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REVASCULARIZATION OF THE RIGHT CORONARY ARTERIAL SYSTEM BY IMPLANTATION OF THE RIGHT INTERNAL MAMMARY ARTERY INTO THE RIGHT VENTRICULAR MYOCARDIUM

by

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

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DEDICATION

TO MY MOTHER, FATHER AND MARY IN
DEEP APPRECIATION FOR HAVING MADE
THIS POSSIBLE.

P R E F A C E

After many years of trial and error it now appears that it is possible to place the surgical treatment of coronary artery heart disease upon a rational, logical and factual basis. There is no longer any doubt that coronary artery disease, whatever its cause, is an obstructive disease which, like other vascular obstructions elsewhere in the body, can only be relieved by surgical measure.

Any surgical procedure designed for the relief of myocardial ischemia aims at restoration of an adequate oxygenated blood supply to the myocardium in order to :

(1) relieve anginal pain

(2) prevent myocardial fiber loss

(3) restore myocardial function.

To attain this objective new multiple arteriolar or larger anastomosis must be made between surrounding systemic arteries and the coronary arteriolar network of the right and left coronary system. Ideally, many arterial channels are needed in order to be sure that the summation of flow is as great, or greater than the total capacity of the patient's coronary arterial system prior to the onset of disease.

Developing such an operation is synonymous to implementing a surgical method for coronary artery insufficiency that will be capable of total and complete myocardial revascularization. In short this has been our aim in the development of the right internal mammary artery implantation to the right ventricular myocardium.

Dr. Arthur M. Vineberg, Department of Cardiac Surgery,

Royal Victoria Hospital, Montreal, has contributed immensely to this work by supervising, encouraging and suggesting, and for this I wish to express my sincere appreciation and gratitude.

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Benjamin Ocampo Zamora, M.D.

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CHAPTER I

INTRODUCTION AND PURPOSE

Inspite of the tremendous progress in the field of cardiovascular surgery within the past few decades, deaths due to heart disease are still one of the top ranking causes.

The gravity of the problem and the urgent need for its solution are reflected in the public health statistics of several countries which reveal this disease to be one of the principal causes of death in the adult population. It has been estimated that approximately two thirds of the deaths from heart disease may be traced directly or indirectly to coronary artery insufficiency. (Rowe 1960).

As regards treatment, the value of medical management is well accepted, even with its limitations. While the controversy over the different procedures of revascularization for an ischaemic heart still continues, it is however now widely accepted that surgery has a definite place in coronary arteriosclerotic heart disease. Surgical measures employed range from cardiac denervation (Jonnesco 1920) for relief of angina by employing a cervico-thoracic ganglionectomy, to implantation of a systemic vessel within the left ventricular myocardium as advocated by Vineberg as early as 1946. Fifteen years of experience has shown clearly that an internal mammary artery implanted into the left ventricular wall forms many anastomoses with the ventricular arteriolar systems. (Vineberg, A.M. 1946, 1947, 1949, 1953, 1955, 1958). Inspite

of this invaluable finding, certain anatomico-pathological facts quickly showed the limitation of this initial procedure. With this point in mind the quest for additional procedures to revascularize the entire myocardiol system led to the development of the Ivalon Sponge Operation (Vineberg et al. 1958, 1959, 1960), and Epicardiectomy, Sero-Pericardiectomy and Free Omental Graft Operation, combined with left internal mammary implantation (Vineberg et al. 1962, 1963, 1965).

These anatomico-pathological findings could be aptly summarized as follows :

1. In man the right coronary artery is predominant in 50% of the cases, i.e. this artery supplies all of the right ventricle, posterior half of the interventricular septum, and a large part of the posterior wall of the left ventricle (Schlesinger 1940). Gross in 1921 and Barnes in 1940 showed that in approximately 75% of hearts most of the posterior ventricular surface is supplied by the right coronary artery.
2. Multiple involvement of coronary arteries by atherosclerosis.
3. Progressive nature of coronary atherosclerotic disease.
4. Inadequacy of the internal mammary artery to supply the entire heart.

These anatomico-pathological facts are the reasons therefore for an operation which will revascularize the entire heart, and for this, the implantation of the right internal mammary artery to the right ventricular myocardium was conceived and subsequently developed.

The development of this procedure has an additional twofold purpose: first, to prove without any reasonable doubt, that the right ventricular wall, and subsequently, the posterior interventricular wall of the heart could be revascularized directly through implantation of the right internal mammary artery.

Secondly with regard to the clinical application of this method, its indications whether it is needed singly or in combination with the other revascularization procedures as the case might demand.

CHAPTER II

ANATOMY OF THE HEART AND THE CORONARY VASCULAR SYSTEM WITH SPECIAL REFERENCE TO THE RIGHT VENTRICLE

The advent of cardiac surgery had placed great importance on the anatomy of this organ; reviving with great interest the descriptions of such masters in the art as Vesalius, Vieussens and others. Numerous names could be added within a span of a century, and in this list we cite a few, specifically Wearn (1928) and Grant (1929). Based on a sound knowledge of this anatomy, cardiac surgery progressed tremendously in all its aspects, and with this goes surgery for coronary heart disease. Practically all the newer surgical procedures for coronary heart disease have been based on a fuller and new understanding of the pertinent underlying anatomy (Kato, 1964).

GENERAL DESCRIPTION OF THE HEART

The heart is a hollow muscular organ, situated in the middle mediastinum enclosed in a fibro-serous sac called the pericardium. The cavity of the fully developed heart is completely separated into right and left halves by an obliquely placed longitudinal septum, and each half consists of a posterior, receiving chamber - the atrium - and an anterior ejecting chamber - the ventricle. Externally a comparatively shallow constriction, the atrio-ventricular groove, indicates the separation of the atria from the ventricles; internally a wide aperture is left between the lower part of each atrium and the posterior part of the corresponding ventricle. Each atrio-ventricular orifice is provided

with a valve which allows the free passage of blood from the atrium to the ventricle, but effectively prevents its return. (Cunningham 1951). The four chambered heart (consisting of right and left atria, right and left ventricles) somewhat resembles a short cone, and is described as having a base and an apex, and three surfaces, sterno-costal, diaphragmatic and left or pulmonary. The base of the heart faces posteriorly and consists largely of the left atrium, but the right atrium forms its right border. The great veins - the four pulmonary veins, the superior vena cava and the inferior vena cava - enter the base, which is therefore the part of the heart that is attached to the posterior pericardial wall. From the base the heart projects downwards to the left, and forward, to end in a blunt apex that is formed mainly by the left ventricle. The surface of the heart from the base to the apex is directed largely inferiorly and is the diaphragmatic surface. The sternocostal surface is anterior. The right margin is actually largely inferior being the fairly sharp edge between the diaphragmatic and sternocostal surfaces, and has been more commonly called the acute margin. (Hollinshead 1962).

THE PERICARDIUM

The pericardium is the fibroserous sac that encloses the heart and with it occupies most of the middle mediastinum.

The pericardium is divided into two basic layers, an outer fibrous layer and an inner serous layer.

The outer fibrous layer is a strong, dense layer of interlacing collogenous bundles with a network of elastic fibers in its deepest part. (Popa, G. T. et al.).

Below it blends with the central tendon of the diaphragm, to which it is firmly bound in front and on the right (Pericardiophrenic ligament). The union to the diaphragm elsewhere is looser. The pericardium is pierced by the inferior vena cava and blends with its adventitia. At its apex and posteriorly it is gradually lost upon the great vessels which enter and emerge from the heart, and it gives sheaths to them - namely the aorta, the two branches of the pulmonary trunk, the superior vena cava, the four pulmonary veins, and the ligamentum arteriosum. Behind the pericardium is bound by loose connective tissue to the structures in the posterior mediastinum. On its lateral aspects it is adherent to the mediastinal pleura, except where separated from it by the phrenic nerves and their accompanying vessels. In front the pericardium forms the posterior boundary of the anterior mediastinum. Two variable, fibrous strands, the sternopericardial ligaments, connect the pericardium above and below with the posterior surface of the sternum. (Gardner et al. 1963).

Congenital absence of the pericardium has been recorded (Moore 1925). There were no noticeable effects on the heart in such instances.

Serous Pericardium. This is a closed sac, the outer parietal layer of which lines the inner surface of the fibrous pericardium and is reflected onto the heart where it is termed the visceral layer or the epicardium. As the visceral layer is reflected onto the heart, it partially ensheaths the great vessels. The visceral and parietal layers, the opposing surfaces of which are lined by mesothelium, are separated by a potential space, the pericardial cavity, and are moistened by a film of

fluid. The majority of the great vessels receive only partial coverings from the visceral layer; thus the superior vena cava is covered in front and on each side; the pulmonary veins in front, above and below; and the inferior vena cava in front and on each side. The aorta and the pulmonary trunk are enclosed together in a complete sheath of the visceral layer. Therefore, when the pericardial sac is opened from the front, it is possible to pass a finger behind them and in front of the atria, from the right to the left side, through a passage called the transverse sinus of the pericardium. The spaces which intervene between the vessels which receive partial coverings from the serous pericardium are also called sinuses; and the largest of them, which is called the oblique sinus, is bounded below and on the right by the inferior vena cava, and above and on the left by the lower left pulmonary vein. (Cunningham 1954).

BLOOD AND NERVE SUPPLY OF THE PERICARDIUM

The fibrous pericardium and the parietal layer of the serous pericardium are supplied by the pericardiacophrenic branches of the internal mammary arteries and by pericardial branches of the bronchial, œsophageal, and superior phrenic arteries. The epicardium is supplied by the coronary arteries.

As regards its nerve supply, the fibrous pericardium and the parietal layer of the serous pericardium are supplied by branches of the phrenic nerve. These branches contain vasomotor and sensory fibers. The epicardium is supplied with vasomotor and sensory fibers from the coronary plexus, but no pain results from stimulation of the epicardium. (Gardner et al. 1963).

RIGHT VENTRICLE

The right ventricle as with the left ventricle is composed, from without inwards of epicardium, myocardium and endocardium. The epicardium or the visceral layer of the serous pericardium was discussed in the previous paragraph.

The myocardium is composed mainly of cardiac muscle fibers. It also contains connective tissue septa, which delimit bundles of cardiac muscle fibers, and a connective tissue skeleton, which supports and gives attachment to the musculature. The thickness of the myocardial layer is proportional to the amount of work that it does, thereby the wall of the right ventricle is very much thinner as compared to the left, the pressure in the pulmonary trunk, (Fig. 1) being much lower than that in the aorta.

Externally, the right ventricle is triangular in form. Its base is directed upwards and to the right, and, in the greater part of its extent, it is continuous with the right atrium, with which it communicates by the atrio-ventricular orifice; but its left and upper angle is free from the atrium, and gives origin to the pulmonary trunk. Its inferior wall rests upon the diaphragm. The left or septal wall bulges into its interior, and on that account the transverse section of the cavity has a semi-lunar appearance. (Cunningham 1951).

The interior of the right ventricle consists of a cavity that resembles a bent tube. This cavity is made up of two parts; an inferior portion or body, which communicates with the atrium through the atrio-ventricular orifice; and an antero-superior part - the infundibulum - which ends in the pulmonary trunk. Within this trunk is the valve of the pulmonary artery which consists of three valvules or cusps. These

cusps are named according to their approximate position, the anterior, right, and left semilunar valvules. At the middle of the free edge of each valvule is a thickening, the nodule, and the thin margin on each side of the nodule is the lunula. The valvules are normally forced tightly together by the pressure of blood in the pulmonary trunk after the ventricle has contracted and is relaxing, and the pulmonary valve thus prevent regurgitation of blood into the ventricle.

Opening below and into the right side of the right ventricle is the right atrio-ventricular ostium . On the ventricular side this ostium is protected by the right atrio-ventricular or Tricuspid valve; the three leaflets or cusps of this valve are attached at their bases to a fibrous ring that surrounds the atrio-ventricular ostium and the free edges of the cusps in the relaxed heart protrude into the right ventricle, where they are attached by fibrous cords the chordae tendinae, to the ends of the protruding, nipplelike papillary muscles. The three cusps of the valve are ventral (usually called anterior), dorsal (usually called posterior) and septal or medial. There is usually, one large anterior papillary muscle, which sends chordae tendinae to both the anterior and posterior cusps. The papillary muscles and chordae tendinae prevent the cusps of the valve from being everted into the atrium by the pressure developed in the contracting ventricle; this pressure closes the valve, and as the size of the ventricle decreases during contraction the papillary muscles also contract so that they maintain constant tension on the cusps. (Hollingshead 1962).

The ridge-like bundles of muscles projecting into the cavity of the ventricle are called the <u>trabeculae carnae</u>. A particularly prominent

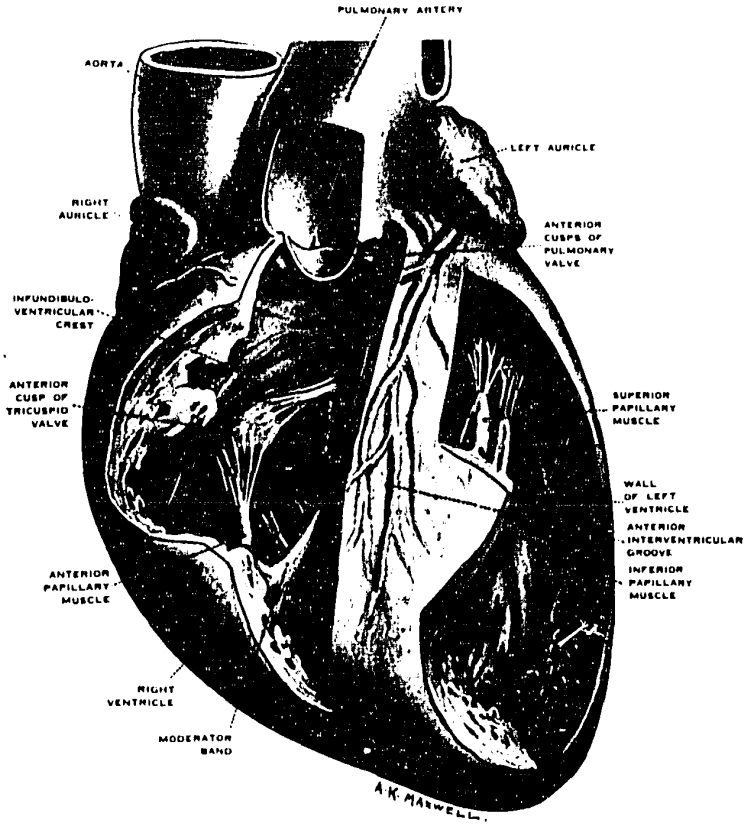


FIGURE 1: Interior of the heart showing the relative thickness of the right ventricle as compared to the left ventricle. (From textbook of human anatomy edited by Hamilton - McMillan Book Company.)

one at the apex of the ventricle that passes from the interventricular septum to the base of the anterior papillary muscle is the septomarginal trabeculae formerly known as the moderator band. This contains the right crus of the atrio-ventricular bundle. This modified trabeculae has been variously designated in the past as the trabecula of Leonardii, and the limbic band of Gross. The significance of this myocardial bridge is that, when present, it conveys the terminal part of the right stem of the bundle of His; it does not serve, as formerly fancied, to restrain the heart wall from overdistension. (Licata 1954).

THE CORONARY VASCULAR SYSTEM

The coronary arteries and veins, so named because they make a ring or crown about the middle of the heart, have been known for centuries. It is only within the past few decades, however, that great emphasis has been given to certain details of the structure of the vessels nourishing and draining the heart in relationship to diseases of the heart. This emphasis reflects the rising rates of illness due to disease of the coronary arteries and recognition that details in the structure and function of the blood vessels of the heart are closely related to possible disturbed mechanisms both in certain forms of heart disease and in the involvement of the heart by extracardiac disease (Licata 1959).

Many excellent investigations of the coronary arterial anatomy have been published. Fundamental studies of the coronary arteries have been contributed by Banchi (1903, 1904), Piquand (1910), Gross (1921), Crainiciaru (1922), Spalteholtz (1924), Grant (1927), Wearn (1936), Schlesinger (1940), Truex and Copenhaver (1947), Soderstrom (1948), Diguglielmo (1954), James and Burch (1958), Ravin and Greever (1946)

Day (1957) and Barry and Patten (1960). The descriptions given by different investigators vary in the some detail but in general, the discrepancies, especially those of the latter authors refer to either the small branches or to the anastomatic circulation.

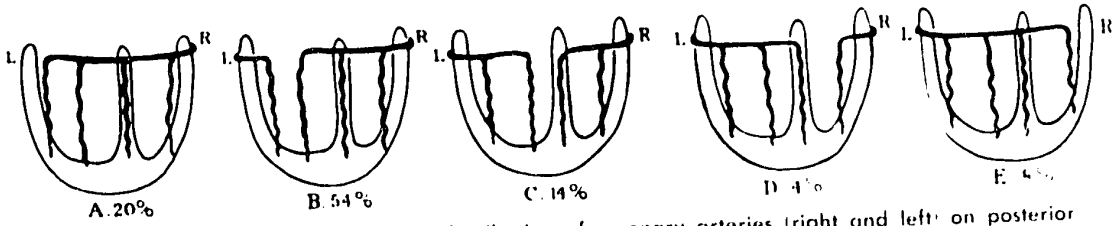
The orifices or openings of the coronary arteries are ordinarily the apertures in the wall of the aorta through which blood passes into the coronary arteries. The orifices, or coronary ostiums, are funnel shaped depressions, somewhat rounded in contour, and ordinarily are found near the center of the sinuses of Valsalva, which are guarded by the right anterior and left anterior leaflets of the aortic valve. In the majority of hearts, there is one orifice for the right coronary artery in the right arterior sinus of Valsalva and one orifice for the left coronary artery in the left anterior sinus of Valsalva.
Main arteries form a complete arch around the coronary sulcus. Off this comes a secondary arch lying in the interventricular sulci. The major branches are on the surface. The branches of the coronary arteries then penetrate the myocardium and form four arteriolar zones - the right coronary, anterior descending, circumflex and septal. (Vineberg 1959).

The Right Main Coronary Artery leaves the ostium and runs from the aorta toward the right and anteriorly behind the base of the pulmonary artery and its sinuses of Valsalva, and in front of and under the right auricular appendage (Fig. 2). This artery continues in the atrio-ventricular sulcus on the posterior surface of the heart (Roberts, J.T.,1959) From this point on variations occur from one specimen to another according to a reciprocal arrangements with the terminal circumflex branch of the left coronary artery for supplying the posterior surface of the heart.

FIGURE 2: Radiographic picture of the right coronary artery and its branches as demonstrated by the Schlesinger radio-opaque mass (normal dogs heart).

According to Gross (1921), the right coronary artery terminates near the acute margin of the heart in four per cent of hearts, near the crux in ten per cent, between the crux or posterior interventricular sulcus and the obtuse margin of the heart in sixty-six per cent and near the obtuse margin of the heart in the remaining twenty per cent. This agrees with the finding of Barnes (1940), (Fig. 3), that in seventy-four per cent of hearts most of the posterior ventricular surface is supplied by the right coronary artery. The branches of the right coronary artery are intermediate in size and often not specifically named. After branches to the wall of the aorta (such as the vasa vasorum), there are one, two or three anterior ventricular branches, usually one lateral branch, one right posterior ventricular branch, and one to three, or even five, left posterior ventricular branches, in addition to the larger posterior descending branch occurring in ninety-two per cent of cases. From the right coronary artery, atrial branches pass over the front, side, and back of the right atrium and to a variable degree, over the back of the left atrium, with practically always one or two anterior atrial branches and one lateral atrial branch, in addition to one or two right posterior and left posterior atrial branches. From these branches of the right coronary artery, specific arteries to the SA node and AV node are usually described, as well as branches to the AV bundle of His and its right branch.

Anterior Descending Artery is possibly the most conspicuous blood vessel of the heart and has been given most attention by pathologists. This artery is one of the direct branches of the left main coronary artery and is a sturdy short vessel running from the left coronary ostium in the left anterior sinus of Valsalva, up to its bifurcation which is usually between 1 mm and 1 cm from the wall of the aorta. The anterior descending



Common patterns in the distribution of coronary arteries (right and left) on posterior surface of human heart. (From Barnes, according to Campbell.)

FIGURE 3: Common patterns in the distribution of coronary arteries (right and left) on posterior surface of human heart. (From Barnes, according to Campbell and cited by Roberts, 1961).

from its origin then runs downward in the anterior interventricular sulcus toward the apex of the heart, giving branches to both ventricles. The ventricular branches of the anterior descending artery are several; they pass from an acutely angled origin to the right and across the anterior surface of the infundibular part of the right ventricle, and lower down over its anterior wall. Arising at a similar angle are several other vessels, approximately 1 mm. in external diameter, which run to the left and apically over the anterior surface of the left ventricle; these anostomose with each other from above and below, and also with the end twigs of the descending branches of the left circumflex coronary artery, especially with the above obtuse marginal branches.

The left circumflex coronary artery is a large artery averaging two to four mm. in external diameter but varying in its size according to a reciprocal arrangement with the other arteries. From its origin it passes under cover of the left auricular appendage forward and then curves toward the left in the anterior left part of the AV sulcus, in front of and above the fibrous ring and anterior leaflet of the mitral valve. In the first 3 to 5 cm. of its course, it is hidden in the layer of adipose tissue and frequently a few strands of cardiac muscle. Running parallel to it and superficial or anterior to it is the great cardiac vein, as it unites with the large atrial vein to form the origin of the coronary sinus. This vein lies at first inferior or apical to the artery, then anterior or superficial to it, then cranial or superior to the artery. The artery then leaves its close attachment to the coronary sinus as it approaches the obtuse, or left, margin of the heart, where it lies on the

inferior or apical floor of the sinus. The artery ends usually between the obtuse margin of the heart and the crux or posterior interventricular sulcus but occasionally may continue into the sulcus as the posterior descending coronary artery. Branches of the left circumflex coronary artery arise at a rather obtuse angle with this trunk and descend almost parallel to it toward the apex but crossing somewhat more toward the left in general direction. In the great majority of hearts (23 and 45%), there are two or three obtuse marginal branches, but sometimes as many as four, five or six such branches descend from the artery over the rounded or obtuse margin of the left ventricle toward the apex where the join in the anastomosis near the vortex anostomosing with terminal branches of the left anterior descending artery and the right coronary artery. (Roberts 1959).

VARIATIONS ON THE CORONARY ARTERIAL PATTERN

The coronary arterial system is not the same on all hearts. According to Gross (1921), the right coronary artery is predominant, it supplying the posterior ventricular surface in 70% to 75% of hearts. Adachi (1928) summarized the distribution of the coronary vessels in 359 human hearts. He stated that 67.7% had an essentially balanced coronary artery system, 26.6%, the right coronary artery was predominant and in 10.7% the left coronary artery was predominant. The findings of Gross agree with the findings of Barnes, that in approximately 74% of hearts, most of the posterior ventricular surface is supplied by the right coronary artery. According to Schlesinger (1940), in about one half (48%), the right coronary artery predominates (Group I), i.e. this artery supplies all of the right ventricle, posterior half of the

interventricular septum, and a large part of the posterior wall of the left ventricle. In about one third (34%), the blood supply is balanced between the two coronary arteries (Group II), i.e., the right coronary supplies only the right ventricle and the posterior half of the interventricular septum and the left coronary artery supplies the left ventricle and the anterior half of the interventricular septum. The smaller group (18%) includes those hearts where the left coronary artery predominates, (Group III), i.e., the left coronary may supply the whole of the left ventricle and the entire interventricular septum anteriorly and posteriorly and also may supply a part of the right ventricle over the posterior surface and anteriorly in the region around the pulmonary conus and on the right ventricular side of the anterior descending.

In fifty per cent of cases there is a third smaller coronary artery, the conus artery, which arises directly from the right anterior sinus of the aorta and supplies the conus arteriosus. (Schlesinger and Zoll 1949).

PENETRATING OR PERFORATING CORONARY ARTERIES

These channels are most important and are quite variable in number, location, and pattern of secondary branching. In general they arise from the deep or buried wall of the main coronary trunks. Some of the penetrating arteries pass directly into the myocardium at an angle which may be acute, perpendicular or obtuse, as well as tortuous in some cases. Whitten (1940) believed that the perforating branches from the vessels supplying the right ventricle penetrated at a more acute angle to the surface of the heart than those penetrating into the myocardium of the

left ventricle, and felt that this accounted for less bending of those in the right ventricle, thereby protecting them from injury leading to atherosclerosis. Other authors have been less impressed with this variation. (Gross and Kugel 1933).

INTRAMYOCARDIAL PLEXUS OF CORONARY ARTERIES

Within the myocardium, the perforating or penetrating coronary arteries fulfill their most important functional role of bringing arterial or oxygenated blood to a richly branching and anastomosing intramyocardial plexus of arterioles, capillaries and veins which penetrate all parts of the myocardium in the four chambers in such a way as to form a network of capillaries around each muscle fiber. There is great variation, however, in the pattern of the larger intramyocardial arteries; there is also disagreement about possibly important relationships of such vessels to bundles or subdivisions of the ventricular muscle. According to earlier workers, the penetrating branches in general pass through the myocardium until approaching the endocardium. From these penetrating branches, horizontal branches pass in the connective tissue septa or planes between the several layers of the ventricular musculature. (Roberts 1959).

ENDOCARDIAL CORONARY ARTERIES

The endocardium, especially in the thicker left ventricle and in the papillary muscles of both ventricles, is supplied in several ways from either the superficial coronary arteries or the cavity through the so-called luminal channels. Arising from the superficial ventricular arteries, the endocardial arteries are terminal small twigs from larger penetrating vessels which have penetrated only a third or more of the

distance from the epicardium to the endocardium; in some cases they are horizontal plexuses of vessels in the endocardium arising from larger penetrating arteries that pass from the epicardial layer to near the endocardium before breaking up into terminal plexus.

ARTERIOLUMINAL CHANNELS AND SINUSOIDS (Fig. 4).

The presence or absence of these channels and sinusoids had been the subject of controversy ever since Vieussens in 1706 and 1715 published the results of his brilliant studies on the heart, demonstrating openings of small size in the endocardium of both ventricles and more commonly in the lining of the atria. Thebesius in 1708 also demonstrated a connection between the coronary veins and the openings in the heart walls. His experiment, simple and convincing, consisted of blowing air into the coronary veins with the heart immersed in water and observing the bubbles of air escape through the openings in the heart wall. In 1798, Abernethy confirmed the results of Vieussens, and, while he did not fully appreciate the significance of his findings, his experiments demonstrated vascular communications between the chambers of the heart and the arterial side of the coronary circuit. Wearn et al (1933) described three types of such connections according to their characteristics of wall structure and lumen. Some of these arterioluminal channels were arterioles or vessels with relatively thick walls and lumens 10 to 30 μ. in diameter. In other areas or sections the vessel was less clearly arterial, with less muscle in the wall, but was arterial in function, as shown by tracing back through the reconstruction to an origin from a coronary artery. A third variation was found in channels with very

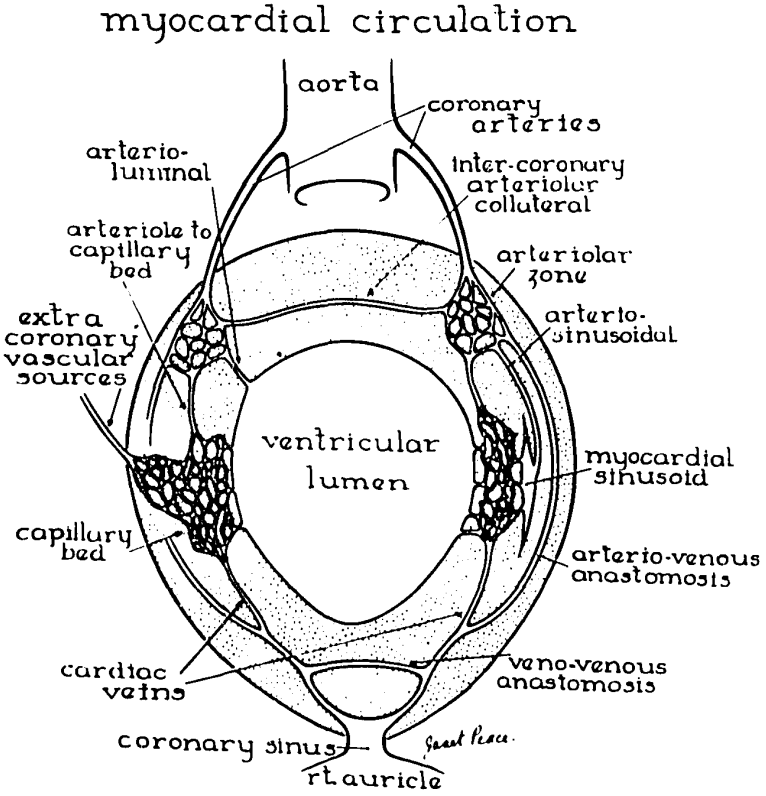


FIGURE 4: Schematic representation of the myocardial circulation, showing its complexities. (Vineberg 1959).

thin walls and lumens of variable size and shape, some of which resembled ordinary capillaries and others of which became expanded into large channels with irregular contour and diameters of 30 to 250 u. The latter were called sinusoids because they resembled the sinusoid described in other organs. Some of each of these types of channels end directly in the pores or openings of the endocardium whereas others go through intermediate phases of capillary networks and venular structure. Some of them communicate directly with the venoluminal channels which connect the lumen of the chambers with the fine terminal tributaries of the coronary veins. Vessels of this group are of the type originally described by Thebesius.

