M. Sc. Experimental Surgery.

AN EXPERIMENTAL STUDY OF REVASCULARIZATION OF THE ISCHEMIC MYOCARDIUM.

by

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PREFACE

The experimental work presented in this manuscript was performed at the laboratory of the Department of Experimental Surgery of McGill University, Montreal. The author's work embraces the year beginning July, 1958 and ending July, 1959. My interest in the carrying out of this project was stimulated by the growing need to find a solution for today's number one killer, in the United States and Canada, coronary heart disease.

The author wishes at this time to express his deep gratitude to the following, whose contributions in each one's phase, figured so importantly in the successful completion of my work:

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Finally, without the continuous help, encouragement, patience and perserverance of my most remarkable wife, Marilyn, the experimental work and preparation of this manuscript would have been impossible.

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CHAPTER I

I N T R O D U C T I O N

Through the ages, coronary artery disease has been plaguing mankind by the millions every year. Many sudden mysterious and dramatic deaths were attributed to this disease, yet people did not know how it worked. It was only during the advent of the 20th century that medical science began to probe this mystery, especially these last 35 years.

This disease is responsible in 80% of all sudden deaths (Munck-1946), one third of all deaths in the United States, and, moreover, it appears to be increasing rapidly every year. It is now considered the number one killer, leaving cancer far behind as number two. Metropolitan Life Insurance figures show a death rate of 78.2 per 100,000 population. Some of the apparent increase was also due to better diagnostic facilities and progressive increase of the aging population. It has been calculated that in 1900 only 13.6% of the population was over 45 years of age, while in 1980, 43% of the population will be over 45 years of age. Accordingly, the problem of this disease will become of increasing importance and be a major concern. The

important fact is that the incidence of the disease is imminently high, 4 to 8 million people in the United States are afflicted, and this, indeed, represents a major national problem. (79, 210, 211, 219, 224).

Coronary artery disease due to atherosclerosis is now being treated as a true disease process rather than an inevitable consequence of the aging process. The etiologic factors are sought by scientists all over the world in an attempt to control and reduce the incidence during the past few years. Pioneer studies have been initiated to determine the possible relationship between ways of life, diet, sex, race, degree of physical activity, emotional stress and strain, toxic substances and other unknown factors.

The findings of White and other workers are as follows:

1. There was a great preponderance of male, the ratio of man to woman was 97 to 3. (2) The mesomorph or the broad muscular person was more likely to be subject to this disease than the endomorph and ectomorph. (3) There is definitely more coronary artery disease in the immediate ancestors of coronary cases than in the ancestors of the control cases. (4) The serum cholesterol average a definitely higher figure in cases of coronary thrombosis. (5) Other factors, such as diet, exercise or lack thereof, the use of tobacco and alcohol and other stress and strain were in one way contributory to the causation of the disease.

It would appear then given the hereditary candidate or host with suseptible age, sex and temperament subjected to a high fat diet and numerous stress and strain, Will in all likelihood develop this disease. (6, 41, 63, 69, 70, 79, 80, 85, 103, 108, 110, 125, 163, 180, 227)

The prognosis of coronary artery insufficiency is poor inspite of various medical therapies, including the use of anticoagulants. Parker in 1946 showed 53.2% five year survival in 3,440 cases followed within the 20 years period of patients suffering from angina pectoris. White, Bland and Miskall found in their(497 cases) of angina pectoris, 445 died with an average duration of of 9.7 years. The immediate mortality in myocardial infarction following acute attack showed 49% survival in 5 years, 31% survival in lo years, 14% survival in 15 years, 5% survival in 20 years and 4% survival in 25 years. (16, 48, 54, 56, 118, 122, 142, 154, 158, 185, 216, 217, 218, 226).

In the symposium of coronary artery disease in 1956, Dr. Robert Levy of New York stated that the causes as well as the therapeutic possibilities of this disease are being actively explored and the approach to its prevention is dimly perceived.

It appears that medicine has had little to offer to those who are struck with coronary artery disease. In the light of the severity of the disease, during

the last 25 years, Beck in 1935 and O'Shaughnessy in 1936 have pioneered in the surgical therapy of this disease by incresing the blood supply to the ischemic heart. Numerous surgeons and physiologist from different countries followed the same trail opened up by their predecessors and contemporaries, and now it is possible to augment more blood to the ischemic hearts by several surgical procedures.

The present study conducted in the Department of Experimental Surgery at McGill University, which is the basis of this thesis, is to evaluate several of the known procedures and devise new ones. In these numerous operations we endeavor to determine how the operations could bring new blood to the ischemic heart, by the application of casein plastics called "Ameroids" around the coronary arteries.

Table I shows the different surgical methods which have been used in the attempt to revascularize the heart. Many of them had transient popularity, and because of high mortality and poor overall results, they were eventually given up. However, a few are being used as standard surgical procedures today, because they prolonged life by increasing the blood supply of the ischemic hearts.

TABLE I

SURGICAL PROCEDURES FOR REVASCULARIZATION OF THE ISCHEMIC MYOCARDIUM

I. GRAF OF TISSUES ON THE HEART.
By using: Pectoral muscle (Beck I-1935); Omentum (O'Shaughnessy-1936); Lung Cardio-pnuemopexy (Prudden-1959); Spleen (Favacchio and Caminiti-1957); Jejunum (Key).

II. PRODUCTION OF ADHESIONS BETWEEN PERICARDIUM, EPICARDIUM AND MYOCARDIUM.
With inflammatory substances like abrasion of the surface of the heart plus asbestos (Beck I); Talcum Cardio-pericardiopexy (Thompson-Raisbeck); Asbestos and 1% Novocaine (Peruzzo and Badright-1957); 5% Sodium Salicylate (Knock); enzymes, phenol, trichlor-acetic acid, etc.

IIII. IMPLANTATION OF EXTRA CARDIAC ARTERIES INTO LEFT VENTRICULAR MYOCARDIUM.
By use of: Internal mammary artery (Vineberg); Carotid artery (Sabiston and Fauteux); Subclavian artery (Fuquay); Splenic artery (Leibow); Homograft and nylon prosthesis (Vineberg and Duchenne, Sabistonet al); Prosthesis implanted from left ventricular cavity to myocardium (Massimo).

IV. COMPLETE OR PARTIAL LIGATION OF CORONARY SINUS AND TRIBUTARIES.
Gross and Blum procedure; Beck I Operation; Fauteux procedure.

V. ARTERIALIZATION OF CORONARY SINUS.
By vein graft with aorta (Beck II); Sinistation of coronary sinus (Hernandez and Lopez): Anastomosis between left inferior pulmonary vein and coronary sinus-Pablo-1959); other procedures like internal mammary and subclavian arteries.

VI. ANASTOMOSIS OF CORONARY ARTERY WITH EXTRA CARDIAC ARTERY.
Like internal mammary artery (Carter and Roth); Subclavian, Carotid artery etc.;Ivalon graft to coronary arteries for anastomotic bridge (Smith and McIntyre).

VII. ENDARTERECTOMY.
By Angelo May and B ailey; Longmire et al.

TABLE I (CONTINUATION)

SURGICAL PROCEDURES FOR REVASCULARIZATION OF THE ISCHEMIC MYOCARDIUM.

VIII. SECTIONS OF NERVE SUPPLY TO HEART.
Peri-coronary neurectomy (Fauteux); Section of rami communicantes and sympathetic chain (Raney); Dorsal rhizotomy (White).

IX. BILATERAL LIGATION OF INTERNAL MAMMARY ARTERY.
Digliotti et al; Glover et al.

X. IVALON SPONGE OPERATION.
(Vineberg, Deliyannis and Pablo)

XI. PRODUCTION OF SURGICAL ANOXIA AND ANOXEMIA.
Fistula between implanted internal mammary artery into left auricle (Carey et al); Arterio-venous fistula between pulmonary artery and left auricle (Lillihei et al and Day et al); Internal mammary artery and vein fistula (Julian et al)

XII. COMBINATION OF ABOVE PROCEDURES.
Internal mammaryartery implantations plus partial ligation of coronary sinus; combination of Beck I and Fauteux procedure; etc.

CHAPTER II.

ANATOMICAL CONSIDERATIONS

A. The Heart and Pericardium: (91, 92)

The heart is about the size of a man's fist, located inside the pericardial cavity. It has four chambers, two atriae and two ventricles.

The pericardium is a membranous covering of the heart divided into fibrous and serous parts. The serous part consist s of parietal and visceral layers, whereas the fibrous part has a parietal layer only.

The fibrous pericardium is cone-shaped sac which contains the heart and its serous pericardium. The inner surface is intimately lined by the parietal layer of the serous pericardium. The base of this sac arise from the roots of the great vessels which either leave or enter the heart. It blends with the adventitia of these vessels.

The serous pericardium forms a closed cavity into which half its wall is invaginated. The cavity contains clear light yellow fluid. The visceral layer or epicardium represents the invaginated part of the serosa and the parietal layer is the uninvaginated part. The aorta and pulmonary arteries are enclosed by a short tube of pericardium which contains plenty of fat.

Since the topographic anatomy of muscle bundles of the heart is not familiar to many, it may be helpful to briefly review it. At least five separate muscle bundles compose the ventricles of which the four principal ones are the superficial sinospiral, superficial bulbospiral, deep sinospiral and deep bulbospiral muscles. The fifth muscle bundle is the scroll muscle. Plate I shows in diagrammatic form the approximate location of the four muscle bundles viewed in transections of the ventricles.

The right ventricle is composed of three muscles, both superficial muscles and deep sinospiral muscle in contrast to the left ventricle which is composed of four muscles. The atriae are made up of an exceedingly thin superficial bundle which runs transversely over both atria and a deep bundle consisting of two sets of looped fibers which arise from the fibrous ring around the atrio-ventricular orifice and pass antero-posteriorly around one or the other atrium. (212, 144,171)

B. Blood Supply of the Heart:

1. The Coronary Arterial Supply: There are two main

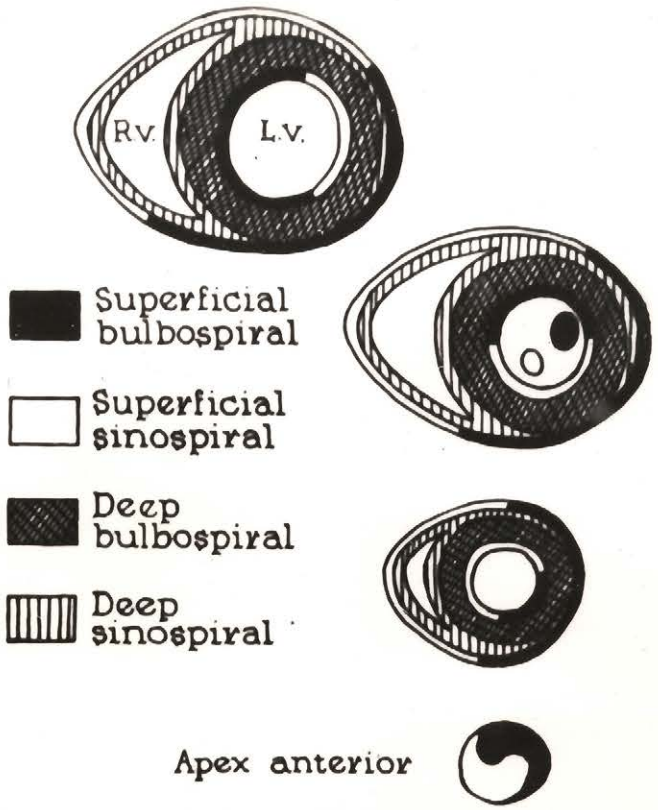


Fig. 1.—Cross-sectional anatomy of the muscle bundles of the human cardiac ventricles.

From: Wartman, W. B.; Sonders, J. C.
Arch. Path. 50: 329, 1950

PLATE NO. 1

Diagrammatic transverse or cross-sectional anatomy of the muscle bundles of the human cardiac ventricles.

coronary arteries, left and right. The left arises from the posterior left sinus of valsalva, while the right from the anterior sinus. The left divides early into an anterior descending branch and a left circumflex branch.

The anterior descending branch down the ventricular groove into the apex of the heart and nourishes the anterior part of the right ventricle, the interventricular septum and the anterior and apical part of the left ventricle.

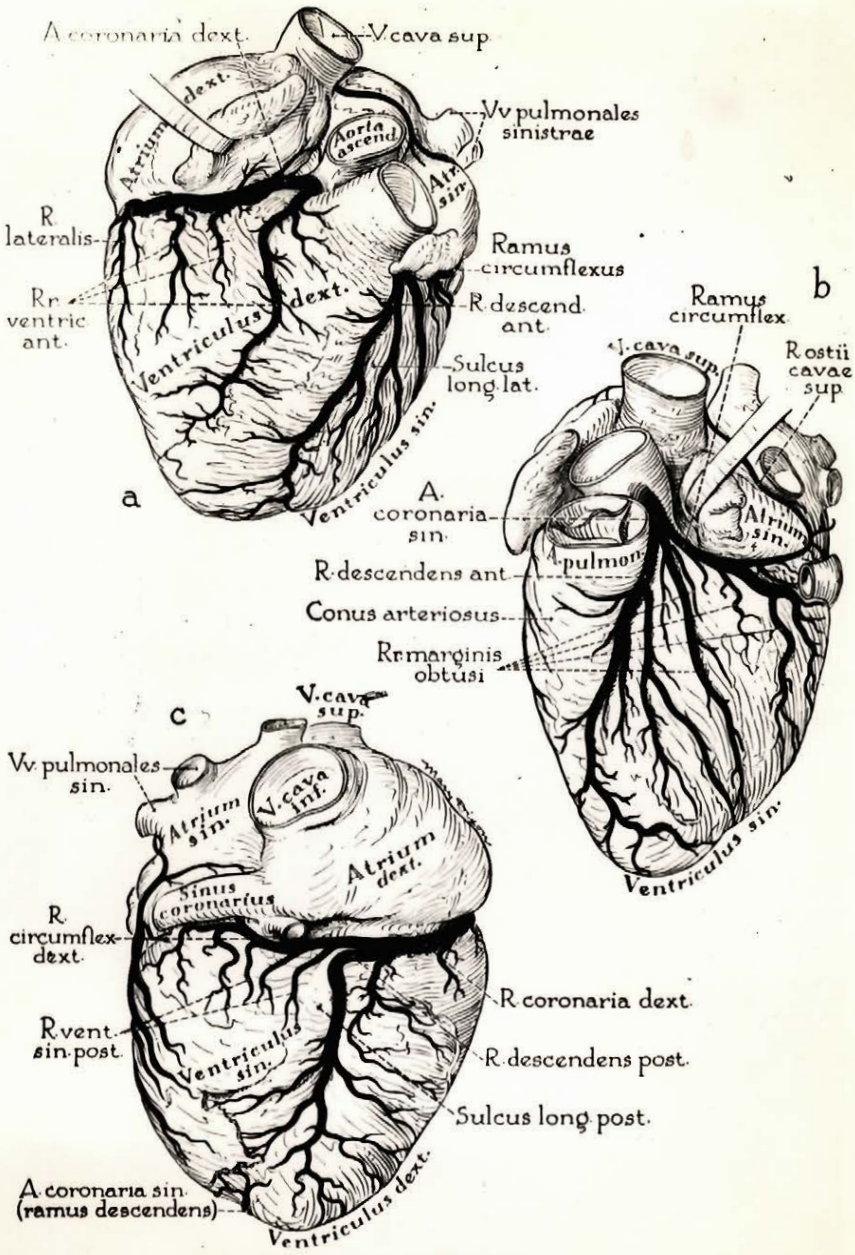
The smaller left circumflex branch curves around the back between the left atrium and ventricle and supplies the upper lateral and posterior basal portion of the left ventricle.

The septal branch arises near the origin of the anterior ascending branch or from the main trunk close to its bifurcation and still in a few cases may arise from the circumflex branch. The septal artery supplies the anterior third of the interventricular septum, anastomosing with the terminal branches of the septal portion of the posterior descending branch of the right coronary artery.

In our series of animals (dogs), this septal branch was found to have arisen from the anterior descending artery in 80%, from the main trunk in 10%, and from the left circumflex artery in 10% of cases.

In Painetto's series (162), the septal artery came from the anterior descending artery in 70% and from the main left coronary artery in 30% of cases.

The right coronary artery does not divide, but runs around the back between the right atrium and ventricle, sending small branches to the sinus node, to the anterior part of the right ventricle and to the posterior base of both ventricles. There is a considerable degree of anastomoses between the terminal branches of these vessels, an anastomoses that increased rapidly when the blood supply into any area is threatened. (165, 167). The right ventricle is supplied as it is by two of the biggest coronary arteries and offering little resistance to systolic coronary blood flow is rarely the seat of infarction. The upper and lateral part of the left ventricle supplied by the proximal branches from both anterior descending and left circumflex vessels is therefore virtually safe. The posterior basal portion is less secured for it is supplied only by the terminal branches, some from the right coronary and some from the left circumflex. In having this double source of nourishment, however, it is still more fortunate than the anterior apex of the left ventricle which is fed almost entirely by terminal rami from the anterior dscending branch of the coronary artery.



Coronary arteries.
***a*, Heart, anterior view. *b* and *c*, Same specimen, lateral views (from the left and the right, respectively).**

PLATE NO. 2.

The coronary arteries and its branches in the anterior and lateral views of the heart. (Taken from Human Anatomy by Anson).

The interventricular septum is supplied anteriorly by perforating branches from the anterior descending coronary artery and posteriorly by perforating branches from the right.

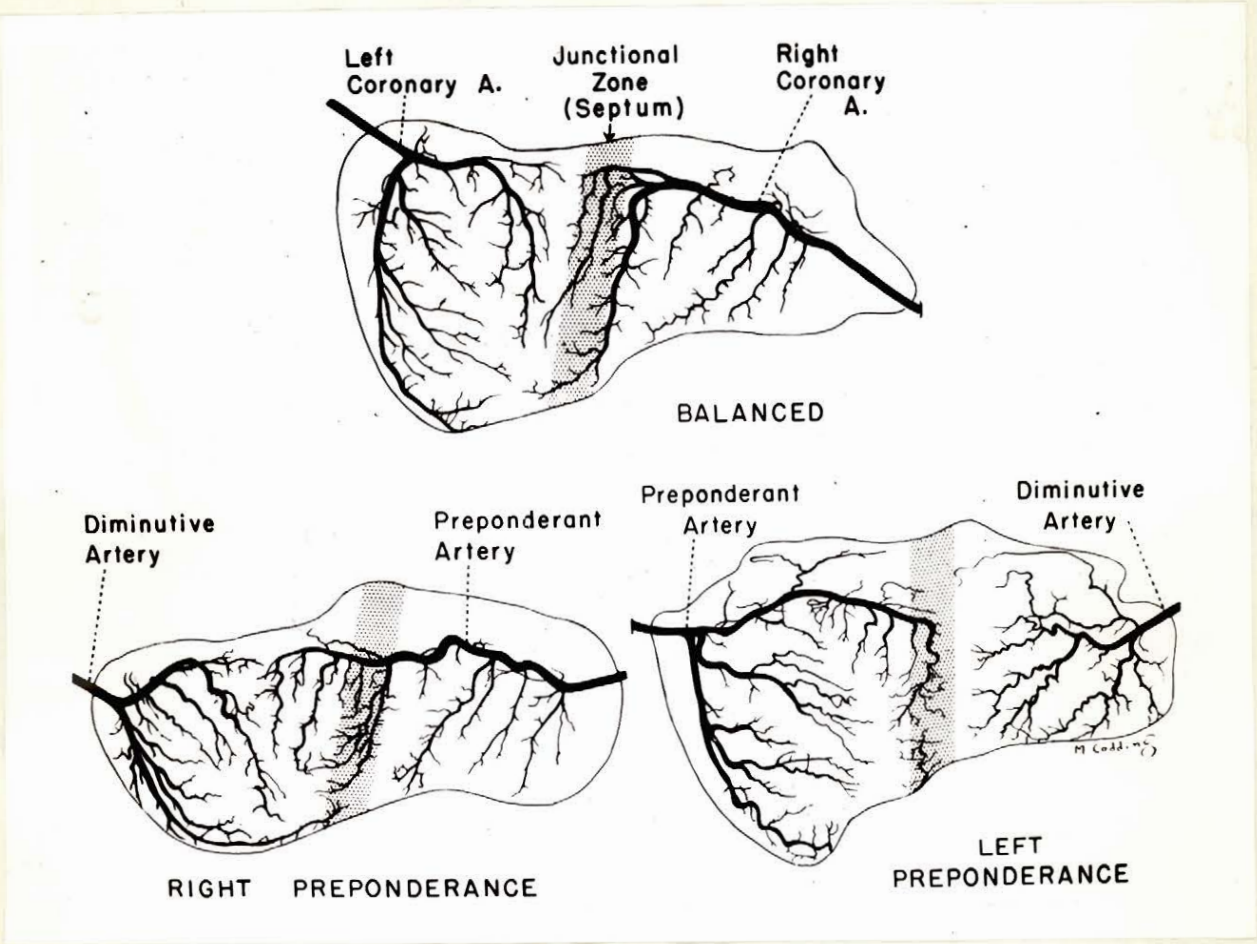
The artery to the sino-auricular node (Ramus ostii cavae superoris) arises from the proximal right coronary artery in 60% and from the proximal left coronary artery in 40% of cases (114). In Hanetto's series in dogs, the sino-auriculo node received blood from the right coronary artery in 75% of cases (162).

The artery to the auriculo ventricular node (Ramus septi fibrosi) penetrates the junction of the interatrial and interventricular septa at this location arising from which every coronary artery passes the crux of the heart. In 85% of cases, this is from the right coronary artery.

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 down the endocardium, where they change their course to make a rich anteriorlar anastomoses. This vascular bed surrounds the muscle bundles arborizing into capillaries which surrounds the individual fibers as a plexus.

In general, it appeared that when the right coronary artery is occluded, there is an infarct in a deep muscle (posterior and basal infarct); when the descending branch of the left coronary artery is occluded the infarct is one or both of a superficial muscle (anterior and apical infarct); when the circumflex branch of the left coronary is occluded the infarct is in either deep or superficial muscles and, finally, when multiple occlusions occurred in different coronary arteries, then, there was only an infarct in more than one muscle bundle (212, 171, 144).

Schlesinger described three types of coronary distributions: 1. Balanced circulation: In 34% the right coronary artery supplies the right ventricle and the posterior half of the interventricular septum. 2. Right coronary preponderance: In 48% the right coronary artery preponderates and supplies not only the whole of the posterior region, but makes contribution to the blood supply of the posterior region of the left ventricle. 3. Left coronary artery preponderance: In the remaining 20% the circumflex branch of the left coronary artery supplies all of the posterior septum as well as some of the contigous portions of the right ventricle. The third group is physiologically least sound, the first group is most sound and the second intermediate. Figure 3 shows diagrammatically these coronary artery distributions.



From: Schlesinger, M. J. American Heart J. 15: 528,1958

PLATE NO. 3.

Schlesinger's three types of coronary distributions.

2. The Coronary Venous System: The cardiac veins mostly accompany the arteries in the sulci and tend to be superficial to them. Five of the six cardiac veins end in the coronary sinus. The coronary sinus is about one and half inches long and it opens into the right atrium at the left of the orifice of the inferior vena cava. The orifice of the coronary sinus is guarded by the Thebesian valve, while the orifice of the inferior vena cava is guarded by the Eustachean valve. At the left end of the coronary sinus, it receives the great cardiac vein which follows the course of the left coronary artery and its interventricular branch of the right coronary artery, called middle cardiac vein, ends in the coronary sinus, so do the inferior ventricular veins from the diaphragmatic surface of the ventricles. The oblique vein is a twig that lies behind the left atrium and ends in the coronary sinus.

The anterior cardiac veins are several good sized venous trunks which lie buried in the subpericardial fat, number from 3 to 5 occupying the sulcus between the right ventricle and auricle. Each is formed by the confluence of many smaller veins which course over the surface of the right ventricle and empty into the right auricle about 4 to 8 mm. superior to the ventricular edge of the tricuspid valve.

There are anastomotic channels from the branches of the great cardiac vein, branches from pulmonary conus and adjacent fat tissues.

In those experiments in which all the major anterior cardiac veins were cannulated, the flow values range from 8.5 to 26.5 cc. per minute. The anterior cardiac vein arises from the coronary arteries, but the main contribution is from the right coronary artery. The major portion, 50 to 92% of right coronary flow, was found to drain via the anterior cardiac vein into the right auricle. The present study reveals that the anterior cardiac veins and not the Thebesian veins constitute the main drainage pathway of the right coronary artery. (97).

The deeper system of veins which communicates directly with the chambers of the heart are the Thebesians veins and they would be discussed in the mycardial circulation.

3. Myocardial Circulation: The heart muscle is provided with a blood supply more complex than any organ of the body. To understand its development, a review of the comparative anatomy and embryology of the hearts of the primitive vertebrae up to human mammalian heart. is necessary.

The lamprey is a spongy nonvascular heart without coronary vessels. Its nourishment comes entirely through intertrabecular spaces from the heart cavities. In frogs, the heart develops a small core of muscle with some vascular supply at the region of the bulbus cordis. The rest of the myocardium remains spongy. (86, 88, 89, 130).

The developing mammalian heart of the rabbit is spongy in its early stage. Coronary veins appear later as outgrowth from the left horn of the sinus venarium and from these branches spread over the surface of the myocardium to communicate with the intertrabecular sinusoidal spaces. Outgrowths from the endocardium give rise to epicardial capillaries which connect with the branches of the coronary vein and probably with the coronary artery later. The coronary artery sprout from the future aorta, spread over the heart and unite with the capillary network already formed by the veins and intratrabecular spaces (35, 87).

Two structures should also be mentioned, the Vieussens channel or arterio-luminal vessels and the Thebesian channels or arterio-sinusoidal vessels, which form direct communication between the arteries or arterioles and the ventricular and

auricular cavities: The first of these to maintain their arteriolar character to the very end of their course; the latter break up shortly into sinusoids which lie between muscle bundles. These vessels resemble capillaries in possessing thin walls made up of endothelium only, but differ from capillaries in their larger diameter which varies from 50 to 250 micra. (188, 193).

However, Wearn has shown that in the human heart there are lake-like spaces called by him as myocardial sinusoids. These lie between groups of muscle bundles and communicate directly with the arteriolar network which pour blood into them via arterio-myocardial sinusoidal vessels. (129, 213, 214).

The function of the Thebesian vessels is no longer obscure today. Numerous investigations using media of different viscosities and at different pressures have injected coronary arteries, coronary veins and Thebesian veins and seem to establish the following facts:

(a) When physiological saline solution or india ink is perfused through a coronary artery, about 90% escape into the lumen of the heart, via the Thebesian veins and very little passes through

the capillaries of the coronary sinus.

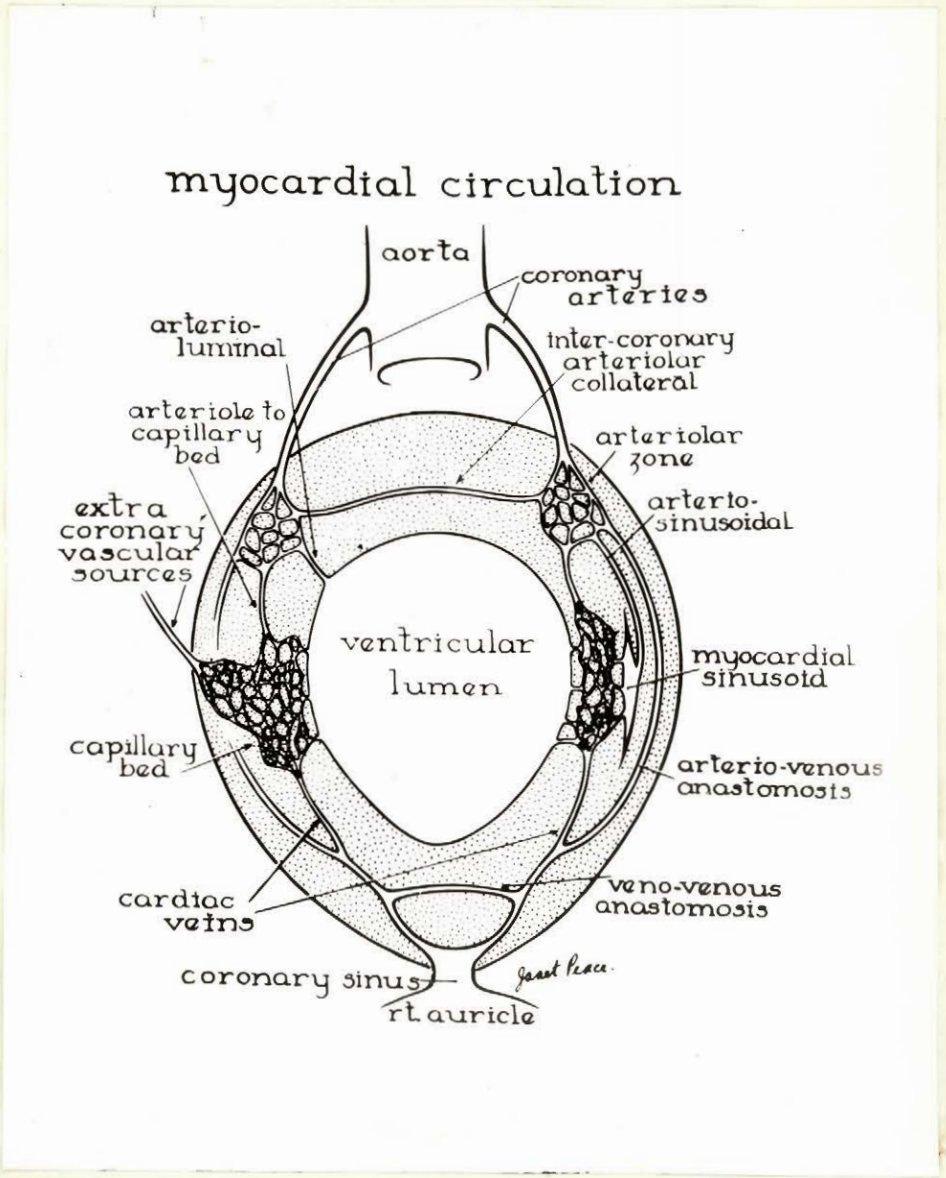
(b) Similarly, when a coronary sinus is perfused most escapes by the Thebesian veins and a little passes through the capillaries to the arteries.

(c) A fluid too viscous to pass through the capillary bed will, when injected in the artery or vein, escape into the lumen of the heart via the Thebesian veins.

(d) A fluid too viscous to flow out through the arteries may yet, when injected into the coronary vein, enter the heart via the Thebesian veins (45, 67).

Evidently, then, the pathway from the coronary vein via the Thebesian veins to the lumen of the heart is wider than from the coronary artery via the Thebesian veins to the lumen, and this in turn is wider than the passage through the capillary bed.

It is found by Batson that when carborundum too large to traverse either the capillaries or Thebesian veins of the heart or capillaries of the lungs are injected during life into the external jugular vein of the dog, they accumulate in large amounts in the coronary sinus and the vein on the surface of the heart. To get there, they must have taken a retrograde course in the veins. (15, 90, 127, 130, 145, 164).



From: Vineberg, A.M.; Deliyannis, T.D. C.M.A.J. 1958

PLATE NO. 4.

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

4. The Collateral Circulation: There are two types of collateral circulation in the heart verified by anatomic and physiologic studies. They are intrapericardial and extrapericardial collateral blood supply. (12, 23, 25, 44, 95, 151, 159, 165, 176, 178).

(a) Intracardiac Collateral Circulation: There is no longer any controversy about the existance of anastomoses between the branches of the coronary arteries to one another. There are no end arteries in the heart and there are no rich anastomoses in all layers of the heart. The main branches of the coronary arteries anastomoses with one another,so do the precapillaries and the capillaries. However, the anastomoses improve with age, the channel becoming wider and in the epicardial fat, they apparently increase in number. If one coronary artery is slowly obliterated, an increased collateral circulation can be established to prevent myocardial ischemia. They are most marked at the functional area supplied by both arteries. The luminal diameters of 20 to 350 micra and lengths ranging from 1 to 5 cm. are found in the human heart.

There are two types of anastomoses, the homocoronary and the intercoronary anastomoses. The homocoronary

anastomoses is between the branches of the coronary artery of the same side and intercoronary anastomoses is between the branches of the two different coronary arteries.

The homocoronary communications are found everywhere except in the immediate subepicardial layers. Intercoronary communications are found in areas supplied by both coronary arteries. They appear in the shape of a cork screw.

These two types of anastomoses are significantly increased in coronary obstruction where there is pressure differential and relative myocardial ischemia. Back flow studies have shown that gradual occlusion of a coronary vessels is followed by increase of 1 cc. to 30 cc. per minute within a period of 30 days. These anastomotic circulations are formed after various pathogic syndrome and can be interpreted as the result of hypertrophic growth of the collateral vessels existing in all human hearts. (Blumgart, 1940).

In normal hearts the intercoronary anastomoses are not larger than 40 micra in diameter. Blumgart believes these vessels will not protect against infarction, but they

could prolong life by allowing some blood supply to the ischemic myocardium.

Prinzmetal claims that the diameter of intercoronary anastomoses does not appear to increase with age. However, he found the largest intercoronary artery communication range from 70-80 micra, verified by injection of graduated glass spheres and radioactive cells.

(b) Extracardiac Collateral Circulation: (112, 123, 126, 133 148, 177). The nourishment of the heart comes principally from the two coronary arteries, which are the first branches of the aorta. It is partically assisted by some blood coming from the heart cavities and also by myriads of anastomotic branches from extracardiac blood vessels.

In 1880, Langer showed anastomoses between the coronary arteries through small branches distributed in the pericardium. He also showed connections between coronary and bronchial arteries by means of the vaso vasorum of the pulmonary artery and aorta.

Subsequently, investigators showed that the branches of the internal mammary arteries through the anterior mediastinal, pericardial and sternal branches together with some

twigs from the pericardio phrenic anastomoses with the branches from the intercostal, bronchial, esophageal and coronary arteries, to form a subpleural mediastinal plexus. These anastomoses take place around the root of the lung pulmonary arteries and veins around the ostia of the superior and inferior vena cava and ;finally, through the intervascular pericardial reflection.

The superior and inferior pericardio phrenic arteries indirectly contribute to these extracardiac collateral circulation through the musculo phrenic and pericardio phrenic branches of the internal mammary arteries.

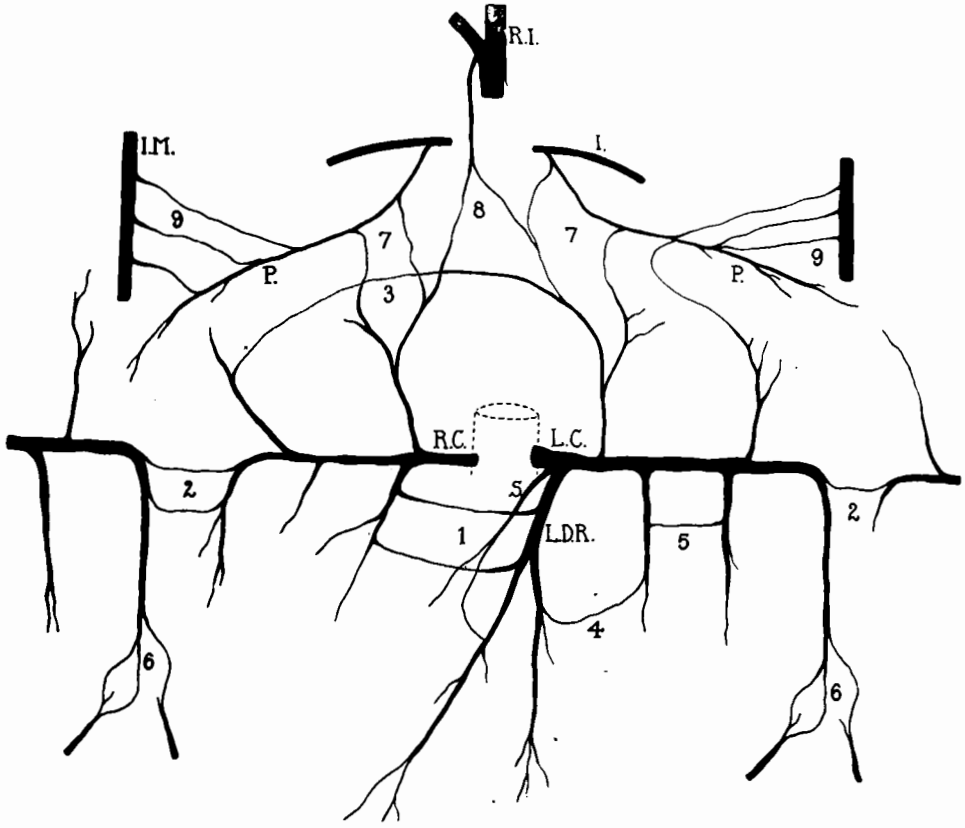
These anastomotic channels have been used in different operations to revascularize the ischemic myocardium.

C. Lymphatics of the Heart (4):

There is very little work and research directed towards the anatomy and physiology of the cardiac lymphatics. Ruddeck is given credit for the first description of the lymphatic drainage of the heart in 1653.

Aagaard in 1924 wrote a detailed monogram on the subject and has summarized the work of others until that date.

The problem was further studied by Pateck in 1939.



From: Mautz, F.R.; Beck, C.S. J. Thoracic Surg. 7: 113, 1937

PLATE NO. 5.

Diagram showing anatomic connections between main coronary arteries and between coronary and extra-cardiac arteries.
(From Mautz and Beck, collateral coronary circulation).

It is believed that the heart possesses a diffuse network of lymphatics and is in a sense a lymphatic sponge.

The subepicardial lymphatics are extremely numerous and diffuse. These lymphatics are small and drain into larger ones which course along the pulmonary branches of the lymphatic vessels to enter a large channels passing through the pericardial reflections with the mediastinum. The subepicardial lymphatics of the anterolateral surface of the left ventricle drain to a node at the junction of the brachiocephalic artery and superior vena cava. The lymphatics of the anterior right ventricle enter a lymph node along the left subclavian artery. The lymphatics of the posterior surface of the heart drain to lymph nodes on the posterior surface of the trachea and main bronchi.

The myocardium possess lymphatic capillaries three times the diameter of the myocardial blood capillaries. Most of these lymphatic capillaries pass directly into the subepicardial capillaries. There are only a few that empty into small subepicardial drainage vessels.

Subepicardial and endocardial lymphatic plexuses are mainly capillaries lying in 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 arterioventricular valves.

During diastole, lymph is driven from subendocardial lymphatics to myocardial plexus and during systole, the lymph from the myocardial plexus forces into the subepicardial lymphatics towards the end of diastole. The pressure of the dilated heart against the pericardium drives the lymph from the subepicardial capillaries into the lymphatic vessels.

The relative importance of the cardiac lymphatics are based upon two considerations. Firstly, the absorption of fluid in pericarditis and secondly, in association with observations in coronary arterial insufficiency. The success of the multiple operations for myocardial ischemia may in one way or another be the result or the contributory effect of the lymphatics of the heart.'

In mitral stenosis, an enoromous dilatation of the lymphatic vessels beneath the viceral pleura around the lung root and along the internal mammary near the phrenic nerve is evidence of the role the lymphatic system plays in this disease.

CHAPTER III.

PHYSIOLOGY OF THE HEART AND ITS CORONARY CIRCULATION.

A. Cardiac Output

The heart is life itself for without it the rest of the body dies. It is the main pump that circulates the blood to and from the tissues. It is always said that man is separated from his grave by cessation of a few heart beats.

The coronary circulation depends upon cardiac output and its resultant driving aortic pressure. In healthy man at rest, the ventricles eject an average of 70 to 80 cc. from each side per heart beat. The minute volume of the heart under basal conditions varies in different individuals from 3 to 4.6 liters. Grollman has shown that the basal cardiac output is a function of the surface area of the body. In the normal person, the minute volume per square meter of body surface, which is called the Cardiac Index, has an average value of 2.2 liters by acetylene method, and 3.2 liters by direct Fick method. The cardiac output is proportional to the basal metabolism. The average basal cardiac output per kilogram body weight is 62 cc. An adult at rest pumps at least 5,500 liters of blood through his body daily. The heart

cavities are believed not to empty completely during rest for it contains around 100 cc. of residual blood at the end of systole.

Cardiac output depends upon the heart rate and stroke volume. The cardiac output in a robust subject may increase nine folds during strenous exercise and oxygen consumption 12 times. It is, therefore, calculated that stroke volume increases over 3 times and that oxygen requirement is satisfied by rise in the circulation rate, an increase in coeffecient of oxygen utilization playing a lesser role.

The physiological conditions that could vary the cardiac output are muscular exercise, temperature, digestion of food, sleep, posture, pregnancy, anxiety, anger and probably certain emotional upsets. The pathological conditions which increase the cardiac output are hyperthyroidism, anemia, anoxemia, fever, angina pectoris, arteriovenous fistula and Pagets disease of the bone. The pathological conditions that reduce cardiac output are (1) cardiac irregularities, like paroxysmal tacchycardia, auricular fibrillation and complete heart block: (2) valvular disease and myocardial failure: (3) myxedema: (4) adherent pericardium and pericarditis with effusion: (5) pneumothorax: (6) haemorrage and surgical shock: (7) arterial hypertension: (8) after operation - 1 to 4 days after

surgery. Cardiac output is increased by drugs like adrenaline, histamine, nitrities, acetylcholine, digitalis strophantin, alcohol in moderate doses and caffeine.

B. Coronary Circulation:

The myocardium is supplied with blood from two main coronary arteries, which rise from the sinus of valsalva of the aorta in normal state. In human beings, Schlesinger describes three types of coronary distributions: (1) right preponderance in 48%. (2) Balanced circulation in 34%. (3) Left preponderance in 18%. The second group is the least vulnerable to arteriosclerotic changes and their effects. The third group appears to be most susceptable while the first group is intermediate with regards to incidence of coronary artery disease.

In the dog, 80% of the blood to the heart is carried by the left coronary artery,(50% by the circumflex branch and 30% by the anterior descending branch) while the remaining 20% is from the right coronary artery.

The hemodynamic principles of coronary circulation are based upon the following hydraulic laws: (1) Blood flow is proportional to the pressure gradient in a system. (2) Flow is proportional to the square of the cross-sectional area

of the vessel or to the diameter of the fourth power. (3) Blood flow is inversely proportional to the viscosity. Blood with normal hematocrit has approximately 5 times the viscous resistance to flow as does water.

Direct measurement of coronary arterial flow can be carried out in open chest dogs by means of a rotameter and in closed chest dogs by means of the nitrous oxide method with coronary sinus catheterization.

The coronary circulation time is about 8 seconds as compared with 20 seconds through the vessels of the limb. About 5% of the total cardiac output of the heart flows through the coronary system and nearly 2 liters would pass through the system. Bing (40) found that by the use of the Morawitz cannula that the average coronary blood flow through 100 grams. of left ventricular tissue was 77 cc. and the oxygen consumption of this unit was 9.4 cc. of oxygen per minute.

Katz and his associates (120) found that theproportion of total coronary flow carried by each of the coronary arteries was found to be widely variable in different individuals. His findings are (1) changes in heart rate alone do not appreciably alter the rate of the total coronary blood flow. (2) the rate

of coronary blood flow varies directly with coronary perfusion pressure, other conditions being constant. (3) When all other variables are kept constant, the total coronary inflow is decreased by raising the mean pressure within the heart cavities and thus, the mean intramuscular tension with their walls. Decreasing the pressures increased the total coronary pressures and tension of each side of the heart alone. (4) When the mean pressure of the heart cavities is changed, the rate of sinus flow varies in a direction opposite to the total coronary inflow, so that the ratio between the two varies widely. Changes in the sinus outflow depend almost entirely on the changes in pressure in the right side of the heart and the pressure in the left side having little effect. (5) The coronary sinus outflow may persistently exceed the total coronary inflow when the mean pressure in the heart cavities and the mean intramuscular tension of their walls are high relative to the coronary perfusion pressure. Changes in pressure in the right heart are more effective than in the left heart.

Katz (119) also found that during relaxation, the pressure within the ventricle dropped below zero level of the system. The amount of the drop was a direct function of the

initial length of the muscle. The source of energy for the sucking action are mainly potential stores created by the contraction process, such as energy of position and of elastic state. The distinction is made between the source of energy for the sucking action and for the flow of the fluid. That relaxation is of similar nature to contraction: Both are dependent on some reversible physiochemical process which alters the elastic state of the muscle between 2 limits, the minimum for the relaxed and the maximum for the contracted heart. Evidence is given to show that the ventricles not only can but does exert a sucking action in the intact mammal. The myocardium possess an extra rich capillary supply. The ventricular muscle is much more vascular than the auricular wall and the auriculo-ventricular bundle. At birth, a single capillary supplies 4 to 5 cardiac fibers. In adult, each muscle fiber receives a capillary blood vessel (Wearn, 214); the hypertrophied heart, therefore, suffers a relative reduction in its blood supply.

Provenza and associates (168) found capillaries of 3 types in the substance of the myocardium as shown in Plate No. 6.

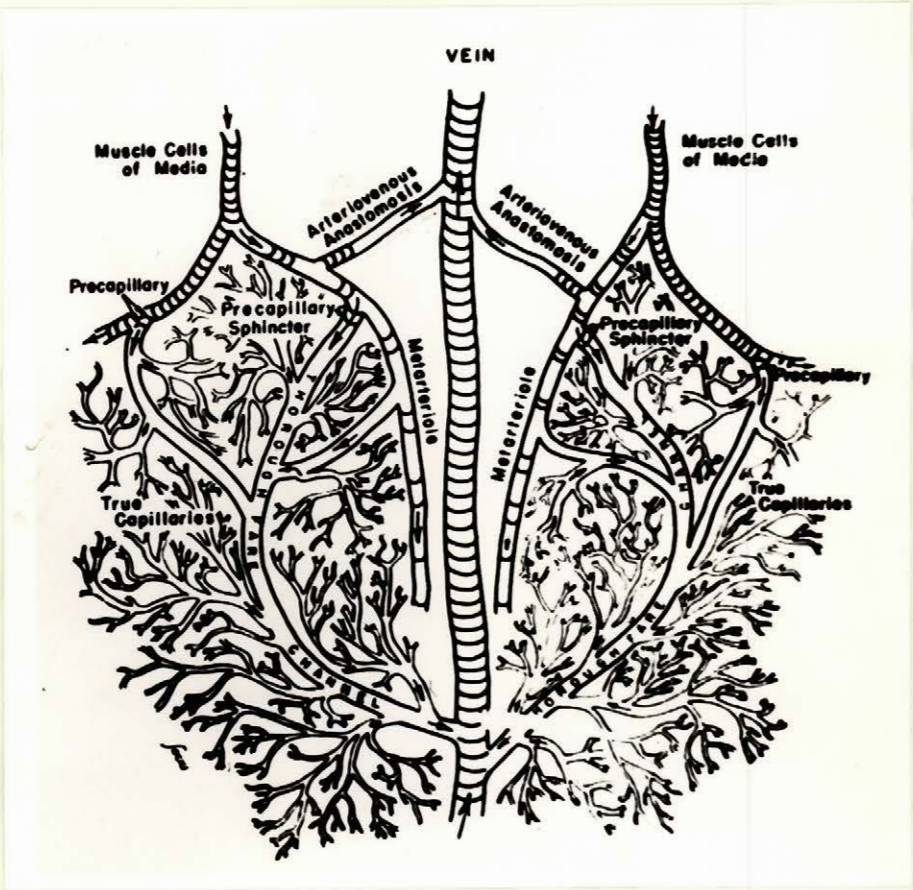


PLATE NO. 6.

