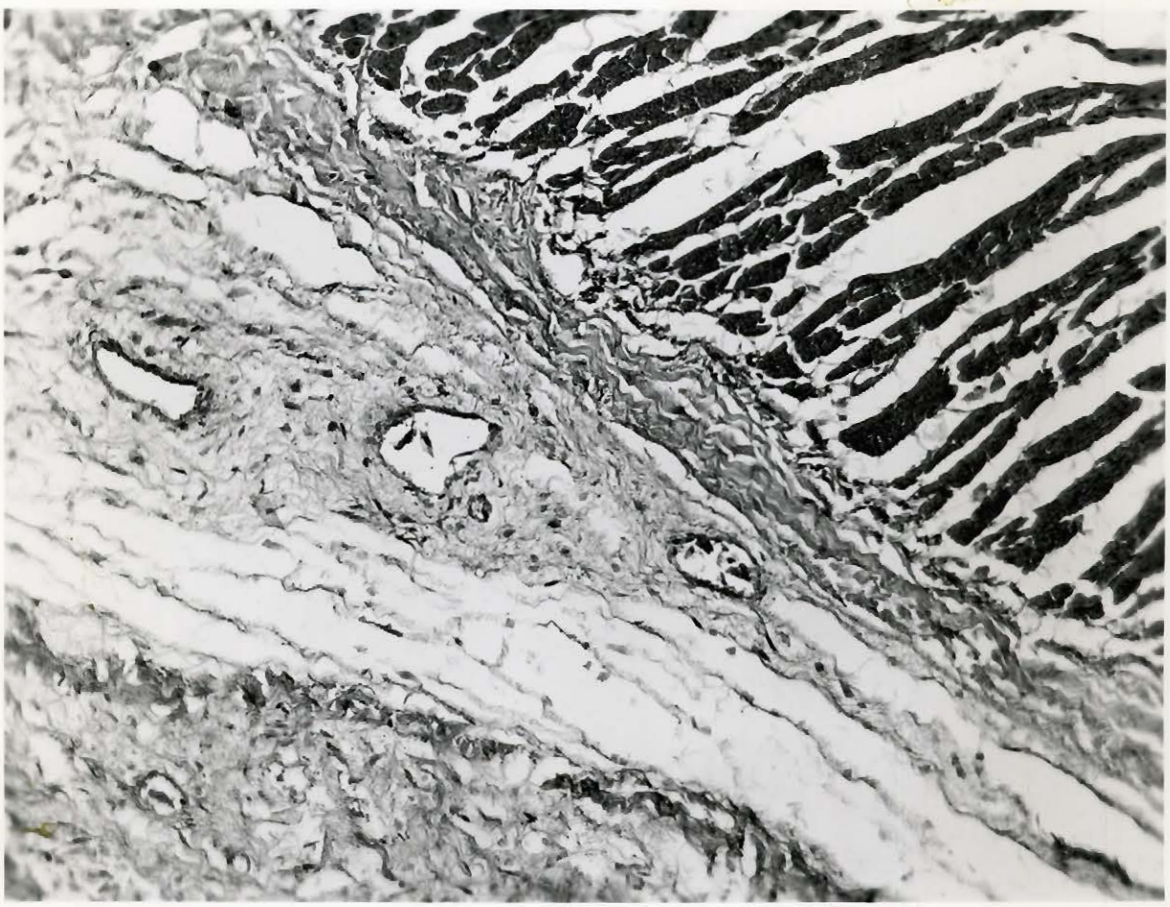

PLATE NO. 25

Dog No. 126 Microscopic section of the junctional area between the lingula and left ventricular muscle. Note thickened epicardium with chronic inflammatory reaction. No vascular communications between the graft and myocardium.

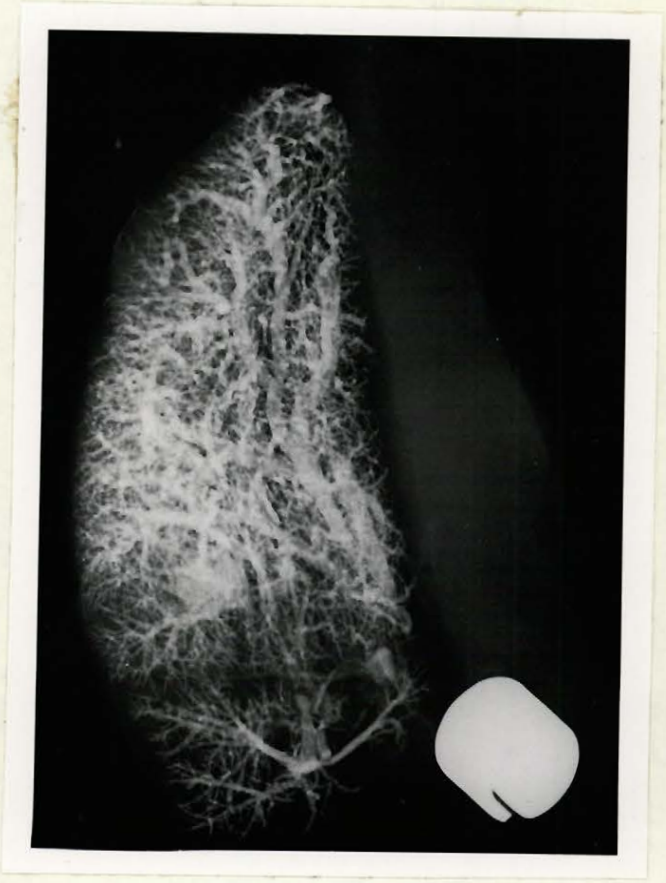

PLATE NO. 26

Dog No. 120 X-ray study of Schlesinger injection through the pulmonary artery of the adherent lung. Note no vascular channels go into the left ventricular myocardium on right.

PLATE NO. 27

Dog No. 350 X-ray study of intercoronary anastomosis in cardiopneumopexy. Note ≠ ≠ intercoronary anastomosis.

SERIES E. IVALON TUBE IMPLANTATION FROM THE AORTA INTO THE LEFT VENTRICULAR MYOCARDIUM

10 dogs weighing between 42 to 52 pounds

In this series specially prepared Ivalon sponge tubes were anastomosed to the side of the aorta and the bleeding distal segments were implanted into the left ventricular myocardium after making a few holes on its side.

Dog No. 94 This animal underwent Ivalon tube implantation operation on November 14th, 1957, and died on December 26th, 1958. The septal branch arose from the circumflex. On post-mortem examination left upper lobe was found to be adherent to the heart and the Ivalon Tube. The tube was partially thrombosed with no anastomotic channels in the myocardium. Arteries within the ameroid were obstructed up to 70% of its lumen.

Dog No. 352 This animal underwent Ivalon tube implantation operation on November 7th, 1957, and died on November 30th, after twenty-three days. The septal branch arose from the anterior descending branch. On post-mortem examination the Ivalon tube was found to be collapsed and thrombosed inside the myocardium. Arteries within the ameroid were obstructed up to 77.5% of its lumen. There were areas of gross infarction at the apex of the heart.

Dog No. 126 This animal underwent Ivalon tube implantation on November 11th, 1957, and died on December 4th, 1957. The ameroid was placed proximal to the septal branch arising from the anterior descending. On post-mortem examination the Ivalon tube was found to be thrombosed from the anastomotic site. Arteries within the ameroid were obstructed 55% of its lumen.

Dog No. 160 This animal underwent Ivalon tube implantation operation on November 15th, 1957, and died on December 6th, 1957. The septal branch arose from the left coronary artery at its bifurcation. On post-mortem examination the synthetic tube was thrombosed beyond the anastomotic site and the upper lobe was adherent to the tube. Arteries were obstructed 80% of its lumen by organized thrombus.

Dog No. 362 This animal underwent Ivalon tube implantation operation on November 4th, 1957, and died on December 4th, 1957. Ameroid was placed proximal to the septal branch which arose from the anterior descending branch. On post-mortem examination the Ivalon tube was found to be partially thrombosed starting at the anastomotic site with the aorta. Arteries within the ameroid were obstructed up to 60% of its lumen.

Dog No. 321 This animal underwent Ivalon tube implantation on October 29th, 1957, and died on November 26th. The septal branch was arising from the anterior descending branch. On post-mortem examination the Ivalon tube was found to be thrombosed. Arteries within the ameroid were obstructed 100% by intimal hyperplasia.

Dog No. 326 This animal underwent Ivalon tube implantation operation on December 9th, 1957, and died on December 29th, 1957. The septal branch was arising from the anterior desdending branch. On post-mortem examination the Ivalon tube was thrombosed completely. The arteries were obstructed 67.5% of its lumen within the ameroids.

Dog No. 339 This animal underwent the Ivalon tube implantation procedure on November 8th, 1957, and died on November 24th, 1957. Septal branch arose from the circumflex branch. On post-mortem examination the implant was found to be completely thrombosed beginning at the anastomosis. Arteries within the ameroid were found to be obstructed 75% of its lumen.

Dog No. 314 This animal underwent Ivalon tube implantation operation on November 14th, 1957, and died on February 26th, 1958. The septal branch arose from the anterior descending branch. On post-mortem examination the Ivalon tube

was found to be thrombosed. On Schlesinger injection study of the coronary tree ∕ ∕ homocoronary and ∕ ∕ intercoronary anastomosis was found. The arteries within the ameroid were obstructed 60% of its lumen.

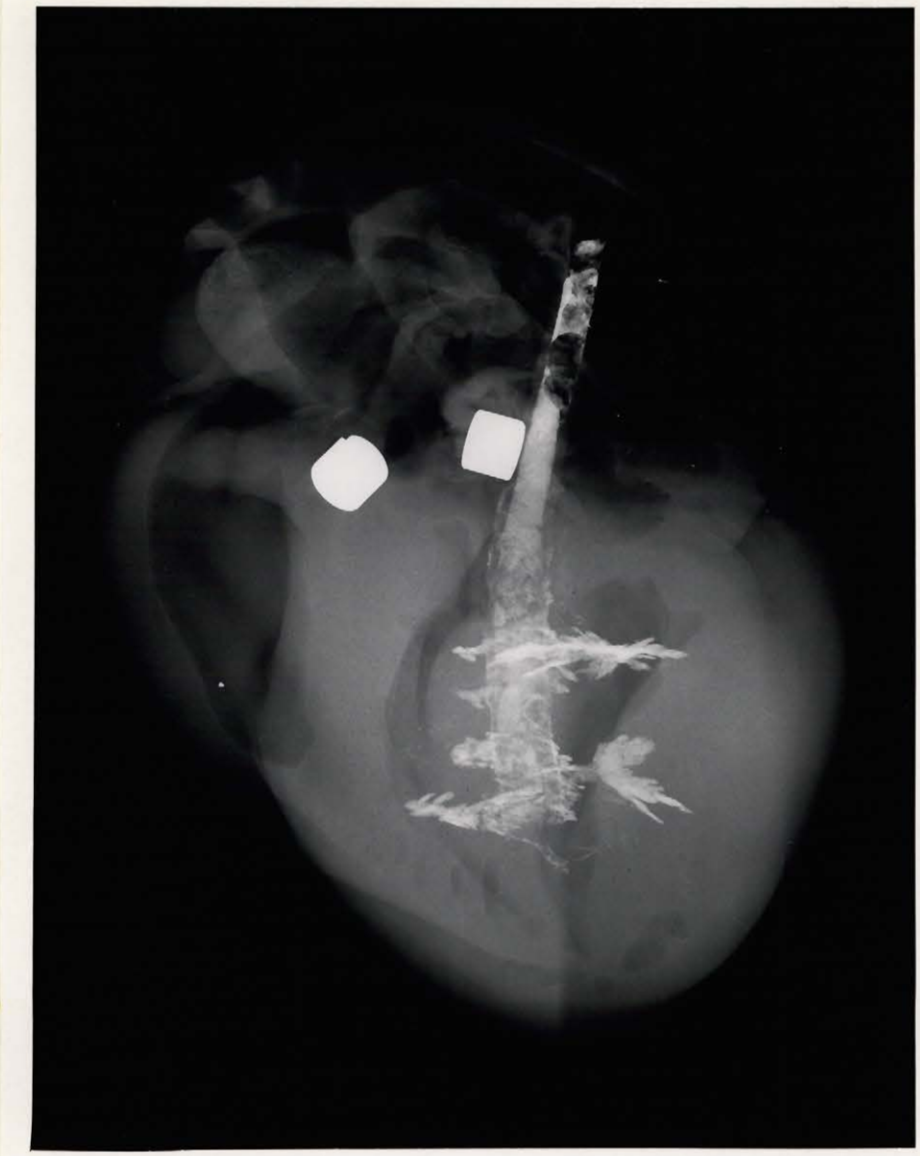

PLATE NO. 28

Dog No. 94 Schlesinger injection through the Ivalon tube implant. Note patent graft but no anastomosis.

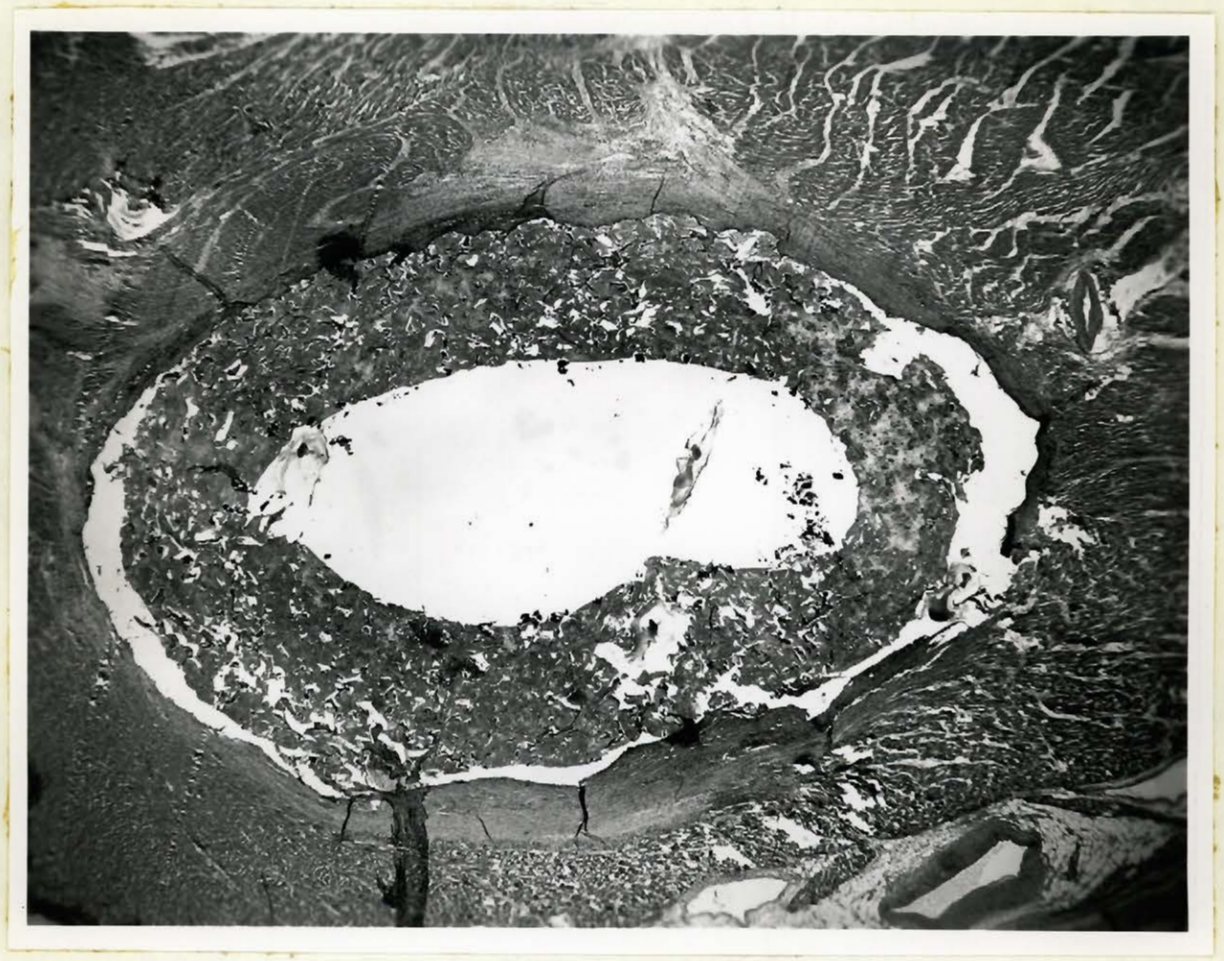

PLATE NO. 29

Dog No. 160 Microscopic section of Ivalon tube through the myocardial tunnel. Note the uneven surface of the Ivalon tube and myocardial fibrosis around it.