INTERCORONARY AND EXTRACORONARY ANOSTOMOSIS

Anostomosis between the several parts of the coronary system are theoretically of great importance. The existence and significance of each of these anostomoses has caused much controversy because of use of various technical methods, often inadequate, by various writers, and perpetuation of dogmatic opinions by authorities who gave little evidence of having usedskillfully enough the available methods for studying such vessels. The concept that each coronary artery and each of its branches was an "end artery" in the sense used by Conheim and others has been based upon failure of thick viscid injected materials to pass from one vessel into others under the pressure used; infarction and death of animals after experimental ligation of coronary artery branches; and incomplete inspection of the connections between vessels in gross specimens and injected hearts (Roberts 1959).

It now seems established beyond question (Gross 1921; Schlesinger 1938, 1940; Prinzmetal 1947; and many others) that the intercoronary anastomoses are fairly abundant between adjacent branches of the coronary arteries at all levels of branching. Careful dissection of the terminal branches of the coronary arteries, especially near the apex, often reveals intercoronary anastomoses which are visible to the unaided eye without injection. After injection of coloured, coagulable or radio-opaque material, numerous anastomoses between the coronary arteries are visible on inspection, dissection, differential corrosion and radiography material, numerous anastomoses between the coronary arteries are visible on inspection, dissection, differential corrosion and radiography of specimens.. These anastomoses are usually of capillary or arteriolar size, except for occasional ones of small arterial or larger size. According to Blumgart et al. (1947), only 15 per cent of normal human hearts were found to have interarterial communications of 30 to 80 u. (micra) in diameter. Prinzmetal and others (1947) injected graduated glass spheres and radioactive red cells into the coronary arteries of normal human hearts and concluded that the largest intercoronary arterial communications range from 70 to 180 micra in diameter (approximately the diameter of arterioles). They also found that the thebesian vessels ranged from 70 to 220 micra in diameter, and that there are direct arteriovenous anastomoses of 70 to 170 micra in diameter, with no significant difference between those of the two ventricles.

The extracoronary anastomoses have generally been ignored in dissections and clinical management of patients, but recently attention has been given them as possible sources for supplementary coronary artery blood flow, either natural or induced. Very little really has been

written about the anostomosis between branches of the coronary arteries and branches of the aorta outside the heart. In a classic study by Hudson et al (1932), the existence of extracardiac anostomosis and their possible contribution to coronary blood flow was placed on a firm basis. By injection into the coronary arteries, the branches of the coronary arteries around the ostia of the pulmonary veins, pulmonary artery, the superior and inferior vena cava, the root of the aorta, and the pericardial reflections about the large vessels were clearly demonstrated and found to anastomose with branches of the internal mammary arteries and other branches of the aorta. Through these anostomosis, injection of the coronary arteries under controlled conditions allowed the injected material to flow into the vasa vasorum of the thoracic aorta and pulmonary artery as well as into vessels of the parietal pericardium, diaphragm, pleural surface of the lungs, brachi, mediastinum, trachea and esophogus. Supplementing this study, Moritz (1932) reported extensive anostomosis between branches of the coronary arteries (especially in the fat pads around the coronary arteries) and the vessels supplying the parietal pericardium in four hearts where the pericardial cavity was obliterated by chronic adhesions.

Although it is clear that the intercoronary and the extracardiac anostomoses are present in various degrees in all hearts, their value in protecting against coronary disease of severe progressive nature is inadequate. Their potential significance, however, is indicated by the finding of hearts with extensively narrowed coronary arteries which have survived with considerable activity and cardiac reserve. In such cases,

it is surmised that the role of the intercoronary anastomoses, the thebesian vessels, and the extracardiac anostomoses must have been very active during life.

BLOOD SUPPLY OF THE CONDUCTING SYSTEM

The SA node in man is usually supplied by a large branch which enters the node and runs through its center while giving lateral branches which anastomose with vessels in the adjacent atrial muscle. This artery of the SA node is a branch of the artery of the ostium of the superior vena cava. In turn, this artery is nearly always a branch of the right coronary artery which arises near its ostium as one of the first arterior atrial arteries. These vessels ascends over the front of the right auricular appendage to reach the sulcus between the ostium of the superior vena cava and the base of the appendage on the roof and posterior wall of the right atrium. This pattern is present in more than 70% of hearts, and in 25% of the cases, the principal stem of the artery of the ostium of the superior vena cava arises from the end of the left coronary artery as a branch of the circumflex branch of the left coronary artery when it forms the posterior descending artery. In some of the other hearts, the artery of the SA node arises from both coronary arteries. The AV node is supplied by a posterior atrial artery supplying the posterior wall and portion of the atrial septum. This artery arises in about 92% of hearts from the posterior portion of the right coronary artery. The right stem of the AV bundle usually receives most of its blood supply from perforating septal branches of the anterior descending branch of the left coronary artery as they penetrate the

interventricular septum. The left stem is supplied by interventricular septal branches from both the right and left coronary arteries, chiefly from the anterior descending branch of the left coronary artery and some small vessels from the posterior descending artery, which is usually a terminal branch of the right coronary artery. The Purkinje fibers receives its blood supply from the various branches of the two coronary arteries supplying the myocardium of the area. (Roberts 1959).

CARDIAC CAPILLARIES

The capillaries of the heart are its most essential vessel, as they nourish the contracting muscle cells and the other tissue elements of the organ. The capillaries begin as small branches of the terminal arterioles which penetrate the fibrous sheath of muscle bundles, usually at a perpendicular or oblique angle. From the branching arterioles, a network of capillaries is formed which wraps the individual muscle fibers in a basket-like covering of small capillaries. The walls of the capillaries are in general smooth and are more or less parallel, as seen in longitudinal section. Most of the capillaries are filled with blood cells, one or two or more columns in width, as contrasted with the arterioles, which are usually empty. The number of capillaries visible in the uninjected heart is much less than the number visible after the heart has been injected by a relatively diluted material capable of penetrating such small channels. This method of completely filling the capillary bed was developed by Wearn (1928). Later, Roberts and Wearn (1938, 1941), injected a large number of human and animal hearts by such a method, finding out the average supply to be 3,342 capillaries per cu.mm. in normal adult human hearts which had an average muscle fiber diameter of 13.9 micra and

a ratio of one capillary for each muscle fiber. These findings were essentially the same in normal hearts of rabbits and dogs.

THE CORONARY VENOUS SYSTEM

The coronary veins, with the role of draining the cardiac capillary bed, are distributed throughout the heart in arrangements which more or less resemble those of the distributing channels of the coronary arteries.

The venous drainage systems of the myocardium are as follows :

(1) The superficial or subepicardial group which empties into the right atrium and consists of the anterior cardiac veins and the coronary sinus, together with associated veins emptying near its mouth, and,

(2) A deeper group of veins which communicate directly with the cardiac chamber.

The Coronary Sinus is the collecting channel for the large veins of the heart. This usually enters on the posterior wall of the right atrium through a somewhat crescentic opening measuring approximately 3 to 8 mm. in transverse diameter. Its tributaries; are the great, small and middle cardiac veins, the posterior vein of the left ventricle, and the oblique veins of the left atrium, all of which, except for the last are provided with valves.

The Great Cardiac Vein: This begins at the apex of the heart. It ascends in the anterios interventricular groove to the coronary sulcus, then turns to the left, passes round the left surface of the heart, and ends in the left extremity of the coronary sinus. It receives the left marginal

vein which ascends from the apex of the heart along the left border.

The Small Cardiac Vein begins at the inferior border of the heart near the apex and passes to the right to the coronary sulcus, in which it turns to the left, and ends in the right extremity of the coronary sinus.

The Middle Cardiac Vein begins at the apex of the heart and passes backwards in the posterior interventricular groove to end in the coronary sinus near its right extremity.

The posterior vein of the left ventricle lies to the left of the middle cardiac vein. It usually ends in the coronary sinus but may join the great cardiac vein.

The Oblique Vein of the left atrium is a slender vessel which descends on the posterior wall of the left atrium, and ends in the coronary sinus. It is a remnant of the embryonic left common cardinal vein and its continuous with the fold of the left vena cava.

VEINS OF THE HEART WHICH DO NOT END IN THE CORONARY SINUS

Minimal cardiac veins of Thebesius: These small vessels connect their orifices in the endocardial surface of the cardiac chambers with the venules, capillaries and sinusoids of the myocardium, and probably at times directly with small arteriolaminal vessels and arterioles. Many of them are short trunks which pass only through a very short distance of the endocardium after being the union of small tributaries in the subendocardium and inner few layers of the myocardium.

SIGNIFICANT DIFFERENCES BETWEEN CANINE AND HUMAN CORONARY ARTERIES

In man, approximately 50% of hearts have the right coronary

artery predominant; 30% have a balanced coronary circulation; and 20% have the left coronary artery predominant. The arterial pattern of the dog heart compares with the situation in man in which the left coronary artery nourishes about 85% of the heart muscle, supplying the whole of the left heart as well as portions of the right ventricle. (Schlesinger 1940).

In the dog there is a large constant artery penetrating the interventricular septum with smaller penetrating arteries entering the septum from the anterior and posterior descending arteries to join it. The canine septal artery originates near the bifurcation of the left coronary artery and enters the septum diagonally in an anterior-to-posterior and apical direction. In human hearts the blood supply to the interventricular septum is principally provided by 4 to 6 equally large branches of the left anterior descending artery.

The canine right coronary artery supplies most of the right atrium and the right ventricle, except the posterior directly adjacent to the interventricular sulci. It does not cross the crux of the heart, whereas the human right coronary crosses the crux in approximately 90% of cases.

The principal blood supply to the SA node in the dog is almost exclusively from a branch of the right coronary artery, originating from the lateral or posterior third. The left coronary artery supplies the atrio-ventricular node.

CHAPTER III

EMBRYOLOGY OF THE HEART AND THE CORONARY VASCULAR SYSTEM WITH SPECIAL REFERENCE TO THE RIGHT VENTRICLE

The organs of the vascular system are among the earliest to begin their development and appear to be the first to assume their functional role. During the first week of its existence, the human embryo relies for nourishment upon its meager inherent stores. After implantation within the uterus early in the second week, nutritive material and oxygen from maternal sources became available, but these must first traverse the surrounding trophoblastic wall, and then by diffusion, reach the individual cells. Rapid increase in size and complexity during the third and fourth weeks renders such processes as diffusion ineffective in distributing the materials necessary for continued growth and in eliminating accumulated wastes. Thus arises the need for an intraembryonic system for transporting metabalites, and, coincident with this need, the vascular system is established in its basic form during the fourth week of embryonic life. (Wilson 1959).

The earliest identifiable cardiac primordia are aggregates of splanchnic mesodermal cells that appear in the cardiogenic plate, beneath the coelom. They arrange themselves side by side as two longitudinal strands, each of which gains a cavity just as primordial vessels do elsewhere in the embryo. These thin-walled endothelial tubes lie within corresponding longitudinal folds of the splanchnic mesodium.

In the cranial half of the future heart the two endothelial vessels quickly fuse into a single tube and their individual mesodermal folds merge into a single trough-like fold which encloses them. As the anterior intestinal portal retreats in a caudal direction, thereby elongating the foregut, opportunity is offered for these paired cardiac primordia to join the median, unpaired portion, already formed. This they do in pace with the enlarging pericardial cavity which progressively incorporates the lateral coelomic canals. Thus the paired cardiac primordia merge progressively until the entire heart is a single organ.

In embryos with but few somites the heart is a simple tube within a tube. The internal, endothelial component is destined to become the actual lining layer of the endocardium; the external, thick covering gives rise to the myocardium and epicardium. Such a heart is suspended by a mesenterial attachment where the lateral margins of the mesodermal folds are reflected upon the ventrolateral sides of the foregut. This mesentery, named the dorsal mesocardium, is only temporary; it is lost before the heart has advanced greatly. A peculiarity of the mammalian heart, in contrast to other vertebrates, is that there is no ventral mesocardium. This is because the coelom arises very early from the coalescence of separate spaces and forms a complete cavity in the region of the heart before the head fold and heart as such begin to differentiate.

The Cardiac Regions: Even while the bilateral cardiac halves are merging, they each bear alternative dilations and constrictions which indicate the future atrium, ventricle and bulbus. The union of the bulbar and ventricular halves is complete in embryos with some nine somites, but

the atria are still paired sacs. Such a heart shows at first three divisions:

(1) The paired atria which receive blood from the primitive veins,

(2) The ventricles or chief pumping region; and

(3) bulbus cordis

Within the next day or two a fourth division, the sinus venosus becomes recognizable as a region distinct from the caudal end of the atrium. At the extreme cranial end of the heart it is convenient to distinguish a fifth division, the truncus arteriosus, which the bulbus continues as a canal that conducts blood into the aortic sac. (Arey, 1965).

Establishment of External Forms: Between the stages of seven and sixteen somites the heart becomes unattached except at its two ends. Extending through and beyond this same period the cardiac tube grows faster than the pericardial chamber in which it lies, and as a result the heart is compelled to bend. The method of asymenetrical growth is such that the entire tube is thrown first into a simple bend and then to a spiralled S. A continuation of this growth process drops the bulbo-ventricular loop still farther caudad and ventrad. At the same time the sinus venosus is drawn out of the septum transversum and its horns partially merge. Both the atrium and sinus shift in a cranial direction until both lie dorsal and cranial to the rest of the heart. This shift is caused by a more oblique position taken by the septum transversum.

These changes thus result in an essential reversal of the original cranio-caudal relation of the primitive parts of the heart,

in addition the venous and arterial ends are brought close together as in the adult. The growing atrium is now constricted dorsally by the sinus venosus and ventrally by the bulbus truncus. For this reason it can enlarge rapidly only in lateral directions, and in so doing forms a sacculation on each side which fore-shadows the future right or left atrium respectively. Meanwhile the right horn of the sinus venosus enlarges more rapidly than the left, owing to an important shift in the blood flow from the left side of the body across the lines, and the sinus itself comes to open into the right side of the common atrium.

As the bulbo-ventricular loop increases in size, the duplication of the wall between its two limbs lags in development and disappears during the fifth week. The result is the merging of the two into a single chamber, the primitive ventricle, which is separated from the atria by a deep coronary sulcus. At about the same time, the ventricle developes a median longitudinal groove that indicates the position of an internal septum already partitioning the unpaired chamber into two chambers. This external groove is the <u>interventricular sulcus</u>. Thus in an embryo of six weeks the heart exhibits the general external shape and markings that characterize it permanently. (Arey 1965).

<u>Establishment of Internal Forms:</u> In an embryo of 5 m.m., the heart contains three as yet undivided chambers:

(1) The sinus venosus, opening dorsally into the right dilation of the atrium;

(2) the bilaterally dilated atrium, communicating, in turn,

by a common atrio-ventricular with :

(3) the primitive ventricle which is beginning to incorporate the bulbus into itself.

Important changes, chiefly concerned with the elaboration of septa and valves, next follows leading to the formation of the four chambered human heart. These developments include:

(1) the partitioning of the common atrium into separate right and left chambers

(2) the division of the atrio-ventricular canal into two canals;

(3) the absorption of the sinus venosus into the wall of the right atrium, and of the pulmonary veins into the left atrium;

(4) the merging of the bulbus into the definitive right ventricle, and the longitudinal division of the bulbus and truncus into aorta and pulmonary artery;

(5) the partitioning of the single ventricle into right and left chambers;

(6) the histogenetic differentiation of the cardiac wall, including the development of valves.

The basis of the partitioning of the heart into right and left sides is largely laid down during the second month of development, but the final phases of this division and the rerouting of blood streams involved can not be completed until after birth when the placenta ceases to be the source of oxygen and lung breathing begins. In the separation of the primitive common atrium into right and left chambers two septa are directly involved. These on the basis of their sequential appearance, are commonly called <u>septum primum and septum secondum</u>. Starting as a crescentic

ridge on the dorsocepholic part of the atrial wall, the septum primum grows toward the atrio-ventricular canal.

At about the same time that this septum primum is making its appearance, the first indications of the impending division of the original common atrio-ventricular canal into a right and left channel become evident. Two local thickenings, one dorsally, the other ventrally located, appear in the walls of the canal. These thickenings are the endocardial cushions of the atrio-ventricular canal. Each cushion consists of a mass of embryonal connective tissue, of the type characteristically appearing in the developing heart at points where septa will fuse, or where elaborate connective tissue structures such as the cardiac valves are destined to be molded. During the sixth week of development the dorsal and ventral cushions are brought into contact with each other by their own growth, and fuse to form a common mass dividing the atrio-ventricular canal. There is then left between the concave margin of septum primum and the growing atrio-ventricular canal cushions a progressively diminishing opening known as the interatrial foromen primum or ostium primun.

While these changes have been occurring, the sinus venosus has been shifted out of the midline so that it opens into the atrium to the right of the newly formed interatrial septum. The heart is now in a critical stage of development. Its simple tubular form has been altered so that the four chambers characteristic of the adult heart are clearly recognizable. But there is as yet no division of the blood stream because there are still open communications from the right to the

left side in both atrium and ventricle. A little further progress in the partition, however, and the two sides of the heart would be completely separated. Were this to occur in the young embryo, the left side of the heart would become almost literally dry. An insignificant amount of blood from the undeveloped lungs is all that would enter it, for the sinus venosus into which systemic, portal and placental currents all enter has, as we have seen, come to open on the right of the interatrial septum. The partitions in the ventricle and in the atrio-ventricular canal do progress rapidly to completion but an interesting series of events takes places at the interatrial partition which assures an adequate supply of blood reaching the left atrium and thence the left ventricle.

Just when it appears that the septum primum is going to fuse with the endocardial cushions of the atrio-ventricular canals, closing the interatrial foramen primum and isolating the left atrium, a new opening is established. The more cepholic part of the septum primum ruptures to form the interatrial foramen secondum. The appearance of a second interatrial communication just as the initial one is closing is of fundamental significance, because the constant presence of an interatrial communication makes it possible for the left atrium to receive, without interruption, a contribution from the blood entering the right atrium. (Patten W. 1953).

Indications of the division of the primitive ventricle into right and left chambers appear at about the same time that the first interatrial septum becomes recognizable. Early in the second month the primary muscular part of the <u>interventricular septum</u> appears at the apex

of the ventricular bend and grows towards the atrio-ventricular canal cushions. For a time there remains an interventricular foramen between the crescentic margin of the interventricular septum and the bottom of the partition in the atrio-ventricular canal. The primary interventricular septum grows rapidly for a time and greatly reduces the size of the interventricular foramen. This reduced interventricular foramen instead of having its closure delayed until after birth, as is the case in the atrium, is closed surprisingly early. Normally all traces of the opening will have disappeared by the end of the second month. The final closure of the interventricular foramen is not, however, accomplished by the continued growth of the main muscular part of the septum. The last remaining opening is closed by a composite mass of connective tissue derived in part from the connective tissue margin of the interventricular septum itself, in part from the base of the endocardial cushions forming the partition in the atrio-ventricular canal, and in part from the conus ridges.

The involvement of the conus ridges in the closure of the interventricular foramen makes it necessary to take up at this point the partitioning of the truncus arteriosus, for the conus ridges are merely prolongations into the ventricle of the ridges which fuse to form the septum aorticum and thus divide the truncus into aortic and pulmonary stems. The partitioning of the truncus begins distally between the roots of the fourth and sixth aortic arches and progresses spirally back through the truncus towards the ventricles. As these ridges grow they cut more and more deeply into the lumen of the truncus and finally meet to form a complete partition, separately an aortic channel leading

into the fourth aortic arches and a pulmonary channel leading into the sixth aortic arches. The fact that these truncus ridges pursue a spiral course as they grow toward the ventricles account for the way the ascending aorta and the main pulmonary trunk twist around each other as they emerge from the ventricles. The same spiralling brings the aortic channel around into a position to receive the blood pumped by the left ventricle, and the pulmonary channel into a position to receive the right ventricular output.

The level at which the aortic and pulmonary valves develope may be regarded as the line of demarcation between the truncus arteriosus and the tapering ventricular outlet called the conus. In the walls of both the aorta and the pulmonary trunk three small pads of young connective tissue develope and bulge into the lumen. Gradually each of these buttonlike masses of intimal connective tissue becomes molded into one of the cusps of the semi-lunar valves of the aorta and of the pulmonary artery. During the later stages of development there is a further rotation of the aorta and the pulmonary stems about each other so that the aortic outlet is carried further to the right behind the pulmonary outlet than was the case at the time these vessels were first separated by the truncus septum.

The final closure of the interventricular foramen with subsequent complete partitioning of the ventricle, is accomplished by a mass of connective tissue derived mostly from the conus ridges and from the right tubercles of the atrio-ventricular canal cushions. This composite mass of connective tissue completing the interventricular septum is at first bulky and loosely organized. As the septal cusps of the atrio-ventricular

valves are molded and as the connective tissue itself becomes more highly differentiated, the interventricular septum at this point of final closure gradually becomes a thin fibrous sheet, known as the membranous part of the interventricular septum. The closure of the interventricular foramen establishes a four-chambered heart which is completely divided into right and left sides except for the valvular mechanism at the foramen ovale . (Patten W. 1953)

In order to discuss the partitioning of the heart in its logical sequence, certain things of less striking importance have been temporarily passed over, specifically the absorption of the sinus venosus into the wall of the right atrium and of the pulmonary veins into the left atrium.

In embryos of about seven weeks the superior vena cava has been formed to return blood from the head end of the embryo, and the inferior vena cava to serve similarly for lower levels of the body. Both vessels drain into the right horn of the sinus venosus. Between the sixth and eighth week the atria increase rapidly in size and the right horn of the sinus venosus, failing to keep pace, is taken up into the wall of the right atrium. By this absorption the superior vena cava of necessity drains directly into the cranial wall of the atrium, while the inferior vena cava opens into its caudal wall. Internally the absorbed sinal wall represents the region between the right sinal valve and the atrial septum; it is known as the sinus venarum and is characterized permanently by a smooth lining. The remainder of the atrium including all of the right auricle, gains a thick and uneven muscular wall.

The final relation of the pulmonary veins to the heart is also the result of an absorptive process through which the left atrium is markedly enlarged. In the embryos of about 6 mm., a single pulmonary vein drains into the caudal wall of the left atrium. This vessel bifurcates into right and left veins which in turn divide again, so that two terminal branches drain each lung. As the atrium grows, these pulmonary vessels are progressively drawn into the atrial wall. As a result, at first one, then two, and finally four pulmonary veins open separately into the left atrium.

EMBRYOLOGY OF THE CORONARY VESSELS:

The several phases in the known development of the coronary blood vessels are as follows :

(1) initial phase of nourishment and drainage of the predominantly spongy wall of the heart by sinusoids;

(2) development of the coronary veins by budding from the coronary sinus;

(3) development of the coronary arteries by budding of branches from the aorta;

(4) penetration of the developing compact myocardium by branches of the coronary veins and arteries;

(5) Compression of large sinusoids into capillaries with a few vestigial remains, as the spongy inner myocardial layer atrophies;

(6) union of some cardiac capillaries with budding regional lymphatic channels to form the cardiac lymphatic vessels. (Roberts 1959).

Phase 1 - nourishment of the heart is entirely by transcellular diffusion and by large sinusoids between the widely spaced muscle fiber trabeculae of the spongy myocardium which makes up practically all of the wall of the heart muscle during the first two or three weeks of embryonic life. These sinusoidal spaces enlarge, fuse and unit with each other resulting into the central hollowing of the pumordial cardiac tube. A sort of tidal circulation through these sinusoids and intertrabecular spaces occurs into which small capillaries open for both nourishment and drainage of the myocardium prior to the establishment of veins and arteries.

Phase 2 - deals with the formation of the coronary veins, by budding from the coronary sinus. Essentially the two cardinal veins (right and left) are involved in its development. In the embryo of about three weeks, the atrium and the sinus venosus becomes distinct chambers, and the two cardinal veins are drawn into the proximal end of the sinus venosus. The sinus venosus is then absorbed into the wall and lumen of the right part of the atrium, and the right cardinal vein follows the same fate. During this same period the left cardinal vein enters the right swelling of the atrium, just to the right of where the secondary interatrial septum is being formed. In the embryo of about the fifth week, the left cardinal vein becomes smaller as the right has become larger. As the large return of blood from the anterior left cardinal vein is lost by being shifted to the right side through the superior vena cava, persistence of the left cardinal vein is maintained by fusion of several of the small tributaries or buds with venous channels which have been developing as drainage channels for the sinosoidal beds of the myocardium.

The four chambered heart is nearly completed in embryos of about fifty days of age. Both superior and inferior vena cava empty directly into the right atrium, and the body of the sinus venosus has completely disappeared into the wall of the atrium. The left horn of the sinus, however, remains and empties into the right atrium near the termination of the inferior vena cava. The terminal portion of this horn will become the coronary sinus. Shortly before the appearance of the coronary arteries the cardiac veins, which drain into the coronary sinus, arise as endothelial buds from the sinus. By the 9th week of embryonic life the coronary veins grow rapidly along the sulci to attain virtually definitive distribution. (Wilson 1959).

Phase 3 - The development of the coronary arteries begins during the seventh week. At this time the coronary vessels are small channels with delicate endothelial lining, arising from the right anterior and from the left anterior part of the aorta. The right and left coronary arteries may arise approximately at the same time, but the left seems to branch earlier into its anterior descending and left circumflex branches. These two branches, as well as the right coronary artery, extend by endothelial budding into the anterior interventricular sulcus and into the left and right AV sulci to reach their permanent position. The smaller branches of the coronary arteries break up into the very rich bed of smaller penetrating vessels and capillaries found throughout the myocardium. Some of them make connection with the endothelium-lined spaces, sinusoids and intertrabecular spaces, forming the arterioluminal channels.

Phase 4 - is the penetration of the myocardium by the terminal budding branches of the coronary arteries and veins so as to communicate

with the capillaries and spaces in the spongy myocardium.

Phase 5 - this phase is characterized by the constriction of most of the intertrabecular spaces into capillaries and small sinusoids resulting in the presence of the accessory coronary vascular system referred to as the thebesian system, or the arterioluminal, arterio-capillary luminal, arteriosinusoidal luminal and venoluminal channels. Since these channels are the result of such a complicated embryogenesis, it is not surprising that their number, distribution and size are variable in the adult heart.