Diagram shows the 3 types of capillaries: (1) Metarteriole. (2) True capillary. (3) Precapillary. (From Provenza and associates (168)).

(1) Metarteriole, which is a continuation of an arteriole. It consists of an endothelial lining surrounded by discontinous muscle. These muscle cells constitute a sphincter; one feature is constant, the lack of continuity between sphincter muscles. (2) True capillary, consist of simple endothelial tube, completely wanting in muscular components. The perithelium consist of very loose type of areolar and reticular connective tissue. This type of capillary may be a continuation of either arteriole or metarteriole. (3) Precapillary is intermediate between the metarteriole and the true capillary. The proximal end of the pre capillary consist of endothelial tube surrounded by one or several muscle cells - precapillary sphinter.

C. Coronary Circulation During Different Phases of the Cardiac Cycle:

In the 17th century, Scaramucci of Italy was the first to recognize the flow through the coronary arteries occurred mainly during diastole, and that a reduced amount of blood enters the vessels during systole owing their compression to the contracting muscle. Lagendorff studied the problem intensively in the perfused isolated heart and our knowledge of this coronary flow during cardiac cycle is based largely upon his work. In recent years, Anrep and his colleagues (8) in England

and Wiggers, Green and Gregg (9, 98, 223) with their associates in America are the outstanding contributors in this field. The two main factors affecting coronary flow are aortic pressure and extravascular compression (120). The intramural flow through the intramyocardial peripheral vessels are directly compressed, while the extramural flow through the superficial coronary branches are both directly and indirectly compressed during systole. Wiggers measured and studied this coronary vessel flow and found that the pressure in the intramyocardial peripheral vessels never rises as high as the aortic pressure any time during cardiac cycle. Two sharp reductions occur in the isometric period, and at the beginning of ejection and the other is in the latter part of the ejection period. The rate of flow is greatest in the midsystole and throughout diastole. The extramural flow resembles that of the intramural flow except that it is completely arrested during early systole and is greater during midsystole and the first half of diastole. As the aortic pressure rises during systole the superficial vessels are distended to accommodate more blood, the extramural flow is then increased over that in the deeper lying and compressed intramural vessels. During early diastole the peripheral vessels are quickly released from

compression and the intramural flow is increased. The blood flow through the right coronary differs from those of the left vessels for the flow during systole may approach or even exceed that during diastole. The coronary flow was found to be increased during digestion by over 80% and about 400% when the dog performs strenous work, according to Essex and his associates. The pressure in the right coronary is lower than in the left coronary, but is considered higher than the pressure in the right ventricle, whereas the pressure in the left coronary sinus is about 10-12 mm.Hg. The flow from the coronary sinus is increased during the latter half of auricular systole and very greatly during ventricular ejection. In coronary perfusion experiments raising the right ventricular pressure increases outflow from the coronary sinus due to diversion of blood from the Thebesian drainage system. If the perfusion pressure is low and the right ventricular pressure high, the flow through the Thebesian vessels may be reversed and blood enters the myocardium from the ventricular cavity.

D. Venous Drainage:

The blood after releasing its oxygen, electrolytes and food nourishments, returns to the right side of the heart through

a superficial and a deep venous system.

(1) The superficial consisted of the coronary sinus, great cardiac vein and anterior cardiac veins usually 2-3 in human and 3-5 in dogs. 50-90% of the blood from the right coronary artery drains into the anterior veins (Gregg, et al). The anterior cardiac veins empty into the right auricle a little above the border of the AV node. The left coronary contributes a variable amount of blood to the anterior cardiac veins which is considerably lesser than the right coronary artery. (96).

(2) The deep venous system consists of a number of small veins which arise in the substance of the myocardium and empty into the right chambers by the Thebesian and other luminal vessels.

(a) Thebesian vessels described by Thebesius in 1708 are small venous channels which open into the auricular and ventricular cavities. Various workers have shown that they communicate with the cavities of the ventricles, especially the right, with the coronary sinus and other coronary veins and hence, with the capillary bed of the ventricular muscle. There are also many channels connecting the cardiac veins with one another and with extra cardiac veins tributary.

Arteriovenous anastomosis are plentiful in the myocardium. (188).

(b) Channels of Vieussens described in 1706. (198).

Wearn demonstrated two types of channels, the arterio luminal and arterio sinusoidal. The arterio luminal vessels are coronary branches from 0.2 to 1.0 mm. in diameter. The arterio sinusoidal vessels are branches of coronary artery which break up into a number of irregular channels varying 50-250 micra in diamter. This channel is referred to as myocardial sinusoid lined by one layer of endothelial cells in its walls which have free anastomosis with one another.

E. Coronary Anastomoses or Communications:

The coronary arteries form 3 types of anastomoses or communications:

1. Potential anastomoses between branches of the coronary artery (homocoronary anastomoses) and with those of another (intercoronary anastomoses). In normal hearts the coronary arteries are eventually end arteries. However, anastomoses between them occurs if gradual occlusion takes place.

2. Communications with cavities of the heart. The Thebesian vessels and channels of Vieussens consisting of arterio luminal and arterio sinusoidal were already described.

3. Extra cardiac anastomoses: Potential anastomoses between auricular twigs of the coronary arteries and branches of the internal mammary and aorta-pericardial, bronchial, phrenic and esophogeal (112). The site of anastomoses is in the pericardial fat and around the opening of the great vessels. Pericardial adhesions increase the extracardiac anastomoses (189). It does not appear that anastomotic communications play any role in supplying blood to normal hearts. Gradual occlusion of the coronary is followed by development of anastomoses as shown by back flow studies (151, 95, 98). In cases of complete occlusion of both coronary arteries, the blood supply of the myocardium, to sustain life, comes from the ventricles or through extracardiac anastomoses or both. Pratt (164) has shown the existance of communications between the coronary system and the ventricular cavities. Katz and his associates (122) showed the same communications by injection of bacteria into the superior vena cava. The bacteria were found in the sinusoidal spaces, capillaries and small arteries of the myocardium.

F. Factors Regulating the Coronary Circulation:

1. The aortic blood pressure: The mean aortic pressure and the

resistance in the peripheral coronary vessels are the most important factors determining the coronary flow (98, 120). The coronary flow is decreased in aortic regurgitation and in arteriovenous aneurysm because there is a sharp fall in the diastolic pressure.

2. Innervation of the coronaries: The coronary vessels are very richly supplied with both vagal and sympathetic fibers. The larger coronary branches are equally innervated by both fibers whereas the arteriolar innervation are mainly through the vagus. In mammals the vagus is vasoconstrictor, while the sympathetic and adrenaline are vasodilator. (8). The vagus exerts its effects through the liberation of acetylcholine. One would expect acetylcholine to reduce the coronary blood flow, but in mammals this chemical dilates the coronaries, an effect which is not abolished by atropine. According to White, a great portion of the coronary constrictor fibers run through the superior cardiac nerve and that its interruption increases the irritation of the myocardium. It appears that the normal and predominant action of the sympathetic impulses in coronary physiology is to produce dilatation, but under pathologic condition, like angina pectoris, the action is reversed; that is, such impulse produces coronary constriction, because of pathological changes in the myoneural

junction (170). Operations devised to relieve pain by the interruption of different pathways are only palliative measures; they remove the warning signal of an impending seizure, but do not solve the patient's real trouble. The operation of Raney (170) is a preganglionic operation; the major portion of the different mechanism is left intact and thus the warning signal is not removed. Horner syndrome is not produced; the different pathways on the operated side are almost entirely interrupted. The operation consists of sectioning of the rami communicantes from the intercostal nerves and section of the sympathetic chain between the 5th and 6 th dorsal ganglion.

3. Coronary reflexes initiated from the abdominal and thoracic vicera have been demonstrated. Stimulation of the abdominal organs has been shown to cause coronary constrictions. A coronary dilator reflex is initiated by a rise in pressure in the right auricle or vena cava. The coronary reflex is not abolished by excision of the stellate ganglia (179), and the sections of the other sympathetic cardiac fibers. Both limbs of the reflex would appear, therefore, to be in the vagus.

4. Oxygen lack and carbon dioxide excess: Anoxia increased

coronary flow very greatly. Reduction of oxygen saturation of the arterial blood below 20% causes maximal dilatation of coronary vessels and a five-fold increase in flow (222). Carbon dioxide and lactic acid in the absence of a reduced oxygen supply caused only a very moderate dilatation of the coronary vessels. Reactive hyperemia is a very pronounced phenomenon of the coronary circulation.

5. Variation in heart rate: In an animal in which the innervation of the heart is intact, the coronary flow is actually increased during cardiac acceleration. However, an increase in heart rate which causes shorteneing of diastole relatively to systole, will decrease the coronary flow. When the rate is slow, other factors remaining constant, the flow is also augmented.

6. Drugs: Nitrites, cyanides, caffeine, camphor, adenosine, mecholyl increases the coronary flow. Histamine, niketamide, atropine and nembutal were found to increase the flow from 60 to 100%.

Thyroxine increases the flow by 250%. Khellin, an active principle from a plant is a powerful coronary dilator. Pituitrin decreases coronary flow by 80%. Alcohol in the concentration of 0.1% or more in the blood causes constriction

of the coronary artery and reduction of coronary flow. (Sulzer).

Drugs which increase coronary flow in normal hearts have apparently little or no effect in increasing the blood supply to an infarcted area.

CHAPTER IV.

PATHOLOGY OF ISCHEMIC HEART DISEASE.

Occlusive disease of the coronary arteries is a part of a general medical disease called arteriosclerosis. It is characterized clinically by angina pectoris, acute coronary insufficiency and cardiac infarction; pathologically, by occlusive coronary atherosclerosis with or without thrombosis and by focal or massive ischemic myocardial necrosis or fibrosis.

Coronary arteriosclerosis is an occlusive process usually of large and medium sized coronary arteries (176) characterized by intimal thickening, lipoid deposits and often calcium deposition, all of which narrow the lumen of the coronary vessel (7). The larger vessels on or near the surface of the heart are particularly involved. Small arteries within the myocardium rarely show any marked sclerosis. The left coronary artery is usually more severely affected than the right because of anatomic characteristic and distribution. The deep branches of the arteries of the left ventricle leave at right angles and pass directly through the

myocardium. The branches of the arteries of the right ventricle spread out in practically the same plane as the larger arteries from which they arise. (220).

Lipoid substances accumulate in the intima in a patchy irregular fashion causing a variable degree of pressure atrophy of the underlying media and sometimes, encroaching in the lumen of the vessel.

The degree of narrowing cannot be accurately assessed by its appearance at necropsy. Duguid and Robertson maintain that an arterioschlerotic vessel per se is dilated and that narrowing of the lumen is only caused by thrombosis.

Although the normal intima and early atheroma are a vascular advance, lesions developed a blood supply from the vaso vasorum (Leary). Some authors disagree, for according to Anderson (7), the intima of normal coronary arteries is without vasa vasorum, but in and around atherosclerotic lesions may be found in capillaries some of which take their origin from the lumen.of the artery. The importance of haemorrhage from these delicate channels in the initiation of coronary thrombosis has been emphasized by Patterson in 1936 and Wartmen in 1938 (212).

Secondary calcification of advanced atherosclerosis may convert the coronary arteries into bony tubes. Erosion or ulceration of atheromatous lesions forms an excellent nidus for secondary thrombosis, which is the common cause of acute coronary occlusion. Atheroma may represent nothing more than intravascular clotting (Duguid, 1948).

A. Etiology of Arteriosclerosis:

The biologic interpretation of arteriosclerosis explains the difficulty some observers have had in determining when physiologic aging ends and disease begins. The doctrine that arteriosclerosis is an inevitable oonsequence of growing old has been largely abandoned, instead it is now believed that arteriosclerosis is closely related to disturbances of metabolism usually acting over a period of time, brought about by heredity, fat ingestion, emotional and physical stress, alcohol and tobacco intake, physical make-up, age sex, race and climate (3, 41, 63, 69, 70, 88, 110, 125, 156). Perhaps there is alteration in the biophysical properties and biochemical structure of the intima itself. The filtration theory of atherogenesis by Page is based on observation that cholesterol deposits may accumulate gradually

over the years in normal individuals, but that they may do so much more rapidly in a far greater degree in the presence of raised blood lipoprotein, if there is high filtration pressure and if there are changes in the ground resistance of the intima increasing permeability. (Wilens, 1947, 1951).

B. Pathological Manifestations:

There is a substantial agreement that coronary heart disease is a manifestation or varying degrees of myocardial ischemia and anoxia. When a coronary artery is narrowed or occluded, the fate of the human being or experimental animal depends upon the amount of blood to the ischemic myocardium (Beck, 32). The responses of the heart are two types: (1) One which concerns the production of electric current. (2) The other which concerns the death of the heart muscle.

(1) Coronary Occlusion, Thrombosis, Embolism: Complete blockage of a coronary may result from thrombosis, progression of the arteriosclerotic process, intramural haemorrhage, syphilis about the coronary openings and embolism. Most coronary occlusions are within 3 - 4 cm. of the openings of the vessels. Leyden in 1884 described the results of coronary obstruction and grouped them into 3 classes:

(a) those with no myocardial changes observable, death having occurred so suddenly that there was no histological changes demonstrable; (b) those giving rise to myomalacia cordis; (c) those due to a slower progressive closure of arteries producing myofibrosis either as disseminated islands or as larger confluent areas of fibrosis.

Whitten in 1930, grouped the life results of fibrosis of occlusion and infarction: (a) those with a large zone of destruction and fibrosis, often associated with thinning of the ventricular wall; (b) those with localized scars producing surface depressions, the infarct lesion generally extending almost through the myocardium in a zone corresponding fairly well with the surface depression; (c) those with the infarct confined to the subendocardial third or fourth of the ventricular wall.

According to Beck (31), coronary occlusion has 3 effects: (a) production of oxygen differential and the current produced by these differentials lead to ventricular fibrillation, then cardiac arrest. One-third of all victims of coronary heart disease has no infarct. The majority of death is due to fibrillation rather than destruction of muscle; (b) death of the heart muscle; (c) heart failed to produce mechanical energy

leading into heart failure and death.

Coronary thrombosis is almost invariably on the bssis of a coronary arteriosclerosis. It is then the final event in blocking a lumen, which is already greatly narrowed. There is always a relation between intramural haemorrhage and thrombosis of the lumen. Small hematoma may precipitate thrombosis inside the lumen of the artery.

Coronary occlusion by emboli is relatively rare because of the protected position of the coronary ostia. If it ever occurs, it is due to fragmentation of vegetations from the adjacent aortic valve.

2. Myocardial Infarction: Grossly, the infarct of the heart wall is primarily a large area of congestion which later undergoes the changes described in coagulation necrosis. The area gradually undergoes decolorization, becomes smaller, more sharply defined, removed from the arterial occlusion and is accompanied by thinning of the heart wall in the late stages. There is only rarely a zone of reactionary hyperemia, fibrosis appears first in the margins and finally extends through the infarct. The removal of necrotic material is accompanied by liquefaction by the action of polymorphonuclear leucocytes, fibroblasts,

polyoblasts and multinucleated giant cells. There is no reason for assuming that true regneration of muscle occurs in the healing of myocardial infarct. (117).

Cicatrization of the myocardial infarct is due to proliferation of pre-existent connective tissue and blood vessels and is not materially different from cicatrization of other organs. (7).

In view of death of muscle fiber followed by fibrosis, replacement with thinning of the ventricular wall may lead to aneurysmal dilatation and cardiac rupture in 5 to 10% of cases. (165).

When necrosis involves the inner layers of the myocardium, mural thrombi frequently form against the damaged myocardium, in fact, they are found in 40-50% of all cases. (Hellerstein and Martin, 1947).

Local pericarditis occurs over superficial necrosis and has been formed in 30-85% of all cases (Wartman and Hellerstein, 1948 (212).

McDonald and associates (152) found that (a) 43% of their pathological specimens had significant coronary occlusive disease; (b) 73% of cases without angina, but with other clinical

symptoms had involvement of 2 or more arteries. Only 10% of these lesions were theoretically curable; (c) angina did not occur unless at least two arteries had extensive involvement. None of the patients with angina had curable lesions. All but one have had previous myocardial infarction ; (d) in general, coronary arteriosclerosis, when clinically manifested, tends to be generalized.

Infarction was more common in the left ventricle than the right ventricle and infarction in the left ventricle was more frequently due to disease of anterior descending branch than of the circumflex branch. The anterior descending branch of the left coronary artery is called the artery of coronary occlusion and the artery of sudden death. Although the right ventricle has fewer blood vessels than the left, it is much more likely to receive an adequate blood supply even with advancing years (Whitten (220).

In dogs, ligation of the circumflex branch of left coronary at its origin results in 90% mortality, while of the anterior descending branch, results in 70%. Ligation of the right coronary at its origin results in 100% mortality. Back flow of 300 ccs. per hour from the anterior descending is enough to save the dog's life, if this artery is ligated and 390 cc.

per hour from the circumflex artery is enough to save life after this artery is ligated. (Beck, 17, 18, 28, 31).

The incidence of infarction was 75% for anterior descending branch; 21% for the right coronary artery and 4% for the circumflex branch of the left coronary artery in human patients. (Bean, 16).

Zoll, Wessler and Schlesinger found intercoronary arterial channels to be found in 9% of normal human heart and about 10% of normal dogs' heart.

Occlusion of a major coronary artery branch for 10 mins. causes subsequent electrocardio-graphic changes in many dogs and gross infarction is produced by occlusion for 25 mins. (Webb, et al, 215)

Occlusion of coronary arteries is the most effective stimulus for production of intercoronary anastomoses. Occlusion plus time equals intercoronary arterial anastomoses. 89% with acute occlusion had intercoronary channels while 100% with chronic occlusion had intercoronary channels (31).

Twelve or more days of 75% narrowing were regarded to produce sufficiently rich anastomotic communications to

protect the myocardium from damage and to permit survival after superimposed acute complete occlusion;freely communicating anstomoses rarely appeared within hours or days, but were abundant after two weeks (44).

CHAPTER V.

HISTORICAL BACKGROUND OF THE DIFFERENT REVASCULARIZATION PROCEDURES REPORTED IN THIS THESIS.

A. Introduction:

In the Harvey Tercentenary Congress in London last June 1957, circulation in different parts of the body, including coronary circulation, were discussed. Historical background with regards to etiology, physiology, pathology and treatment both medical and surgical were reviewed and presented by different representatives of 16 countries. It was the consensus that arteriosclerosis would probably be better understood in the next hundred years and then may be prevented. Until that time comes, different research laboratories are discovering new facts and surgery has taken a foothold in the therapy of coronary artery disease.

Beck and O'Shaughnessy pioneered revascularization of the ischemic myocardium by their famous operations associated with their names in 1935 and 1936, respectively. Since then, new surgical therapies have come and gone, and it was implied that some had transitory popularity. Nevertheless, surgery of the heart is here to stay. A brief tabulated summary of these procedures appears in Table I.

A detailed historical review of the surgical procedures performed in this laboratory for the year 1958-59 is hereby presented.

B. Ivalon Sponge Operation (208, 209):

In 1957, Constantine at McGill University used thin slices of marine sponge and Deliyannis of Montreal Cardiology Institue, in the same year, used dry marine sponge powder. Both were abandoned because most of the animal died from severe reaction and pericardial effusion.

Since 1951, plastic sponge manufactured by Clay Adams of New York was used as a framework for living tissues. Grindlay and Waugh of Rochester, Minnesota in 1951 reported its use to reinforce abdominal aneurysms. In 1952, Gale and associates of Madison, Wisconsin used ivalon sponge prosthesis following resection in pulmonary tuberculosis. By using this sponge as plombage, the dead space created following resection was filled and accompanied by a minimal amount of reaction.

Deliyannis, while a resident in the Chicago Municipal Sanatorium in 1956, where ivalon plombage was used in lung resections, noted that the sponge was moderately vascularized during subsequent operations on the same patients. This puzzled him, so when he came to Maisonneuve Hospital in 1957, under the direction of Vineberg

he used for the first time, thin sheets of one-eight of an inch thick Ivalon sponge for revascularization of the ischemic hearts in a series of 14 dogs, whose coronary arteries had Ameroid constrictors. Three dogs survived 30 days and the rest were sacrificed two and one half to four months after operation. The sacrificed dogs showed no evidence of myocardial infarction. Microscopically, the interstices of the sponge contained blood vessels filled with red blood cells. There was no evidence of arteriolar connections between these vessels and the arterioles of the myocardium. He used retrograde injection of the coronary sinus with india ink which reached the area of the sponge and the lumen of the heart. There was no definite conclusion to his work because normally retrograde india ink injection of the coronary sinus of normal hearts will go into the lumen of the heart. This was proven many years ago by Thebesius, Pratt and Wearn. Verbal conversation with Deliyannis, before he left Maisonneuve Hospital in 1958, lead me to believe that he did not have much faith in the procedure and that he predicted that the ivalon sponge would be replaced by fibrous tissues, if left long enough on the surface of the heart.

Vineberg, on the other hand, believing that some protection was given to those dogs of Deliyannis for them to survive the ameroid constrictors and live many months. As a matter of fact, he was the first one to use successfully the ivalon sponge in revascularization of ischemic human hearts in the early 1958.

In view of lack of sufficient scientific proofs of how the ivalon sponge operation works, we have reinvestigated the operation at the Department of Experimental Surgery of McGill University from July 1,1958 to June 30, 1959.

Two series of Ivalon Sponge Operations were performed as Series II-A and Series II-B, which are described in Chapter VIII of this thesis.

Ivalon sponge is a white polyvinyl alcohol sponge produced by treating foamed polyvinyl alcohol with formaldehude. It is soft and resilient when wet and hard when dry. The sponge can easily be sterilized easily by boiling in water for 30 minutes and allowing this sponge to remain in water until cool. It has a framework of continous intercellular spaces, which permits

the infiltration of fibrous tissues and new blood vessels. Ivalon surgical sponge is separately manufactured under carefully controlled conditions, compared to the ordinary household sponge, in order to avoid foreign body reaction which might result from contamination. Furthermore, the sponge will not support mold or bacterial growth. It is inert and harmless to living tissues.

C. Implantation of the Internal Mammary Artery into Left Ventricular Myocardium and Partial Coronary Sinus Constriction: (194-206 inclusive)

In 1946, Vineberg first implanted the left internal mammary artery into the left ventricular myocardium in dogs, and subsequently, to many human patients since 1950. During the span of 13 years, many hundreds of dogs were subjected to this type of operation by different Research Fellows in this laboratory, studying them physiologically, technically and pathologically for more refinement and modifications as the case may be.

The original Vineberg procedure as reported in the literature and as mentioned by Rodriquez in An Atlas of Cardiac Surgery, consisted of the following; 1. The left internal mammary artery is dissected free from the chest wall from the 6th to 4th intercostal spaces, transectimg very carefully

between catgut #3-0 ligatures, the intercostal branches. The distal end of the artery is ligated with cotton.

2. The artery is implanted into the ventricular tunnel 1 cm. deep and 2 and 1/2 cm. long, created by a small straight mosquite hemostat forceps, without tension, torsion, kinking and injury to the artery. The end of the artery, which is ligated with cotton, is tied to an anchoring suture of cotton at the region where the tunnel ends.

3. Before the artery is drawn into the tunnel, the 6th intercostal artery and 2 or more branches are cut so that blood escapes freely through the openings into the surrounding myocardial tunnel.

4. The pre-pericardial fat pads are applied over the surface of the myocardium which is stripped off the epicardial covering.

5. Recent additional modification: partial coronary sinus ligation to 3 mm. diameter.

A study shows that new blood is brought to the myocardium because no hematoma is produced after the artery is allowed to bleed continuously inside the myocardial tunnel. Histologically, anastomoses between the arteriolar branches of the implanted artery to the branches of the arteriolar branches of the coronary arteries takes place, approximately 5-6 months

after implantation. 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. Mortality is reduced after anterior descending branch of the left coronary artery is ligated. Finally, there is better chance for the internal mammary artery to grow and give branches in a ischemic myocardium, than in a normal well supplied myocardium.

The critics of this procedure has been numerous because the results they obtained in their laboratories could not duplicate those obtained in this laboratory. The surgical and medical literature has been flooded by this discouraging poor result from different authors, that the popularity of the procedure has waned temporarily. Nachlas and associates (158) found that the internal mammary implant in pigs became obliterated in 4 weeks. Maniglia and Bakst (139) showed after 6 months following implantation that the lumen of the artery has narrowed from 50% to 10% of the normal caliber. Glenn and his associates (81, 82) reported that the implanted artery showed narrowing of the lumen due to intimal proliferation and the other changes were those of organization and channeling. The report in the literature appeared to have

changed since 1958, when other reseachers, like Bellman and Frank (36), Bakst and Loewe (134), Pearl and associates (160), Duchene et al (64) have shown that the implants remained patent and anastomoses were formed with the branches of the coronary arteries. They also reported better survivals and better protections to the ischemic hearts by physiological studies. Pearl and Bakst have recently reported that good implantation of the arteries occurred in ischemic myocardiums far better than in normal non-ischemic hearts. The purpose of the operation appeared consummated for it is the treatment of coronary insufficiency and the operation of choice now and in the future for it really brings new extra cardiac blood to the impoverished heart, which is on the brink of death.

D. Beck I: Abrasion of the Epicardium; Asbestos Poudrage and Partial Ligation of the Coronary Sinus. (17, 18, 19, 22, 23, 25, 26, 27, 28, 29, 30, 34).

Beck has pioneered the work in revascularization of the ischemic heart. In 1935, he started with grafting pectoral muscle to the surface of the heart, followed by poudrage of powdered beef bone. Subsequently, through series of animal experimentations, he brought forth the Beck I procedure. It consisted of theabrasions of the lining of the parietal pericardium and also of the epicardium,

narrowing of the coronary sinus to a diameter of 3 mm., application of powdered asbestos 0.3 grams to the surface of the heart and finally, the application of mediastinal fat as a graft to the surface of the heart. Beck claims that this operation increases average back flow from 228 cc per hour to 510 cc per hour, or an increase of 282 cc per hour. Recently, he has tried to replace the mechanical epicardial abrasions by the application of 5% trichloracetic acid and his results showed average back flow of 10.1 cc per minute or 606 cc per hour. This modification is still in the experimental stage, although he has already tried it in some human cases. The Beck I operation produces an inflammatory reaction on the surface of the heart which in turn, produces and opens intercoronary arterial channels. The operation rarely adds new blood from outside sources. It redistributes its own blood, so that the heart can enjoy a balanced circulation. Beck believes that the heart resists blood from outside sources and while it is not impossible to produce extra coronary anastomoses between the hearts and grafts, they can not be produced with any degree of regularity.

Gross in 1935 has shown ligation of the coronary sinus provided far greater extractions of oxygen from the blood in the capillary bed, stimulation of intercoronary anastomoses, reduction of size of infarct when left anterior descending branch of left coronary artery was ligated. Subsequently, different authors have substantiated these findings. For this reason, it was incorporated in the Beck operation to increase survival rates and prolongation of life. Beck I operation prevents the mechanism, death, which is the main cause in 90% of cases, secondary to oxygen and electrical differential at the periphery of the anoxic zone and normal heart tissue. The difference in electrical potential electrocutes the heart by producing ventricular fibrillation and then cardiac arrest. One third of coronary attacks or death does not show any myocardial infarction. The other cause of death is death of the muscle mass, which leads into cardiac failure. This proceudre is at present the most popular, for it is easy to perform, has very low mortality, (8%), and has a good immediate result (64, 140).

E. Thompson and Raisbeck Procedure (Cardio-pericardiopexy) (148, 189, 190).

In 1932, Hudson, Moritz and Wearn have recommended the pericardium as a source of collateral circulation for the pericardium receives branches from the aorta, internal mammary, esophageal, phrenic, bronchial, mediastinal and coronary arteries. Cardio-pericardiopexy was first used by Beck and O'Shaughnessy.

In 1942, Thompson and Raisbeck first introduced 0.3 grams of sterile talcum powder (U.S.P.), hydrous magnesium silicate into the pericardial sac. The powder produced a foreign body reaction characterized by fibrinous pericarditis. There was inflammatory reaction involving the pleura, pericardium, epicardium and adjacent myocardium. Augmentation of coronary circulation was produced in three ways: 1. Formation of new channels between the main coronary arteries. (2) Dilatation and proliferation of already existing inter-coronary channels. (3) Formation of new extra-cardiac channels from the grafted pericardium. (148). All of these actions were due to foreign body granuloma reactions to the irritant effect of the talcum powder, accompanied by the hyperemic and increased vascularity. Subsequently,

different authors have instilled chemicals into the peri-cardial cavity to produce cardio-pericardiopexy. Some of these chemicals are phenol, acetic acid, HCl, trichloracetic acid, sodium, salicylate, enzymes, etc. Various surgeons, who have used the procedures, showed good results because it is easy to perform, has low mortality rate and has produced immediate effect and action. However, other authors, like Gage and associates (77), Gross and associates (102), showed that cardio-pericardipexy failed to protect the experimental animal against coronary occlusion.

F. Cardio-Pericardiopexy: By the Use of 5% Sodium Salicylate:

This is another procedure like the Thompson-Raisbeck procedure which works on the same physiological principle of producing non-suppurative fibrous pericardiopexy through lysis of the epicardium. The other chemical methods of de-epi-cardialization were: (1) phenol, used by Harkin and associates (107); (2) resorcinol; (3) cresol; (4) thiophenol; (5) thiocresol; (6) barbiturates, salts; (7) ether; (8) chloroform; (9) aliphatic alcohols; (10) acetic acid; (11) lactic acid; (12) phosphoric acids; (13) salicylic acid; (14) acetyl salicylic acid; (15) trichloracetic acid; (16) and lastly, salicylates salts.

Knock of Presbyterian St. Luke's Hospital in Chicago, first used sodium salicylate solution in hypertonic glucose in conjunction with implantation of multiple omental loops for revascularization by cardio-mentopexy (124). SHe claims that simple application of sponge soaked in 5% sodium salicylate solution to the ventricles for a few minutes, allowed easy removal of long strips of epicardium from both right and left ventricles. No other authors in the literature has used 5% sodium salicylate alone for revascularization of the ischemic myocardium. In this laboratory, we have tried this chemical in a series of five dogs to find out its efficacy in terms of physiological, pathological survival and X-ray findings.

G. Arterialization of the Coronary Sinus by Anastomoses of Left Inferior Pulmonary Vein to Coronary Sinus and Partial Ligation of coronary Sinus: A New Procedure. (Pablo)

The principle of arterialization and of the reversal of the flow of blood through the coronary sinus and its ramifications was first suggested by Roberts (172) and was first successfully carried out in experimental animals and human beings by Beck andhis co-workers. Bailey and his associates (12) confirmed the results of Beck and he has advocated its use in occlusive disease of the coronary

arterial system, produced by atherosclerosis and in congenital anomalies where coronary arteries take origin from the pulmonary artery. It has been shown that the coronary sinus and its tributaries possess continuity with the capillary bed of the left ventricle and septum. The coronary sinus also has several collateral channels leading to the lumen of the right atrium. Arterialization of the coronary sinus permits arterial blood to enter the capillary bed of the left heart by retrograde flow through the tributaries of the coronary sinus. Following arterialization, branches of the coronary sinus establish epicardial anastomoses with the small cardiac veins of the right ventricle. Through these anastomoses, the right ventricle also receives arterial blood. The collateral channels also return the major outflow to the lumen of the right atrium, which acts as a safety valve. The two measurements of benefits are less mortality and infarction, which indicate that the anastomoses can and does supply the myocardium with a sufficient amount of arterial blood (12, 14, 23, 24)

Hahn and Kim (105) studied histological changes after arterialization of the coronary sinus. The original vein had undergone marked alterations so that it was difficult to

identify intima media and adventitia. The graft was a tube of fibrous tissue lined by endothelium. The media and adventitia were composed of collagenous and coarse elastic fibers. Finally, it was found that the grafted vessel becomes occluded in 6 months by intimal proliferation and thrombus formation. At present, Dr. Beck and other surgeons have given up this procedure, because of difficulty in the technical aspect, high mortality, multiple surgical procedures and finally, the graft becomes blocked.

In the present procedure, we are using the left inferior pulmonary vein, which carries arterial blood and which has a lower pressure than a systemic artery, thus preventing ultimate blockage of the anastomoses. Partial ligation of the coronary sinus is also performed, like in Beck I, in order to augment the reversal of flow through the coronary sinus and promote intercoronary anastomoses and bring more blood to the capillary bed. This operation could be performed in one single procedure. (20, 66, 94, 95, 100, 101).

CHAPTER VI.

OBJECTIVES AND PROBLEMS OF REVASCULARIZATION OF THE ISCHEMIC MYOCARDIUM.

The death from coronary heart disease has reached an enormous proportion to become not only an individual problem, but also national as well. In the United States alone in 1950, the death from cardiovascular disease was at the rate of 2,040 each day, 85 every hour and 1.25 every minute. One-third of all deaths in the U. S. were due to this number one killer. (189).

There is an increase in coronary death of 114% over a period of 7 years. The increase among physicians was 240%. It appears to be that coronary heart disease is an occupational hazard of the medical profession. It does not spare even those who know the disease, and who treat the disease itself. (189).

Since the medical treatment for these coronary cripples is insufficient and very unsatisfactory, surgical treatment has taken a foothold in its therapy. Many years ago the heart was a forbidden territory and a no man's land for the surgeons, but today, it is the main street of cardiac surgery.

All revascularization procedures done in human beings have been tried and given the stamp of approval after hundreds and thousands of experimentation in animals. They have been studied in all angles, physiologically, pathologically, technically, radiologically, etc. They were also submitted for careful scrutiny and discussion before surgical meeting of top level cardiac surgeons, physiologists and cardiologists.

The pathology of the heart could be understood better after knowing it physiologically. The purpose of any treatment is to restore as much as possible of the heart to its normal function.

In myocardial ischemia the limit of adjustment between blood demand and supply which has been called the coronary reserve may be exceeded by an increase in myocardial demand or rationale of surgery in the treatment of coronary heart disease is to increase the coronary supply. The treatment consisted of interruption of the nerve supply, especially the sympathetic nervous system, removal of the thyroid gland when necessary, and finally, the operation on the heart itself. The objective is the augmentation and distribution of the coronary circulation which is produced in 3 ways:

(1) Formation of new channels between the main coronaries. (2) Dilatation and proliferation of already existing intercoronary channels. (3) Formation of new extracardiac channels (190).

The other problem is the simulation of the disease in experimental animals. There were various ways of experimental production of coronary insufficiency performed and then, results are controversial and inconclusive. Furthermore, revascularization procedures are performed long before the disease has occurred, which is not the case with human beings. The ideal way is to produce the disease and then treat it afterwards, just like treating human cases.

In the Department of Experimental Surgery At McGill University, Litvak in 1956-57 simulated coronary insufficiency by the use of ameroid casein plastic in steel jacket whose rate of constriction of the coronary arteries were slow, fairly constant and reasonably predictable in vivo. These dogs subjected to ameroid constrictors will die at an average of 20 to 26 days, if no revascularization procedures are done on them (132).

For the above reasons, the application of ameroid constrictors and revascularization procedures were performed simultaneously which are compared to the control series

of ameroid constrictors alone.

The following operations carried out in different series all had ameroid constrictors as follows:

Series I: Ameroid constrictors for control
Series IIA: Ivalon sponge operation.
Series IIB: Ivalon sponge operation.
Series III: Implantation of left internal mammary artery into left ventricular myocardium with partial coronary sinus ligation.
Series IV: Beck I operation.
Series V: Thompson-Raisbeck operation.
Series VI: Cardio-pericardiopexy by use of sodium salicylate.
Series VII: Arterialization of coronary sinus by anastomoses with left inferior pulmonary vein.

The various revascularization procedures will be compared to the control series and also between one another as to their efficacy on the following basis:

1. Survival time and mortality rate for the different procedures.

2. Intracardiac anastomoses like homocoronary and intercoronary anastomoses by injection of new Schlesinger mass.

3. Extracardiac anastomoses as shown by injection studies of intact heart.

4. Presence and location of infarctions by slicing the hearts and by microscopic findings.

5. Number of arterioluminal vessels and number of these vessels that went into the lumen of the heart.

6. Extent of coronary occlusion of ameroids treated coronary arteries by microscopic studies.

7. Patency and extent of occlusion of implanted internal mammary artery and anastomoses between left inferior pulmonary vein and coronary sinus by microscopic studies.

8. Position of septal artery.

9. Presence of dye in the intramyocardial blood vessels.

10. Pertinent microscopic findings.

CHAPTER VII.

EXPERIMENTAL MYOCARDIAL ISCHEMIA.

A. Review of Previous Methods:

Coronary artery disease is very common in human beings and could be easily produced in a susceptible host.

In the experimental anaimals, especially in dogs, coronary artery disease with coronary insufficiency is difficult to produce and stimulate as in human subjects. It is for this very reason why numerous setbacks in the research for the treatment of this disease lies.

Since the late 18th Century, numerous methods have been tried experimentally and clinically in order to produce the gradual occlusion of blood vessels, including the coronary arteries. The reports in the literature are voluminous, its statistics are inadequate with regards to effectiveness, mortality and extent of infarction.

Arterial occlusion could be produced by external compressing devices, by means of loops, springs, screws, tape, bands, clamps, like the Goldblatt clamps, and gadjets infinitum, which have been developed and tried by numerous investigators, like Halsted, Neff, Burchell, etc. The main

disadvantage of this method is infection invading the artifidal sinus from the outside, haemorrhage, compression atrophy about the wall and unpredicability of effective occlusion.

Arterial occlusion of internally obstructing the arteries like fascial plugs, tubes, springs, polyethylene tube, vinyl acetate and thrombogenic materials, like magnesium and aluminum wires, were performed. These foreign bodies within the vessels produce rapid thrombosis, plus danger of embolism, and finally, recanalization in some instances, which may or may not be desired.

Injection of irritant solutions, like iodine, silver nitrate, acriflavine, silicon, sodium morrhuate, into the tunica adventitia of the arteries were also used. The results were variable from mild to marked fibroplasia with resultant narrowing of the vascular lumen.

The most popular method in many laboratories in Canada, U. S. and other countries, is the ligation of one or more branches of the left coronary artery by means of suture ligatures, like cotton, silk or tape. This is usually done in a few weeks or days following revascularization procedures in normal or non-ischemic hearts. It is compared to putting the cart before the horse.

Furthermore, it has been proven that revascularization procedures were usually ineffective in non-ischemic hearts, where blood supply is normal. There is no need of extra blood in a normally nourished heart. (134, 160).

In recent years and in different laboratories, experimental production of gradual vascular occlusion by the use of cellophane, polyethylene, dicetyl-phosphate and finally, a combination of cellophane plus dicetyl-phosphate were tried by Abbott in 1949, Shapiroff in 1950, and Litvak of McGill University in 1956-57 (132).

The result of the experimental procedures showed with certain unpredictable periods, variable amounts of fibrotic reaction in the tunica adventitia and secondary narrowing of the arterial lumen. At no time was the free flow of blood in any of these arteries impeded because arterial pulsation and free flow of blood from the cut end of the artery distal to the wrapping were present.

The unsatisfactory results with cellophane and dicetyl-phosphate prompted a further search for a more suitable means of occluding arteries.

B. Gradual Occlusion of Coronary Arteries by Means of Ameroids. (Compressed casein plastic in a steel jacket, 132).

In 1954, Berman of Indianapolis, first reported casein plastic material as a means of producing gradual occlusion of blood vessels in experimental animals and man in a predictable time. Casein plastic is a hygroscopic casein derivative which absorbs water slowly. This material could occlude blood vessels if it is encased in a capsule or shell rigid enough to withstand peripheral expansion of the casein.

The casein plastic bars or rods are fitted into a stainless steel sleeve 1 mm. in thickness. The lumina of the casein plastic jacket are cut to different sizes by means of a metal drill. A longitudinal slot is made along the side of the sleeves through the steel and casein plastic into the lumen by means of a metal saw. The purpose of the longitudinal slot is to provide a means of slipping it over a vessel which is flattened momentarily. Encasement of the material in stainless steel directed the expansion of the plastic towards the previously cut lumen.

Glycerine coating of these sleeves produced a slight reduction in the rate of luminal obliteration over the entire

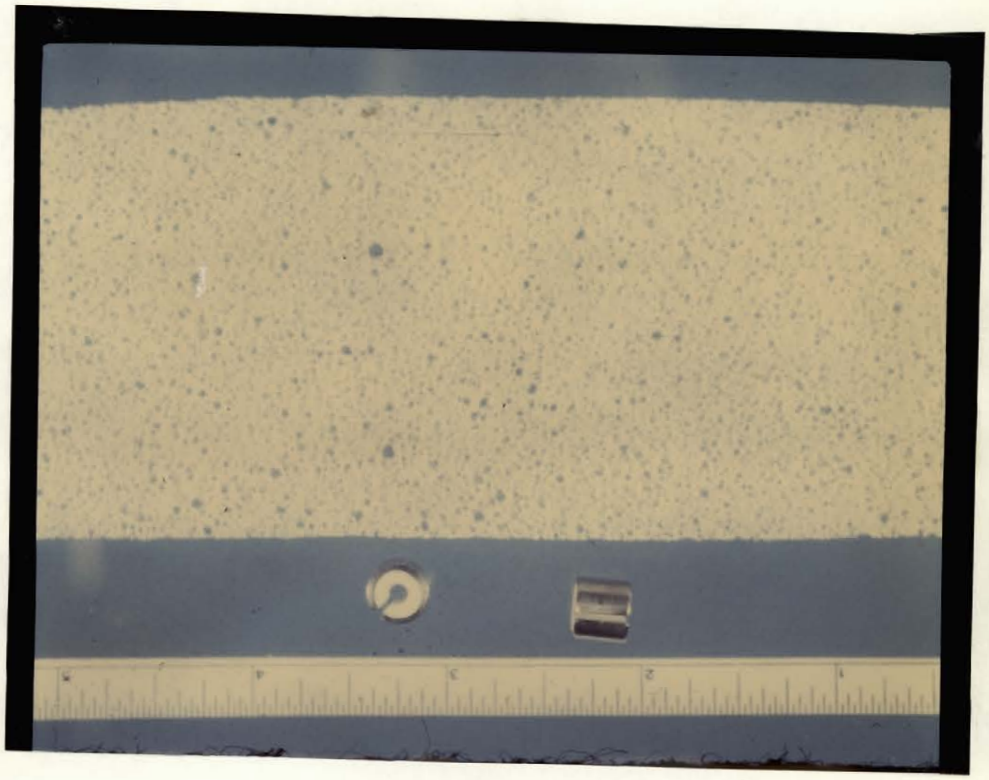


PLATE NO. 7.

Photograph shows a strip of Ivalon surgical sponge, (Clay-Adams) 1/16 inch in thickness; 2 casein plastic 'ameroids' in stainless steel jacket, and a ruler to show the relative size of its lumen, which is about 0.103 of an inch.

test period and occlusion occurs in 12 days. Rapid swelling of the plastic is noted. Petrolatum or vaseline coating of the sleeve produced no obliteration or alteration in the initial expansion of the plastic for 20 days. This is followed by a more gradual diminution in the size of the lumen over the remaining test period.

John Litvak of the Department of Experimental Surgery in 1956-57 tried this compressed casein plastic, called ameroid, in a stainless steel jacket clinically in dogs, using peripheral and coronary arteries. There is evidence that the time of occlusion of these arteries can be predicted with much success in order to produce artery or coronary insufficiency. These ameroids without coating of vaseline or petrolatum placed around the anterior descending and circumflex branch of the left coronary artery close to their respective point of origin, produced in 12 test dogs death which ranged from 2 to 26 days with an average of 15 days. When the ameroids with a lumen of 0.110 inch, coated with petrolatum were used, the average survival in Litvak's series was 20 days and in Mahanti's series was 26 days.

Microscopic examination of all sleeved encased coronary artery segments, revealed that occlusion probably

resulted from 3 mechanisms: (a) There is mechanical narrowing of the vessel by the swelling force of the casein plastic, thus making it the most potent factor in causing gradual vascular occlusion. (b) Fibroblastic responses of the arterial tunicae at the site of the sleeve application probably helped in narrowing the functional lumen. (c) Intraluminal thrombi are found which had organized and gradually filled the lumen of the artery in direct relation to the amount of time of sleeve application. Intraluminal thrombi appear to form eccentrically from the walls of the tunica intima and progressively filled the lumen.

These microscopic findings correlated with the clinical course of the experimental animals suggest that total anatomical occlusion of these coronary arteries was not necessary for production of myocardial infarction and insignificant alteration to the depolarization of the conducting system of the heart.

In the present studies of artificial myocardial ischemia, we use a modified technique of storage, sterilization and coating of the ameroid prior to its usage in the control and different revascularization series.

The modified technique presently used is as follows: The standard size ameroids with internal lumen of 0.103 of an inch. are measured by calipher and then placed on a steel rod, 6 in. in length, which will snugly fit into the lumen. This is purposely done to prevent gradual obliteration of the lumen from the desired size. The ameroids in stainless steel rods are placed in an airtight dessicator containing soda lime in its bottom. The soda lime absorbs moisture in the bottle and thus prevents expansion of the casein plastic; the ameroid is always kept dessicated dry.

On the day of operation the ameroids are obtained from the dessicator and placed inside a clean bottle containing fresh white petrolatum (U.S.P). The bottle is loosely covered and placed inside the autoclave for 10 minutes at 20 lbs. pressure or 15 minutes at 15 lbs. pressure. The ameroids become sterilized and at the same time, are coated with the melted petrolatum. The sterilized ameroids are allowed to cool and its internal lumen measured and verified to the desired size of 0.103 of an inch by means of sterile known steel rods before they are used in the different surgical procedures. Plate No. 8 shows the glass dessicator containing ameroids and soda lime.

PLATE NO. 8.

Photograph of an airtight glass dessicator containing Ameroids and soda lime.

CHAPTER VIII.

MATERIALS & METHODS.

A. EXPERIMENTAL ANIMAL.

In cardiac experimental research, dogs, especially the mongrel bred, are used not only in the Department of Experimental Surgery at McGill University, but also in other laboratories in Canada and the U. S. Mongrel dogs are preferred because of their fairly good resistance to infections and other diseases and also they tolerate operative insult and trauma very well. They are easy to procure at any time of the year, and are easier to care fore postoperatively for they are domesticated. Furthermore, the dog's heart has great resemblance to that of the human, anatomically and physiologically. Experimental results are comparable because the same type of animal is used practically in every research laboratory.