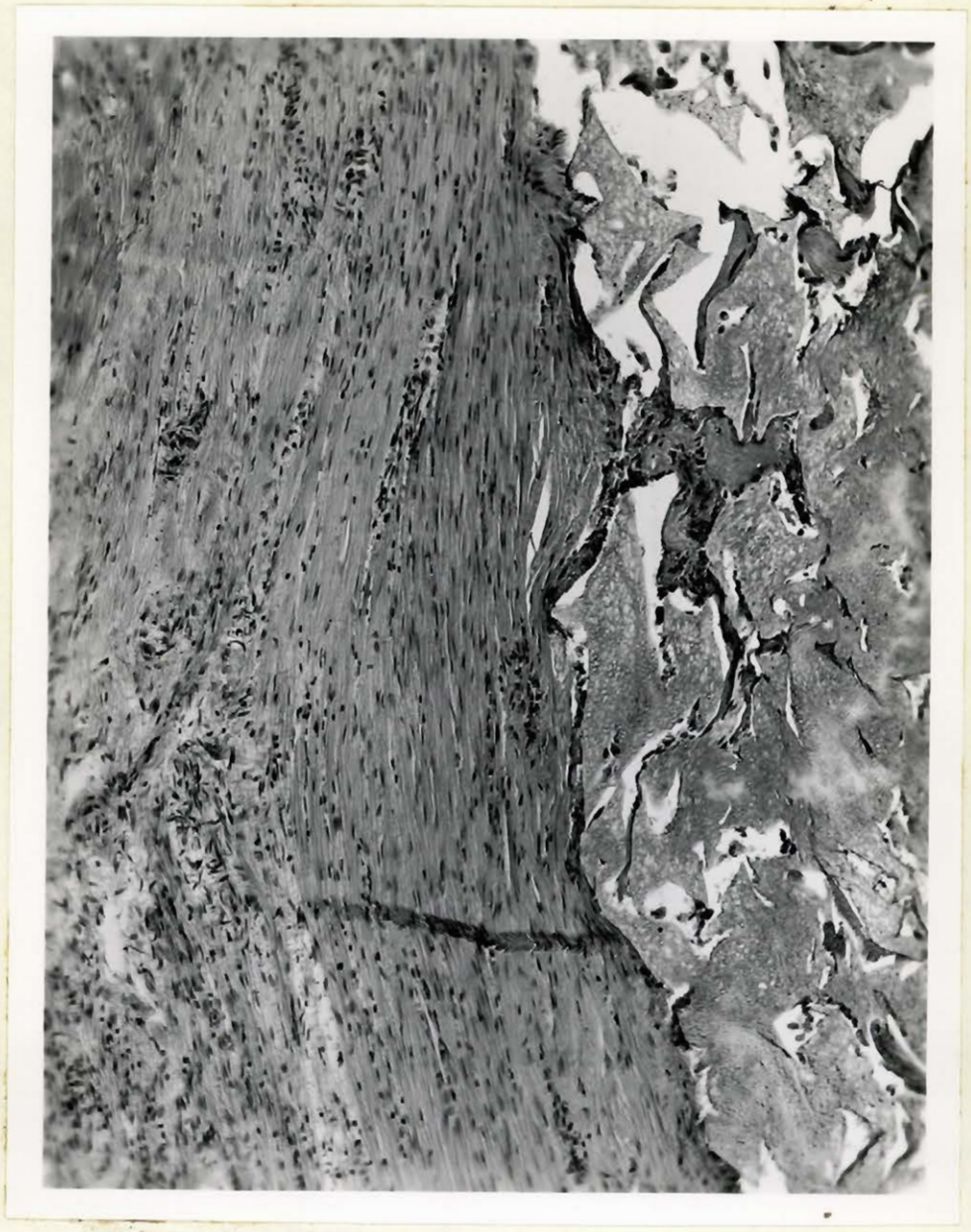

PLATE NO. 30

Dog No. 160 Microscopic section of the myocardium around the Ivalon tube implant. Note chronic inflammatory reaction in the myocardium with fibroblasts adjoining the sponge.

SERIES F- INTERNAL MAMMARY LIGATION - AS MODIFIED BY DR. BLALOCK.

Dogs weighing between 42 to 50 lbs.

Dog No. 171, 354, 153, 119, 324, 334, 353, 23, 120, 17 were operated on for left internal mammary artery ligation in the second interspace for evaluation of its benefit in coronary insufficiency produced by gradual occlusion by ameroids. All the branches of the subclavian artery proximal and distal to the origin of the left internal mammary were ligated to gain the maximum hypertensive effect in the pericardiophrenic branch which was also ligated near the diaphragm. The average survival of these animals was 25 days, the same as the control series. The manner of death was also similar to the control series.

On post-mortem examination the pericardiophrenic branch does not seem to be larger than at the initial operating time. This branch is also very variable from small to moderate size in vivo. By injection of India ink through the divided internal mammary artery, the pericardiophrenic with its branches could be traced as far as the small capillaries over the aorta and pulmonary artery. This was only formed in dogs No. 354, 324 and 23. There was no ink in the coronary arterial system of the left ventricle as shown by other authors. There were larger

branches than the pericardiophrenic from the left internal mammary artery proximal to the second interspace supplying the mediastinal fat. These vessels were usually more readily injected than the pericardiophrenic which arises just at the origin of the internal mammary artery from the subclavian. artery.

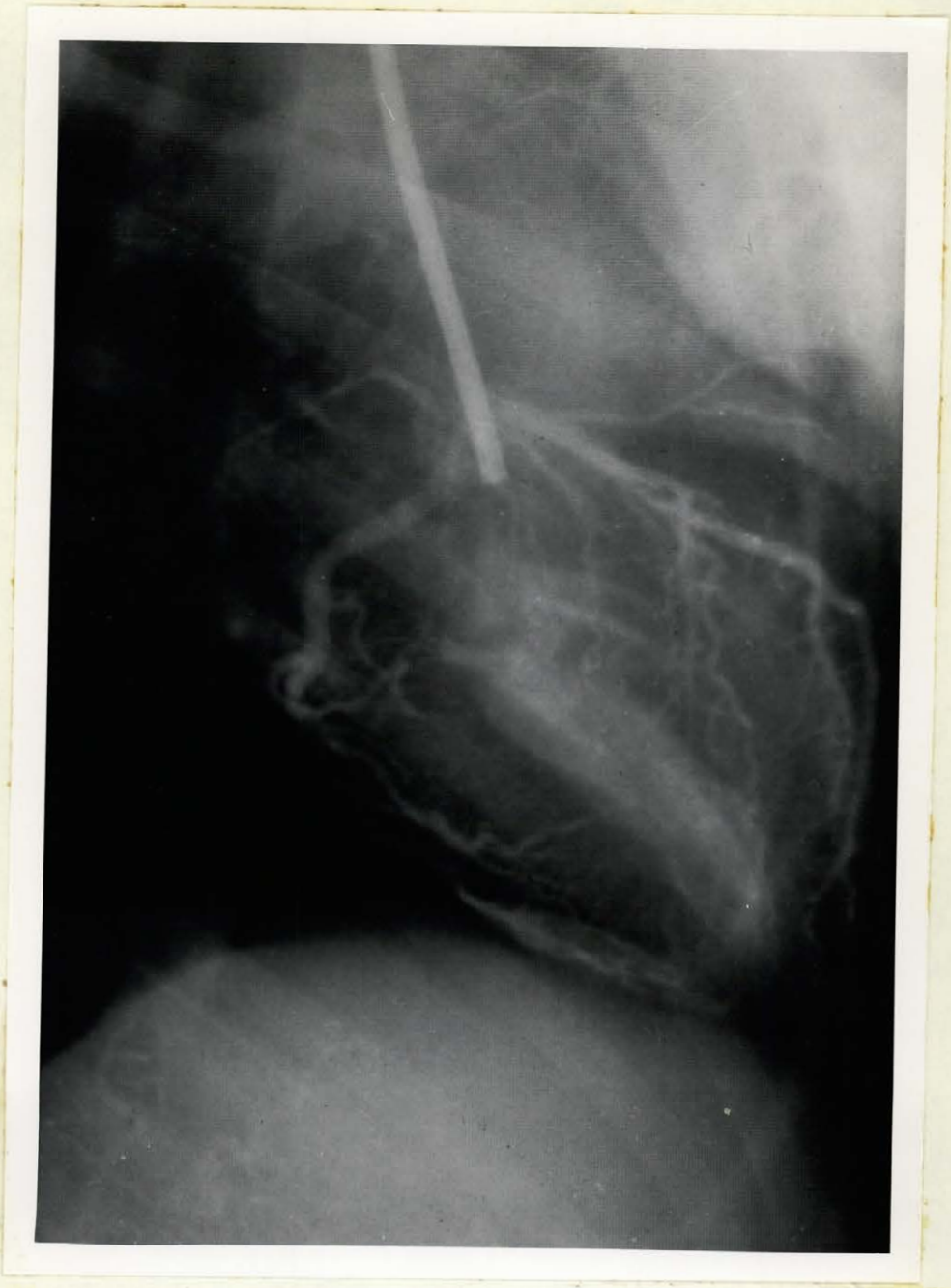

PLATE NO. 31

Normal Dog Coronary arteriogram through left common carotid artery. Note vizualisation of all the main branches of left coronary artery and main trunk of right coronary artery. Catheter tip has slipped inside after injection.

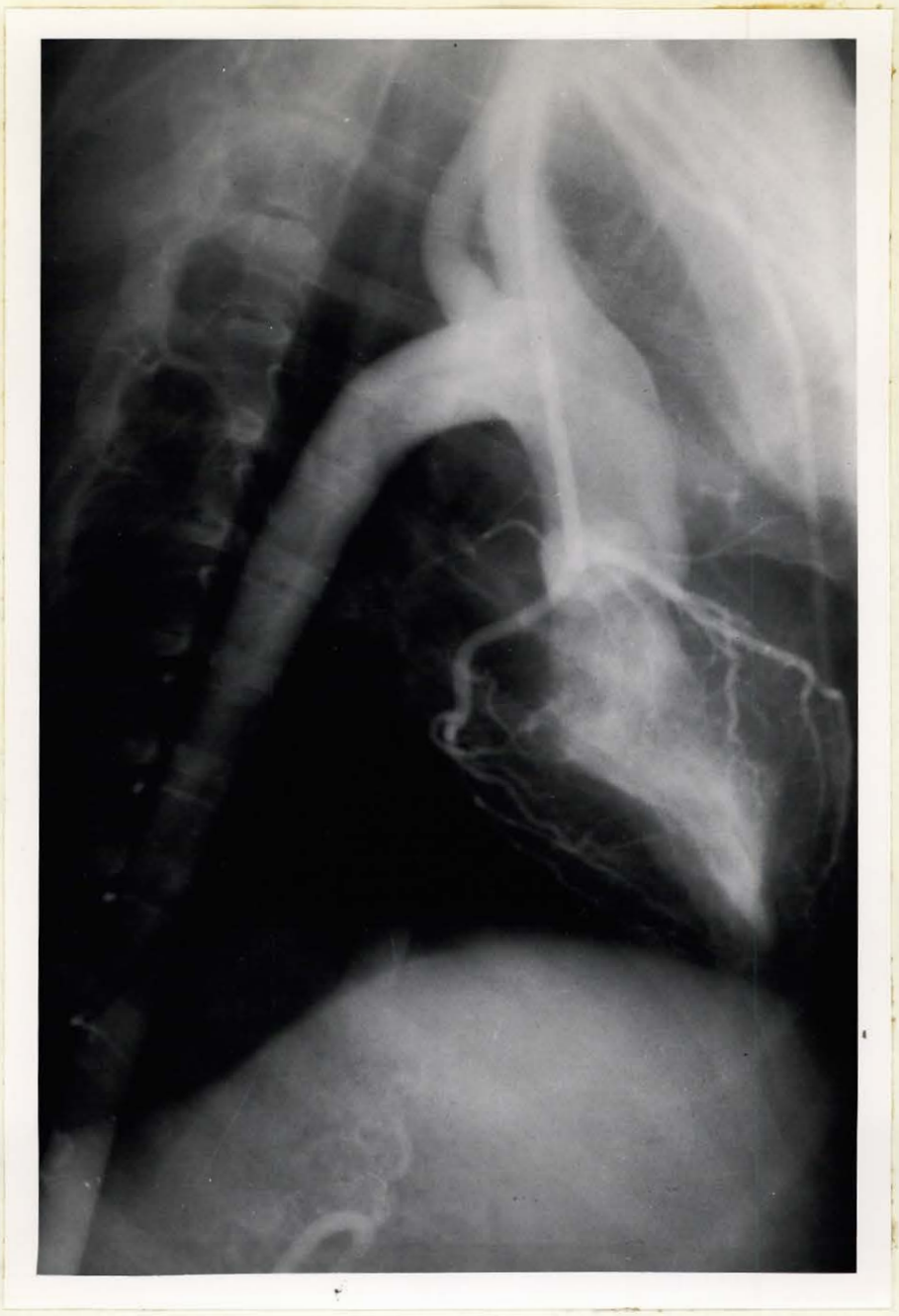

PLATE NO. 32

Normal Dog Another view of normal coronary arteriogram.

Note visualization of both coronaries.

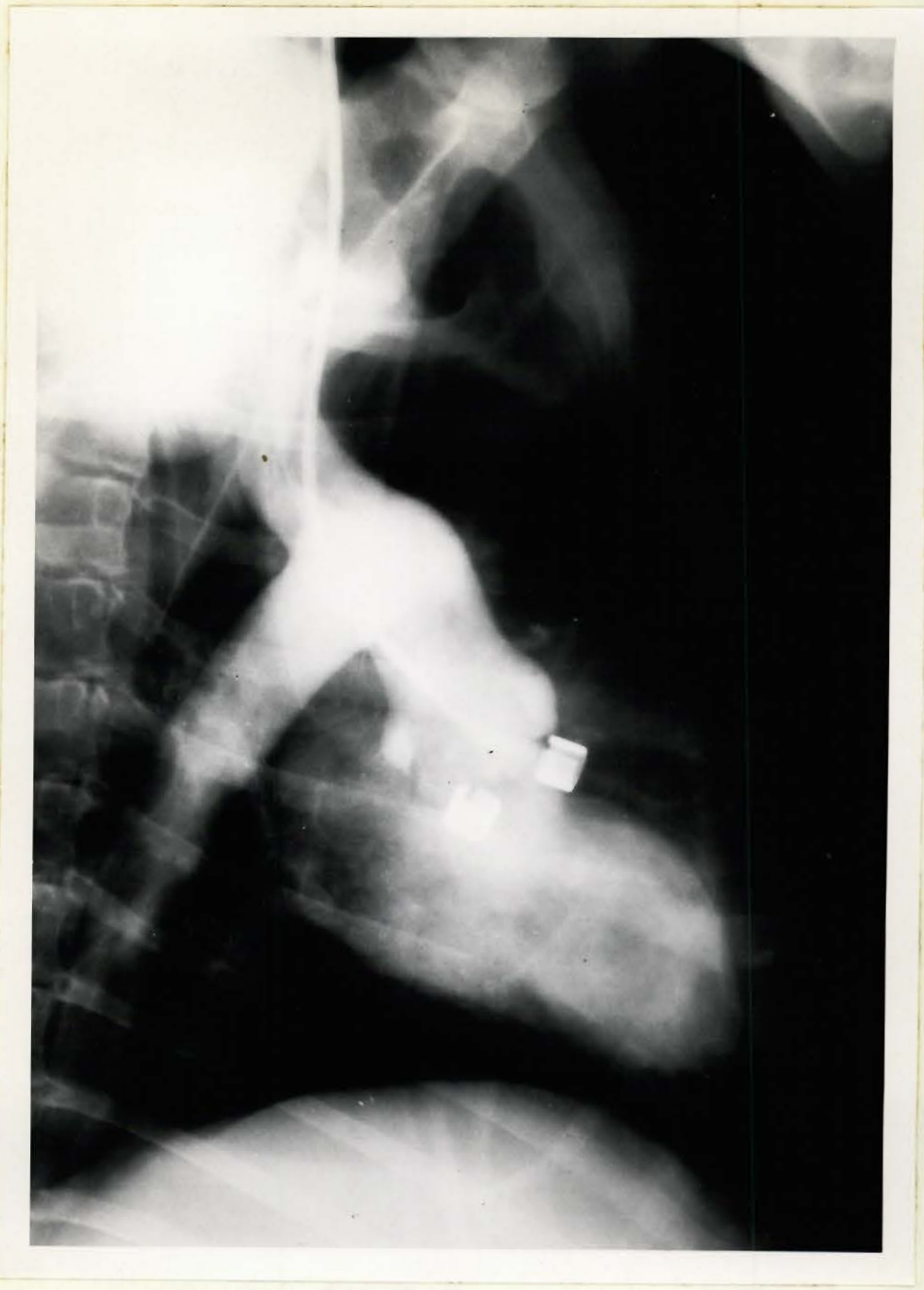

PLATE NO. 33

Dog No. 153 Coronary arteriogram in a dog with vaselinized ameroid constrictors around the anterior descending and circumflex branch. Note visualization of right coronary artery but there is no dye passing through circumflex and very little through the anterior descending branch.