Phase 6 - this phase deals with the development of the lymphatic system in the heart wherein really very little is known. By inference these channels may develope somewhat as do others peripheral lymphatic vessels. After the formation of the primary lymphatic sacs and channels, by about the seventh week, extensions of the smaller channels from the primary sacs and channels take place by the growth of endothelial sprouts. These are at first solid and then, as they extend, become hollow to form lymphatic vessels.

CHAPTER IV.

THE PHYSIOLOGY OF THE CORONARY CIRCULATION

The solution of problems dealing with the coronary circulation depends upon the development of adequate preparation and methods, and the overcoming of instrumental difficulties. Such consideration should reveal, in part, the proper basis for the interpretation of past and future studies of the coronary system.

PREPARATIONS:

The objectives of studies of the coronary circulation are knowledge of :

(1) the determinants of coronary flow;

(2) determination of the oxygen uptake (Coronary flow X arteriovenous oxygen difference) by the myocardium;

(3) and the relation of the above to the work of the heart in states of normalcy, of increase or decreased stress, and of disease in man.

These objectives are far from being realized. (Gregg 1959).

Much information has been gained, however, from experimental preparations, in which the coronary circulation has been studied with the heart in various degrees of separation from the rest of the animal.

The use of the isolated, perfused heart by Langendorff in 1899, laid the groundwork for the understanding of the fundamentals of the coronary circulation. Originally the heart was suspended and the coronary arteries perfused under constant temperature and pressure with oxygenated saline through a canula in the aorta. Total venous return was measured by overflow from the right atrium and ventricle. With

this procedure, studies have been made not only in animal hearts, but also in human hearts, by Kountz et al (1932, 1934). To obviate the effects of cardiac contraction and thus reduce the number of uncontrolled variables, the perfused, quiescent or arrested heart was used by Wiggers in 1909, and the fibrillating heart by Katz, Weinstein and Jochim in 1935. In the different experiments, the coronary arteries were perfused under a constant pressure or with the naturally pulsating aortic pressure.

Morawitz and Zahn (1941) developed a canula for insertion into the coronary sinus via the right atrium. The flow through it was pressured to quantitate total venous return from the vessels of the heart. This investigation enabled the experimenter to study coronary flow with the beating heart in situ as well as in the isolated heart preparation. However, experimental work soon showed that the coronary blood drained by this channel represented only a fraction of the total coronary venous outflow. The reliability of the use of the method, therefore, depends upon the constancy of the fraction drained through the coronary sinus.

Other methods utilized to measure coronary flow are through the use of the Pitot tube, orifice meter, rotameter, bubble flowmeter, the thermostromuhr and most recently by the electromagnetic flowmeter.

The thermostromuhr is usually placed around the coronary artery, and its disadvantages is that it requires a surgical procedure for placement plus problems in its calibration with failure to distinguish forward and backward flow. Both the orifice meter and the rotameter have been used extensively in investigations, and the former has furnished information concerning phasic flow since, depending on the pressure gradient across an

orifice, it is sensitive to rapid changes both in volume and direction of flow; the latter which measures flow by its ability to elevate a suspended body in a vertical tube has been most valuable where determination of mean flow is desired. (Rowe 1960). The bubble flowmeter has been used in pharmacologic and physiologic investigations of coronary flow (Eckenhoff et al 1947) and the electromagnetic flowmeter has its advocates. As with any flowmeter the biggest problem will be its calibration, however, this disadvantage is offset by the tremendous advantage it offers, especially the electromagnetic miniature type.

Another method of note worth mentioning is the nitrous oxide (N_2O) method. This method has been widely used for determining coronary flow because of its ready application to the intact anaesthetized animal and to the unanaesthetized human. Certain basic problems are involved in the N_2O method of determining coronary flow, not the least of which is the procedure of cardiac catherization where a certain amount of apprehension on the part of the subject is natural. In addition, placement of the catheter in the coronary sinus may be difficult based on the anatomic characteristics of the thebesian and Eustachian values. There is a further disadvantage since the method requires a ten minute "steady state" to determine a single coronary flow. An even greater disadvantage is the fact that it is not possible to measure flow continuously.

BASAL DATA:

In the resting state the coronary data for dog and man agree. With the left ventricular cardiac work index approximately 3.5 to 4.6 kg.,

left coronary flow approximates 72 to 85 ml/100 gm. left ventricle per minute (Table 1). Although the heart can remove essentially all oxygen from the coronary blood in its passage through the myocardium, normally about two thirds is extracted with an arterio-venous difference of 12 to 14 ml. and a coronary sinus value of 4 to 5 ml. This extraction changes little with increased stress, signifying that the oxygen supply is well balanced with metabolic demands (Rowe et al 1956).

In the anesthetized dog, the circulation time from the central coronary artery to the coronary sinus approximates 4.5 secs. (Mena et al 1961). In normal patients the coronary transit time (with I^{131} injection) varies from 6.5 to 11 secs. Exercise and nitroglycerin which increase coronary flow (nitrous exide method) decrease the transit time (increased coronary flow velocity) while the valsalva maneouver, which increases the circulation time, decreases coronary flow. (Gregg 1950).

Oxygen uptake per 100 gm. left ventricle is 8 to 10 ml/min., of which a considerable portion occurs during diastole or the resting state. The resting metabolism (absence of heart rate, cardiac output, and arterial blood pressure) during cardiac arrest by vagal stimulation or potassium injection in hearts with perfused coronary arteries approximate 2.5 ml/100 grm. left ventricle per minute or about 25 to 30 per cent of that at the prior working level. The metabolism of the non-working (but slowly beating) heart, obtained by rapid exanguination is about the same, while that of the fibrillating heart is considerably greater. Oxygen consumption during systole averages about three times that in diastole for the same period. (Paul et al 1954)

TABLE I

NORMAL VALUES FOR CORONARY BLOOD FLOW IN THE DOG (ROWE, 1960)

Coronary Flow/Min./100 Gm. of left ventricle = 70 - 90 cc.

Oxygen Extraction/100 cc. of left coronary blood = 10 - 15 cc.

Work of left ventricle (CO x BP) = 3 - 5 Kg. - M./Min.

$$\text{EFFICIENCY} = \frac{\text{Work of Left Ventricle}}{\text{Energy Equivalent of Oxygen Used by Left Ventricle.}}$$

$$\times 100 = 15 - 20\%.$$

Various studies have indicated that the human heart metabolizes glucose, lactate, and pyruvate and fatty acids. Considerable variability has been noted in the relation of these substances to metabolism, but the reason for such variability has not been apparent. Nevertheless, it is concluded that under basal postabsorptive conditions about 35 per cent of the energy of the heart comes from the utilization of carbohydrates, 67 per cent from amino acids. (Bing 1954-1955).

Determinants of Coronary Flow:

Accurate estimates of the changes in the gross vasomotor state of of the coronary vascular bed are of prime importance to an understanding of the mechanisms which control coronary flow. As in any other vascular bed, the influences controlling coronary blood flow are comprised of both physical and chemical factors.

Physical factors: Coronary flow is related to the pressure difference (effective pressure) between the central coronary artery (identical to aortic pressure) and the right atrium divided by the sum of the viscous resistances to flow in the epicardial portion of the artery and in the peripheral coronary bed. (Gregg 1959). Viscous resistance to flow is determined by the static and dynamic effects of the viscosity of the blood and the bore of the blood vessels. Since the arterial resistance is negligible, the mean coronary diameter and hence flow are controlled by the effective intravessel pressure and by two peripheral mechanisms, active changes in the state of the small mass of intravascular smooth muscle built into the coronary vessels, and the mechanical or passive effect on flow exerted during ventricular systole by the large extravascular muscle mass around the coronary vessels.

Insight into the complexity of the integrating action of these three flow determinants has been obtained from recording of the peripheral coronary pressure and the phasic, or moment to moment changes, in coronary inflow and outflow in the epicardial arteries and veins. (Fig.5). At the onset of isometric contraction of the left ventricle, there is an abrupt decrease in the left coronary inflow (solid line) or even the appearance of backflow. With the rise in aortic pressure, forward flow increases initially and rapidly, only to decrease to a new intermediate level in late systole. With the onset of isometric relaxation, coronary flow increases significantly, peaking at early diastole and then declining progressively. The veloscity of coronary inflow differs somewhat from the estimated intramyocardial flow (dotted line). The deficit during isometric contraction is caused by the compressing action of the myocardium on the coronary capillaries, forcing blood into the superficial vessels. Early in the period of ejection, the flow excess is caused by the uptake of blood in the superficial coronary arteries; in diastole the excess is caused by the uptake of blood to fill the previously compressed capillaries. These demarcations of flow are much less obvious in the right coronary inflow pattern, which roughly resembles the prevailing aortic pressure curve. Thus, blood is flowing through the myocardium throughout the cardiac cycle, except possibly for a brief period in each systole in the left coronary artery. In the left coronary artery, the systolic rate of flow is less than that during disastole; in the right coronary artery, the systolic rate

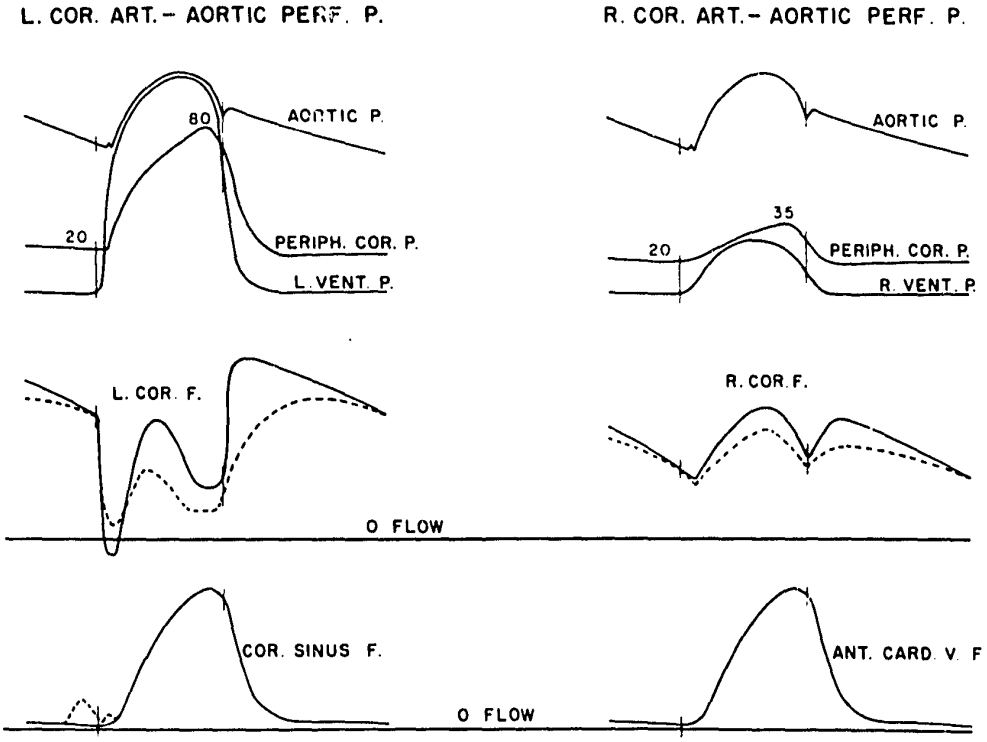


FIGURE 5: Series of curves relating variations in left and right coronary inflow, coronary sinus, and anterior cardiac vein flow to aortic pressure, ventricular pressure and peripheral pressure.

of flow equals or exceeds the diastolic. (Gregg 1959).

CHEMICAL FACTORS:

The chemical composition of the blood and tissue fluids within the heart has been found to be of great importance in determining the volume of coronary flow. Asphyxia, in which the carbon dioxide content of the blood increases and the oxygen content decreases simultaneously from cessation of breathing, is accompanied by a large increase in coronary inflow in the anaesthetized dog. Within thirty to sixty seconds after cessation of respiration, the flow in both systole and diastole increases averaging about 200 per cent, and occurs before any significant change in aortic pressure or heart rate. (Green et al. 1942). The coronary response to carbon dioxide increase and decrease pH is minimal as reported by Eckenhoff et al (1947); resulting into the conclusion that in Green's experiment the main chemical stimulus to the increase coronary flow was the anoxia, and not the hypercapnia.

Many dynamic functions of the heart such as increase in systemic blood pressure, cardiac output, cardiac work, heart rate, etc. will result into active coronary dilatation with increased coronary flow, and decreased coronary resistance. However, the best correlation of coronary flow is with oxygen consumption. This is so because, since normally most oxygen is removed from the coronary blood and the level of coronary sinus oxygen is fairly constant, the increased metabolic demands by the myocardium must be met by increased coronary flow. Therefore, the determinants of coronary

flow are also the determinants for oxygen uptake by the heart, and coronary flow must closely parallel oxygen consumption. (Alella et al. 1955, 1956; Case et al 1954; Katz, A.M. et al 1955; Sarnoff et al 1958b).

The preceding discussion suggests that an increase in metabolism (increased oxygen demand) and/or decreased supply of oxygen are the primary antecedents which give rise to active coronary dilation and increasing coronary flow. It could be that both are effective through a local hypoxia. This general pattern of active coronary regulation together with the indicated passive control is believed to operate in most states of increased stress.

REPONSE PATTERNS OF CORONARY CIRCULATIONS:

The heart and the coronary system may react in different ways to various primary stresses. The stresses conveniently divide themselves into those in which the work load of the systemic system is increased or is decreased.

(1) Coronary response to primary stress states generally resulting in increased cardiac activity:

Heart Rate: When the heart rate is increased considerably by electrical stimulation of the myocardium, aortic blood pressure, minute cardiac output, and work increase, while the stroke volume and the stroke work decrease. Simultaneously, minute coronary flow and oxygen usage increase, coronary resistance decreases, oxygen extraction is unchanged, but the coronary flow and oxygen consumption per beat decrease. Since acceleration of the heart means proportionally greater

time per beat and per minute in systole than in diastole and since in systole coronary flow is less than in diastole, it would be anticipated that increased heart rate per se should reduce coronary flow. Since it does not, it must be that increased flow is due to arteriolar dilatation from the increased metabolic activity. (Gregg 1959).

Transfusion: Augmentation of ventricular blood by increasing venous return and hence circulating blood volume through infusion has a dinical counterpart in the load placed upon the human heart by transfusion. The increasing coronary flow is partially explainable on a mechanical basis, since the slowing of the heart should increase coronary flow per beat and per minute by increasing diastolic time in which flow is greater.

Nervous Influences: No critical evidence has been adduced that stimulation of vagal fibers to the heart causes coronary flow changes not explainable on some other basis, such as a change in heart rate. However, stimulation of the cardiac fibers from a stellate ganglion increases mean left coronary flow as the resultant of a decrease in systolic flow and a large increase in diastolic flow. (Gregg 1959).

Exercise: It would be expected that exercise which increases cardiac work would stimulate the coronary circulation. In man and dog left coronary flow and oxygen consumption increase and the coronary arterio-venous oxygen difference does not change. (Lombardo et al, 1953).

Anemia: The coronary system participates actively in the circulatory adjustments to anemia. For hemaglobin values of 10 gm. or more, the systemic circulation is essentially unaltered and the compensation of the coronary system to the decreased oxygen - carrying capacity

is similar to that with hypoxia, that is, an increased coronary flow without change in oxygen uptake. When the hemaglobin valves reach to 6 or 8 gr., the response of the systemic circulation is manifested by tachychardia, increased cardiac output and a fall in peripheral resistance. The coronary flow may now triple, and oxygen uptake is considerably increased. The increase in coronary flow is related in part to the decreased blood viscosity and in larger part to the active dilatation associated with myocardial hypoxia, which, in turn, arises from the low hematocrit and from the increased metabolism.

Valvular Lesions : Acute elevation of right ventricular pressure by pulmonary artery constriction initially decreases right coronary flow, to be followed quickly by a maintained increase in systolic, diastolic and mean flow in the right coronary artery, and to some extent, in the left coronary artery. Upon release, right coronary flow temporarily increases still further. The coronary response to elevation of left ventricular pressure by aortic constriction central to the coronary ostia is similar to that with pulmonary artery stenosis. In both instances, the sustained flow increase indicates a dominant influence of active coronary dilatation over the increased mechanical flow - inhibiting effect of increasing extravascular compression which earlier was dominant. These maintained changes in the coronary circulation could well be the early response in the human being to gradual moderate stenosis of the corresponding valves. (Gregg et al, 1943, 1944).

(2) Coronary Response to primary stress states generally resulting in decreased cardiac activity.

Heart failure - The heart shares with other types of muscle the characteristic that an optimum exists beyond which further stretching reduces the force of contraction and leads to myocardial failure. Results available indicate that in human cardiac failure, coronary blood flow is slightly reduced and oxygen consumption per unit weight of left ventricle are normal for oxygen, carbon dioxide, glucose, lactate, pyruvate, fatty acide, amino acids and Ketones. (Bing 1954-55). However, when consideration is given to the usual cardiac hypertrophy and increased heart weight, there is noted a decrease in the amount of work performed per unit of oxygen consumed and a decrease in cardiac efficiency.

Shock - Oligemic shock in dogs is characterized during the hypotensive phase by a decrease in cardiac output, systemic blood pressure, cardiac work, stroke volume, stroke work, and by an increase in heart rate and an adequate central venous pressure. Coronary flow and coronary resistance are greatly decreased. Coronary flow is generally greater and the resistance generally less than can be accounted for by a simple decline in arterial blood pressure. (Opdyke et al 1947). At the same time the oxygen uptake decreases and the coronary arterio-venous oxygen difference is generally unchanged. (Hackel et al. 1955). With restoration to normal systemic blood pressure by reinfusion, coronary flow is greater and flow resistance is less than at equivalent arterial blood pressure in the pre-shock state, and the augmented flow is maintained after circulation failure subsequently intervenes.

Hypothermia: The associated changes that occur which tend to reduce the coronary flow are a diminution in blood and muscle temperatures, cardiac output, heart rate, cardiac work, oxygen usage by the heart, an

increased blood viscosity, and a great lengthened period of ventricular systole. Opposing these factors are the relaxation of the major coronary vessels, which is known to occur with hypothermia, and dilatation of the coronary bed caused by the hypotension per se. As a resultant of these determinants, coronary flow is decreased at low temperature. Myocardial function appears to be adequate. However, many hearts are apparently not too far from failure, because if total venous inflow occlusion (which decreases coronary flow close to zero) is now added to permit open cardiotomy, myocardial failure supervenes, as evidenced by elevation in mean right atrial pressure and post mortem findings. This trend can be reversed by perfusion of the coronary system with small volumes of oxygenated blood. (Lombardo et al. 1957).

Physiologic effects of Drugs on Coronary flow and myocardial metabolism.

The effects of and the mechanisms of action of different drugs have been studied by different authors in the isolated heart, fibrillating heart, heart-lung preparation, and heart in situ. It is not believed that these studies are significant except with the heart in situ, for not only can a drug have different effects on the hearts of two different preparations, but also many of the drugs have extracardiac effects on pulse rate and the metabolism of other organs, on respiration, and other activities of the body which may, in themselves, so alter the cardiac load or coronary vasomotor state as to overshadow the local coronary effect.

Drugs may be effective in changing the myocardial blood supply through alteration of the blood pressure and/or vasomotor state of the normal and collateral coronary vascular channels. In addition, certain of the drugs alter blood flow by modifying the vigor of cardiac contraction.

It is a simple matter to determine experimentally whether a given drug increases or decreases coronary flow with the heart in situ. Khellin, Papaverine, the nitrites, xanthines, acetylcholine, epinephrine, paradrine, coramine, histamine, all increase coronary flow, while pitressin decreases coronary flow.

Pitressin: Of the drugs used clinically this is the only one which decreases coronary flow by all methods of study, and increases the total peripheral resistance to flow, i.e., flow decreases in the presence of an increased central coronary pressure. (Green, H.D. 1940). The sustained reduction in coronary inflow occurs throughout the cardiac cycle following its injection into a coronary artery. It is believed that this drug acts by direct effect on the coronary arterioles, but a decrease in cardiac metabolism and vigor of contraction or an increase in extravascular support have not been ruled out as the cause of the flow decrease.

Nitrites and Xanthines: These drugs increase coronary flow by nearly all methods of study and in nearly all preparations. (Boyer et al 1941). This is based on the vaso-dilating effect of these drugs on the coronary vessels. This could arise from a direct effect of the drug on the coronary vessels, although a change in cardiac metabolism and work (decrease) cannot be ruled out as the cause of the flow increase.

Epinephrine and Acetylcholine: Since the generally accepted theory of autonomic nerve transmission is based on the liberation of acetyleboline and epinephrine-life substances, the coronary flow effects with these agents are of particular interest in connection with coronary innervations. In most dog preparations including the fibrillating heart,

heart-lung preparation, and heart beating in situ, intracoronary artery injection of epinephrine increases coronary blood flow. In the latter preparation, its effect on the coronary flow pattern is similar to that obtained during stimulation of cardiac accelerator nerves. There is also an associated increase in cardiac metabolism and in vigor of contraction. (Markwalder et al 1941). Regarding its dilating effect per se on the coronary vessels, the evidence is conflicting. In the small dose range (0.02 to 0.2 micrograms), a significant increase in coronary flow is seen without change in heart rate or blood pressure, which indicates a significant dilater effect on the coronary vessels. Thus initial flow augmentation might then indicate a direct dilater action on the coronary vessels, although even here, an early metabolic influence cannot be ruled out. At all events, with the larger doses most of the coronary flow increase can be due to the larte increase in cardiac metabolism.

Acetylcholine, intra-arterially, increases coronary blood flow in the dog. If the dose is properly chosen, this response in the heating heart occurs without a significant change in blood pressure or heart rate. The increased flow response is completely abolished after atropine. This drug then increases the mean bore of the coronary vessels, since the flow is elevated in the presence of a normal or lower central coronary blood pressure.

Opiates: Few studies have been made of the action of morphine and its derivatives on the coronary circulation. Papaverine increases left coronary inflow in the anaesthetized dog. (Foltz et al. 1948), while the blood pressure and heart rate may be unchanged or the former decreased. The cardiac work and metabolism are stated not to be increased by this drug.

CHAPTER V

THE PATHOLOGY OF CORONARY ARTERY HEART DISEASE

More people die of disease of the coronary arteries than of any other disease. As man's life span lengthens, the relative incidence of disability and of death from this cause continues to increase. It is encouraging, therefore, to note that increasing study is being devoted to the causes, treatment and prevention of coronary disease.

Galen (138-201 A.D.) first applied the name"coronary" to the larger arteries of the heart and Lobstein (1833) coined the term arteriosclerosis.

The first correct diagnosis of coronary thrombosis made during life and verified at autopsy was reported by Hammer in 1878; but the classic description of clinical coronary thrombosis with substantiation by autopsy findings was published by Herrick in 1912.

Coronary artery disease is characterized pathologically by intimal atherosclerosis producing narrowing of the lumen and frequently occlusion; physiologically, by a reduced oxygen tension of the myocardium resulting from a disproportion between oxygen supply and demand; and clinically, by variable manifestations ranging from mild chest pain to myocardial infarction, which may be followed by congestive failure or death.

CHANGES IN CORONARY ARTERIES ATTRIBUTABLE TO AGE

The principal change in the coronary arteries attributable to age is a thickening of the intima (Wolkoff 1929). The thickness of the

intima of the coronary arteries exceeds that of other muscular arteries and increases progressively with age. The considerable thickness of the intima of these vessels is related to the special mechanical factors, such as pressure and tension, to which these arteries are subjected. At birth the intimal layer is relatively thin, and consists of a single well-formed layer of elastic fibers which is covered by a layer of flat endothelium. In childhood the thickness of the intima is about equal to that of the media; during the third and fourth decades intimal thickness becomes maximal; in middle age and in old age the intima is several times as thick as the media. The thickening is brought about (1) by splitting off the internal elastic lamina from the internal limiting lamella, with formation of a musculo-elastic layer; (2) by splitting of the internal limiting lassella with formation of a prominent elastic-hyperplastic layer; and (3) by formation in most cases, on the inner aspect of the hyperplastic layer, of a layer of connective tissue. (Gould, 1953). Gross et al. (1934) demonstrated changes in the myocardial arteries which are related to age and to location within the heart. These changes, which they call fibro-elastic metamorphosis, consist of elastification of the media, elastic-hyperplastic changes in the intima, fusion of these two layers, atrophy of smooth muscle fibers and development of irregular patches of connective tissue. With respect to time and frequency of appearance these changes occurred earliest and most often at the following sites, in decreasing order; posterior papillary muscle of the left ventricle, interventricular septum, left ventricle, pulmonary conus and atria.

Eventually there results a gradual diffuse distension of the

coronary arteries both in a transverse and longitudinal direction, so that the vessels become longer as well as wider and assume a tortuous course. This results from progressive deterioration of the elastic tissue and is not accompanied by any characteristic histologic change. Thus during the average life span, the cross-sectional area of arteries increases six to seven times, and the number of macroscopically visible arteries is doubled. (Blumenthal 1959).

PATHOGENESIS OF ARTERIOSCLEROSIS

Much has been written regarding the etiology of arteriosclerosis but the problem is still unsolved. Blumenthal (1959) introduced the concept of response potentials of vascular tissue in the pathogenesis of arteriosclerosis. According to this concept, atheriosclerosis is regarded as a complex mixture of degenerative and reparative processes leading to increased rigidity, diminished elasticity and decreased caliber of arteries.

In general, etiologic agents capable of eliciting response of vascular tissue components fall into three categories.

(1) inflamatory,

(2) metabolic, and

(3) hemodynamic

In this section then, diseases of the coronary arteries are presented within this frame of reference.

Inflamatory Factors in Coronary Artery Disease: This falls into several groups, i.e. infectious, allergic, toxic, and those of unknown etiology. Infectious disease which may involve the coronary arteries are syphillis, tuberculosis, Brucellosis, typhus, typhoid and subacute bacterial endocarditis. In most instances of infectious coronary arteritis, the lesion probably results from a bacteremia.

In SBE, however, the lesion may be embolic in nature. As to allergic coronary arteritis, fatal cases have been reported following respiratory infections, antisyphilitic therapy, injections of serum, tetanus antitoxin, or typhoid vaccine, and due to drug hypersensitivity. Such fatal accidents may be caused by an acute swelling of the arterial intima (acute urticaria). It is conceivable that non-fatal cases of this type might progress to a stenotic sclerotic lesion of coronary arteries. Involvement of the coronary arteries in various collagen diseases has been observed, but frequently these involve primarily the more distal segments of the coronary circulation. Occasionally, the larger vessels may be involved in Periarteritis nodosa. Some forms of necrotizing arteritis are difficult to categorize from a pathogenetic point of view. They can be produced experimentally by a variety of substances, some hormonal, others chemical and possibly toxic.

The foregoing observations suggest that there is strong evidence that an inflamatory basis for coronary arteriosclerosis may be considerably more frequent than is generally realized. Whether such imflamatory lesions uniformly involve all such segments of the coronary circulation or only the intramyocardial portions remains in doubt. Nevertheless, severe involvement of the intramural channels may produce a peripheral resistance which might secondarily involve the larger coronary segments on a hemodynamic basis. (Blumenthal 1959).

Metobolic factors in Coronary Artery Disease: In recent years, lipid metobolic factors, particularly those associated with cholesterol metabolism, have received considerable attention in the etiology of coronary arteriosclerosis. Data to support this concept

fall essentially into the following categories:

(1) The presence of cholesterol and other lipids in atheromotous plaques in concentrations similar to those found in the circulating blood.

(2) The experimental production of atherosclerosis by the elevation of plasma lipids, including cholesterol.

(3) The increased incidence of atherosclerosis in various clinical states of hypercholesterolemia and hyperlipemia.

(4) The finding of quantitative, and possibly qualitative, differences from normal of plasma lipid transport in atherosclerotic individuals.

(5) A seemingly close relationship between intake of dietary lipids, including cholesterol, and the incidence of atherosclerosis in various population groups.