In our studies, mongrel dogs, which were healthy and fairly young, with weights ranging from 37-56 lbs. were used. Both sexes are represented and no pregnant ones were used in the series. Originally, we wish to limit our dogs to weights between 40-50 lbs. so that the hearts are of uniform size for production of coronary insufficience by ameroid constrictors.

B. ANESTHESIA.

The dogs did not have any premedication except that they had nothing by mouth the night and morning prior to operation. They were put to sleep by means of intravenous nembutal with the dose of 1 gm. per 5 lbs. thus maintaining third plane of anesthesia for about 3-4 hours. An endotracheal tube with an inflatable cuff or balloon was introduced into the trachea via the oral cavity to maintain a patent airway at all times. After the balloon was properly inflated, the endotracheal tube was connected to a Hiedbrink anesthesia machine and automatic Jefferson respirator, using plus 15 and minus 5 mm. of pressure of 95% oxygen and 5% carbon dioxide mixture. Fresh soda lime was always used in the anesthesia machine. Sometimes, additional numbutal was given if the anesthesia became light during the operative procedure.

C. OPERATIVE PROCEDURES:

After the animal was put to sleep, the left chest and upper abdomen were shaved by an electric razor. Then, the dog was positioned on the operative table on its right side with the left side uppermost. The four extremities were fastened and immobilized to the upper and lower posts on the side of the table. An aluminum contact plate of the Bovie

machine was anchored to one of the hind legs which was previously shaved.

The operative area was thoroughly cleansed with green liquid soap and water several times followed by the application of several layers of tincture of merthiolate 1 to 1,000 solution. Finally, the operative site was draped with sterile towels anchored to the skin by towel clips, followed by large surgical sheets.

The skin was incised from the sternum anteriorly to the line of the transverse process posteriorly and was made through the 4th or 5th intercostal space, depending upon the procedure for proper exposure of the field of operation. The subcutaneous tissue and different layers of the chest muscle and pleura were transected by a sharp knife, scissor or by a Bovie cautery. Small bleeders were electrocoagulated while big ones were ligated with cotton #10. The edges of the incision were draped with sterile towels and the adjacent ribs were spread 6 or 8 inches apart by a Burford or Tofiay self-retaining retractors for perfect operative exposure.

The rest of the detailed technique depends upon the type of revascularization procedure. However, the control series and all other revascularization series had coronary

artery insufficiency, produced by application of vaselinized ameroids around the origins of the anterior descending and circumflex branches of the left coronary artery. Individual procedures of the different series would then be described.

SERIES I: OPERATION FOR CONTROL WITH AMEROIDS.

The chest was opened and adjacent ribs were separated by rib retractors to the desired field of exposure. The heart was in free view after the left lung was displaced posteriorly by retraction with a lung forceps.

The pericardium was incised parallel and anterior to the left phrenic nerve from the base of the heart to its apex. All pericardial bleeders were ligated with #5-0 black silk sutures. The pericardial flaps were retracted by #3-0 black silk sutures and anchored either to the rib retractor or operative sheet. The left coronary artery and the origins of the anterior descending and circumflex branches together with their corresponding veins were identified, and exposed after the left auricular appendage was retracted by #3-0 black silk which was tied to a tiny portion of its tip. The anterior descending and circumflex branches were isolated about 1/2 inch just beyond their origin from the left coronary

artery following incision of the epicardium.

Elevated ligatures of cotton #25 with guidance of curved blunt probes were placed under each vessel. A segment of each vessel was lifted by 2 adjacent elevated ligatures set appart and a sterile vaselinized ameroid slipped around it, using a Lahey cystic duct clamp. After this was completed, all traction sutures were removed and the pericardium was closed by interrupted #5-0 black silk. Antibiotic powder of penicillin and streptomycin was sprinkled inside the left pleural cavity followed by gradual full expansion of the lobes of the left lung, which were put back in their anatomical place. The thoracotomy incision was closed in layers by using interrupted #25 cotton pericostal suture to approximate the two adjacent ribs. Continuous #10 cotton was used for the different layers of muscle and interrupted #30 stainless steel wire for the skin. The lung was fully reinflated after the air in the left pleural cavity was withdrawn through a rubber catheter. The above procedure was carried out routinely in order to establish gradual coronary insufficiency before the revascularization procedures were performed, at the time of operation. All other series will be compared to this control series.

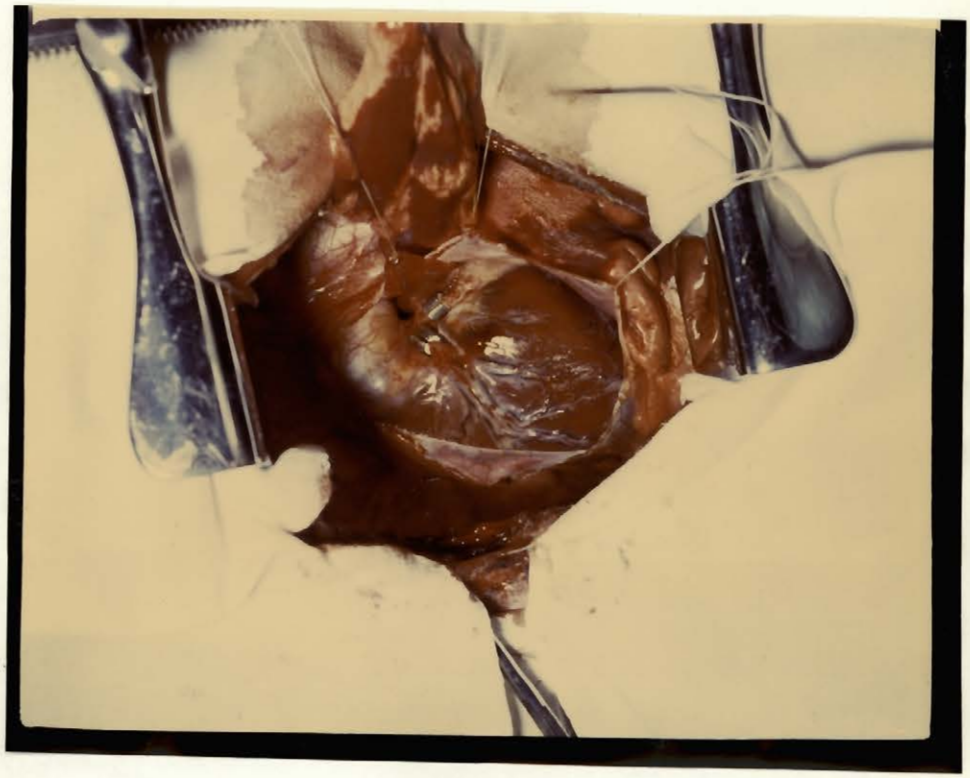


PLATE NO. 9.

Photograph of the heart showing the ameroids around the anterior descending and circumflex branches of the left coronary artery. Pericardium is reflected by means of stay sutures.

SERIES IIA & IIB: IVALON SPONGE OPERATION: A NEW REVASCULARIZATION PROCEDURE.

All steps are the same as in the control series up to the completion of the insertion of the ;ameroid constrictors.

In Series IIA, the epicardium or visceral serous pericardium on the anterior surface of the left ventricle and a part of the adjacent right ventricle was removed mechanically by dissection and by scraping with a Beck burr, deep enough to remove subepicardial fat and to lay bare the myocardial tissue. Moderate bleeding from scraped small blood vessels were encountered. A piece of ivalon sheet 1/16 in. thick sterilized by boiling for 30 minutes, was sutured by interrupted #5-0 black silk to the raw bleeding area of the heart. The fibrous pericardium, including the adjacent parietal serous pericardium overlying the anterior surface of the left ventricle, were removed mechanically and by sharp dissection, leaving alone the pericardial fat, containing branches of the pericardiophrenic artery and its respective collaterals. This pericardial fat containing blood vessels were then applied by a few sutures to the ivalon sponge, which acts as a sandwich meshwork between the pericardial blood vessels and myocardium.

Finally, the rest of the fibrous pericardium were closed by interrupted sutures of #3-0 black silk. All residual blood in the left pleural cavity were removed and antibiotic powder sprayed inside. The chest incision was closed in the same way as in the control series.

In Series IIB, the epicardium and subepicardial fat in the anterior and posterior surfaces of the left ventricle and adjacent part of the anterior surfaces of the right ventricle were removed mechanically by scraping with a Beck burr, until the myocardium was exposed. Also, moderate bleeding from scraped tiny epicardial blood vessels was encountered. In the process of scraping, care was taken not to injure moderate sized blood vessels. A bigger piece of sterile Ivalon sponge 1/16 inch. was sutured interruptedly around the entire left ventricle and part of the anterior surface of the right ventricle. The fibrous pericardium including the adherent parietal serous pericardium, overlying the scraped area of the heart were removed mechanically and by sharp dissection, except the small residual posterior portion which was scarped by a Beck burr. The pericardial fat containing blood vessels was also sutured interruptedly to the ivalon sponge and the

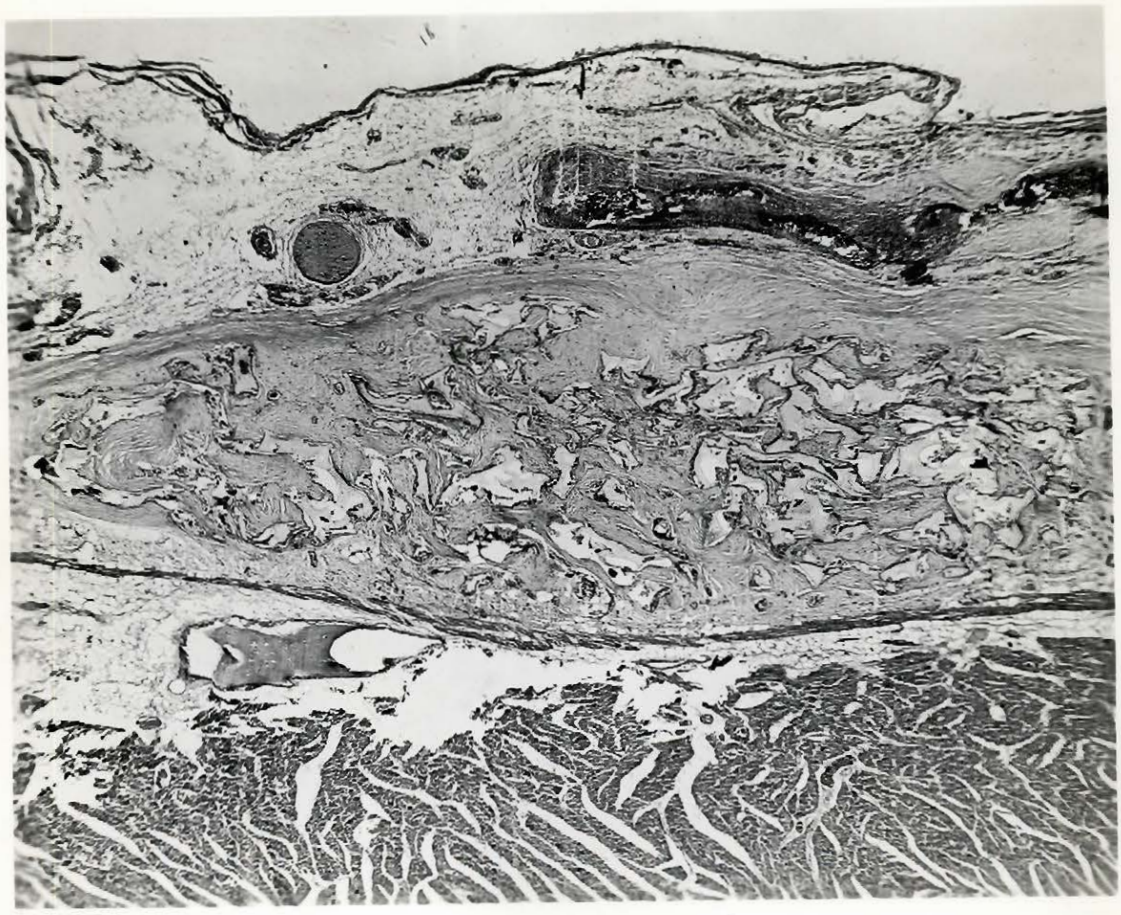


PLATE NO. 10-A

Microphotograph showing ivalon sponge interpose between bare myocardium and pericardial fat pad containing blood vessels filled with dye. The ivalon sponge contains endothelial lined spaces filled with dye and red blood cells. There are some hyalinized fibrous tissue. Myocardium has dilated spaces called sinusoids, but apparently, there is no visible dye in them. Specimen obtained from ivalon dog 24-441, which was sacrificed 98 days after operation (x 10).

rest of the pericardium closed in the same manner. Any blood in the left pleural cavity was removed and antibiotic powder sprayed inside. The chest incision was closed in the same way as the control series. From our results, Series IIB was a better revascularization procedure than Series IIA.

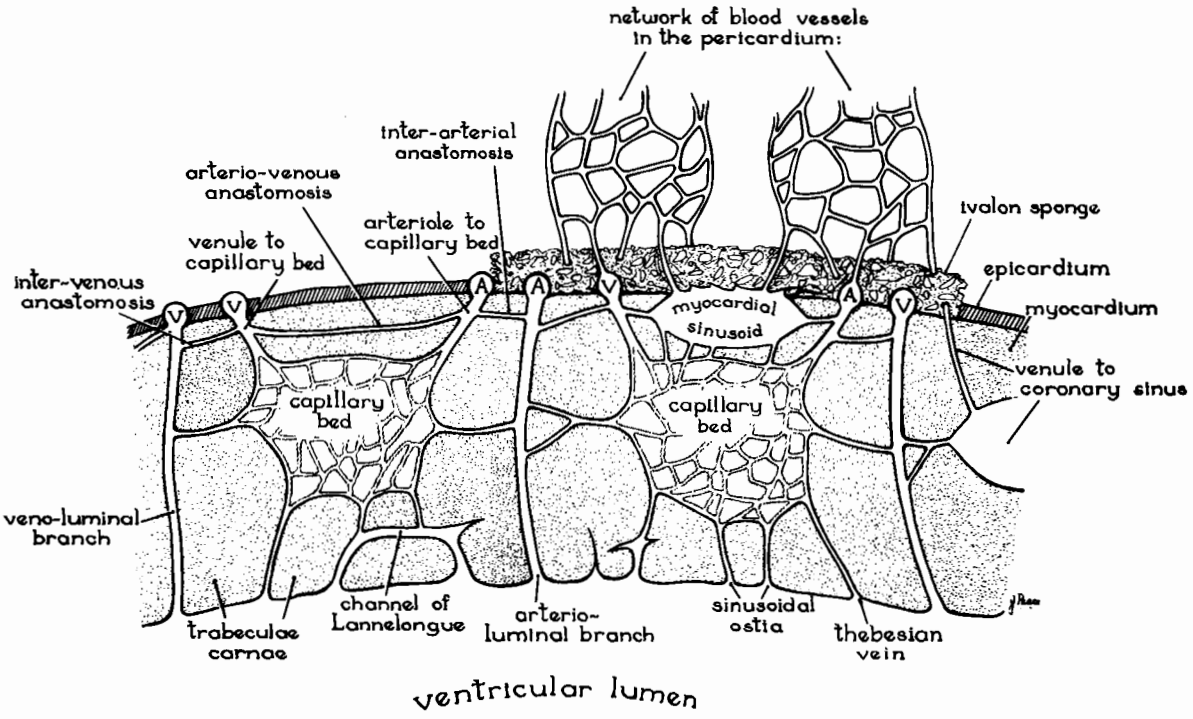
It appears that in the human being the fibrous pericardium and parietal serous pericardium could not be dissected away from the pericardial fat containing blood vessels because they are too adherent. In this case, scraping with a Beck burr is the only solution.

SERIES III: INTERNAL MAMMARY ARTERY IMPLANTATION INTO THE LEFT VENTRICULAR MYOCARDIUM AND PARTIAL CONSTRICTION OF CORONARY SINUS. (MODIFIED VINEBERG PROCEDURE):

The chest was opened through the fourth intercostal space following the control series procedure up to the completion of the application of the ameroid constrictor, in order to produce coronary insufficiency.

The operator then went to the other side of the operating

Myocardial Circulation



A modification of Vineberg's Myocardial circulation (209)

PLATE NO. 10.

Diagram showing the relationship of the Ivalon sponge to the anastomoses of network of blood vessels in the pericardium to the myocardial blood vessels, sinusoids, capillary bed, coronary sinus and ventricular lumen.

table, facing towards the inner surface of the sternum, where the left internal mammary was located. The subcostal muscle was partially excised and the parietal pleura incised along the course and surface of the internal mammary artery, which was gradually freed from the chest wall, after transecting between black silk sutures #5-0, all intercostal branches from the subclavian artery down to the 6th interspace. The internal mammary was handled meticulously so that no injury to the vessel in the form of subadentitial hematoma, bruising and narrowing of the lumen from ligature of the intercostal branches. The internal mammary was transected between 2 #10 cotton ligatures distal to the 6th intercostal artery which was the biggest of the intercostal branches. The proximal ligature was made long because it would be used at a later stage in the procedure.

The operator then went back to the previous side of the table and continued the operative procedure. The transected internal mammary artery was now pulled gently towards and applied over the left ventricle in various positions until the most favourable site was found for implantation into the myocardium, with the same tension possessed by the artery when it was anchored to the chest wall. An anterior stitch of

cotton #10 was placed towards the apex of the heart just distal to the proposed myocardial tunnel. A 4 mm. incision of the epicardium was made proximal and closed to the anchoring stitch. This represented the lower end of the tunnel. A mosquito hemostatic forcep was introduced through the incision to a depth of 1 cm. in the ventricular wall and the tunnel was extended 2.5 cm. proximally and horizontally beyond the point of introduction. The hemostat was directed along the projected ideal line of tunneling and it was spread a few times, in order to make a patent tunnel and open up the epicardial opening well on the surface of the heart. The ligature at the end of the internal mammary was then drawn through the tunnel by means of a mosquito hemostatic forcep. However, before the artery was drawn into the tunnel, the ligated 6th intercostal artery and 2 or 3 more branches were cut close to their origin, so that blood escaped freely from their opening into the tunnel. No scalloping of the internal mammary artery was done. Care was taken to prevent angulation, kinking or torsion of the implanted artery. The cotton ligature on the end of the artery was then tied to the anchoring apical suture, securing a normal tension for the implanted artery. Bleeding from the opening of the tunnel

if any, was controlled by light application of a gauze sponge for a few minutes.

By slight elevation and rotation of the heart, the coronary sinus was seen as a dilated thin venous structure emptying into the right auricle. A circumferential #2-0 black silk suture was passed around the sinus by reversing the needle through an arch corresponding to the curvature of the needle. The suture is tied over a 3 mm. Beck probe, so that appropriate partial ligation of the lumen was maintained. The coronary sinus partial ligation could be performed prior to the implantation of the internal mammary artery. Finally, the prepericardial fat pads were applied over the de-epicardialized myocardium and the edges of the fat pads were joined to the edges of the fibrous pericardium, in its closure by interrupted silk sutures. Antibiotic powder was sprayed inside the left pleural cavity after extravasated blood was withdrawn. The chest incision was closed in anatomical layers as in the control series.

This was a modified Vineberg procedure because of the following: (1) The left internal mammary artery was dissected from the chest wall, not only from the 4th to 6th intercostal

spaces, but also from the subclavian artery down to the 6th interspace. (2) No scalloping of the implanted internal mammary artery which was done in other procedures. (3) There was a lesser chance of kinking of the artery in any position the heart may assume postoperatively. (4) There was a stronger pressure in the internal mammary artery and more free flow of blood inside the tunnel after it was dissected from the subclavian artery down the 6th intercostal space. This was also contributed to the prevention of thrombo sis of the implanted artery. (5) The coronary sinus was partially ligated to 3 mm. size, which was not performed in the original Vineberg procedure.

From the survival results and X-ray studies, it appeared that this procedure will be the procedure of choice in the future.

SERIES IV: BECK I OPERATION.

The pericardium was opened posterior to the phrenic nerve in an extension of 8-9 cm., a transverse incision is then made from the midportion of the latter incision and carried towards the root of the lung. Two sutures of #2-0 silk were applied to the corners of the pericardial flaps for retraction. Ameroid constrictors were applied in the same manner as the control

series.

The heart is retracted medially with the left hand so as to visualize the coronary sinus,which was a bluish thin vessel emptying into the right auricle. A circumferential suture of #2-0 black silk on an atraumatic needle was applied carefully in reversed fashion and then withdrawn through an arc corresponding to the curve of the needle. The ligature was tied over a 3 mm. Beck probe which was placed along the wall of the vessel to facilitate proper reduction of the lumen. The probe was slipped out of the ligature after tying. Both the anterior and posterior surfaces of the left ventricle were abraded gently with a Beck burr, avoiding injury to coronary vessels. The parietal pericardium over the corresponding area of the heart was also abraded in the sameway. Moderate amounts of asbestos powder about 0.3 grams, were sprayed or spread over the abraded surface of the heart. The dissected pre-pericardial fat pads were applied directly over the abraded surface of the heart and thensutured to the edges of the pericardial flaps then closed with interrupted silk sutures #3-0. The chest incision was closed in anastomical layers, as in the control series, following full expansion of the left lung.

SERIES V. CARDIO-PERICARDIOPEXY (THOMPSON, RAISBECK PROCEDURE).

The chest was opened in the left 5th interspace and ameroid constrictors applied in the same way as the control series. The pericardium was opened anterior and parallel to the left phrenic nerve. About 0.5 grams of sterile talcum powder (magnesium silicate U.S.P) was spread widely over the anterior and posterior surfaces of the heart. The pericardium was closed by interrupted suture of #3-0 black silk. The chest wall incision was closed in anatomical layers without drainage as in the control series.

SERIES VI: CARDIO-PERICARDIOPEXY BY APPLICATION OF 5% SODIUM SALICYLATE. A NEW PROCEDURE FOR MYOCARDIAL REVASCULARIZATION:

The left side of the chest was opened through the 5th interspace and ameroid constrictors were applied in the same manner to produce gradual coronary insufficiency. In this procedure, instead of using sterileasbestos and talcum, we have tried experimentally sterile 5% sodium salicylate. The solution was applied directly in several layers to the anterior and posterior surfaces of the heart with right and left ventricle by use of a medicine dropper or by gauze sponge.

After application of the solution, it appeared that the epicardium of the heart became whitish and dull and the condition of the blood vessels showed no change. The pericardial flaps were then closed by interrupted sutures of #3-0 black silk. The chest wall incision was again closed in anatomical layers without drainage as in the control series.

SERIES VII: ARTERIALIZATION OF THE CORONARY SINUS BY ANASTOMOSES OF LEFT INFERIOR PULMONARY VEIN: A NEW MYOCARDIAL REVASCULARIZATION PROCEDURE.

Ameroid constrictors were applied as in the control series. The pericardium was opened longitudinally, posterior and parallel to the left phrenic nerve from the base of the heart down to the apex. A transverse incision was then made from the midportion of the latter incision and carried to the root of the left lung. Two sutures of #2-0 silk were applied to the corners of the pericardial flaps for retraction. The coronary sinus was identified inthe auriculoventricular groove before it emptied into the right atrium. The site of anastomoses was determined and then isolated. A #2-0 silk suture on an atraumatic curved needle was passed completely around the sinus about 1/2 cm. from its terminus. Great care was taken that the needle did not puncture the sinus. This suture was used later in the procedure.

Two #5-0 arterial silk sutures wedged upon atraumatic needles were passed longitudinally into the most prominent aspect of the sinus wall. The bites were about 3 mm. long parallel to and about 3 mm. apart from each other and acted as stay sutures. The inferior pulmonary vein of the left lower lobe was identified and isolated up to its terminus in the left auricle. The vein was tried for alignment several times to the coronary sinus site of anastomoses, so that when anastomoses was done, no tension on the suture line occurred. Having satisfied this criteria, the left inferior pulmonary vein was ligated close to its terminus by means of black silk #2-0. The vein was transected between the tied ligature and a bulldog clamp about 1 cm. apart, for cuff allowance needed for the anastomoses. A segment of the coronary sinus was exteriorized within the jaws of a special curved sinus clamp as shown in Plate No. 11. A No. 11 Bard Parker bistoury scalpel was used to make a longitudinal slit between the stay sutures. The size of the slit depended upon the size of the inferior pulmonary vein, usually 4 -5 mm. The sinus lumen was flushed with solution of heparin. A 36 inch. #5-0 silk suture with atraumatic curve needle at each end was used to attach the end of the pulmonary vein to the inferior extremity of the incision in the sinus. The suture was tied so that both ends are of equal length. One end of the

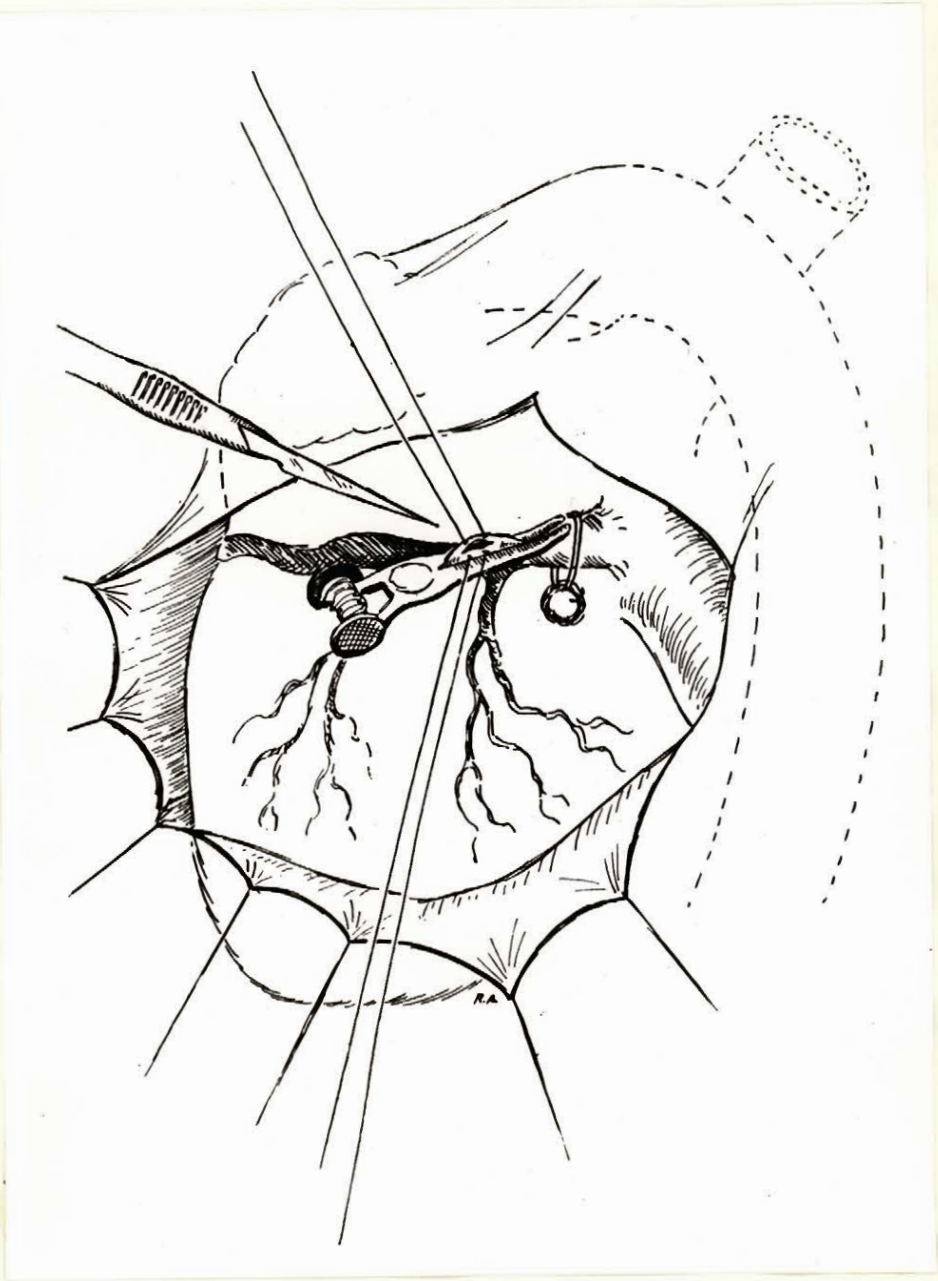


PLATE NO. 11.

Photograph shows a No. 11 Bard Parker bistoury scalpel made a longitudinal slit in the coronary sinus isolated by a special curved sinus clamp. Incision is spread by stay sutures and will be the site of anastomoses.

suture was used to perform the anastomosis of the anterior lip of the incision using a continuous running suture. The needle at each bite passed from the adventitial side of the vein about 1 and 1/2 mm. apart. When the suture line reached the stay sutures, the latter were removed. Each stitch was individually picked up and tightened after suture line was finished. The suture line on the other side of the vein was similarly applied and the free end was tightened and then tied to the end of the initial suture. The sinus clamp was removed after completion of anastomoses ; permitting oxygenated blood to flow into the coronary sinus down to the left auricle. The suture line was inspected for leaks and additional stitches applied, if necessary. Finally, the coronary sinus distal to the anastomoses was tied over a 3 mm. Beck probe placed along the sinus wall to facilitate proper reduction of the lumen. The probe was slipped out of the ligature after tying. After this was done the coronary sinus blood down the cardiac vein became pink and their walls moderately distended. There was no change in the heart rate and heart contraction. The completed inferior pulmonary vein and coronary sinus appears in Fig. 12. The pericardium was sutured by interrupted silk sutures giving enough room for passage of anastomoses. The lung was put

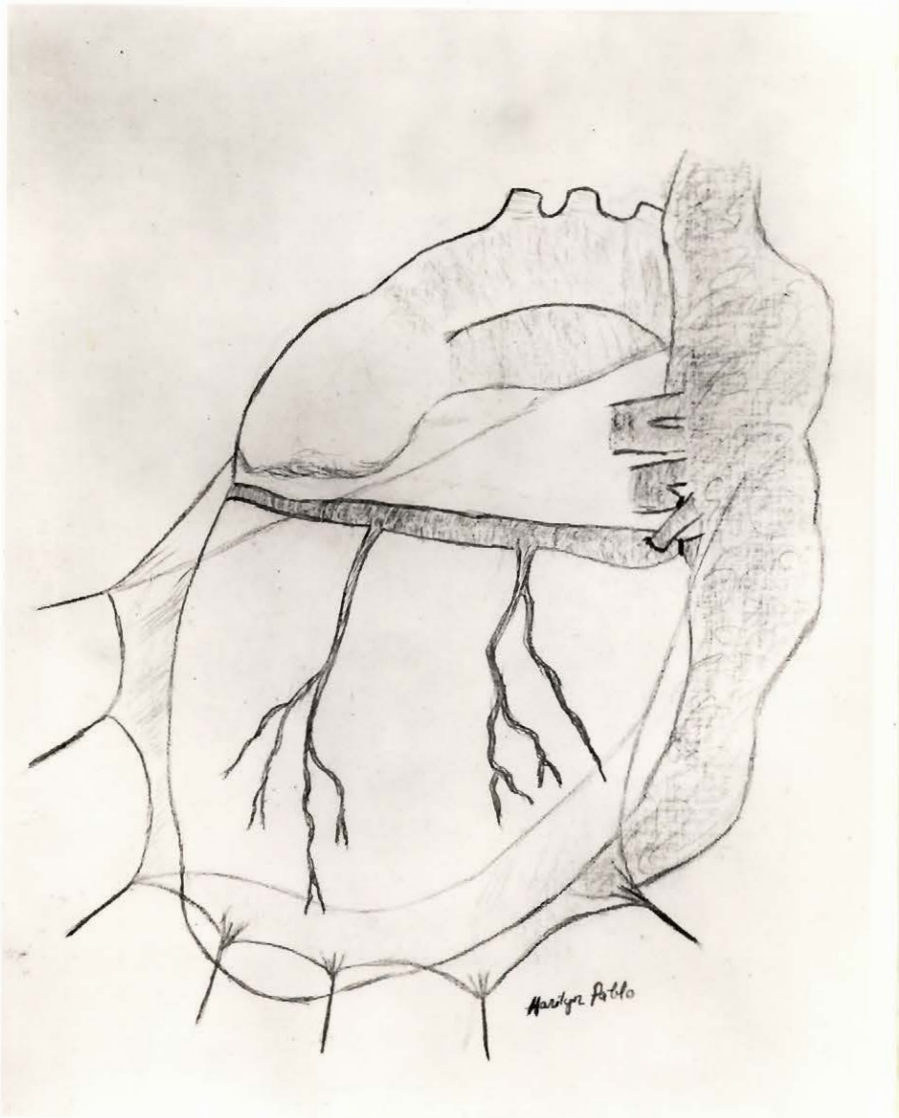


PLATE NO. 12.

Photograph shows the completed anastomoses between the coronary sinus and left inferior pulmonary vein. The coronary sinus is ligated to 3 mm. in luminal diameter by black silk #3.

back in its anatomical place and then carefully inflated. The chest wall was closed in layers in the same way as the control series.

D. CARE OF THE POSTOPERATIVE ANIMAL.

The dogs were carefully watched after completion of the surgical procedures. They remained aided with the Jefferson respirator until they recovered from anesthesia. As soon as they could breathe on their own, the endotracheal tube was removed and the dogs were carefully watched for possible respiratory or cardiac arrest. After they had passed from these dangers, they were brought to their individual cages and followed postoperatively for 4-7 days. Finally, they were sent to the farm for boarding until they died or brought back for sacrifice.

E. POSTMORTEM EXAMINATION

1. Gross examination of dead dogs: Within twelve hours after death of each dog, a routine gross autopsy was performed. Any dog dying of chest wall infection, empyema, pneumonia, pleural effusion, distemper and other intercurrent dog diseases not related to the operations, were discarded from the series.

The dogs that died of myocardial ischemia, infarction, congestive failure and the like, their hearts were removed en masse

with extravascular supply intact as per operation performed. The specimen was then refrigerated in physiological saline solution for relaxation of muscular specimen.

2. Gross examination of hearts: Hearts were examined for adherent pieces of lung, pericardial inflammation and pericardial blood vessels which were not disturbed before injection were done. Any noticable infarction, myocardial softening, thinning, rupture or necrosis were recorded with regards to their specific locations.

After injection and X-ray studies were performed, the hearts were placed in jars containing 10% formalin and physiological saline solution for 48-72 hours. Then, they were sectioned for verification of infarctions, necrosis and rupture, especially with regards to location and muscle bundle involvement. They were also sectioned for more X-ray studies with regards to presence of dyes in the arterioluminal vessels and their extension to the heart's lumen. Lastly, they are sectioned in order to secure specimen for microscopic studies. The hearts were sectioned in three different ways: (a) Transversely - from base of heart down to apex in 1/2 cm. thickness. (b) Sagital sections - from the left side of the heart up to the right side of the heart. This is a perpendicular vertical section

of ventricular wall of 1/2 cm. thickness. All of these serial sections were laid down in order for X-ray pictures.

F. MICROSCOPIC EXAMINATION.

Segments of anterior descending and circumflex branches of the left coronary artery with ameroid constrictors were obtained for sections, proximal, at midportion and distal portion to ameroid, to determine amount of narrowing of lumen and micropscopic reasons for narrowing. Segments of implanted internal mammary artery and inferior pulmonary vein coronary sinus anastomosis were also obtained for determination of patency, narrowing of lumen at different levels, proximal, middle and distal portions with microscopic findings to substantiate the narrowing were recorded.

G. INJECTION STUDIES.

With the use of the new Schlesinger mass of intact and isolated hearts.

This will be discussed separately in Chapter IX.

H. TABULATION OF RESULTS.

All results were recorded and tabulated carefully on big graphing paper with regards to the following: dog number, sex, weight, date of operation, date of death, date of sacrifice,

number of days of survival, gross postmortem findings, position of septal artery, extent of occlusion of coronary arteries with ameroids, of implanted internal mammary artery, of inferior pulmonary vein coronary sinus anastomoses, X-ray findings with regards to anastomoses, arterioluminal blood vessels in myocardial wall, microscopic findings and remarks. All these will be discussed in detail in Chapter X, entitled Summary of Protocol.

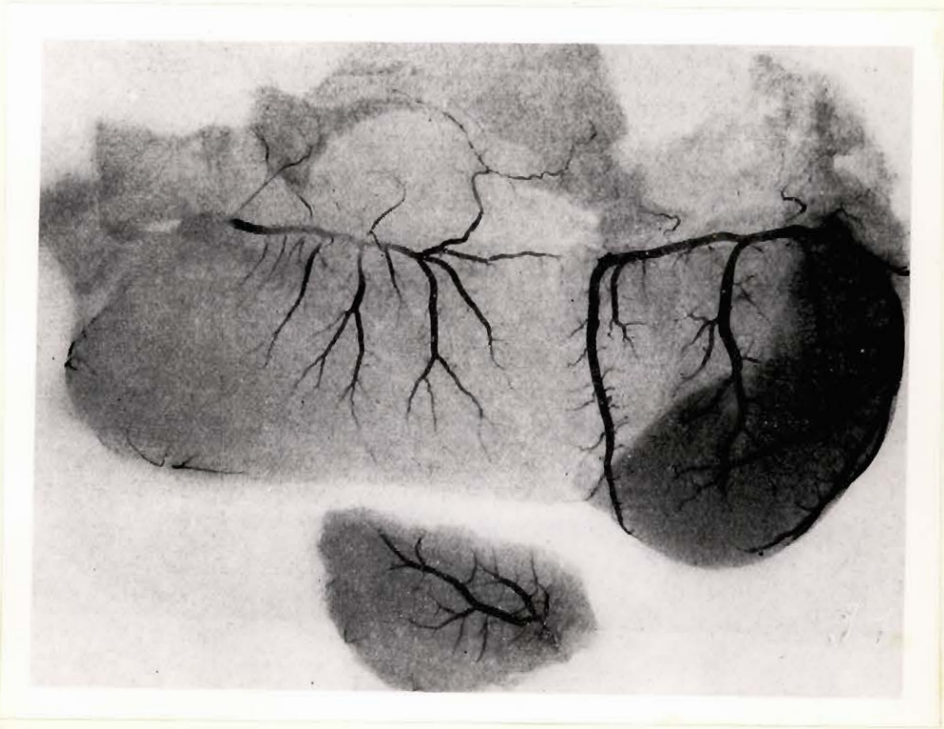


PLATE NO. 13.

The coronary system of the dog's heart injected spread out and radiographed according to the Schlesinger method.

CHAPTER IX.

INJECTION OF NEW SCHLESINGER MASS AND X-RAY STUDIES.

A. Materials and Composition:

The new Schlesinger mass consists of a mixture of gelatin, potassium iodide and barium sulfate. It was apparently prepared by Dr. Monroe Schlesinger, immediately before he died in 1957. The injection of this barium mixture could be carried out at room temperature, thus avoiding the unnecessary apparatus and water bath required with lead agar and other mixtures, which solidify at room temperature. It satisfies the criteria of being uninjurious to tissues, of having sufficient radio-opacity and of penetrating with smaller arterioles. Its viscosity is nearer to that of blood than the viscosity of other mixtures. The comparison of viscosity as compared to blood are as follows: barium mixture to blood is 1.5 to 1; lead agar (at 45°C) to blood is 3:1; and barium gelatin to blood is 18:1. This new mixture lends itself easily to the addition of water soluble dyes. Its viscosity could be determined by means of viscosity conversion concentration, where in you prepare certain mixtures at a definite time of solidification, to suit the length of the injection studies.

B. Apparatus.

The injection apparatus consists of a source of pressure, in this case, compressed air from a side wall outlet, with a constant pressure reservoir, a needle valve, a manometer and feeding bottles joined to each other by flexible tubing. The connections must be airtight. The needle valve and large U-shaped mercury manometer,constructed by the author of this thesis, are inserted in the line between the source of pressure and the feeding bottles. The needle valve acts as as a bleeder to reduce the pressure of the source to that desired in the vessels. The constructed injection apparatus appears in Plate No. 15.

C. Preparation of Specimen.

Metal cannulas with plunged mouths of suitable diameter are tied into the desired vessels which are gently flushed with a few ccs. of saline to free them of air and to identify leaks so that they may be stopped. The injection could be performed with hearts still intact in the chest cavity or in isolated hearts suspended on a stand so as to allow free access to all surfaces.

D. Technique.

With the apparatus assembled and specimens ready for injection, proceed as follows:

PLATE NO. 14.

Photograph showing the new Schlesinger mass, consisting of gelatin K I, barium mixture, with different color dyes and equipment for injection.

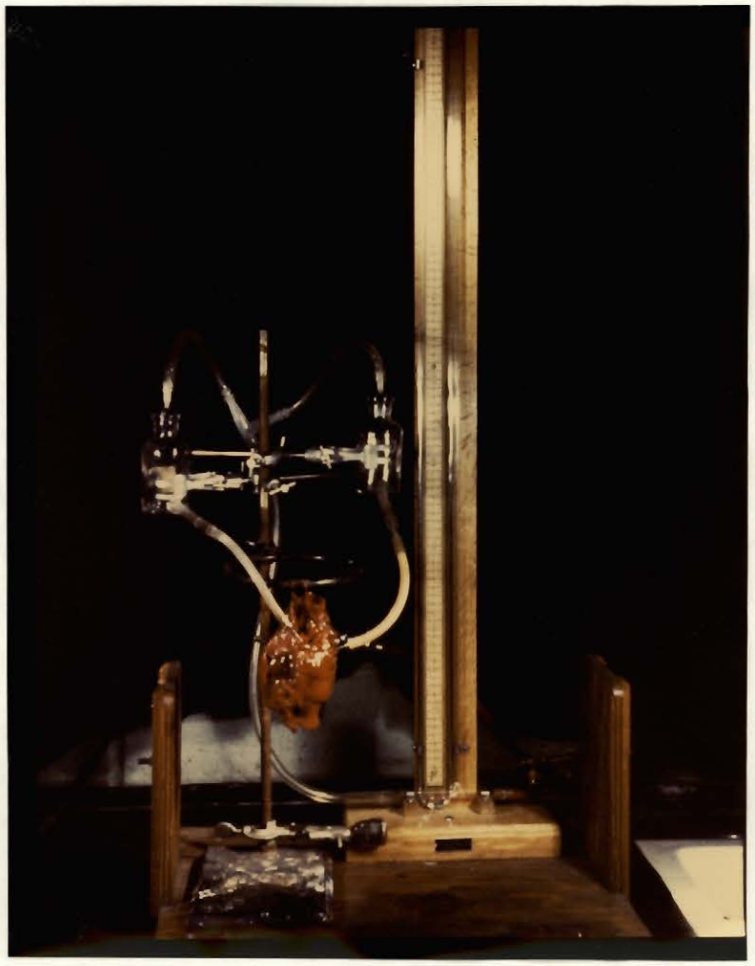


PLATE NO. 15.

Photograph shows the new injection apparatus, consisting of a needle valve, U-shaped mercury manometer, two feeding bottles, flexible tubing and an iron stand where heart is suspended freely.

1. Shake the gelatin KI barium mixture mass of desired quantity predetermined to distribute the barium sulfate evenly; avoid bubbles.

2. Pour the mass inside the feeding bottles and add the specific amount of dye solution. Mix the two solutions well.

3. Add formalin in the concentration previously determined. Shake container well while adding formalin; avoid bubbles.

4. Begin injection immediately after the addition of formalin. Injection is began at a pressure well below that eventually desired in order to determine troublesome leaks not previously discovered. If there is no leak, the pressure is then raised to 140-170 mm. of mercury. Injection is completed usually within 10-20 minutes or as soon as there is no further flow as indicated by a stable level of the mass in the feeding bottles. The cannulas and tubing are then clamped until solidification has taken place. The injection apparatus is disassembled immediately after the cannulas and tubing have been clamped; at this time, the mass is still fluid enough to allow easy cleaning of the feeding bottles and of the attached tubing. X-ray pictures of the specimen are taken after solidification of the injection mass. Different colors could be used to determine region of anastomosis andidentify respective blood vessels.

Finally, 10% formalin and physiological normal saline solution, are used to fix the hearts in for 48-72 hours, prior to sectioning.

E. Injection of Intact Heart Through the Left Subclavian Artery and Aorta: New Technical Procedure.

This injection method was primarily utilized in order to evaluate the efficiacy of various revascularizations in augmenting coronary circulation via its extracardiac collaterals. This was performed mainly in dogs that survived ameroid constrictors through various revascularization and a few normal dogs. The dogs were anesthetized with the usual dosage of nembutal. The left side of the chest and upper abdomen were shaved and the dogs placed on the operating table. The legs were strapped to the 4 posts of each corner of the table.

The left chest was opened through the 4th intercostal space, one space above the previous incision in order to avoid postoperative adhesions especially adherent lung to the chest wall. During the procedure, the dog was allowed to breathe by itself and in view of an open thoractomy, it gradually died, usually in a period of one to one and a half hours, While the dog was still alive, the left subclavian was cannulated with a metal cannula distal to its take off from the aorta. However,

the brachial, thyrocervical and vertebral arteries were ligated, leaving the internal mammary and costocervical arteries and their respective branches intact.

Another metal cannula was placed into the aorta through the proximal stump of the subclavian artery. The descending thoracic aorta above the diaphram was ligated with umbilical tape and a plastic cardiac cannula was passed into the left ventricular cavity via the left common carotid in retrograde to serve as an outlet for extra ventricular pressure. The cannula was tied above the origin of the coronary arteries, by umbilical tape at the arch of the aorta between the left common carotid and innominate arteries. The arch of the aorta was also tied just distal to the take off of the left common carotid artery. The metal cannulas and plastic cardiac cannula were flushed with physiological normal saline solution, containing heparin to prevent clotting of blood.

The barium mixture was then injected by means of the injection apparatus first through the subclavian cannula immediately after the dog died while its blood had not yet coagulated. The injection lasted for 20 minutes at 140-170 mm.Hg. pressure.

Immediately left lateral chest X-ray was taken to visualize the internal mammary arteries and its branches especially the pericardiophrenic and other collaterals that went to the heart.

The second injection was through the aorta in order to visualize the intercostal, bronchial, esophageal, medistinal, pericardial, subcostal and superior phrenic arteries which all participate in the subpleural plexus, and extra cardiac collateral anastomoses. Another left lateral chest X-ray was again taken. Any radio-opaque material that had gone to the heart to fill up the coronary arteries and ventricular cavities must have come from the extra cardiac collateral blood vessels. After the X-rays were taken and the barium mixture had solidified, the heart was removed for more examination, further injections and X-rays of the coronary arteries and implanted internal mammary artery or inferior pulmonary vein-coronary sinus anastomoses, as the case may be.