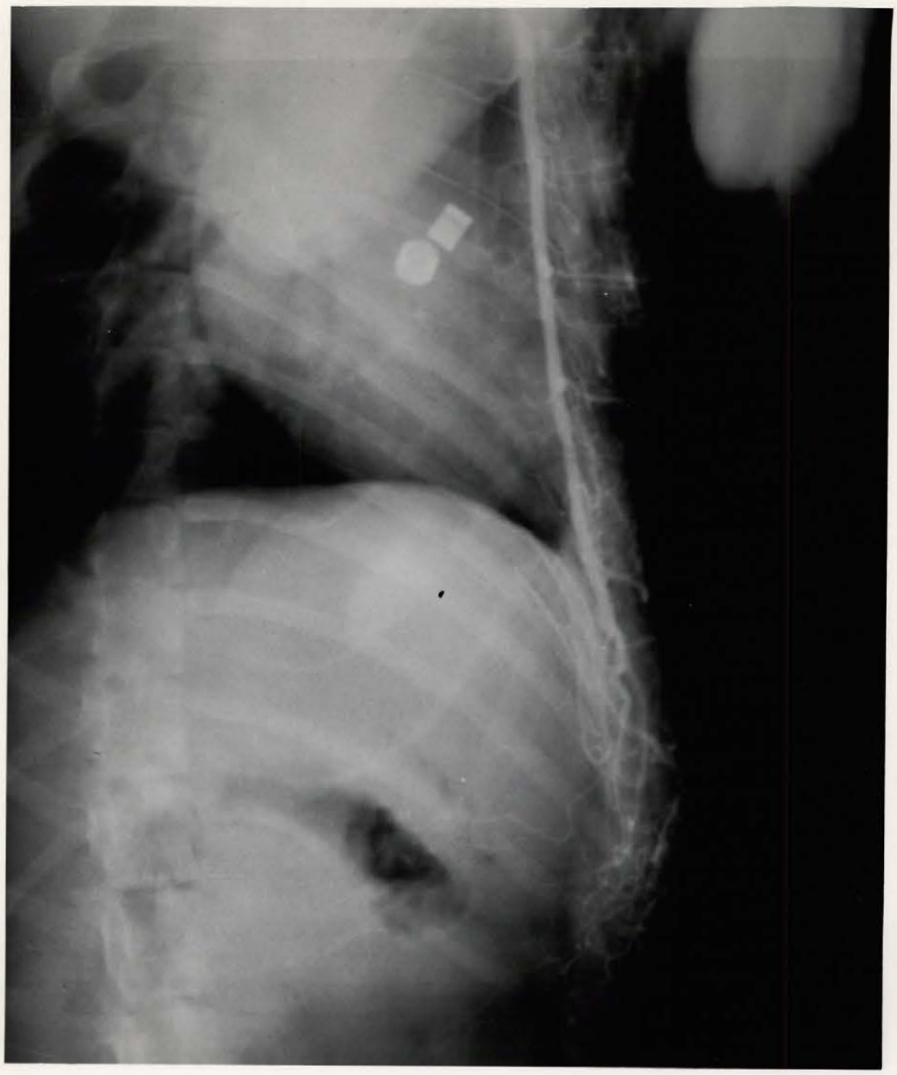

PLATE NO. 34

Dog No. 313 Angiographic study of extracoronary vascular supply of the left ventricular myocardium. Note left internal mammary with all its branches visualized but no dye goes into the myocardium.(Beck I operation.)

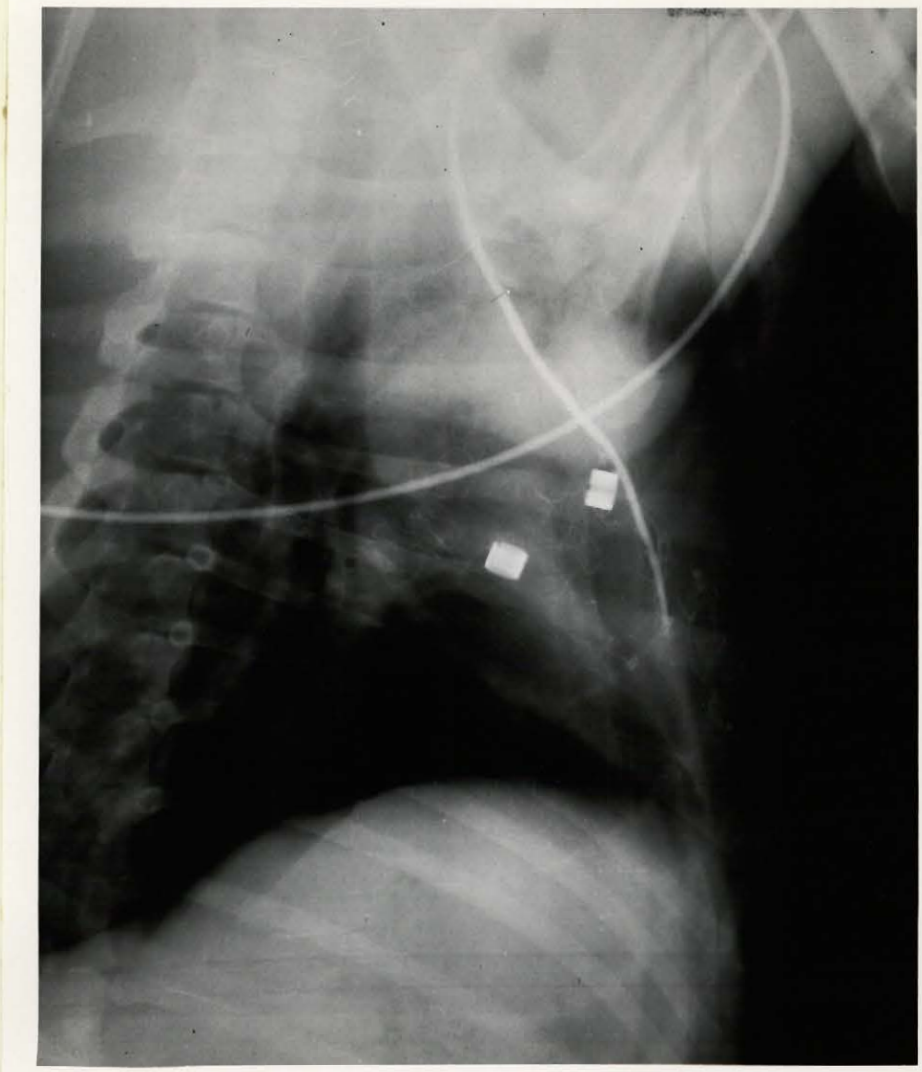

PLATE NO. 35

Dog No. 151 Extracoronary arteriogram through left internal mammary artery. Note the dye in the patent artery visualized inside the left ventricular myocardial tunnel.

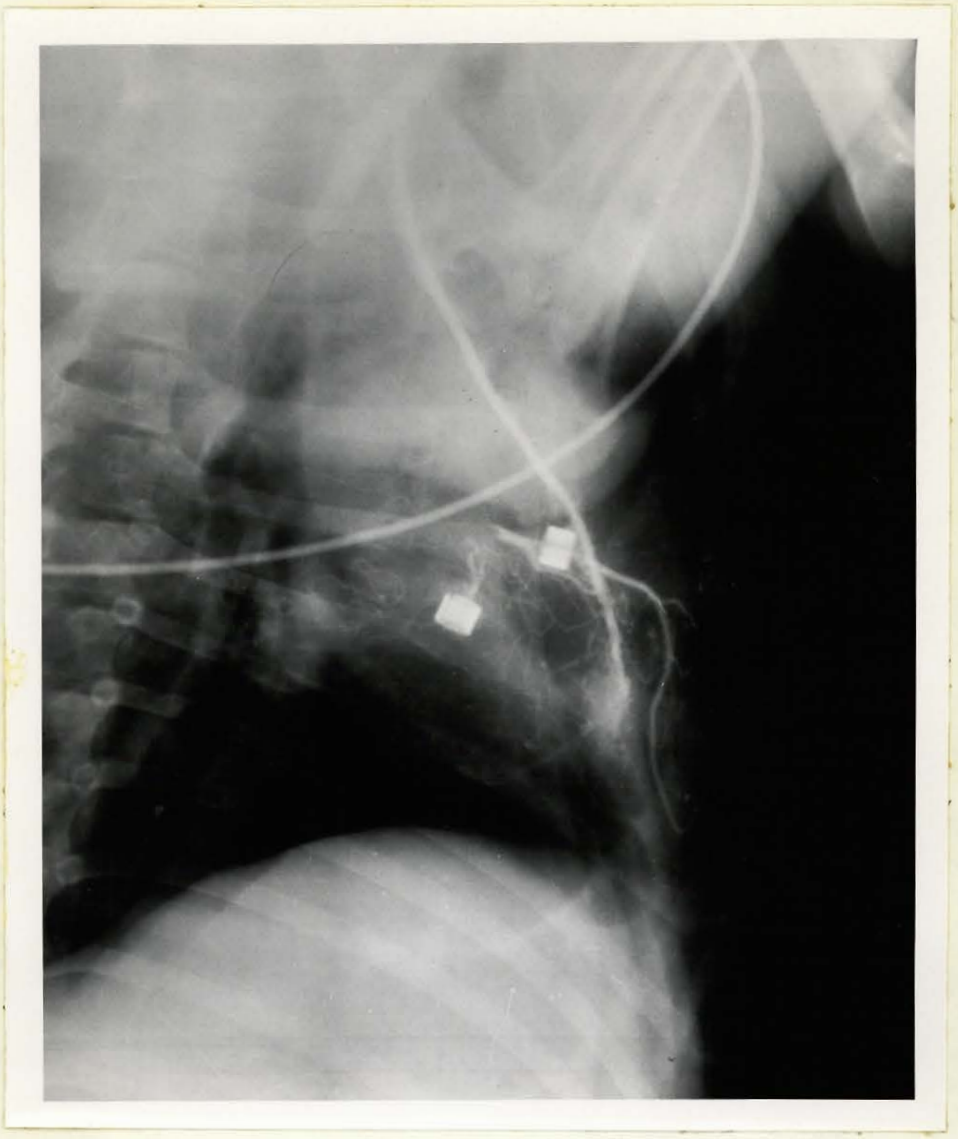

PLATE NO. 36

Dog No. 151 Continuation of extracoronary arteriogram through the left internal mammary artery. Note the dye in the anterior descending branch in communication by arteriolar anastomosis. Also note the septal branch arising proximal to the ameroid is in communication with the implant.

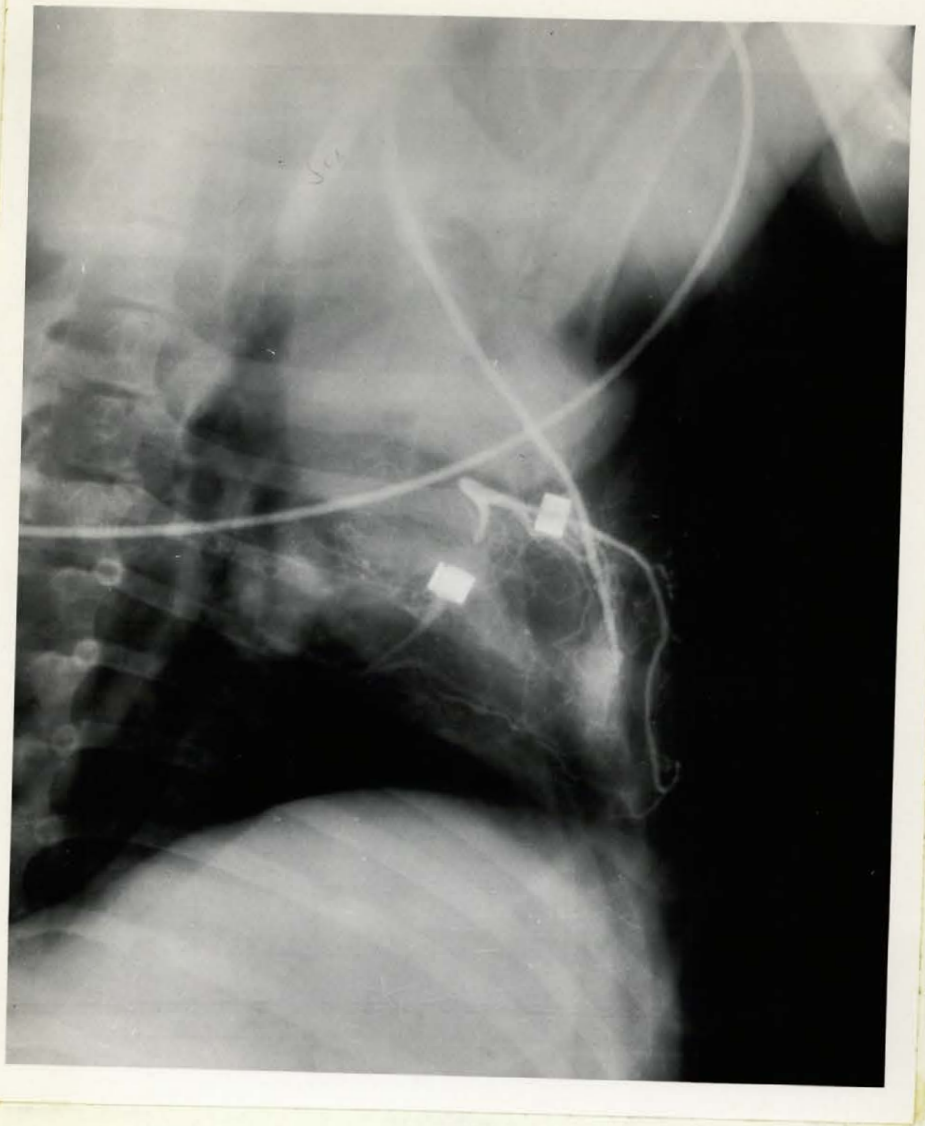

PLATE NO. 37

Dog No. 151 Continuation of Plate No. 36. Note the dey in branches of the circumflex artery and visualization of more arteriolar anastomotic branches.