Experimental Atherosclerosis: Atheromatous vascular lesions resembling those of human atheroslcerosis have been produced experimentally in rabbits, guinea pegs, hamsters, pigs and chicken by feeding large quantities of cholesterol or animal fat. (Katz, L. 1953, Leary, T. 1934). A pronounced hypercholesterolemia precedes the development of the atheromotous lesions and is presumed to be the primary disturbance leading to intimal cholesterol deposition.

Many objections have been raised to the validity of applying these experimental observations to the explanation of human atherosclerosis. Attempts to produce atherosclerosis by cholesterol feeding in a variety of carnivorous or omnivorous animals have been very difficult and the distribution of atherosclerotic lesions in hervivorous animals differ from that in human atherosclerosis. The quantity of cholesterol fed to rabbits is proportionately far in excess of that usually taken by man,

and the resulting hypercholesterolemia has no counterpart in the majority of cases of human atherosclerosis. Atherosclerosis in man appears to be related more to the arterial reactions, degeneration and repair than to the level of serum cholesteral, which is the determinant in the rabbit. The lesions of experimental atherosclerosis in the rabbit and chiefly in the reticular-enothelial tissues and parenchymal organs are not as prominent in the coronary or cerebral arteries as in human atherosclerosis. However, some of the objection to any analogy between experimental atherosclerosis in rabbits and human atherosclerosis appears to have been overcome by the experimental production of generalized atherosclerosis in chicken by the subcutaneous injection of diethylstilbestral (Chaikoff et al 1948), and also in the rhesus monkey by maintaining pyridoxine deficiency (Rinehart et al 1954). This resembles human atherosclerosis, particularly in that the cerebral and coronary arteries are involved.

In general, proponents of the lipid metabolic theory believe that elevated serum lipid lead to a deposition of these substances in the intima and that this process initiates plaque formation. There appears, then, a clearly definable area in which lipid metabolic factors play a primary role; this includes familial hyperlipemia and hypercholesterolemia and certain other metabolic disease entities associated with a prolonged, almost continuous elevation in serum lipids. There is also another area in which the evidence for a primary role of lipid factors is at best only suggestive. To attribute all or most cases of coronary artery disease to lipid metabolic factors may tend to exclude a consideration of other, at least equally important factors.

HEMODYNAMIC FACTORS OF CORONARY ARTERY DISEASE

An analysis of hemodynamic factors operating in the coronary circulation offers the best prospect for accounting for the distribution of intimal plaques, if not also for their pathogenesis. The effects on arteries of such factors have been considered by some as reparative reactions to "wear and tear" injury and by others as compensatory in character, serving to maintain hemodynamic equilibriums. Serial studies on progressive phases through which intimal plaque developement proceed indicate that in the large majority of instances the lesion respresents a progressive response of vascular tissue components to hemodynamic forces, in which the appearance of lipids is a late development and may represent an incidental by product of the reactive process. In addition, the complications of thrombosis, aneurysm formation, and rupture are best accounted for on an hemodynamic basis. These important hemodynamic factors which deserve consideration in the development of arteriosclerosis of the coronary artery system are the following :

(1) blood pressure - hydrostatic tension;

(2) Cardiac thrust;

(3) Vibration;

(4) Gravity effect - static pressure;

(5) Flow characteristics

(6) Shearing forces (Blumental H. 1959)

The role of hemodynamic forces in the patherogenesis of degenerative vascular disease derives its strongest support from direct observations on human postmortem material along with a correlation with recognized physiologic phenomena. It suffers particularly from a

lack of experimental reproduction. In large part this is due to a difficulty in setting up experimental conditions which reproduce or intensify known operating hemodynamic conditions. This area of investigation needs considerable development. (Blumenthal 1959).

MACROSCOPIC APPEARANCE OF CORONARY ATHEROSCLEROSIS:

1. ATHEROMA. The first macroscopic changes occur in the form of yellowish minute (pin-head sized) spots of lipoid material visible beneath the intima, which are round and scarcely elevated above the surface. They were encountered by Wolkoff as early as the beginning of the second decade, and was also noted in one half of the subjects during the second decade of life, in two thirds of these during the third decade of life and in the coronaries of all persons after their fortieth year. The process, in general increases in severity with age.

2. FIBROUS PLAQUES. Beginning at about age thirty, the fatty spots, in part or whole, become covered by hyaline - like connective tissue, forming rounded or irregular plaques of white colour which encroach upon the lumen. Fibrous plaques may be encountered without accompanying lipoid deposits and in such cases one may not always be able to determine if the fibrosis was preceded by lipoid deposits or if it was a primary change. Duguid (1946) is of the opinion that not infrequently coronary thrombosis is followed by fatty degeneration, and that fibrosis results from the organization of the clot; in such cases Duguid believes that thrombosis may be a factor in the production of coronary atherosclerosis rather than a consequence of it.

3. CALCIFICATION. In later decades, the plaques become calcified, or they may show ragged ulceration of the intimal surface, frequently with

secondary thrombosis. In middle age or later, the main stems and main branches of the coronaries frequently show scattered plaques, often with points of narrowing of the lumen, particularly at sites of branching. At such points of constriction, thrombosis is favoured. Again there may be more or less diffuse atherosclerosis with thickening and rigidity of the wall, sometimes with calcification. Such rigid vessels often have narrow lumina; at other times the lumina are wider than normal, as a result of loss of elasticity, presumably because of age, and the vessels are tortuous. Thus, sclerosis may be focal or diffuse, present with or without narrowing of the lumen, and with partial or complete occlusion. (Gould 1953).

MICROSCOPIC APPEARANCE OF CORONARY ATHEROSCLEROSIS.

The primary and predominant lesions occur in the intima. There is uncertainty as to the very earliest lesions. According to Kletz (1915) and others the initial change is the presence of lipid-containing macrophages (foam cells) in the subendothelial layer of the intima. Shortly thereafter, if not simultaneously, there are deposits of lipoidal material in the ground substance of the intima as well as in the large mononuclear foam cells. The initial foci of lipid within and outside the macrophages coalesce to form lipid-rich intimal plaques. Vacuolar degeneration and swelling of the metachromatic gound substance and collagen framework of the intima are also observed in early lesions. According to Aschoff L. (1932), and others, these changes, including the deposition of mucoid ground substance, the formation of fibroblasts and collagen and the proliferation of elastic tissue, are primary and the deposition of lipids secondary.

Subsequent thickening of the intima results from a proliferation of reactive or reparative connective tissue, from increased deposition of lipids within and outside of foam cells, the formation of new capillaries, calcification and rarely bone formation. The internal elastic lamella may be displaced and fragmented. Sometimes it disappears while newly formed, delicate elastic fibrils arise in atherosclerotic plaque.

The changes which follow the initial internal lipoidosis and degeneration appear to represent attempts at repair or the consequences of disturbances in nutrition. Normally the intima receives most or all of its nutrition by imbibition from the arterial lumen. The deposition of lipid and the formation of new cellagen to repair the damaged intima result in significant thickening of this layer of the artery. In consequence, imbibition from the lumen, even when supplemented by that from the adventitial vasa vasorum, is inadequate to nourish all portions of the thickened intima. Newly formed capillaries arise in the intima, occasionally from the lumen but more frequently from the vasa vasorum (Gross et al 1934). From this viewpoint the intimal capillaries represent a granulation tissue type of reparative structure designed to compensate for local nutritional deficiencies.

Subsequent changes appear to be determined by the ability of these new nutritive channels to keep pace with increasing lipid and other degenerative changes and fibrosis. A deficiency in nutrition results in necrosis of the atherosclerotic plaque. The atheromotous plaque often causes an unilateral thickening of the vessel wall and an eccentric lumen. The atheroma may extend to the surface and rupture

through the intima emptying its contents into the lumen and producing an atheromatous ulcer. Later on calcium is deposited around the atheromotous focus as well as in the thickened fibrous hyalinized areas of the intima. (Friedberg, C. 1956).

Changes in the media are much less prominent and consist of atrophy of the muscular and elastic elements. This is probably the result of compression by the thickened intima. The atrophic changes produce thinning and sometimes almost complete disappearance of the medial layer of the artery. (Friedberg C, 1956).

The adventitial changes are less striking, but frequently irregular patches of fibrosis and focal collections of lymphocytes simulate inflamatory lesions. (Gerlis, L. 1956).

INCIDENCE AND LOCALIZATION OF CORONARY ARTERY OCCLUSION:

The ground work for the determination of the incidence and localization of occlusions in coronary heart disease was begun by Wolkoff in 1929 when he showed that only five out of one hundred and twenty hearts he studied exhibited more severe atherosclerotic changes in the right coronary than in the left. The breakthrough in this field, however, was based on the extensive work of Schlesinger (1938), and Schlesinger & Zoll (1941), documenting this different sites of occlusions and its predilection, by an injection and dissection study of 400 hearts. (Fig. 6.). These authors reported 2.5 occlusions per heart; the left anterior descending was involved in 39%, the main stem of the right coronary was diseased in 34%, and the left circumflex branch in 27% of cases. A_t the Royal Victoria Hospital, in a series of 150 cases studied in preparation for surgery by cine coronary angiography, a review of 53 cases showed 3.1 lesions per diseased heart (Vineberg 1966).

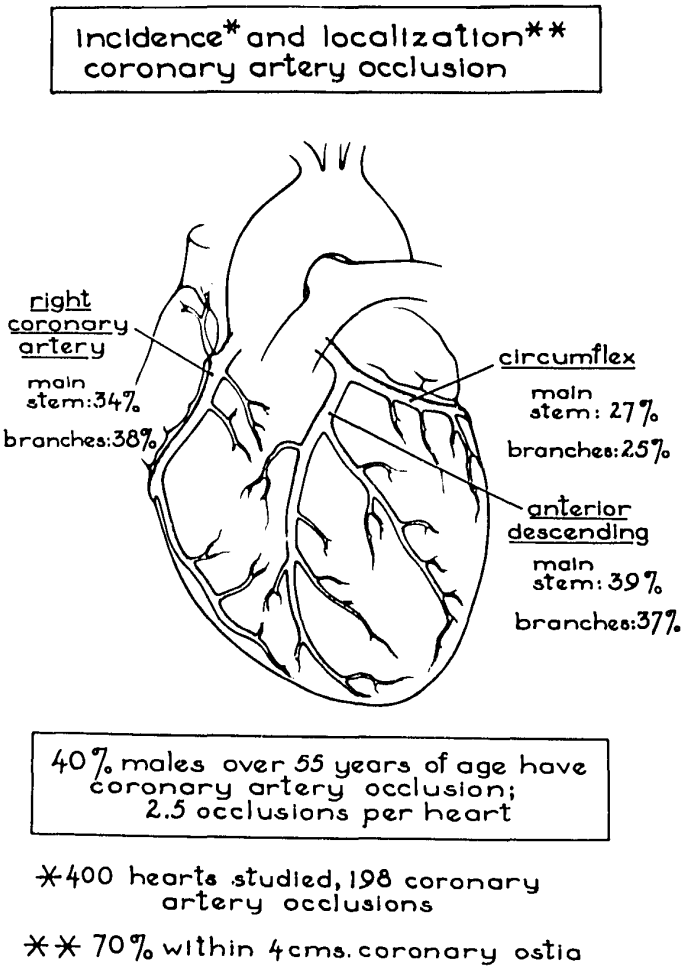


FIGURE 6: Diagram showing incidence and localization of coronary artery occlusion. In 70% of cases lesion is within four cm. of the major coronary arteries. The frequency of disease in the right coronary artery should likewise be noted. (Vineberg 1964).

Schlesinger & Zoll's original work showed that most zones of segmental occlusion were less than 5 mm. in length, 50% of them occurring within 2.5 cm. of the origin of the trunk, and 70% were localized to the proximal 4 cm., thus making it almost impossible for natural collaterals to form proximal to the points of occlusion. They also showed that the coronary arteries are mostly diseased in their epicardial courses, and that the vast myocardial network of arterioles lying within the myocardium are usually disease-free. It was also demonstrated that the coronary arteries supply definite myocardial zones. (Fig. 7), and that there are numerous arteriolar-sized branches running between these zones (Fig. 8). This type of communication between arteriolar zones or between arteries has been termed collaterals, and this exists in 9% of normal hearts, and in practically all diseased hearts. (Vineberg, 1964). From this study it is clear that coronary artery disease reduces the size of the total coronary inflow tract. The surgical treatment of coronary artery heart disease should be directed then towards this occlusive nature.

Schlesinger (1940) and others have also reported that 32% of hearts will show occlusion in the distal coronary artery branches (Fig. 9). Where there is coronary artery occlusion and where it has been shown that the proximal or main coronary inflow tracts are not diseased, these hearts will form intercoronary anastomosis and develope collaterals which will supply oxygenated blood to the ischemic zones made by the occluded distal artery (Vineberg and Walker, 1964).

MYOCARDIAL INFARCTION:

Myocardial infarction signifies the necrosis or death of

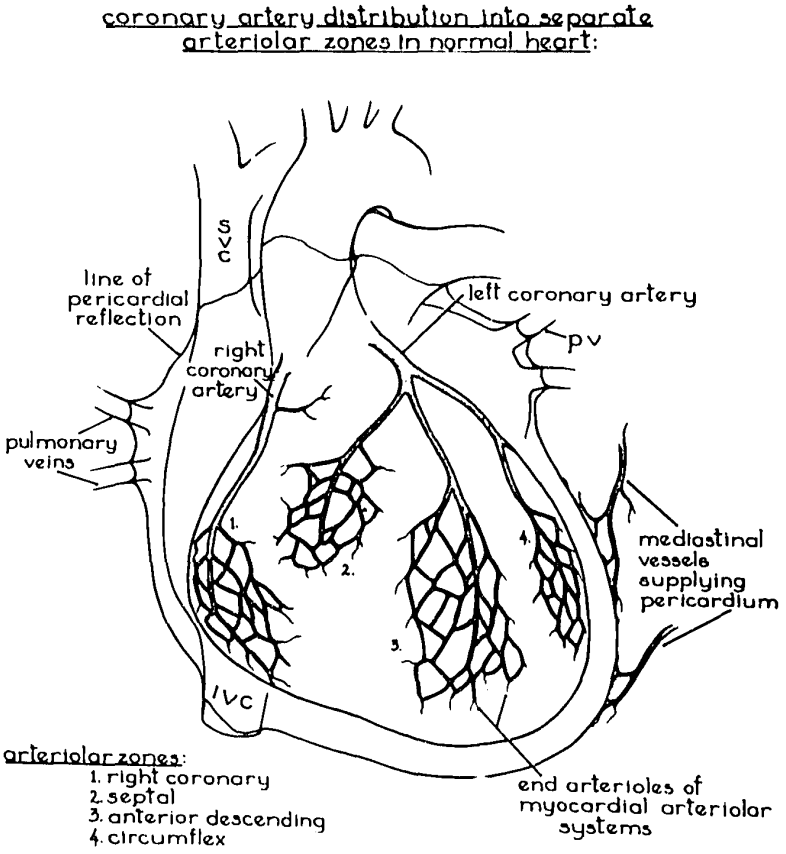


FIGURE 7: Diagram showing right and left coronary arteries dividing into arteriolar zones. (Vineberg 1964).

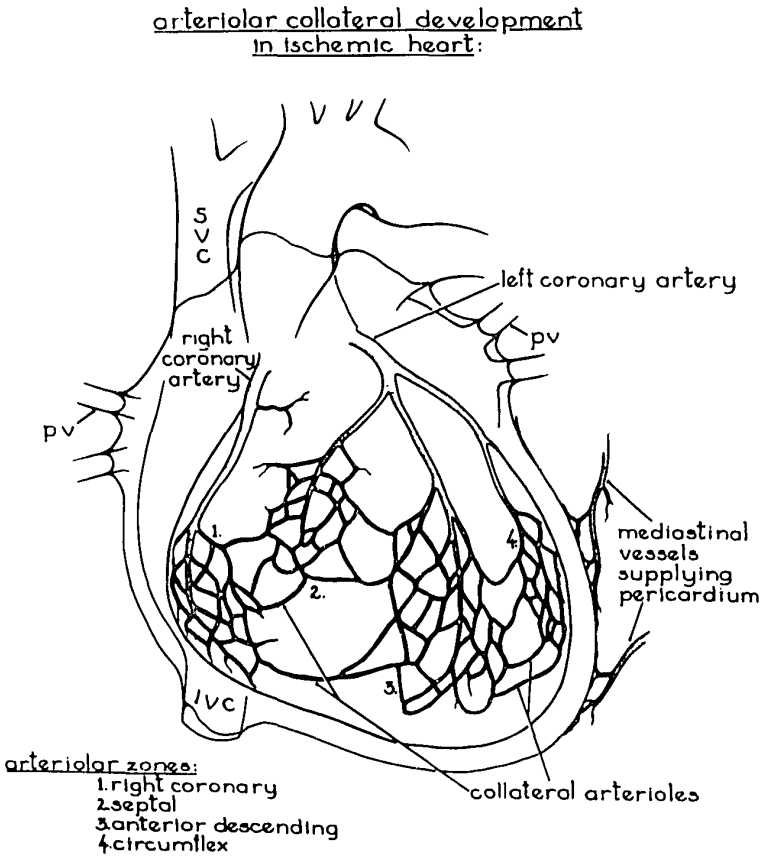


FIGURE 8: Diagram demonstrating the presence of numerous arteriolar sized branches joining arteriolar zones. These are collaterals that could be divided either into intercoronary or homocoronary anastomosis. (Vineberg 1964).

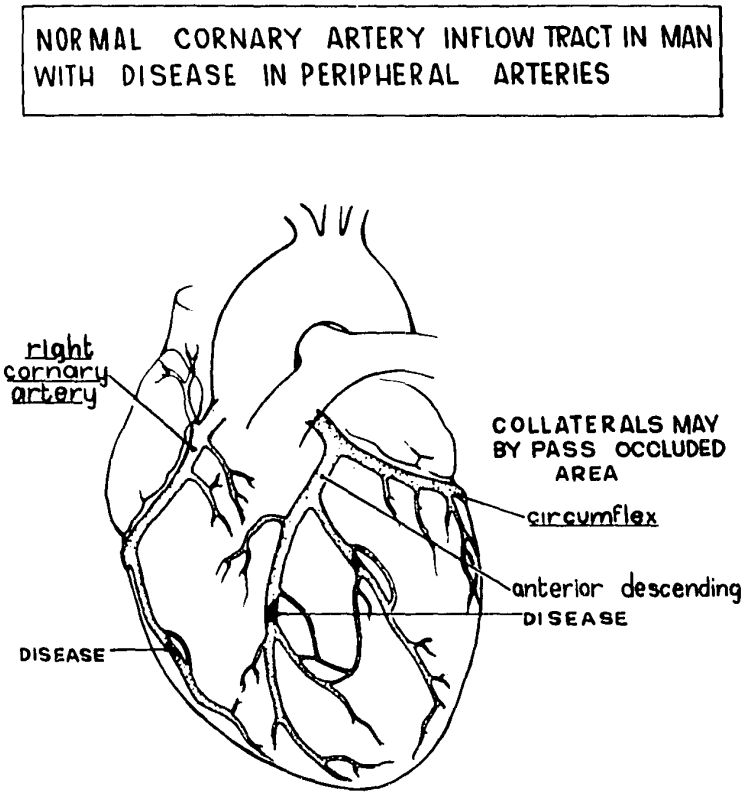


FIGURE 9: Diagram showing occlusion in the distal coronary artery branches. (Vineberg 1964).

a portion of heart muscle because of an interruption or curtailment of its blood supply. While it is usually the result of an acute coronary occlusion, infarction of the myocardium may also occur without mechanical obstruction of a coronary artery, following a sharp reduction in the volume or oxygen content of the coronary blood, due to circulatory or hematologic disturbances.

Gross changes ordinarily do not develope for five or six hours after an acute attach. The earliest change is a loss of lustre of the necrotic muscle. This soon becomes pale, dry and somewhat swollen. The border of the infarcted and living muscle is usually irregular. Within a day or two the muscle assumes a clay colour if the infarct is diffuse or a streaked yellow appearance if the infarct is patchy. The yellow color is explained by fatty degeneration of the necrotic muscle fibers and, at the border of necrotic areas, by infiltration with polymorphonuclear leucocytes, particularly within the first five or six days of the infarct. There may be considerable liquefaction necrosis with disappearance of many muscle fibers, thus accounting for much of the loss of thickness of the myocardial wall after healing of large infarcts. The border of the infarct may be reddish because of hyperemia of adjacent vessels or hemonhagic from extravasation of blood from these vessels; at the end of one week the reddish colour may in part be explained by young granulation tissue. After the first week or ten days, the border becomes depressed owing to the shrinkage following removal of neciotic muscle. The depressed zone becomes progressively wider and paler, and the granulation tissue is replaced by fibrous tissue, and after two or three months by a white scar (Gould,1953).

If the infarct extends to the epicardial surface a pericarditis developes which usually is largely fibrinous but may have some hemorrhagic or purvulent component; with survival of the patient, it heals by organization and scarring. If the infarct extends to the endocardial surface, a thrombus usually forms at the site. The resulting thrombus may cause narrowing of the lumen of the ventricle or the site of thrombosis may be marked by aneurysmal bulging of the ventricular wall.

In hemorrhagic areas of infarction involving a good portion of the thickness of the cardiac wall, there may be rupture of the wall with fatal hemopericardium. More often, however, infarcts undergo organization and are replaced by whitish scars, sometimes with a trace of pigment apparent. (Gould 1953).

MICROSCOPIC CHANGES IN MYOCARDIAL INFARCTION IN MAN.

Molloy et al (1939) described the microscopic changes in myocardial infarcts in the hearts of 72 persons in whom the onset of clinical findings enabled them to determine the age of the infarct. Their microscopic findings are summarized as follows :

1. Necrosis of muscle, connective tissue and smaller blood vessels. Necrosis does not become evident for 5 or 6 hours. The muscle fibers then become hyaline, while the striation become less evident; the nuclei undergo pyknosis, karyorrhexis or karyolysis.

2. Hemorrhage is usually focal rather than diffuse and extravasations are relatively rare. The venules and capillaries are hyperemic.

3. Fat varies in amount depending on the suddenness of infarction and previous sufficiency of circulation. Most of the fat is found at the periphery of the infarct. The fat is removed by the macrophages

at the same time as the necrotic muscle.

4. Infiltration with polymorphonuclears begins at about five hours, starting at the edges of the lesion and spreading centrally. It is present in the interstitial tissue and about the blood vessels and gradually extends into the secrotic tissue. At 24 hours, the infiltration is slight, with beginning degeneration of leucocytes; at five days many of the polymorphonuclears are necrotic, and thereafter they gradually disappear. Mallory et al (1939) suggested that the polymorphonuclears may produce an enzyme which aids in the breakdown and phagocytosis of the muscle.

5. Ingrath of blood vessels and connective tissue. Beginning on the 4th day new blood capillaries grow into the infarcted area, starting peripherally. Fibro blasts accompany the blood vessels into the infarcted area.

6. Removal of necrotic muscle. Infiltration by pigmintad macrophages. Simultaneous with the ingrowth of new capillaries and fibroblasts, macrophages invade and phagocytize the necrotic tissue. Occasionally giant cells may appear. After about ten days, one mm. of necrotic peripheral muscle has been removed, and after six weeks active absorption of necrotic muscle may still be present. At two months, necrotic muscle fibers have generally been completely removed.

7. Lymphocytes and plasma cells appear as soon as absorption of muscle starts, are fairly prominent during the third week and disappear about the same time as the pigmented macrophage.

8. Collagen, produced by the fibroblasts appear first at 12 days, is prominent at three weeks and maximum at two to three months. The amount of collagen provides a good indication of the age of the infarct.

9. Pericarditis. Fibrinous pericarditis appear within 24 hours. Organization of the exudate begins at eight days and is complete at four weeks. The pericardial reaction also provides a basis for judging the age of the infarct.

10. Endocardial thrombus. Thrombosis begins as early as five days but may occur much later. Its organization begins on the ninth day and complete organization may be present on the sixteenth day.

MYOCARDIAL INFARCTION WITHOUT CORONARY OCCLUSION:

Myocardial infarction without any evidence of coronary occlusion had been reported by several authors in the past. Bean in 1938 had a series of 300 myocardial infarcts, wherein 20% were associated with arterial narrowing but no thrombosis. In four hearts the coronary arteries showed no significant change. Gross and Sternberg (1939) reported that in 15 hearts with extensive infarction the coronaries showed insignificant intimal changes and scant narrowing of the lumina. It should be pointed out that in 13 of these cases the patients had associated hypertension. Wartman and Hellerstein (1948) in a study of 160 infarcted hearts found neither disease nor occlusion of the coronary arteries in 3.8 per cent, while Yater et al (1948) in a study of 114 hearts with gross myocardial infarct found 8 without any occlusion at all of the coronary vessels.

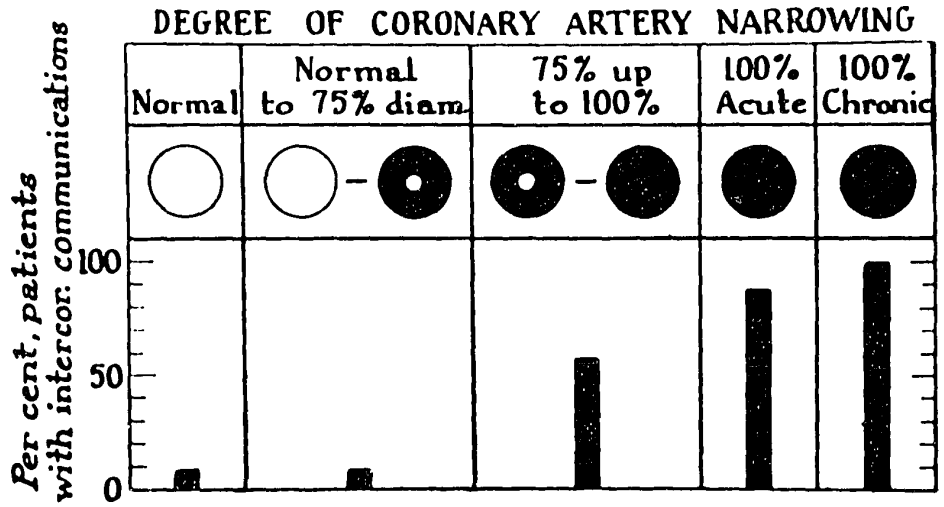
It has been postulated that infarction without coronary occlusion may be caused by a "relative" ischemia which may be temporary. In support of this view, it has been pointed out that in most instances they are associated with hypertension, a condition in which vasoconstrictor phenomena is prominent and in which myocardial hypertrophy has increased

the nutritional demands of the heart.

CORONARY OCCLUSION WITHOUT MYOCARDIAL INFARCTION

Blumgart et al (1941) explained the occurence of complete coronary occlusion as severe narrowing of one or more coronary arteries without evidence of myocardial infarction, by the slow progress of the obstructing lesion which allows sufficient time for the formation of an adequate collateral coronary circulation. Karsner (1949) stated that he has not observed infarction to result from gradual occlusion of the coronary arteries by arteriosclerosis. Holyoke (1945), by injection of the coronary arteries by Schlesinger's method found old occlusions in 11 hearts, in 3 of which no old infarcts were present; he also encountered five hearts with recent occlusions, two of which showed no recent infarction; Ravin and Geever (1946) demonstrated coronary occlusion in 18 injected hearts; in five of these eighteen, infarction was absent.

Such observations imply that the development of collateral coronary channels is a response to coronary artery insufficiency and diminished myocardial oxygenation. There is usually no significant formation of such collaterals until narrowing of the coronary arteries exceeds 75 per cent of the lumen diameter; at this point, about 58% of hearts have a demonstrable collateral circulation. With complete acute occlusion, the frequency is about 80 per cent, and with complete chronic (atheromotous) occlusion the incidence increases to 100 per cent. (Zoll et al 1951). (Fig. 10).