F. Injection of Isolated Heart.

The hearts that were subjected to this injection, are all postmortem hearts, except those whose coeonary arteries were filled up during the injection of intact hearts. All frozen hearts were defrosted and allowed to return to room

temperature, usually 37-38 degrees, before barium mixture injections were carried out. If the heart underwent internal mammary procedure, then the extra cardiac portion of that artery was cannulated first and then subjected to injection via the injection apparatus. The implanted artery on X-ray was examined for patency, branching and anastomoses with the branches of both coronary arteries. This was followed by the cannulization of the right coronary and left coronary arteries, proximal or distal to the ameroids, as the case may be. If the heart underwent inferior pulmonary vein-coeonary sinus anastomoses, the inferior pulmonary vein was first cannulated and injected, followed by the coronary arteries. For the other revascularization procedures, only the coronary arteries were cannulated and injected proximal or distal to the ameroid constrictors. X-ray pictures are taken after each blood vessel has undergone injection with the barium mixture: The injection usually lasting 10 minutes, while the heart was suspended on a stand of the injection apparatus. Various colors of dyes were used for each blood vessel injected. Finally, the hearts were spread out by the Schlesinger method and X-rays were taken to show

homocoronary and intercoronary anastomoses.

After all of this was done, the hearts were reconstructed to their normal shape by interrupted cotton sutures. They were placed for 48-72 hours in a jar contining 10% formalin with physiological normal saline solution for preservation.

G. Sectioning or Slicing of the Hearts.

Preserved hearts were sectioned in 3 different ways:

1. Transverse or horizontal sections from base of the heart down to the apex in 1/2 cm. thickness. This was especially good in locating infarctions in the different muscle bundles of the heart.

2. Sagital or perpendicular sections from the left side of the heart up to the right side of theheart in 1/2 cm. thickness.

3. Coronal right angle vertical section of ventricular walls in 1/2 cm. thickness.

All these serial sections were laid down in order on a piece of paper for X-ray pictures and at times for colored photography. The purpose of the sectioning or slicing of the heart was fourfold: (1) To locate the infarcted area in the different muscle bundles. (2) To determine the number of arterioluminal vessels in the different slices, taking note of the number that went into the lumen.

(3) To determine if the dye had entered the ventricular lumen.

(4) Lastly, the heart was sectioned in order to obtain specimens for microscopic studies.

PLATE NO. 16.

Photograph showing the heart sliced transversely in 1/2 cm. thickness, spread out serially to show location of injected dye and myocardial infarction with regards to muscle bundles.

PLATE NO. 17.

Photograph showing the heart sliced sagitally in 1/2 thickness, spread out serially to show the location of the injected dyes and myocardial infarction with regards to the ventricular wall.

CHAPTER X.

SUMMARY OF PROTOCOL

SERIES I: OPERATION FOR CONTROL WITH AMEROIDS.

General Summary and Results:

1. Number of dogs - 16
2. Sex: male 12; female 4.
3. Weight: between 38-52 lbs.
4. Mortality: 12 dogs. Percentage: 75%
   Average survival in days of mortality dogs: 19 days.
5. Survival: 4 dogs Percentage: 25%
   Average survival in days of sacrificed dogs: 171 days.
6. Position of septal artery: Percentage:
   a) from anterior descending branch: 12 75%
   b) from circumflex branch: 2 12.5%
   c) from main left coronary artery: 2 12.5%
7. Injection of coronary arteries:
   a) proximal to ameroids: 5
   b) distal to ameroids: 10
   c) from extracardiac injections: 0
   d) cannula in ventricular cavity: 0 No cannula: 15
8. Extent of coronary artery occlusions:
   a) average percentage for anterior descending branch: 87.5%
   b) average percentage for circumflex branch: 84%
   c) combined average percentage: 85.9%
9. Coronary anastomoses:
   a) Intracardiac anastomoses:
      1. Average for surviving dogs: homocoronary ***
         intercoronary **
      2. Average for mortality dogs: homocoronary 1.27 times*
         intercoronary 0.45 times *
      3. Overall average: homocoronary 1.66 times *
         intercoronary 0.86 times *
   b) Extracardiac anastomoses: None
10. Arterioluminal vessels:
    a) Average number: 11 vessels
    b) Average number of vessels communicating with lumen of heart: 1

11. Presence of dye in intramyocardial vessels:
    a) Number of hearts with dye: 9
    b) Number of hearts without dye: 7
    c) Surviving dogs: all hearts had dye in the intramyocardial vessels.
    d) Mortality dogs: 5 out of 12 had dye in intramyocardial vessels.

12. Section or slicing of hearts:
    a) transverse or horizontal sections: 7
    b) sagitial or vertical section: 1
    c) coronal, right angle to lumen: 3
    d) no sections of heart: 4

13. Location of infarction:
    a) anterior wall: 4
    b) posterior wall: 4
    c) Postero-lateral wall: 3
    d) No myocardial infarction: 4
    e) all mortality dogs had myocardial infarction
    f) all surviving dogs had no myocardial infarction.

14. Microscopic findings:
    a) endocardial portion: 8
    b) Middle and endocardial portions: 3
    c) epicardial and endocardial portions: 1
    d) no myocardial fibrosis: 4
    e) all mortality dogs had myocardial fibrosis.
    f) all surviving dogs had normal myocardium.

Individual Summary

Dog 1-378: This was a male, 40 lbs., mongrel dog, which was operated on July 28, 1958 and died on the farm September 1, 1958. It survived the operation and lived 34 days. Twelve hours after death, postmortem examination showed the left lung was adherent to the surface of the heart, presence of anterior wall infarction of the left ventricle and the septal

artery arose from the AD artery. Coronary artery occlusions showed AD-95%, C-80%, combined occlusion-87.5%, which were due to intimal proliferation and thrombus formation. Extensive myocardial fibrosis in the inner 1/3 of the myocardium was present. There was no dye in the intramyocardial blood vessels. No X-ray was obtained.

Dog 3-408: A 40 lb. male, mongrel dog, lived 13 days was operated on 8-4-58 and died on 8-17-58. Post mortem examination showed anterior wall infarction of the L.V. and the septal artery arose from the AD artery. The coronary arteries were injected with dye distal to the ameroids, without ventricular cannula, showed ** homocoronary, * intercoronary anastomoses, Coronary artery occlusions showed AD-98%, C-75%and combined occlusion 86.5% which were due to intimal proliferation and thrombus formation. Transverse or horizontal sections of the heart were performed. Microscopic sections revealed fibrosis in the middle and inner thirds of the myocardium. There was no dye in the intramyocardial blood vessels and none in the heart's lumen. Coronary arteries had some intimal proliferation and their lumen filled with dye. There were 10 arterioluminal vessels and only one small twig communicated with the lumen of the heart.

Dog 4-380: A 40 lb. male mongrel dog, lived 10 days was operated on 8-6-58 and died on 8-16-58. Post mortem examination showed anterior wall infarction of the L.V. and the septal artery arose from the circumflex artery. The coronary arteries were injected with

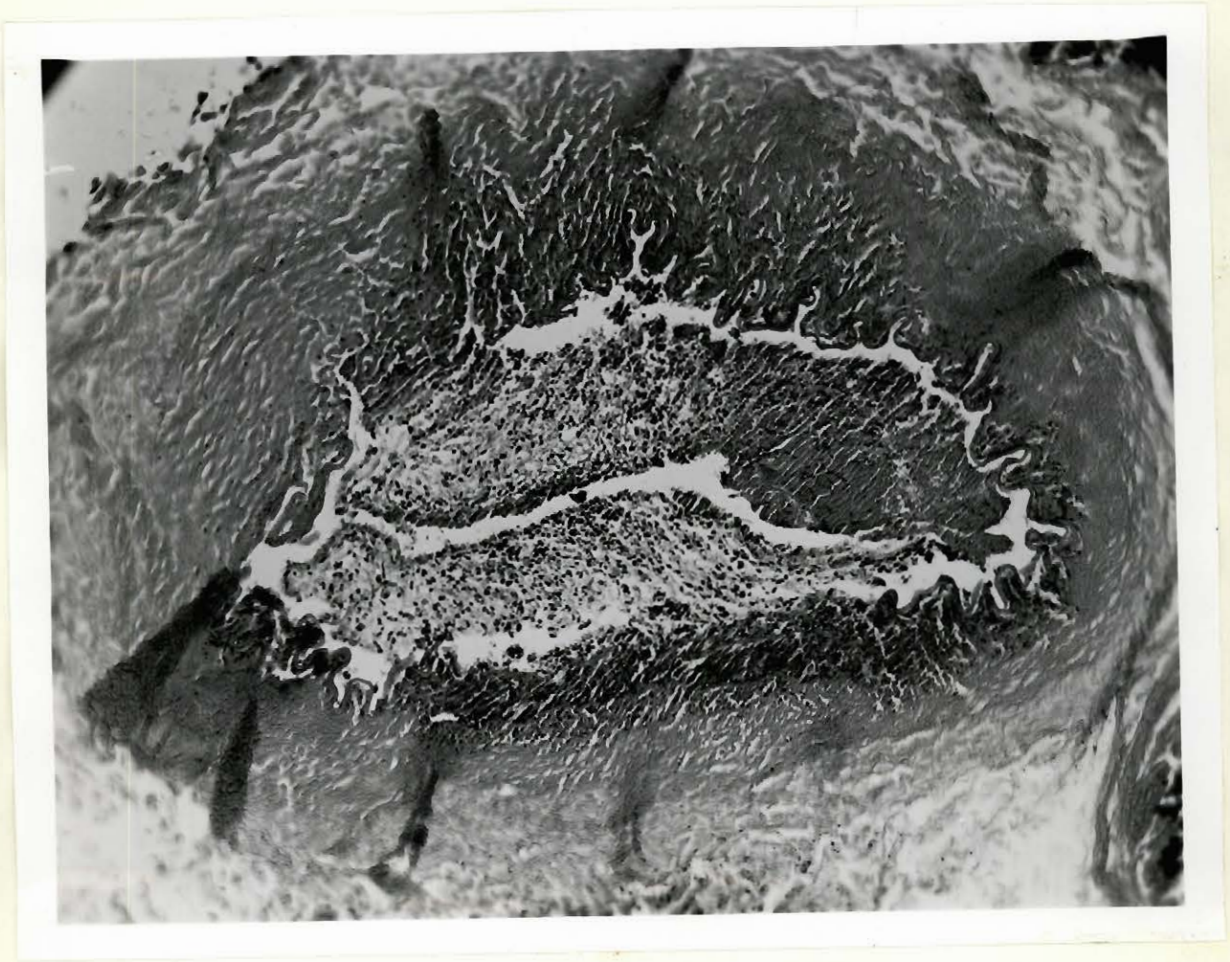


PLATE NO. 18.

Photograph shows section of anterior descending branch of left coronary artery in the midportion of ameroid constrictor of Dog 3-408. The occlusion is due to intimal proliferation and thrombus formation. (x90).

dye distal to the ameroids,without ventricular cannula showed ** homocoronary, * intercoronary anastomoses,12 arterioluminal vessels, 2 of which communicated with the lumen of the heart. Coronary artery occlusions showed AD-95%, C-70% and combined occlusion-82.5%, were due to intimal proliferation and thrombus formation. Transverse sections of the heart were done. Microscopic examination revealed extensive fibrosis in the middle and inner thirds of the myocardium. Superficial coronary arteries had some intimal proliferation and their lumen contained dye.

Dog 5-244: A 38 lb. female mongrel dog, lived 33 days was operated on 8-6-58 and died on 9-9-58. Postmortem examination showed posterior wll infarction of the L.V. and the septal artery arose from the AD artery. The coronary arteries were injected with dye proximal to the ameroids, without ventricular cannula showed ** homocoronary and 0 intercoronary anastomoses. Coronary artery occlusion showed AD-85%, C-95% and combined occlusions-90%, which were due to intimal proliferation and thrombus formation. Microscopie findings revealed fibrosis in the inner 1/4 of the myocardium. Some dye was found in the intramyocardial blood vessels, but none went into the lumen of the heart. Superficial coronary arteries had intimal proliferation and their lumen were filled with dye.

PLATE NO. 19.

Photograph showing section of circumflex branch of left coronary artery in the distal portion of the ameroid constrictor of dog 4-380. Arterial occlusion is due to intimal proliferation and thrombus formation. (x 40).

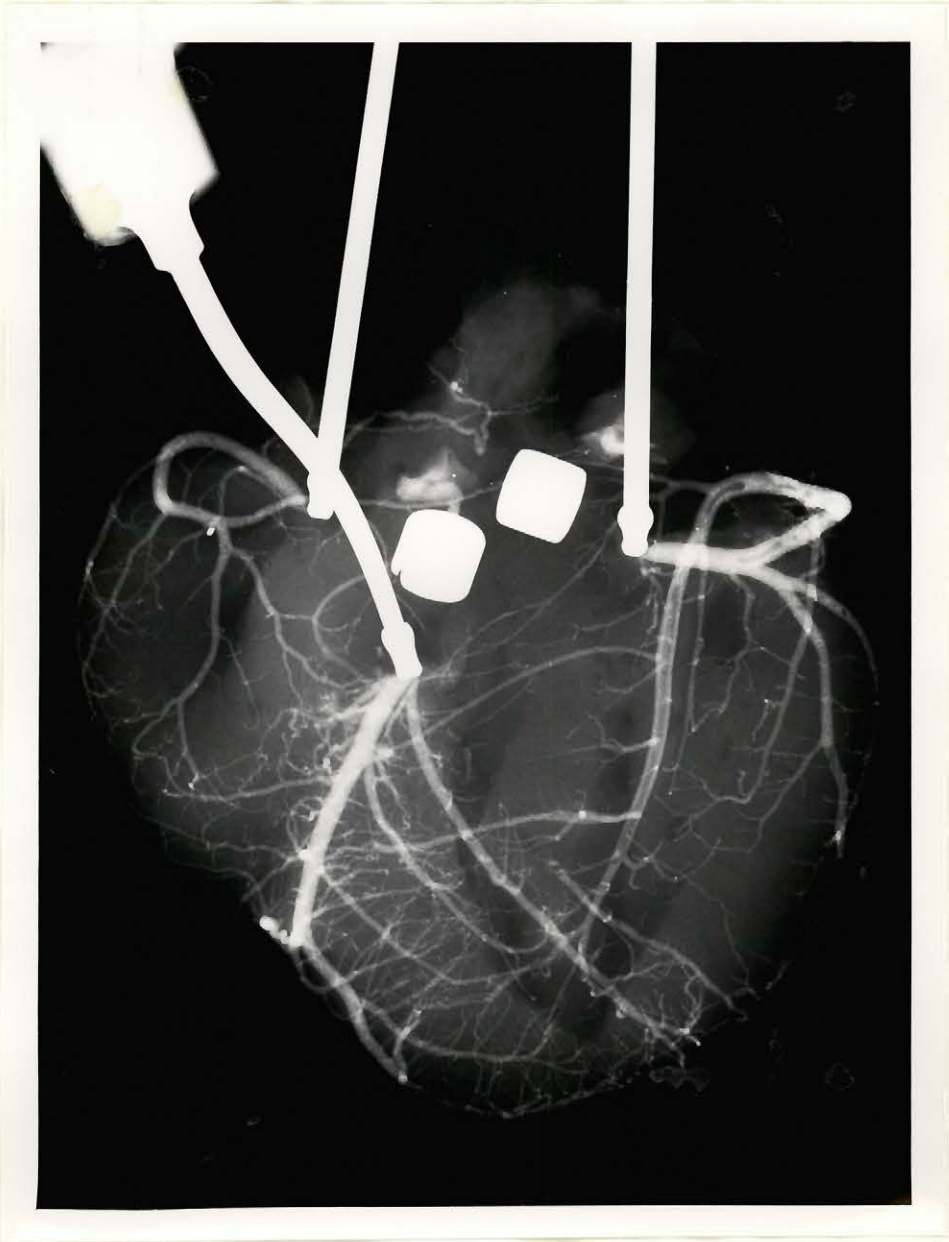


PLATE NO. 20.

Photograph showing heart of dog 4-380, injected with the new Schlesinger mass, distal to ameroids. Note the presence of a few homocoronary and intercoronary anastomoses.

Dog 6-405: A 40 lb. male mongrel dog, lived 6 days was operated on 8-7-58 and died on 8-13-58. Postmortem examination showed postero-lateral infarction of the L.V. and the septal artery came from the circumflex artery. The coronary arteries were injected with dye proximal to the ameroids, without ventricular cannula showed 0 homocoronary and 0 intercoronary anastomoses. Coronary artery occlusions showed AD-75%, C-80% and combined occlusions-77.5%, which were due to intimal proliferation and thrombus formation. Microscopic findings revealed patches of fibrosis in the inner 1/2 of the myocardium. There was no dye in the intramyocardial blood vessels and none was seen in the ventricular lumen. Superficial coronary arteries had very little intimal proliferation.

Dog 14-308: A 50 lb. male,mongrel dog, lived 195 days was operated on 8-21-58 and sacrificed on 3-4-59. Postmortem examination showed no visible gross infarction of the L.V. and the septal artery arose from the AD artery. The coronary arteries were injected with dye, distal to the ameroids, without ventricular cannula showed *** homocoronary, ** intercoronary anastomoses, 5 arterioluminal vessels, none communicated with the heart's lumen. Coronary artery occlusions were AD-95%, C-80% and combined occlusion-87.5%, which were due to intimal proliferation and thrombus formation.

The heart was sliced transversely 1/2 cm. in thickness. Microscopic examination revealed normal appearance of the myocardium, presence of dye in the intramyocardial blood vessels, but none in the heart's lumen. There were plenty of blood vessels between the pericardium and epicardium.

Dog 28-413: A 40 lb. female, mongrel dog, lived 167 days was operated on 9-18-58 and sacrificed on 3-4-59. Postmortem examination showed no visible gross infarction and the septal artery arose from the AD artery. The coronary arteries were injected with dye distal to the ameroids, without ventricular cannula showed ** homocoronary,** intercoronary anastomoses, 10 arterioluminal vessels, but none communicatedd with the heart's lumen. Coronary artery occlusions showed AD-80%, C-70% and combined occlusion-75%, which were due to intimal proliferation and thrombus formation. The heart was sliced transversely and the microscopic sections revealed the myocardium normal, some dye in the intramyocardial blood vessels, but none went into the lumen of the heart.

Dog 30-381: A 38 lb. female, mongrel dog, lived 16 days was operated on 9-22-58 and died on 10-6-58. Postmortem examination showed anterior wall infarction of the L.V. and the septal artery arose from the main left coronary artery. The coronary arteries were injected with dye distal to the ameroids, without ventricular cannula showed

* homocoronary, 0 intercoronary anastomoses, 9 arterio-luminal vessels, one of which communicated with the lumen of the heart. Coronary artery occlusions were AD-100%, C-95% and combined occlusion-97.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced transversely and microscopic sections revealed strips of fibrosis in the endocardial portion of the myocardium. Dye was found in the intramyocadial vessels.

Dog 32-313: A 38 lb. male, mongrel dog, lived 161 days was operated on 9-2-58 and sacrificed on 3-4-59. Post mortem examination showed no visible myocardial infarction and the septal artery arose from the AD artery. The coronary arteries were injected with dye, distal to the ameroids, without ventricular cannula, showed *** homocoronary, ** intercoronary anastomoses, 8 arterio-luminal vessels, one of which communicated with the heart's lumen. Coronary artery occlusions showed AD-70%, C-85% and combined occlusion-77.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced transversely and microscopic setions revealed normal myocardium, with some dye in the intramyocardial blood vessels.

Dog 1-303: A 44 lb. female, mongrel dog, lived 28 days was operated on 10-20-58 and died on 11-18-58. Post-mortem examination showed posterior wall infarction of

the L.V. and the septal artery arose from the AD artery. The coronary arteries were injected with dye proximal to the ameroids, without ventricular cannula, showed 0 homocoronary and 0 intercoronary anastomoses. Coronary artery occlusions showed AD-90%, C-955% and combined occlusion-92.5%, which were due to intimal proliferation and thrombus formation. Microscopic examination revealed fibrosis in patches of the middle and inner portions of the myocardium. There was no dye in the intramyocardial blood vesels.

Dog 2-387: A 44 lb. male, mongrel dog, lived 30 days was operated on 10-30-58 and died on 11-20-58. Post mortem examination revealed anterior wall infarction of the L.V. and the septal artery arose from the AD artery. The coronary arteries were injected with dye, proximal to the ameroids, without ventricular cannula, showed ** homocoronary and * intercoronary anastomoses. Coronary artery occlusions showed AD-95%, C-85% and combined occlusion-90%, which were due to intimal proliferation* and thrombus formation. Microscopic sections showed patches of fibrosis in the epicardial and endocardial portions of the myocardium. There was no dye in the intramyocardial blood vessels and none entered in the heart's lumen. Between the epicardium and pericardium, there were round cell and fibrous tissue reactions.

Dog 3-430: A 46 lb. male, mongrel dog, lived 25 days was operated on 11-26-58 and died on 12-21-58.

Postmortem examination showed posterior wall infarction and the septal artery arose from the AD artery. The coronary arteries were injected with dye proximal to the ameroids, without v entricular cannula, showed ** homocoronary, 0 intercoronary anastomoses, 9 arterioluminal vessels, one of which communicated with the heart's lumen. Coronary artery occlusions showed AD-80%, C-100% and combined occlusion-90%, which were due to intimal proliferation and thrombus formation. The heart was sliced transversely and microscopic sections revealed fibrosis in the endocardial side of the myocardium. There was no dye in the intramyocardial blood vessels and none entered in the heart's lumen.

Dog 5-495: A 40 lb. male, mongrel dog, lived 12 days was operated on 12-11-58 and died 1-2-59. Postmortem revealed anterior wall infarction extending to the posterior wall of L.V. and the septal artery arose from the AD artery. The coronary arteries were injected with dye distal to the ameroids, without ventricular cannula, showed * homocoronary, 0 intercoronary anastomoses, 9 arterioluminal vessels, one of it communicated with the heart's lumen. Coronary artery occlusions showed AD-90%, C-95% and combined occlusion-92.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced transv ersely and microscopic setions revealed fibrosis in the middle and inner 1/3 of the myocadium. No

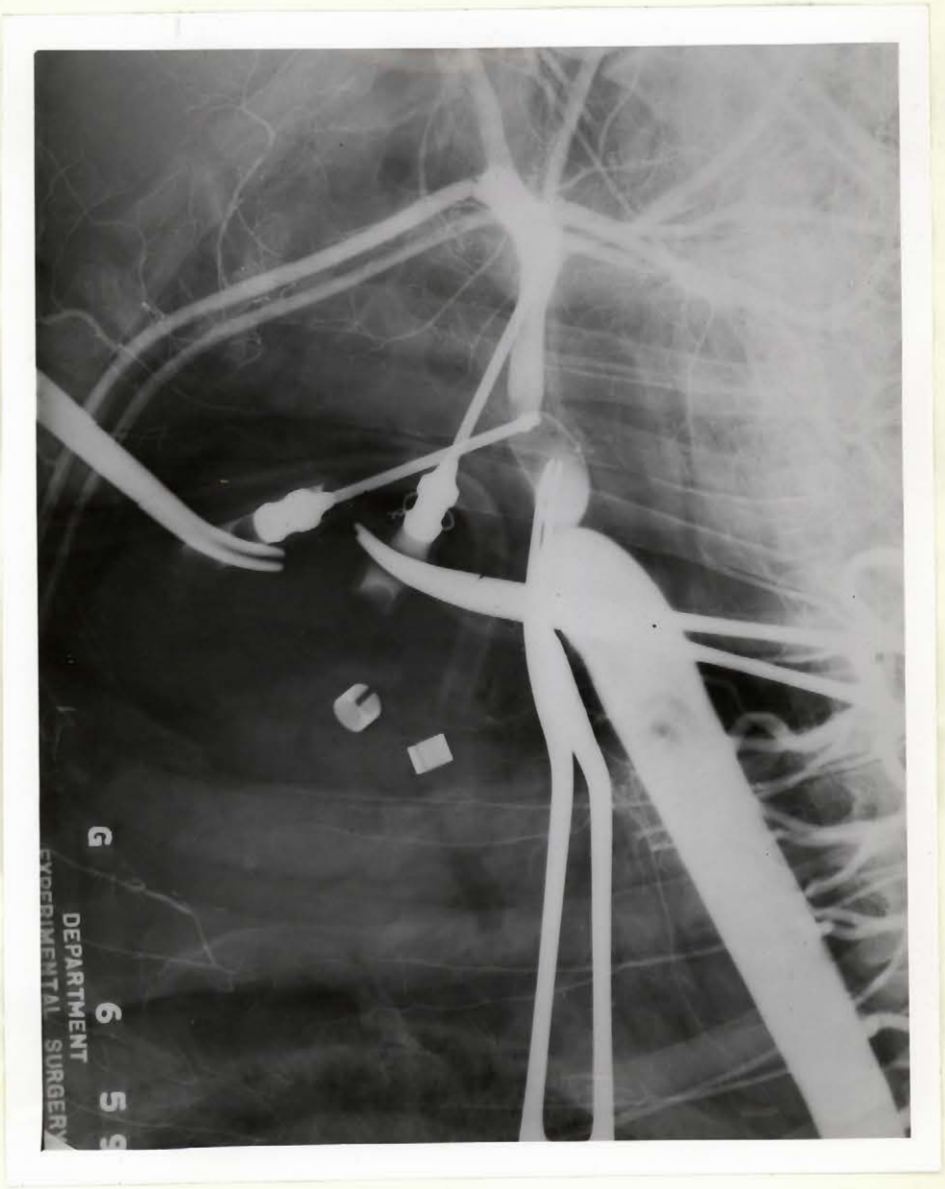


PLATE NO. 21.

X-ray photograph showing injection of intact heart with Schlesinger mass through the left subclavian artery and aorta. There is a cannula inside the ventricular cavity and the aorta is tied with umbilical tape distal to the coronary ostiae, so that no dye could enter the coronary arteries. Very little unit of blood vessels converging towards heart and no coronary anastomoses present. Note presence of two ameroids. (Control dog 8-472).

dye was found in the intramyocardial blood vessels.

Dog 7-422: A 52 lb. male, mongrel dog, lived 9 days was operated on 4-15-59 and died on 4-25-59. Post mortem examination showed posterior wall infarction of the L.V. and the septal artery arose from the AD artery. The coronary arteries were injected with dye distal to the ameroids, without ventricular cannula, showed ** homocoronary, * intercoronary anastomoses, 20 arterioluminal vessels, 2 of which communicated with the lumen of the heart. Coronary artery occlusions showed AD-65%, C-78% and combined occlusion-71.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced coronally in 1/2 cm. thickness . Microscopic sections revealed fibrosis in the inner 1/3 of the myocardium and the dye was present in the intramyocardial blood vessels.

ADDENDUM

Injection of the intact heart through the left subclavian and aorta with dye in three normal dogs (Dogs No. 2-353, 3-400, and 8-422) showed extracardiac arteries went to the pericardium. No dye went to the coronary arteries or its branches and none ent ered the ventricular lumen of the heart.

SERIES IIA: IVALON SPONGE OPERATION

General Summary and Results:

1. Number of dogs: 10

2. Sex: males 6, females 4

3. Weight: between 37 1/2 - 53 lbs.

4. Mortality: 6 dogs Percentage 60%
   Average survival in days of mortality: dogs: 12.6 days.

5. Survival: 4 dogs Percentage 40%
   Average survival in days of sacrificed dogs: 170 days.

6. Position of septal artery: Percentage:
   a) from anterior descending branch: 7 70%
   b) from circumlfex branch: 2 20%
   c) from main left coronary artery: 1 10%

7. Injection of coronary arteries:
   a) proximal to ameroids: 6
   b) distal to ameroids: 4
   c) from extracardiac injections: 3
   d) cannula in ventricular cavity: 0 No cannula: 10

8. Extent of coronary occlusions:
   a) average percentage from anterior descending branch: 88.8%
   b) average percentage for circumflex branch: 89%
   c) combined average percentage: 88/9%

9. Coronary anastomoses:
   a) intracardiac anastomoses:
      1. Average for surviving dogs: homocoronary 2.8 times *
         intercoronary 1.8 times *
      2. Average for mortality dogs: homocoronary 1.8 times *
         intercoronary 0.33 of *
      3. Overall average: homocoronary **
         intercoronary 0.9 of *
   b) Extracardiac anastomoses: 1 case.

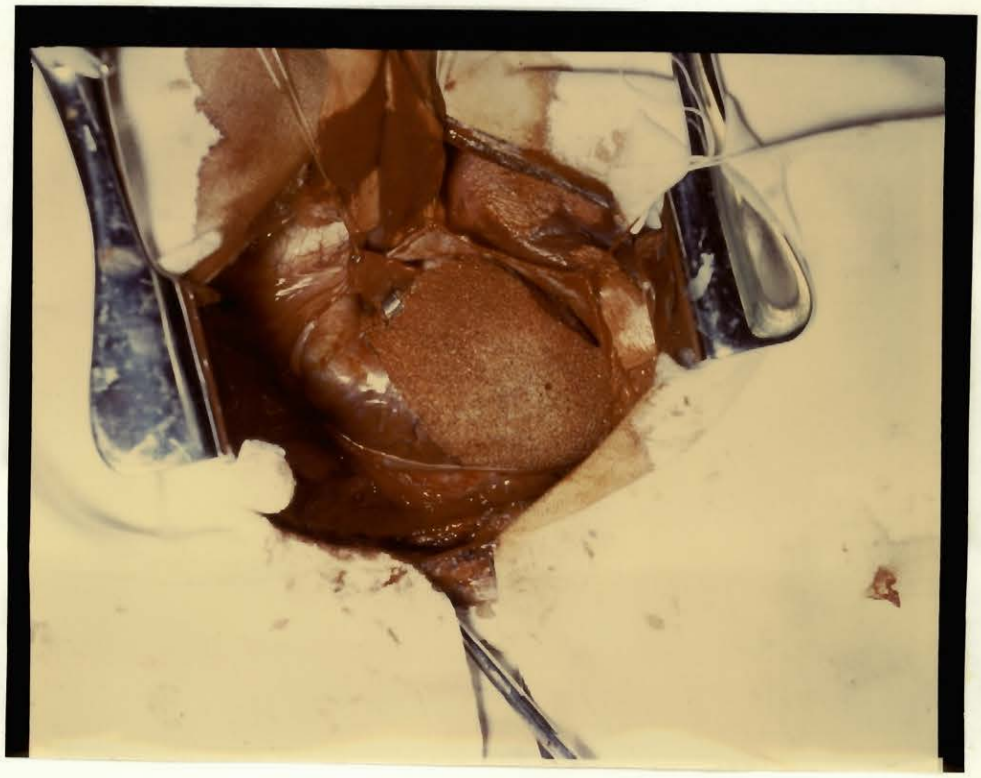


PLATE NO. 22.

Photograph showing sterile ivalon sponge overlaid and sutured to surface of scraped myocardium on the anterior and posterior portions of left ventricle. Pericardium is seen retracted by stay sutures and ameroids are still partly visible.

10. Arterio-luminal vessels:
    a) Average number: 21.6 vessels.
    b) Average number of vessels communicating with the lumen of the heart: 5.6 vessels.

11. Presence of dye in intramyocardial vessels:
    a) Number of hearts with dye: 9
    b) Number of hearts without dye: 1
    c) All surviving dogs had dye in intramyocardial vessels.
    d) All mortality dogs except one had dye in the intramyocardial vessels.

12. Sections or slicing of hearts:
    a) Transverse or horizontal sections: 2
    b) Sagital or vertical sections: 3
    c) Coronal right angle to lumen: 3
    d) No sections of heart: 2

13. Location of infarction:
    a) anterior wall of left ventricle: 0
    b) posterior wall of left ventricle: 5
    c) combined anterior and posterior wall: 1
    d) no myocardial infarction: 4
    e) All mortality dogs except one nad myocardial infarction.
    f) All surviving dogs did not have any infarction.

14. Microscopic findings: Presence and location of myocardial fibrosis:
    a) Endocardial portion: 5
    b) Middle portion: 1
    c) Epicardial portion: 0
    d) No myocardial fibrosis: 4

Individual Summary:

Dog 4-414:

This was a 50 lb. male, mongrel dog operated on October 27, 1958 and sacrificed on May 13, 1959. It lived 199 days. Post mortem examination showed the left lung was adherent to the surface of the heart, absence of visible infarction of the heart and the septal

arose from the AD artery. Injection of the intact heart through the left subclavian artery and aorta without ventricular cannula showed extracardiac arteries went to the pericardium, but none filled the coronary arteries. The coronary arteries were injected with dye distal to the ameroids showed ** homocoronary, ** intercoronary anastomoses, 19 arterioluminal vessels, 5 of which communicated with the heart's lumen. Coronary artery occlusions showed AD-95%, C-100% and combined occlusion-97.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced coronally and microscopic sections revealed small patches of fibrosis in the inner 1/3 of the myocardium. The ivalon sponge contained cellular fibrous tissue with marked hyalinization and with small number of blood vessels. The sponge material was reduced and a small number of giant cells were seen. Between sponge and myocardium were blood vessels showing extensive intimal proliferations with diminution of lumen calibre. In additional sections the vascular channels in the sponge were of medium size and somewhat more numerous than described above. Dye in the intramyocardial vessels were seen.

Dog 6-403: A 44 lb. male, mongrel dog, lived 9 days was operated on 11-6-58 and died on 11-15-58. Postmortem studies revealed posterior wall infarction of the L.V. and the septal artery arose from the AD artery. The coronary arteries were injected with dye proximal to the ameroids without ventricular cannula, showed ** homocoronary, 0 in-

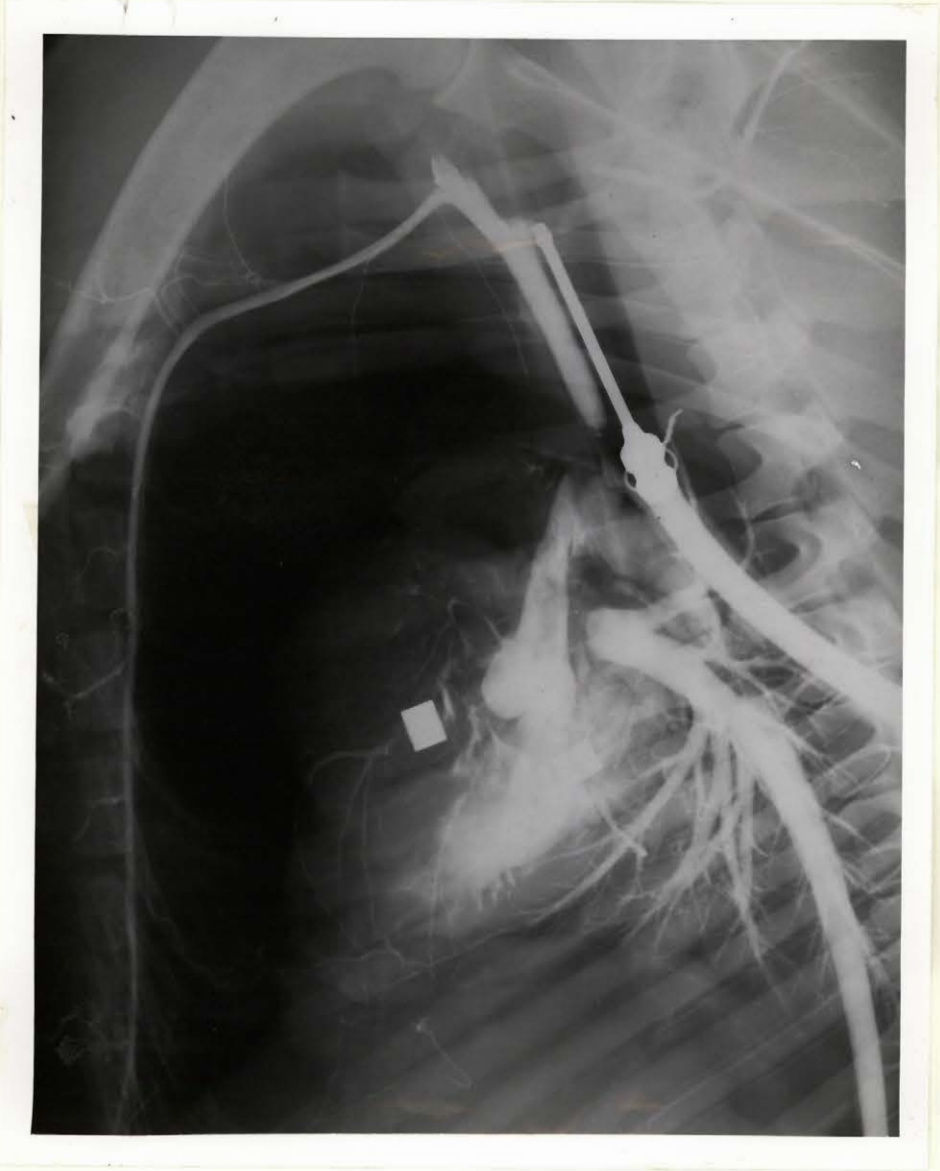


PLATE NO. 23.

X-ray microphotograph of left ventricle of ivalon dog 4-414, sacrificed at 199 days after operation. Note ivalon sponge on surface of the myocardium, which is slightly filled with dye together with intramyocardial vessels. In spite of improved coronary circulation due to operation, patches of fibrosis could still be seen in inner 1/3 of myocardium. Myocardial sinusoids could be seen connected with surface of heart, but are not filled with dye. This finding does not agree with with primitive type of heart nourishment.

tercoronary anastomoses and the occlusions showed AD-85%, C-85% and the combined occlusion-85%, which were due to intimal proliferation and thrombus formation. Microscopic studies revealed small patches of fibrosis along the inner border of the endocardium. The ivalon sponge contained red blood cells in clumps with moderate amount of dye. Plenty of small blood vessels were forming and growing with small amount of fibrous tissue and hyalinization. In certain areas, there were foreign body giant cells grouped together. Between the sponge and the myocardium were coronary blood vessels filled with dye and their lumen narrowed by some intimal proliferation. The intramyocardial blood vessels and some myocardial sinusoids contaied the injected dye.

Dog 8-153: A 42 lb. male, mongrel dog, lived 15 days was operated on 11-13-58 and died 11-28-58. Post mortem examination showed posterior wall infarction of the L.V. and the septal artery arose from the AD artery. The coronary arteries were injected with dye, proximal to the ameroids, without ventricular cannula, showed 0 homocoronary, 0 intercoronary anastomoses, 14 arterio-luminal vessels, none of which communicated with the heart's lumen. Coronary artery occlusions showed AD-75% C-95% and combined occlusion-85%, which were due to intimal proliferation and thrombus formation. The heart was sliced sigitally and microscopic studies revealed tiny patches of fibrosis in the middle third of the myo-

cardium. Intramyocardial blood vessels contained dye, but none went in the sinusoids and lumen of the heart. The ivalon sponge contained rich cellular fibrous tissue, with some hyalinization, some giant cells and blood vessels filled with red blood cells.

Dog 11-371: A 40 lb. female, mongrel dog, lived 3 days was operated on 11-24-58 and died 11-27-58. Postmorrem examination showed anterior and posterior wall infarction and the septal artery arose from the AD artery. The coronary arteries were injected with dye proximal to the ameroids, without ventricular cannula, showed * homocoronary, and 0 intercoronary anastomoses. The coronary artery occlusions showed AD-90%, C-90% and combined occlusion-90%, whcih were due to intimal proliferation and thrombus formation. Microscopic studies revealed patches of fibrosis in the endocardium. Some dye was seen in the intramyocardial blood vessels, but no dye entered heart's lumen.

Dog 12-143: A 40 lb. female, mongrel dog, lived 174 days was operated on 11-27-58 and sacrificed on 5-20-59. Postmortem examination showed absence of visible infarction and the septal artery arose from the main left coronary artery. Injection of the intact heart with dye through the left subclavian artery and aorta without ventricular cannula showed extracardiac arteries went to the pericardium and filled the coronary arteries and finally entered the heart's lumen. Coronary arteries showed *** homocoronary, ** intercoronary, *** extracardiac anastomoses, 21

arterioluminal vessels, 4 of which communicated with the heart's lumen. The coronary artery occlusions showed AD-95%, C-75% and combined occlusion-85%, which were due to intimal proliferation and thrombus formation. The heart was sliced coronally and microscopic studies revealed normal myocardium. The intramyocardial blood vessels contaied dye, but none in the myocardial sinusoids. The ivalon sponge contained fibrous tissue with hyalinization and a number of blood vessels. Between the sponge and myocardium were numerous blood vessels containing dye.

Dog 13-429: A 37 lb. female, mongrel dog, lived 177 days was operated on 12-3-58 and sacrificed on 5-29-59. Postmortem studies showed absence of gross infarction and the septal artery arose from the AD artery. Injection of intact heart with dye through the left subclavian artery and aorta, without ventricular cannula, showed extracardiac arteries went into the pericardium, but no filling of the coronary arteries. The coronary arteries were injected distal to the ameroids, which showed *** homocoronary, * intercoronary anastomoses, 25 arterioluminal vessels, 4 of which communicated with the heart's lumen. Coronary artery occlusions showed AD-95%, C-80% and combined occlusion-87.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced coronally and microscopic studies revealed same findings as of Dog 12-443.

Dog 14-444: A 53 lb. male, mongrel dog, lived 21 days was operated on 1-16-59 and died on 2-6-59. Post

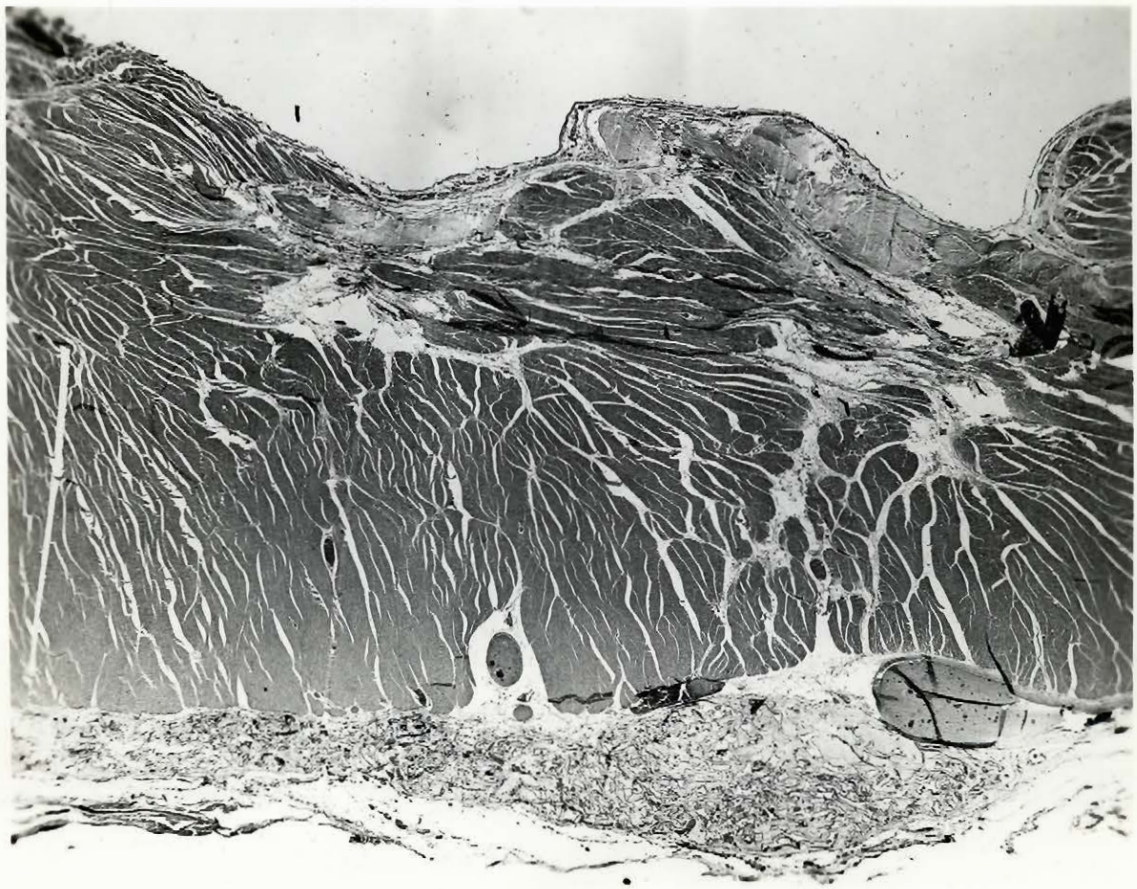


PLATE NO. 24.

X-ray photograph of ivalon dog 12-443 whose intact heart is injected with the new Schlesinger mass through left subclavian artery and aorta, showing branches of pericardio phrenic, IMA, intercostal, esophageal and bronchial arteries in pericardium, and dye filled up coronary arteries and lumen of heart. No dye went to coronary and ventricular lumen from the aorta for it was ligated above the sinus of valsalva. Pulmonary vessels and descending thoracic aorta are also filled with dye.

mortem revealed presence of posterior wall infarction of L.V., and the septal artery arose from the AD artery. The coronary arteries were injected with dye distal to the ameroids, without ventricular cannula, which showed *** homocoronary, * intercoronary anastomoses, 33 arterioluminal vessels, 10 of which communicated with the heart's lumen. No dye entered the ventricular lumen. Coronary artery occlusions showed AD-98%, C-95% and combined occlusion-96.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced transversely and microscopicstudies revealed extensive fibrosis in the middle third of the myocardium. Intramyocardial blood vessels contained dye. The ivalon sponge had rich cellular fibrous tissue with marked hyalinization moderate number of blood vessels and dye in the meshes of the sponge. There was plenty of foreign body giant reaction.

Dog 15-435: A 44 lb. male, mongrel dog, lived 20 days was operated on 2-2-59 and died 2-22-59. Postmortem revealed posterior wall infarction and the septal artery arose from the AD artery. The coronary arteries were injected with dye distal to the ameroids, without ventricular cannula, showed *** homocoronary, * intercoronary anastomoses, 28 arterioluminal vessels, 12 of which communicaed with the heart's lumen. The coronary artery occlusions showed AD-85%, C-80% and combined occlusion-77.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced tran sversely and microscopic studies revealed normal myocardium. Dye was present in the intramyocardial blood vessels. The

ivalon sponge contained dye, hyalinized fibrous tissues, some blood vessels and foreign body giant cell reaction. Between the ivalon and the myocardium were coronary arteries with intimal proliferation which contained dye.

Dog 16-425: A 42 lb. female, mongrel dog, lived 130 days, was operated on 12-17-58 and sacrificed on 4-26-59. Postmortem showed absence of gross infarction and the septal artery arose from the circumflex artery. The coronary arteries were injected with dye, distal to the ameroids, without ventricular cannula, which showed *** homocoronary, ** intercoronary anastomoses, 24 arterioluminal vessels, 10 of which communicated with the heart's lumen. The coronary artery occlusions showed AD-100%, C-100% and combined occlusion-100%, which were due to intimal proliferation and thrombus formation. The heart was sliced sagitally and microscopic studies revealed the myocardium was normal and intramyocardial blood vessels contained dye. The spaces of the ivalon sponge were filled with partial hyalinized fibrous tissue, some thin walled blood vessels and a few areas of foreign body giant cell reaction.