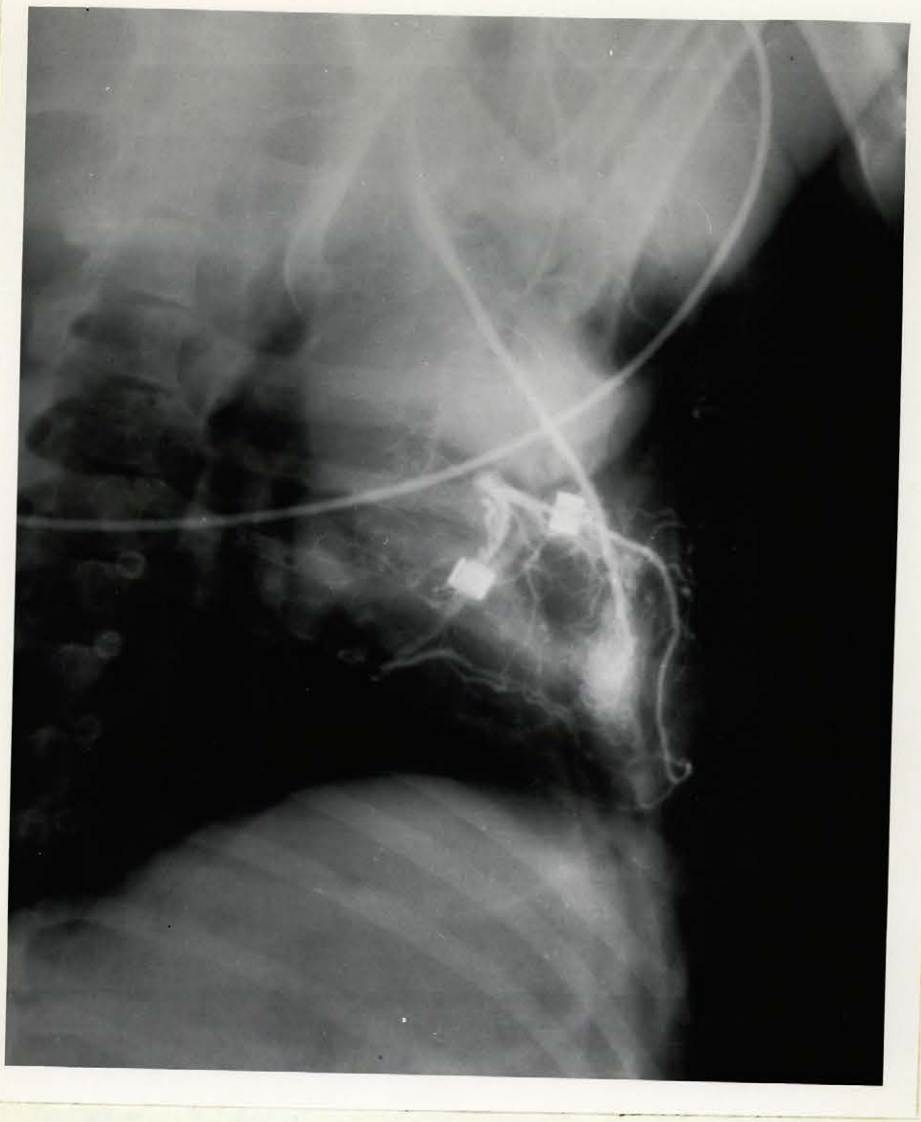

PLATE NO. 38

Dog No. 151 Continuation of Plate No. 37. Note the visualization of the circumflex and anterior descending branch at its bifurcation by retrograde flow through the septal branch. Note also dye in coronary venous system.

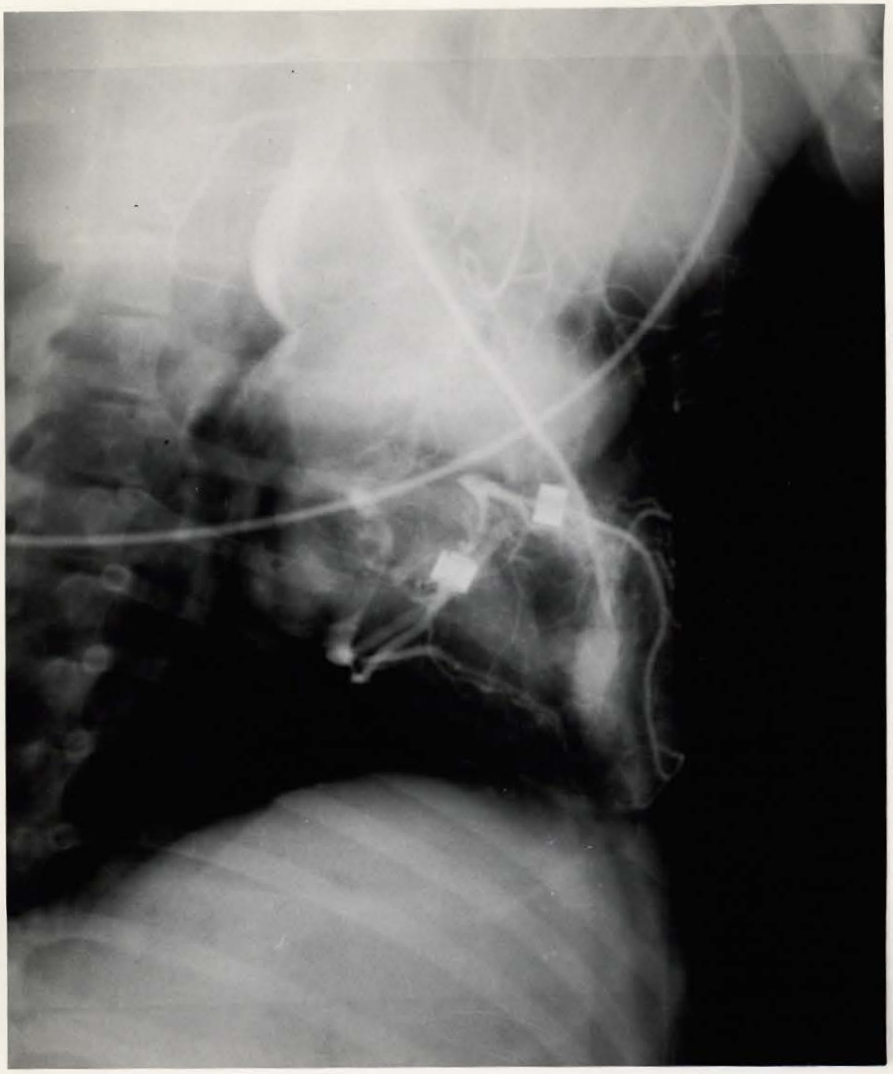

PLATE NO. 39

Dog No. 151 Continuation of Plate No. 38. Note well visualized anterior descending and circumflex arteries by the dyes passing from the implant through the arteriolar anastomosis. Note athe coronary sinus as the dye drains out.

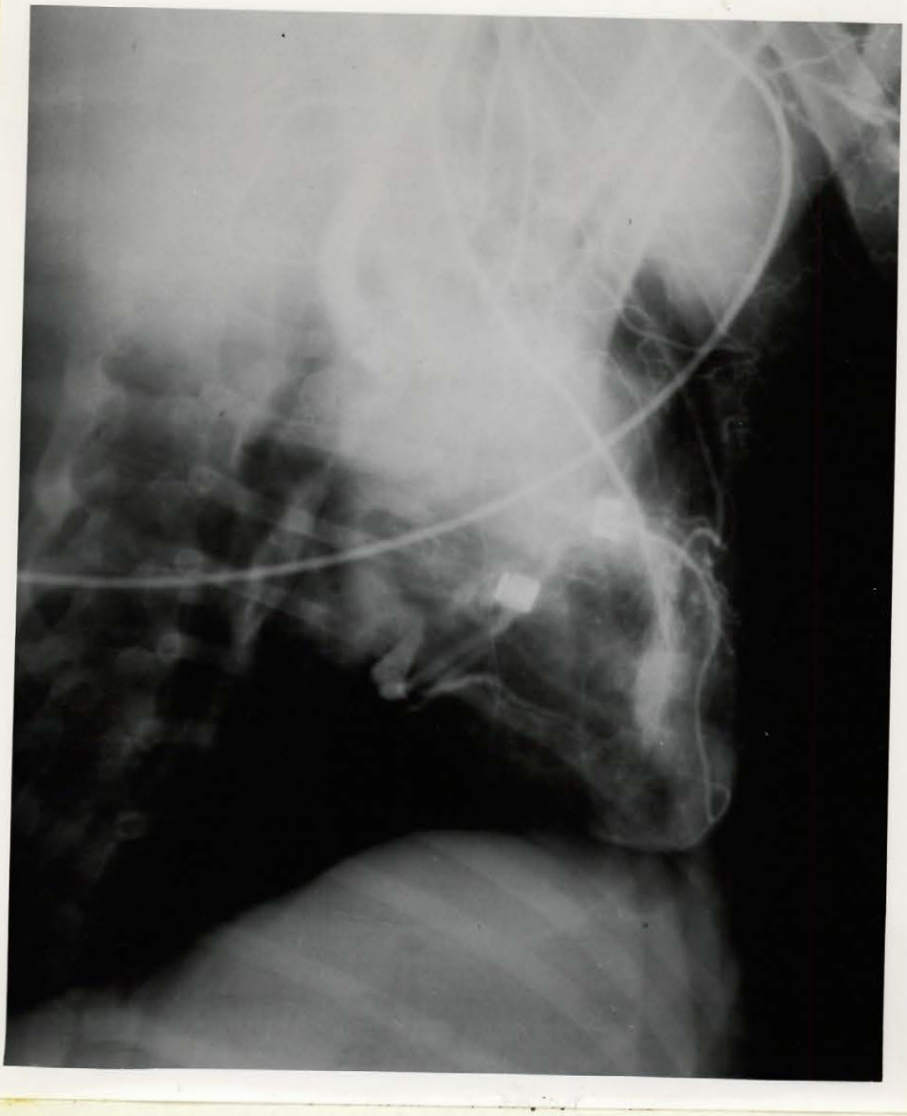

PLATE NO. 40

Dog No. 151 Continuation of Plate No. 39. Note the dye is being cleared away from the coronary arterial system into the coronary sinus.

NORMAL CONTROL

All animals between 43 to 50 lbs.

NORMAL CONTROL

All animals between 43 to 50 lbs. average

Dog No.	Date of Operation	Date of Death	Duration Lived	Gross Findings	X-Ray Findings	Aneroid Section Amount of Closure	Arteriogram	Septal Branch	Remarks
153	Dec. 31	Feb. 10	41 days	Lingula adherent.	HC + + IC +	87%	yes	AD	No visualisation of circumflex Branch. Right coronary artery well demonstrated and anterior descending branch faintly seen.
348	Dec. 31	Feb. 4	35 days	Infarction of the apex.	HC + IC +	70%		Bifurcation.	
119	Feb. 10	March 5	25 days	Upper lobe adherent. Infarction present.	HC + + IC +	90%		AD	
373	Feb. 20	March 20	30 days	Lung adherent, gross infarction.	IC + HC +	75%		L.C.	
375	Feb. 24	March 10	16 days	Lung adherent	HC + + IC +	75%		Coronary	
376	March 6	April 2	28 days		HC + IC +	80%		AD	
126	March 17	April 8	21 days	Gross infarction. Lung adherent.	HC + IC +	68%		AD	
328	Feb. 10	Feb. 30	20 days	Lung adherent.	HC + IC +	65%		AD	
372	March 5	April 5	30 days	Lung adherent.		72%		AD	
176	March 17	April 2	17 days		IC + HC +	87%		L.C.	
Average Survival			26 days		Normal type of anastomosis.				

IC : Intercoronary
HC : Homocoronary

BECK I

All animals between 44-52 lbs.

Dog No.	Date of Operation	Date of Death	Duration Lived	Gross Findings	Septal Branch
313	Sept. 8	March 18 (Sacrificed)	190 days	In all the specimens the lingula or left upper lobe was adherent. No pericardial cyst formation in any of them. No gross infarction of myocardium - but it is difficult to recognise.	Coronary
171	Sept. 13	Oct. 6	23 days		AD
314	Sept. 16	Dec. 14	88 days		AD
116	Sept. 17	Oct. 18	30 Days		AD
303	Sept. 18	Oct. 6	18 Days		(Circumflex)
145	Sept. 18	Oct. 6	18 Days		Coronary
307	Sept. 19	Oct. 12	23 days		AD
94	Sept. 23	Oct. 9	16 days		Coronary
141	Sept. 27	Oct. 19	22 days		AD
136	Dec. 27	Jan. 16	19 days		AD

( ) Ameroid Proximal to Septal Branch

BECK I

All animals between 44-52 lbs.

X-Ray Findings	Ameroid Section	Arteriogram	Myocardium	Remarks
IC + + + + HC +	85%			No visualisation of extracardiac blood supply.
IC - None HC +	82.5%			
HC + IC + +	80%			
HC + IC +	85%			
HC + IC +	65%			
HC + IC -	70%			
IC + HC +	92.5%			
IC + HC +	90%			
IC + HC +	85%			
HC IC -	75%			Sections shows thickened pericardial layer infiltrated with chronic inflammatory cells and fibroblasts. Not a picture of granuloma. No vascular communications.

HC : Homocoronary
IC : Intercoronary

IMPLANT AND CORONARY — All animals

SINUS CONSTRICTION — between 42-50 Lbs.

Dog No.	Date of Operation	Date of Death	Date Sacrificed	Life Duration	Gross Findings	Septal Branch	X-Ray Findings	Arteriogram	Ameroid Section	Remarks
13	Aug. 1st		April 16	256 days	Artery soft. Left upper lobe adherent.	AD	Injection taken. Anastomosis		85%	
123	Aug. 5	Oct. 9		56 days	Artery soft.	Circumflex	Injection taken Arterial anastomosis.		82.5%	
168	Aug. 9		April 25	236 days	Patent artery. Methylene blue circulates through the implant.	AD	Excellent anastomosis		67.5%	But no visualisation.
309	July 29		April 18	260 days	Methylene blue easily circulates.	AD	Good arterial anastomosis		75%	
151	Aug. 30		April 4	214 days	Implant is soft with branches from the internal mammary over the adherent lung.	Coronary	Good anastomosis		85%	Excellent arteriogram animal expired due to blockage of the artery for more than 1 hr.
175	Sept. 4		April 8	214 days	Soft.	AD	Fair anastomosis		67.5%	
17	Sept. 5		March 24	199 days	Soft.	AD	Fair anastomosis		72.5%	
301	Sept. 12		April 24	222 days	Soft.	AD	Patent artery No anastomosis		60%	
319	Jan. 30	Feb. 21		22 days	Thrombosed.	Coronary	None		45%	Plain catgut not Dissolved.
145	Jan. 29	Feb. 18		20 days	Artery blocked. Left upper lobe adherent crossing the ameroid jacket. Plain catgut not dissolved.	Circumflex	None			Plain catgut not dissolved.

CARDIOPNEUMONOPEXY

Animals between 43-52 lbs.

Dog No.	Date of Operation	Date of Death	Date Sacrificed	Life Duration	X-Ray Findings	Gross Findings	Microscopic	Arter-iogram	Arterial lumina Within ameroid	Septal Branch	Remarks
25	Oct. 9		April 4	175 days	I.C. + + + Injection through pulmonary artery did not take.				65%	AD	
329	Oct. 3	Oct. 27		24 days	Injection through pulmonary artery did not take.				100%	AD	
120	Sept. 26	Nov. 25		60 days	Injection did not take in myocardium. Pulmonary artery well injected.				75%	Coronary	
135	Sept. 27	Oct. 8		22 days	Lung separated - not well adherent.				60%	Circumflex	
358	Oct. 10	Nov. 13		33 days	Pneumonia in the adherent lobe.				80%	AD	
350	Oct. 3	Oct. 27		24 days	Injection did not take. Blood in chest.				65%	AD	
94	Dec. 4		April 23	139 days	Retrograde did not take.				77.5%	AD	No visualisation of Bronchial artery anastomosis
106	Jan. 3	Jan. 28		25 days	Injection did not take through pulmonary artery.				50%	Coronary	
126	Jan. 16	Jan. 30		14 days	Congestion of the adherent lobe.				75%	Coronary	
		Average		57 days							

Ameroid placed proximal to septal branch.

4 more died of distemper and other, lung complications.

Common complications of pneumopexy - as pneumonia, Separation of lobe after anchoring, Haemorrhage were found in 25 percent of cases.

No vascular Communications. Signs of inflammatory reaction in the muscle.

CARDIO-AORTIC IVALON TUBE IMPLANT

Dog No.	Date of Operation	Date of Death	Duration Lived	Septal Branch	X-Ray Findings
94	Nov. 14	Dec. 26	41 days	Circumflex	Patent but no anastomosis.
352	Nov. 7	Nov. 30	23 days	AD	
126	Nov. 11	Dec. 4	23 days	(AD)	
160	Nov. 15	Dec. 6	21 days	Coronary	
362	Nov. 4	Dec. 4	30 days	(AD)	
321	Oct. 29	Nov. 26	28 days	AD	
326	Dec. 9	Dec. 29	20 days	AD	
339	Nov. 8	Nov. 24	16 days	Circumflex	
314	Nov. 14	Feb. 26	102 days	AD	HC + + IC + +

All others were thrombosed on gross examination.

Average days.. .....

IC : Intercoronary
HC : Homocoronary

( ) proximal to Septal Branch

CARDIO-AORTIC IVALON TUBE IMPLANT

Gross Findings	Ameroid Closure of arterial lumen	Remarks
Partially thrombosed	70%	
Tube collapsed Thrombosed	77.5%	Gross infarction at the apex.
Thrombosed	55%	
Thrombosed - partially starting at the anastomosis	80%	
Thrombosed	60%	
Thrombosed	100%	
Thrombosed	67.5%	
Thrombosed	75%	
Thrombosed	60%	

On most of the specimens the Ivalon tube was covered and firmly adherent by lingula or left upper lobe.

