EXPERIMENTAL ATTEMPTS TO INCREASE THE BLOOD SUPPLY TO THE DOG'S HEART BY MEANS OF CORONARY SINUS OCCLUSION*

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This report deals with experimental attempts to alter the blood supply of the dog's heart in such manner as to render it less susceptible to the infarctions which follow sudden occlusion of the anterior descending branch of the left coronary artery.[1] Inasmuch as the ultimate objective of this work is its application to those conditions in the human heart which are associated with myocardial ischemia (angina pectoris of vascular origin generally due to sclerotic or thrombotic coronary occlusion), three practical desiderata were kept in mind: (*a*) the production of an adequate functional increase in the blood supply to the heart; (*b*) the employment of a method requiring a minimum of manipulation; (*c*) the attainment of the desired results after a minimum lapse of time.

In 1921, Gross (1) showed that there are three vascular mechanisms in the blood supply to the human heart which probably serve as compensatory means to ward off the results following coronary artery narrowing or occlusion. The first and most important of these mechanisms is a gradual and consistent widening of intramyocardial anastomotic channels which occurs with increasing age. A conspicuous portion of these anastomotic channels are situated in the interventricular septum. The second compensatory mechanism is the age period development of rami telae adiposae, vessels which lie in the epicardial mantle and anastomose with the myocardial vascular ramifications on the one hand, and with periaortic

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[1] This vessel will be referred to in this report as the left anterior descending branch.

and peripulmonic vessels on the other. The third mechanism is the existence of anastomoses between the myocardial and pericardial vascular ramifications and extracardiac vessels (bronchial arteries, arteriae mammariae internae, and diaphragmatic vessels). These studies were subsequently confirmed and extended by Campbell (2), Davis (3), Robertson (4), Hudson, Moritz, and Wearn (5), and by Gross and Kugel (6). That these mechanisms may at times adequately compensate for coronary artery occlusion was suggested by Gross (1) in a series of injection studies on the human heart. Apparently, the adequacy of the compensatory mechanisms depends upon the slowness of the occluding process in the coronary arteries or their branches.

A fourth possible compensatory mechanism which has been emphasized by Wearn (7) is the so called Thebesian backflow. This author believes that under certain circumstances the heart may be nourished by means of retrograde circulation by way of the Thebesian vessels. This theory has received considerable attention and has been both supported and refuted by many experiments.

Recently, augmentation of these extracardiac anastomoses by means of epicardiectomy (stripping of the epicardium) was attempted by Beck, Tichy, and Moritz (8), and by Beck and Tichy (9). Simultaneously, and in graded stages, a gradual occlusion of the coronary arteries and their branches was produced. Some of the dogs tolerated this procedure to a point of considerable narrowing of the coronary bed. No statistical data of the mortality rate are presented, although the authors indicate that this was high. Encouraged by these observations, Beck (10) engrafted the left pectoral muscle on the heart of a patient in whom a diagnosis of coronary sclerosis and angina pectoris was made. $3\frac{1}{2}$ months after the operation the patient was alive and claimed to be well.

More recently, Robertson (11) carried out experiments in dogs in an effort to determine the validity of the Thebesian backflow theory. The coronary sinus, main veins, and coronary arteries were tied off in several stages. In a typical experiment the procedure lasted approximately 6 months. Robertson observed that the venous ligatures were well tolerated by all animals. Following the first coronary artery ligation which closed the main trunks at their origin, the dogs survived for at least some hours. The majority, however, died within 24 to 48 hours. Three showed no ill effects (no data are furnished on the number of animals used). From his experiments and microscopic studies, Robertson concluded that little or no nutritive function developed in the Thebesian vessels but that this depends on the pericardial adhesions.

None of the above mentioned authors reports control experiments on gradual occlusion of the coronary bed without previously or simultaneously producing pericardial adhesions. Inasmuch as gradual coronary artery occlusion by itself leads to compensatory dilatation of intramyocardial anastomoses, the interpretation of their results is open to question. In a recent discussion on the factors concerned

in the development of collateral coronary circulation during slow coronary occlusion, Wiggers (12) has stressed the importance of pressure gradients in distending minute potential communications. Furthermore, Beck and Tichy (9) have already found that vascularization of the myocardium from a collateral bed was slight, and in some experiments, completely absent if the coronary circulation was normal. It seems, therefore, that before applying the epicardiectomy or cardiopexy procedures to the human heart it would be advisable to obtain direct experimental evidence that such pericardial adhesions alone (*i.e.*, without simultaneous coronary artery occlusion) lead to sufficient augmentation of the cardiac vasculature to permit of subsequent sudden coronary artery occlusion with a decrease in the extent of infarction. Apart from these objections, however, the authors themselves observe that the procedures are extremely hazardous and time-consuming. They, therefore, fail to fulfill the criteria considered necessary for a practical method which could be applied to the human heart.