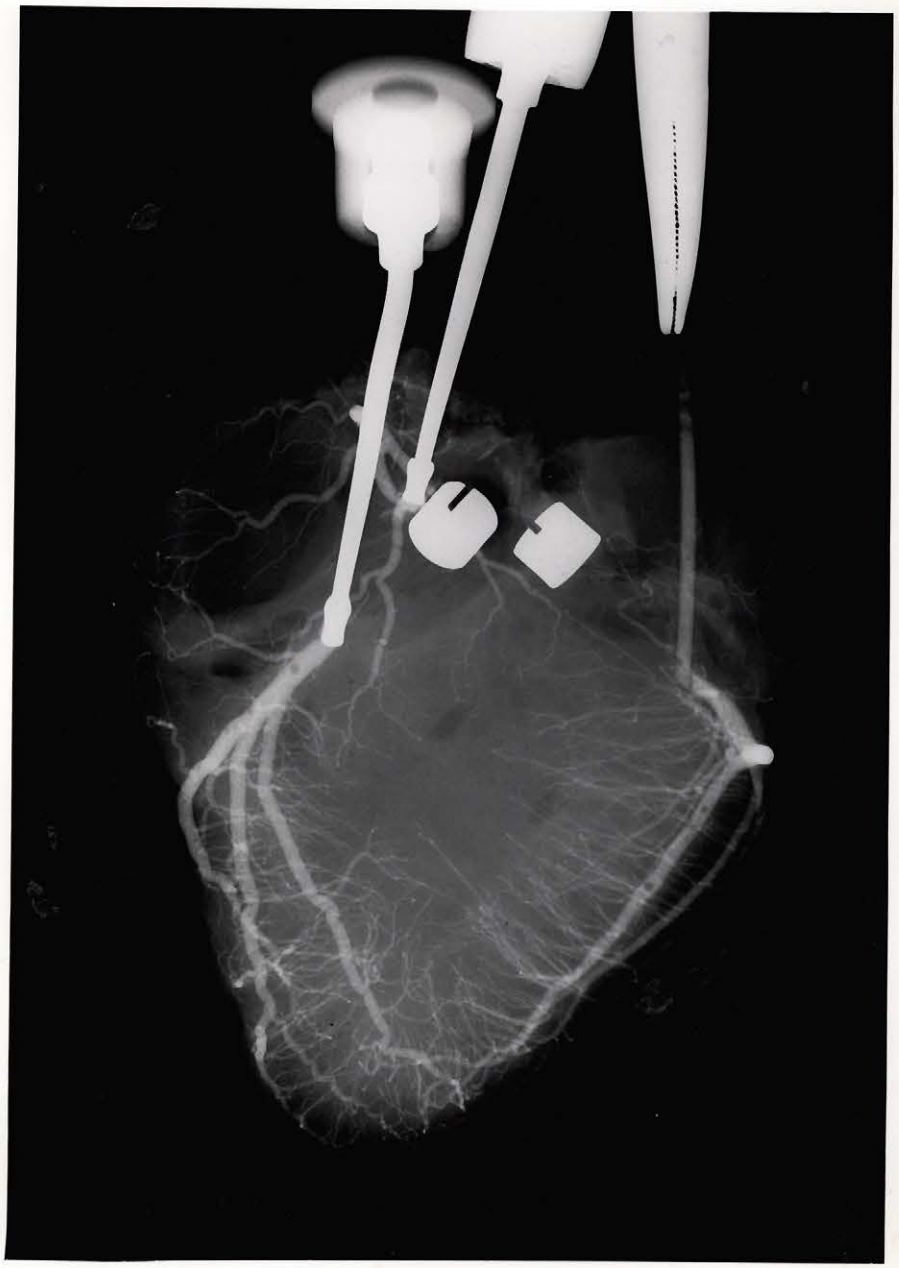


PLATE NO. 25

X-ray photograph showing heart of ivalon dog 15-435, injected with new Schlesinger mass, distal to the ameroids. Note numerous palisading of the arterio-luminal vessels and the tremendous homocoronary and increcoronary anastomoses.

SERIES IIB: IVALON SPONGE OPERATION

General Summary and Results:

1. Number of dogs: 10

2. Sex: males 8; females 2

3. Weight: between 37-44 lbs.

4. Mortality: 5 dogs Percentage: 50%
   Average survival in days of mortality dogs: 51.8 days.

5. Survival: 5 dogs Percentage: 50%
   Average survival in days of sacrificed dogs: 87 days.

6. Position of septal artery: Percentage:
   a) from anterior descending branch: 6 60%
   b) from circumflex branch: 2 20%
   c) frommain left coronary artery: 2 20%

7. Injection of coronary arteries:
   a) proximal to ameroids: 0
   b) distal to ameroids: 10
   c) from extracardiac injection: 6
   d) cannula in ventricular cavity: 3 No cannula: 7

8. Extent of coronary occlusions:
   a) average percentage form anterior descending branch: 86%
   b) average percentage from circumflex branch: 91.3%
   c) combined average percentage: 88.6%

9. Coronary anastomoses:
   1. Intracardiac anastomoses:
      Average for surviving dogs: homocoronary 3.4 times *
      intercoronary 2.4 times *
      Average for mortality dogs: homocoronary 2.8 times *
      intercoronary *
      Average overall: homocoronary 3.2 times *
      intercoronary: 1.7 times *
   2. Extracardiac anastomoses: 1 case

10. Arterioluminal vessels:
    a) average number: 23.3 vessels
    b) average number communicating with lumen of the heart: 6.4

11. Presence of dye in intramyocardial vessels:
    a) number of hearts with dye: 10
    b) number of hearts without dye: 0
    c) all surviving dogs had dye in the intramyocardial vessels.
    d) all mortality dogs had dye in the intramyocardial vessels.

12. Sections or slicing ofhearts:
    a) transverse or horizontal sections: 2
    b) sagital or vertical sections: 0
    c) coronal, right angle to lumen: 8
    d) no sections of heart: 0

13. Location of infarction:
    a) anterior wall of LV: 1
    b) posterior wall of LV: 2
    c) postero-lateral wall of L.V.: 1
    d) no infarction: 6.

14. Microscopic findings: Presence and location of myocardial fibrosis:
    a) endocardial portion: 4
    b) middle portion: 0
    c) middle and endocardial portion: 0
    d) no myocardial fibrosis: 6

Individual Summary:

Dog 19-395:

This was a 43 lb. male mongrel dog operated on February 13, 1959 and died April 16, 1959. It lived 62 days. Postmortem showed left lower lobe was adherent to the surface of the heart, presence of slight posterior wall infarction of L. V., and the septal artery arose from the AD branch. Injection of coronary

arteries with dye, distal to the ameroids, without ventricular cannula, showed ** homocoronary, * intercoronary anastomoses, 13 arterioluminal vessels, 3 of which communicated with the heart's lumen. Coronary artery occlusions showed AD-75%, C-100% and combined occlusion-85%, which were due to intimal proliferation and thrombus formation. The heart was sliced transversely and microscopic studies revealed fibrosis in the inner 1/2 of the myocardium. Intramyocardial blood vessels contained dye, but none in the myocardial sinusoids. The ivalon sponge had hyalinized fibrous tissue, some thin-walled blood vessels, injected dye and some foreign body giant cells. Between the sponge and the myocardium were coronary blood vessels with intimal proliferation and their lumen contained dye.

Dog 20-303: A 40 lb. male, mongrel dog, lived40 days was operated on 2-16-59 and died on 3-28-59. Postmortem revealed postero-lateral infarction of the L.V., and the septal artery arose from the AD artery. The coronary arteries were injected with dye, distal to the ameroids, without ventricular cannula, showed *** homocoronary, * intercoronary anastomoses, 12 arterioluminal vessels, 3 of which communicated with the heart's lumen. The coronary artery occlusions showed AD-70%, C-100% and combined occlusion-85%, which were due to intimal proliferation and thrombus formation. The heart was sliced transversely and microscopic sections revealed patches of fibrosis in the endocardial side of the myocardium. Intramyocardial blood vessels contained dye, but none in the myocardial sinusoids.

The ivalon sponge contained hyalinized fibrous tissue, some thin-walled blood vessels, injected dye and foreign giant cells. Between the sponge and the myocardium were coronary vessels with intimal proliferation containing dye in their lumen.

Dog 24-441: A 42 lb. male, mongrel dog, lived 98 days was operated on 2-23-59 and sacrificed on 6-1-59. Postmortem showed absence of gross infarction and the septal artery arose from the AD artery. Injection of the intact heart with dye through the left subclavian artery and aorta with ventricular cannula showed extracardiac arteries went to the pericardium. None filled the coronary arteries and the lumen of the heart. Injection distal to the ameroids showed *** homocoronary, ** intercoronary anastomoses, 21 arterioluminal vessels, 7 of which communicated with the heart's lumen. The coronary arter occlusions showed AD-95%, C-90% and combined occlusion-92.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced coronally and microscopic studies revealed normal myocardium, dye was present in the intramyocardial vessels and myocardial sinusoids. The iva-sponge contained partially hyalinized fibrous tissue, thin-walled blood vessels and few areas of foreign body reaction. In the inner pericardium was suture material and foreign body granuloma.

Dog 28-450: A 44 lb. mongrel dog, lived 89 days was operated on 3-6-59 and sacrificed on 6-3-59. Postmortem

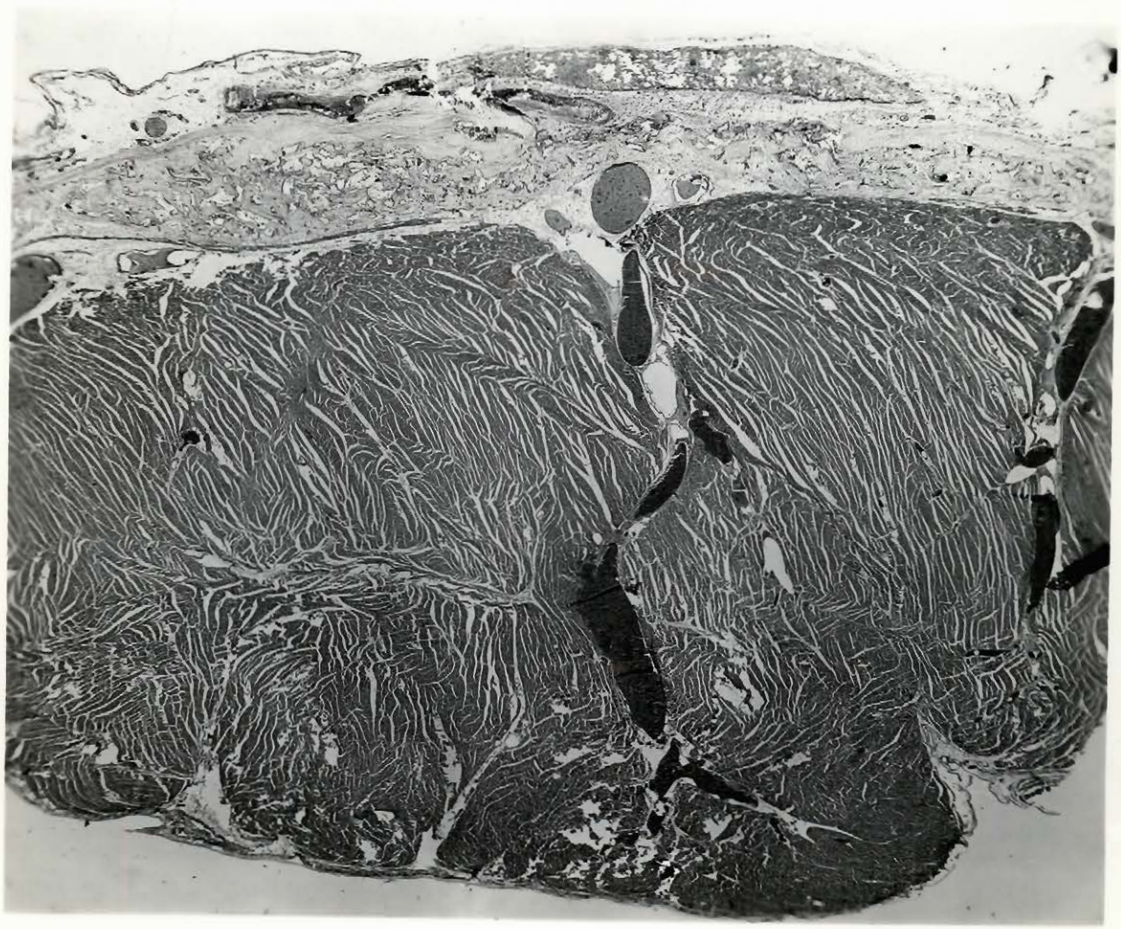


PLATE NO. 26

Photomicrograph is from heart of ivalon dog 24-441 which died 98 days after operation. Section shows myocardium is normal with dye in the intramyocardial vessels and myocardial sinusoids. Ivalon sponge contains partially hyalinized fibrous tissue, thin-walled blood vessels and a few areas of foreign body giant cell reaction (x 10).

studies showed absence of gross infarction and septal artery arose from the main left coronary artery. Injection of intact heart with dye through the left subvlacian artery and aorta, with ventricular cannula, showed extra cardiac arteries went to the pericardium. There was no filling of the coronary arteries and none entered the lumen of the heart. The coronary arteries were injected distal to the ameroids, which showed *** homocoronary, ** intercoronary anastomoses, 20 arterioluminal vessels 3 of which communicated with the heart's lumen. The coronary occlusions showed AD-100%, C-95% and combined occlusion-97.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced coronally and microscopic sections revealed normal myocardium with dye in the intramyocardial vessels. The ivalon sponge contained fibrous tissue, large and small blood vessels and moderate amounts of foreign body giant cell reaction.

Dog 30-159: A 38 lb male, mongrel dog , lived 106 days was operated on 3-11-59 and sacrificed on 6-15-59. Postmortem showed absence of gross infarction and septal artery arose from the AD branch. Injection of intact heart with dye through theleft subclavian artery and aorta, with ventricular cannula showed extracardiac arteries went into the pericardium. There was no filling of the coronary artery. Injection distal to the ameroids showed *** homocoronary, ** intercoronary anastomoses, 29 arterioluminal vessels, 6 of which communicated with the heart's lumen. The

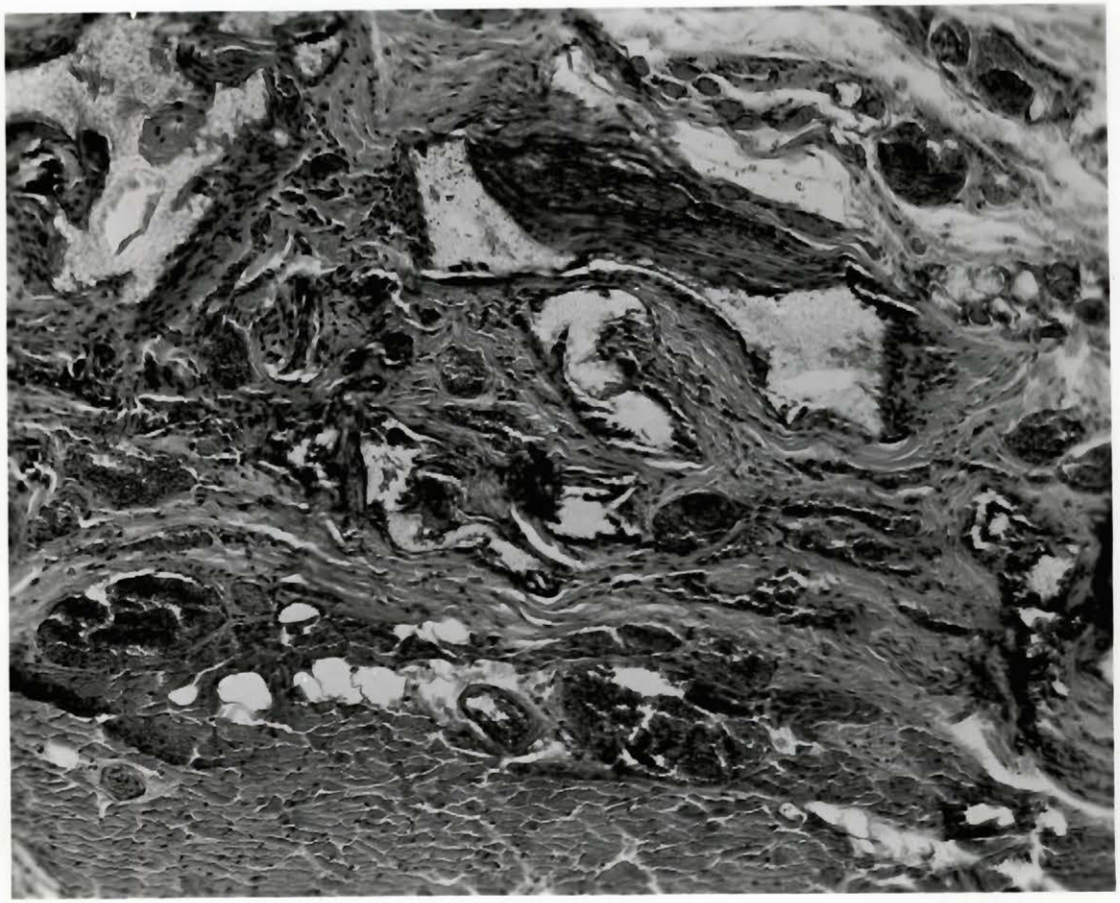


PLATE NO. 27

Photomicrograph taken from heart of ivalon dog 25-325 which survived 90 days. Section shows normal myocardium with dye in intramyocardial vessels. Ivalon sponge contains fibrous tissue, large endothelial lined vascular channels, hyalinized fibrous tissue and foreign body giant cell reaction. (x 100).

coronary occlusions showed AD-75%, C-95% and combined occlusion-85%, which were due to intimal proliferation and thrombus formation. The heart was sliced coronally and microscopic studies revealed normal myocardium and intramyocardial vessels were filled with dye. The ivalon sponge contained more fibrous tissue, less vascular channels and less foreign body giant cell reaction.

Dog 31-388: A 40 lb. male, mongrel dog, lived 62 days was operated on 3-11-59 and died on 5-12-59. Post mortem showed small infarction in the posterior wall of L.V., and septal artery arose from the circumflex artery. The coronary arteries were injected with dye distal to the ameroids, without ventricular cannula, showed *** homocoronary, 0 intercoronary anastomoses, 27 arterioluminal vessels, 7 of which communicated with the heart's lumen. Coronary occlusions showed AD-90%, C-80% and combined occlusion 85%, which were due to intimal proliferation and thrombus formation. The heart was sliced coronally and microscopic studies revealed large fibrosis containing dilated vascular spaces in the inner portion of the myocardium, and intramyocardial blood vessels contained dye. The ivalon sponge had fibrous tissue, foreign body giant cell reaction, a subacute granulomatous inflammation with lymphocytes, plasma cells and moderate sized vascular channels.

Dog 35-470: A 46 lb. female, mongrel dog, lived 53 days was operated on 5-1-59 and sacrificed on 6-22-59.

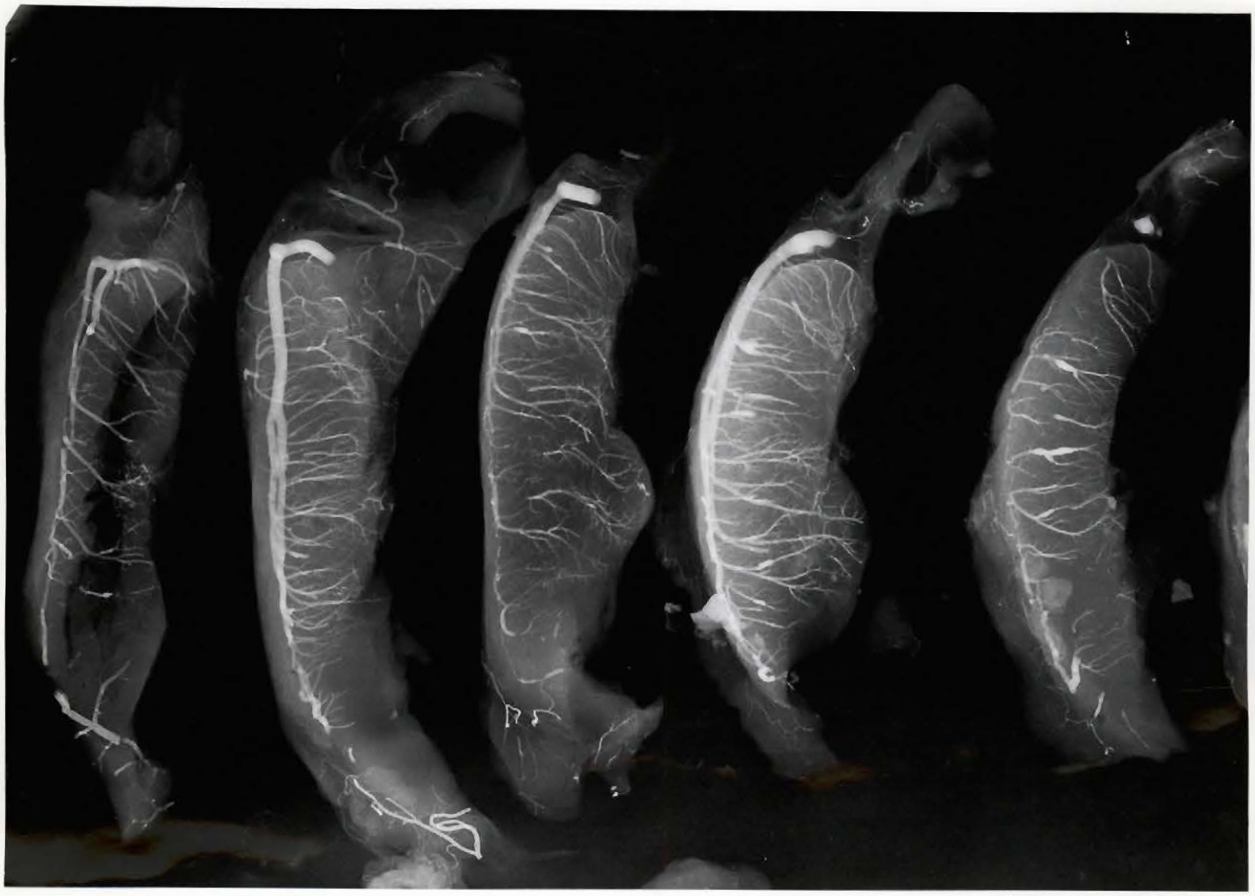


PLATE NO. 28

X-ray photograph of coronal-right angle to lumen slices of heart of ivalon dog 35-470, sacrificed 53 days after operation. There are about 27 arterioluminal vessels, 10 of which communicate with the lumen of the heart.

Postmortem showed no gross infarction and septal artery arose from the AD artery. Injection of the intact heart with dye through the left subclavian artery and aorta with ventricular cannula showed extracardiac arteries went to the pericardium. The circumflex and AD branches became filled with dye indicating extracardiac anastomoses. Injection of the coronary arteries showed **** homocoronary, *** intercoronary anastomoses, 27 arterioluminal vessels, 10 of which communicated with the heart's lumen. Coronary occlusions showed AD-80%, C-100% and combined occlusion-90%, which were due to intimal proliferation and thrombus formation. The heart was sliced coronally and microscopic studies revealed normal myocadium and intramyocardial blood vessels contained dye. The ivalon sponge had hyalinized fibrous tissue, thin-walled blood vessels, injected dye and moderate amount of foreign body giant cells.

Dog 37-478: A 43 lb. female, mongrel dog, lived 40 days was operated on 5-6-59 and died on 6-15-59. Postmortem showed absence of gross infarction and septal artery arose from the circumflex artery. Injection of the intact heart with dye through the left subclavian artery and aorta, with ventricular cannula, showed extracardiac arteries went to the pericardium, but did not fill up the coronary arteries. The coronary arteries were injected distal to the ameroids, which showed *** homocoronary, * intercoronary anastomoses, 18 arterioluminal vessels, 5 of which

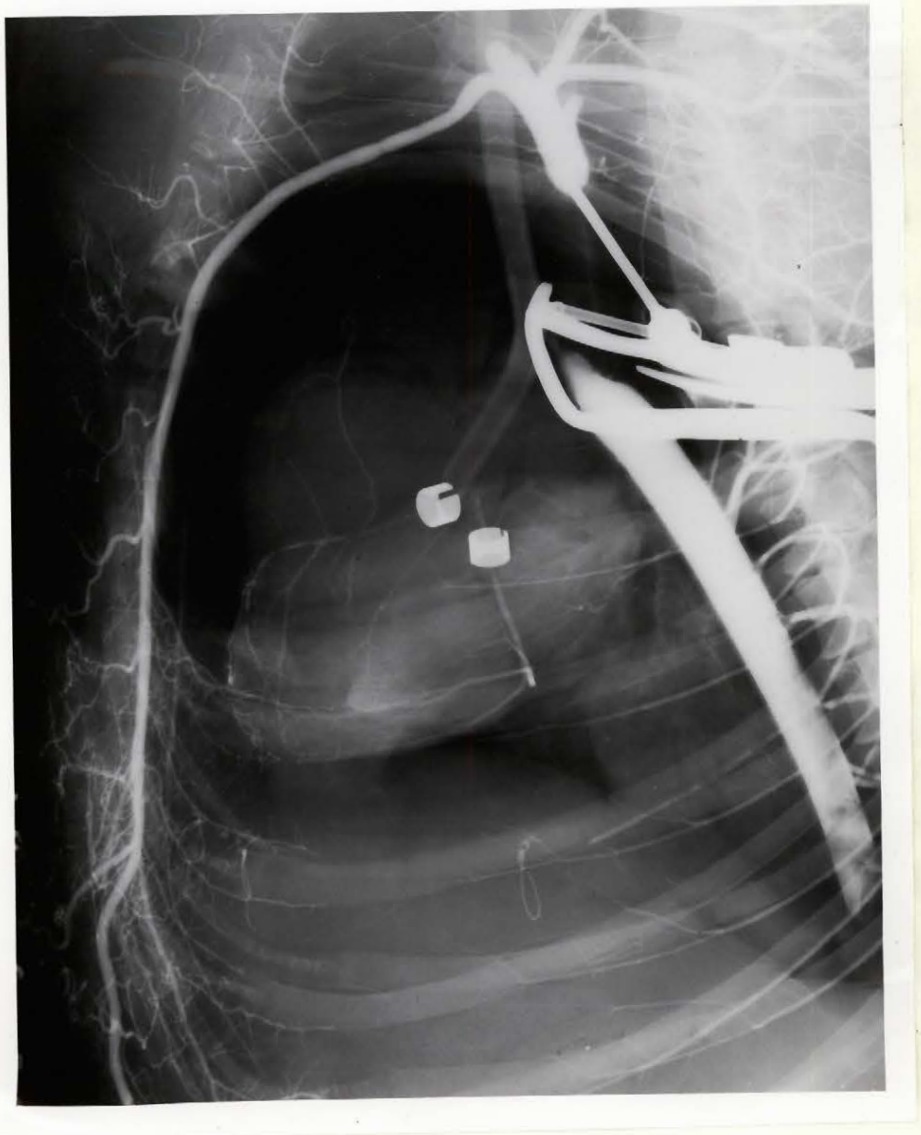


PLATE NO. 29.

X-ray photograph of ivalon dog 35-470 which was sacrificed 53 days after operation. Injection of intact heart with new Schlesinger mass through the left subclavian artery and aorta, shows branches from pericardio phrenic, IMA, intercostal, esophageal and bronchial arteries goes to the pericardium. The circumflex and AD branches are filled with dye indicating extracardiac anastomoses. There is a ventricular cannula.

communicated with the lumen of the heart. Coronary artery occlusions showed AD-85%, C-85% and combined occlusion-86.5% which were due to intimal proliferation and thrombus formation. The heart was sliced coronally and microscopic studies revealed normal myocardium and the intramyocardial blood vessels contained dye. The ivalon sponge contained fibrous tissue, thin-walled blood vessels, injected dye and moderate amount of foreign body giant cell reaction.

SERIES III: IMPLANTATION OF LEFT INTERNAL MAMMARY ARTERY TO THE LEFT VENTRICULAR MYOCARDIUM AND PARTIAL LIGATION OF THE CORONARY SINUS.

Summary and Results:

1. Number of dogs: 10

2. Sex: males 6, females 5

3. Weight: between 37 1/2 - 55 lbs.

4. Mortality: 3 dogs Percentage 30%
   Average survival in days of mortality dogs: 26 days

5. Survival: 7 dogs Percentage 70%
   Average survival in days of sacrificed dogs: 237 days.

6. Position of septal artery: Percentage
   a) from anterior descending branch: 7 70%
   b) from circumflex branch: 2 20%
   c) from main left coronary artery: 1 10%

7. Injection of the coronary arteries:
   a) proximal to ameroids: 3
   b) distal to ameroids: 6
   c) from extracardiac injections: 4
   d) cannula in ventricular cavity: 0 No cannula: 10

8. Extent of coronary occlusion:
   a) average percentage from anterior descending branch: 79%
   b) average percentage from circumflex branch: 87%
   c) combined average percentage: 83%

9. Occlusion and patency of implanted internal mammary:
   a) average proximal occlusion: 17%
   b) average midportion occlusion: 34%
   c) average distal portion occlusion: 51.5%

10. Coronary anastomoses:
    a) Intracardiac anastomoses:
       1. Aver. for surviving dogs: homocoronary 2.7 times *
          intercoronary 1.4 times *

2. Aver. for mortality dogs: homocoronary 1.66 times *
intercoronary 0.66 times *
3. Overall average: homocoronary: 2.4 times *
intercoronary 1.2 times *

b) Extracardiac anastomoses: 4 cases.

11. Arterioluminal vessels:
a) average number of vessels: 26.6
b) average number communicating with lumen of heart: 4.6

12. Presence of dye in intramyocardial vessels:
a) number of hearts with dye: 8
b) number of hearts without dye: 2
c) all surviving dogs had dye in the intramyocardial vessels, except one.
d) all mortality dogs had dye in the intramyocardial vessels, except one.

13. Sections or slicing of hearts:
a) transverse or horizontal sections: 0
b) sagital or vertical sections: 0
c) coronal, right angle to lumen: 7
d) no section of heart: 3

14. Location of infarction:
a) anterior wall of LV: 0
b) posterior wall of LV: 3
c) no myocardial infarction (normal): 7

15. Microscopic findings: presence and location of myocardial fibrosis.
a) endocardial portion: 4
b) middle portion: 1
c) epicardial portion: 1
d) no myocardial fibrosis (normal): 4

Individual Summary:

Dog 17-408:

This was a 45 lb. male, mongrel dog operated on August 27, 1958 and sacrificed May 20, 1959. It lived 267 days. Post-mortem showed left lower lung lobe was adherent to the surface

of the heart, absence of gross infarction and the septal artery arose from the AD artery. Injection of intact heart with dye through the left subclavian artery and aorta, without ventricular cannula, showed the dye passed through implanted IMA into all the coronary arteries and finally into the lumen of the heart. There were *** homocoronary, ** intercoronary anastomoses, 29 arterioluminal vessels, 9 of which communicated with the heart's lumen. Implanted IMA occlusions showed proximal-10% , mid-20% and distal pertion-30%. Coronary artery occlusions showed AD-70%, C-100% and combined occlusion-85%. All these occlusions were due to intimal proliferation and thrombus fomation. The heart was sliced coronally and microscopic studies showed normal myocardium and presence of dye in the intramyocardial blood vessels.

Dog 22-161: A 55 lb. male, mongrel dog, lived 245 days was operated on 9-8-58 and sacrificed on 5-11-59. Postmortem showed absence of gross infarction and septal artery arose from the circumflex artery. Injection of intact heart with dye through the left subclavian artery and aorta, without ventricular cannula, showed the IMA was patent, but no branching because the lumen was accidentally blocked by a bubble of air during the injection. The coronary arteries did not fill up and nodye entered the lumen of the heart. Injection distal to the ameroids showed ** homocoronary, ** intercoronary anastomoses, 20

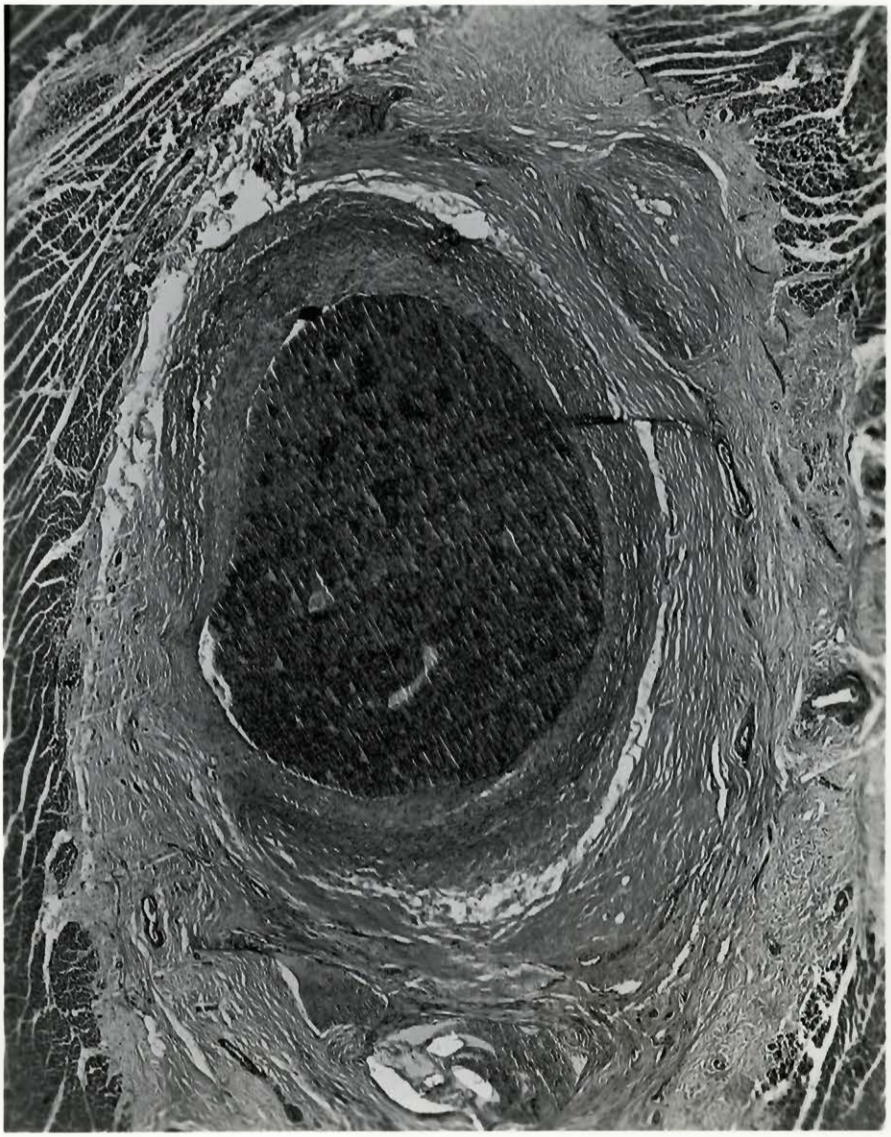


PLATE NO. 30.

Photomicrograph of mid portion of internal mammary artery implanted into left ventricular tunnel. Lumen is narrowed about 15% due to intimal proliferation and contains injected dye. Adventitia also shows dense collagenous cuff. Specimen obtained from IMA dog 23-397 sacrificed 258 days after operation. (x 35).

arterioluminal vessels, 5 of which communicated with the heart's lumen. Coronary artery occlusions showed AD-80%, C-95% and combined occlusion-87.5%, while IMA showed proximal-40%, mid portion-65% and distal portion-80%, which were all due to intimal proliferations and thrombus formation. The adventitia of the IMA showed collagenous cuff. The heart was sliced coronally and microscopic studies revealed fibrosis in the inner third of the mycocardium and the intramyocardial vessels contained no dye.

Dog 23-397: A 45 lb. male, mongrel dog, lived 258 days was operated on 9-9-58 and sacrificed on 5-25-59. Postmortem showed absence of gross infarction and septal artery arose from the AD branch. Injection of intact heart with dye, through the left subclavian artery and aorta, without ventricular cannula, showed IMA was parent with early branching. There was no filling of the coronary arteries and no dye entered the lumen of the heart. Injection distal to the ameroids showed ** homocoronary, * intercoronary anastomoses, 16 arterioluminal vessels, 3 of which communicated with the heart's lumen. Coronary artery occlusiona showed AD-90%, C-85% and combined occlusion-87.5%, while IMA showed proximal portion-10%, mid portion-15% and distal portion-30%, which were all due to intimal proliferation and thrombus formation. The adventitia of IMA contained a dense collagenous cuff with moderate number of arterioles and small sized arteries. The heart was sliced coro-

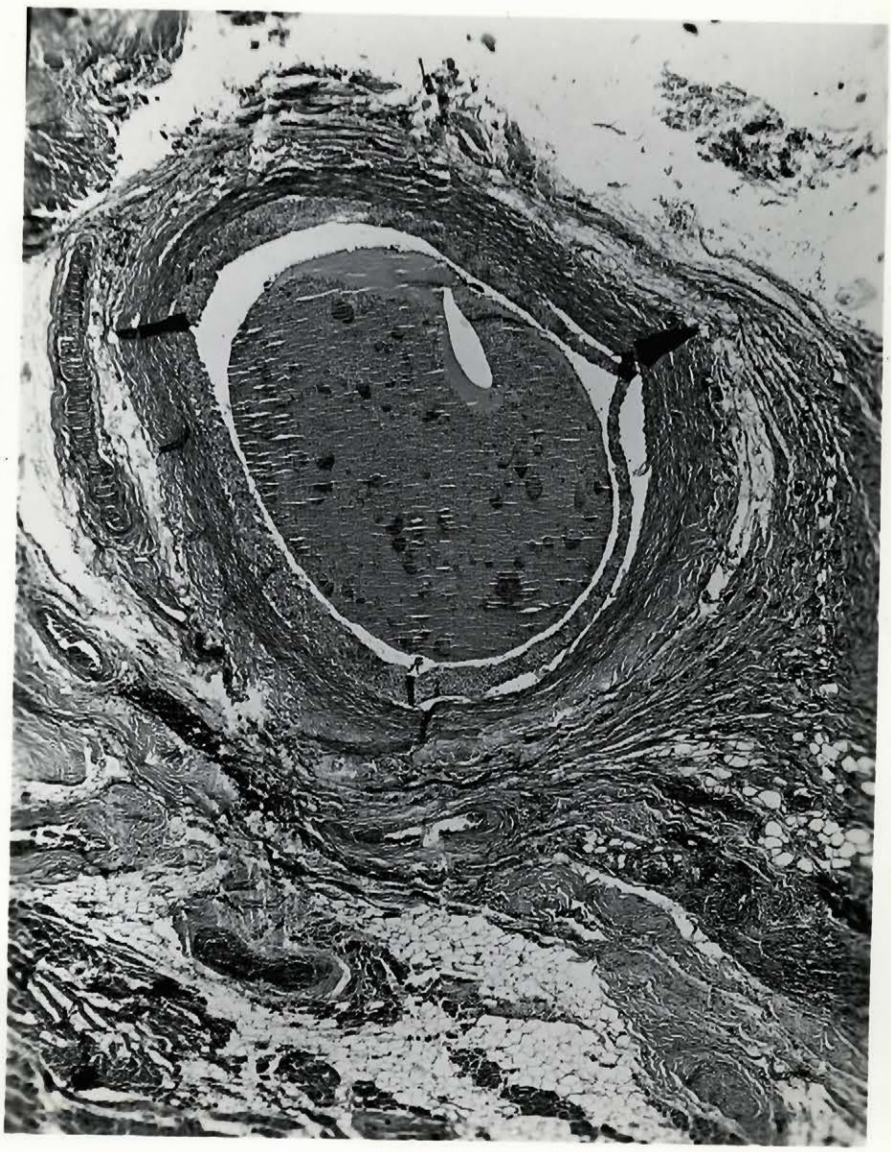


PLATE NO. 31.

Photomicrograph of proximal portion of internal mammary implanted into left ventricular tunnel. Presence of intimal obliteration, narrowing the lumen about 10%. Inside the lumen is the injected dye. The adventitia contains dense collagenous cuff; Specimen obtained from IMA dog 23-397, sacrificed 258 days after operation. (x 35).

nally and microscopic studies revealed slight fibrosis in the endocardial side of the myocardium and intramyocardial blood vessels contained dye.

Dog 25-404: A 40 lb. female, mongrel dog, lived 252 days was operated on 9-11-58 and sacrificed on 5-21-59. Postmortem showed absence of gross infarction and septal artery arose from the AD branch. Injection of the implanted IMA without ventricular cannula, showed patency, but it gradually narrowed distally with some branching of small size. Injection distal to the ameroids showed *** homocoronary, 0 intercoronary anastomoses, 17 arteriluminal vessels, 4 of which communicated with the heart's lumen. Coronary artery occlusions showed AD-100%, C-90% and combined occlusion-95%, while implanted IMA showed proximal-20%, mid-40% and distal portion-60%, which were all due to intimal proliferation and thrombus formation. The adventitia of IMA contained collagenous cuff with arterioles. The heart was sliced coronally and microscopic studies revealed normal myocardium and intramyocardial blood vessels had injected dye.

Dog 26-374: A 41 lb. female, mongrel dog was operated on 9-15-58 and sacrificed on 5-29-59. Postmortem showed absence of gross infarction and septal artery arose from the main left coronary artery. Injection through IMA with dye, without ventricular cannula, showed artery was patent in the myocardial tunnel with numerous branchings. Coronary arteries were injected distal to the ameroids, showed **

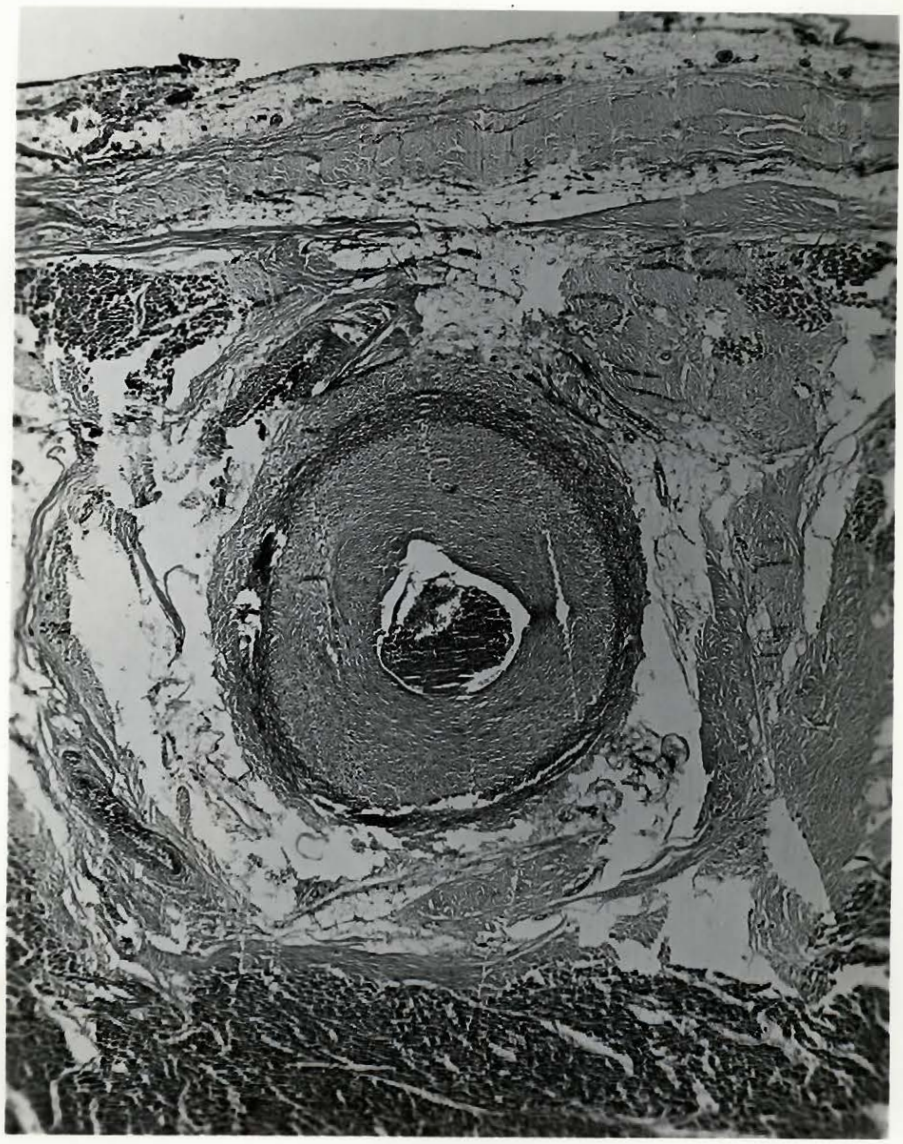


PLATE NO. 32.

Photomicrograph is from IMA dog 25-404, sacrificed 252 days after operation. Section is taken from distal portion of implanted IMA, which is narrowed 60% in its lumen by intimal proliferation. There is a dye inside the center of its lumen. The adventitia contains some collagenous cuff. (x 35).

homocoronary, * intercoronary anastomoses, 15 arterio-luminal vessels, 2 of which communicated with the heart's lumen. Coronary artery occlusions showed AD-80%, C-60% and combined occlusion-70%, while implanted IMA showed proximal-10%, mid-30% and distal portion-45%, which were all due to intimal proliferation and thrombus formation. Adventitia of IMA contained some collagenous cuff. The heart was sliced coronally and microscopic studies revealed normal myocadidum and dyes were present in the intramyocardial blood vessels.

Dog 31-405: A 44 lb. male, mongrel dog, lived 25 days was operated on 9-24-58 and died on 10-19-58. Post mortem showed posterior wall infarction of L.V., and septal artery arose from AD branch. Injection of implanted IMA with dye, without ventricular cannula, showed artery was patent with some narrowing and no branching. Coronary arteries were injected distal to the ameroids which showed * homocoronary,0 intercoronary anastomoses and no dye entered the heart's lumen. Coronary artey occlusions revealed AD-50%, C-90% and combined occlusion-70% while implanted IMA showed proximal-30%, mid-50% and distal portion-80%, which were all due to intimal proliferation and thrombus formation. Microscopic studies revealed fibrosis in the epicardial portion of the myocardium and intramyocardial blood vessels contained dye.