CHAPTER XI

SUMMARY OF RESULT

Section 1

Series A

This is the control series with vaseline treated ameroid constrictors around the anterior descending and circumflex branch to produce coronary insufficiency. This is to be compared with other operations to test the efficacy of the procedure. Of the ten animals prepared this way, the survival rate was between sixteen to forty-one days, with an average of twenty-six days. On post-mortem examination in eight out of ten hearts the lung was adherent. The septal branch was arising from the anterior descending in six; three from the left coronary and one from the circumflex. Section through ameroids revealed blockage by organized thrombus or intimal proliferation from sixty-five to one hundred percent of its lumen with an average of 74.9 percent. Schlesinger injection study and x-ray, revealed only + intercoronary anastomosis, which is normal and + to + + homocoronary anastomosis. Seven out of the ten animals suddenly died when in some form of excitement as combat or jumping for food. The accurate manner of death of the other three could not be obtained. Section through

the heart showed infarction in the endocardial surface of the left ventricle and interventricular septum in seven out of ten hearts.

Series B

In this series, ten animals were prepared with the Beck I operation on ameroid treated dogs. Of the ten animals, nine died in a similar manner as the controls, between nineteen to eighty-eight days, with an average of 28.5 days. On post-mortem examination the lingula or left upper lobe of the lung was adherent to the heart. The septal branch arose from the anterior descending in six hearts; three from left coronary and one from the circumflex artery. The ameroid was proximal to the septal branch which arose from the circumflex artery. Microscopic section through the ameroid constrictors revealed an average of eighty percent blockage of the lumen, varying from 65 to 92.5%. Schlesinger injection study revealed + intercoronary and + homocoronary anastomosis in all the nine animals which died between nineteen to eighty-eight days. In none of these nine hearts was Schlesinger mass seen to fill the pericardium. On microscopic section the epicardium and adherent pericardium was found to be thickened and infiltrated with chronic inflamm-

atory cells and fibroblasts. There was no sign of granuloma formation and no blood vessel communications between the pericardium and the myocardium.

In dog No. 313, an arteriogram was done in vivo by cannulation of internal mammary artery which did not demonstrate any blood supply from the vascular mediastinal fat pad into the left ventricular myocardium after one hundred and ninety days. The animal was sacrificed and Schäsinger injection study revealed + + + + intercoronary and + homocoronary anastomosis. Section through ameroid revealed eighty-five percent obstruction of arterial lumen.

Series C

In this series left internal mammary implantation into the left ventricular myocardium with constriction of coronary sinus was carried out on eleven dogs with vaselinized ameroid constrictors. One dog developed ventricular fibrillation after coronary sinus constriction. The ligature was removed and the heart defibrillated. The above animal was not included in the comparing series. Seven out of ten animals survived more than two hundred days after which they were sacrificed. On some of them, arteriogram in vivo was done before sacrifice. The other three out of ten survived from twenty to fifty-six days. The animals during sacrifice or post-mortem examination revealed the left lung to be adherent

to the heart and to the internal mammary artery in all ten animals. The septal branch arose from anterior descending in six hearts, from the left coronary at its bifurcation in two others and from circumflex branch in the other two. In all the seven animals, during the sacrifice procedure, methylene blue was injected into the soft implanted artery outside the heart. Dye showed immediately in the left ventricular myocardium and in the branches of the coronary arteries. Schlesinger injection study of the implant showed open arteries in eight hearts with anastomoses in seven. Angiography in vivo was done on dog No. 168 and 151. Cannulation of the internal mammary was not successful in dog No. 168. In dog No. 151, which was a success, dye from the implanted artery circulated through the arteriolar anastomosis with the coronary arteries and went out through the coronary sinus. In two of the three animals which died between twenty to fifty-six days, the internal mammary was completely blocked and did not take Schlesinger injection. Interestingly enough, in these two animals, plain 00000 catgut was used to ligate the branches of the internal mammary artery instead of 00000 black silk as it was out of stock at that time. These plain catgut were not dissolved and the artery felt beaded and hard at the site of catgut ligation.

Section through the arteries within the ameroid revealed an average of seventy-three percent blockage of the lumen by organized thrombus or intimal proliferation.

Series D

In this series cardiopneumonopexy as described by Bloomer and his associates was carried out on ten animals (47, 48, 119). Eight out of ten survived fourteen to sixty days with an average of twenty-four days. The other two (dog No. 25 and No. 94) were sacrificed after one hundred and seventy-five and one hundred and thirty-nine days respectively. On post-mortem examination pneumonia in the adherent lobe, haemorrhage and separation of lobe from the heart were found in four out of the eight animals. These are the common complications of pneumonopexy as has been mentioned by several other authors. Retrograde injection of Schlesinger mass through the pulmonary artery, where possible, was done and in none of the specimens, could Schlesinger mass be found in the ventricular myocardium. Microscopic section of the artery within the ameroid revealed seventy-two percent obstruction of the lumen on the average. The septal branch arose from the anterior descending branch in five hearts, from the bifurcation of the

left coronary artery in four and from circumflex branch in the other. Angiography of the bronchial artery for visualization of the blood supply to left ventricular myocardium was negative on dog No. 94. Microscopic section of the cardiopulmonary junction did not show any vascular communications. There were signs of chronic inflammatory reaction in the myocardium underneath the lung. Dog No. 125 which survived for one hundred and seventy-five days revealed + + + intercoronary anastomosis. In dog No. 94 no x-ray study could be made accurately due to faulty injection.

Series E

In this series Ivalon tube anastomosed to the descending aorta was implanted into the left ventricular myocardium on ten animals with vaselinized ameroids. All the animals died within an average of twenty-seven days. The septal branch arose from the anterior descending in six cases, from the coronary artery at its bifurcation in three and from the circumflex branch in the other dog. On post-mortem examination, nine out of ten implants were completely thrombosed beginning at the anastomosis with the aorta. One was partially thrombosed and did take Schlesinger injection revealing a patent tube but no anastomosis. In all the

specimens the left upper lobe of the lung was firmly adherent to the graft, but the implant could be separated very easily from the myocardium indicating its foreign body nature. Microscopic section of the artery through the ameroid revealed seventy-one percent blockage of the arteries. No angiographic study was done as there was no living animal after three months.

SERIES F - INTERNAL MAMMARY ARTERY LIGATION

All the ten animals died in a similar manner as to the controls, suggestive of no protection whatsoever by this method. Moreover pericardiophrenic was usually found to be a very small branch of the left internal mammary artery in comparison to other branches arising from it in the dogs.

India ink injection study did not reveal any anastomotic communication with the coronary arterial system. During the time of operation one could see the fine capillary anastomosis over the pulmonary artery continuous with branches of left anterior descending. But it must be too small to be of any clinical significance and as far as the myocardial revascularisation is concerned.

In some of the animals, the application of ameroids at the bifurcation of the left coronary artery destroys or occludes the fine branches supposed to be in communication with extracoronary arterial system at the root of the heart. This may be one of the reasons for the absence of India ink travelling as far as these fine communications in some of the hearts.

CHAPTER XII

DISCUSSION

A. In the control series of vaseline treated ameroids around the anterior descending and circumflex branch, the animals survived on the average for twenty-six days. The branches of the left coronary artery were obstructed due to intimal proliferation or organized thrombus up to 74 percent of its lumen, with microscopic evidence of myocardial infarction involving the inner surface of the left ventricle and the interventricular septum (see page 67). The manner of death of these animals was also interesting to note, as most of them died in some form of excitement such as combat or jumping for food, during which state the constricted arterial lumen could not supply enough blood to the overworking myocardium. From the gross, microscopic and angiographic study, as well as the manner of death observed, it can be concluded that the ameroid casein plastic does produce myocardial infarction due to coronary insufficiency in a predictable time and is similar in nature to the human condition from the clinical and pathological point of view.

These ten hearts were studied for development of

new intercoronary anastomoses due to the gradual blockage of the arterial lumen. It may be mentioned again that Schlesinger injection study reveals only arterioles larger than 40 micra in diameter. However, anastomotic communication less than 40 micra are of little clinical significance (38).

Blumgart and his associates reported that twelve or more days of 75 percent narrowing were required to produce anastomotic communication sufficient to protect the myocardium. In the present control series of ten animals, all of them survived beyond twelve days and the left coronary artery branches were narrowed up to 74 percent. None of them revealed any new intercoronary anastomoses.

It can be concluded that it takes a much longer time than twenty-six days for the development of new intercoronary anastomoses, sufficient to protect the myocardium from gradual occlusion of coronary arteries.

B. BECK I

In this series the Beck I operation was performed on ten animals with vaselinized ameroids. Nine animals survived twenty-eight days on the average. In this group death occurred in a similar manner as in the control group.

There were no complications like pericardial cyst formation in any of the specimens. These nine hearts also did not reveal any intercoronary anastomosis by Schlesinger injection study despite the Beck I operation and gradual obstruction of the left coronary arterial lumen to 80 percent. Beck and his associates have reported that intercoronary communication develops as early as two days (13), and collaterals to the heart develop as early as three weeks (152). The discrepancy may be due to the fact that their study was not done by Schlesinger injection technique and the anastomotic channels which were shown were less than 40 micra in diameter. On microscopic examination in all our specimens the epicardium and inner layer of pericardium were not destroyed completely. There was thickening with chronic inflammatory cells and fibroblasts in the epicardium in contrast to the findings of others who have reported formation of granulomas with communicating vascular channels between the pericardium and myocardium (198, 199).

The tenth animal survived for one hundred and ninety days in spite of the blockage of the coronary arterial lumen to 80 percent and revealed four plus intercoronary anastomosis. This animal was sacrificed after angiography to visualize extramyocardial supply through the vascular mediastinal fat.

This was negative. This application of vascular mediastinal fat pad is one of the steps of the Beck procedure. Mautz and Beck make no claim as to the amount of blood that can be transported to the heart through these new vessels. Only in the late stage of the coronary arterial obstruction does blood actually flow into the heart through extracardiac anastomosis, since it is only in severe coronary arterial obstruction that these vessels have been seen to persist and enlarge.

In our experimental animals the coronary arterial obstruction can be considered as severe as it kills them. Despite this there is no evidence of extracardiac anastomosis.

The main reason for the survival of the lone dog out of ten was the good intercoronary anastomosis which could overcome the effect of obstruction. From our studies it could be concluded that intercoronary anastomosis develops sometime beyond twenty-eight days after the Beck I operation in the dogs treated by vaselinized ameroids for production of coronary artery insufficiency.

C. LEFT INTERNAL MAMMARY IMPLANTATION INTO LEFT VENTRICULAR MYOCARDIUM WITH CONSTRICTION OF CORONARY SINUS

In this series, left internal mammary implantation into the left ventricular myocardium with simultaneous constriction of coronary sinus to 3 millimeter was done on ten dogs. The main reason for adding this extra step is to find out if the surgical benefit could be increased beyond the 76 percent which was attained with the implant alone at the present time. Drs. Vineberg and Walker recently reported one hundred cases with 76 percent improvement.

In this experiment seven out of ten animals survived more than two hundred days. They were sacrificed after angiography was done. All these seven had open arteries with good anastomosis. One out of the other three animals which survived less than two hundred days had an open left internal mammary artery without any anastomosis. The other two implants were completely blocked. Surprisingly enough, in these two animals the blockage of the implant is attributed to the use of catgut for ligature of the branches of the internal mammary artery. Catgut was used in these two animals because of the unavailability of silk during the time of operation. These catgut sutures did not dissolve even after four to six weeks and the arteries felt hard and beaded near the ligation of

its branches.

As it has already been discussed, the coronary sinus constriction was added with the idea that it will provide greater extraction of oxygen from blood in the capillary bed and stimulation of intercoronary communication. Moreover, the ameroid casein goes into a burst of expansion in the first eight to ten days when the coronary sinus ligation will be beneficial as the arteriolar anastomosis is not fully developed in the early weeks of implantation. Baily states that simple ligation of the coronary sinus may be considered as a total revascularization procedure although a lesser degree of intercoronary development is obtained by this. However, our experiments discount this being a total revascularization procedure as the animals did not survive with the Beck I operation in which this is one of the important steps. However, it undoubtedly has some value as shown by all the previous studies.

Statements that the benefit of implant procedure is due to the development of intercoronary are not valid as in our study, and recently by several other groups, it is proved that the implant communicates with the coronary arterial system by anastomotic arteriolar channels. Angio-

graphic study in vivo in our experiments clearly depicts the course of blood through the ventricular myocardium. In addition there are other proofs by injection and x-ray studies. Recently Bakst and Loewe reported 90 percent filling of the anterior descending branch of the left coronary artery through the internal mammary implant when performed in the ischaemic heart, as reported in the American Journal of Cardiology, March, 1958. The retrograde flow from the anterior descending was 12 cc. per minute in contrast to 3.8 cc. in Harken's modified de-epicardiliazation with 95 percent phenol and 5.5 cc. by Thomson procedure. They have come to the conclusion that the combination of implant and Thomson procedure is an effective operation to protect both anterior and posterolateral portions of the left ventricle.

As has been mentioned, the infarction in ameroid treated animals occurred in the deeper surface of the left ventricle and interventricular septum near the endocardium which also is the case in human hearts. In 1940 King published a critical essay on the grafting procedures in general in which the vascular communication occurs between the vessels of the graft and the epicardial vessels.

The graft applied to the surface of the heart can do very little to supply the deeper layers where the infarction generally occurs. Moreover, in most of our studies there does not seem to be any vascular communication between these grafts and the myocardium. A similar observation of King and Freidbacker is that a fibrous tissue layer develops between the graft and the heart which gradually tends to contract due to scar tissue formation in spite of the demand for their existence in our experiments with induced myocardial ischaemia.

CARDIOPNEUMOPEXY

SERIES D -

In this series the pulmonary aftery to the left lingula was ligated to stimulate bronchial artery dilatation as reported by Bloomer and his associates (49). The lingula was then anchored to the left ventricular myocardium after application of phenol as advocated by Harkins to destroy the epicardial barrier. Although this operation has been carried on human patients, no experimental evidence of vascular communication to the ischaemic myocardium has yet been reported.

Bloomer's experiments were carried out on normal hearts with the application of silvernitrate on the left ventricular myocardium. They reported that the connection between the bronchopulmonary and coronary circulation occurs between 9 and 20 weeks after surgery as revealed by Vinyl plastic corrosion. However their was no evidence in our experiments by Schlesinger injection study of any communications. Moreover most of our animals died before the uptimum time for the development of vascular communication.

In this series eight out of the ten animals died within an average of 24 days due to coronary insufficiency produced by ameroids. The anterior descending and circumflex branches were obstructed to 72% of its cross-section.

Pneumonia in the adherent lobe, haemorrhage, separation of the lobe, pneumothorax and atelectasis are the common complications of pneumopexy. In these experiments 4 out of 8 animals died of these complications. Two other animals which survived beyond 130 days were sacrificed after angiography to visualise the bronchial arterial communications into the left ventricular myocardium. The angiography was negative and on exploration the lungs were firmly adherent to the heart. Schlesinger injection study through the pulmonary artery did not reveal any injection mass in the myocardium. The possible cause of survival of these animals was thought to be due to new intercoronary anastomosis. Schlesinger injection study, dog No. 25, showed + + + intercoronary anastomosis and in dog No. 94, no conclusions could be made accurately due to faulty injection. It seems if there were any vascular communication between the lingula and the myocardium at all, it must be less than 40 micra since it did not take Schlesinger injection.

Histologic examination of the junctional area between the heart and lung did not reveal any vascular communication. There was a fibrotic reaction associated with signs of chronic inflammation in the myocardium underneath the adherent lung.

Prudden (165A) even improved Bloomer's procedure to produce a high pressure cardiopneumopexy by a direct

anastomosis of the subclavian to the pulmonary artery of the left lower lobe. His results were also disappointing. He found the interface between the onlay and myocardium filled with a connective tissue barrier which prevented effective vascular communication.

Our experiments also reveals the same picture in this series of experiments of coronary insufficiency by gradual occlusion.

In conclusion onlay grafts of highly vascular tissue do not revascularize the myocardium to a degree sufficient to protect the heart from coronary insufficiency.

SERIES E - IVALON TUBE IMPLANTATION FROM THE AORTA INTO THE LEFT VENTRICULAR MYOCARDIUM.