The well known clinical observation that anginal pains not infrequently disappear during an attack of right sided heart failure led one of us to the thought that increased tension in the coronary sinus might accomplish the same result. Because of this and other theoretical considerations as well as anatomical observations, it appeared desirable to determine whether an increase in intramyocardial collateral circulation would follow coronary sinus obturation, and if so, whether the increase was associated with functional enhancement of the myocardial nutrition. In previous communications we have briefly described the results obtained in dogs by the employment of this method (13), the details of a relatively simple technique for occluding the coronary sinus (14), and the electrocardiographic (15) changes which follow complete and partial occlusion of the coronary sinus by various techniques. We have shown that the procedures employed by us can be performed within 20 minutes, and apparently produce a rapid increase in the extent of the coronary bed in the dog's heart. Furthermore, the dilatation of the intramyocardial collateral circulatory channels thus produced is apparently so extensive and abundant that in the majority of otherwise normal dog hearts prepared in this manner it becomes difficult or impossible to induce in-

farction by subsequent sudden occlusion (division between ligatures) of the left anterior descending branch 2 cm. below the aortic ostium of the left circumflex coronary artery. It is the purpose of this report to describe in greater detail the results obtained in a larger series of animals and to add a number of observations on the effects of the various procedures employed to produce complete or partial occlusion of the coronary sinus, and on their effectiveness in preventing or minimizing the results of subsequent acute occlusions of the left anterior descending branch.

Methods

The methods employed in these experiments are listed in Table I. The dogs weighed approximately 15 kilos. All procedures were carried out under pernoston or nembutal anesthesia. The method of approaching the coronary sinus has been described in detail in a previous report (14). With the dog under anesthesia, a skin incision is made in the right fifth intercostal space extending from the border of the sternum to the mid-axillary line. The chest cavity is entered through this incision and artificial respiration is employed. Care must be taken to avoid hyperventilation or insufficient aeration. After deflation of the right lung by compression with moist pads, an incision 6 cm. long is made in the pericardium parallel to and 0.5 cm. anterior to the phrenic nerve. The incision should extend 1 cm. cephalad to the atrioventricular sulcus. This exposes the coronary sinus. Ligature is effected by passing a blunt needle deep to the coronary sinus in an oblique direction. The point of entry of the needle should be located on the atrial side about 1 cm. from a dimple or puckering which marks the ostium of the coronary sinus. The point of emergence of the needle should lie on the ventricular side 0.5 cm. from the dimple.

As may be seen from Table I, escharotics were used in some experiments in order to produce thrombosis of this vessel, or such considerable perivenous sclerosis as would tend to narrow or occlude the vessel from without. 1 to 2 cc. of the escharotic were injected around the mouth of the coronary sinus (perisinus injection) or within its lumen. The escharotics used were 5 per cent and 10 per cent aqueous solutions of sodium morrhuate, 30 per cent aqueous solution of sodium salicylate, and tincture of green soap (U. S. P.). In order to introduce the escharotic into the coronary sinus, several methods were employed. One was the introduction of a cannula transauricularly. The cannula is fashioned with a pear-shaped extremity in order to prevent the escharotic from being washed out of the coronary sinus by blood flow. The cannula, filled with the escharotic, is introduced through an opening in the right atrium around which there has first been placed a purse-string suture. With little experience the cannula is inserted into the mouth of the coronary sinus, at which site it may be visualized and felt manually (through the visceral pericardium). The cannula is kept in place and 1 to 2 cc. of the escharotic

is injected into the coronary sinus. After 10 minutes, the cannula is removed and the purse-string suture in the atrium closed off.

TABLE I

Operative Mortality Rate Associated with Coronary Sinus Occlusion in Dogs

	No. of dogs	No. surviving	No. dying within 24 hrs.	Operative mortality rate (within 24 hrs.)
				per cent
Complete coronary sinus occlusion				
Ligation	46	31	15	33
Dissection and ligation	16	9	7	44
Ligation and injection*	8	4	4	50
Intrasinus injection* through transauricular cannula	2	1	1	50
Intrasinus injection* with temporary occlusion†	17	7	10	59
Total	89	52	37	= 42
Partial coronary sinus occlusion				
Ligation	6	6	0	0
Dissection and ligation	2	2	0	0
Ligation and injection*	4	3	1	25
Perisinus injection*	14	12	2	14
Intrasinus injection* through transauricular cannula	2	2	0	0
Intrasinus injection* with temporary occlusion	11	10	1	9
Total	39	35	4	= 10
Unsuccessful coronary sinus occlusion				
Ligation	7	7	0	0
Dissection and ligation	1	1	0	0
Ligation and injection*	3	3	0	0
Perisinus injection*	1	0	1	100
Intrasinus injection* through transauricular cannula	4	2	2	50
Intrasinus injection* with temporary occlusion	5	2	3	60
Total	21	15	6	= 29

* Escharotics were injected as indicated in text.

† Temporary occlusion by ligature or digital.

Another method of temporarily retaining the escharotic in the coronary sinus was by digital compression of the vessel, or better still, by a temporary ligature. In these experiments, the escharotic is introduced into the distal portion of a coronary sinus by means of a hypodermic syringe. After 5 to 10 minutes the occlusion is released. Recently, we have been attempting to inject the escharotic through a cannula introduced through the right jugular vein. Our observations following the use of this procedure are as yet incomplete.

In order to occlude the left anterior descending coronary branch, the left chest is entered through the third intercostal space, artificial respiration being simultaneously applied. The pericardium is exposed from above the conus to the apex for a distance of 4 cm. from the latter. After carefully exposing the left anterior descending branch and its venae comites, approximately 2 cm. from the left circumflex coronary ostium, two suture ligatures are placed about it and the artery is divided between them. It is most important to emphasize the necessity of cutting the artery between ligatures since ligature alone of the artery is not infrequently unsuccessful for the production of complete occlusion.

In some of the experiments, topical injections or applications of alcohol or cocaine solutions were made around the region of the coronary artery occlusion in an effort to avoid possible nervous factors influencing the vascular system. The results of these experiments were inconclusive.