Dog 25-321: A 40 lb. male, mongrel dog, lived 23 days was operated on 10-22-58 and died 11-13-58. Inject-

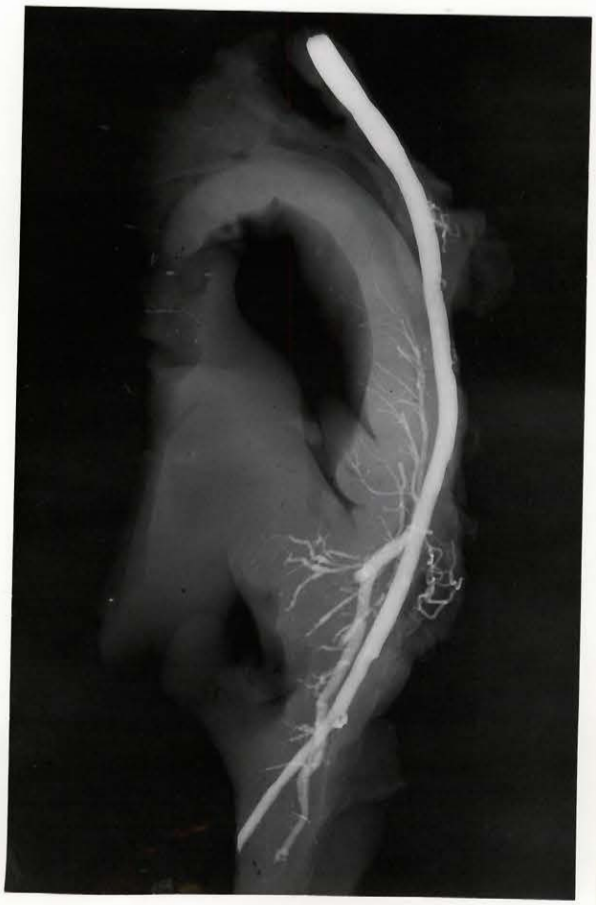


PLATE NO. 33.

X-ray photograph of sliced portion of left ventricle where internal mammary artery is implanted. It shows artery is patent, filled with dye and shows numerous branching inside the tunnel. Specimen is obtained from heart of IMA dog 26-374, sacrificed 255 days after operation.

ion of the implanted IMA, without ventricular cannula showed artery was patent with beginning branchings. Coronary arteries were injected proximal to ameroids which showed ** homocoronary and * intercoronary anastomoses. Coronary artery occlusions showed AD-100%, C-60% and combined occlusion-80%, while implanted IMA showed proximal-20%, mid-40% and distal portion-60%, which were all due to intimal proliferation and thrombus formation. Adventitia of IMA contained collagenous cuff. Microscopic studies showed fibrosis in the middle 1/3 of the myocarduim and presence of dye in the intramyocardial blood vessels.

Dog 37-332: A 52 lb. female, mongrel dog, lived 31 days was operated on 10-24-58 and died on 11-23-58. Post mortem showed posterior wall infarction of L.V., and septal artery arose from the circumflex branch. Injection of implanted IMA, without ventricular cannula showed artery was patent with early branching. Coronary arteries were injected proximal to the ameroids which showed ** homocoronary, and * intercoronary anastomoses. Coronary artery occlusions showed AD-60%, C-100% and combined occlusion-80%, while implanted IMA showed proximal-10%, mid-30% and distal portion-40%, which were all due to intimal proliferation and thrombus formation. Microscopic studies revealed fibrosis in the endocardial side of the myocardium and no dye in intramyocardial vessels.

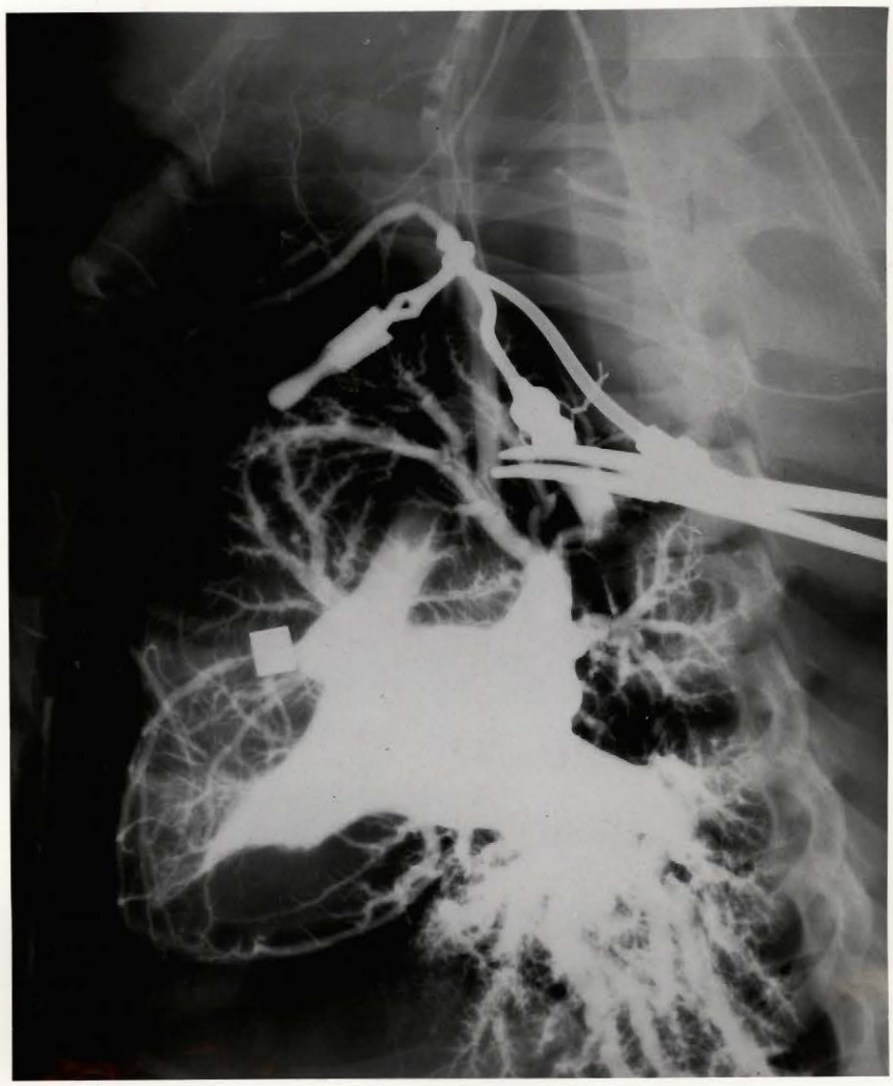


PLATE NO. 34

X-ray photograph of injected intact heart with new Schlesinger mass through left subclavian artery, shows implanted internal mammary patent. Through its anastomoses, the coronary arteries were filled and dyes went into the lumen of the heart and pulmonary vessels. Specimen taken from IMA dog 38-382, sacrificed 196 days after operation.

Dog 38-382: A 43 lb. male, mongrel dog, lived 196 days was operated on 11-21-58 and sacrificed on 6-5-59. Postmortem showed absence of gross infarction and septal artery arose from the AD branch. Injection of intact heart with dye through the left subclavian artery and aorta, without ventricular cannula, showed implanted IMA was patent with branching. It filled the coronary arteries and dye entered the heart's lumen. Some vessels going to the lungs were filled with dye. Coronary artery occlusions showed *** homocoronary, ** intercoronary anastomoses, 26 arterioluminal vessels, 4 of which communicated with the heart's lumen. Coronary occlusions showed AD-100%, C-95% and combined occlusion-97.5%, while implanted IMA showed proximal-10%, mid-30% and distal portion-50%, which were all due to intimal proliferation and thrombus formation. The heart was sliced coronally and microscopic studies revealed patches of fibrosis in inner 1/3 of myocardium and presence of dye in the intramyocardial blood vessels.

Dog 40-432: A 37 lb. female, mongrel dog , lived 185 days was operated on 12-8-58 and sacrificed on 6-11-59. Postmortem showed absence of gross infarction and the septal artery arose from the AD branch. Injection of the intact heart with dye through the left subclavian artery and aorta, without ventricular cannula, showed IMA in the myocardial tunnel was patent and dye filled all the coro-

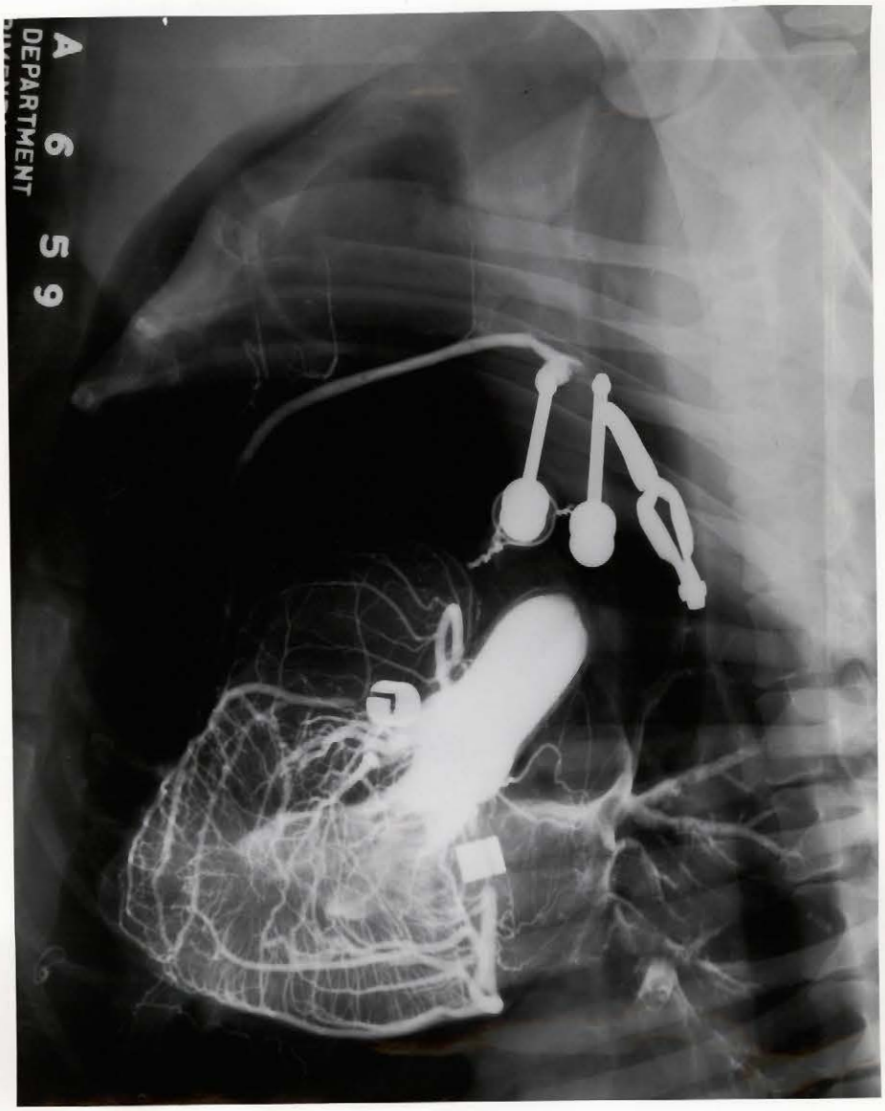


PLATE NO. 35

X-ray photograph show injection of intact heart with the new Schlesinger mass through the left subclavian artery. The IMA implanted in the ventricular myocardium is patent for dye passed through into the coronary arteries, lumen of the heart and pulmonary blood vessels. There is no ventricular cannula. Ameroid constrictors are seen with occlusion fo the anterior descending and circumflex branch of the left coronary artery. Specimen is taken from IMA dog 40-432, sacrificed 185 days after operation.

nary arteries and also entered the lumen of the heart. Some of the dye filled the blood vessels of the lungs and the base of the aorta. Coronary arteries showed *** homocornary, ** intercoronary anastomoses, 30 arterio-luminal vessels, 6 of which communicated with the lumen of the heart. Coronary artery occlusions showed AD-60% C-95% and combined occlusion-78.5%, while implanted IMA showed proximal-10%, mid portion-20% and distal portion 40%, which were all due to intimal proliferation and thrombus formation. The heart was sliced coronally and microscopic studies showed normal myocardium and the presence of dye in the intramyocardial blood vessles.

SERIES IV: BECK I OPERATION: (ASBESTOS CARDIO-PERICARDIOPEXY WITH PARTIAL LIGATION OF THE CORONARY SINUS.

General Summary and Results:

1. Number of dogs: 10

2. Sex: males, 7. females 3.

3. Weight: between 40-46 lb.s

4. Mortality: 6 dogs Percentage 60%
   Average survival in days of mortality dogs: 24.6 days.

5. Survival: 4 dogs Percentage 40%
   Average survival in days of sacrificed dogs: 60 days.

6. Position of septal artery: Percentage:
   a) from anterior descending branch: 7 70%
   b) from circumflex branch: 1 10%
   c) from main left coronary artery: 2 20%'

7. Injection of coronary arteries:
   a) proximal to ameroids: 0
   b) distal to ameroids: 10
   c) from extracardiac injections: 4
   d) cannula in ventricular cavity: 4 No cannula: 6

8. Extent of coronary artery occlusions:
   a) average percentage for anterior descending branch: 85.3%
   b) average percentage for circumflex branch: 83.5%
   c) combined average percentage: 84.4%

9. Coronary anastomoses:
   a) Intracardiac anastomoses:
      1. Average for surviving dogs: homocoronary ***
         intercoronary 1.8 times *
      2. Average for mortality dogs: homocoronary **
         intercoronary *
      3. Overall average: homocoronary: 2.5 times *
         intercoronary *
   b) Extracardiac anastomoses: 0

10. Arterioluminal vessels:
    a) average number of vessels: 18.8
    b) average number of vessels communicating with lumen of heart: 4.3

11. Presence of dye in intramyocardial vessels:
    a) number of hearts with dye: 7
    b) number of hearts without dye: 3
    c) all surviving dogs had dye except one.
    d) all mortality dogs had dye except one.

12. Sections or slicing of hearts:
    a) transverse or horizontal sections: 2
    b) sagital or vertical sections: 3
    c) coronal, right angle to lumen: 5
    d) no sections of the heart: 0

13. Location of infarction:
    a) anterior wall: 1
    b) posterior wall: 3
    c) postero-lateral wall: 2
    d) no infarction. 4

14. Microscopic findings: presence and location of myocardial fibrosis:
    a) endocardial portion: 5
    b) middle portion: 2
    c) no myocardial fibrosis: 3.

Individual Summary:

Dog 1-332:

This was a 40 lb. male mongrel dog operated on March 2, 1959 and died March 20, 1959. It lived 18 days. Postmortem showed left lung adherant to chest wall and surface of the heart, presence of postero-lateral infarction of LV., and the septal artery arose from the circumflex branch. Coronary arteries were injected with the new Schlesinger mass, distal to the

ameroids, which showed ** homocoronary, * intercoronary anastomoses, 13 arterioluminal vessels, 3 of which communicated with the heart's lumen. Coronary artery occlusions showed AD-90%, C-85% and combined occlusion-87.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced transversely. microscopic studies revealed patches of fibrosis in inner 1/4 of myocardium, nodye in the intramyocardial blood vessels. On the surface of the myocardium was a moderate giant cell foreign body reaction with glistening foreign body, small number of dilated cappilaries, fibrosis and chronic inflammatory reaction. Between the pericardium and myocardium were coronary vessels with intimal proliferation and dye.

Dog 2-453: A 40 lb. male, mongrel dog, lived 18 days was operated on 3-16-59 and died on 4-3-59. Post mortem showed postero-lateral wall infarction and septal artery arose from AD branch. Coronary arteries were injected with dye distal to the ameroids, without ventricular cannula, which showed * homocoronary, * intercoronary anastomoses, 19 arterioluminal vessels, 7 of which communicated with the heart's lumen. Coronary artey occlusions showed AD-80%, C-95% and combined occlusion-87.5% which were due to intimal proliferation and thrombus formation. The heart was sliced transversely and nodye in heart's lumen. Microscopic sections revealed patches of fibrosis in inner 1/4 of myocardium and dye in intramyo-

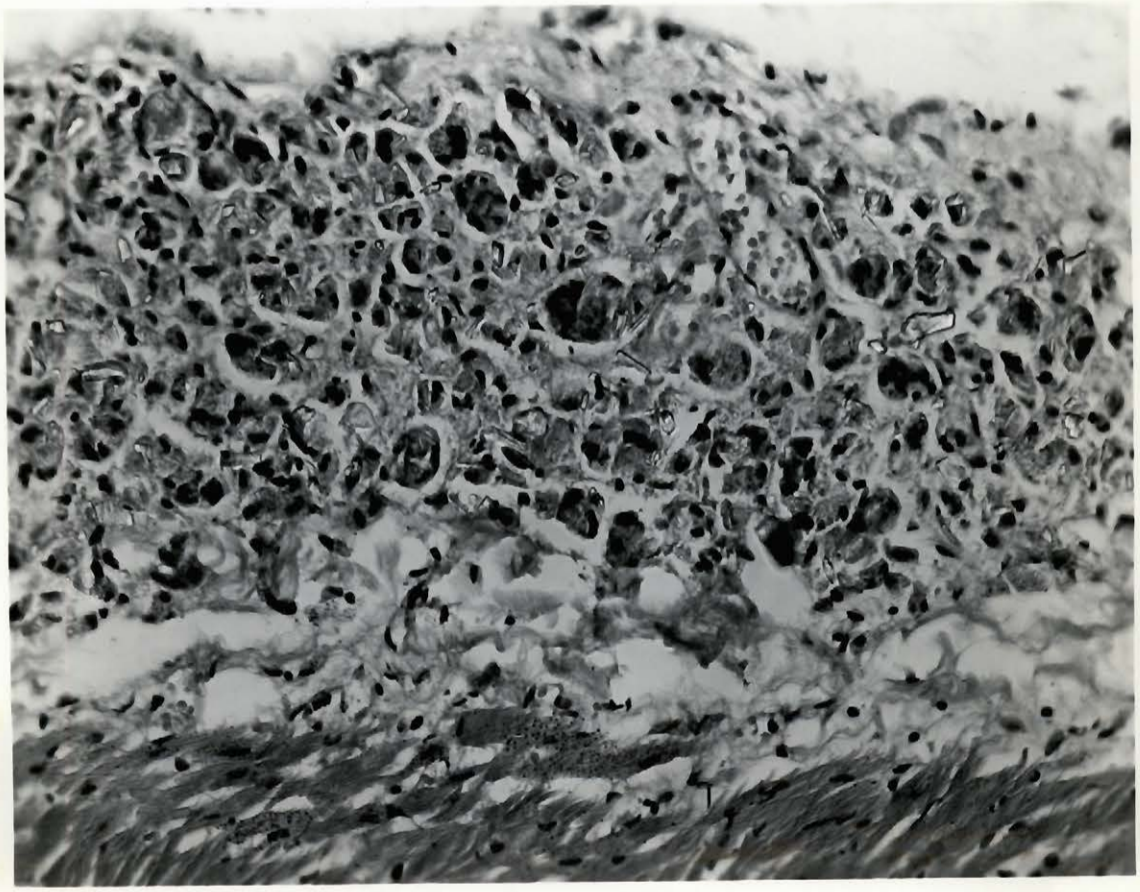


PLATE NO. 36.

Photomicrograph is from Beck I dog 3-435, which died 32 days after operation. Section shows the epicardial layer of myocardium has marked foreign body giant cell reaction with glistening foreign bodies (asbestos). There are dense fibrous tissue, some relatively small number of dilated capillaries, numerous foreign body giant cells are seen. (x 175).

cardial blood vessels. On the epicardium were moderate foreign body giant cell reaction and chronic inflammation with small cappilaries.

Dog 3-435: A 45 lb. male, mongrel dog, lived 32 days was operated on 4-1-59 and died 5-3-59. Postmortem revealed septal artery arose from the AD branch. Coronary arteries were injected with dye, distal to the ameroids, without ventricular cannula, showed ** homocoronary, * intercoronary anastomoses, 17 arterioluminal vessels, 5 of which communicated with heart's lumen. Coronary artery occlusions showed AD-98%, C-95% and combined occlusion-96.5%, whcih were due to intimal proliferation and thrombus formation. The heart was sliced sagitally and microscopic sections revealed fibrosis in inner 1/3 of myocardium and no dye in intramyocardial blood vessels. On the epicardium was a marked foreign body giant reaction with asbestos particles. There were dense fibrous tissues, small number of dilated cappillaries and larger vessels in this tissue.

Dog 4-413: A 42 lb female, mongrel dog, lived 26 was operated on 4-3-59 and died on 4-29-59. Postmortem showed septal artery arose from the main left coronary artery. The coronary arteries were injected with dye distal to the ameroids, without ventricular cannula, showed *** homocoronary, * intercoronary anastomoses, 20 arterioluminal vessels, 5 of which communicated

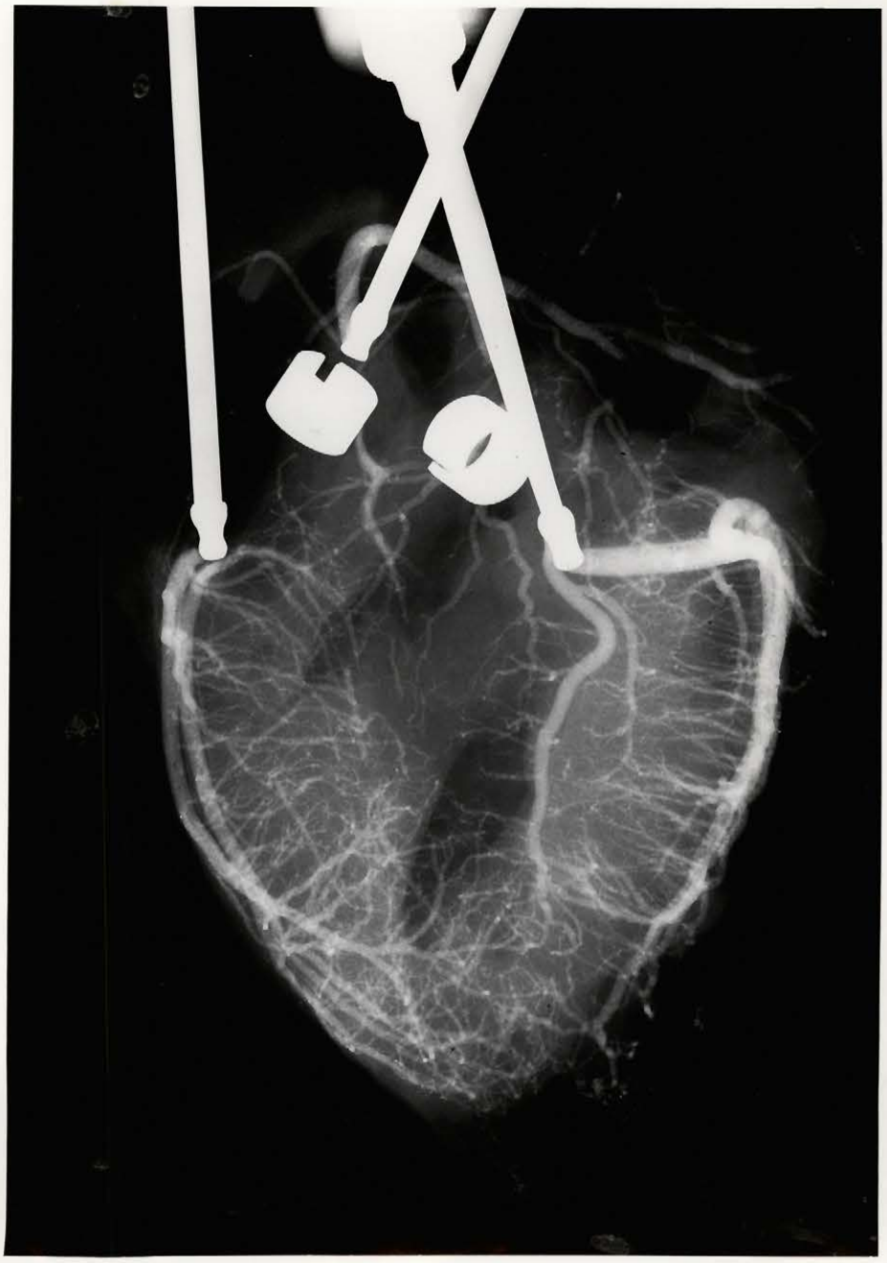


PLATE NO. 37.

X-ray photograph of heart injected distal to the ameroids which shows *** homocoronary and * intercoronary anastomoses. The ameroids are shown in place. Picture taken from Beck I dog 4-413, which died 26 days after operation.

with the heart's lumen. No dye entered the cavity of the heart. Coronary artery occlusions showed AD-100%, C-75% and combined occlusion-87.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced sagitally. Microscopic studies revealed fibrosis of the endocardial portion of the myocardium and dye in intramyocardial blood vessels. On the epicardial side of myocadium were found fibrous tissues, foreign body giant cell and small number of blood vessels. Between pericardium and myocardium were coronary vessels with intimal proliferation and dyes.

Dog 5-447: A 40 lb male, mongrel dog, lived 70 days was operated on 4-8-59 and sacrificed on 6-17-59. Postmortem showed septal artery arose from the AD branch. Injection of intact heart with dye through the left subclavian artery and aorta, with ventricular cannula, showed extracardiac arteries went into the pericardium. There was no filling of the coronary arteries and no dye entered the heart's lumen. Injection distal to the ameroids showed ***homocoronary, ** intercoronary anastomoses, 20 arterioluminal vessels, 5 of which communicated with the lumen of the heart. Coronary artery occlusions showed AD-75%, C-100%, and combined occlusion-87.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced coronally. Microscopic studies showednormal myocardium, but no dye in intramyocardial blood vessels. The zone of foreign body giant cell reaction was narrow. It was surrounded with dense hyalinized fibrous tissue

with small number of vascular channels.

Dog 6-662: A 44 lb. male, mongrel dog, lived 45 days was operated on 4-13-59 and died on 5-28-59. Post mortem showed extensive posterior wall infarction of L.V., and septal artery arose from the AD branch. Coronary arteries were injected with dye distal to the ameroids, without ventricular cannula, showed *** homocoronary, * intercoronary anastomoses, 31 arterioluminal vessels, 5 of which communicated with the heart's lumen. No dye entered the lumen of the heart. Coronary artery occlusions showed AD-85%, C-65% and combined occlusion-75%, which were due to intimal proliferation and thrombus formation. The heart was sliced coronally. Microscopic sections revealed extensive fibrosis in the middle 1/2 of the myocadium and dye in intramyocardial blood vessels. Presence of fibrous tissue and foreign body giant cell reaction with few blood vessels on surface of heart.

Dog 7-468: A 44 lb. female, mongrel dog, lived 9 days was operated on 4-15-59 and died on 4-24-59. Post mortem showed extensive posterior wall infarction and septal artery arose from the AD branch. The coronary arteries were injected distal to the ameroids without ventricular cannula showed ** homocoronary, * intercoronary anastomoses, 10 arterioluminal vessels, none of which communicated with the heart's lumen. Coronary artery occlusions showed AD-80%, C-75% and combined occlu-

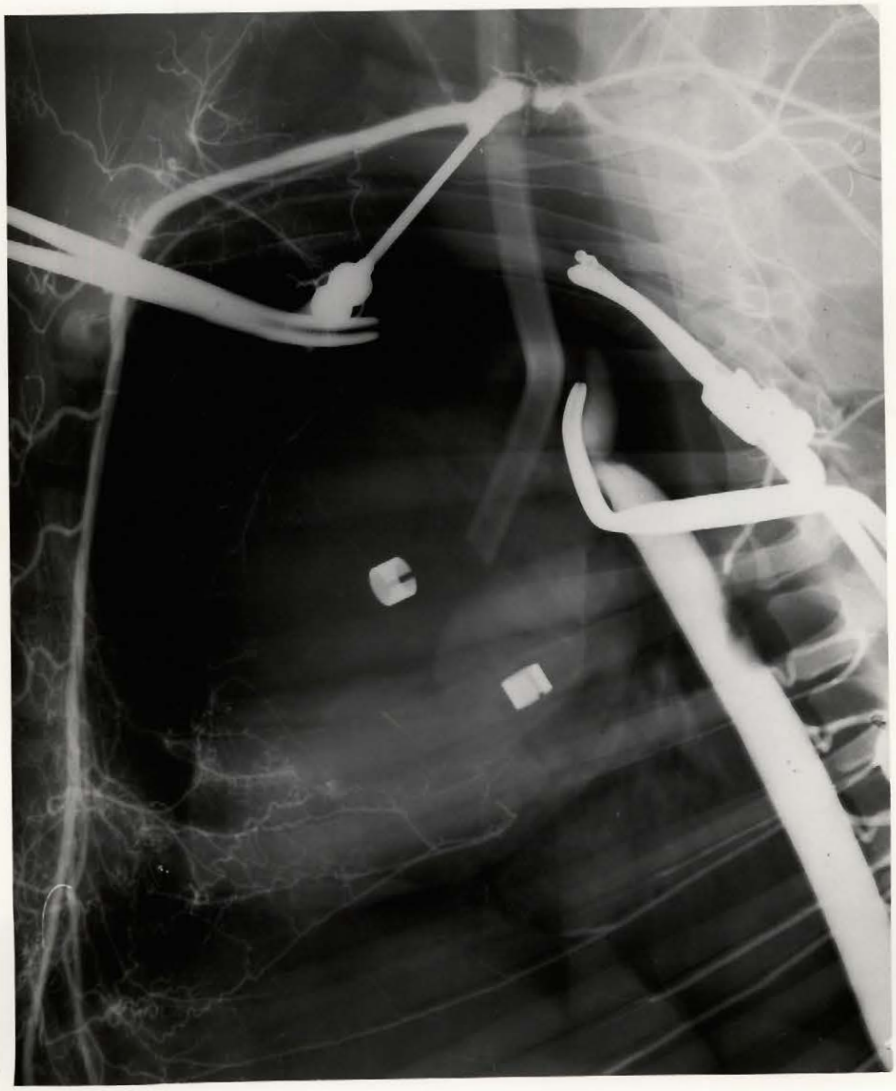


PLATE NO. 38.

X-ray photograph of injected intact heart with the new Schlesinger mass through left subclavian artery and aorta. The branches of the pericardio phrenic, IMA and intercostal arteries are filled with dye, but did not communicate with the coronary arteries. The ameroids and ventricular cannula are present. Picture taken from Beck I dog 8 454, which was sacrificed 62 days after operation.

sion-77.5%, which were due to intimal proliferation and thrombus formation.Microscopic studies revealed extensive fibrosis in inner 1/3 of the myocardium and dye in intramyocardial blood vessels. On the epicardial side of myocardium was hyalinized fibrous tissue, some blood vessels and foreign body giant cell reaction.

Dog 8-454: A 43 lb. male, mongrel dog, lived 62 days was operated on 4-17-59 and sacrificed on 6-18-59. Post mortem revealed absence of grss infarction and septal artery arose from the main left coronary artery. Injection of intact heart with dye through the left subclavian artery and aorta, without ventricular cannula, showed extracardiac arteries went to the pericardium. There was no coronary and ventricular filling with dye. Coronary arteries were injected distal to the ameroids showed *** homocoronary, * intercoronary anastomoses, 20 arteriolumi-nal vessels, 5 of which communicated with the heart's lumen. Coronary occlusions showed AD-100%, C-95% and combined occlusion-97.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced coronally. Microscopic sections revealed fibrosis on the endocardial side of myocardium and dye in intramyocardial blood vessels. The epicardial surface of myocardium contained hyalinized fibrous tissue, blood vessels and giant cells.

Dog 9-484: A 46 lb. female, mongrel dog, lived 55 days was operated on 4-22-59 and sacrificed on 6-16-59. Postmortem showed absence of gross infarction and septal

artery arose from the AD branch. Injection of intact heart with dye through the left subclavian artery and aorta showed extracardiac arteries went to the pericardium. It filled the coronary arteries and the dye entered the heart's lumen. Dye that was in the ventricle came out of the cannula inserted in the cavity of the heart. Coronary arteries showed *** homocoronary, * intercoronary anastomoses, 23 arterioluminal vessels, 4 of which communicated with the heart's lumen. Coronary artery occlusions showed AD-65%, C-60% and combined occlusion-62.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced coronally. Microscopic studies revealed normal myocardium and dye in intramyocardial vessels. The asbestos layer on the surface of myocardium was thin win hyalinized fibrous rim, contained occasional small capillaries and foreign body giant cell reaction.

Dog 10-400: A 45 lb. male, mongrel dog, lived 54 days was operated on 4-24-59 and sacrificed on 6-17-59. Postmortem showed absence of gross infarction and septal artery arose from the AD branch. Injection of intact heart with dye through left subclavian artery and aorta showed extracardiac arteries went to the pericardium. There was no filling of the coronary arteries and lumen of heart. Injection distal to the ameroids showed *** homocoronary, ** intercoronary anastomoses, 15 arterio-

luminal, 4 of which communicated with the lumen of the heart. Coronary artery occlusions showed AD-80%, C-90% and combined occlusion-85%, which were due to intimal proliferation and thrombus formation. Microscopic studies revealed normal myocardium and dye was present in intramyocardial blood vessels. The asbestos layer was thick and contained fobrous tissue, moderate number of capillaries and foreign giant cell reaction. There were womewhat larger blood vessels found in the granulation tissues.

SERIES V: THOMPSON-RAISBECK OPERATION: CARDIO-PERI-CARDIOPEXY BY THE USE OF TALCUM.

General Summary and Results:

1. Number of dogs: 10

2. Sex: males 6, females 4.

3. Weight: between 38-50 lbs.

4. Mortality: 8 dogs Percentage: 80%
   Average survival in days of mortality dogs: 12.4 days.

5. Survival: 2 dogs: Percentage: 20%
   Average survival in days of sacrificed dogs: 69.5 days.

6. Position of septal artery: Percentage:
   a) from anterior descending branch: 7 70%
   b) from circumflex branch: 1 10%
   c) from main left coronary artery: 2 20%

7. Injection of coronary arteries:
   a) proximal to ameroids: 2
   b) distal to ameroids: 8
   c) from extracardiac injections: 2
   d) cannula in ventricular cavity: 1 No cannula: 9

8. Extent of coronary occlusions:
   a) aver. percentage from the anterior descending branch: 80%
   b) aver. percentage from circumflex branch: 79%
   c) combined average percentage: 79.5%

9. Coronary anastomoses:
   a) Intracardiac anastomoses:
      1. Aver. for surviving dogs: homocoronary ***
         intercoronary **
      2. Aver. for mortality dogs: homocoronary 1.5 times *
         intercoronary 0.75 of *
      3. Overall average: homocoronary 1.8 times *
         intercoronary *
   b) Extracardiac anastomoses: 0

10. Arterioluminal vessels:
    a) Average number of vessels: 16.9
    b) Average number of vessels communicating with the lumen of the heart: 1.6

11. Presence of dye in intramyocardial vessels:
    a) number of hearts with dye: 6
    b) number of hearts without dye: 4
    c) all surviving dogs had dye
    d) the mortalitydogs had dye in only one half of the cases.

12. Sections or slicing of hearts:
    a) transverse or horizontal sections: 3
    b) sagital or vertical sections: 2
    c) coronal, right angle to lumen: 5
    d) no sections of the heart: 0

13. Location of infarction:
    a) anterior wall of LV: 4
    b) posterior wall of LV: 1
    c) postero lateral wall of LV: 1
    d) no gross infarction: 4

14. Microscopic findings: Presence and location of myocardial fibrosis:
    a) endocardial portion: 3
    b) middle portion: 0
    c) epicardial portion: 0
    d) scattered areas: 2
    e) no myocardial fibrosis: 5

Individual Summary:

This was a 50 lb. male mongrel dog operated on February 11, 1959 and died February 24, 1959. It lived 13 days. Postmortem showed left lung was ahderent to the surface of the heart, presence of anterior wall infarction and septal artery arose from the AD branch. The coronary arteries were injected proximal to the ameroids, and showed * homocoronary and * intercoronary

There were 11 arterioluminal vessels, 2 of which communicated with the heart's lumen. There was no cannula and dye in the ventricular lumen as shown by transverse sections of the heart. Coronary occlusions showed AD-85%, C-60% and combined occlusion-72.5%, which were due to intimal proliferation and thrombus formation. Microscopic studies revealed strips of fibrosis along endocardial portion of myocardium and no dye in the intramyocardial blood vessels. The epicardial layer contained hyalinized fibrosis with some blood vessels and foreign body giant cell reaction due to talcum.

Dog 2-119: A 48 lb. female, mongrel dog, lived 10 days was operated on 2-25-58 and died on 3-7-59. Postmortem showed postero-lateral infarction and septal artery arose from the circumflex branch. Injection proximal to the ameroids without ventricular cannula, showed ** homocoronary, * intercoronary anastomoses, 8 arterio luminal vessels, one of which communicated with the heart's lumen. Coronary occlusions showed AD-65%, C-75% and combined occlusion-70%, which were due to intimal proliferation and thrombus formation. The heart was sliced transversely. Microscopic studies revealed fibrosis in endocardial portion of myocardium and no dye in intramyocardial blood vessels. Epicardium had hyalinized fibrosis, little amount of capillaries and giant cells.

Dog 3-344: A 38 lb. male, mongrel dog, lived 12 days was operated on 3-2-59 and died on 3-14-59. Post mortem showed anterior wall infarction and septal art-

ery arose from the AD branch. Injection distal to the ameroids without ventricular cannula showed * homocoronary, 0 intercoronary, anastomoses, 15 arterioluminal vessels, none of which communicated with the heart's lumen. Coronary occlusions showed AD-55%, C-85% and combined occlusion-70%, which were due to intimal proliferation and thrombus formation. The heart was sliced transversely. Microscopic studies revealed tiny fibrosis in myocadium and some dye in intramyocadial vessels. In epicardium were foreign body giant cell reaction, few capillaries and hyalinized fibrous tissues.

Dog 4-474: A 46 lb. male, mongrel dog, lived 73 days was operated on 4-8-59 and sacrificed on 6-10-59. Postmortem showed absence of gross infarction and septal artery arose from the AD branch. Injection of intact heart with dye through left subclavian artery and aorta, without ventricular cannula, showed extracardiac arteries went to the pericardium. The coronary arteries and ventricular lumen did not fill with dye. Injection distal to the ameroids showed AD-95%, C-80% and combined occlusions-87.5%, which were due to intimal proliferation and thrombus formation. There were *** homocoronary, ** intercoronary anastomoses, and the heart was sliced transversely. Microscopic studies revealed normal myocardium and dye in intramyocardial vessels. Epicardial layer had giant cells, hyalinized fibrosis and capillary spaces.

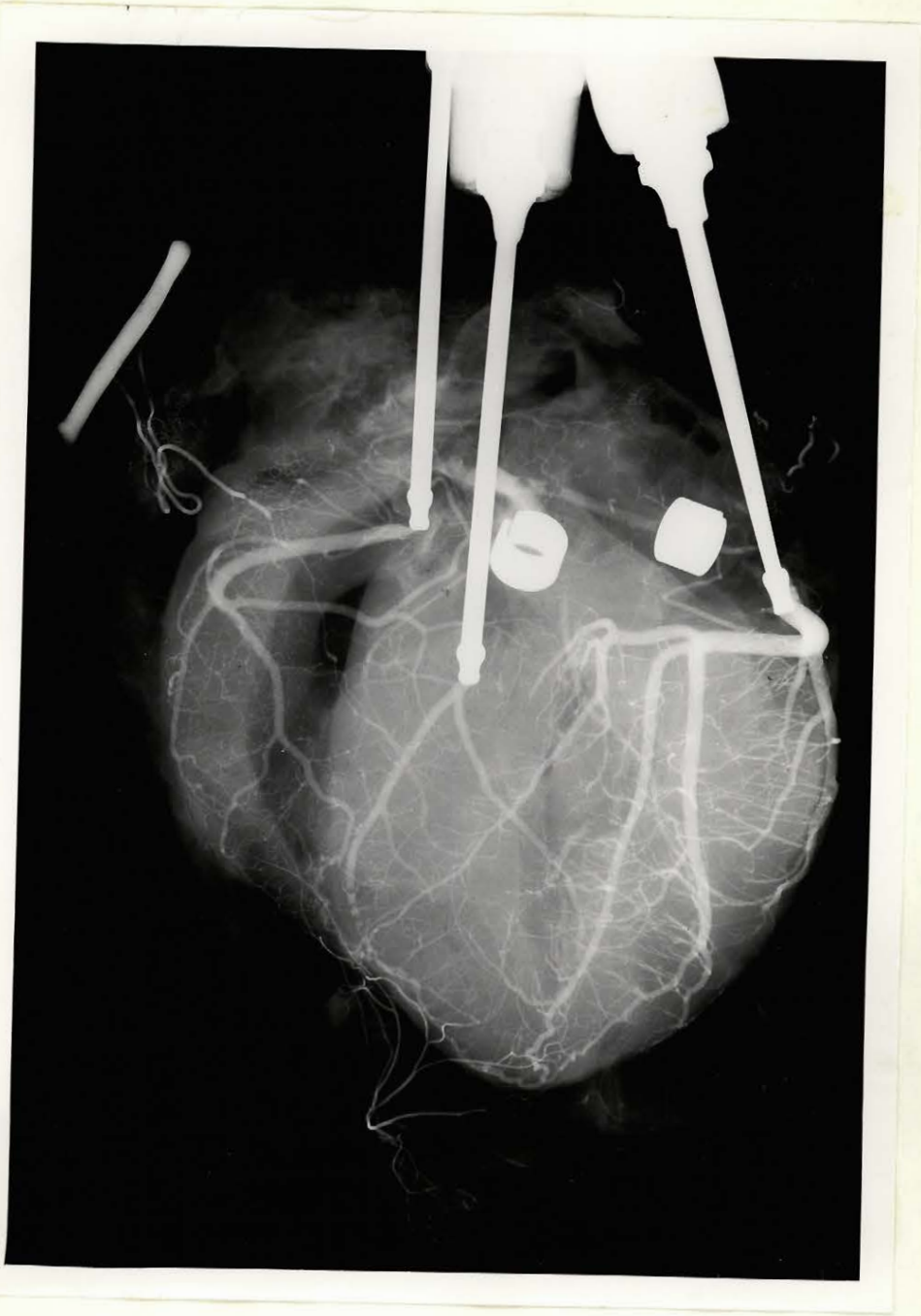


PLATE NO. 39.

X-ray photograph of heart injected distal to ameroids which shows *** homocoronary and ** intercoronary anastomoses. Picture taken from talcum dog 4-474, which was sacrificed 73 days after operation.

Dog 5-476: A 48 lb. male, mongrel dog, lived 18 days was operated on 4-10-59 and died on 4-28-59. Post mortem showed posterior wall infacrion and septal artery arose from the main left coronary artery. Injection distal to the ameroids without ventricular cannula showed ** homocoronary, ** intercoronary anastomoses, 16 arterioluminal vessels, 2 of which communicated with the heart's lumen. Coronary artery occlusions showed*AD-95%, C-85% and combined occlusion-87.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced sigitally. Microscopic studies revealed fibrosis in inner 1/3 of myocardium and no dye in intramyocardial blood vessels.

Dog 6-473: A 46 lb. female, mongrel dog was operated on 4-13-59 and sacrificed on 6-18-59 and lived 66 days. Postmortem showed septal artery arose from AD branch. Injection of intact heart with dye through left subclavian artery and aorta, with ventricular cannula, showed extracardiac arteries went to the pericardium. No filling of coronary arteries and heart's lumen. Injection distal to the ameroids showed *** homocoronary, ** intercoronary anastomoses, 21 arterioluminal vessels, 2 of which communicated with the heart's lumen. Coronary artery occlusions showed AD-100%, C-90% and combined occlusion-95%, which were due to intimal proliferation and thrombus formation. The heart was sliced coronally. Microscopic sections revealed normal myocardium and dye in

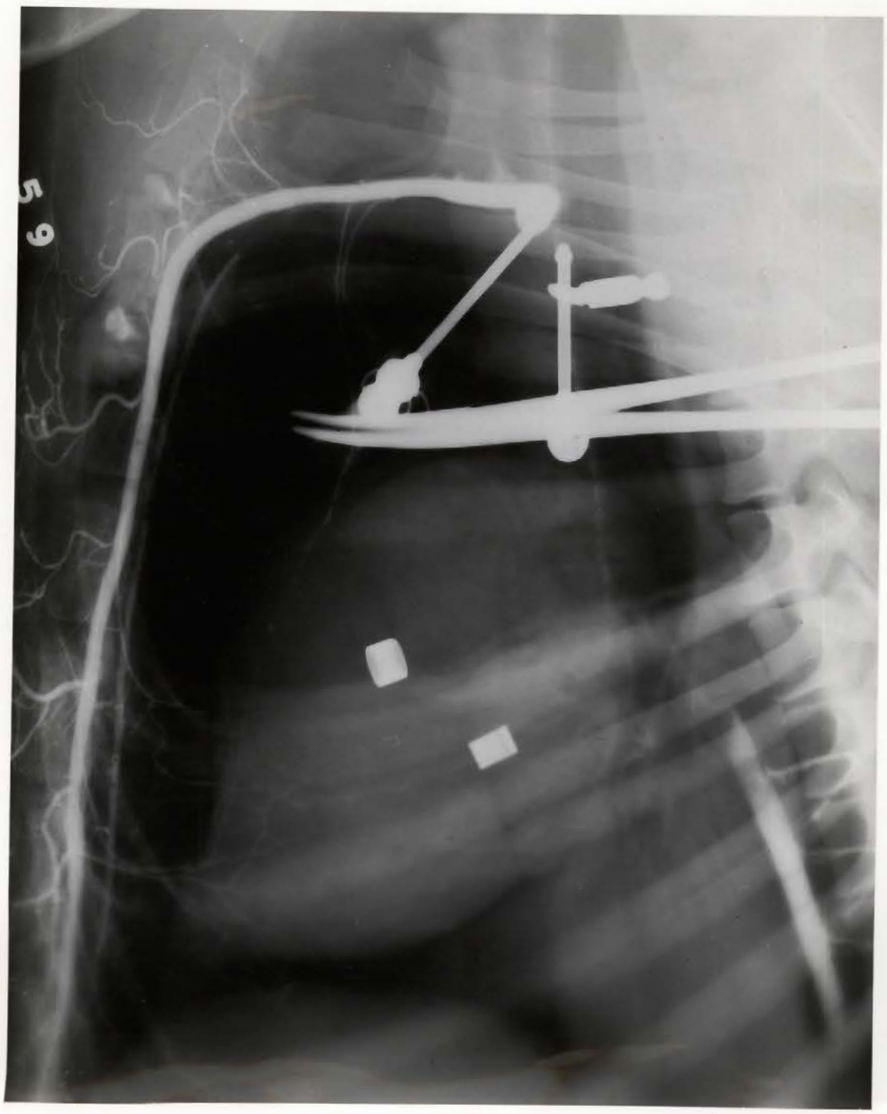


PLATE NO. 40

X-ray photograph of injected intact heart with new Schlesinger mass through left subclavian artery and aorta, which showed no extracardiac anastomoses. Picture taken from talcum dog 4-474 sacrificed 73 days after operation.

intramyocardial vessels. The Epicardium showed hyalinized fibrosis, foreign body giant cell reactions and few new capillaries.