In this series Ivalon tube anastomosed to the descending aorta was implanted into the left ventricular myocardial tunnel. This was carried out on ten animals with vaseline treated ameroids. All the ten animals died within an average of 27 days as the control group. Nine out of the ten grafts thrombosed at the time of post-mortem examination. The thrombosis was extending from the anastomotic site towards the myocardium. There was no thrombus extending into the aorta at the time of autopsy to account for embolism. In one of the grafts which was partially thrombosed, Schlesinger injection and x-ray study did not reveal any communication with coronary arterial system.

The operation itself and the anastomosis of graft is quite satisfactory from the point of technique as one could see the pulsation in the graft at the time of operation. There is no reports published in the literature regarding the Ivalon tube implantation in human cases, although ivalon has been used extensively in intracardiac and vascular repairs. Recently Dr Vineburg reported using the ivalon sponge for myocardial revascularisation.

Smith has used the nylon tube prosthethic graft for implantation in human hearts and has been satisfied with the results. But this procedure is still in experimental stage and there is no long term follow up as regards the thrombus formation and its efficacy in coronary arterial insufficiancy.

In conclusion, Ivalon tube implantation, inspite of its advantage over other types of prosthetic grafts thromboses quite early and does not protect coronary arterial insufficiency produced by ameroid constrictors. Moreover ivalon tube acts as a foreign body and produces chronic inflammatory reaction around the myocardial tunnel.

INTERNAL MAMMARY ARTERY LIGATION

In this series, the animals died after 26 days sustaining the average as in the control group. Previous to the present series, a study was made on ten animals with bilateral internal mammary ligation treated with dry ameroids. Schlesinger injection was found to be too viscus to pass through the distal branches of the pericardiophrenic artery to show the communication with the coronary arterial system. It was modified in the present series by ligating the distal branches of the subclavian and the distal end of the peridardiophrenic to gain the maximum hypertensive effect as suggested by Dr. Blalock. This was carried out on 10 animals with vaselinised ameroid constrictors. In these animals India ink was injected into the divided internal mammary artery but in none of the specimens was the ink found in the myocardium. It could be seen to have traveled as far as the periaortic and pulmonary capillaries when the pericardium was reflected.

In the last two years, several experiments have been carried out in different centers to find objective evidence of increase blood supply into the myocardium by bilateral internal mammary ligation. After the concept of the Italian authors like Fieschi, Battezzali, Tagliaferro and De Marchi, Glover and group have reported on 135 human cases with 68% improvement in relief of pain and discomfort.

Adams (5) reported his results of experiments on fresh cadavers followed by operation on 4 cases. On fresh cadavers he measured the flow rate in the aorta, internal mammary artery and pericardiophrenic artery. After the occlusion of the internal mammary artery there was no increase in minute volume of flow from the pericardiophrenic artery.

Out of the 4 human cases operated on, the pain disappeared before the vessels were ligated. In his cases symptomatic improvement was not supported by objective clinical tests in any of these cases. Similar is the observation by Glover in his cases. Adams concludes: "The symptom relieving effectiveness of a patient will succeed, of belief in his physicians word, and of confidence in his surgeons procedure" has once again been demonstrated "as a triad of facts".

In conclusion the bilateral internal mammary ligation does not lead to any demonstrative benefit in protecting the heart from coronary insufficiency produced by gradual occlusion. There was no objective evidence of communication with corronary arterial system.

CHAPTER XIII

SUMMARY AND CONCLUSIONS

1) A brief review of the anatomical, physiological and pathological considerations with regard to the problem of myocardial revascularization is described.

2) A survey of various methods of producing coronary artery insufficiency has been presented and the technique adopted in the experiments has been described.

3) A casein plastic (ameroid) in a stainless steel jacket when placed around the anterior descending and circumflex branches has been shown to produce coronary artery insufficiency in a predictable time, averaging twenty-six days in control animals.

4) Coronary artery insufficiency produced in the dogs by ameroid constrictors is similar to the human condition of coronary artery disease from the clinical, anatomical and pathological point of view.

5) The lumen of the arteries within the ameroids are obstructed on an average of 74% due to intimal proliferation or organized thrombus formation. The infarction produced by such a procedure is confined to the inner surface of the left ventricle and interventricular septum.

6) The gradual occlusion of the coronary artery resulting in an average of 74% reduction of lumina in a twenty-six day period does not stimulate the development of any new intercoronary anastomoses sufficient to protect the myocardium.

7) In the Beck I procedure, intercoronary anastomoses of sufficient size to protect against coronary artery insufficiency produced by ameroid constrictors occurred in only one out of ten animals.

8) Further angiographic studies of Beck I material revealed no evidence of collateral anastomotic channels between the vascular mediastinal fat pad and the coronary arterial system in the myocardium.

9) The operation of left internal mammary implantation and simultaneous coronary sinus partial occlusion up to 3 mm. has been shown to produce the best protection against coronary artery insufficiency produced by ameroid constrictors. Seven out of ten animals survived beyond six months with good arteriolar anastomosis; eight out of ten arteries were patent.

10) The flow of dye through the implant and its communication with the coronary arterial system was studied in vivo. The angiogram of dog No. 151 is shown on page 136 - 142.

11) The use of plain catgut in ligating the branches of the left internal mammary seems to be injurious and tends to thrombus formation. In the two animals which had complete thromboses plain catgut was used.

12) Coronary sinus ligation did not appear to influence the percentage of mammary coronary anastomoses by implant alone.

13) Surface grafts like cardiopneumopexy did not reveal any evidence of vascular communications between the bronchial arterial system of the graft and the left ventricular myocardium as shown by Schlesinger mass injection and angiographic study.

14) Surface grafts of highly vascular tissue did not revascularize the myocardium. A connective tissue barrier developed at the interface between the graft and heart muscle. This is probably due to incomplete destruction of the epicardium which acts as a strong barrier for revascularization.

15) In one of the surviving animals out of ten, cardiopneumopexy led to the development of intercoronary anastomosis as shown by Schlesinger injection study.

16) Bilateral internal mammary ligation did not protect the animal heart with coronary artery insufficiency. There was no evidence of anastomotic communication between the pericardiophrenic and the extracardiac branches of the coronary artery in the myocardium by India ink or Schlesinger injection study.

17) Implantation of a prosthetic tube, like Ivalon, from the aorta to the left ventricular myocardium failed due to thrombosis in 90 percent of the cases. The thrombosis usually started at the anastomotic site.

1. Anrep, G.V. -- Studies in Cardiovascular Regulation -- Lane Medical Lectures, Strafford Univ. Publ. Univ. Series, M.Sc. Series, 3-199-1936 -- Cited by Gregg.

2. Anrep, G.V. and Bing, B. -- Significance of Diastolic and Systolic Blood Pressure for Maintenance of Coronary Circulation, J. Physiology, 64-341-1928.

3. Anrep, G.V., Blalock, A., and Hammouda, M. -- Distribution of Blood in the Coronary Vessels -- J. Physiology, 67-87-1929.

4. Anrep, G.V. and Segal, H.M. -- The Regulation of the Coronary Circulation -- Heart, 13-239-1926.

5. Adams, R. -- Internal Mammary Ligation for Coronary Insufficiency - An Evaluation - N.Eng.J.Medicine, 258-113-58.

6. Allison, P.R. and Sabiston, D.C. -- Experimental Studies on the Cardiac Lymphatics -- Surgical Forum - P.271:1957.

7. Allen, D.S. -- Cardio stathorrhaphy- Splinting the Flaccid Myocardium of Coronary Occlusion by Surgical Procedure.J.Tho.Surg. 22:609:1951

8. Bailey, C.P. et al (Geckler, G.D., Truex, R.C., Likoff, W., Neptune, W.B., Angulo, A.W., and Antonius, N.) -- The Anatomic (Histologic) Basis and Efficient Surgical Technique for the Restoration of Coronary Circulation -- J. Thor. Surg., 25-143-1953.

9. Batson, O.V. and Bellet, S. -- The Reversal of Flow in the Cardiac Veins -- Am.Heart J., 6-205-1931.

10. Beck, C.S. -- The Development of a New Blood Supply to the Heart by Operation -- Ann.Surg., 102-801-1935.

11. Beck, C.S. -- Coronary Sclerosis and Angina Pectoris, Treatment by Grafting New Blood Supply on the Myocardium -- S.G. and O. 64:270,1937.

12. Beck, C.S. -- The Coronary Operation -- Am.Ht.J. 22-539-1941.

13. Beck, C.S. -- Principles Underlying the Operative Approach to the Treatment of Myocardial Ischaemia -- Ann.Surg.118:788,1943.

14. Beck, C.S., Tichey, V.L. and Moritz, A.R. -- The Production of a Collateral Circulation to the Heart -- Proc.Soc.Exp.Biol. and Med. 32:759,1935.

15. Beck, C.S. -- Revascularization of the Heart -- Ann.Surgery 128:854,1948.

16. Beck, C.S. -- Revascularization of the Heart - Surgery 26:82,1949.

17. Beck, C.S. -- Operation for Coronary Artery Disease -- Postgrad.Med. 14(2):95, Aug.1953.

18. Beck,C.S. and Mako, A.E. -- Venous Stasis in the Coronary Circulation (Experimental Study) -- Am.Ht.J. 21:767, June 1941.

19. Beck, C.S., Stanton, E., Batiuchok, W., and Leik, E. -- Revascularization of Heart by Graft of Systemic Artery into Coronary Sinus -- J.A.M.A. 137:436:1948.

20. Beck, C.S. -- Revascularization of the Heart -- N.Y.State Med. Journal -- 49:1727:1949.

21. Beck, C.S., and Leighninger, D.S. -- Operation for Coronary Artery Disease -- J.A.M.A.156:1226:547.

22. Beck, C.S. -- Coronary Heart Disease -- American Journal of Surgery -- 95:743:1958.

23. Beck, C.S. -- Coronary Heart Disease -- An Evaluation and Criticism of Present Day Concept -- Am.J.Cardiology -- 1:547:1958.

24. Beck,C.S. -- Coronary Artery Disease -- Annals of Surgery -- 145:439:1957.

25. Beck, C.S. -- Symposium on Coronary Artery Disease -- Diseases of the Chest -- 31:247:1957.

26. Beck, C.S., and Brofman, B.L. -- The Surgical Management of Coronary Artery Disease, Background, Rational and Clinical Experience. Annals of Int.Medicine -- 45:975:1956.

27. Beck, C.S., and Leighninger, D.S. -- Operation for Coronary Artery Disease -- Arch.Surg. -- 70:143:1955.

28. Beck, C.S. -- Operation for Coronary Artery Disease -- Annals of Surg. -- 141:24:1955.

29. British Medical Journal -- Surgery of Coronary Artery Disease -- Editorial -- 5025:997:57.

30. Blumgart, H.L., Zoll, P.M., Friedberg, A.S., and Gilligan, D.R. -- Experimental Production of Intercoronary Arterial Anastomoses; Functional Significance -- Circulation, 1:10-Jan.1950.

31. Blumgart, H.L., Zoll, P.M., Paul, M.H., and Norman, L.R. -- The Effect of Experimental Acute Coronary Occlusion on Stimulation of Intercoronary Collateral Anastomosis -- Transactions of the Association of American Physician - 68:155-1955.

32. Brofman, B.L., Leighninger, D.S., and Beck, C.S. -- Electrical Instability of the Heart - Circulation 13:161:1956.

33. Bennet, A.L. and Still, E.U. -- An Improved Method of Measuring Blood Flow -- Am.J.Physiol.105-4,1933.

34. Best, C.H. and Taylor, N.B. -- Physiological Basis of Medical Practice -- Ch.28 4th Edition 1943. The Williams and Wilkins Co., Baltimore.

35. Bing, R.J., Hammond, M.M., Handlesman, J.C., Powers, S.R., Spence, F.C., Eckenhoff, J.E., Goodvale, W.T., Hafkenscheil, J.H., and Kety, S.S. -- The Measurement of Coronary Blood Flow, Oxygen Consumption and Efficiency of the Left Ventricle in Man-- Am.Ht.J., 38:1,1949.

36. Bland, E.F., and White, P.D. -- Coronary Thrombosis (With Myocardial Infarction) -- Ten Years Later -- J.A.M.A.117:1171-1173,1941

37. Blum, L. and Gross, L. -- Technique of Experimental Coronary Sinus Ligation -- J.Thor.Surg. 5:522,1937.

38. Blumgart, H.L., Schlesinger, M.J. and Davis, D. -- Studies on the Relation of Clinical Manifestations of Angina Pectoris, Coronary Thrombosis and Myocardial Infarction to Pathological Findings -- Am.Heart J. 19:1, 1940.

39. Bohening, A., Jochim, K., and Katz, L.N. -- The Thebesian Vessels as a Source of Nourishment for the Myocardium. -- Am. J. Physiol., 106:183-200, 1933.

40. Brooks, B., and Martin, K.A. -- Simultaneous Ligation of the Vein and Artery -- J.A.M.A., 80:1678,1953.

40a. Baltezati, M., Tagliaferro, and DeMachi, G. -- La Leg uture dille due arterie mammarie interne nei disturbi di vascolari zzazione del Miocardio. 46:1178, 1955 Minerva Medica.

41. Baroldi, G., and Mantero, O.,Scomazzoni, G. -- The Collaterals of the Coronary Arteries in Normal and Pathologic Hearts -- Circulation Research -- 4:223:1956.

42. Baronofsky, I.D., Hanon, D.W., and Turback, C.E. -- Cardiojejunopexy for Coronary Artery Disease - Surgery 39:3:1956.

43. Bakst, A.A., Goldberg, H., and Baily, C.P. -- The Effect of Acute Occlusion of the Coronary Sinus on the Coronary Circulation -- Circulation Research 2:410:1954.

44. Benscome, S.A., and Vineberg, A. -- Histologic Studies of the Internal Mammary Artery after Implantation into the Myocardium. - Am.H.Journal 45:571, 1953.

45. Bakst, A.A., Costos-Durieux, J., Goldberg, H., and Baily, C.P. -- Protection of the Heart by Arterialization of the Coronary Sinus - J.Thoracic Surg. 27:433, 1954.

46. Bakst, A.A., Maniglia, R., Adam, A., and Baily, C.P. -- The Physiologic and Pathologic Evaluation of the Implantation of the Internal Mammary Artery into the left Ventricular Myocardium for the treatment of Coronary Artery Disease - Surgery 38:349, 1955.

47. Bakst, A.A., Adam, A., Goldberg, H., and Baily, C.P. -- Arterialization of the Coronary Sinus in Occlusive Coronary Artery Disease -- J.Thor.Surgery - 29:188, 1955.

48. Bloomer, W.E., Stein, H.E., and Liebow, A.A. -- Application of Induced Pulmonary Arterial Collateral Circulation as Collateral Supply to the Heart. -- Proc.Soc.Exp.Biol.,N.Y. 86:202, 1954.

49. Bloomer, W.D., Harrison, W., Lindkog, G.E., and Liebow, A.A. -- Respiratory Function and Blood Flow in the Bronchial Artery after ligation of the Pulmonary Artery. Am.J.Phys. 151:317, 1949.

50. Baily, C.P. -- Surgical Treatment of Coronary Insufficiency -- Diseases of the Chest -- 27:477, 1955.

51. Bellman, S., and Frank, H.A. -- Vascular Channels Established by Implantation of a Systemic Artery into the Myocardium -- Ann. Surg. -- 147:425, 1958.

52. Boone, A.W., and Hubbell, D.S. -- Observations on Production of Pericardial Adhesions and Ligation of Coronary Arteries -- S.G.O. 87:9, 1948.

53. Bledsoe, A. -- Collateral Cardiac Circulation -- Illinois Medical Journal 108:220, 1955.

54. Barker, W.F., Gkawakami, G., Diesh, G., Clifford, C., and Fong, R. -- Experimental Coronary Artery Occlusion -- Western Journal of Surgery, 65:297, 1957.

54a. Buller, W.K., -- An Experimental Study of the Internal Mammary Artery Implanted in the Left Ventricular Myocardium with Special Reference to Variations in the Operative Procedure as it Affects the Implant and to Blood Flow characteristics Through the Implant -- Thesis for M.S.C., 1953, 54.

55. Carter, B.N., Gall, E.A., and Wadsworth, C.L., -- Cardiopneumopexy and collateral circulation. Surgery, 25:489, 1949.

56. Canon, J.A., Clifford, C.A., and Barker, D. G. -- Accurate Diagnostic Coronary Arteriography in the Dog -- Surgical Forum, 6:197:1956.