After death of the dogs, autopsy was performed and the hearts were injected under standardized conditions with a barium sulfate suspension in gelatine using the method described by Gross (1, 16). It is to be noted that this method injects the coronary tree as far as the arterioles and precapillaries. Since the injection mass does not reach the capillary bed, this method offers more reliable information concerning the extent of the arterial tree than one which fills the capillary bed and enters the veins, such as used by Beck and his associates. The barium sulfate-injected hearts were fixed in 10 per cent neutralized formalin saline.[2] Roentgenograms were then taken of the intact heart as well as of serial slices of the specimen 7 mm. thick, cut transversely from base to apex.

Electrocardiographic records were taken before and during anesthesia, when the pericardium was opened, after dissection of the vessel or after passing the ligatures, immediately after tying and cutting the vessels, after the closure of the chest, and finally at various intervals (hourly or daily) until the dog died or was sacrificed. The electrocardiographic changes following coronary sinus occlusion have already been reported elsewhere in detail (Gross, Silverman, and Master (15)). Since these findings are of some significance in elucidating the results obtained in these experiments, reference will be made to them in this report. In addition, observations on the electrocardiographic changes following occlusion of the left anterior descending branch will be mentioned briefly. This will be taken up more fully in a subsequent report.

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[2] Solution of formaldehyde U. S. P. 10 parts, 1 per cent sodium chloride solution 90 parts. This solution is rendered neutral with a weak alkali.

EXPERIMENTAL

1. Results Following Sudden Complete Occlusion of the Left Anterior Descending Branch 2 Cm. below the Ostium of the Left Circumflex Coronary Artery

In order to compare the results of sudden complete coronary artery occlusion upon dogs which had withstood coronary sinus obliteration, with control animals in which no previous manipulation had been carried out, sudden occlusion of the left anterior descending coronary branch was produced in 53 dogs. The operation was performed under pernoston or nembutal anesthesia in the manner previously

TABLE II

Results of Sudden Left Anterior Descending Branch Occlusion in Control Dogs and in Dogs Prepared by Preliminary Coronary Sinus Occlusion

Preliminary procedure	No. of dogs	No. dying within 24 hrs.	Operative mortality rate (within 24 hrs.)	No. of dogs surviving sudden L.A.D.* occlusion	Average size of infarct
			per cent		
Control	53	28	53	25	24 dogs, 5 x 5 cm. 1 dog, 1 x 1 cm.
Complete coronary sinus occlusion	29	16	55	13	7 dogs, no infarct 2 dogs, 1 x 1 cm. 4 dogs, 3 x 3 cm.
Partial coronary sinus occlusion	29	9	31	20	2 dogs, no infarct 2 dogs, 1 x 1 cm. 7 dogs, 3 x 3 cm. 9 dogs, 5 x 5 cm.
Unsuccessful coronary sinus occlusion	13	9	67	4	3 dogs, 3 x 3 cm. 1 dog, 5 x 5 cm.

* Left anterior descending branch.

described. 28 of these dogs died within 24 hours of the operation (Table II). Death was generally due either to surgical shock or to ventricular fibrillation. The significance of these two factors will be taken up in the discussion. It was found that when dogs survived for over 24 hours the mortality rate, due to the operative procedure, dropped sharply. In this report, therefore, the mortality rate will refer to death taking place within 24 hours of the operative procedure.

In a series of studies at present being carried on by Gross, Mendlowitz, and Schauer (17), the cardiovascular dynamics in these dogs were carefully investigated. In brief, the outstanding features following such occlusion of the left anterior descending branch are diminished cardiac output and delay in cyanide

circulation time. In a number of hearts there was present a darkening of the anterior wall (beginning infarction). On injection, the vascular tree usually showed a large filling defect. In all cases the remainder of the coronary tree was similar to that found in normal animals.

Twenty-five dogs were sacrificed at periods ranging from 36 hours to 12 weeks. Most of the dogs were permitted to survive 1 week. In 24 of these dogs, the hearts showed a large infarcted area on the surface of the left ventricle bordering the interventricular septum and apex. These infarctions averaged 5 x 5 cm. on the surface. In one heart, the infarct measured 1 x 1 cm. The injection invariably disclosed a filling defect of the coronary tree (Figs. 1, 2, 3, and 4) which corresponded roughly to the size of the infarct. In ten dogs the remaining vasculature was similar to that seen in the intact heart. In seven, the arterial tree was somewhat dilated, suggesting the possibility of a beginning compensatory process.

The electrocardiographic changes which were most frequently associated with the left anterior descending branch occlusion consisted of RT_1 elevations and ST_2 and ST_3 depressions. In approximately one-third of the dogs these electrocardiographic changes occurred in such combinations as were not found in dogs which had previously undergone coronary sinus occlusion.

2. Results Following Sudden Complete Occlusion of the Coronary Sinus

The coronary sinus was completely occluded[3] in 89 dogs by the methods listed in Table I. Immediately after occluding the coronary sinus, whether by ligature or cannula, a turgidity was noticed of the entire heart. The superficial veins became engorged and the left ventricle became cyanotic up to and slightly beyond the interventricular grooves. Occasionally, ecchymotic spots appeared on the surface of the left ventricle. The right ventricle retained its normal color except for a strip adjacent to the interventricular grooves, particularly on the posterior aspect of the heart.