Presence of intercoronary arterial anastomosis in human hearts with various degrees of stenosis. (From Zoll et al. Circul. 1951.)

FIGURE 10: Diagram showing relationship of coronary artery narrowing to the presence of intercoronary anastomosis in human hearts.

CHAPTER VI

THE SURGICAL TREATMENT OF CORONARY ARTERY HEART DISEASE.

In myocardial ischemias and especially in coronary disease, some patients sustain severe myocardial damage and are incapacitated beyond the stage of satisfactory recovery. Surgery may offer these patients a chance for further rehabilitation which cannot be secured by non-surgical methods. During the course of coronary disease, a change from ischemia to hyperemia of the myocardium can give some protection from further serious damage by the ischemic process. Thus the value of surgery in coronary disease is chiefly that of rehabilitation, protection and the prolongation of life. (Thompson 1959).

A review of surgical interventions in coronary artery heart disease showed that the surgical efforts have been directed along several distinct and differing lines. They may be considered as : (Table 2)

(1) Efforts to relieve the anginal syndrome by interrupting the nervous innervation of the heart - cardiac denervation.

(2) Efforts to reduce the work load of the heart by reducing the bodily metabolism.

(3) Efforts to improve the vascularization of the heart by adding (a) a new source of blood to the myocardium or (b) to enhance the benefits derived from some of the remaining existing sources of myocardial nutrition.

CARDIAC DENERVATION: In the first or "symptomatic approach" beginning with Jonnesco (1920) an attempt was made to relieve angina by blocking

TABLE II

SURGICAL PROCEDURES FOR THE TREATMENT OF CORONARY HEART DISEASE

NEUROSURGERY TO BLOCK AFFERENT PAIN PATHWAYS

Cervicothoracic ganglionectomy - Jonnesco (1916)
Chemical nerve block - Swetlow (1926)
Posterior rhizotomy - Hoven and King (1942)
Pericoronary neurectomy - Fauteux and Svensen (1946)

REDUCTION OF GENERAL METABOLISM

Total thyroidectomy - Blumgart and Levine (1933)
Radioactive destruction of the thyroid gland

DEVELOPMENT OF COLLATERALS, ANASTOMOSES, OR BOTH

Ligation of cardiac vein - Fauteux (1940)
Ligation of coronary sinus - Gross and Blum (1935)
Bilateral ligation of internal mammary artery

DIRECT ATTACK ON DISEASED CORONARY ARTERIES

Resection and graft substitution of occluded coronary artery - Murray
Endarterectomy - Bailey (1957)

MYOCARDIAL VASCULARIZATION BY EXTRACARDIAC BLOOD

Surface grafts:
  Pectoral muscle - Beck (1935)
  Omentum - O'Shaughnessy (1936)
  Lung - Lezius (1937, Carter (1949)
  Lung and ligation of pulmonary artery - Liebow (1950)
  Pericardial fat pad - Vineberg (1954)
  Skin - Moran (1952)
  Jejunum - Key (1954)
Arterialization of coronary sinus - Beck (1948)
Cardiopericardiopexy:
  Bone chips, asbestos, etc. - Feil and Beck (1937)
  Talc - Thompson (1939)
Ventricular arterialization by vascular implants
  Internal mammary artery implant - Vineberg (1946-1957)
  Splenic artery implant - Liebow (1956)
  Carotid artery implant - Sabiston and Blalock (1956)
Graft from aorta to myocardium
  Single - Vineberg and McIntosh (1954-1957); Sabiston and Blalock (1956); Smith (1957)
  Double - Vineberg and Duchesne (1957)

the sympathetic nervous system which largely is responsible for mediation of pain sensation of cardiac origin. Danielopolu (1926), Coffey and Brown (1923), Mandl (1925, Swetlow (1926), and White (1935), have suggested various methods of surgical interruption of the cervical and dorsal sympathetic nervous system. Mandl has advised the use of procaine injections into the upper four or five dorsal sympathetic ganglia. Swetlow used alcohol injected paravertebrally along the first five dorsal nerve roots. Singer in 1927 suggested dorsal laminectomy and section of the posterior nerve roots for angina pectoris. Raney in 1939 advised surgical interruption merely of the upper thoracic preganglionic fibers (white rami communicantes) in order to avoid the production of Horner's syndrome.

While the relief of anginal pain afforded by the various procedures upon the sympathetics frequently is gratifying, it is also felt that an operation upon the sympathetic nervous system for the relief of angina pectoris essentially is only palliative. It would seem self-evident that the gross organic lesions associated with coronary atherosclerosis cannot be improved by interruption of sympathetic nervous pathways.

REDUCTION OF METABOLIC DEMANDS OF THE MYOCARDIUM.

The second surgical approach was aimed to reduce the work load of the heart by reducing the bodily metabolism. Obviously with a lessened oxygen need the limited myocardial and coronary reserve must become more nearly adequate. Therefore, Blumgart et al (1933) suggested total thyroidectomy in euthyroid patients in order to produce a great but controllable) reduction in bodily metabolism. The development of

myxedema can be prevented by careful management with hormonal products. Blumgart (1931) and Altschule and Volk (1935) showed both a reduction in the speed of blood flow and a diminution in the cardiac volume output incident to hypothyroidism. Eppinger and Levine (1939) showed that removal of the thyroid gland altered the response of the cardiovascular system to adrenalin injections which reliably could produce characteristic anginal episodes in patients with myocardial ischemia.

Destruction of the thyroid gland by X-Ray irradiation has been tried with the same objectives, but has never found much favour. Radioactive isotopes of iodine (I^{131}) have been recommended essentially for the same purpose by Blumgart et al. (1950).

Unfortunately, surgically or medically produced myxedema is commonly associated with hypercholesterolemia and this conceivably might cause the underlying arteriosclerosis to advance more rapidly.

In general it would seem that such methods of extreme reduction of body metabolism to reduce the work load of the heart, while perhaps theoretically sound, have the effect physiologically and psychologically of transforming an individual into an almost vegetative existence; at this point more or less this operation has been abandoned.

INCREASING THE BLOOD SUPPLY OF THE HEART:

Finally, many attempts have been made, in some way, surgically to increase the blood supply of the myocardium. The following surgical procedures have been attempted:

(1) Direct approach to diseased coronary arteries.

(2) Encouragement of the development of collaterals and/or anastomosis

(3) Myocardial revascularization by extracardiac blood.

The direct surgical approach is aimed at increasing arterial inflow through the coronary arteries by removal of the occlusive lesion or by deliberate resection of the narrowed (atherosclerotic) segment of the coronary artery and its replacement by a vascular graft.

Endarterectomy for myocardial ischemia was first advocated by Dos Santos in 1947. Absalon et al (1959) demonstrated the feasibility of performing an endarterectomy on the coronary arteries in the cadaver. May (1957) successfully performed coronary endarterectomies on animals without death or disability. May and Baily (1958) have reported six patients upon whom coronary endarterectomy was successfully performed. More recently successful reports of the same procedure were reported by Longmire and Cannon (1958), Sabiston (1960), Hallen, (1963), and Effler et al. (1964).

Murray (1953) has reported the deliberate resection of the narrowed segment of the anterior descending coronary artery and its replacement by vascular graft in five human patients. Acute ischemia of the segment of myocardium supplied by this vessel was prevented by perfusion of the distal portion of the vessel by way of a branch during the period of actual accomplishment of the surgery.

Inspite of these successful reports, there is still nevertheless a notably restrained enthusiasm in regard to this mode of treatment for coronary arterial disease. The limited extent of the clinical application of this direct approach for myocardial ischemia is in direct contrast to its widespread use in peripheral vascular disease. Yet it is neither a lack of patients who need relief of myocardial

ischemia nor a lack of qualified surgeons which has limited the acceptance of this procedure. The cause appears to be in the very nature of coronary disease itself and the technical problems peculiar to it.

DEVELOPMENT OF COLLATERALS AND/OR ANASTOMOSIS:

Development of collaterals and/or anastomosis as a means of increasing the blood supply to the ischemic myocardium was advocated by several investigators as another way to alleviate coronary insufficiency. The encouragement of the development of collateral and/or anastomosis solely should not, however, be considered a basic treatment but as only part of a procedure which distributes arterial blood to the heart without introducing extra-cardiac blood. (Vineberg 1959).

Robertson (1934) attempted to nourish the myocardium with venous back flow by experimental ligation of the cardiac vein. In 1937, Gross et al. ligated the coronary sinus in experimental animals in an attempt to cause congestion of the myocardium and to enhance its intrinsic vascularity in order to protect it against subsequent ligation of the coronary arteries. It was their hope that the vascular congestion consequent to ligation of this great normal venous drainage system would stimulate an overdevelopment of the normally existing communications between the deeper myocardial sinusoids and the cardiac chambers.

Subsequently Fauteux (1946), ligated the great cardiac vein in human patients in an attempt to alter favourably the course of coronary insufficiency. He reported his results in ten patients with precordial pain, seven of whom had returned to work. Ripstein (1948) analyzed the results of forty cases and reported that 72% of the group had benefitted from the procedure.

The effect of venostoris on the coronary system was investigated by Beck et al. (1941). They concluded that the beneficial effect did not justify clinical application. However, by 1954, Beck had employed the principle of reversal of venous flow in revising the Beck I operation. This procedure consists of partial coronary sinus occlusion, production of a sterile pericarditis, and grafting of mediastinal fat to the pericardium, and was designed to provide an equal distribution of the collateral blood supply to the heart (Beck 1957, 1958).

The bilateral ligation of the internal mammary arteries was first suggested by Fieschi in Italy in 1939, (cited by Battezatti et al, 1955), and employed in a number of patients with coronary artery disease by De Marchi and Associates (1959). This procedure was frequently combined with poudrage or retrosternal-neurclysis. The rationale of this operation is based upon the known presence of anastomatic channels between the pericardiophrenic arteries, arising from the internal mammary arteries, and the coronary circulation through the pericardial fat pads and pericardial reflections over great vessels. This anastomatic bed is capillary in nature. According to the proponents of this operation, bilateral ligation of the internal mammary arteries increases the rate of blood flow down the pericardiophrenic artery, thus causing the blood to flow into the coronary bed. Glover et al. (1951) employed this technique in the treatment of coronary artery heart disease, reporting relief of angina in 68% of the patients with an operative mortality of 7%. Sabiston and Blalock (1958) and numerous other investigators have demonstrated no evidence of value in bilateral internal mammary artery ligation. Even under special laboratory conditions permitting an increase in flow in the

ligated mammary arteries, no significant increase in retrograde coronary flow nor protection of the heart against coronary arterial occlusion could be demonstrated.

Final judgment with regard to this procedure must be reserved until clear cut evidence is shown that ligation of the internal mammary artery either does or does not convert the capillary pericardiophrenic-coronary anastomosis into arteriolar-sized communications. (Vineberg 1959).

MYOCARDIAL REVASCULARIZATION BY EXTRACARDIAC SOURCE:

The particular aim of this revascularization procedure is the bypass points of coronary artery occlusion by connecting an extra cardiac source of blood to the ventricular myocardium distal to these points of obstruction. Theoretically, this is a sound concept based upon the pathologic state that exists in human coronary artery disease. Practically, this has been a most difficult and perplexing problem, particularly in reference to :

(1) introduction of a volume of blood large enough to relieve myocardial ischemia,

(2) equal distribution of the extracardiac blood throughout the myocardium

(3) maintenance over months and years of the new extracardiac source of blood pathways. (Vineberg 1959).

Several procedures have been developed over the years trying to fulfill these three criteria, some failing, some partially successful. Our right internal mammery artery implantation to the right ventricular myocardium falls under this category of myocardial revascularization ----- by extracardiac source; the procedure was developed

with the particular aim to answer the criteria set forth above.

In reviewing the history of this particular type of revascularization we have to mention Beck who in 1929 experimentally produced a chemical pericarditis by the intrapericardial injection of Dakin's solution, but concluded that it was not safe for clinical use. Hudson and co-workers (1932), Moritz et al (1932), noted an increased extra-cardiac coronary anastomosis in four patients who had died of pericarditis.

In 1935 Beck produced a sterile pericarditis by mechanical abrasion of the epicardium and inner surface of the pericardium. The adhesions which developed between the two surfaces enhanced the anastomatic channels (Beck 1935(a), 1935(b), 1935(c), 1941, 1943). Thompson in 1939 reported the creation of cardio-pericardial adhesions by direct application of talc (Magnesium sillicate) to the heart. Similar reports were given by Thompson and Raisback (1942, 1949) and Dack et al. (1953). Schildt, Stanton and Beck (1943) had noted a consistent overdevelopment of the intercoronary anastomosis as a result of the instillation of powdered asbestos into the pericardium. They concluded that powdered asbestos, another sillicate, was superior to talc, to phenol and to all of the other substances tested for that purpose. Currently, the production of pericarditis is rarely employed alone, but more usually as an adjunet to some other procedure, such as ligation of the coronary sinus (Beck, 1955, 1958) (Beck and Brofman 1956).

SURFACE GRAFTS: Many types of tissue have been grafted to the surface of the left ventricle in the hope that these grafts would furnish the myocardium with a fresh extracardiac source of oxygenated blood.

(a) Cardio-omentopexy: O'Shaughnessy (1936) was the first to try cardio-omentopexy. In this operation a vascular flap of omentum was brought up through the diaphragm and affixed to the anterior surface of the left ventricle, where it formed anastomatic channels between the vessels of the omentum and the heart. At present this operation is no longer employed clinically.

(b) Pectoral muscle transplant to the heart: This procedure was advocated by Beck and Tichy in 1935. In this procedure the chest wall is opened, the pericardium incised, and a pedicled flap of the pectoralis major muscle and its vascular fat is sutured directly on to the heart wall. In his first group of 12 patients on whom he operated, Beck (1949) recorded a mortality of 50%. This dropped to 15% in his later series of 13 patients. The high mortality and the equivocal results have led nearly all surgeons to abandon this procedure. The incorporation of a direct artery or vein implant with the muscle offers better possibilities. Other substances besides the muscle may carry blood to the myocardium.

(c) Cardiopneumonopexy (Lezius): The principle of this procedure was to permit the heart to become adherent to the lung. Lezius in 1937 used the lower and the middle lobe of the left lung and grafted them to the myocardial surface in animals. He reported that if the heart became adherent tothe lung, sufficient collateral circulation, at times, developed so that when the coronary artery was ligated the animal did not always die. Carter et al (1949) used asbestos powder to produce vascular adhesions between the heart and lung. They were able to cut the mortality in dogs following a ligation of the anterior

descending branch of the left coronary artery to nearly 1 in 3 if the cardiopneumonopexy had been performed. Reismann et al. (1950) established the communication by suture graft. Both Lezius and Carter demonstrated blood vessel channels between the pulmonary and coronary vessels, but information concerning the direction of blood flow, the volume of blood delivered through the new channels and the direction are not available. Garamella and associates (1956) performed experimentally, a segmental resection of the lung, debrided the epicardium with 30% acriflavine, then grafted the pulmonary segmenal cleavage surface to the myocardium. Based on reports that ligation of the pulmonary artery would increase flow of the bronchial artery, Kline and associates (1956) occluded the left pulmonary artery before producing adhesions between the lung and myocardium with the application of silver nitrate.

(d) Pericardial Fat Pad Grafts: In this operation, the medial diaphragmatic and phrenic fat pads are detached from the fibrous pericardium. The epicardium covering the surface of the myocardium is then removed by sharp dissection and the fat pads are applied to the surface of the heart. It has been shown by Vineberg et al (1954) that in the partially ischemic heart, arteriolar communication develops between the grafted pericardial fat pads and the coronary circulation. Vineberg also showed that in one patient, 18 months after operation, retrograde injection of the circumflex artery revealed the injection mass to enter the diaphragmatic fat pad.

(e) Skin Pedicle and Jejunuh Grafts: Other surface grafts which have been attempted experimentally include a skin pedicle graft described by Moran et al (1952) and a jejunum graft by Key et al (1954). An isolated loop of jejunum with its blood

supply intact was delivered through the diaphragm, its mucosa stripped and the denuded surface sutured to the myocardium. Key reported that 75% of the jejunal pedicle vessels were open, with 61% anastomosis between the jejunum and the coronary vessels. The type of anastomosis was almost capillary, but they suggest that the amount of blood delivered through multiple capillary anastomosis would equal that produced by several small arteries. Baronofsky (1954, 1956) and Hannon and Baronofsky (1956), modified Key's technique by suturing the free end of a Roux-y-jejunal segment to the heart muscle. The jejunal graft is probably too major a procedure to be used in the treatment of human beings with coronary artery disease since it involves - as in cardio-omentapexy - an abdeminothoracic approach.

ARTERIALIZATION OF THE CORONARY SINUS:

Batson (1931) demonstrated that the heart can be kept alive and beating in an isolated state by perfusing it through the coronary venous system. This has been corroborated by many workers and led to the idea of anastomosing an artery to the coronary sinus, first described by Roberts et al (1943), using the subclavian, brachiocephalic and innominate arteries.

Beck (1948), after a considerable period of animal experimentation, finally developed a reliable surgical technique, by which the coronary sinus can be arterialized utilizing a vein graft to unite the sinus with the aorta. By incompletely ligating the coronary sinus close to its ostium at a subsequent operative stage, a sizable portion of the shunted blood may be directed into the myocardium by retrograde flow through the tributaries of the coronary sinus. There

was a 3 to 6 weeks interval between the two operations, and this procedure became known as the Beck II operation. Seven patients with coronary artery insufficiency were operated upon, with quite a high mortality. The Beck II operation has been given up by Beck and by others because of its high mortality and because it was shown by Eckstein et al (1954) that retrograde perfusion of the coronary bed or through the graft lasts for about five weeks and then looses functional contact with it, probably because of obliterative venous change caused by high arterial pressure in the venous bed.

VENTRIBULAR ARTERIALIZATION BY VASCULAR IMPLANTS

With the anatomico-pathological facts of coronary heart disease based on Schlesinger & Zoll's (1941) findings, Vineberg in 1945 attempted to graft a large systemic artery into the left ventricular myocardium. This was the very first attempt in such a kind of revascularization procedure. The artery chosen was the left internal mammary artery. He proposed then that if such an artery could be grafted into the left ventricular myocardium, then any blood descending through it into the arterioles of the myocardium should bypass the points of coronary artery occlusion. (Fig. 11). Several years were spent in overcoming initial difficulties such as angulation, scarring and answer to the question why some arteries are patent and why some are not. Thus, the internal mammary artery implant operation underwent five years of laboratory testing from 1945 to 1950, before human application. (Vineberg, 1946, 1950), (Vineberg and Jewitt, 1947).

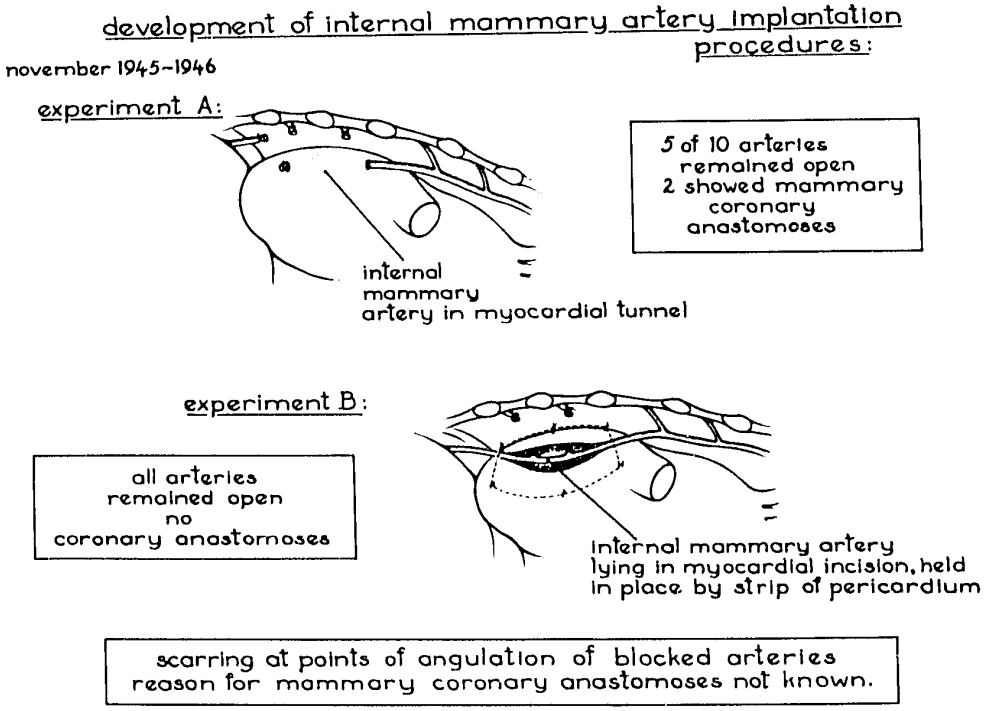


FIGURE 11: Diagram showing the first two attempts at transplanting the left internal mammary artery into the left ventricle. (Vineberg 1964).

The internal mammary artery was detached from the chest wall between the 6th and 4th interspace, divided between ligatures, and the proximal end buried within a tunnel made in the myocardium. In its new location the transplanted vessel remains open because of side branches which are left open at the time of implantation and which bleed into vascular spaces surrounding the internal mammary artery within the tunnel. (Fig. 12). The implanted vessel commences to bud at the end of 12 days and between 3 and 6 weeks it sends out numerous arteriolar or larger branches which anostomose with the surrounding arteriolar network lying within the myocardium. These findings were all shown by digestion cast studies. This digestion cast studies were made by injecting the implanted internal mammary artery with a vinyl plastic from 10 days to seven months postoperatively in the dog. (Vineberg 1964). The results of this cast studies disproved totally the theory of Glenn (1950), who reported a modification of the implant operation, leaving the end of the artery open in the myocardial tunnel. He then suggested that the branches from the implanted internal mammary artery were granulation tissue which tended to disappear within six weeks.

It has been shown both in animals and in man, that where there is myocardial ischemia the implanted vessel remains patent and does not close off by intimal proliferation when studied 9 months to 3 years after implantation. (Vineberg 1959).

Regarding those who reported blocked arteries, such as Bailey and Neptune (1955), in a study of 18 animals, Vinebergs technique

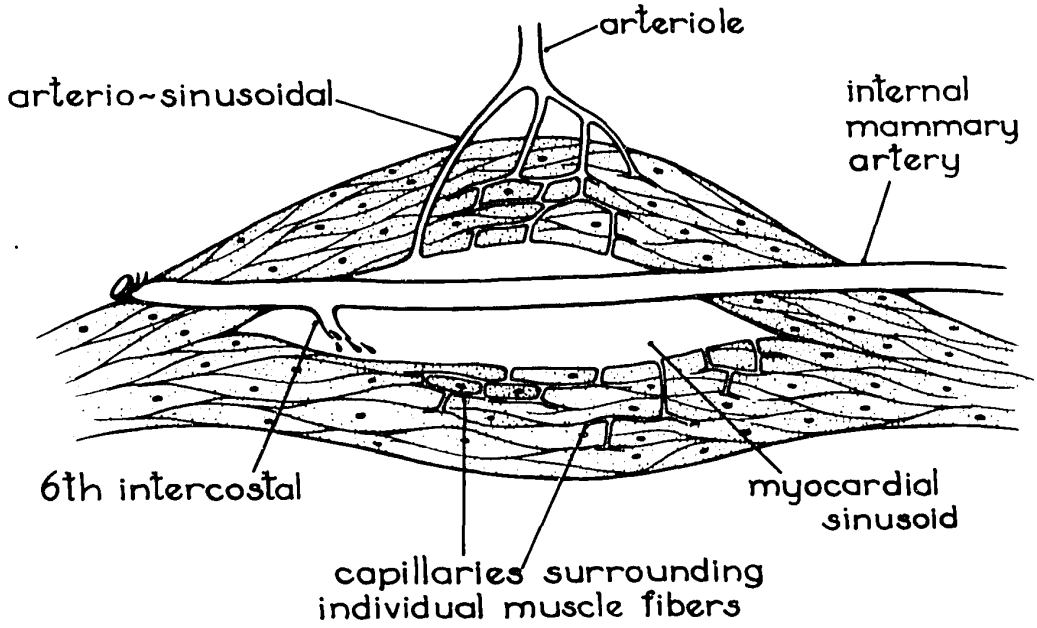


FIGURE 12: Schematic illustration of the internal mammary artery implant with open side branch. Initial runoff from the implanted artery enters the myocardial sinusoid. (Vineberg 1958).

of implantation was not carried out and myocardial ischemia was not produced. Many workers have since confirmed his work (Sabiston 1957) (Fuquay et al. 1955).

Measurement of blood flow through implanted internal mammary arteries five to seven months after implantation was studied by Buller (1950). It was found that up to 55 cc. per minute were delivered from the coronary sinus. (Vineberg and Buller (1955), Vineberg et al(1955).

TREATMENT OF HUMAN CORONARY ARTERY HEART DISEASE BY INTERNAL MAMMARY ARTERY IMPLANTATION.

The treatment of human coronary artery insufficiency by internal mammary artery implantation started in April, 1950. Since then Vineberg has operated upon 94 patients (Vineberg and Walker 1964). The results in patients who had no angina at rest, without exciting cause are most satisfactory. (Vineberg 1964). In the favourable group, there are 75 patients, of whom 63 have been followed for six months to 12 years. In the first four years, there was an operative mortality of 25 per cent. During the past 8 years, 63 consecutive patients have been operated upon with two operative deaths, or a mortality of 3.2%.

Thus, the Vineberg series of 63 patients followed up six months to 12 years, 64% were improved and 75% returned to work. Their figures are rather close to those obtained in experimental animals in which 71% mammary-coronary anastomosis occurred. (Vineberg 1964).

Vineberg has studied 16 human hearts from 60 hours up to four years post-operatively, after internal mammary artery implantation. In this series there were 11 implanted arteries widely patent (68%), which is close to the number of patent arteries in animal ischemic hearts. Four of these were patent when examined one and a half to four years after

surgery. Two living patients have recently shown by cine angiography to have patent arteries branching in the myocardium, 7½ and 10 years post-operatively. Both are well and pain free. (Vineberg 1964).

There has been modifications of the standard Vineberg implant operation (Fig 13 (a) and 13 (b)). One of these has been made by Sewell (1962) who implants the internal mammary artery along with the vein and some chest wall tissues into the myocardial tunnel. Sewell implants the artery with the vein and claims that the vein helps to keep the artery open. It has, however, been found that there is no communication between the artery and vein at any time after implant and that the internal mammary vein became blocked within a few days after implantation. (Vineberg and Walker 1964). Another modification has been made by Effler (1963), who uses a longer myocardial tunnel - Effler's Myocardial Tunnel - into which he implants the internal mammary artery, are from one and one half to two inches long, whereas the tunnel made for the standard Vineberg implant operation is one to one and a half inches long.