Dog 7-481: A 40 lb. male, mongrel dog, lived 10 days was operated on 4-17-59 and died on 4-27-59. Post mortem showed anterior wall infarction and septal artery arose from AD branch. Injections distal to the ameroids without ventricular cannula, showed ** homocoronary, * intercoronary anastomoses, 22 arterioluminal vessels, 3 of which communicated with the heart's lumen. Coronary occlusions showed AD-100%, C-80% and combined occlusion-90%, which were due to intimal proliferation and thrombus formation. The heart was sliced cronally and no dye was found in heart's lumen. Microscopic studies revealed fibrosis in endocardial portion of myocardium and dye in intramyocardial vessels. Epicardial layer has extensive area of giant cell reaction, some capillaries and fibrosis.

Dog 9-464: A 40 lb. female, mongrel dog, lived 13 days was operated on 4-24-59 and died on 5-7-59. Postmortem showed absence of gross infarction and septal artery arose from the AD branch. Injection distal to the ameroids without ventricular cannula showed * homocoronary, * inter coronary anastomoses, 18 arterioluminal vessels, one of which communicated with heart's lumen. Coronary artery occlusions showed AD-75%, C-90% and combined occlusion-82.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced coronally and no dye

PLATE NO. 41.

Photomicrograph of heart which shows extensive foreign body giant cell reaction, some hyalinized fibrosis and some new capillaries in the epicardial layer. Picture taken from heart specimen of talcum dog 9-464. (x 200).

was found in the lumen of the heart. Microscopic studies showed normal myocardium and dye in intramyocardial vessels. Epicardial layer had foreign body giant cell and some hyalinized fibrosis and some new capillaries.

Dog 10-452: A 42 lb. female, mongrel dog, lived 26 days was operated on 4-25-59 and died on 5-20-59. Postmortem showed no gross infarction and septal artery arose from the AD branch. Injection distal to the ameroids without ventricular cannula, showed * homocoronary, 0 intercoronary anastomoses, 10 arterioluminal vessels, none of which communicated with the heart's lumen. Coronary occlusions showed AD-80%, C-75% and combined occlusion-77.5% which were due to intimal proliferation and thrombus formation. The heart was sliced coronally and no dye was seen in cavity of heart. Microscopic studies revealed normal myocardium and dye in intramyocardial vessels. The epicardium contained foreign body giant cell reaction, hyalinized fibrosis and some cappillaries.

SERIES VI: CARDIO-PERICARDIOPEXY WITH SODIUM SALICYLATE 5% SOLUTION.

General Summary and Results:

1. Number of dogs: 5

2. Sex: males 3, females 2

3. Weight: between 35-52 lb.s

4. Mortality: 4 dogs Percentage: 80%
   Average survival in days of mortality dogs: 13 days

5. Survival: 1 dog Percentage: 20%

6. Position of septal artery: Percentage:
   a) from anterior descending branch: 3 60%
   b) from circumflex branch: 1 20%
   c) from main left coronary artery: 1 20%

7. Injection of coronary arteries:
   a) proximal to ameroids: 3
   b) distal to ameroids: 2
   c) from extracardiac injections: 1
   d) cannula in ventricular cavity: 0 No cannula: 5

8. Extent of coronary artery occlusions:
   a) aver. percentage for anterior descending branch: 83%
   b) aver. percentage for circumflex branch: 75%
   c) combined average percentage: 78.8%

9. Coronary anastomoses:
   a) Intracardiac anastomoses:
      1. Average for surviving dogs: homocoronary ***
         intercoronary *
      2. Average for mortality dogs: homocoronary: *
         intercoronary 0
      3. Overall average: homocoronary: 1.4 times *
         intercoronary 0.8 times *
   b) Extracardiac anastomoses: 0

10. Arterioluminal vessels:
    a) average number: 17
    b) average number of vessels communicating with the lumen of the heart: 1.7

11. Presence of dye in intramyocardial vessels:
    a) number of hearts with dye: 2
    b) number of hearts without dye: 3
    c) the survival dogs had dye in the intramyocardial vessels.
    c) all mortality dogs had no dye in the intramyocardial vessels, except one.

12. Sections or slicing of hearts:
    a) transverse or horizontal sections: 3
    b) sagital or vertical sections: 0
    c) coronal, right angle to lumen: 1
    d) no sectioning of heart: 1

13. Location of infarction:
    a) anterior wall: 2
    b) posterior wall: 2
    c) no gross infarction: 1

14. Microscopic findings: Presence and location of myocardial fibrosis.
    a) endocardial portion: 2
    b) middle portion: 1
    c) epicardial portion: 1
    d) no fibrosis: 1

Individual Summary:

Dog 1-433:

This was a 46 lb. male, mongrel dog operated on January 29, 1959 and sacrificed June 9, 1959. It lived 132 days. Postmortem showed left lung adherent to surface of heart, absence of gross infarction and the septal artery arose from AD branch. Injection of intact heart, with new Schlesinger

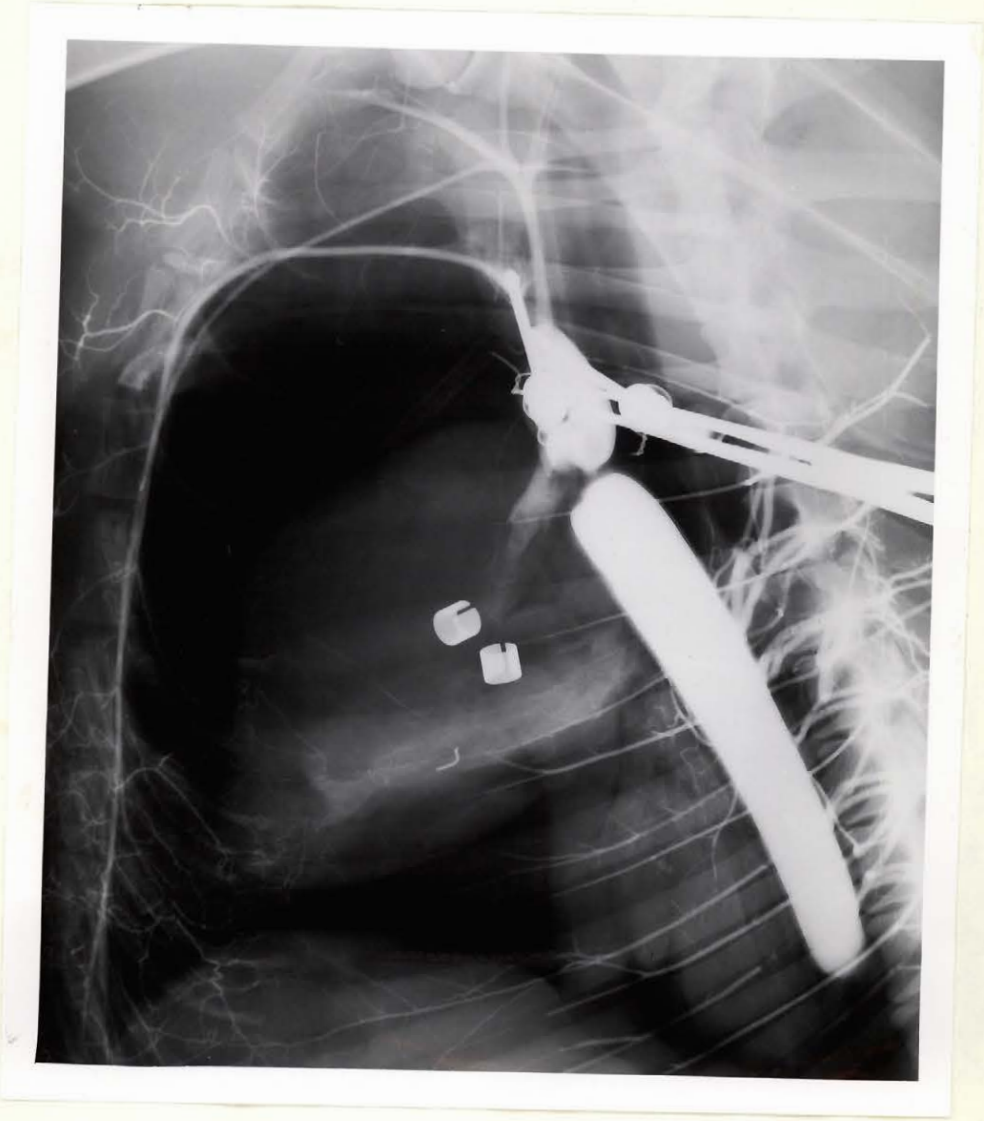


PLATE NO. 42

X-ray photograph of injected intact heart through left subclavian artery and aorta, showing branches from pericardio phrenic, IMA, intercostals going to pericardium. There is no filling of coronary arteries, indicating no extracardiac anastomoses. Picture taken from salicylate dog 1-433, which was sacrificed 132 days after operation.

mass through left subclavian artery and aorta, without ventricular cannula, showed extracardiac arteries went to the pericardium. Injection distal to the ameroids showed *** homocronary, * intercoronary anastomoses 28 arterioluminal vessels, 4 of which communicated with heart's lumen. Coronary artery occlusions showed AD-80%, C-98% and combined occlusion-89%, which were due to intimal proliferation and thrombus formation. The heart was sliced coronally and nodye found in lumen of heart. Microscopic sections revealed patches of fibrosis in the epicardial side of myocardium and dye in intramyocardial vessels. Epicardium contained inflammatory cells interposing some fibrous tissue and scanty capillaries.

Dog 2-412: A 35 lb. dog, lived 17 days was operated on 1-28-59 and died on 2-14-59. Postmortem showed infarction in posterior wall of L.V., and septal artery arose from the circumflex branch. Injection proximal to the ameroids without ventricular cannula, showed * homocoronary,0 intercoronary anastomoses, 8 arterioluminal vessels, none of which communicated with the heart's lumen. Coronary occlusions showed Ad-70%, C-95% and combined occlusion-82.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced transversely. Microscopic sections revealed fibrosis in inner 1/3 of myocardium and no dye in intramyocardial vessels. Epicardium contained hyalinized fibros is and some capillaries.

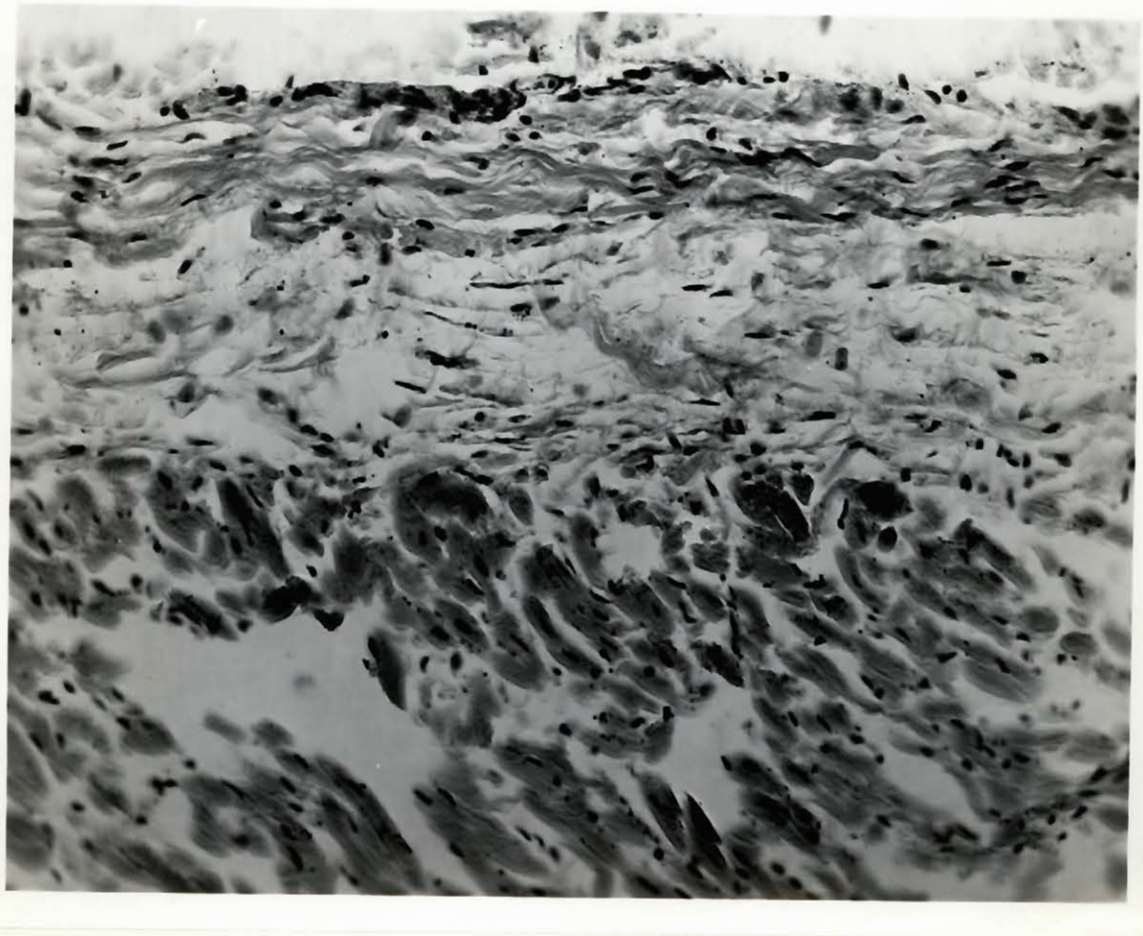


PLATE NO. 43.

Photomicrograph of section of heart showing hyalinized fibrosis with some capillaries in the epicardial layer of the myocardium. Picture taken from heart of salicylate dog 2-412, which died 17 days after operation. (x 200).

Dog 3-428: A 52 lb. female, mongrel dog, lived 12 days was operated on 2-2-59 and died on 2-14-59. Post-mortem showed anterior wall infarction and septal artery arose from the AD branch. Injection proximal to the ameroids without ventricular cannula showed * homocoronary, 0 intercoronary anastomoses, 7 arterioluminal vessels, none of which communicated with the heart's lumen. Coronary artery occlusions showed AD-95%, C-65% and combined occlusion-75%, which were due to intimal proliferation and thrombus formation. The heart was sliced transversely and nodye was found in ventricular cavity. Microscopic sections revealed fibrosis in endocardial portion of myocardium and no dye in intramyocardial vessels. Epicardium contained granulomatous reaction, fibrosis and some capillaries.

Dog 4-414: A 46 lb. male, mongrel dog, lived 20 days was operated on2-4-59 and died on 2-24-59. Post-mortem showed anterior wall infarction and septal artarose from the AD branch. Injection proximal to the ameroids, without ventricular cannula, showed * homocoronary, 0 int ercoronary anastomoses, 19 arterioluminal vessels, 3 of which communicated with the heartIs lumen. The heart was sliced transversely and dye was found in ventricular cavity. Microscopic sections refibrosis in the middle third of the myocardium and dye in the intramyocardial vessels. Epicardium contaied

granulomatous reaction, fibrosis and some small blood vessels. Coronary occlusions showed AD-90%, C-60% and combined occlusion-75%, which were due to intimal proliferation and thrombus formation.

Dog 5-336: A 52 lb. female, mongrel dog, lived 3 days was operated on 2-9-59 and died on 2-12-59. Post mortem showed posterior wall infarction and septal artery arose from the AD branch. Injection of the coronary arteries distal to the ameroids, without ventricular cannula, showed * homocoronary and 0 intercoronary anastomoses. Coronary artery occlusions showed AD-80%, C-65% and combined occlusion-72.5%, which were due to intimal proliferation and thrombus formation. Microscopic sections revealed normal myocardium and no dye in the intramyocadial blood vessels. The epicardium showed granulomatous reaction, fibrosis and no new capillaires.

SERIES VII: ARTERIALIZATION OF CORONARY SINUS WITH LEFT INFERIOR PULMONARY VEIN ANASTOMOSES.

General Summary and Results:

1. Number of dogs: 5

2. Sex: males, 4 and females 1

3. Weight: between 40-50 lbs.

4. Mortality: 3 dogs Percentage: 60%
   Average survival in days of mortality dogs: 23 days.

5. Survival: 2 dogs Percentage: 40%
   Average survival in days of sacrificed dogs: 188 days.

6. Position of septal artery: Percentage:
   a) from anterior descending branch: 4 80%
   b) from circumflex branch: 0 -
   c) from main left coronary artery: 1 20%

7. Injection of the coronary arteries:
   a) proximal to ameroids: 1
   b) distal to ameroids: 4
   c) from extracardiac injections: 1
   d) cannula in ventricular cavity: 0 No cannula: 5

8. Extent of coronary artery occlusions:
   a) aver. percentage for anterior descending branch: 90%
   b) aver. percentage for circumflex branch: 86%
   c) combined average percentage: 88%

9. Coronary anastomoses:
   a) Intracardiac anastomoses:
      1. Aver. for surviving dogs: homocoronary 2.5 times * intercoronary **
      2. Aver. for mortality dogs: homocoronary 2.6 times * intercoronary *
      3. Overall average: homocoronary 2.6 times * intercoronary *
   b) Extracardiac anastomoses: 0

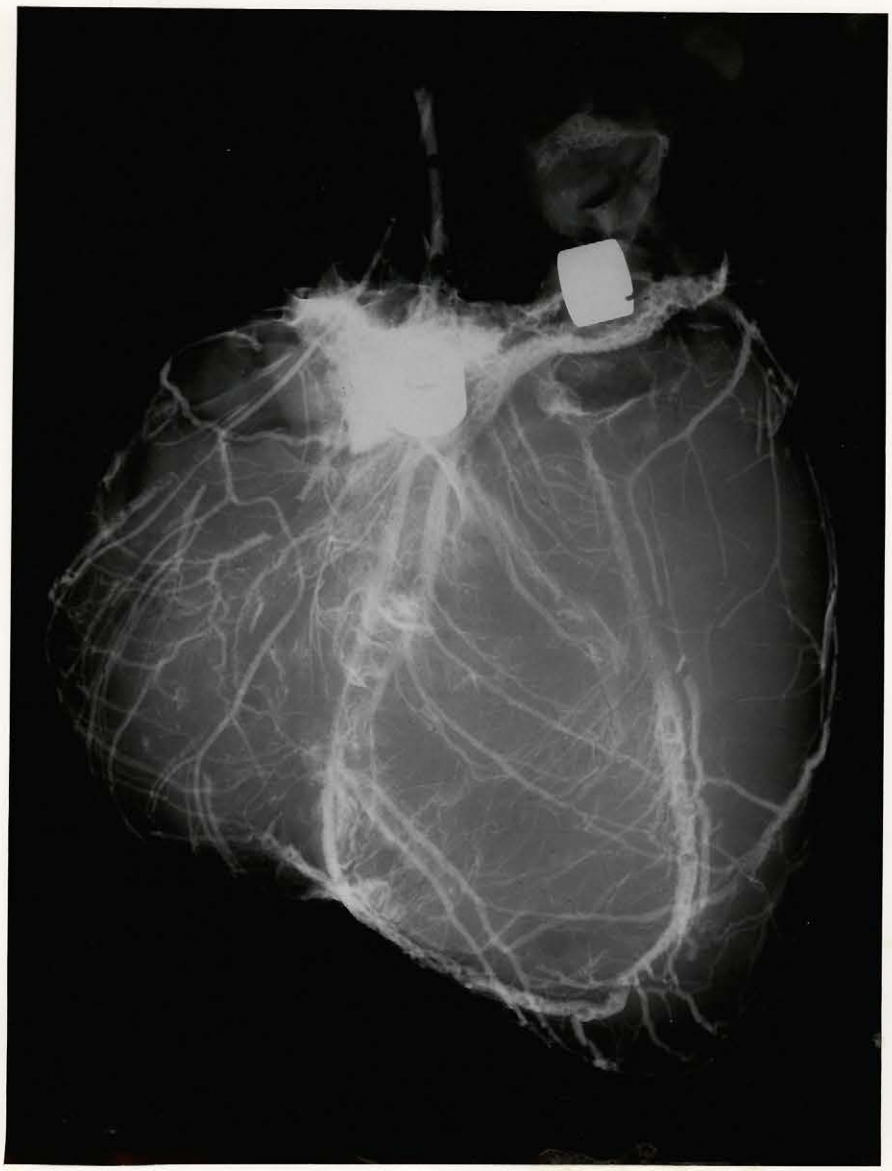


PLATE NO. 54.

X-ray photograph of heatt whose coronary sinus and inferior pulmonary vein anastomoses was injected with dye. The anastomoses is patent and coronary arteries showed good anastomoses. Picture taken of heart of PV dog 1-390, which was sacrificed 90 days after operation.

10. Arterioluminal vessels:
    a) average number of vessels: 15.5
    b) average number of vessels communicating with lumen of heart: 4

11. Presence of dye in intramyocardial vessels:
    a) number of hearts with dye: 5
    b) number of hearts without dye: 0
    c) all surviving dogs had dye
    d) all mortality dogs had dye

12. Sections or slicing of hearts:
    a) transverse or horizontal sections: 3
    b) sagital or vertical sections: 0
    c) coronal, right angle to lumen: 1
    d) no sections of heart: 1

13. Location of infarction:
    a) anterior wall: 0
    b) posterior wall: 2
    c) anterior and posterior walls: 1
    d) no infarction: 1

14. Microscopic findings: Presence and location of myocardial fibrosis:
    a) endocardial portion: 2
    b) middle portion: 1
    c) epicardial portion: 0
    d) no myocardial fibrosis: 1

Individual Summary:

Dog 1-390:

This was a 41 lb. male mongrel dog operated on August 18, 1958 and sacrificed on November 7, 1958. It lived 90 days. Postmortem showed left lung was adherent to chest wall and surface of the heart, absence of infarction and septal artery

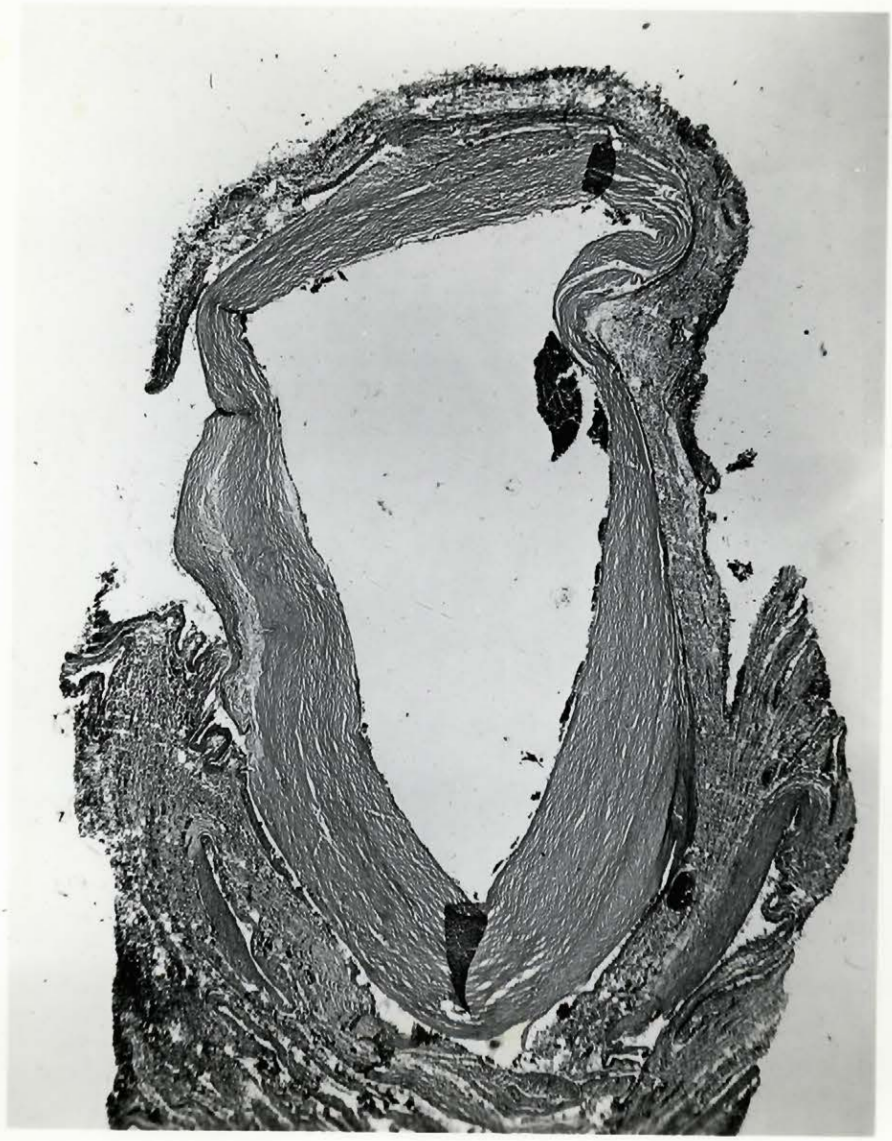


PLATE NO. 45

Microphotograph of a section of coronary sinus anastomoses with left inferior pulmonary vein. The sinus is patent with slight intimal proliferation. Picture taken from PV dog 2-364, sacrificed 287 days after operation.

arose from the AD branch. Injections proximal to the ameroids without v entricular cannula showed ** homocoronary, and ** intercoronary anastomoses. Coronary occlusions could not be determined for the spicemen was lost, and therefore no sections could be obtained.

Dog 2-363: A 50 lb. male, mongrel dog, lived 287 days was operated on 8-21-58 and sacrificed on 6-4-59. Postmortem showed septal artery arose from the AD branch. Injection of the intact heart through the left subclavian artery and aorta without ventricular cannula showed extracardiac arteries went to the pericardium. There was no filling of the coronary arteries. Injections distal to the ameroids showed *** homocoronary, ** intercoronary anastomoses, 15 arterioluminal vessels, 6 of which communicated with the heart's lumen. Coronary occlusions showed AD-85%, C-95% and combined occlusion-90%, which were due to intimal proliferation and thrombus formation. The heart was sliced coronally. Inferior pulmonary vein and coronary sinus anastomos is was patent with some intimal thickening, so much so that the sinus appeared like an artery. Microscopic sections revealed normal myocardium and dye in the intramyocardial vessels and sinusoids. Epicardial layer showed plenty of new blood vessels filled with blood. There was very little fibrous tissue reactions.

Dog 4-177: A 44 lb. male, mongrel dog, lived 24 days was operated on 10-15-58 and died on 10-13-58. Post

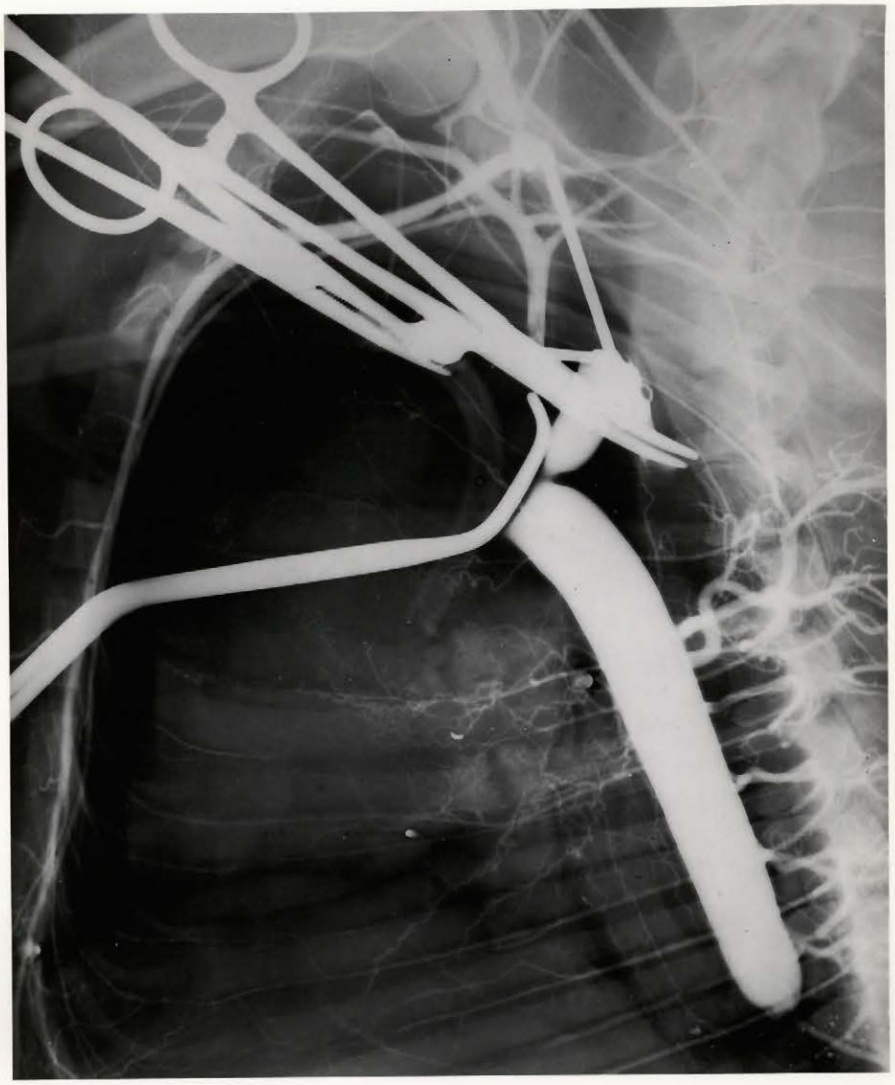


PLATE NO. 46-A

X-ray photograph of normal dog 3-400 injected with the new Schlesinger mass in an intact heart, through left subclavian artery and aorta. There is a ventricular cannula. There is no extracoronary anastomoses seen in spite of the fact that the aorta and its branches are filled with dye.

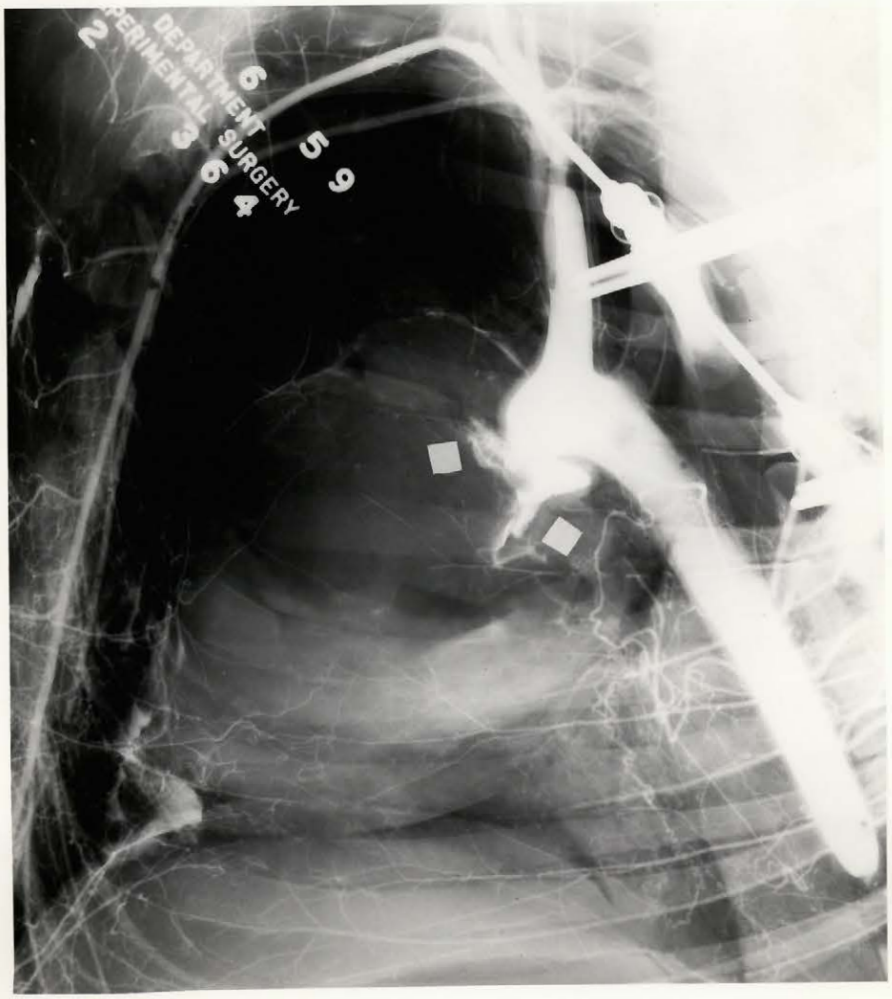


PLATE NO. 46

X-ray photograph of injected intact heart with the new Schlesinger mass through the left subclavian artery and aorta, shows branches from pericardio phrenic, IMA, intercostals, esophageal and bronchial arteries which go to the pericardium, but no filling of coronary arteries, indicating absence of extracardiac anastomoses. Picture taken from PV dog 2-364, sacrificed 287 days after operation.

mortem showed posterior wall infarction and the septal artery arose from the main left coronary artery. Injectdistal to the amerois without ventricular cannula showed *** homocoronary, * intercoronary anastomoses, 17 arterioluminal vessels, 3 of which communicated with the heart's lumen. Coronary artery occlusions showed AD-95%, C-80% and combined occlusion-87.5%, which were due to intimal proliferation and thrombus formation. The heart was sliced transversely and no dye was found in the lumen of the heart. Microscopic sections revealed fibrosis in middle third of myocardium and dye in intramyocardial vessels. Between epicardium and myocardium were capillaries.

Dog 5-312: A 40 lb. female, mongrel dog, lived 12 days; was operated on 10-29-58 and died on 11-10-58. Postmortem showed anterior and posterior wall infarctions and septal artery arose from the AD branch. Injection distal to the ameroids without ventricular cannula, showed ** hocoronary, * intercoronary anastomoses, 17 arterioluminal vessels, 4 of which communicated with the heart's lumen. Coronary occlusions showed AD-90%, C-90% and combined occlusion-90%, which were due to intimal proliferation and thrombus formation. The heart was sliced transversely. Microscopic sections revealed fibrosis in epicardial portion of myocardium and dye in intramyocardial vessels. Between pericardium and epicardium there was plenty of

blood filled capillaries.

Dog 6-399: A 50 lb. male, mongrel dog, lived 28 days was operated on 11-5-58 and died on 12-3-58. Postmortem showed posterior wall infarction and septal artery arose from the AD branch. Injections distal to the ameroids, without ventricular cannula showed *** homocronary, * intercoronary anastomoses, 13 arterioluminal vessels, 3 of which communicated with the lumen of the heart. Coronary artery occlusions showed AD-90%, C-80% and combined occlusion-85%, which were due to intimal proliferation and thrombus formation. The heart was sliced transversely and no dye was found in the cavity of the heart. Microscopic sections revealed fibrosis in the endocardial portion of the myocardium and dye in the intramyocardial blood vessels. There were blood filled capillaries between pericardium and epicardium.

TABLE 11 SERIES 1 CONTROL WITH AMEROIDS

Dog Number	Date of Operation	Date of Death or Sacrifice	Time Lived in days	Position of Septal Artery	Location of Infarction	Homocoronary Anastomoses	Inter Coronary Anastomoses	Extra Cardial Coronary Anastomoses	No. of Arterio-luminal vessels & those communicating with lumen of heart	Dye in intramyocardial Vessels	Sectioning of heart	Extent of Coronary Occlusion	Location of Myocardial Fibrosis
L-378	7-28-58	9-1-58	34	AD	Anterior wall	No X Ray For		Specimen	was lost.			87.5%	
3-408	8-4-58	8-17-58	13	AD	Anterior wall	± ±	±	0	10' (1)	0	transverse	86.5%	Fibrosis-inner 1/3 a/ Myocardium
4-380	8-6-58	8-16-58	10	C	Anterior wall	± ±	±	0	12 (2)	±	transverse	82.5%	Middle and inner 1/3
5-344	8-6-58	9-9-58	33	AD	Posterior wall	± ±	0	0	Not done	±		90.%	Inner ½ of Myo - cardium
6-405	8-7-58	8-13-58	6	C	Postero-Lateral wall	0	0	0	Not done	0		77.5%	Inner ½F Myocardium
14-308	8-21-58	3-4-59	195 *	AD	None	± ± ±	± ±	0	5 (0)	±	Transverse	87.5%	None
28-413	9-18-58	3-4-59	167 *	AD	None	± ±	± ±	0	10 (0)	±	Transverse	75%	None
30-381	9-22-58	10-6-58	16	LC	Anterior wall	±	0	0	9 (1)	±	Transverse	97.5%	Endocardial Portion
32-313	9-24-58	3-4-59	161 *	AD	None	±-± ±	± ±	0	8 (1)	±	Transverse	77.5%	None
6-303	10-20-58	11-18-58	28	AD	Posterior wall	0	0	0	Not done	0	None	92.5%	Middle & inner portion of Myocardium
2-387	10-30-58	11-20-58	30	AD	Anterior wall	± ±	±	0	Not done	0	None	90%	Epicardial and Endocardial Portion
3-430	11-26-58	12-21-58	25	AD	Postero-lateral wall	±	0	0	Not done	0	None	90%	Endocardial Portion
4-418	12-4- 58	5-15-59	162 *	LC	None	± ± ±	± ±	0	17 (1)	±	Coronal	96.5%	Tiny fibrosis in Endocardium
5-405	12-11-58	1- 2-59	12	AD	Anterior Posterior walls	±	0	0	9 (1)	0	Transverse	92.5%	Middle and inner 1/3
6-390	2- 2-59	2-19-59	17	AD	Postero-Lateral wall	±	±	0	Not done	±	Sagital	84%	None
7-422	4-15-59	4-24-59	9	AD	Posterior wall	± ±	±	0	20 (2)	±	Coronal	71.5%	Inner 1/3 of Myocardium

AD- Anterior descending branch
C- Circumflex Branch
LC- Lef Coronary Artery
O- None
*- Surviving Dogs

TABLE III Series II A IVALON SPONGE OPERATION

Dog Number	Date of Operation	Date of Death or Sacrifice	Time Lived in Days	Position of Septal Artery	Location of Infarction	Homocoronary Anastomoses	Inter Coronary Anastomoses	Extra Cardial Coronary Anastomoses	No. of Arterio-luminal vessels & those communicating with lumen of heart	Dye in intramyocardial Vessels	Sectioning of heart	Extent of Coronary Occlusion	Location of Myocardial Fibrosis
4-414	10-27-58	5-13-59	199 *	AD	None	x x	x x	0	19 (5)	x	Coronal	97.5%	Inner 1/3
6-403	11-6-58	11-15-58	9	AD	Posterior wall	x x	0	0	0 (0)	x	None	85%	Along Endocardium
8-153	11-13-58	11-23-58	15	AD	Posterior wall	0	0	0	14 (0)	x	Sagital	35%	Inner 1/3
9-369	11-17-58	12- 5-58	18	AD	Posterior wall	x	0	0	9 (2)	0	Sagital	85%	Inner 1/3
11-371	11-24-58	11-27-59	3	C	Anterior & Posterior walls	x	0	0	0 (0)	x	None	90%	Along Endocardium
12-443	11-27-58	5-20-59	174 *	LC	None	x x x	x x	x	21 (4)	x	Coronal	85%	None
13-429	12- 3-58	5-29-59	177 *	AD	None	x x x	x	0	25 (4)	x	Coronal	34.5%	None
14-444	1-16-59	2- 6-59	21	AD	Posterior wall	x x x	x	0	33 (10)	x	Transverse	96.5%	Middle 1/3
15-435	2- 2-59	2-22-59	20	AD	Posterior wall	x x x	x	0	28 (12)	x	Transverse	77.5%	None
16-425	12-17-58	4-26-59	130 *	C	None	x x x	x x	0	24 (10)	x	Transverse	100%	None

TABLE IV SERIES 1 1-B IVALON SPONGE OPERATION

Dog Number	Date of Operation	Date of Death or Sacrifice	Time lived in days	Position of Septal-Artery	Location of Infraction	Homocoronary Anastomoses	Inter Coronary Anastomoses	Extra Cardial Coronary Anastomoses	No. of Arterio-luminal vessels & those communicating with lumen of heart	Dye in intramyocardial Vessels	Sectioning of heart	Extent of Coronary Occlusion	Location of Myocardial Fibrosis
19-395	2-13-59	4-16-59	62	LD	Posterior Wall	x x	x	0	13 (3)	x	Transverse	37%	Inner ½
20-303	2-16-59	3-23-59	40	AL	Posterior Lateral wall	x x x	x	0	12 (3)	x	Transver-	85%	Along Endocardium
24-441	2-23-59	6- 1-59	93 *	AD	None	x x x	x x	0	21 (7)	x	Coronal	92.5%	None
25-325	3- 4-59	6- 2-59	90 *	LC	None	x x x x	x x x	0	34 (11)	x	Coronal	95%	None
26-353	3- 4-59	4-23-59	55	AL	Anterior Wall	x x x x	x x	0	32 (9)	x	Coronal	82.5%	Inner ¼
29-450	3- 6-59	6- 3-59	89 *	LC	None	x x x	x x	0	20 (3)	x	Coronal	97.5%	None
30-159	3-11-59	6-15-59	106 *	AD	None	x x x	x x	0	27 (7)	x	Coronal	90%	None
31-383	3-11-59	5-12-59	62	C	Posterior Wall	x x x	x	0	27 (7)	x	Coronal	95%	Along Endocardium
35-470	5- 1-59	6-22-59	53 *	AL	None	x x x x	x x x	x	27 (10)	x	Coronal	90%	None
37-478	5- 6-59	6-15-59	40	C	None	x x x	x	0	13 (5)	x	Coronal	36.5%	None

Table V Series III Implantation of the Internal Mammary Artery into left Ventricular Wall

Dog Number	Date of Operation	Date of Death or Sacrifice	Partial Ligation of Time Lived in Days	Position of Septal Artery	Location of Coronary Infarction	Sinus Homocoronary Anastomoses	Inter Coronary Anastomoses	No. of Arteriolominal Vessels & those communicating with lumen of heart	Dye in intramyocardial Vessels	Sectioning of heart	Extent of Coronary Occlusion	Extent of Ima Implant Occlusion	Extra Cardial Coronary Anastomoses	Location of Myocardial Fibrosis
17-408	8-27-58	5-20-59	267 *	AD	None	x x x	x x	29 (9)	x	Coronal	85%	Prox.10% Mid. 20% Distal30%	x	None
22-161	9- 8-58	5-11-59	245 *	C	None	x x	x x	20 (5)	0	Coronal	87.5%	Prox.40% Mid 65% Distal80%	0	Middle 1/3
23-397	9- 9-58	5-25-59	258 *	AD	None	x x	x	16 (3)	x	Coronal	87.5%	Prox.10% Mid 15% Distal30%	0	None
25-404	9-11-58	5-21-59	252 *	AD	None	x x x	0	17 (4)	x	Coronal	95%	Prox.20% Mid 40% Distal60%	0	None
26-374	9-15-58	5-29-59	255 *	LC	None	x x	x	15 (2)	x	Coronal	70%	Prox.10% Mid 30% Distal45%	x	None
31-405	9-24-58	10-19-58	25	AD	Posterior Wall	x *	0	None	x	None	70%	Prox.30% Mid 50% Distal80%	0	Outer 1/3
35-321	10-22-58	11-13-58	23	AD	Posterior Wall	x x	x	None	x	None	80%	Prox.20% Mid 40% Distal60%	0	Middle 1/3
37-332	10-24-58	11-23-58	31	C	Posterior Wall	x x	x	None	0	None	80%	Prox.10% Mid 30% Distal40%	0	Inner 1/3
38-382	11-21-58	6- 5-59	196 *	AD	None	x x x	x x	26 (4)	x	Coronal	97.5%	Prox.10% Mid 30% Distal50%	x	Inner 1/3
40-432	12- 8-58	6-11-59	185 *	AD	None	x x x x	x x	30 (6)	x	Coronal	78.5%	Prox.10% Mid 20% Distal40%	x	None

TABLE VI Dog Number	SERIES IV Date of Operation	Beck 1 Date of Death or Sacrifice	Operation Time Lived in Days	Position of Septal Artery	Location of Infarction	Homocoronary Anastomoses	Inter Coronary Anastomoses	Extra Cardial Coronary Anastomoses	No. of Arterio luminal Vessels & those communicating with lumen of heart	Dye in intramyo Cardial Vessels	Sectioning of heart	Extent of Coronary Occlusion	Location of Myocardial Fibrosis
1-332	3- 2-59	3-20-59	18	C	Postero-Lateral wall	x x	x	0	13 (3)	0	Transverse	37.5%	Middle ½
2-454	3-16-59	4- 3-59	13	AD	Postero-lateral wall	x	x	0	19 (7)	x	Transverse	37.5%	Inner ½
3-435	4- 1-59	5- 3-59	32	AD	Anterior wall	x x	x	0	17 (5)	0	Sagital	96.5%	Inner 1/3
4-413	4- 3-59	4-29-59	26	LC	Posterior wall	x x x	x	0	20 (5)	x	Sagital	87.5%	Close to Endo-Cardium
5-447	4- 8-59	6-17-59	70 *	AD	None	x x x	x x	0	20 (5)	0	Coronal	87.5%	None
6-462	4-13-59	5-28-59	45	AD	Posterior wall	x x x	x	0	31 (5)	x	Coronal	75%	Middle ½
7-468	4-15-59	4-24-59	9	AD	Posterior wall	x x	x	0	10 (0)	x	Sagital	77.5%	Inner 1/3
8-454	4-17-59	6-18-59	62 *	LC	None	x x x	x	0	20 (5)	x	Coronal	97.5%	Endo-Cardial Portion
9-434	4-22-59	6-16-59	55 *	AD	None	x x x	x	x	23 (4)	x	Coronal	62.5%	None
10-430	4-24-59	6-17-59	54 *	AD	None	x x x	x x	0	15 (4)	x	Coronal	85%	None

TABLE VII SERIES V Thompson-Raisbeck Operation

Dog Number	Date of Operation	Date of Death or Sacrifice	Time Lived in Days	Position of Septal Artery	Location of Infarction	Homocoronary Anastomoses	Inter Coronary Anastomoses	Extra Cardial Coronary Anastomoses	No. of Arterio Luminal Vessels & those communicating with lumen of heart	Dye in Intra Myocardial Vessels	SEction-ing of heart	Extent of Coronary Occlusion	Location of Myocardial Infarction
L-419	2-11-59	2-24-59	13	AD	Anterior Wall	x	x	0	11 (2)	0	Transver-se	72.5%	Along Endo-Cardium
2-119	2-25-59	3- 7-59	10	C	Postero-Lateral wall	x x	x	0	8 (1)	x	Transver-se	70%	Along Endo-Cardium
3-344	3- 2-59	4-14-59	12	AD	Anterior wall	x	0	0	15 (0)	x	Transver-se	70%	Scattered Fibrosis
4-474	4- 8-59	6-10-59	73 *	AD	None	x x x	x x	0	25 (3)	x	Coronal	87.5%	None
5-476	4-10-59	4-28-59	18	LC	Posterior wall	x x	x x	0	16 (2)	0	Sagital	87.5%	Inner 1/3
6-473	4-13-59	6-18-59	66 *	AD	None	x x x	x x	0	21 (2)	x	Coronal	95%	None
7-481	4-17-59	4-27-59	10	AD	Anterior wall	x x	x	0	21 (2)	0	Sagital	62.5%	Scattered Fibrosis
8-483	4-22-59	5-14-59	22	LC	Anterior wall	x x	x	0	22 (3)	x	Coronal	90%	Close to Endocardium
9-464	4-24-59	5- 7-59	13	AD	None	x	0	0	18 (1)	x	Coronal	82.5%	None
10-452	4-24-59	5-20-59	26	AD	None	x	0	0	12 (0)	x	Coronal	77.5%	None