Thirty-seven of these dogs died in less than 24 hours. The remaining dogs survived or were permitted to survive for a period up to 6 months after the coronary sinus occlusion. The average survival was approximately 4 weeks. Death under 24 hours was generally associated with evidence of surgical shock, although cardiac asphyxia due to the sudden venous congestion may have played a rôle. In this group of experiments, occlusion by the ligature method was associated with the lowest mortality rate. It must be noted, however, that in this experiment the attempts made in the use of the escharotic method were relatively crude as we were endeavoring to determine the optimum escharotic fluid and the effective dose to be employed. As a result, the escharotic method showed a mortality rate which was probably in excess of that which could be secured by the use of milder escharotics. In a number of dogs the venous thrombosis was so extensive and the necrosis of the myocardium so marked that this undoubtedly led to the death of the animal.

[3] The extent of coronary sinus occlusion was always determined at autopsy.

Immediately following complete occlusion of the coronary sinus, the following electrocardiographic changes were consistently observed: elevation of the RT transition, notching and downward direction of the main QRS deflection, inversion of the T wave, and temporary slowing of the heart rate. Large T waves of a transitory nature were occasionally noted. Partial heart block was noted in two dogs. The slowing of the heart rate lasted a few minutes and took place only when ligature was employed. The fact that it did not take place when escharotics alone were used indicates that the slowing is not due to irritation at the mouth of the coronary sinus. When the coronary sinus was dissected before ligation, the immediate records showed no downward direction of the QRS deflection, notching of the QRS was less frequent, the T waves were inverted and the RT transition was elevated. When escharotics alone were used for the occlusion, the electrocardiographic changes were inconstant. All electrocardiographic changes tended to return to normal within 2 to 4 weeks.

After death of the dogs, the hearts were injected with a barium sulfate suspension in gelatine and roentgenograms were taken. In most instances, the coronary artery tree showed considerable dilatation (Fig. 5), as compared to that found in intact dogs' hearts (Fig. 1). The vascular channels were on the whole wider, and more vessels were generally visible.

In order to determine whether this increase in the extent of the coronary tree was associated with a corresponding functional improvement in the nutrition of the myocardium, dogs which had survived coronary sinus occlusion were submitted to subsequent sudden left anterior descending branch occlusion. If it could be shown that the incidence and extent of infarction is thereby reduced, this would suggest that the widening of the vascular channels is associated with a better perfusion during life or that a more extensive shunt mechanism is provided so that additional vascular channels may more easily take over the function of the occluded vessels.

3. Results Following Complete Occlusion of the Left Anterior Descending Branch 2 Cm. below the Ostium of the Left Circumflex Coronary Artery in Dogs Which Had Survived Complete Coronary Sinus Occlusion

In 29 dogs which had survived complete coronary sinus occlusion for a period of time varying from 1 to 8 weeks (average 4 weeks), sudden left anterior descending branch occlusion was performed in the manner described above (Table II). Sixteen of these dogs succumbed during the first 24 hours following the left anterior descending branch occlusion. No infarct or discoloration was seen on the surface of the heart. On injection, most of the hearts showed an enrichment in vasculature. Only one heart showed a filling defect on injection.

Thirteen dogs survived or were permitted to live for a period of time ranging from 3 days to 6 weeks (average 1 week) following the left anterior descending branch occlusion. In seven of these, no infarcts were present (Figs. 5, 6, 7, and 8). In two, a very small infarct measuring 1 x 1 cm. was found. In four, infarcts definitely smaller than those almost invariably found in the control animals, were present in the dogs' hearts. These averaged 3 x 3 cm. on the surface. The only filling defects at times noted on injection were those corresponding to the infarcts. Almost invariably the coronary tree was considerably enriched and dilated.

Unfortunately electrocardiographic studies were made only on those dogs which died in less than 24 hours or in those which presented small infarcts. The most frequent findings were elevation of RT_1 and depression of ST_2 and ST_3. The incidence of these changes was similar to that found in the control group 1. On the other hand, certain combinations of changes, *e.g.*, elevation of RT_1, ST_2, and ST_3, etc. were not found. This therefore, also suggested an influence of the preliminary coronary sinus occlusion.

In spite of the improvement in the nutrition of the myocardium as indicated by the decreased incidence and diminished extent of the infarctions, complete coronary sinus occlusion did not lower the mortality rate following subsequent left anterior descending branch occlusion (Table II). Undoubtedly, therefore, the factors responsible for death were not inhibited by the enrichment of the coronary tree. What these factors may be, and the relative importance of each will also be taken up in the discussion.

4. Results Following Partial Occlusion of the Coronary Sinus

In 39 dogs partial coronary sinus occlusion was produced by the procedures listed in Table I. Four of these dogs died within 24 hours. Six dogs succumbed to snuffles within 4 days to 6 weeks after the operation. The hearts were injected and showed a somewhat increased vascular bed. This, however, was not as consistent as in those in which the coronary sinus was completely occluded. The remaining dogs were permitted to survive for periods up to 6 weeks (average 1 week) at which time they were submitted to left anterior descending branch occlusion. Electrocardiographic findings in these dogs were qualitatively similar to those described in the dogs in which total coronary sinus occlusion had been produced. The QRS changes, however, were less constant.

5. Results Following Sudden Complete Occlusion of the Left Anterior Descending Branch 2 Cm. below the Ostium of the Left Circumflex Coronary Artery in Dogs Which Survived Partial Coronary Sinus Occlusion

The left anterior descending coronary branch was completely occluded in 29 dogs which survived partial coronary sinus occlusion for periods of from 1 to 6

weeks. In the majority of instances the partial coronary sinus occlusion in this series followed injection of escharotics into or around the coronary sinus. Of the 29 dogs in which sudden occlusion of the left anterior descending branch was produced, nine died within 24 hours after the operation (Table II). In three of these, vascular filling defects, but no discoloration or infarction, was noted.