57. Carey, L.S., Fuquay, M.C., Dahl, E.V., and Grindly, J.H. -- Myocardial Revascularization in the dog - Effect of Creation of a Temporary Fistula between an Implanted Artery and Left Atrium. Surgical Forum - 6:216:56.

58. Chardack, W.M., Bolgan, F.J., Olson, K.C.,Gage, A.A., and Farnworth, W.E. -- The Mortality Following Ligation of the Anterior Descending Branch of the Coronary Artery in Dog -- Annals of Surgery, 141:443:1955.

59. Cancellette, L. De Sautis, M., and Marchini, M. -- Vineberg Cardiac Revascularization operation - Experimental Study -- Archino di Chirurgia del Torece -- 11:115:57.

60. Davies, D.T., Mansell, H.E., and O'Shaughnessy, L. -- The Surgical Treatment of Angina Pectoris and Allied Conditions -- Lancet 1:1:1928.

61. Davis, D.J. -- The Periaortic Fat Bodies -- Arch. Path. & Lab. Med. -- 4:937:1927.

62. Donald, D.E., and Essex, H.E. -- Studies on the Chronic Effects of Ligation of the Canine Right Coronary Artery -- Am.J. Physiology -- 176:431:1954.

63. Duguid, J.B., and Robertson, W.B. -- Effects of Atherosclerosis on the Coronary Circulation. Lancet, 268:525:55.

64. Devera, L.B., Gold, H., and Corday, E. -- Simultaneous Comparison of Antigrade and Collateral Coronary Blood Flow. Circulation Research 6:26:1958.

65. Duchesne, E.R., and Vineberg, A. -- An Experimental Study of the Effects of Mechanically induced Ischaemia upon the Mammary Coronary Anastomoses. Surgery, 43:837:1958.

66. Drinker, C.K. -- The Lymphatic System, its part in regulating composition and of tissue fluid -- Lane Medical Lecture, Stanford University, 1942.

67. Dack, S. -- Cardio-pericardiopexy for treatment of Coronary artery disease. Am.Heart Journal, 45:772:1953.

68. Eckenhoff, J.E., Hofkenscheil, J.H., Harmel, M.H., and Goodale, W.T., Lubin, M., Bing, R.J., and Kety, S.S. -- Measurement of Coronary Blood Flow by the Nitrous Oxide Method -- Am.J.Physiol., 152:356, 1948.

69. Eckenhoff, J.E., Hofkenscheil, J.J., and Landmesser, C.M.-- The Coronary Circulation in the Dog. -- Am.J.Physiol., 148:582-596, 1949.

70. Eckenhoff, J.E., Hofkenscheil, J.H., Landmesser, C.M. and Harmel, M. -- Cardiac Oxygen and Metabolism and Control of Coronary Circulation. -- Am.J.Physiol., 149:634, 1947.

70a. Endry, J.C. -- The Clinical Significance o f the Findings of Calcified Coronary Arteries Diagnosed by x-ray in vivo. Cardiologia 29:426, 1956.

71. Eckstein, R.Q., Hornberger, J.C., and Sano, T. -- Acute Effects of Elevation in Coronary Sinus Pressure. -- Circulation 7 (3), 422, 1953 (March.

72. Eckstein, R.W., and Leighninger, D.S. -- Chronic Effects of Aortacoronary Sinus Anastomosis of Beck in Dogs. -- Circ. Research, 2:60, 1954.

73. Eckstein, R.V., Smith, G., Eleff, M., and Demming, J. -- The Effect of Arterialization of the Coronary Sinus in Dogs on Martality following acute Occlusion. -- Circulation 6:16, 1952.

74. Eckstein, R.W., Stroul, M., Dowling, C.V., Eckel, R., and Pritchard, W. H. -- The Response of Coronary Blood Flow following Stimulation of Cardiac Accelerator Nerves. -- Fed. Proc. 8:38, 1949.

75. Edwards, J.E. -- Pathologic Spectrum of Occlusive Coronary Arterial Disease. -- Laboratory Investigation 5:475, 1956.

76. Edwards, J.E., Burnside, C., Swarm, R.L., and Lansing, A.I. -- Arteriosclerosis in the Intramural and Extramural portions of Coronary Arteries in the Human Heart. Circulation, 13:235, 56.

77. Fauteux, M. -- An Experimental Study of the Surgical Treatment of Coronary Disease (Coronary Vein Lig'n). -- S.G.O. 71:151, 1940.

78. Fauteux, M. -- Surgical Treatment of Angina Pectoris (Coronary Vein Ligation). -- Am.Surg., 124:1041, Dec.1946.

79. Fauteux, M. -- Treatment of Coronary Disease with Angina Pectoris by Periocoronary Neurectomy with Ligation of the Great Cardiac Vein.-- Am.H.J. 31:260, 1946.

79a. Ferrari, A., and Ballaire, L. -- Attempted revascularization of the Heart by means of Ligation of the Internal Mammary Artery. -- Minerva Medica. 12:197, 1957.

80. Fauteux, M. -- Traitement Preventif de la Fibrillation Ventricular du Cours de la Maladie Coronaries. -- Union Med. du Canada. 75:368, 1946.

81. Fauteux, M. -- Anastomose de l'Artere Mammaire Interne avec le Sinus Coronarien. -- Union Med. Canada 75:347, 1946.

82. Fuquay, M.C., Carey, L.S., Dahl, E.V., Kirklen, J.W., and Grundlay, J.H. -- Myocardial Revascularization: A Comparison between Internal Mammary and Subclavian Artery Implantation in the Dog. Surgical Forum, 6:211:1955.

83. Fox, J.R., and Hughes, F.A. -- Experimental Protection of Dog Heart against Coronary Artery Ligation, use of Pericardial Irritant Poudrage and a Pedicle Graft Containing the Left Gastric Vessel. South, M.J. - 48:599, 1955.

84. Glenn, F. and Beal, J.M. -- The Fate of an Artery Implanted in the Myocardium. -- Surgery 27 (No.6) Pp.841-847, June 1950.

84a. Garamella, J.J., George, V.P., and Hay, L.J. -- A Corelative Study of Peripheral Coronary Pressures and Coronary Arteriography following Coronary Occlusion. S.G.O. 105:89, 1957.

85. Grant, J.C.B. -- A Method of Anatomy. -- Williams and Wilkins Co., Baltimore, 3rd Edit., 1944.

86. Grant, R.T. and Viko, L.E. -- Observations on the Anatomy of the Thebesian Vessels. -- Heart 15:103, 1929.

87. Green, H.D. and Gregg, D.E. -- The Relationship between Differential Pressure and Blood Flow in a Coronary Artery. -- Am.J.Physiol., 130:97, 1940.

88. Green, H.D. and Gregg, D.E. -- Changes in the Coronary Circulation following Increased Aortic Pressure Augmented Cardiac Output, Ischaemia and Valve Lesions. -- Am.J.Physiol. 130:126, 1940.

89. Green, H.D., Gregg, D.E. and Wiggers, C.J. -- The Phasic Changes in Coronary Flow Established by Differential Pressure Curves. -- Am.J.Physiol., 112:627, 1935.

90. Gregg, D.E. -- Studies of the Venous Drainage of the Heart. -- Am.J. Physiol., 151:13, 1947.

91. Gregg, D.E., -- Coronary Circulation in Health and Disease. -- Lea and Febiger, 1950 Philadelphia.

92. Gregg, D.E. and Dewald, D. -- Immediate Effects of Coronary Sinus Ligation on the Dynamics of the Coronary Circulation. -- Proc. Soc. Exper. Biol. & Med., 39:203, 1938.

93. Gregg, D.E. and Green, H.D. -- Effects of Viscosity, Ischaemia, Cardiac Output and Aortic Pressure of Coronary Blood Flow Reassured under a constant Perfusion Pressure. -- Am.J.Physiol. 130:108, 1940.

94. Gregg, D.E. and Shipley, R.E. -- Changes in right and left Coronary Artery Inflow with Cardiac Nerves Stimulation. -- Am.J.Physiol., 141:382, 1944.

95. Gregg, D.E., Shipley, R.E. and Bidder, T.G. -- The Anterior Cardiac Veins. Their Functional Importance in the Venous Drainage of the Right Heart. - Am.J.Physiol., 139:732, 1943.

96. Gregg, D.E., and Dewald, D. -- The immediate effect of the Occlusion of the Coronary Veins on Collateral Blood Flow in the Coronary Arteries. Am. J.Physiology, 124:435, 1938.

97. Green, H.D. and Wigria, R. -- Effects of Asphysia, Anoxia and Ischaemia on Coronary Flow. -- Am.J.Phys. 135:277, 1942.

98. Grey -- Grey's Anatomy -- Editors: T.B.Johnson and J.Whillis, Longman, Green & Co., Toronto, 29th Edit., 1942.

99. Gross, L.B. -- The Blood Supply to the Heart in its Anatomical and Clinical Aspects -- Paul H. Hoeber Co., New York, 1921.

100. Gross, L.B. and Blumm, L. -- Effects of Coronary Occlusion on Dog's Heart with total coronary sinus Occlusion. -- Proc. Soc. Exp. Biol., N.Y., 32:1578, 1935.

101. Gross, L., Blumm, L. and Silverman, G. -- Experimental Attempts to Increase the Blood Supply to Dog's Heart by means of Coronary Sinus Occlusion. -- J. Exp. Med.65:91, 1937.

102. Griffin, J.C., Hardy, J.C., and Turner, M.D. -- Does Internal Mammary Ligation increase Arterial Flow to the Myocardium. -- Surgical Forum. 7:325, 1958.

103. Glover, R.P., Danta, J.C., Kyle, R.H., Beard, J.C., Trent, R.G., and Kitchell, J.R. -- Ligation of Internal Mammary Arteries as a means of increasing Blood Supply to the Myocardium. -- J. Thor. Surgery, 34:661, 1957.

104. Garamello, J.J., George, V.P., Anderson, J.G., Ditmanson, M.L., and Hay, L.J. -- Modified Cardiopneumopexy employing Pulmonary Segmental Resection -- A Mortality Infarct Study. Annals of Surg. 146:864, 1957.

105. Grant, R.T. -- Development of the Cardiac Coronary Vessels in the Rabbit. Heart, 13:261, 1926.

106. Grice, P.G., Rodrigues, R.W., Kajikini, H., Riben, A., and Shumacker, H.B. -- Intrapericardial Asbestos in Experimental Coronary Artery Ligation. Surgery, 40:757, 1956.

107. Gross, H., Bloomberg, A.E., and Rosenblatt, M. -- Failure of Cardiopericardiopexy to protect pigs againt acute Coronary Occlusion. J.Thor.Surg. 33:679, 1957.

108. Guglieluno, L., and Guttadauro, M. -- Roentgenologic visualization of the Coronary Arteries in Living Subjects. Scientia Medica, Italica, 3:466, 1955.

109. Hahn, R.S., Kim, M. and Beck, C.S. -- Vascularization of the Heart -- Observations on the Circulation Following Arteriolization of the Coronary Sinus. -- Am.J.H., 44:772,1953.

110. Hahn, R.S., and Kim, M. -- Revascularization of the Heart (Histologic Changes after Arterialization of the Coronary Sinus). Circulation, 5:870, 1952.

111. Han, O, and Deterling, R.A. -- Evaluation of Contrast Media Employed for Aortic and Coronary Visualization. Surgical Forum. 7:320, 1957.

112. Hill, L. and Rowlands. -- Oxygen requirements of the Heart. -- Heart 3:219, 1912.

113. Hannon, D.H., Alden, J.F., Sprafka, J.L., Katz, Y.J., and Baronofsky, I.D. -- Staged Occlusion of the Coronary Arteries and Studies under low Oxygen tension. J.Thor.Surg. 32:1,1956.

114. Hudson, C.L., Moritz, A.A. and Wearn, J.T. -- The Extra Cardiac Anastomosis of the Coronary Arteries. -- J.Exper.Med. 56:919-925, 1932.

115. Heinbecker, P., and Barton, W.A. -- Operation for Development of Collateral Circulation in the Heart. -- J.Thoracic 9:431, 1940.

116. Johnson, J.R. and Wiggers, G.J. -- The alleged validity of Coronary Sinus Outflor as a Criterion of Coronary Reactions. -- Am.J.Physiol., 118:38, 1937.

117. Johnson, A.S., Fairschild, P.G., and Fulton, F. -- Visualization of Coronary Sinus Graft and Venous Pathways of the Heart in Living Dogs. Am.J.Roentgenology,Radium Therapy & Nuclear Medicine. 72:648:1954.

118. King. E.S. -- Artificial Collateral Circulation to the Heart: some critical comments on its value. -- Australia and New Zealand J.Surg., 10:8, 1940.

119. Kline, J.L., Stein, H., Bloomer,W.E., and Liebow, A.A. -- The Application of an Induced Bronchial Collateral Circulation to the Coronary Arteries by Cardiopneumonopexy. -- Am.J.Path., 32:663, 1955.

120. Katz, L.N., Jochim, K., and Bohning, A. -- The effect of the Extravascular Support of the Ventricles on the Flow in the Coronary Vessels. Am.J.Phys. 122:236, 1938.

121. Kimura, E., Suzuki, N., Kanazawa, T., Ho, Y., Harigeri, N., Yamamoti, E., Kamagai, S., Suzuki, Y., and Obera, F. -- Experimental Studies on the Coronary Insufficiency and Coronary Occlusion. Tohuku Journal of Exp.Med. 66:33, 1957.

122. Kowmacki, R.J. -- Collateral Circulation to the Heart by means of Cardiopneumonopexy and Lingular Vein Ligation. Archives of Surgery, 76:106, 1957.

123. Katz, L.N., and Jochim, K. -- Observations on the Innervation of the Coronary Vessels of the dog. Am.J.Phys.126:395, 1939.

124. Klemme, R.M. -- A Simple Operation Procedure for the Relief of Anginal Pain. J.Int.C.Surg. 10:272, 1947.

125. Leary, T., and Wearn, J.T. -- Two cases of complete Occlusion of both Coronary Orifices. Am.Heart Journal. 5:415, 1929.

126. Levene, C.I. -- The early Lesions of Atheroma in the Coronary Arteries. Journal of Path. & Bact. 72:79, 1956.

127. Leighninger, D.S. -- Surgical Treatment for Coronary Arterial Disease. Angiology 6:395, 1955.

128. Leighninger, D.S. -- A Laboratory and Clinical Evaluation of operations for Coronary Artery Disease. J.Thor.Surg.30:397, 1955.

129. Litvak, J. -- Experimental Production of gradual Vascular Occlusion. Thesis 1956-1957.

130. Lezius, A. -- Die Anatomischen und Funktionellar Grundlagen der Kunstlichen Blutuersirigbg des Hertzmuskles duch die lunge bei Coronarurterian Verschluss. Arch.J.Klin.Chir. 191:101, 1938. (Cited by Carter, Wall, and Wadsworth)

131. Lezius, A. -- Die Kunstliche Blutuersorggung des Hertzmuskles. Arch. F.Klin.Chir. 189:343, 1937.

132. Lowe, T.E. -- Some principles governing the supply of Blood to the Myocardium in Occlusive Arterial Disease. Am.Heart Journal. 21:326, 1941.

133. Lowenfel, A.B., Newman, C.G., Wade, W.H., Vonwedel, J., Lord, J.W., and Hinton, J.W. -- The Effects of gradual Occlusion of the Coronary Arterial Circulation in dogs and pigs. Surgical Forum, 7:302, 1957.

134. Lendrum, B., Kondo, B., and Katz, L.N. -- The role of Thebesian Drainage in the Dynamics of Coronary Flow. Am.J.Phys. 1945,143:243

135. Mimico, G., Balchum, O.J., Owens, J.C., and Swan, H. -- Experimental chronic Myocardial Insufficiency produced by Coronary Artery Embolization. Surgical Forum. 6:204, 1956.

136. Milch, E. Zimdahl, W.T., Egan, T.W., Anderson, A.A., and David, J. -- Experimental Prevention of sudden death from Acute Coronary Occlusion in the dog. Am.Heart J. 50:483, 1955.

137. Mathes, M.E., Holman, E., and Reichert, F.L. -- Study of the Bronchial, Pulmonary, and Lymphatic Circulation of the Lung under various Pathologic Conditions. J.Thor.Surg. 1:339, 1932.

138. Maniglia, R. and Bakst, A.A. -- Revascularization of the Myocardium by Aorta to Coronary Sinus Anastomosis. Surgery, 39:786, 1956.

139. Murray, G., Hilano, J., Porcheron, R., and Roschlan, W. -- Surgery of Coronary Heart Disease. Angiology, 4:526, 1953.