Other modifications with more or less similar results have been obtained by Bloomer and Liebow (1964) when they implanted the splenic artery into the myocardium and by Sabiston and Blalock, who have implanted the carotid artery in animals. Smith and McIntyre (1958) reported the implantation into the myocardium of prosthetic grafts from the aorta. This last technique has been submitted to clinical trial in two instances with seeingly good results, but Sabiston and Fonkalsrud (1958)

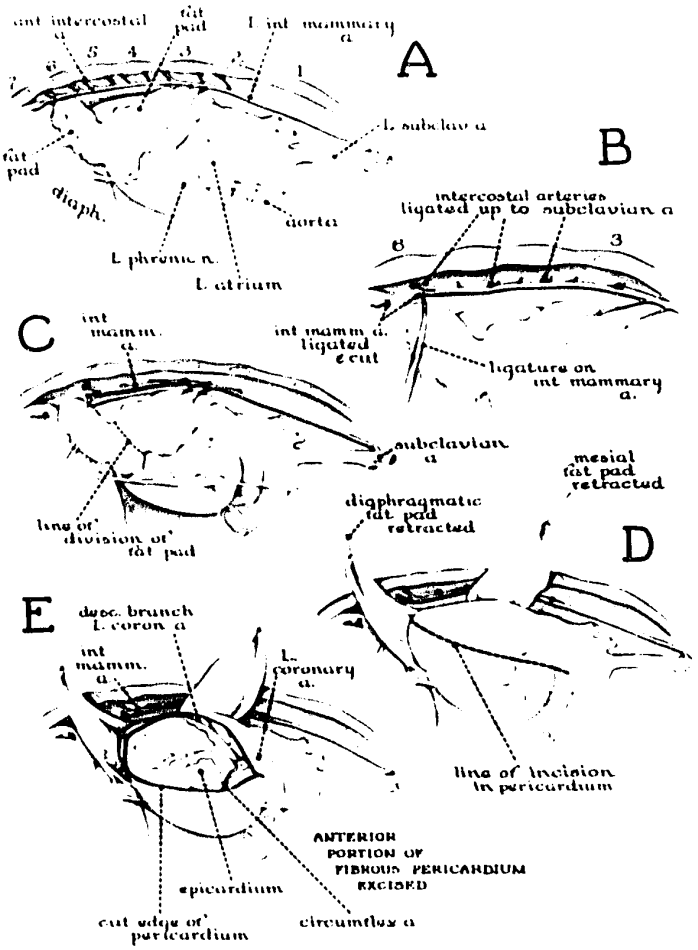


FIGURE 13(a): The Vineberg internal mammary implantation and the ivalon sponge operation for coronary artery heart disease.

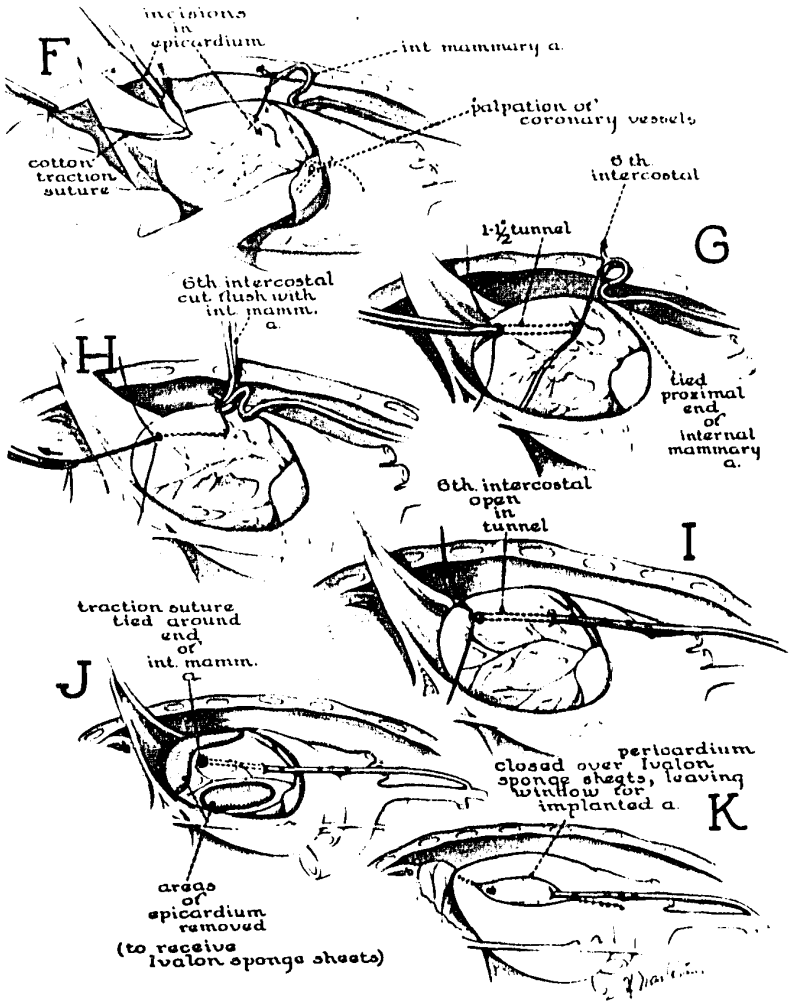


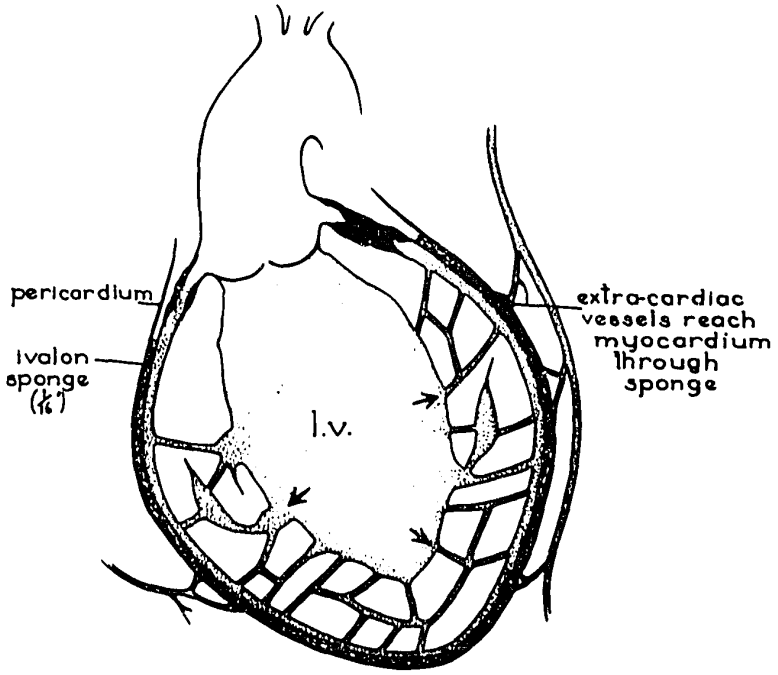
FIGURE 13(b): The Vineberg internal mammary implantation and the ivalon sponge operation for coronary artery heart disease.

found that in dogs, the graft became impervious after 44 days.

IVALON SPONGE OPERATION: This operation was introduced by Vineberg and Delyannis in 1958. The operations consists of removal of the epicardium (epicardiectomy), suturing strips of Ivalon Sponge to the bared myocardium removing the serous pericardium, and finally closing the pericardium. The principle of the operation is based on the syphoning action of the Ivalon Sponge and epicardietomy, wherein oxygenated blood from the left ventricular lumen is syphoned into the left ventricular wall. (Vineberg and Becerra 1961). (Figure Number 14). . The hydrostatics of the myocardial circulation is markedly altered when there is narrowing of the coronary inflow tract. Multiple myocardial vascular spaces are emptied by ventricular systole. During diastole, because the coronary inflow tract is constricted a comparative vacuum is left unfilled within the myocardial spaces. Removal of the epicardium loosens the myocardial structure and encourages syphoning of blood from the left ventricular lumen.

The Vineberg Ivalon Sponge operation underwent $3\frac{1}{2}$ years of laboratory testing before human application in a case of ventricular failure caused by coronary artery insufficiency (Vineberg, 1964). Thirty patients have undergone the Ivalon Sponge operation, with three deaths, a 10% mortality. The majority of these patients appeared to be hopeless at the time of operation. Two thirds had chronic ventricular failure, and over two thirds also had had two to four myocardial infarctions. Of these patients, 80% showed post-operative improvement which is similar to the percentage of animal survivals from ameroid constriction after

d. Vineberg sponge operation:



blood from ventricular lumen siphoned into myocardium.

FIGURE 14: Diagram demonstrating blood from the ventricular lumen syphoned into myocardium in the ivalon sponge operation.

sponge operation. Likewise reduction in heart size has accompanied the improvement. (Vineberg 1964).

VINEBERG'S TRIPLE OPERATION: (Epicardiectomy, Sero-Pericardietomy, Free Omental Graft and Left Internal mammary artery implantation.)

Again, this operation has been extensively tested in the laboratory before its clinical application. Vineberg noting the limitation of the internal mammary artery implantation operation, decided to look for a combined procedure that will revascularize not only the left ventricle, but also the right ventricle or posterior ventricular wall. Kato (1965 showed in 94 experimental animals that the free omental graft operation (Fig.15) plus epicardiectomy, sero-pericardiectomy and internal mammary implantation produced the best results with regards to the survival rates and prevention of the ischemic damage of the myocardium under the triple ameroid coronary occlusion test (100% lethal test used in control animals). Following this combined operation 80% of the animals so treated survived; in 73% of these survivors no gross or microscopic evidence of myocardial fibrosis was found. Injection studies in the surviving animals demonstrated that anastomoses had been established between the vessels of the omental graft and those of the mediastinum, pericardium, aorta and chest wall on one side and those of the coronary system on the other. The mediastinal, pericardial, aortic, and chest wall omental and omental-coronary anastomoses were so extensive that not only were all coronary vessels filled following injection of the thoracic aorta, but the implanted left internal mammary artery was filled in a retrograde manner. In addition to the development of multiple mediastinal-omental-myocardial anastomoses, these animals all had extensive mammary-coronary anastomoses when studied 190 to 460 days post-operatively.

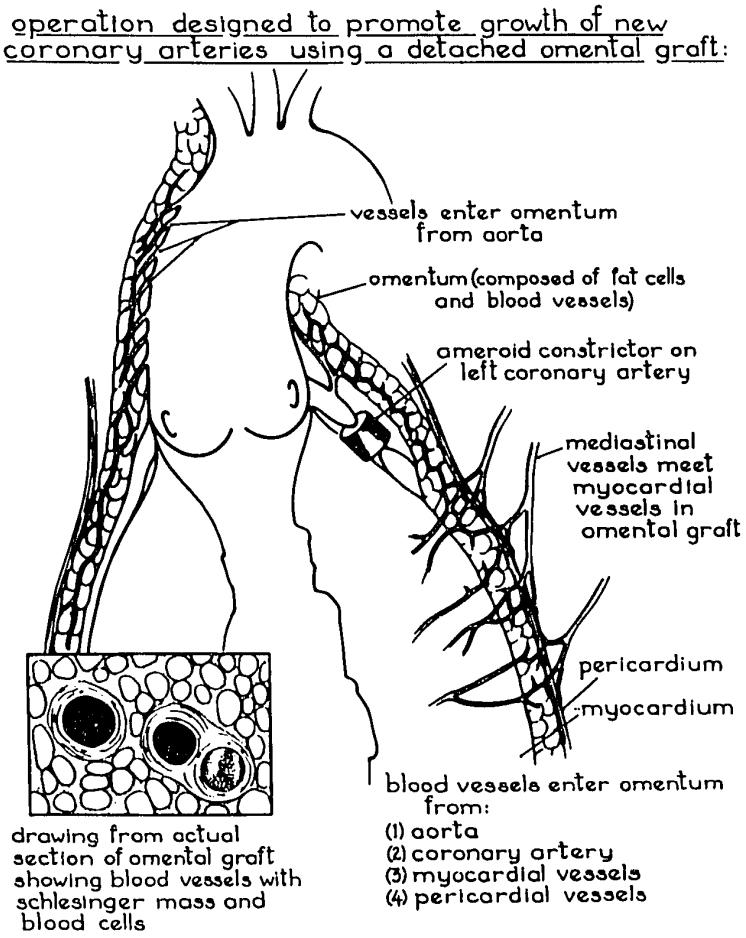


FIGURE 15: Diagram illustrating the free omental graft operation. (Vineberg 1963).

Human application of this combined procedure has been done by Vineberg since around $2\frac{1}{2}$ years ago. In his present series, so far 62 patients underwent this combined operation (Vineberg 1966). He divided his patients in to two groups pre-operatively :

(1) Those with no angina at rest - 45 patients.

(2) Those with angina at rest without apparent cause - 17 patients.

The results on the 45 patients under group (1) showed two operative deaths, an operative mortality of 4.4%. Postoperatively 33 patients had slight or no pain and 6 had decreased pain, i.e. 87% showed improvement. Thirty patients returned to work; 18 of these (47%) had been unable to work before operation. Among the 17 patients in group (2), there were four operative deaths, a mortality of 24%. Eight have had no pain and three have had less pain, so that 11 are improved (76%). There were three late deaths, leaving nine patients still improved (65%). Preoperatively, only one in this group was working full time, now, postoperatively nine are working full time, using few if any nitroglycerin tablets. The degree of left ventricular enlargement has been reduced in four cases out of 20 (25%). Eleven patients of the original 17 (65%) in congestive failure are no longer in failure. It is expected that with the passage of time these will experience steady improvement with respect to left ventricular enlargement and failure. (Vineberg A.M. 1966).

CHAPTER VII

EXPERIMENT

For many years it has been clear that the internal mammary artery when it remains fully patent is only capable of supplying sufficient blood to maintain the health of the left ventricle. This was brought to Vineberg's attention in 1956 when one of his patients who had undergone internal mammary artery implantation four years previously died of a ruptured right ventricular aneurysm. A study of this patient's heart revealed that the only patent artery in the heart was the internal mammary artery, and that the left ventricular muscle appeared to be healthy. This and other cases led to the quest of additional means of relieving myocardial ischemia caused by right coronary artery disease.

The results of the Ivalon Sponge operation on animals were quite encouraging but it was found that it was impossible to suture the sponge to the posterior surfaces of the right and left ventricles and to the anterior surface of the right ventricle. In addition to the fact that the internal mammary artery was not sufficiently large to supply the entire heart in the presence of progressive coronary artery occlusion, it is also known that a certain percentage of implanated internal mammary arteries, both in animal and in humans, become obstructed or narrowed. Because of the above reasons, the combined Vineberg procedure was soon developed. Prior to the development of this procedure (Right Internal Mammary Implant), Vineberg's combined operation is the only procedure that answers the criteria for a complete revascularization of the heart. In this particular procedure, the right ventricular wall and the posterior interventricular wall is revascularized indirectly through the epicardiectomy

and the free omental graft application. The right internal mammary implant operation is the second procedure then that will revascularize an ischemic myocardium en toto, with an added advantage that it revascularizes the right ventricular myocardium and the posterior interventricular wall in a direct way, and that is by formation of adequate sized arterioles that produce anastomoses between the different arteriolar zones in the right and left coronary arterial system.

METHODS AND PROCEDURES

1. EXPERIMENTAL ANIMALS:

Fifty-seven healthy adult mongrel dogs of both sexes of around two to four years of age were selected for this experimental study. The weight of all these dogs were chosen between 40 and 50 lbs. in order to have a uniform size of hearts and approximate diameter of the coronary arteries.

These animals were used because of the ease in their management. Likewise their relative accessibility and the similarity of the physiopathology in their cardiovascular system to that of humans make them the ideal experimental animal for this particular procedure. Furthermore, they have been used for numerous studies of a similar nature, which further increases their merit in these experiments as a basis for comparison of our results with those of others.

2. PRE-OPERATIVE CARE:

All of these dogs used in this particular procedure were admitted to a community cage at the Donner Building, McGill University,

around 2-3 days prior to surgery. Canine distemper vaccine and anti-canine distemper - hepatitis - leptospira canicola serum were administered as instructed during this period.

They were placed on nothing per orem at least 12 hours prior to surgery. In some cases enemas were given the night prior to surgery to prevent bowel movements during the actual procedure.

3. ANAESTHESIA:

No pre-medications were given.

The animals were anaesthetized with intravenous sodium pentobarbital (nembutal 6%). The dosage was 30 mg. per kg., through the cephalic vein in either forelimb. This intravenous anaesthesia is usually adequate to maintain the animal for the entire procedure; however, if indicated during surgery, an additional dosage of sodium pentobarbital was given intermittently through the lingual vein. The trachea was intubated with a No. 42 French Cuffed Davol tube. Respiration was maintained via the endotracheal tube with 40% of oxygen and 60% of air, positive pressure 15 cm. H_2O, rate 16, using a Bird Respirator (Mark 8) and Ruben non-rebreathing valve. During surgery, the lungs were re-inflated every 20 minutes. At the time of closure of the thoracotomy, the lungs were fully expanded. At the end of the operating procedure, the endotracheal tube was removed when the animal returned to spontaneous respiration.

4. POSITION AND PREPARATION OF ANIMALS:

In all cases the animals were placed in the right lateral position. The four extremities were fastened to the upper and lower part on the side of the operating table. As regards preparation the

left thoracic and abdominal wall of the dog was clipped with an electric razor. The skin was prepared aseptically with tincture of metaphen 1:200 (Nitromersol tincture, N.F.).

5. OPERATION:

The operation was strictly conducted with the same sterile precautions used in a human operating room. The incision was made a few cm. lateral to the sternum anteriorly to the transverse process of the 6th thoracic vertebrae posteriorly, around the 5th left intercostal space. The edges of the skin incision were protected with skin towels. The incision was then carried down through the subcutaneous tissue and muscular layers and each bleeders clamped and ligated accordingly, or occasionally the Bovie electrocautery was used. The left 5th intercostal space was identified and access to the thoracic cavity was then made by going through the parietal pleura just above the upper border of the left 6th rib. A Finochietto chest retractor was used for exposure.

After the left lung was retracted posterolaterally with a wet towel, the pericardium was opened vertically, anterior and parallel to the left phrenic nerve. All bleeders were accordingly clamped and ligated.

PLACEMENT OF AMEROID CONSTRICTORS:

Myocardial ischemia was produced in each animal by the gradual occlusion of the right coronary artery at its origin by the use of the ameroid constrictors. (Fig. 16)

The ameroid constrictor is a plastic product made of casein,

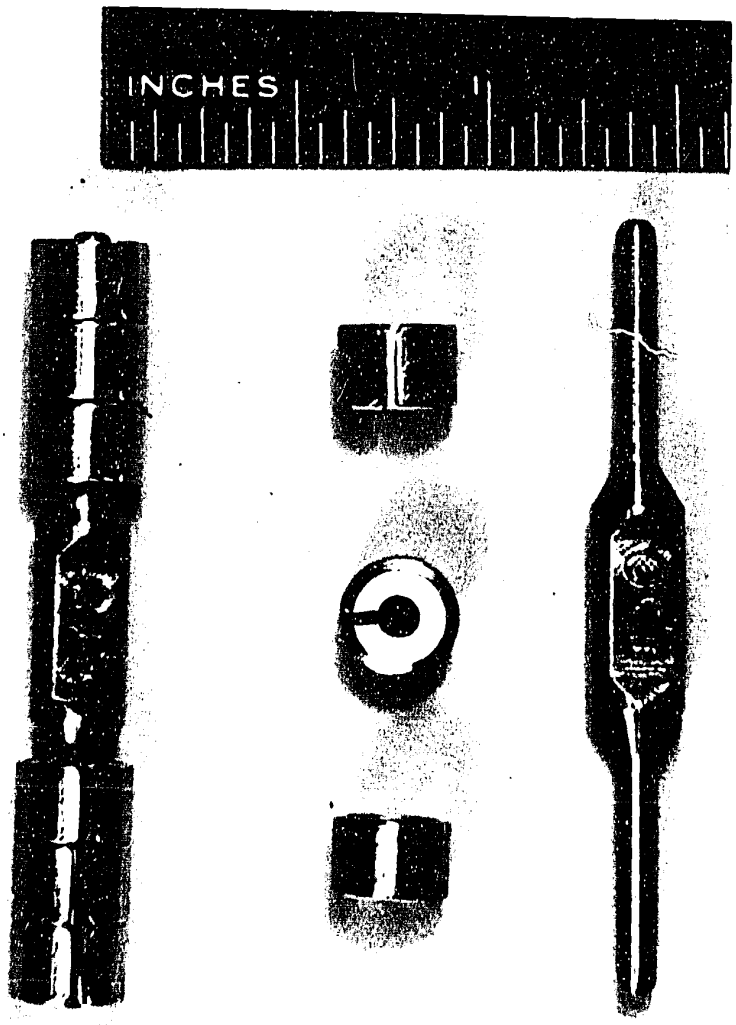


FIGURE 16: Aneroid constrictors and its measurement.

which expands upon absorption of water or moisture because of its hygroscopic properties. Casein plastic is prepared by mixing powdered rennet casein with water. By extrusion under increased pressure and temperature, rods of varying dimensions are formed. The rods are hardened for a prolonged period in formalin. The ameroid has a central lumen drilled to a specific diameter of 0.110 inch. (3mm.). This hygroscopic substance is encased in a rigid steel jacket so as to prevent peripheral expansion. Leading from the periphery into the central lumen is a communicating slot large enough (1 mm.) for the introduction of the coronary artery. The limitation to expand peripherally results consequently in internal expansion, and thereby narrows the central lumen. The ameroids are stored in a dessicator prior to their use and are eventually sterilized in a container of vaseline in a water bath for around an hour prior to the operation. The initial dessication storage prevents water absorption prior to sterilization and the vaseline forms a thin coating, thus delaying the absorption of tissue fluids. This is done in order to give more time for the heart to re-establish its circulation either naturally or by means of revascularization procedures. Litvak (1957) reported that the dry ameroid placed in saline solution reduces its central bore from 0.110 to 0.06 inch in 26 days. Vaseline coated ameroids absorb less water and consequently their rate of swelling is diminished. Such ameroid constrictors reduce their central luminae from 0.110 to 0.707 in 32 days and to 0.0708 inch in 54 days.

Prior to placement of the ameroid, the right auricular

appendage was retracted for proper exposure of the right coronary artery at its origin. The right coronary sulcus was brought into the operative field by left rotation of the heart with the left hand during the dissection of the right coronary artery and ameroid placement. If abnormal heart beats occurred, the procedure was temporarily stopped. In order to place the ameroid constrictor at the origin of the right coronary artery, the artery was freed accordingly from the surrounding tissues. Any branch arising from the trunk, from the origin to the planned area of ameroid constrictor application, was cut between legatures. A cotton ligature was used to retract the artery for a few seconds which helped to slide the artery into the slot and hence into the central lumen of the ameroid constrictor. After placing the artery through the slot and into the lumen, the ameroid was rotated 180° to prevent it from coming off the artery. The placement of the constrictor around the origin of the right coronary artery was carried out as quickly as possible to reduce the sugical risk caused by manipulation around the vicinity of the SA node with resulting arrythmia.

CONTROL GROUP: The procedure described above was exactly done on this group of 20 dogs. In short, these dogs on the control group underwent an ameroid placement on the origin of their right coronary artery, followed by closure of the pericardium in a loose fashion. Closure of the chest cavity will be described later.

OPERATED GROUP: Implantation of the right internal mammary artery within the right ventricular myocardium.

This group consists of three subgroups, the division being based on the technique and site of implantation of the right internal mammary artery on the right ventricular myocardium, and the length of the tunnel created.

Subgroup 1: (Fig.17) Seven dogs. The technique used in this subgroup was the needle technique and the site of implantation was in the outflow

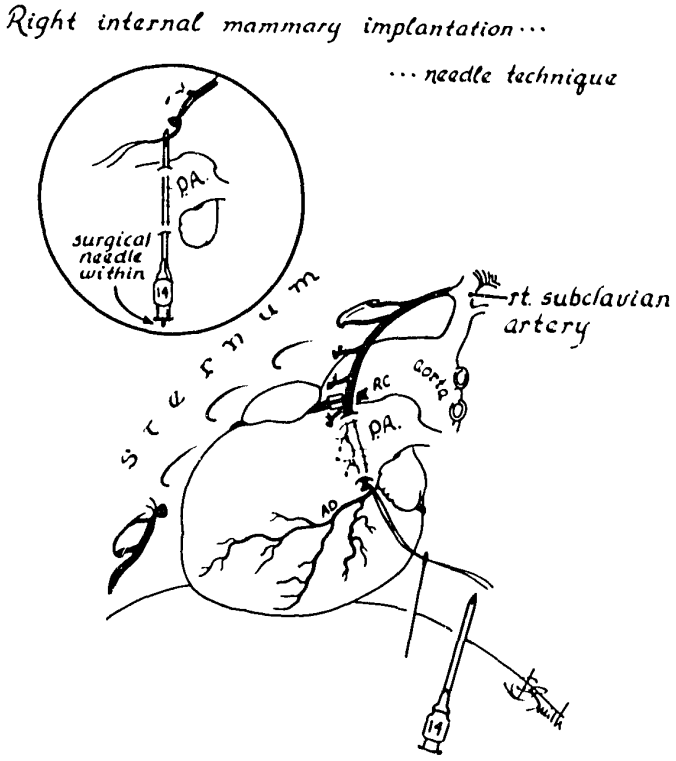


FIGURE 17: Diagram illustrating technique and implantation site for the right internal mammary operation. (Subgroup I).

tract of the right ventricle. The needle technique was called as such since a gauge # 14 hypodermic needle was used to create the tunnel within the right ventricular wall. In this way the frequent complication of perforation of the thin right ventricular wall was minimized. With the # 14 needle within the right myocardial wall, a straight surgical needle was then guided in. The ligature around the end of the mobilized right internal mammary artery was threaded in the eye of the surgical needle and pulled in through the hypodermic needle. In this way, once both needles are pulled out we have the artery implanted nicely within the tunnel. Prior to implantation of the artery two of its side branches were left bleeding, thereby leaving an actively bleeding vessel implanated within the right myocardial wall. Between the chest wall and tunnel the artery was left slack enough but not excessively so; undue angulation at either end was not desirable. When the position of the implanted artery was satisfactory, a mattress sature (3-0 silk) was placed around the projecting tip and it was secured to the right ventricle. Any bleeding from the proximal or distal end of the tunnel was usually controlled by light pressure with a gauze sponge. The length of the tunnel created in this particular procedure was around 2 to 3 c.m.

Subgroup 2: Ten Dogs. Site of implantation in this subgroup was the same as in subgroup (1) - the outflow tract. (Fig. 18.) The difference was in the length of the tunnel. (4 cm. in this subgroup), and the technique of implantation. The hemostat (mosquito) was used to create the tunnel in the right ventricular wall. In all cases the axis

Right internal mammary implantation ···

··· outflow tract ~ tunnel technique

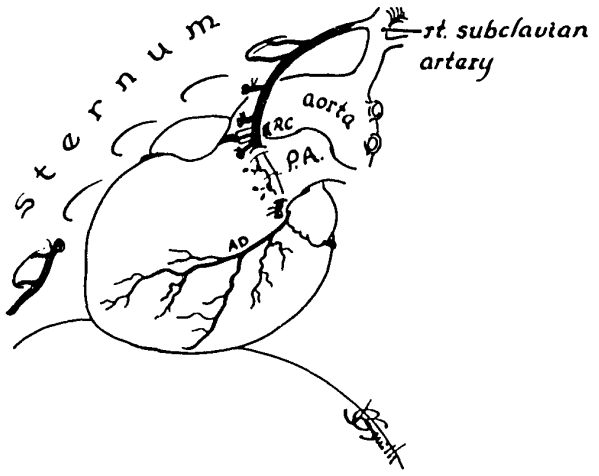


FIGURE 18: Diagram illustrating technique and implantation site for the right internal mammary operation. (Subgroup II).

and length of the tunnels were fixed by two stab wounds in the right ventricular myocardium. The tip of a hemostat was then inserted into the distal stab wound, and the instrument was guided to the proximal stab wound. As the hemostat advanced, the blades were alternately spread and closed to separate myocardial muscle layers. Implantation was accomplished by introducing the hemostat through the full length of the tunnel, grasping the ligature on the tip of the artery and drawing the artery with its two bleeding side branches into the myocardial tunnel. The tip of the implanted artery was then exteriorized at the exit point. Bleeding from perforation of the right ventricle (a complication that occurred in 2% of the cases), was easily controlled by light pressure with a gauze sponge and in some cases by suturing with 3-0 silk at the site of puncture. As regards tension and fixation of artery, the technique of subgroup one was followed.