Of 20 dogs which survived the left anterior descending branch occlusion for periods of from 1 day to 3 weeks (average 1 week) all but two showed an increase in the vascular bed. In two dogs there was no infarction. In two, the infarctions measured 1 x 1 cm. on the surface, in seven the infarctions averaged approximately 3 x 3 cm., and in nine the infarction was of the usual extent, averaging approximately 5 x 5 cm. on the surface. On injection, filling defects were present in the vascular tree corresponding to the presence and size of the infarct. The remainder of the coronary bed was usually increased in extent. The electrocardiographic changes were studied largely in the group of animals showing infarctions. They were similar to those described in group 3.

It appears from the above mentioned findings that in spite of the incomplete coronary sinus occlusion, there occurred a definite though moderate improvement in the nutrition of the heart so that in half of the dogs the infarctions following subsequent sudden left anterior descending branch occlusion were either absent or considerably smaller than those observed in the control group. Moreover, since the mortality rate following the left anterior descending branch occlusion was considerably lower (31 per cent) than in the group in which the preliminary coronary sinus occlusion was complete (55 per cent) or in which the preliminary coronary sinus occlusion was unsuccessful (67 per cent), it would indicate that partial, or perhaps gradual coronary sinus occlusion is the desirable approach to the problem. These observations, however, should be confirmed on a larger series of animals.

6. Results Following Unsuccessful Coronary Sinus Occlusion

The manipulations listed in Table I under the entry Unsuccessful coronary sinus occlusion were carried out in 21 dogs. In some (ligation), the coronary sinus was deliberately manipulated without intention to produce occlusion. The purpose of this was to discover whether dilatation of the coronary tree followed such manipulation, and in order to study the electrocardiographic findings. In the remaining dogs absence of coronary sinus occlusion was due to faulty technique. Electrocardiographic changes in this group were infrequent but were similar qualitatively to those described for the other groups (Nos. 3, 4). Their presence, together with the fact that subsequent left anterior descending branch occlusion appeared to

produce a smaller infarct in some of the dogs, suggested that a transient narrowing of the coronary sinus may have been present following the injection of escharotics. Six of these dogs died in less than 24 hours after operation. Two survived for periods of 1 and 3 weeks, respectively, and were sacrificed for anatomical studies. The remaining dogs were employed for the experiments described in the next group.

7. Results Following Sudden Complete Occlusion of the Left Anterior Descending Branch 2 Cm. below the Ostium of the Left Circumflex Coronary Artery in Dogs Which Had Survived Unsuccessful Occlusion of the Coronary Sinus

The left anterior descending branch was completely occluded in thirteen dogs which survived unsuccessful[4] coronary sinus occlusion for a period of from 1 to 6 weeks. Nine dogs died within 24 hours after the operation (Table II). Vascular defects were present in only two of these. No discoloration of the myocardium or other evidence of infarction was present.

Of four dogs which survived for an average period of 1 week, one showed an infarct measuring 5 x 5 cm. on the surface of the left ventricle and the other three showed smaller infarcts averaging 3 x 3 cm. It is thus seen that even in this group there seems to be a tendency for the infarcts resulting from sudden left anterior descending branch occlusion to be somewhat smaller than those found in the control group 1. Furthermore, as was indicated above, the occasional occurrence of some of the characteristic electrocardiographic changes (confined to those animals in which escharotics had been used), the somewhat more extensive vascular tree, and the lower incidence of vascular filling defects suggest the possibility that a transient occlusion was present in this group. In further support of this view was the perisinus thickening found in several of the hearts in which perisinus infiltration was employed.

DISCUSSION

In appraising the therapeutic value of coronary sinus occlusion as carried out in the experiments herein described, several pertinent facts must be borne in mind. First, the left anterior descending branch occlusion was complete and sudden. These experiments, therefore, differ in this important respect from those reported by Beck and his coworkers and by Robertson. Secondly, the results of such sudden coronary occlusion in unprepared dogs were completely controlled and are well known. In our control series of 53 dogs in which this procedure was carried out, 28 died in less than 24 hours. Roughly speaking, therefore, the mortality rate may be considered to

[4] As subsequently determined at autopsy.

be approximately 50 per cent. This agrees with the findings of previous investigators. In a number of dogs dying in less than 24 hours there was present evidence of beginning infarction in the heart (myocardial discoloration and early softening). Furthermore, in all the specimens which were injected, a filling defect was noted in the coronary tree. Of the 25 dogs which survived over 24 hours, all showed infarction of the heart and in 24 of these the surface of the infarct averaged 5 x 5 cm. approximately 1 week following the occlusion. Large filling defects of the coronary tree were noted on injection.

In sharp contrast to these findings are those following left anterior descending branch occlusion in animals which had survived occlusion of the coronary sinus for periods of time varying from 1 to 8 weeks (average 4 weeks). When the coronary sinus occlusion had been complete, irrespective of the technique used for this purpose, there was a pronounced beneficial effect on the incidence and extent of the infarction following complete and sudden left anterior descending branch occlusion. In over half of the dogs no infarction resulted. (Most of the animals were killed approximately 1 week after the left anterior descending branch occlusion.) In the remainder, the infarctions were considerably smaller than expected. The vasculature was on the whole increased and the filling defects on injection were either absent or small.