140. Murray, G. -- Surgical Treatment of Coronary Thrombosis. Canadian M.A.J. 67:100, 1952.

141. Moritz, A.R., Hudson, C.L., and Orgaris, E.S. -- Augmentation of the Extracardiac Anastomosis of the Coronary Arteries through Pericardial Adhesions. J.Exp.Medicine, 56:927, 1932.

142. Maniglia, R., and Bakst, A.A. -- Implantation of the Left Internal Mammary Artery in the Myocardium - A Histopathological Evaluation after Six Months. Archives of Surgery, 73:187, 1956.

143. Marcus, E., Hasbronck, E., and Wong, S.N. -- Myocardial Revascularisation - Experimental and Clinical Critique. 74:225, 1957.

144. Moir, T.W., and Pritchard, W.H. -- Study of the Hemodynamic Effects of the Aortocoronary Sinus Graft Operation in Patients with Coronary Artery Disease. Circulation, 16:1070, 1957.

145. Massimo, M. -- Myocardial Revascularization from Left Ventricle. J.Thor.Surg. 27:672, 1957.

146. Markwalder, J. and Starling, E.H. -- A Note on some Factors which determine the Blood Flow through the Coronary Circulation. J.Physiol., 47:275, 1914.

147. Mautz, F.R. and Beck, C.S. -- The Augmentation of Collateral Coronary Circulation by Operation. J.Thorac.Surg., 7:113, 1937.

148. Mautz, F.R. and Gregg, D.E. -- Dynamics of Collateral Circulation following Chronic Occlusion of the Coronary Arteries. Proc.Soc.Super.Biol. & Med. 36:797, 1937.

149. McLaughlan, J. -- The Experimental use of Ivalon Arterial Grafts. Surgery, 42:717, 1957.

150. Miller, W.D. -- An Experimental Study on the Development of Anastomosis between the Coronary circulation and the Left Internal Mammary Artery Implanted into the Left Ventricular Myocardium. M.Sc. Thesis, 1950, McGill.

151. Moe, G.H. and Visscher, M.B. -- The Distribution of Coronary Blood Flow. Blood, Heart, Circulation. A.A.A.S.Publ. 13:100, 1940.

152. Moritz, A.R. and Beck, C.S. -- The Production of a Collateral Circulation to the Heart (Pathological Anatomy Study). Am. Heart J., 10:974-880, 1935.

153. Mozen, H.E. -- Surgical Treatment of Coronary Artery Disease. Surgery, 42:394, 1957.

154. Niloff, P.H. -- An Experimental Study of Collateral Coronary Circulation produced by Transplanting the Left Internal Mammary Artery to the Left Ventricular Myocardium. M.Sc. Thesis McGill.

155. Notkovich, H. -- Anatomy of the Bronchial Arteries of the dog. J.Thor.Surg. 33:242, 1957.

156. O'Shaughnessy, L. -- An Experimental Method of Providing a Collateral Circulation to the Heart. Brit.J.Surg. 1936, 23, 665.

157. O'Shaughnessy, L. -- Surgical Treatment of Cardiac Ischaemia. Lancet, 1:185, 1937.

158. Okubo, T., and Kuroda, S. -- Experimental Study on Surgery on the Coronary System. The Nagaya Journal of Med.Science, 17:129, 1954.

159. Paul, M.H., Norman, L.R., Zoll, P.M., and Blumgart, H.L. -- Stimulation of Intrarterial Coronary Anastomosis by exp. Acute Coronary Occlusion. Circulation, 16:608, 1957.

160. Palumbo, L.T. -- Angina Pectoris, relief by new Surgical Approach. Medical Times, 84:1066, 1956.

161. Patek, P.R. -- The Morphology of the Lymphatics of the Human Heart. American Journal of Anatomy, 64:203, 1939.

162. Pearl, F., Joseph, P., and Cizet, C. -- Technique of Implantation of the Internal Mammary Artery into the Myocardium of the dog.

163. Pratt, F.H. -- The Nutrition of the Heart Through the Vessels of Thebesius and the Coronary Veins. Am.J.Physiol., 1:86, 1898.

164. Prinzmetal, M., Bergman, H., Kruger, H.E., Schwartz, L.L., Simkin, B., and Sobin, S.S. -- Studies of the Collateral Circulation of Beating Human and dog Hearts with Coronary Occlusion. A.M.H.J., 35:689, 1948.

165. Prinzmetal, M., Kayland, S., Margoles, C., and Tragerman, J. -- A Quantitative Method for Determining Collateral Coronary Circulation. J.Mt.Sinai Hosp., 8:933, 1941.

165a. Prudden, J.F. -- A Study of the Effectiveness of "High Pressure" Cardiopneumonopexy in Myocardial Revascularization. S.G.O., 106:702, 1958.

166. Prinzmetal, H., Simkin, B., Bergman, H.C., and Kruger, H.E. -- Studies on the Coronary Circulation. Am.Heart Journal, 33:420, 1947.

167. Raymen, J., Johnson, C., and Wiggen, J. -- The Alleged Validity of Coronary Sinus Outflow as a Criterion of Coronary Reaction. Am.J.Physiology, 118:38, 1937.

168. Ripstein, C.B. -- The Results of Surgical Treatment of Coronary Artery Disease. C.M.A.J., 59:52, 1948.

169. Roberts, J.T., Brown, R.S., and Roberts, G. -- Nourishment of Myocardium by way of Coronary Veins. Fed.Proc.Bult. 3:90, 1943.

170. Robertson, H.F. -- The Vascularization of the Epicardial and Periaortic Fat Pads. Am.J.Path., 6:209, 1930.

171. Robertson, H.F. -- The Physiology, Pathology, and Clinical Significance of Experimental Coronary Sinus Obstruction. Surgery, 9:1, 1941.

172. Robertson, H.F. -- The Reestablishment of Cardiac Circulation during Progressive Coronary Occlusion. Am.Heart Journal, 10:533, 1935.

173. Rudbeck, O. -- Cited by Mascagni, P. -- Vasorum Lymphaticorum corpous humani histona et achonographia. P.Carli Senis. 1787.

174. Sabiston, D.C., Fauteux, J.P., and Blalock, A. -- An Experimental Study of the Fate of Arterial Implants in the Left Ventricular Myocardium. Annals of Surg.,145:927, 1957.

175. Saphir, O., Ohrunger, L., and Wong, R. -- Changes in the Intramural Coronary Branches in Coronary Arteriosclerosis. Archives of Path., 62:159, 1956.

176. Sarnoff, S.J., Braunwald, E., Welch, G.G., Carr, R.B., Starnsby, W.N., and Mantz, R. -- Hemodynamic Determinants of Coronary Flow Effects on Changes in Aortic Pressure and Cardiac Output in the Relationship between Myocardial Oxygen Consumption and Coronary Flow. Am.J.Phys., 192:157, 1958.

177. Scarmucci, Dianio Parmeuxe 1689. Cited by Parker from Haller's Elements, Physiology Pub. 1718, Lib.IV, 459.

178. Schlesinger, M.J. -- An injection-dissection Study of Coronary Artery Occlusion and Anastomosis. Am.H.Journal, 15:528, 1938.

179. Schlesinger, M.J. -- Relation of Anatomic Pattern to Pathologic Conditions of Coronary Arteries. Arch. of Path., 30:403, 1940.

180. Schlesinger, M.J. -- Significant Variation in the Anatomic Pattern of the Coronary Vessels. Am.Assoc. for Adv.Sc. No.13, p.61-72.

180a. Schlesinger, M.J., and Zoh, P.M. -- Incidence and Localization of Coronary Artery Occlusion. Arch. Path., 32:178, 1941.

180b. Sabiston, D.C., and Fonkalsand, E.W. -- Experimental Implantation of Arterial Homograft into the Ventricular Myocardium. S.G.O., 106:709, 1958.

181. Sewell, W.H., and Koth, D.R. -- Experimental Coronary Occlusion using a Polytheylene Tube. - A Preliminary Report. Yale Journal of Biology & Medicine, 27:187, 1954.

182. Shipley, R.E., Shipley, L.J., and Wearn, J.T. -- The Capillary Supply in Normal and Hypertrophic Hearts of Rabbits. J.Exp.Med., 65:29, 1937.

183. Selman, M.W. -- Experience in the Beck Operation for Coronary Artery Disease. Diseases of the Chest, 28:1, 1955.

184. Shumacher, S.H., and Riben, A. -- A Study in Coronary Occlusion with particular reference to the lack of effect of Experimentally Produced Myocardial Infarction upon Exercise Tolerance. Surgery, 37:890, 1955.

185. Shapiroff, B.G. -- The use of the Auricular Appendage as an Autogenous Myocardial Graft. J.Thor.Surg., 22:631, 1957.

186. Siderys, H., Grace, P.F., Schumacker, H.B., and Riben, A. -- Occlusion of the Great Cardiac Vein and Coronary Artery Ligation. S.Gn.O., 102:18, 1956.

187. Smith, S., Beasley, R.N., Richard, H., Hoyt, H., Eugene, B., Edgar, W.H. -- Auxiliary Myocardial Vascularization by Prosthetic Graft Implantation. S.Gn.O., 104:263, 1957.

188. Smith, J.M. -- Concerning Anatomy of the Coronary Arteries. Am.J.M.Sc., 156:706, 1918.

189. Smith, F.R. -- Coronary Artery Collateral Circulation Developed by Heart Lung Graft. Anatomical Records, 119:95, 1954.

190. Spencer, F.C., Merill, D.L., Powers, S.R., and Bing, R.J. -- Coronary Blood Flow and Cardiac Ozygen Consumption in Unaesthetized dogs. Am.J.Phys., 160:149, 1950.

191. Stanton, E.J., Schildt, P., and Beck,C.S. -- The Effect of Abrasion of the Surface of the Heart upon Intercoronary Communications. Am.Heart J., 22:529, 1941.

191a. Shumway, N.E., Gliedman, L.M., Lewis, F.J. -- An Experimental Study of the Use of Polyvinyl Sponge for Aortic Graft. S.G.O., 100:703, 1955.

192. Stella, G. -- The Part Played by the Thebesian Vessels in the Blood Supply to the Heart. Am.J.Phys., 73:36, 1931.

193. Stewart, J.D., Birchwood, E., and Wells, H.G. -- The Effect of Arteriosclerotic Plagues on the Diameters of the Lumen of the Coronary Arteries. J.A.M.A., 104:736, 1935.

194. Thal, A.P., Richard, L.S., and Murray, M.J. -- Coronary Arteriography in the Adult Human. Surgical Forum, 7:328,1958.

195. Thal, A., Perry, J.F., Miller, F.A., and Wagensteen, O.H. -- Direct Suture Anastomosis of the Coronary Arteries in the dog. Surgery, 40:1023, 1956.

196. Tennant, R. -- The Effect of Coronary Occlusion on Myocardial Contraction. Am.J.Phys., 112:357, 1935.

197. Theis, F.V. -- Ligation of Artery and Concomitant Veins in Operation on large Blood Vessels. Arch.Surg., 17:224, 1938.

198. Thomson, S.A. -- The Development of Pericardial Adhesions following talc. Proc.Soc.Exp.Biol., 40:260, 1939.

199. Thomson, S.A. and Plachta, A. -- Cardiopexy and Coronary Artery Disease. J. Thor.Surg., 27:64, 1954.

200. Thornton, J.J., and Mantz, F.R. -- Experimental Methods for producing Chronic, Progressive Coronary Arterial Occlusion. Am.H.J., 19:404, 1940.

201. Thornton, J.J., and Gregg, D.E. -- The Effect of Chronic Venous Occlusion on Coronary Arterial and Venous Haemodynamics. Am.J.Physiol., 128:179, 1939.

202. Ungerleider, H., Kerkof, A.J., and Fahr, G. -- Venous Pressure as a Factor in Determining Collateral Circulation in the Heart. Proc.Soc.Expr.Biol. & Med., 37:703, 1938.

203. Viensseus -- Nouvelle Decouvertes sur le Colur (1708). Cited by L. Gross, Paul B. Hoffer, New York, 1921.

204. Vineberg, A.M. -- Development of an Anastomosis between the Coronary Vessels and a Transplanted Internal Mammary Artery. C.M.A.J., 55:117, 1947.

205. Vineberg, A.M., and Jewett, B.L. -- Development of an Anastomosis between the Coronary Vessels and a Transplanted Internal Mammary Artery, C.M.A.J., 56:609, 1947.

206. Vineberg, A.M. -- Development of Anastomosis between the Coronary Vessels and a Transplanted Internal Mammary Artery. J.Thoracis, 18:839, 1949.

207. Vineberg, A., Miller, W.D. -- Internal Mammary Coronary Anastomosis in the Surgical Treatment of Coronary Artery Insufficiency. C.M.A.J., 64:204, 1957.

208. Vineberg, A. -- Treatment of Coronary Artery Insufficiency by Implantation of the Internal Mammary Artery in to the Left Ventricular Myocardium. J.Thoracic, 23:42, 1952.

209. Vineberg, A., and Miller, D. -- Functional Evaluation of an Internal Mammary Coronary Anastomosis. Am.H.J., 45:873, 1953.

210. Vineberg, A. -- Internal Mammary Artery Implant in the Treatment of Angina Pectoris. C.M.A.J., 70:367, 1954.

211. Vineberg, A. -- Coronary Artery Insufficiency with Left Ventricular Enlargement and failure Treated by Epicardectomy and Mediastinal Cardio-omentopexy. C.M.A.J., 71:281, 1954.

212. Vineberg, A., Munro, D.D., Cohen, H., and Buller, W. -- Internal Mammary Implant. J.Thoracic, 29:1, 1955.

213. Vineberg, A., Munro, D.D., Cohen, and Buller, W. -- Four Years' Clinical Experience with Internal Mammary Artery Implantation in the Treatment of Human Coronary Artery Insufficiency including Additional Experimental Study. J.Thoracic, 29:32, 1955.

214. Vineberg, A. and Walker, J. -- Six Months to Six Years' Experience with Coronary Artery Insufficiency treated by Internal Mammary Implant. Am.Heart J., 851:54, 1957.

215. Vineberg, A., and McMillan, G.C. -- The Fate of Internal Mammary Artery Implant in the Ischaemic Human Heart. Diseases of the Chest, 33:64, 1958.

216. Von Haller, A. -- First Lines of Physiology. First Amer. Edition, Troy, Ohio, Penniman & Co. 1803.

217. Von Wedel, J., Stone, P.W., Newman, C.G., Lord. J.W., Jr., Hinton, J.W., and Moran, R.E. -- Revascularization of the Heart by a Pedicle Skin Flap. Science, 116:3013,319, 1952.

218. Wearn, J.T. -- The Extent of the Capillary Bed of the Heart. J.Exp.Med., 47:273, 1928.

219. Wearn, J.T. -- The role of the Thebesian Vessels in the Circulation of the Heart. J.Exp.Medicine, 47:293, 1928.

220. Wearn, J.T., Mettrer, S.R., Klumpp, T.G., and Zschiesche, A.B. -- The Nature of the Vascular Communications between the Coronary Arteries and the Chambers of the Heart. Am.H.Jour. 9:143, 1933.

221. Wiggen, C.J., and Cotten, F.S. -- Studies on the Coronary Circulation. Am.J.Physiology, 106:9, 1933.

222. Wearn, J.T. -- Morphology, Functional Alterations of Coronary Circulation. Bulletin N.Y.Acad. of Med. 2nd Ser. 17:754, 1941.

223. White, P.D., and Bland, E.F. -- The Prognosis of Angina Pectoris and Coronary Thrombosis - A Study of 500 Cases of the former and 200 Cases of the latter. Am.H.Journal, 7:1, 1957.

224. Wiggen, C.J. -- The Physiology of the Coronary Circulation. In Levy, R.L. (ed) Diseases of the Coronary Arteries and Cardiac pain, New York, 1936, McMillan Co.

225. Wiggen, C.J. -- The Physiology in health and disease. Lea & Febiger. Philadelphia, 1934.

226. Wiggen, C.J. -- The Interplay of Coronary Vascular Resistance and Myocardial Compression in Regulating Coronary Flow. Circ. Research, 2:271, 1954.

227. Woodruff, C.S. -- Studies on the Vasavasonum. Am.J.Path., 2:567, 1926.

228. Zoll, P.M., Norman, L.R., and Casin, S. -- The Effects of Vasomotor Drugs and Anaemia on the Intercoronary Anastomosis. Circ., 6:832, 1952.