Subgroup 3. 20 Dogs. The same technique of implantation was used in this subgroup as in subgroup 2, the tunnel technique with the aid of a hemostat (mosquito). The site of implantation was, however, different from the first two subgroups, with the length of the tunnel being particularly slightly larger (4.5 to 5 cm.) in this case. The site chosen for implantation was the superior lateral aspect of the right ventricle almost parallel to the direction of the right main coronary artery, and going just beneath its main ventricular branches. (Fig. 19). As in the two previous subgroups, once the position and tension of the implanted artery was judged satisfactory, a mattress suture

Right internal mammary implantation ···

··· tunnel — superior lateral aspect : rt. ventricle

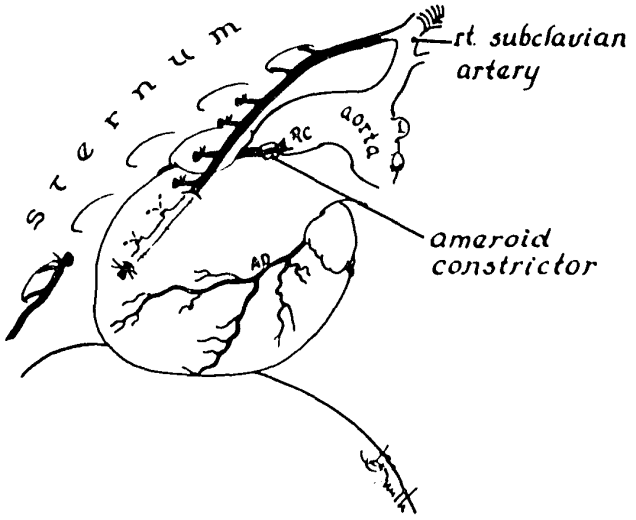


FIGURE 19: Diagram illustrating technique and implantation site for the right internal mammary operation. (Subgroup III).

was placed around the projecting tip to secure the artery to the wall of the right ventricle.

Exposure and mobilization of the Right Internal Mammary Artery prior to implantation:

Access to the right chest cavity was accomplished by retraction of the lung and the heart posteriorly, and by going through the very thin mediastinal pleura separating the left from the right chest cavity. The internal mammary artery is visible down to the third intercostal space, then it passes behind the sternocostalis muscle. The sternocostalis muscle was incised from the 6th to the 5th interspace and was dissected medially from the chest wall as a flap to expose the underlying artery. The internal mammary artery was then freed of overlying pleura, fascia and muscle from the 5th up to the level between the 1st and 2nd intercostal space. Once the right mammary artery was mobilized, all the intercostal branches were accordingly identified and isolated, then ligated with 5-0 silk suture and divided. At the level of the 5th and 6th interspaces, however, the side branches of the artery were preserved, since each side branch at this level is considered as a potential source of revascularization. In the mobilization of the internal mammary artery, a meticulous technique has to be employed. Preferred instruments for dissection were blunt nerve hooks, long-handled scissors, smooth forceps and long-handled right angled clamps. The mobilized right internal mammary artery was left in continuity in the chest wall. After preparation of the tunnel (site of tunnel and technique of implantation depending on what group the

animal belongs) the operator returned to the prepared internal mammary artery and divided this between ligatures (2-0 silk), just above branching of the mammary artery into its two terminal branches, the superior epigastric artery and the musculophrenic artery. The mobilized artery was then drawn away from the chest wall and the two side branches cut as far away from the parent vessel as possible. In this study two side branches were left actively bleeding. Implantation was then accomplished as described in each group.

The entire procedure could be summarized as follows :

(1) Routine left sided thoracotomy and access to the right chest cavity through mediastinal pleura.

(2) Mobilization of the right coronary artery as its origin.

(3) Mobilization of the right internal mammary artery from the 5th to the 1st intercostal space.

(4) Correct placement of the ameroid on the origin of the right coronary artery.

(5) Implantation of the right internal mammary artery into the right ventricular myocardium.

CLOSURE: The pericardium was approximated loosely with 3-0 merseline suture, if no implantation procedure was to be done. Otherwise in all implanted cases the pericardium was left unopposed to prevent any adhesions between the implanted vessel and the artery which in effect later on might cause kinking of the vessel.

Two No. 16 French catheters with multiple openings at the

end were introduced in the chest cavity, one on each side and brought out through separate openings an inch below the left thoracotomy skin incision. Closure of the chest wall was done in a routine fashion approximating the adjacent ribs with "0" merseline sutures in an interrupted fashion. A rib approximater was used to bring the two ribs together. The thoracic wall was closed in layers, using continous 3-0 merseline sutures for muscles, then interrupted mattress 3-0 merseline for the skin. During the closure of the chest, the rubber catheters were connected to two under-water drainage bottles. In case of control animals only one chest tube was used.

6. IMMEDIATE POST-OPERATIVE CARE:

The animal received 2 cc. of Fortimycin (400,000 units of Penicillin and 1 gm. Streptomycin) and 600,000 units of Bicillin intramuscularly.

The chest tubes were removed after no more air or fluid was seen coming from the thoracic cavity.

After spontaneous respiration was noted the endotracheal tube was removed. The animal was moved to an individual cage in the recovery room.

7. POST-OPERATIVE CARE:

Twenty four hours after surgery the animal was transferred to a community cage from the individual cages in the recovery room. After 7 days and the general condition of the animal permits it, the dog was then sent to the farm for further chronic care.

During the post-operative period at the Donner Building, 5th floor, close observation was taken to prevent untoward complications.

Thoracentosis was performed if any fluid or air accumulation was noted. If necessary the animal was kept there two or three weeks in an individual cage.

POSTMORTEM STUDIES

All dogs underwent numerous postmortem studies on the day of death or sacrifice. The dog was sacrificed with intravenous administration of heparin (2 mg./kg.) and pentobarbital sodium (60 mg./kg. of body wt.).

The dog was then bled through a canula in the femoral artery after a femoral cutdown.

Thoracotomy was performed through the left-fourth intercostal space, and then access made into the chest cavity with the aid of a self-retaining retractor. Both lungs were examined extensively to determine any possible pathology present. Attention was then focused to the heart and the implanted internal mammary (i.e. if dog belongs to implanted group). The heart with the implanted internal mammary artery was then removed en toto, severing the artery just as it comes off the subclavian. The internal mammary artery was cannulated with a medium sized polyethelene tube and injected with Schlesinger Mass , at pressures ranging between 100 and 120 mm. of Hg. The new Schlesinger Mass (Schlesinger M. 1938) consists of a suspension of lead phosphate in agar, which sets quickly thus permitting immediate radiography and cutting of the fresh unfixed specimen. This injection mass does not pass through vessels less than 40 micra in diameter. During the process of injection, the state of filling of the internal mammary artery was carefully noted, including the presence of branching and anastomosis with right and left coronary

arterial system, grading this accordingly. Then the heart was X-rayed, taking several exposures in an AP and a slightly oblique position.

In cases wherein there is no filling of the coronary arterial tree by the internal mammary injection, then the right and left coronary ostia were cannulated with metal cannulae and injected respectively with the Schlesinger mass. Separate X-Rays were taken after injection of each coronary artery.

When the Schlesinger mass had solidified, the heart was unrolled following Schlesinger's technique (1938) and X-Rayed in order that the intercoronary anastomoses could be studied along with the channel formed (in cases of successful implants) to by-pass the area of ameroid coronary artery obstruction.

The extent of anastomoses was graded and recorded as follows: (Vineberg et al 1962):

No anastomoses	0
Anastomoses present	X
Good anastomoses	XX
Complete anastomoses	XXXX

In the control group the heart was also removed in its entirety then both coronary ostia cannulated and injected with Schlesinger mass. The right coronary opening was injected first to determine in a way the degree of occlusion produced by the ameroid in the origin of the right coronary. This was followed by injection of the left coronary ostia. The filling of the left coronary system was carefully noted especially in reference to the frequency of anastomoses between the branches of the left anterior

descending artery and branches of the right coronary artery. Separate X-Rays were taken after injection of each coronary artery. Unrolling of the heart follows this procedure, with another X-Ray film right after.

HISTOPATHOLOGICAL STUDIES:

The heart of each animal (implanted and control group) was examined grossly and microscopically for presence or absence of ischemic myocardial damage. The right ventricle as well as the interventricular septum were sectioned in many places to determine the extent of microscopic infarction or fibrosis. The right ventricle was cut transmurally from the base to the apex, about 0.8 cm. apart. The interventricular septum as well was sectioned horizontally from the anterior to the posterior portion, about 1.0 cm. apart. The extent of myocardial infarction or fibrosis was graded as follows:

No myocardial infarction or fibrosis	0
Focal or scattered	X
Moderate	XX
Massive	XXX

The patency of the implanted internal mammary artery was determined over its entire length of the myocardial tunnel as the percentage of the original arterial sectional area of the lumen. The extent and frequency of mammary-coronary anastomoses also were recorded.

The portion of the right coronary artery lying within the ameroid constrictor was dissected away from the heart and removed from the ameroid constructor. Multiple microscopic sections were taken to determine the extent of narrowing of the lumina of the right coronary artery. This has been recorded as the percentage occlusion of the original coronary sectional area of the lumen.

PATENCY DETERMINATION OF ARTERIAL LUMEN:

Patency studies on the histological sections were done with a Zeiss binocular miscroscope with the slide placed on top of graph paper (80 divisions per inch) fastened to the stage.

Patency percentages were obtained by ratio of the number of squares occupied by the lumina divided by the total area occupied by the vessel.

RECORDS AND TABULATIONS

All the findings of individual animals were carefully recorded and tabulated in each group.

TABLE III (1)

INDIVIDUAL ANIMAL RECORDS

CONTROL GROUP

DOG NO.	SEX	WEIGHT (lbs.)	DATE OF OPERATION	DATE OF DEATH OR SACRIFICE	POST-OPERATIVE COURSE
271*	M	40	27 July '65	3 Feb. '66	uneventful
856*	F	46	3 Sept. '65	3 Feb. '66	uneventful
884	M	48	15 Sept. '65	13 Oct. '65	uneventful
838*	M	45	21 Sept. '65	3 Feb. '66	minor wound infection otherwise uneventful
230*	M	45	29 Sept. '65	2 Feb. '66	uneventful
405*	F	45	14 Oct. '65	10 March '66	uneventful
129	F	45	28 Oct. '65	3 Dec. '65	uneventful
816*	M	44	29 Oct. '65	16 Feb. '66	minor wound infection
340*	F	44	5 Nov. '65	2 Feb. '66	uneventful
264*	F	40	12 Nov. '65	16 Feb. '66	uneventful
484*	M	46	24 Nov. 65	17 March '66	uneventful
419*	M	46	1 Dec. '65	10 March '66	uneventful
446*	M	45	2 Dec. '65	17 March '66	minor wound infection
433*	M	48	9 Dec. '65	23 March '66	uneventful
466*	M	44	10 Dec. '65	23 March '66	uneventful
450*	M	43	14 dec. '65	23 March '66	uneventful
425*	F	48	5 Jan. '65	23 March '66	uneventful
412*	F	40	21 Jan. '66	24 March '66	uneventful
470*	M	43	1 Feb. '66	24 March '66	uneventful
401*	F	44	8 Feb. '66	24 March '66	uneventful

* sacrificed

TABLE III (2)

INDIVIDUAL ANIMAL RECORDS
IMPLANTED GROUP -
SUBGROUP I.

DOG NO.	SEX	WEIGHT (lbs.)	DATE OF OPERATION	DATE OF DEATH OR SACRIFICE	POST-OPERATIVE COURSE
278*	M	50	16 July '65	13 Sept. '65	uneventful
254*	M	42	22 July '65	4 Oct. '65	uneventful
272*	M	45	23 July '65	4 Oct. '65	uneventful
274	M	41	26 July '65	7 Aug. '65	uneventful
213*	F	41	5 Aug. '65	3 Nov. '65	uneventful
864*	F	44	7 Sept. '65	10 Nov. '65	uneventful
877*	M	42	9 Sept. '65	16 Nov. '65	uneventful

* sacrificed

TABLE III (3)

INDIVIDUAL ANIMAL RECORDS
IMPLANTED GROUP -
SUBGROUP II

DOG NO.	SEX	WEIGHT (lbs.)	DATE OF OPERATION	DATE OF DEATH OR SACRIFICE	POST-OPERATIVE COURSE
946*	F	45	16 Sept. '65	20 Jan. '66	uneventful
248*	M	46	22 Sept. '65	20 Jan. '66	uneventful
256*	M	42	23 Sept. '65	27 Jan. '66	upper part of wound resutured on 4th post-operative day
223	F	42	27 Sept. '65	24 Nov. '65	uneventful
505*	M	40	28 Sept. '65	25 Jan. '66	uneventful
456*	M	50	4 Oct. '65	25 Jan. '66	uneventful
273*	M	45	6 Oct. '65	19 Jan. '66	uneventful
704	F	45	7 Oct. '65	6 Nov. '65	wound infection, lower aspect of wound
460*	F	45	13 Oct. '65	19 Jan. '66	uneventful
220*	M	46	18 Oct. '65	27 Jan. '66	Thoracentesis 8 cc clear yellow fluid

* sacrificed

TABLE III (4)

INDIVIDUAL ANIMAL RECORDS
IMPLANTED GROUP -

SUBGROUP III

DOG NO.	SEX	WEIGHT (lbs.)	DATE OF OPERATION	DATE OF DEATH OR SACRIFICE	POST-OPERATIVE COURSE
802*	M	45	19 Oct. '65	27 Jan. '66	uneventful
209*	M	43	22 Oct. '65	2 Feb. '66	uneventful
302*	M	42	25 Oct. '65	3 Feb. '66	uneventful
869*	M	43	26 Oct. '65	2 Feb. '66	uneventful
833*	M	45	27 Oct. 65	3 Feb. '66	uneventful
482*	F	42	1 Nov. '65	9 Feb. '66	uneventful
447*	F	50	2 Nov. '65	10 Feb. '66	uneventful
476	M	47	10 Nov. '65	31 Jan. '66	uneventful
849*	M	47	15 Nov. '65	10 Feb. '66	uneventful
469	F	45	11 Nov. '65	14 Dec. '65	uneventful
889	F	45	9 Nov. '65	30 Dec. '65	uneventful
488*	M	40	6 Dec. '65	24 Feb. '66	uneventful
407*	F	43	23 Nov. '65	17 Feb. '66	uneventful
429*	F	41	17 Nov. '65	24 Feb. '66	minor wound infection
420	M	44	7 Dec. '65	4 Jan. '66	uneventful
406*	M	45	13 Dec. '65	23 Feb. '66	Thoracentesis 10 cc. clear yellow fluid 7th post-operative day
474*	M	41	7 Jan. '66	30 March '66	uneventful
451*	M	41	11 Jan. '66	30 March '66	uneventful
404*	F	44	18 Jan. '66	30 March '66	uneventful
459 *	M	46	12 Jan. '66	30 March '66	uneventful

* Sacrificed

TABLE IV (1)

CONTROL GROUP

DOG NO.	PERCENTAGE OCCLUSION RIGHT CORONARY ARTERY	INFARCTION GROSS (RECENT AND HEALED) RIGHT VENTRICLE	INTER-VENTRICULAR SEPTUM	MICROSCOPIC (RECENT AND HEALED) RIGHT VENTRICLE	INTER-VENTRICULAR SEPTUM
271*	77%	0	0	0	0
856*	100%	0	0	0	0
884	96%	1 x 2 cm.recent posterior lateral wall	0	+++ recent	0
838*	100%	0	0	0	0
230*	92%	3 x 2 cm.posterior wall, healed	0	++ old, healed	0
405*	95%	0	0	0	0
129	96%	0	0	+++ recent posterior wall	0
816*	85%	0	0	0	0
340*	94%	0	0	0	0
264*	87%	0	0	0	0
484*	87%	0	0	+++ old, healed antero-lateral wall	0
419*	98%	0	0	+ to ++ recent antero-lateral wall	0
446*	92%	3 x 3 cm.antero-lateral wall,old	0	+++ old, healed	0
433*	100%	0	0	++ old, healed posterior wall	0
466*	92%	0	0	+ old, healed antero-lateral wall	0
450*	70%	0	0	0	0
425*	88%	0	0	+ old, healed antero-lateral wall	0
412*	100%	0	0	+ recent necrosis focal posterior wall	0
470*	97%	0	0	++ recent antero-lateral wall	0
401*	89%	2 x 2 cm.antero-lateral wall, old	0	++ old, healed	0

* sacrificed

TABLE IV (2)

IMPLANT SUBGROUP I

DOG NO.	PERCENTAGE OCCLUSION RIGHT CORONARY ARTERY	INFARCTION GROSS (RECENT AND HEALED) RIGHT VENTRICLE	INFARCTION GROSS (RECENT AND HEALED) INTER-VENTRICULAR SEPTUM	INFARCTION MICROSCOPIC (RECENT AND HEALED) RIGHT VENTRICLE	INFARCTION MICROSCOPIC (RECENT AND HEALED) INTER-VENTRICULAR SEPTUM
278*	95%	0	0	0	0
254*	90%	0	0	0	0
272*	86%	0	0	0	0
274	94%	posterior wall 2 x 2 cm. recent	0	++ recent	0
213*	100%	0	0	+ (fibrosis) antero-lateral wall	0
864*	97%	0	0	0	0
877*	92%	0	0	0	0

* Sacrificed

TABLE IV (3)

IMPLANT SUBGROUP II

DOG NO.	PERCENTAGE OCCLUSION RIGHT CORONARY ARTERY	INFARCTION			
		GROSS (RECENT AND HEALED)		MICROSCOPIC (RECENT AND HEALED)	
		RIGHT VENTRICLE	INTER-VENTRICULAR SEPTUM	RIGHT VENTRICLE	INTER-VENTRICULAR SEPTUM
946*	77%	0	0	0	0
248*	90%	0	0	0	0
256*	65%	0	0	0	0
223	94%	0	0	++ healed antero-lateral wall	0
505*	92%	0	0	0	0
456*	93%	0	0	0	0
273*	91%	0	0	0	0
704	89%	0	0	++ (subendocardial infarction	0
460*	100%	0	0	0	0
220*	90%	0	0	+ fibrosis antero-lateral wall	0

* sacrificed

TABLE IV (4)

SUBGROUP III

DOG NO.	PERCENTAGE OCCLUSION RIGHT CORONARY ARTERY	INFARCTION GROSS (RECENT AND HEALED) RIGHT VENTRICLE	INTER-VENTRICULAR SEPTUM	MICROSCOPIC (RECENT AND HEALED) RIGHT VENTRICLE	INTER-VENTRICULAR SEPTUM
802*	95%	0	0	0	0
209*	100%	0	0	0	0
302*	88%	0	0	0	0
869*	95%	0	0	0	0
833*	100%	0	0	0	0
482*	98%	0	0	0	0
447*	80%	0	0	0	0
476	91%	0	0	0	0
849*	100%	0	0	++endocardial fibrosis antero-lateral wall	0
464	100%	Posterior Wall recent 2 x 2 cm.	0	+++ recent infarct	0
889	100%	Antero-lateral wall 3 x 3 cm. recent	0	++ recent infarct	0
488*	86%	0	0	0	0
407*	100%	0	0	0	0
429*	88%	0	0	0	0
420	90%	0	0	+++ recent infarct antero-lateral wall	0
406*	96%	0	0	0	0
474*	100%	0	0	0	0
451*	81%	0	0	0	0
404*	96%	0	0	0	0
459*	88%	0	0	0	0

* sacrificed

TABLE V

PERCENTAGE OF INFARCTION - GROSS AND MICROSCOPIC

(1)	Control Group - - -	60%	(Massive	= 20%
			(Moderate	= 25%
			(Scattered foci	= 15%
(2)	Implant Group -			
	No. I - - - - - - - -	28%	(Massive	= 0%
			(Moderate	= 14%
			(Scattered foci	= 14%
	No. II - - - - - - - -	30%	(Massive	= 0%
			(Moderate	= 20%
			(Scattered foci	= 10%
	No. III - - - - - - - -	20%	(Massive	= 10%
			(Moderate	= 10%
			(Scattered foci	= 0%

AVERAGE PERCENTAGE OCCLUSION OF THE RIGHT CORONARY ARTERY WITHIN THE AMEROID CONSTRICTOR PER GROUP

Control	= 86.7%
(1) Subgroup I	= 93.4%
(2) Subgroup II	= 87.1%
(3) Subgroup III	= 93.6%

TABLE VI

COMPARATIVE RESULTS OF THE DIFFERENT GROUPS IN RELATION TO CORONARY OCCLUSION, MORTALITY RATE AND PERCENTAGE MYOCARDIAL INFARCTION

	AVERAGE PERCENTAGE OCCLUSION OF RIGHT CORONARY ARTERY	MORTALITY RATE PERCENTAGE	MYOCARDIAL INFARCTION		
			GROSS PERCENTAGE	MICROSCOPIC PERCENTAGE	AVERAGE PERCENTAGE INFARCTION
Control (20 dogs)	86.7%	10%	20%	60%	60%
Implanted Group:					
Subgroup I (7 dogs)	93.4%	14%	14%	28%	28%
Subgroup II (10 dogs)	87.1%	20%	0%	30%	30%
Subgroup III	93.6%	20% *	10%	20%	20%

* 4 deaths out of 20. One of the mortalities showed no evidence of myocardial infarction (gross or microscopic). Postmortem studies revealed pneumonia as cause of death. Actual mortality rate = 15%

TABLE VII (1)

IMPLANTED GROUP

SUBGROUP I

PERCENTAGE PATENCY OF THE IMPLANTED INTERNAL MAMMARY ARTERY AND EXTENT OF MAMMARY -RIGHT CORONARY ANASTOMOSES AND MAMMARY LEFT ANTERIOR DESCENDING ANASTOMOSES IN A "PLUS" GRADING

DOG NO.	PERCENTAGE PATENCY INTERNAL MAMMARY ARTERY	EXTENT OF MAMMARY - RIGHT CORONARY ANASTOMOSES	EXTENT OF MAMMARY - ANTERIOR DESCENDING ANASTOMOSES
278*	10%	0	0
254*	20%	0	+
272*	35%	0	0
274	28%	0	0
213*	2%	0	0
864*	2%	0	0
877*	47%	0	0

Average Percentage Patency	=	20.5%
Average Mammary - Right Coronary anastomosis	=	0%
Average Mammary - anterior descending anastomosis	=	14%

* sacrificed

TABLE VII (2)

IMPLANTED GROUP

SUBGROUP II

PERCENTAGE PATENCY OF THE IMPLANTED INTERNAL MAMMARY ARTERY AND EXTENT OF MAMMARY - RIGHT CORONARY ANASTOMOSES AND MAMMARY LEFT ANTERIOR DESCENDING ANASTOMOSES IN A "PLUS" GRADING

DOG NO.	PERCENTAGE PATENCY INTERNAL MAMMARY ARTERY	EXTENT OF MAMMARY - RIGHT CORONARY ANASTOMOSES	EXTENT OF MAMMARY - ANTERIOR DESCENDING ANASTOMOSES
946*	40%	+++	+++
248*	53%	0	0
256*	62%	0	0
223	20%	0	0
505*	5%	0	0
456*	20%	0	0
273*	7%	0	0
704	15%	0	0
460*	72%	0	0
220*	60%	0	0

Average percentage patency of internal mammary artery = 34.9%

Percentage of mammary -right coronary anastomosis = 10%

Percentage of mammary -anterior descending anastomosis = 10%

* sacrificed

TABLE VII (3)

IMPLANTED GROUP

SUBGROUP III

PERCENTAGE PATENCY OF THE IMPLANTED INTERNAL MAMMARY ARTERY AND EXTENT OF MAMMARY - RIGHT CORONARY ANASTOMOSES AND MAMMARY LEFT ANTERIOR DESCENDING ANASTOMOSES IN A "PLUS" GRADING

DOG NO.	PERCENTAGE PATENCY INTERNAL MAMMARY ARTERY	EXTENT OF MAMMARY - RIGHT CORONARY ANASTOMOSES	EXTENT OF MAMMARY - ANTERIOR DESCENDING ANASTOMOSES
802*	54%	+++	+++
209*	50%	+++	+++
302*	67%	+++	+++
869*	70%	+++	+++
833*	60%	+++	+++
482*	72%	+++	+++
447*	64%	+++	+++
476	65%	+++	+++
849*	50%	+++	+++
464	52%	0	0
889	65%	0	0
488*	65%	++	0
407*	67%	+++	+++
429*	54%	0	0
420	80%	+++	0
426*	35%	+	0
474*	71%	+++	++
451*	75%	+++	++
404*	70%	+++	++
459*	64%	0	0

Average percentage patency of internal mammary artery = 62.7%
Percentage of mammary - right coronary anastomosis = 80%
Percentage of mammary - anterior descending anastomosis = 65%

* sacrificed

TABLE VIII

AVERAGE NUMBER OF SURVIVAL DAYS IN IMPLANTED GROUP EITHER DIED OR SACRIFICED

IMPLANTED GROUP

Average number of days (Subgroup I)	= 62.1 days
Average number of days (Subgroup II)	= 99.2 days
Average number of days (Subgroup III)	= 80.7 days

TABLE IX

RELATIONSHIP SHOWING PERCENTAGE OF ANASTOMOSIS BETWEEN ANTERIOR DESCENDING ARTERY AND BRANCHES OF RIGHT CORONARY ARTERY IN CONTROL GROUP IN "PLUS" GRADING

DOG NO.	PERCENTAGE OF ANASTOMOSIS BETWEEN ANTERIOR DESCENDING ARTERY AND RIGHT CORONARY ARTERY
271*	0
856*	0
884	0
838*	++
230*	0
405*	++
129	0
816*	0
340*	0
264*	0
484*	0
419*	++
446*	++
433*	0
466*	0
450*	0
425*	0
412*	0
470*	++
401*	0

Percentage of anastomosis = 25%

* sacrificed

TABLE X

COMPARATIVE SUMMARY OF RESULTS IN IMPLANTED GROUP

	AVERAGE NUMBER OF SURVIVAL DAYS (DIED AND SACRIFICED)	AVERAGE PATENCY OF INTERNAL MAMMARY ARTERY	AVERAGE PERCENTAGE OF MAMMARY - RIGHT CORONARY ANASTOMOSES	AVERAGE PERCENTAGE OF MAMMARY - LEFT ANTERIOR DESCENDING ANASTOMOSES
Subgroup I (7 dogs)	62.1 days	20.5%	0%	14%
Subgroup II (10 dogs)	99.2 days	34.9%	10%	10%
Subgroup III (20 dogs)	80.7 days	62.7%	80%	65%

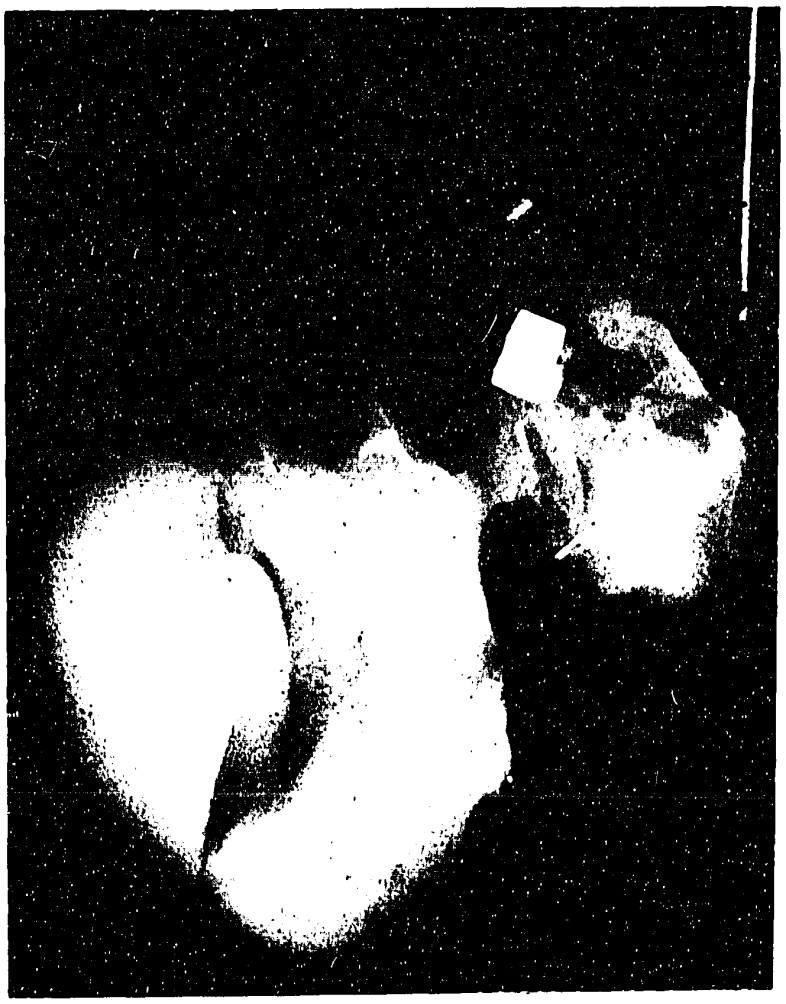


FIGURE 19(a): Experimental animal No. 278 had right internal mammary artery implantation to the right ventricular myocardium. (Needle technique - site: outflow tract). This animal belonged to subgroup I. 58 days after operation the animal was sacrificed for postmortem studies. The right internal mammary was injected with Schlesinger mass. The implanted vessel was noted to be partly obliterated within as could be seen in the picture. Patency of the implanted internal mammary artery was measured to be 10%. Likewise no evidence of mammary - coronary anastomosis.