When the coronary sinus occlusion was incomplete or transient there were still present evidences that the myocardial nutrition had improved. In these animals the infarctions were present almost as frequently as in the control group but in approximately half of them the size of the infarctions as well as the vascular filling defect were considerably diminished. Moreover, in the animals which survived for less than 24 hours, filling defects were generally smaller in size and myocardial discoloration was never noted. One must conclude from these observations that at least in the experimental animal (dog) complete or even partial occlusion of the coronary sinus, whether this be permanent or transient, affords a definite method of anatomically and functionally enriching the coronary bed to such an extent that infarction may be either completely prevented or minimized.

There are several factors which enter into the incidence of mortality in these experiments: surgical trauma (anesthesia, shock, postoperative pneumonia, etc.); injury to the myocardium due to the ischemia following left anterior descending branch occlusion; secondary phenomena of cardiovascular damage (ventricular fibrillation, decreased cardiac output, etc.), and possible injury to the myocardium due to the venous congestion following complete coronary sinus obturation (turgidity of the heart, slowing of heart rate, electrocardiographic changes, etc.). The factors attendant on the surgical procedure itself, *i.e.*, due to anesthesia and thoracotomy, remain more or less constant in all experiments. Opposing the mortality factors relevant to cardiac injury, however, is the enrichment of the circulation following the coronary sinus occlusion. When this coronary sinus occlusion is complete there is evidence that in spite of the functional improvement in myocardial nutrition, the sudden venous congestion itself may be an added trauma. The desideratum, therefore, is a proper balance between the beneficial effects of the improved circulation and the undesirable effects due to possible myocardial injury.

With these considerations in mind, an analysis of the experiments described in this report assumes added significance. As noted above, the mortality rate following sudden complete left anterior descending branch occlusion was 53 per cent. The only group in which this was materially reduced was that in which a preliminary partial coronary sinus occlusion was present (31 per cent). Furthermore, the primary mortality rate of partial coronary sinus occlusion was very low (10 per cent). Of the methods used to produce partial coronary sinus occlusion, perisinus injection of escharotics appears up to the present to be the most satisfactory and to give the most consistent results. If these observations can be confirmed on a larger series of animals it would indicate that a partial occlusion of the coronary sinus strikes a satisfactory balance between the undesirable and beneficial factors. Thus, on the one hand, it is associated with sufficient enrichment of the coronary bed to reduce the mortality rate and the extent of the infarction otherwise following sudden occlusion of the left anterior descending branch and, on the other hand, it either does not damage the myocardium or it does not produce sufficient myocardial damage

to maintain or enhance the mortality rate of the subsequent sudden, complete occlusion of the left anterior descending branch. It is only when the coronary sinus obturation is sudden and complete or when it is inadequate or transient that the mortality rate following sudden occlusion of the left anterior descending branch again rises to the expected level in spite of the fact that there may be some improvement in the vascular nutrition. It appears desirable, therefore, that improved methods be sought for which might produce a partial, or perhaps better, gradual occlusion of the coronary sinus.

In appraising the results of these experiments in terms of application to the human heart, it is to be noted that sudden occlusion of the left anterior descending branch by the methods employed in these experiments is far more drastic than the occurrence of thrombosis in the human heart. The latter occurs in a myocardium which has almost invariably already developed compensatory changes in the coronary tree as a result of gradual coronary narrowing (sclerotic). Furthermore, the thrombotic process itself probably lasts for at least several hours. The beneficial results following the several procedures outlined above, therefore, were obtained under the most adverse of conditions, such as are not encountered in the human heart. Furthermore, it is to be noted that cardiopexy procedures produce little or no vascularization of the myocardium in the intact heart. Assuming, therefore, that some modification of the cardiopexy procedure might lead to beneficial results, this operation should be carried out only when the myocardium is severely damaged. Coronary sinus occlusion, on the other hand, apparently produces a considerable enhancement in the vascular nutrition even of the normal heart. This suggests its possible application both in advanced cases as well as in mild cases of coronary artery disease as a preventative against the results of subsequent arterial occlusion.

SUMMARY AND CONCLUSION

Sudden occlusion of the left anterior descending branch approximately 2 cm. below the ostium of the left circumflex coronary artery in the dog's heart produces a mortality rate of approximately 50 per cent. In dogs weighing approximately 15 kilos surviving more than 24 hours (average 1 week), an infarction is produced which al-

most invariably measures 5 x 5 cm. on surface. Following coronary sinus obturation such secondary sudden occlusion of the left anterior descending branch is followed either by no infarction or by a reduction in the size of the infarct. The success of the procedure, quite apart from the mortality rate, depends upon the completeness of the coronary sinus obturation. On the other hand, sudden and complete coronary sinus obturation by itself is associated with a high operative mortality and apparently does not affect the mortality rate following subsequent sudden left anterior descending branch occlusion. Partial persistent obturation of the coronary sinus, however, is in itself associated with a low operative mortality. Furthermore, its experimental production in dogs appears to lower the mortality rate following subsequent sudden occlusion of the left anterior descending branch and to diminish the extent of the infarction.