TABLE V 111 SERIES V1 Cardio- PERICARDIO PEXY WITH 5% SODIUM SALICYLATE

Dog Number	Date or Operation	Date or Death or Sacrifice	Time Lived in Days	Position or Septal Artery	Location or Infarction	Homo-Coronary Anastomoses	Inter-Coronary Anastomoses	Extra Cardial Anastomoses	No. or Arterio-Luminal Vessels and those communicating with Lumen or heart	Dye in Intra-Myocardial Vessels	Sectioning or heart	Extent or Coronary Occlusion	Location or Myocardial Infarction
1-433	1-28-59	6-9-59	132 *	AD	None	x x x	x	0	28 (4)	x	Coronal	89%	Tiny patches in Epi-Cardial Layer
2-412	1-28-59	2-14-59	17	C	Posterior Wall	x	0	0	8 (0)	0	Transverse	82.5%	Inner 1/3
3-423	2- 2-59	2-14-59	12	AD	Anterior Wall	x	0	0	7 (0)	0	Transverse		Close to Endo-Cardium
4-416	2- 4-59	2-24-59	20	AD	Anterior Wall	x	0	0	19 (3)	x	Transverse	75%	Middle 1/3
5-336	2- 9-59	2-12-59	3	LC	Posterior Wall	x	0	0	None	0	None	72.5%	None

SERIES V111 ARTERIALIZATION OF CORONARY SINUS WITH LEFT INFERIOR VEIN ANASTOMOSES

Dog Number	Date of Operation	Date of Death or Sacrifice	Time Lived in Days	Position of Septal-Artery	Location of Infarction	Homo-Coronary Anastomoses	Inter Coronary Anastomoses	Extra-Cardial Anastomoses	No. of Arterio-Luminal Vessels and those Communicating with Lumen of Heart	Dye in Intra Myocardial Vessels	Sectioning of Heart	Extent of Coronary Occlusion	Location of Myocardial Infarction
L-390	8-18-58	11- 7-59	90*	AD	None	x x	x x	0	SPECIMEN WAS LOST.				
2-364	8-21-58	6- 4-59	287 *	AD	None	x x x	x x	0	15 (6)	x	Coronal	90%	None
4-177	10-15-58	11-13-58	29	LC	Posterior Wall	x x x	x	0	17 (3)	x	Transverse	87.5%	Middle 1/3
5-312	10-29-58	11-10-58	12	AD	Anterior and Posterior Walls	x x	x	0	17 (4)	x	Transverse	90%	Epi - Cardial Side
6-399	11- 5-58	12- 3-58	28	AD	Posterior Wall	x x x	x	0	13 (3)	x	Transverse	85%	Endo-Cardial Layer

TABLE IX TABLE OF GENERAL SUMMARY AND RESULTS

Series Number	Mortality and Percentage	Average Survival in days of Mortality cases	Survival and Percentage	Average Survival in days of Survival Cases	Position of Septal	Injection of Coronary Arteries in Relation to Ameroids	Extent of Coronary Occlusion	Coronary Anastomoses Overall Average	Arterio-Luminal Vessels and No. Communicating with Lumen of heart	Dye in Intra-Myocardial Vessels	Sections of heart	Location of Infarction in ventricular wall	Location of Myocardial Fibrosis
SERIES 1	12 dogs 75%	19 Days	4 dogs 25%	171 Days	AD 75% C 12.5% LC 12.5%	Prox. 5 Distal-10 Extra-Cardial-0	35.9%	Homo-coronary 1.66 (x) Inter-coronary 0.86 (x) Extra-Cardial-0	11 (1)	with Dye 9 without Dye 7	Transverse 7 Sagital 1 Coronal 3 None 4	Anterior4 Posterior 4 Post-Lateral 3 None 4	Endo - Cardial 8 Middle & Endo-Cardial 3 Epi-Cardial & Endo- Cardial 1 None 4
SERIES 11-A	6 dogs 60%	12.6 Days	4 dogs 40%	120 Days	AD 70% C 20% LC 10%	Proximal 6 Distal 3 Extra Cardial 3	33.9%	Homo-Coronary x x Inter-Coronary 0.9 (x) Extra Cardial-1	21.6 (5.6)	With Dye 9 Without Dye 1	Transverse 2 Sagital 3 None 2	Anterior 0 Posterior 5 AnteriorX Posterior 1 None 4	Endo-Cardial 5 Middle 1 None 4
Series 11-B	5 dogs 50%	51.6 Days	5 dogs 50%	37 Days	AD 60% C 20% LC 20%	Proximal 0 Distal 10 Extra-Cardial 6	33.6%	Homo-Coronary 3.2 (x) Inter-Coronary 1.7 (x) Extra-Cardial 1	23 (6.4)	With Dye 10 Without Dye 0	Transwer-se 2 Sagital 0 Coronal 8	Anterior 1 Posterior 2 Post-Lateral 1 None 6	Endo-Cardial 4 Middle 0 None 6
SERIES 111	3 dogs 30%	26 Days	7 dogs 70%	237 Days	AD 70% C 20% LC 10%	Proximal 3 Distal 6 Extra-Cardial 4	33%	Homo-Coronary 2.4 (x) Inter-Coronary 1.2 (x) Extra-Cardial 4	26.6 (4.6)	With Dye 8 Without Dye 2	Transver-se 0 Sagital 0 Coronal 7 None 3	Anterior 0 Posterior 3 None 7	Endo-Cardial 4 Middle 1 Epi-Cardial 1 None 4

TABLE IX TABLE OF GENERAL AND SUMMARY RESULTS CONTINUATION

Series Number	Mortality and Percentage	Average Survival in days Mortality cases	Survival and Percentage	Average Survival in days of Survival Cases	Position of Septal	Injection of Coronary Arteries in Relation to Ameroids	Extent of Coronary Occlusion	Coronary Anasto-moses Overall Average	Arterio-Luminal Vessels and No. Communicating with Lumen of heart	Dye in Intra-Myocardial Vessels	Sections of heart	Location of Infarction in Ventricular wall	Location of Myocardial Fibrosis
SERIES IV	6 dogs 60%	24.6 Days	4 dogs 40%	60 Days	AD 70% C 10% LC 20%	Proximal 0 Distal 10 Intra-Cardial 4	84.4%	Homo-Coronary 2.5 (x) Inter-Coronary (x) Intra-Cardial 0	13.8	With Dye 7 Without Dye 3	Transverse 2 Sagital 3 Coronal 5	Anterior 1 Posterior 3 Post-Lateral 2 None 4	Endo-Cardial 5 Middle 3 None 3
SERIES V	2 dogs 20%	12.4 Days	2 dogs 20%	69.5 Days	AD 70% C 10% LC 20%	Proximal 2 Distal 3 Intra-Cardial 2	78.5%	Homo-Coronary 1.3 (x) Inter-Coronary (x) Intra-Cardial 0	16.9 (1.6)	With dye 6 Without Dye 4	Transverse 3 Sagital 2 Coronal 5	Anterior 4 Posterior 1 Post-Lateral 1 None 4	Endo-Cardial 3 Scattered 2 None 5
SERIES V1	4 dogs 30%	13 Days	1 dog 20%	132 Days	AD 60% C 20% LC 20%	Proximal 3 Distal 2 Intra-Cardial 1	70.3%	Homo-Coronary 1.4 (x) Inter-Coronary 0.8 (x) Extra-Cardial 0	17 (1.7)	With Dye 2 Without Dye 3	Transverse 3 Coronal 1 None 1	Anterior 2 Posterior 2 None 1	Endo-Cardial 2 Middle 1 Epi-Cardial 1 None 1
SERIES V11	3 dogs 60%	23 Days	2 dogs 40%	183 Days	AD 80% C 0 % LC20%	Proximal 1 Distal 4 Extra-C Cardial 1	80%	Homo-Coronary 2.6 (x) Inter-Coronary (x) Extra-Cardial 0	15.5 (4)	With Dye 5 Without Dye 0	Transverse 3 Coronal 1 None 1	Anterior 0 Posterior 2 Anterior and Posterior 1 None 2	Endo-Cardial 1 Middle 1 None 1

CHAPTER XI.

D I S C U S S I O N

SERIES I. CONTROL WITH AMEROIDS.

Coronary artery disease with its accompanying coronary insufficiency, coronary occlusion and myocardial infarction is indeed hard to simulate and produce in experimental animals. Several mechanical and chemical methods, as described in Chapter VII, were used which had numerous setbacks and disadvantages. More recently, local Beta radiation by implantation of radioactive Yttrium pellets along side a coronary artery (149) and by the use of high molecular substances like polysaccharides, (180), were tried with success, but appeared more complicated and possessed some disadvantages.

In this present control series, 16 dogs were used, 12 of which were males and 4 females. Their weights ranged from 38-52 lbs. Vaselinized ameroid casein plastics in steel jackets were placed around the anterior descending and circumflex branches of the left coronary arteries, in order to produce coronary insufficiency and myocardial ischemia. The rate of coronary occlusions were slow, fairly constant and reasonably predictable.in vivo (132). The average survival in days of dogs with coronary artery constrictors by ameroids in Litvak 's series was 20 days.

and in Mahanti's series was 26 days.

In both series, the ameroids were 0.110 of an inch in luminal diameters. In the present series the average survival in days was 19 days, because the luminal diameters of the ameroids used were 0.103 of an inch, a bit smaller than the two previous series.

In this series, the mortality rate (12 dogs) was 75% and the survival rate could be accounted for by the fact that in this series of animals 10% had intercoronary anastomoses already existing. Further more, the anterior descending branch arises from the left coronary artery in dogs in most cases. It is suggested that the posterior descending branch arose from the right coronary artery in some of the dogs which might explain why they survived the ameroid coronary constrictors.

The septal artery arose in 75% of the cases from the anterior descending branch, 12.5% from the circumflex branch and 12.5% from the main left coronary artery.

The coronary arteries were injected with the new Schlesinger's mass in 5 hearts proximal to the ameroids and in 10 hearts distal to the ameroids. None of these hearts had a cannula in the ventricular cavity during injection.

Schlesinger's injection study revealed only arterioles larger than 40 micra in diameter. Anastomotic communications less than 40 micra were of little clincal significance. (42).

According to Blumgart and associates (43, 44) at least 12 or more days of 75% coronary artery occlusions were required to produce anastomotic communications, sufficient to protect the myocardium.

In this series the combined percentage of coronary artery occlusions for both anterior and circumflex branches of the left coronary arteries were 85.5%, sufficient to produce coronary insufficiency and myocardial ischemia. The coronary artery occlusions were due to intimal proliferation and thrombus formation. It seems that more than 19 days were required for the development of new intercoronary anastomoses in order to protect the myocardium.

All surviving dogs showed *** homocoronary and ** intercoronary anastomoses, presence of more arterioluminal vessels and more communicated with the lumen of the heart and finally, the heart had dye in the intramyocardial vessels.

In contrast, the mortality dogs showed 1.27 times * homocoronary and 0.45 times * intercoronary anastomoses, fewer arterioluminal vessels and 5 out of 12 only had dye in the intramyocardial vessels. The mortality dogs, it would appear did not develop or have already present

enough anastomoses, so that all of them died with myocardial infarction. The surviving dogs which developed or had present naturally sufficient number of coronary anastomoses to give them myocardial protection, so all their hearts were normal on microscopic examination.

The above findings and results will be on the basis for evaluation of various revascularization procedures.

SERIES II-A. IVALON SPONGE OPERATION TO ANTERIOR SURFACE OF HEART.

This procedure entailed the removal of the epicardium or serous visceral pericardium on the anterior surface of the left ventricle and a part of the adjacent right ventricle; removal of the parietal serous pericardium and fibrous pericardium, overlying the same area of the heart, by means of mechanical dissection and by scraping with a Beck burr. A sterile ivalon sponge, 1/16 of an inch in thickness was anchored by sutures on the surface of the bared and partially bleeding myocardium and layer of pericardial fat pad containing plexus of blood vessels. The ivalon sponge has a framework of continous intercellular spaces, which permit the infiltration of new blood vessels and fibrous tissue, and this acts as a connecting link between blood

vessels of the pericardial plexus and myocardial channels and arterioles.

In this series, 10 dogs were used, 6 males and 4 females, with weights ranging from 37 and 1/2 to 53 lbs. Coronary insufficiency was produced by vaselinized ameroid constrictors.

The survival rate (4 dogs) was 40% and the average survival in days until sacrificed was 120 days. In this series, ameroids with lumina of 0.103 of an inch were used, whereas, in the Deliyannis series in which ameroid survival with ivalon sponge operation was 85%, the lumina of the coronary constrictors were 0.110 of an inch. The smaller the ameroid constrictors cause coronary artery occlusion faster and cause less time for development of intra and extra coronary anastomoses.

The septal artery arose in 70% from the anterior descending branch, 20% from the circumflex branch and 10% from the main left coronary artery.

The combined average percentage of coronary artery occlusion was 88.9% which was sufficient to produce coronary artery insufficiency. The occlusion was due to intimal proliferation and thrombus formation.

The surviving dogs did not have any myocardial infarction or myocadial fibrosis. The mortality dogs had posterior wall infarction in 5 dogs and a combination of anterior and posterior infarctions in one dog. Surprising,

there was no anterior wall infarction of the left ventricle alone in this series of 10 dogs.

Microscopic sections showed that myocardial fibrosis was located in the endocardial portion of 5 hearts, middle portion in one heart and none in the epicardial portion of the myocardium. These facts suggest that the ivalon sponge when applied upon the anterior surface of the left ventricle protects the area from myocardial ischemia caused by the coronary ameroid constrictor.

In all but one that died of ischemia, infarction in posterior part of left ventricle where there was no sponge application provides additional evidence, that the sponge operation protects the myocardium against ischemia. It should be pointed out that Deliyannis placed ivalon sponge on both anterior and posterior surfaces of the left ventricle.

The coronary anastomoses in the surviving dogs showed 2.8 times * homocoronary and 1.8 times intercoronary anastomoses, giving the myocardium enough blood nourishment to protect it from coronary occlusion by ameroid constrictors. The coronary anastomoses in the mortality dogs was 1.8 times * homocoronary and 0.33 times * intercoronary anastomoses which was almost the same as in the control series, affording the heart no protection whatsoever.

The average arterioluminal vessels in this series was 21.6 vessels, 5.6 of which communicated with the heart's lumen. All surviving dogs had dye in the intramyocardial

blood vessels and in the mortality dogs also all hearts except one had their intramyocardial vessels filled with dye.

In dog 12-443 which was sacrificed after 174 days extracardiac anastomoses were noted. Injection of the intact heart with new Schlesinger's mass, through the left subclavian artery and aorta showed branches of the pericardiophrenic, IMA, intercostal, esophageal and bronchial arteries went to the pericardium, filling up the coronary arteries and lumen of the heart with dye. This proved that the ivalon sponge operation resulted in development of anastomoses between the extra cardiac arteries and the myocardial cardiac arterioles.

By microscopic sections, the ivalon sponge showed the presence of rich cellular fibrous tissue, a moderate number of good sized blood vessels and the injected Schlesinger's mass in spaces of the sponge. In the dogs that were sacrificed early the ivalon sponge contained more blood vessels, less hyalinized fibrous tissue and more foreign body giant cell reaction. However, in the sacrificed dogs many months later, the picture was different for the ivalon sponge contained less but bigger blood vessels, more hyalinized fibrous tissue and much reduced foreign body giant cell reaction.

SERIES II- B. IVALON SPONGE OPERATION TO ANTERIOR AND POSTERIOR SURFACE OF HEART.

This series and procedure is different from Series II-A with definite improvement in results. The epicardium and subepicardial fat in the anterior and posterior surfaces of the left ventricle and adjacent right ventricle were removed mechanically by plain dissection and with Beck burr especially on the posterior surface, until the myocardium was bared and bleeding in order to open up arterioles and sinusoids. The fibrous pericardium and parietal serous pericardium overlying the bared heart was removed mechanically by wet sponge or gauze and by sharp dissection except the extreme posterior portion which was scraped with Beck burr. A large piece of sterile ivalon sponge 1/16 of an inch in thickness was anchored by a few sutures between the surface of the bared myocardium and pericardial fat pad containing plexus of vessels. The sponge served as a medium for blood vessels and other surrounding tissues to grow and give additional blood from the outside to the ischemic heart.

In this series, 10 dogs were used 8 males and 2 females, weights ranged between 37-44 lbs. The mortality rate (5 dogs) was 50% with average survival time when sacrificed was 87 days. This is a bit better than Series II-A which had survival rate of 40%.

The septal artery arose in 60% of cases from the anterior descending branch, 20% from the circumflex branch and 20% from the main left coronary artery.

The combined average for coronary occlusion was 88.6%, almost the same as in Series II-A, but slightly higher than the control series.

The coronary anasromoses for the surviving dogs showed 3.4 times * homocronary and 2.4 times * intercoronary anastomoses, while the mortality dogs showed 2.8 times * homocoronary and * intercoronary anastomoses. The overall average of coronary anastomoses was higher in comparison to Series II-A, and the control series.

The arterioluminal vessels showed an average of 23.3 vessels, 6.4 of which communicated with the lumen of the heart, as compared with the control series which showed an average of 11 vessels, one of which communicated with the lumen of the heart. All the hearts in this series contained dye in their intramyocardial blood vessels, indicating a better blood nourishment to the myocardium.

Dog 35-470, which underwent injection of the intact or in situ heart with the new Schlesinger's mass, through the left subclavian artery and aorta, revealed branches of the pericardio-phrenic, IMA, intercostal, esophageal and bronchial arteries communicating with the coronary arteries by extracardiac anastomoses on the surface of the heart,

which added extra needed blood to the ischemic myocardium.

All the suviving dogs showed normal myocardium, with out infarction and fibrosis, because the hearts developed intercoronary, homocoronary and extra-cardiac anastomoses. All the mortality dogs had myocardial infarction and fibrosis, except one.

Microscopic sections showed the ivalon sponge contained partially hyalinized fibrous tissues, plenty of thin-walled blood vessels and a few areas of foreign giant cell reaction. These new blood vessels in the ivalon sponge, which were arteriolar or larger in size, connected the pericardial plexus of vessels with myocardial vessels, thus provide channels for increasing extra cardiac blood supply of the heart. In view of the dire necessity of extra blood to keep the heart alive, these new blood vessels theoretically might enlarge in size particularly, since the ivalon sponge is gradually removed by the macrophages and foreign body giant cells and this has proven to be true by microscopic studies. The hearts that were sacrificed after several months had less and lesser fibrous tissue in the region of the ivalon sponge.

To summarize this procedure, the following has been done and the results of accomplishments are hereby reported.

1. The serous visceral pericardium, serous parietal pericardium and finally the thick fibrous pericardium were removed mechanically and by the use of Beck burr, which allowed the growth of branches of pericardial plexus of vessels into the ivalon sponge meshes as support and stimulant and then anastomosed with the myocardial blood vessels and sinusoids. In coronary artery disease with old infarction and fibrosis, the serous visceral pericardium or epicardium lost its functional and physiological elasticity, because it adhered with the fibrous tissues to the scarred myocardium. Removal of this restraining fibrotic epicardium gave the myocardium freedom to contract and relax within the physiological requirements and at the same time received the much needed blood.
2. Increased survival rate from the 25% of the control series to 50% of the ivalon series.
3. Increased arterioluminal vessels, both in number and in communication with the heart's lumen. In the ivalon sponge series in which it was applied on the anterior and posterior surfaces of the left ventricle the average arterioluminal vessels were 23.3 vessels, 6.4 of which communicated with the lumen of the heart, whereas in the control series the average arterioluminal vessels were 11 vessels, one of which communicated with the heart's lumen.

5. Presence of dye in all intramyocardial vessels, which came from the injected coronary arteries in all the hearts, indicating better myocardial nourishment and circulation. There were only 2 hearts where dye was present in the myocardial sinusoids.
6. All hearts from surviving dogs were free from myocardial infarction and fibrosis.
7. Presence of new blood vessels in the ivalon sponge connecting the myocardial, pericardial and extrapericardial blood vessels by anastomoses.
8. This new revascularization procedure could be used in conjunction with any of the following; partial ligation of the coronary sinus, ligation of pulmonary vein of left middle lobe in dogs or lingula in man, or implantation of IMA into the ventricular myocardium.

SERIES III: IMPLANTATION OF THE LEFT INTERNAL MAMMARY ARTERY INTO THE LEFT VENTRICULAR MYOCARDIUM AND PARTIAL LIGATION OF CORONARY SINUS.

The implantation of the left internal mammary artery into the left ventricular myocardium and partial ligation of the coronary sinus is an unique procedure for it brings extra needed blood to the ischemic myocardium, through extracardiac method and also allows the myocardium to extract more oxygen from its blood supply. This procedure in the recent 2 years has gained popularity as shown by articles in surgical

journals. Some critics have turned advocates of the procedure, like Bakst and Loewe (134), Bellman and Frank (36), Pearl and Citret (160) and many more. They are fully convinced that the best way to revascularize an ischemic myocardium is to bring in a new blood supply instead of just redistributing the inadequate blood, as advocated by Beck. He claims that the hearts resist blood from extracardiac sources is definitely not true because an IMA implanted into an ischemic myocardium will thrive, grow and remain patent and finally, produce arteriolar anastomoses, if IMA implantation is properly and correctly performed without kinking, tension, torsion and trauma to this delicate life saving blood vessel.

Bakst and Loewe in 1958 (134) reported that internal mammary artery implantation in an ischemic heart produces extra coronary arterial anastomoses, for he demonstrated good filling of the anterior descending artery in 90% of their spicemens and of the circumflex artery in 25% and of the right coronary artery as well in 10%.

Pearl and Citret (160) claims that IMA implanted in the non ischemic heart becomes occluded or severely stenosed in 89%, but if IMA is implanted in an ischemic heart, it becomes patent and successfully implanted in 82%.

Bellman and Frank (36) showed that implanted IMA remained patent in 13 out of 14 casa. The artery gave

intramyocardial branches with the average of 1 to 5 mm. in length and about 0.5 mm. in diameter. All the implants were narrowed terminally and were surrounded by a membrane of thin non-constrictive scar tissue. The distal third of the implants established 1 to 4 branches which emerged from the tunnel to anastomose with the branches of the coronary arteries.

Duchene and associates (64) termed the IMA implantation as the operation of the future for revascularization of the ischemic myocardium after evaluating it with several other procedures.

In this present series, 10 dogs were used, 6 males and 4 females, whose weights ranged between 37 1/2 to 55 lbs. The survival rate (7 dogs) was 70% and the average was 237 days at the time of sacrifice. On the other hand, the mortality rate (3 dogs) was 30% with an average survival of 26 days.

All the implanted IMA remained patent, although there was gradual narrowing of its lumen terminally. The average occlusion of the implanted IMA was 17% in proximal portion, 34% in mid portion and 51.5% in distal portion. The occlusions were due to intimal proliferation, very slight thrombus formation and the adventitia of the artery contained dense collagenous cuff in which there was a moderate number of arterioles and small sized arteries.

The injection of the intact heart in situ with the new Schlesinger's mass in 3 dogs injected by this technique showed the dye entered the Implanted IMA and filled all the coronary arteries and its branches, the blood vessels of the lungs and finally, the ventricular lumen. These injection studies indicated that the heart was supplied with the dye solely from the implanted IMA. No dye could have entered through the coronary ostia because the base of the aorta was isolated by a clamp and a ligature of umbilical tape and unlike the ivalon sponge operation in dogs , no dye entered the heart from the mediastinal branches of the aorta. All the hearts in this series showed a patent IMA, except one which showed no branching, the lumen of the artery was accidentally blocked with a large bubble of air during the injection.

This new injection method of extra cardiac vessels with intact heart in situ provides an objective method of outlining extra cardiac coronary anastomoses, in order to evaluate the various procedures designed to augment the coronary circulation via its collaterals, especially the extracoronary arterial collateral circulation. This dye perfusion and injection experiment is aptly described in Chapter VIII- Materials and Methods.

The extent of average combined coronary occlusions by ameroid constrictors was 83%, which was more than enough for the requirement for development of intracardiac coronary arterial circulation. The occlusion was due to

intimal proliferation and thrombus formation. The average intracardiac anastomoses for all the surviving dogs was 2.7 times * of homocoronary and 1.4 times of * of intercoronary anastomoses and for all the mortality dogs, 1.66 times* of homocoronary and 0.66 * of intercoronary anastomoses, which was equivalent to the control series. In these mortality dogs, no protection from death was afforded by the insufficient coronary anastomoses.

The average number of arterioluminal vessels was 26.6, 4.6 of which communicated with the lumen of the heart, which was 2 1/2 times more than the control series of 11 arterioluminal vessels, one of which had communication with the heart's lumen.

All the dogs in this series had dye in the intramyocardial blood vessles, except one each for the surviving and mortality dogs. This showed clearly the greater amount of blood and dye by injection that had circulated in the myocardium for nourishment via its myriads of capillaries.

All surviving dogs showed normal myocardium without infarction, while those of the mortality dogs, infarctions were located in the posterior wall of the left ventricle. The finding was significant for the internal mammary artery implant gave protection to the anterior wall where it was in the mortality dogs, and complete protection to both anterior and posterior walls of the left ventricles in the surviving dogs.

Myocardial fibrosis on microscopic sections were absent in almost all the hearts of the surviving dogs, except 3, where tiny fibrosis was noted in the endocardial or inner portion of the myocardium. All the mortality dogs had extensive fibrosis in the myocardiumm which were mostly on the endocardial portion. These findings suggest that in the normal animal heart nourishment and blood supply of the myocardium comes mainly from the coronary arteries and not from the ventricular lumen via the intraluminal vessels.

SERIES IV. BECK I OPERATION: CARDIO-PERICARDIOPEXY (ASBESTOS) PARTIAL LIGATION OF CORONARY SINUS.

According to Beck, death from coronary artery disease occurs with or without warning. There are 2 types of death produced by the disease; one is due to fibrillating current that destroys the heart beat, and the other is muscle destruction, due to inadequate blood supply. Most of the deaths are due to the first type and it can be prevented by surgical procedures as shown in the laboratory animals and human patients. The Beck I operation produces inflammatory reaction on the surface of the heart, by the irritant action of asbestos, which in turn, opens up already existing intercoronary anastomoses. The operation rarely brings new blood from the outside sources, except in one case in this series. Partial coronary sinus ligation stimulated collateral branches , so that it redistributes

its own blood in order that the heart can enjoy a balanced circulation and prevent development of oxygen and electrical differentials. (34). However, it appears that it does not remedy the actual lack of sufficient blood required by a normal working heart. Since coronary artery disease is a progressive occlusion of the arteries, and gradual deprivation of blood to the myocardium, it appears that the best therapy is not only to redistribute the blood in the heart, but also to bring extra coronary blood.

This operation increases the average backflow from 228 cc. per hour to 510 cc. per hour or an increse of 282 cc. (151).

Recently, Beck has tried to replace epicardial abrasion by the use of 5% trichloracetic acid to the epicardium. This was a preliminary study and further tests and evaluations are indicated.

In this series of 10 dogs were used, 7 males and 3 females, whose weights ranged between 40-46 lbs. The morlity rate (6 dogs) was 60% and the survival rate (4 dogs) was 40%. The average survival in days for the mortality dogs was 24.6 days and for the sacrificed dogs was 60 days.

The combined average percentage of coronary artery occlusion was 84.5%, which was more than enough to create

coronary insufficiency and even death to the animals, if no revascularization procedure was performed. The occlusion was due to intimal proliferation and thrombus formation.

The development of coronary anastomoses for surviving dogs was *** homocoronary and 1.8 (*) intercoronary anastomoses. This anastomoses brought enough blood to the heart in order to survive the occlusion produced by the ameroid constrictors. The average coronary anastomoses for the mortality dogs on the other hand was ** homocoronary and * intercoronary anastomoses was almost equivalent to the control series; that was why these dogs died.

The average arterioluminal vessels was 18.8 vessels, 4.3 of which communicated with the lumen of the heart. The increased number of vessels were especially present in the surviving dogs as compared to the mortality dogs, which had a lesser number of vessels.

All surviving hearts had dye in the intramyocardial vessels, except one and all mortality hearts also, except two. This operation appeared to have increased the myocardial blood supply as shown by a higher survival rate compared to the control series.

The septal artery arose in 70% of cases from the anterior descending branch, 10% from the circumflex branch and 20% from the main left coronary artery.

Only Dog 9-484, which underwent injection of intact heart with the new Schlesinger mass through the left subclavian artery and aorta showed branches from the pericardio phrenic, intercostals, IMA, esophageal and bronchila arteries, which went to the pericardium. It also filled up the coronary arteries and the lumen of the heart, so much so that the dye came out of the ventricular cannula. In this specific dog that had BECK I operation, extracardiac anastomoses took place.

All sacrificed dogs showed absence of any myocardial infarction because of the successful revascularization. However, all mortality dogs had myocardial infarctions, 5 out of 6 located in the posterior wall, indicating that the myocardium was not protected, especially the posterior wall of the left ventricle.

Microscopic sections also showed that all the sacrificed dogs did not have any fibrosis, except one, and all the mortality dogs had myocardial fibrosis, 5 out of 6 located in the endocardial portion. This indicated that the

Beck I operation brought blood from the coronary to the myocardium mainly and practically a small amount came from the ventricular lumen.

All the specimens showed the presence on the surface of the myocardium of moderate giant cell foreign body reaction with glistening foreign body (asbestos), small number of dilated capillaries, moderate fibrous tissue reactions and in some areas, some chronic inflammatory reaction. This proved that revascularization took place by means of vascularized foreign body granulomas. The fate of the new blood vessels depended upon the replacement and obliteration by fibrous tissue. Only time factor and subsequent study of follow-up of long time survivors could foretell the outcome of these few blood vessels.

SERIES V: THOMPSON-RAISBECK OPERATION: CARDIO-PERICARDIOPEXY BY USE OF TALCUM.

The rationale of surgery in the treatment of coronary artery disease is to decrease the myocardial demand or increase the coronary blood supply to the heart itself. This procedure apparently increases the blood supply to the heart by means of creating an acute inflammatory lesion in the pericardial

sac by production of acute non-suppurative serous and s ero-fibrinous pericarditis, by the irritant effect of talcum powder, this actively stimulating hyperemia. As a result of hyperemia, there is dilatation of intracardiac and extra-cardiac coronary anastomoses. The inflammatory reaction involves all structure of mediastium, including pleura, peri-cardium, epicardium, adjacent myocardium, esophagus and lungs (187, 190). Thompson and associates claim that their results was good in the laboratory and also in human patients. Moritz and associaties (148) substantiate the efficacy of the procedure, for they found 7 cases of human hearts rich in extracardiac anastomoses with coronary arteries following partial or complete obliteration of the pericardial sac by fibrous adhesions.

However, Gage and associates (77) found that cardio pericardiopexy did not protect the animals against thrombi caused by insertion of thrombogenic wire. Poudrage did not promote formation of collaterals beyond which can be expected to occur from gradual occlusion induced in the arterial lumen.

Gross and associates (102) claimed that no beneficial

effects resulted from the talc cardio pericardiopexy in protecting the pig's heart against subsequent ligation of the coronary artery.

In view of the existing controversial results, this' procedure was tried in this laboratory on 10 dogs, 6 males and 4 females, whose weights ranged from 38-50 lbs.

The mortality rate (8 dogs) was 80% and the survival rate (2 dogs) was 20%. The average survival in days for the mortality dogs was 12.4 and of the sacrificed dogs was 69.5 days.

The combined average coronary occlusion was 79.5% which is much lower compared to the control series, but slightly above the 75% that Blumgart claimed would produce coronary anastomoses. Furthermore, this amount of occlusion killed most of the dogs except two, in spite of poudrage procedure. The occlusion was due to intimal proliferation and thrombus formation.

The average coronary anastomoses for the surviving dogs was *** homocoronary and ** intercoronary anastomoses, which were sufficient to protect the myocardium. On the other hand, the mortality dogs had only 1.5 times (*) homocoronary and

0.75 (*) intercoronary anastomoses, which was almost the same as the control series resulting in the death of the dogs in 12.4 days after operation. In this series there was no extracardiac anastomoses formed at all to assist revascularization.

There were 16.9 arterioluminal vessels, 1.6 of which communicated with the lumen of the heart. This number was almost the same as the control series. All surviving dogs had dye in the intramyocardial vessels while the mortality dogs had dye only in half their number.

All the surviving dogs showed no myocardial infarction. However, in the mortality dogs, majority of the infarctions occurred in the anterior wall of the left ventricle which was in agreement with the findings of Bakst and Loewe (134). They claimed that talcum poudrage gives protection to the posterior wall of the left ventricle.

Microscopic sections showed that all the surviving hearts had normal myocardium and most of the fibrosis in the mortality hearts were located in the endocardial portion of the myocardium. All hearts in this series showed that the epicardium had hyalinized fibrosis, little number of capillaries and moderate amount of foreign body giant cell reaction.

Talcum poudrage did not protect the animal against coronary artery occlusion by ameroid constrictors whichi is in agreement with the findings of Gage and Gross and associates.

SERIES VI: CARDIO-PERICARDIOPEXY WITH SODIUM SALICYLATE 5% SOLUTION:

This is a new procedure tried in this laboratory to stimulate revascularization of the ischemic myocardium. Physiologically, it works by lysis or chemical destruction of the epicardium, which will produce non-suppurative fibrous cardio-pericardiopexy and hyperemia. No other laboratory has used this solution solely for revascularization purposes.

In this series, 5 dogs were used, 3 males and 3 females, whose weights ranged between 35-52 lb.

The mortality rate (4 dogs) was 80% and the survival rate (1 dog) was 20%. The survival in days of the mortality dogs was 13 days, while of the sacrificed dogs was 132 days.

The average extent of coronary artery occlusions was 78.8%, which was sufficient to produce coronary insufficiency and myocardial ischemia. The occlusion was due to intimal proliferation and thrombus formation.

The coronary anastomoses for the surviving dogs showed *** homocoronary and * intercoronary anastomoses and for the mortality dogs * homocoronary and 0 intercoronary anastomoses. There was no extracardiac anastomoses shown by injection of the intact heart. The number of anastomoses is just equal to that of the control series. The high mortality rate resulted from the absence of sufficient coronary anastomoses for protection.

The average arterioluminal vessels was 17 vessels, 1.7 of which communicated with the lumen of the heart. The surviving hearts had dye in the intramyocardial vessels, while the mortality dogs hearts had no dye in the intramyocardial vessels, except one. Both of these findings indicated that the procedure failed to increase blood supply and circulation in the myocardium.

Myocardial infarction was absent in the lone surviving dog while myocardial infarctions were present in all the mortality dogs. The fibrosis was mostly located in the endocardial portion of the myocardium.

All the evidence and results indicate that this procedure afforded no protection to the myocardium against coronary occlusion by ameroid constrictors. The lone survivor fell within the group of dogs which had normal intercoronary anastomoses. like those in the control series.

SERIES VII: ARTERIALIZATION OF THE CORONARY SINUS WITH THE LEFT INFERIOR PULMONARY VEIN ANASTOMOSES.

Several revascularization procedures of the ischemic myocardium are in current use today not only in the laboratory but also in human beings. While it is not impossible to produce intracardiac and extracardiac anastomoses between heart and grafts, they cannot be produced in any degree of regularity (34).

The search for other methods of bringing extra needed blood to the ischemic heart appears to augment total coronary circulation in the face of progressive and severe diminution of blood supply as in coronary heart disease, is still going on. The internal mammary artery implantation and Beck II operation were the first ones to have come out for this specific physiological purpose. The first one has held it own with enough statistical proof for its continuance, while Beck II has fallen by the wayside because the graft between the aorta and coronary sinus in 6 months time becomes obliterated by intimal proliferation and thrombus formation. The vein graft could not tolerate the onslaught of the systemic pressure. The operation would have been a success, only if the oxygenated blood is delivered to the coronary sinus at a

a tolerable pressure. The answer to this requirement comes from the inferior pulmonary vein which is lying 1 or 2 cm. away from the coronary sinus. It contains oxygenated blood with a pressure of approximately 10/0 mm. of mercury. On the other hand, the pressure in the left auricle is about 6/2 mm. Hg. and in the right auricle and coronary sinus about 4/0 mm.Hg. Since fluid flows from high to low pressure, then blood from the inferior pulmonary vein would easily flow into the coronary sinus and right auricle. However, to reverse the flow of the oxygenated blood to the myocardial capillaries, partial coronary sinus ligation to 3 mm. is required. Furthermore, Gross ;and Blum (100) have shown that coronary sinus partial ligation, allowed enough time to extract effectively the much needed oxygen from the blood, can be successful.

On these physiological principles, the arterialization of the coronary sinus by anastomoses with the left inferior pulmonary vein, plus 3 mm. partial ligation of the coronary sinus, was conceived and tried by the author of this thesis for the first time in 5 dogs, 4 males and 1 female, whose weights ranged betwe n 40-50 lbs.

The mortality rate (3 dogs) was 60% and the survival rate (2) dogs) was 40%. The average survival in days of the mortality dogs was 23 days and of the sacrificed dogs was 188 days. One of the surviving dogs (Dog 2-364) would still be alive if not sacrificed 287 days after operation.

The extent of combined average coronary occlusions was 88%, sufficient enough to produce coronary insufficiency and myocardial ischemia. The occlusion was due to intimal proliferation and thrombus formation. The septal artery arose from the anterior descending branch in 80% of the cases and from the main left coronary artery in 20%.

The average coronary anastomoses for the surviving dogs was 2.5 times * homocoronary and ** intercoronary anastomoses. On the other hand, the mortality dogs had 2.6 times * homocoronary and * intercoronary anastomoses. The two surviving dogs had extracardiac anastomoses established.

The average arterioluminal vessels was 15.5, 4 of which communicated with the lumen of the heart. All hearts of both mortality and sacrificed dogs had dye in their intramyocardial vessels indicative that more blood had gone into the myocardial tissues.

The surviving dogs had no myocardial infarction and fibrosis, while the mortality dogs had them in the endocardial portion of the myocardium.

In dog 2-364, which survived 287 days, injection of left inferior pulmonary vein showed the dye went into the coronary sinus, its tributaries and then into the lumen of the heart. The anastomoses between the inferior pulmonary vein and the coronary sinus was patent with some intimal thickening, so much so that it appeared like an artery. The epicardial layer of the myocardium showed plenty of new blood vessels filled with blood. There was very little fibrous tissue reaction.

Takeuchi, ligated the pulmonary vein of the left middle lobe in dogs and then sutured it to the pericardial sac. Asbestos poudrage was applied between the surfaces of the sutured lung and pericardium. He noted that subsequent congestion and healing created marked adhesions between the lobe and surrounding structures. Engorgement and bleeding from the lung disappeared at the end of one month due to the large collaterals which developed. The mortality rate of ligated anterior descending branch in 23 dogs was 21.5% and was 0% for the protected dogs. (232)

Shumway, (233) used retrograde coronary sinus perfusion for direct vision surgery of acquired aortic vavular diseases. The coronary circulation was reversed by cannulating the coronary sinus with Foley catheter and arterialized blood from the extracorporeal apparatus was used to supply the heart. The color of the myocardium remained pink through out the procedure.

The above works of Takeuchi and Shumway coroborate the rationale of the arterialization of the coronary sinus with the left inferior pulmonary vein as a treatment of coronary artery disease with coronary insufficiency.

There is enough evidence that the new procedure has produced a relatively good survival rate and brought more blood to the ischemic myocardium. More survivals would be expected after the technique of the operation is refined and perfected by the individual operators.

CHAPTER XII.

SUMMARY AND CONCLUSIONS.

1. A brief review of the anatomy, physiology and pathology of the heart is described especially with regards to revascularization of the ischemic myocardium.

2. Historical background of the different revascularization procedures in coronary artery insufficiency is described.

3. The objectives, problems and difficulties in simulating myocardial ischemia in experimental animals and then the revascularization of their ischemic myocardium are presented.

4. A brief review of the different methods used in the production of coronary insufficiency and myocardial ischemia in experimental animals are described.

5. The vaselinized ameroid casein plastic in steel jacket, when placed around the anterior descending and circumflex branches produced coronary occlusions at a slow fairly constant and predictable rate averaging 19 days in control animals, is comparable to the coronary artery occlusion and insufficiency in human beings.

6. The extent of coronary artery occlusion produced by ameroid constrictor had a combined average percentage of

85.9% which was due to intimal proliferation and thrombus formation. The infarction produced was mostly located in the endocardial portion of the myocardium.

7. The gradual occlusion of the coronary artery to the average reduction of its lumen of 85.9% in 19 days is not sufficient and long enough to allow natural production of new intercoronary anastomoses for the protection of the myocardium.

8. The new method of injecting the intact heart in situ with new Schlesinger's mass, through the left subclavian artery and aorta is an objective test to visualize the effects of various revascularization procedures and augmentation of the coronary circulation via its extracardiac collaterals is described.

9. The ivalon sponge operation stimulated the production and dilatation of homocoronary and intercoronary anastomoses, two to three times that of the control, and also created well established extracardiac anastomoses which were demonstrated in two cases which augmented the coronary circulation.

10. The ivalon sponge operation increased the number of arterioluminal vessels, two to three times and the vessels communicated with the lumen of the heart five to six times that compared to the control series. The myocardial sinusoids were filled up with dye

only in two hearts out of 20. All the 20 hearts, except 1, had dye in the intramyocardial blood vessels, indicating an increase in myocardial circulation.

11. The ivalon sponge served as a framework for the growth of new blood vessels and endothelial lined channels, which connect the pericardial plexus of vessels with the myocardial blood vessels in the arteriolar level for the new Schlesinger's mass to pass through vessels with a diameter of 40 micra.

12. The ivalon sponge gives more protection to the ischemic myocardium when applied on both the anterior and posterior surfaces of the heart or left ventricle than when applied to the anterior surface only. Myocardial infarction occurred in the wall of the ventricle not protected by the ivalon sponge. All hearts that received protection from the ivalon sponge showed no myocardial infarction and fibrosis at all.

13. All hearts unprotected by the ivalon sponge as shown in the mortality group, whowed myocardial fibrosis in the endocardial portion of the myocardium. This indicates that these hearts did not get any blood supply from the lumen of the of the heart and practically all nourishment of the myocardium came from

the coronary arteries and its intramyocardial branches.

14. The implantation of the internal mammary artery into the myocardium and partial ligation of the coronary sinus is the operation of choice and of the future, for it has the highest survival rate of 70% as compared to all the other revascularization procedures.

15. With proper handling and careful technique all the internal mammary arteries dissected free from the 6th intercostal space up to the subclavian artery, remain patent when implanted into the ventricular myocardium. All except one showed early to full branching and anastomoses with that of the coronary arteries and their intramyocardial branches. The lone one which showed no branching accidentally became blocked with a large bubble of air during the injection. The narrowing of the implanted internal mammary arteries were slight to moderate gradual tapering obliteration distally to about 50%, caused by intimal proliferation and thrombus formation and presence of dense collagenous cuff in which there were moderate number of arterioles and small sized arteries.

16. The internal mammary artery operation promoted the increse of homocoronary and intercoronary anastomoses

almost twice the control number. The number of arterio-luminal vessels increased twice and the vessels communicating with the lumen of the heart increased 4 1/2 times compared to the control series.

17. In the internal mammary artery series, all hearts both surviving and mortality dogs had dye in the intramyocardial vessels, except one in each group. All hearts of surviving dogs showed no myocardial infarction and all hearts of the mortality dogs had infarctions in the posterior wall, because the implanted internal mammary arteries have given protections to the anterior wall where they were implanted.

18. Three out of 10 dogs, the hearts in situ were injected with new Schlesinger's mass through the left subclavian artery and aorta. In these 3 cases, the internal mammary arteries and extracardiac collaterals supplied dye to all the coronary arteries and its branches, and finally, the dye entered the lumen of the hearts. Injected in the same way the rest of the dogs may have demonstated the same findings as above.

19. In Beck I procedure, intercoronary anastomoses of sufficient size to protect against coronary artery insufficiency,

produced by ameroid constrictors occurred in 4 out of 10 dogs. There was a slight increase in the number of arterio-luminal vessels and those which communicated with the lumen of the heart. All the surviving dogs had dye in the intramyocardial vessels except one and all mortality dogs had dye in the intramyocardial vessels, except two.

20. Injection of the intact heart with the new Schlesinger mass through the left subclavian artery and aorta failed to show collateral anastomotic channels between the vascular mediastinal fat pad and the coronary arterial system in the myocardium.

21. Beck I proceudre produces, on the surface of the myocardium, a moderate foreign body giant cell reaction due to irritating asbestos powder, small number of dilated capillaries and some fibrous tissue chronic inflammatory reaction.

22. Cardio-pericardiopexy by the use of talcum (Thompson-Raisbeck procedure) did not protect the animals against the ameroid constrictors. Poudrage did not promote formation of enough collateral beyond which can be expected from gradual occlusion induced by the ameroids.

23. In Thompson-Raisbeck procedure, myocardial infarction occurred in the anterior wall of the left ventricle, which is in

agreement with the findings of Bakst and Loewe. They claimed that talcum poudrage gives protection of the posterior wall of the left ventricle.

24. Cardio-pericardiopexy by the use of 5% sodium salicylate did not protect the animal against ameroid constrictors.

25. The arterialization of the coronary sinus with anastomoses of the left inferior pulmonary vein plus partial ligation of the coronary sinus to 3 mm. in diameter produced 40% survival rate because of increased number of ontercoronary, homo-coronary and extracardiac anastomoses. The arterioluminal vessels had received both in average number and number of vessels communicating with the lumen of the heart. Dyes were present in the intramyocardial vessels of all the hearts and in the myocardial sinusoids of one of the surviving hearts, indicative of improved myocardial circulation.

26. The inferior pulmonary vein-coronary sinus operation produced no infarction in the myocardium of the surviving dogs, while the mortality dogs had posterior wall infarction and endocardial fibrosis. The two surviving dogs are still alive, if not sacrificed at 90 and 287 days, respectively. The latter had lived over 9 months, well over the 6 months period, the vein graft of the Beck II operation usually became obliterated by intimal proliferation and thrombus formation.

27. There is enough evidence that the arterialization of the partially ligated coronary sinus has produced a relatively good survival rate brought about by augmentation of the coronary circulation, both intracardially and extracardially. A higher survival rate in the future would be expected after the technique of the operation is refined and perfected by the operators.

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