W1 : RR 1-(5): Experimental animal No. 2% had right internal mammary artery implantation to the right ventricular myocardium (tunnel technique - site: outflow tract). This animal belonged to subgroup II. 17½ days after operation, animal was sacrificed for postmortem studies. The right internal mammary was injected with Schlesinger mass. It is to be noted that the implanted artery is patent all throughout the tunnel but with no evident mammary - coronary anastomosis. Patency of the artery was judged to be 6%.

FIGURE 20: Experimental animal No. 4-2 had right internal mammary artery implantation to the right ventricular myocardium (tunnel technique - site: superior lateral aspect of right ventricle). 101 days after operation this animal was sacrificed for postmortem studies. The right internal mammary artery was injected with Schlesinger mass under pressure of 100 mm. of Hg. Thorough visualization of the right coronary arterial tree was noted, plus filling of the left coronary arterial system through anastomosis with the left anterior descending artery.

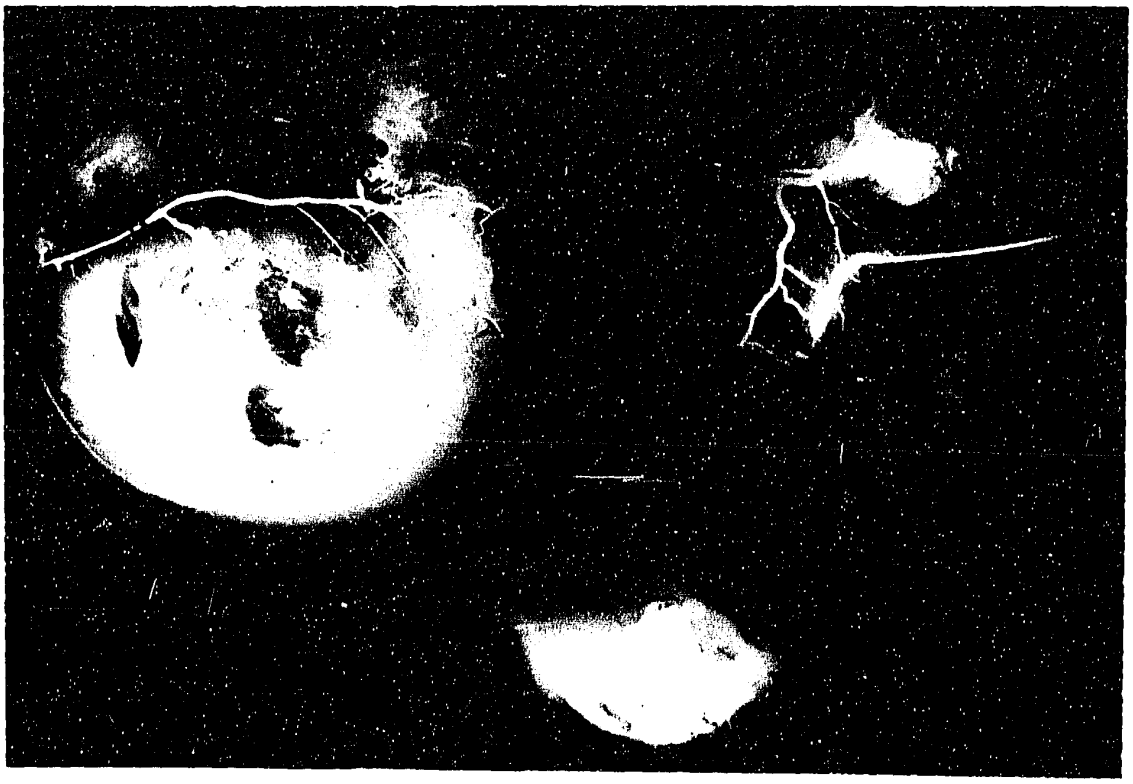


FIGURE 21: The same animal (# 482) with the heart unrolled by the Schlesinger method. Note the extensive anastomosis around site of implantation.

FIGURE 22: Photomicrograph of the X-Section of the implanted internal mammary artery of the same animal (# 452). There was almost no intimal proliferation and Schlesinger mass could be seen within the lumen of the main vessel and likewise in the myocardial branch noted on the lower left hand corner.

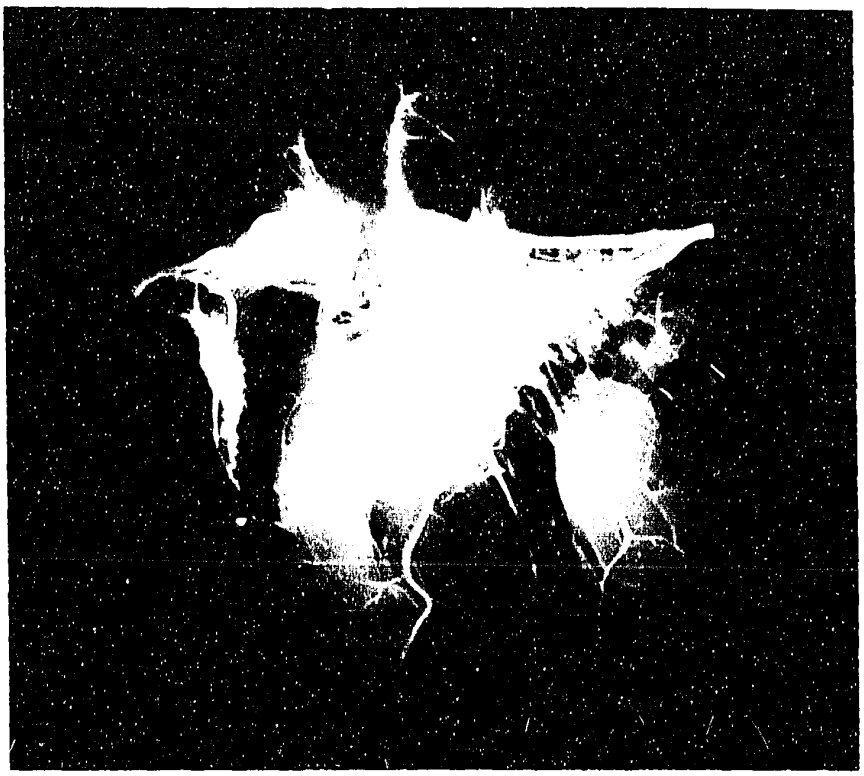


FIGURE 23: The animal (# 407) underwent postmortem studies 93 days after right internal mammary artery implantation to the right ventricular myocardium (tunnel technique; site - superior lateral aspect of right ventricle). Injection of the right internal mammary artery with Schlesinger mass shows extensive mammary - right coronary and mammary - left anterior descending anastomosis.

FIGURE 24: Same animal (# 407) with the heart unrolled showing extensive mammary - coronary anastomosis.

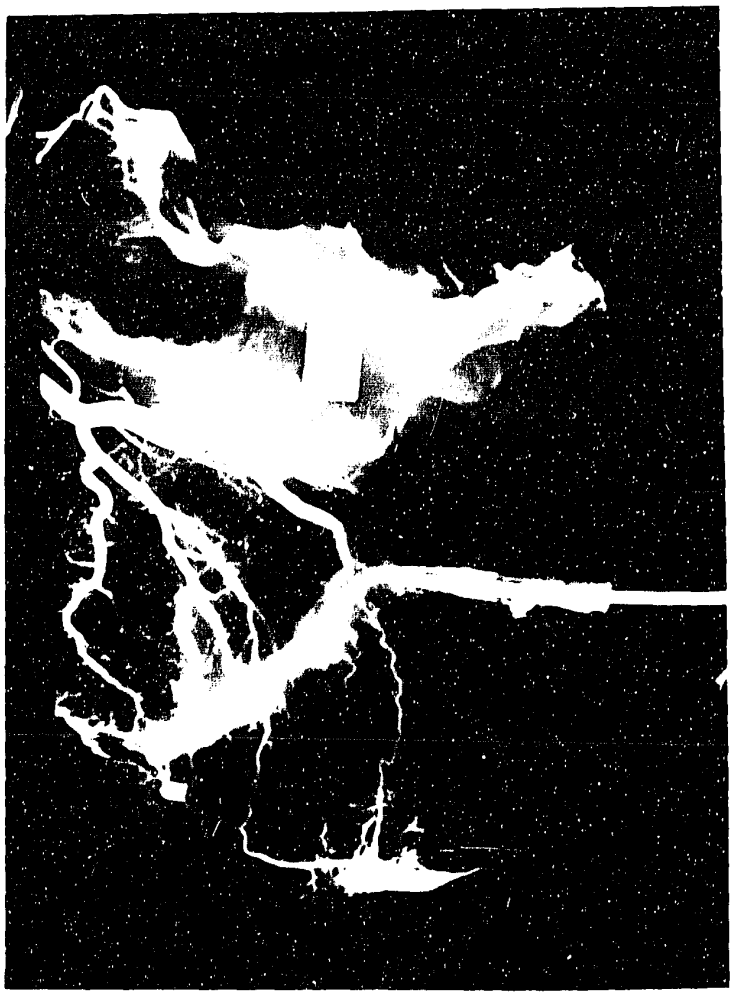


FIGURE 25: Same animal (# 407) showing the blown up picture of the site of implantation of the right internal mammary artery in the right ventricular myocardium. Note extensive anastomotic channels formed around the entire length of the implanted vessel.

RESULTS

The results of this entire work are tabulated in such a way to give as expansive a coverage as possible of the entire project. Individual and averaged-group distribution records are presented for clarification and correlation of results, this leading to definitive conclusions.

CONTROL GROUP:

In this group of 20 dogs (12 males and 8 females weighing an average of 44.4 lbs.), the average per cent occlusion of the right coronary artery was 86.7% ranging from 100% to 70%. The mortality rate was 10%, since two animals died out of the entire group of 20. Massive recent infarction (+++) was evident on these two animals that expired.

Grossly, only four hearts (20%) showed definitive infarction of the right ventricle. Microscopically, infarction was evident in 12 hearts, either recent or healed, giving us a significant figure of 60% in the control group. In all the animals that infarcted, pathology was evident only in the right ventricle; the interventricular septum completely free on all cases. Four animals (20%) out of the twenty showed massive myocardial infarction or fibrosis on the right ventricle, five animals (25%) showed moderately severe myocardial infarction, and 3 animals (15%) showed microscopic scattered foci of myocardial necrosis. Eight animals (40%) were entirely disease-free. Anastomoses between the anterior descending branch of the left coronary artery was noted in five animals giving us a 25% intercoronary anastomoses.

IMPLANTED GROUP:

SUBGROUP I: (The needle technique; artery implanted on outflow tract). There were 7 experimental animals (five males, two females, weighing an average of 43.5 lbs.) in this subgroup. The average percentage occlusion of the right coronary artery was 93.4% ranging from 100% to 86%. There was one mortality (14%) which showed gross and microscopic evidence of recent moderately severe infarction. In all, there were two animals exhibiting infarction or fibrosis, thereby giving an average infarction percentage of 28% (old and recent).

The average percentage patency of the implanted internal mammary artery was 20.5% ranging from 47% to 2%. There was no evidence of mammary- right coronary anastomoses (0%). In one animal there was a mammary - anterior descending anastomoses (14%). The average number of survival days (sacrificed-died) was 62.1 days.

SUBGROUP II (Tunnel technique; artery implanted on outflow tract). There were 10 experimental animals in this subgroup; 6 males, 4 females, weighing an average of 44.2 lbs. The average percentage occlusion of the portion of the right coronary artery within the ameroid constrictor was 87.1%. There were two mortalities (20%), both showing evidence of myocardial infarction by microscopic examination. Out of the ten animals in the entire group, a total of 3 (30%) were noted to have microscopic infarction ranging from a moderately severe (++) subendocardial infarction, to scattered (+) foci of necrosis.

The average patency of the implanted right internal mammary artery was 34.9%, ranging from 72% to 5% patency.

In one animal, injection of the implanted right internal mammary

artery with Schlesinger mass showed extensive filling of the right coronary arterial system. The left coronary arterial system was also filled through the left anterior descending artery. Therefore, we have a 10% mammary - right coronary anastomoses, and 10% mammary - left anterior descending anastomoses.

For this group the average number of survival days (died and sacrificed) was 99.2 days.

SUBGROUP III (Tunnel technique; artery implanted on superior lateral aspect of right ventricle). In this group of 20 experimental animals (13 males, 7 females, with an average weight of 43.9 lbs.), the average percentage occlusion of the right coronary was 93.6%. There were 4 mortalities out of 20; a 20% mortality rate. Out of these four animals, two showed massive (+++) recent infarction, and one showed a moderately severe (++) recent myocardial infarction. The 4th animal that expired showed no evidence of myocardial infarction either grossly or microscopic. Death in this particular case was attributable to pneumonia which was noted on postmortem examination. Aside from these 3 animals with recent infarcts, another dog showed microscopic evidence of a moderately severe endocardial fibrosis; all in all a 20% infarction rate (recent and old) for this particular group.

The average patency of the implanted internal mammary artery was 62.7%, as compared to 20% in subgroup I and 34% in subgroup II. It is interesting to note that not one of the animals in subgroup III had a patency of less than 50% of the implanted internal mammary artery.

Injection of the implanted internal mammary artery showed extensive

or complete anastomoses with the right coronary arterial system in 16 animals; an 80% mammary - right coronary anastomoses. Likewise, the same injection resulted into complete filling of the left coronary arterial system through anastomoses with the left anterior descending artery in 13 animals; a 65% mammary - left anterior descending anastomoses.

The average number of survival days (died and sacrificed) was 80.7 days).

DISCUSSION

Any surgical procedure designed for the relief of myocardial ischemia should be capable of answering several criteria in order for it to be judged an adequate revascularization procedure. First, it must bring adequate oxygenated blood to the right and left coronary arterial trees; Second, it must provide equal and even distribution of all oxygenated blood reaching the heart muscle; and third, it must be a procedure that will not only protect but also maintain the integrity of the myocardium in the years to come (life long protection).

A decade or so ago, such a statement might have been considered futile or even foolish, but in the realm of the present, it is the only valid criteria that could be set forth to judge a revascularization procedure. Developing such an operation is almost synonymous to implementing a surgical method for coronary artery insufficiency that will be capable of total and complete myocardial revascularization. In short, this is our purpose in the development of the right internal mammary artery implantation to the right ventricular myocardium.

Certain anatomico - pathological facts were considered in the formulation of the above criteria, namely:

(1) multiple involvement of the coronary arteries by Atherosclerosis

(2) Progressive nature of coronary atherosclerotic disease

(3) Preponderance of the right coronary arterial tree

in man - this is predominent in 50% of cases, i.e., it supplies all of the right ventricle, posterior half of the interventricular septum, and a large part of the posterior wall of the left ventricle (Schlesinger, 1940). Likewise, Gross in 1921 and Barnes in 1940 showed that in 75% of hearts most of the posterior ventricular surface is supplied by the right coronary artery.

(4) Inadequacy of the left internal mammary artery after implantation to supply the entire heart.

This fact was brought to Vineberg's attention in 1956 when one of his patients who had undergone internal mammary artery implantation four years previously died of a ruptured right ventricular aneurysm. Postmortem examination showed that the only patent artery in the heart was the internal mammary artery, and that the left ventricular muscle appeared to be healthy. Another patient who was pain free for six years after left implantation had recurrence of anginal pain. Cine coronary angiographic examination of the internal mammary artery showed the implant widely open perfusing the left ventricular myocardium $7\frac{1}{2}$ years postoperatively but not the right ventricle which was ischemic due to a blocked right coronary artery (Vineberg 1966).

EVALUATION OF RESULTS: In the discussion of the overall results, the following will be dealt with separately in order to give a clear picture of the final outcome of this study:

(1) Mortality and survival rate

(2) Survival of the myocardium

(3) Demonstration by means of radio opaque injection mass

of extracardiac and intercoronary anastomostic channels arteriolar or larger in size.

SURVIVAL OF THE ANIMAL: Coronary artery constriction was developed in this study by the use of the ameroid constrictor applied around the origin of the right coronary artery. It is a well known fact that the arterial pattern of the dog's heart is similar to that of man except for the left coronary artery predominance.

Thus animal survival will not be a criteria in the final evaluation of this study. Basically, our main aim was not to utilize the right coronary artery as an animal survival test, but to compare myocardial muscle survival in the implanted and non-implanted group. In addition the production of myocardial ischemia in the right ventricle was considered necessary to stimulate the implanted internal mammary artery to form mammary coronary anastomosis.

Mittal et al (1966), utilizing the right coronary artery as a "test ligation" model in the dog got a mortality rate of 4% in a series of 50 dogs, leading him to conclude that employment of the right coronary artery for test ligation experiment does not appear acceptable.

Lumb et al (1963) finding the close similarity in coronary artery distribution between pigs and man (right coronary predominance), ligated the right coronary artery of the pig, close to its origin. He used 20 experimental animals, with death ensuing in all 20, giving him a 100% mortality.

The mortality rate in this study reveals an almost

similar pattern for all the group. We have a 10% mortality (2 out of 20) for the control group; 14% for subgroup I (1 out of 7); 20% for subgroup II (2 out of 10) and 15% for subgroup III (3 out of 20). As previously stated we will not attempt to correlate mortality rate with the other findings. The only thing worth pointing out, however, is the relation of recent infarction to all the deaths in the different groups, both implanted and control. In the control group this could be explained on the basis of no inter-coronary anastomoses; in the implanted group on the basis of absence of mammary - coronary anastomoses and intercoronary anastomoses. An exception to this is a dog in subgroup II that expired with no evidence of infarction except for some old microscopic focal fibrosis. The most plausible explanation is on the basis of myocardial ischemia leading to ventricular fibrillation and death.

SURVIVAL OF THE MYOCARDIUM:

Myocardial survival in the face of continued and progressive ischemia is one of the valid tests for any revascularization procedure. There seems little doubt that failure to relieve ischemia eventually results in the death of myocardial fibers and their replacement by scar formation. Continued myocardial ischemia may result in myocardial hypertrophy or acute myocardial infarction with resultant massive myocardial fiber loss. Our results shows this fact clearly. On our control group of 20 animals, we have a total infarction percentage of 60%, both gross and microscopic. Grossly, infarction was evident in only 4 out of 20 animals (20%), but microscopically myocardial necrosis was noted in 12 of the 20 animals accounting for the 60% total

rate. Significance of these figures could easily be appreciated when compared with the infarction percentage of the implanted group, which were 28% for subgroup I, 30% for subgroup II and 20% for subgroup III. There is no doubt that extracardiac blood via the implanted right internal mammary artery afforded some form of protection to the slowly progressive ischemic process produced by the ameroid constrictor. This is the basic explanation for the much lower infarction rate in Subgroup III, where extensive mammary - right coronary, and mammary - left anterior descending anastomosis were noted. For subgroups I and II, such explanation is not valid entirely since the percentage of mammary - right coronary and mammary left anterior descending anastomoses were quite low. Most likely the combined effects of homocoronary and intercoronary anastomosis formation entered into play here. However,whatever the actual explanation is, the low infarction figures in these two groups, as compared with control, indicates that an open implant gives some protection to the myocardium: This is not surprising as Austin (1966), using flow meters on the left internal mammary artery, has shown a 5 c.c. per minute flow immediately after implantation.

RADIOGRAPHIC DEMONSTRATION OF MAMMARY - CORONARY ANASTOMOSIS:

Vineberg as early as 1946 showed clearly that an internal mammary artery implanted into the left ventricular wall forms many anastomoses with the ventricular arteriolar system. Since then, numerous other investigations had duplicated and verified his results. A thorough review of literature failed to reveal a similar procedure

being tried on the right ventricle, except for an almost similar work done by Sabiston and Fauteux in 1959, when they implanted the carotid artery on the right ventricular myocardium.

Physiologically, the right ventricle differs in a lot of ways from the left ventricle, especially in regards to pressure changes during the cardiac cycle. Aside from the work done by Sabiston and Fauteux (1959), no other investigation has been made regarding the implantation of a high pressure vessel in a low pressure system such as the right ventricle. We have shown through our results that it is possible to produce extracardiac anastomoses in this low pressure system.

We used 3 groups of animals in the implanted series to determine if there will be any difference in regards to patency of the implant and anastomotic formation by :

(1) varying the site of implantation

(2) Varying the length of the tunnel and implanted artery,

(3) varying the technique of tunnel formation

Results showed a great variation in the three subgroups, with subgroup III exhibiting the highest percentage of mammary - right coronary and mammary left anterior descending anastomoses; 80% and 65% respectively. In this subgroup a longer length of artery was implanted (4.5 to 5 cm.) and the site of implantation chosen was just beneath the branches of the main right coronary artery on the superior lateral aspect of the right ventricle. The tunnel was created by the spreading effect of a hemostat. Average patency of the internal mammary artery in this subgroup was 62.7% (ranging from 50% to 80% patency),

compared to average patency of 34.9 for subgroup II and 20.5% for subgroup I. As previously described in the chapter of method and procedures, the meedle technique was used to create the tunnel in subgroup I, with the outflow tract as the implantation site. For subgroup II, the spreading effect of a hemostat was used to create the tunnel with the site remaining the same as in subgroup I.

It is definite then that the technique in creating the tunnel affects patency of the implanted mammary artery. The needle technique was utilized to minimize right ventricular cavity perforation, but apparently the tunnel created by needle insertion is not wide enough mechanically for the implantation of the vessel. This results in compression followed by inadequate perfusion with subsequent development of intimal proliferation; thus accounting for the low mammary artery patency percentage of 20.5% in this subgroup.

In the case of subgroup II, the low patency percentage of the implanted vessel and the low percentage of mammary - coronary anastomosis cannot be ascribed to the technique in tunnel creation; since an exactly similar method was followed in subgroup III. The logical explanation might be found on the site of implantation and length of the implanted vessel.

Sabiston and Fauteux (1959) trying to find the explanation for the continued patency of the majority of arterial implants within the ventricular myocardium compared this with his previous work of similar implants into organs such as the sterno-cleidomastoid muscle, spleen and liver. He found a very early and high percentage of occlusion in these vessels, leading him to suggest

that the rhythmical contraction of the ventricle is responsible for the persistent patency of implants in the heart. Whether there is any pressure differential in force of contraction of the myocardium in the outflow tract and the anterolateral wall of the right ventricle is something to consider seriously, since it would be a logical explanation for the big difference in percentage patency and percentage of mammary - coronary artery anastomosis formations in these two sites. Another plausible explanation in regard to the site of implanation is implanting the artery in a site which brings it in close proximity to branches of the right coronary artery (subgroup III). It is but logical to assume that this close proximity initiates early anastomosis between the mammary artery and the branches of the coronary artery especially if there is some pressure gradient in the area produced by the slow occlusion of the coronary artery by the ameroid constrictor.

As to the influence of the length of the tunnel, we have noted on blown up pictures of the anastomatic site (mammary - coronary) that anastomosis not only occurred at the site where the two side branches were left open but did also occur in the other part of the implanted artery, leading us to believe that a longer tunnel will be more beneficial, as was verified by the higher percentage of patency and mammary coronary anastomosis in subgroup III.

Another salient point to verify is the 65% occurrence of mammary - left anterior descending anastomosis in our series in subgroup III. The possibility that this is just a normally occurring anastomosis between the two coronary systems has occurred to us. In our control group of 20 animals the left coronary artery

was injected with Schlesinger mass to determine the normally occurring anastomosis between the left arterior descending artery and the right coronary arterial system. Only in five out of the 20 animals (25%) were these intercoronary anastomosis noted. Thus it is clear that the implanted right internal mammary not only forms anastomosis with the right coronary arterial system, but also with the left coronary arterial tree through the anterior descending artery.

Thus arterialization of the right coronary arterial system by implantation of the right internal mammary artery into the right ventricular myocardium is definitely possible. Clinically, the success of this procedure has definite significance; We feel that this procedure, in combination with other revascularization methods (left internal mammary implantation, epicardiectomy and free omental graft operation) may be the ideal revascularization procedure since it answers all the criteria set forth for a complete and total revascularization of the ischemic myocardium. A combination of these procedures will ensure formation of many arterial channels that are needed to be certain that the summation of flow will be as great or even greater than the total capacity of the patients coronary arterial system prior to the onset the disease. The formation of this multiple extracardiac arteriolar anastomosis will thus provide continued relief from myocardial ischemia in the face of progressive coronary artery disease.

By itself this procedure has a lot of possible indications. First, it will be the procedure of choice in cases of non-patency of a previously implanted left internal mammary artery. Experimental and clinical experience has shown that a certain percentage of implanted

internal mammary arteries will thrombose - roughly 20%. (Vineberg and Walker 1964). Second, a right internal mammary artery implantation could be performed in cases of traumatic occlusion of the right coronary artery. Vineberg has utilized this procedure once for this indication recently. (Vineberg, 1966). Third, in patients who had a previous left internal mammary implantation but because of the progressive nature of the atherosclerotic process now need additional source of extra coronary blood.

SUMMARY AND CONCLUSIONS

(1) Fifty-seven healthy adult mongrel dogs of both sexes weighing 40 lbs to 50 lbs and between 2 - 4 years of age were utilized in this experimental study. A minimal period of $2\frac{1}{2}$ months and a maximal period of $3\frac{1}{2}$ months were allowed before the surviving animals were sacrificed for the postmortem studies.

(2) Myocardial ischemia was produced by placement of an ameroid constrictor around the origin of the right coronary artery. The coronary artery occlusion was slow, adequate, constant and predictable.

(3) Animals in the control group (no revascularization procedure done) exhibited the highest percentage infarction rate (60%) among the different groups.

(4) Animals in the implanted subgroup I had a percentage infarction rate of 28%, mammary-coronary anastomosis was only evident in 14% of cases.

(5) Animals in the implanted Subgroup II had an average infarction percentage of 30%, and mammary-coronary anastomosis was present only in 10% of cases.

(6) Animals in the implanted Subgroup III gave the best overall results, showing an infarction rate of only 20% with extensive formation of mammary - right coronary anastomoses (80%), and mammary - left anterior descending anastomoses (65%).

(7) Reasons were given to explain the variations in results in the different subgroups, with final correlation of the overall findings.

(8) Indications for the clinical use of the right internal mammary artery implantation to the right ventricular myocardium were given, either as an operation in combination with other procedures, or as a single procedure.

In summary, an operation was devised that revascularizes the right ventricular myocardium, posterior interventricular wall, and the posterior part of the interventricular septum in a direct way, and that is by formation of adequate sized arteriolas that produces anastomoses between different arteriolar zones in the right and left coronary arterial system. This procedure, in combination with other revascularization methods, answers all the criteria set forth for a complete and total revascularization of an entire ischemic heart.

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