In the introduction to this report it was pointed out that there are three important desiderata to the problem of improving the coronary circulation in the human heart. The findings herein reported fulfill these requisites to an encouraging degree. It has been shown that following the outlined procedures, a functional increase in the blood supply to the heart can be produced in a significant proportion of experimental animals, this varying with the nature of the experimental procedure. The manipulation is simple, can be performed in the dog within approximately 20 minutes, and does not lead to appreciable pericardial adhesions. Increase in the nutrition of the myocardium is noted 1 week after the experimental procedure. Although no experiments employing sudden left anterior descending coronary branch occlusion were carried out sooner than 1 week, there is available anatomic evidence that within possibly 24 hours after coronary sinus occlusion a dilatation of the vascular bed occurs. In subsequent experiments attempts will be made to determine whether this early vascular dilatation is adequate to compensate for subsequent sudden left anterior descending branch occlusion.

A discussion is given of the results following various coronary sinus occlusion procedures in which it is indicated that it is desirable to produce a partial or gradual occlusion in order to lower the mortality rate both of the initial procedure as well as of the subsequent sudden arterial occlusion. Experiments thus far reported on cardiopexy

operations are lacking in evidence that they are associated with appreciable improvement in the vascular nutrition of the myocardium.

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EXPLANATION OF PLATES

PLATE 4

FIG. 1. Anteroposterior view of injected dog's heart 9 days after sudden complete occlusion of the left anterior descending branch 2 cm. below the ostium of the left circumflex coronary artery. Arrow marks site of left anterior descending branch occlusion. A, right ventricle; B, interventricular septum; C, left ventricle. Note large vascular filling defect (X) and infarct at apical region.

FIG. 2. Cross section through middle of dog's heart illustrated in Fig. 1. A, right ventricle; B, interventricular septum; C, left ventricle. Note small vascular filling defect (X) and infarct in anterior wall of left ventricle.

FIG. 3. Cross section half way between middle and apex of dog's heart illustrated in Fig. 1. A, right ventricle; B, interventricular septum; C, left ventricle. Note large vascular filling defect (X) and infarct in anterior wall of left ventricle.

FIG. 4. Cross section through apex of dog's heart illustrated in Fig. 1. A, right ventricle; B, interventricular septum; C, left ventricle. Note large vascular filling defect (X) and infarct in anterior wall of left ventricle.

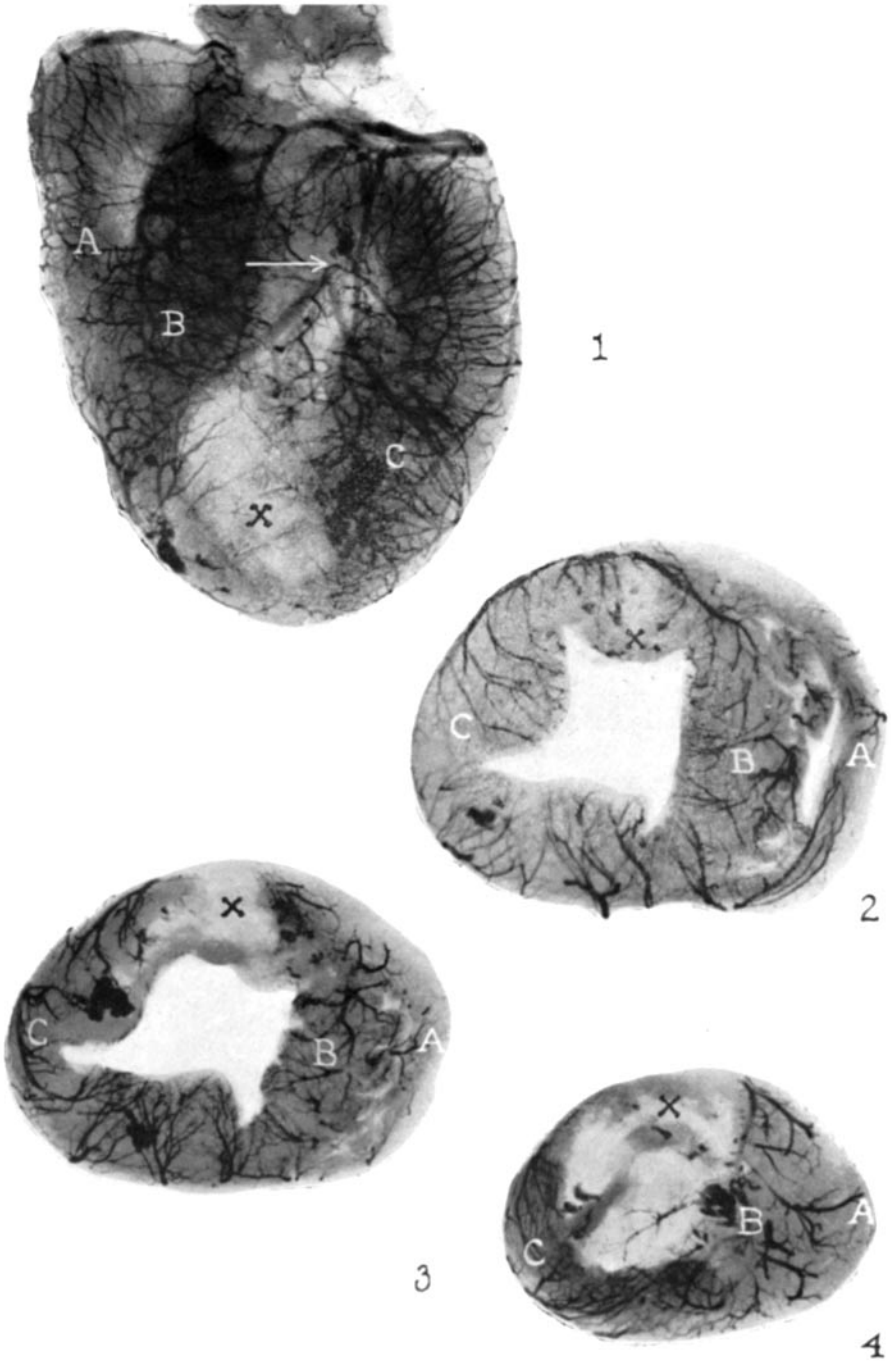
PLATE 5

FIG. 5. Anteroposterior view of injected dog's heart 2 weeks after sudden complete occlusion of the left anterior descending branch 2 cm. below the ostium of the left circumflex coronary artery. 4 weeks prior to the occlusion of the left anterior descending branch, the coronary sinus was completely occluded. Note extensive coronary tree. Arrow marks site of left anterior descending branch occlusion. A, right ventricle; B, interventricular septum; C, left ventricle.

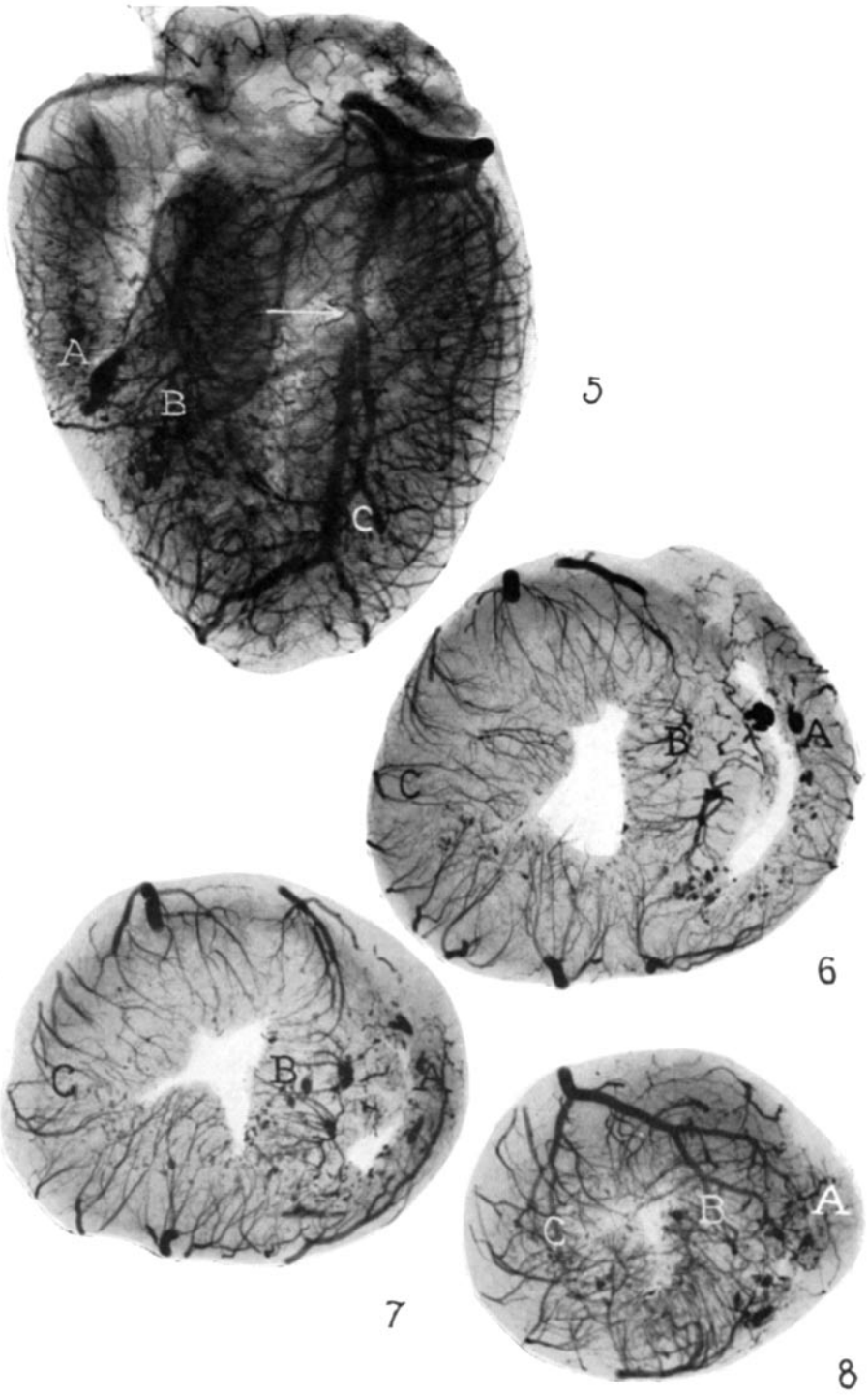
FIG. 6. Cross section through middle of dog's heart illustrated in Fig. 5. Anterior wall is uppermost. A, right ventricle; B, interventricular septum; C, left ventricle. Note absence of filling defect or infarct.

FIG. 7. Cross section half way between middle and apex of dog's heart illustrated in Fig. 5. Anterior wall is uppermost. A, right ventricle; B, interventricular septum; C, left ventricle. Note absence of filling defect or infarct.

FIG. 8. Cross section through apex of dog's heart illustrated in Fig. 5. Anterior wall is uppermost. A, right ventricle; B, interventricular septum; C, left ventricle. Note absence of filling defect or infarct.



(Gross *et al.*: Coronary sinus occlusion)



(Gross *et al.*: Coronary sinus occlusion)