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THE PHYSIOLOGIC EXPLANATION OF THE CHANGES IN THE CORONARY CIRCULATION PRECIPITATED BY AORTIC-CORONARY SINUS ANASTOMOSIS^{1, 2}

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In recent years we have been able to confirm the observations made by Hahn and Beck (1) in demonstrating a significant protection against ventricular fibrillation following coronary artery ligation in dogs in which a chronic aortico-coronary sinus anastomosis has been produced (2). Our recent interest lies in the physiologic explanation of this protection. Accordingly, we have outlined a series of experiments to elucidate two major points with respect to chronic arterialization of the coronary sinus in dogs: 1) whether retrograde blood flow occurs; and 2) if retrograde blood flow does occur, whether or not this blood first traverses a capillary bed. The following information was therefore first secured in normal control dogs: 1) coronary sinus pressure and oxygen content of coronary sinus blood; 2) quantitative determination of retrograde blood flow following circumflex coronary artery ligation from a point distal to the ligature; and 3) determination of oxygen content and saturation of blood samples taken simultaneously from the pulmonary artery, aorta, and the distal end of the cut circumflex coronary artery. Inasmuch as any operation on the heart, by producing pericardial adhesions, might be presumed to alter these findings, we felt it essential to repeat these experiments in dogs having previously had nondescript cardiac procedures. When possible, dogs were used in which unsuccessful arterialization of the sinus had been previously performed, with subsequent thrombosis of the

graft. These experiments were repeated in dogs in which successful arterialization of the sinus had been performed. Moreover, in these dogs coronary sinus pressure, retrograde flow from the distal cut end of the ligated coronary artery, and oxygen content data were obtained with the graft open and closed.

METHODS

Group A constituted the normal control, and consisted of ten mongrel dogs whose weights varied between 11 and 17 kilograms. They were anesthetized with 0.5 cc. of halatal per kg., after which artificial respiration was maintained using intermittent positive pressure. The left chest was opened between the fourth and fifth ribs, the pericardium was opened, and the coronary sinus was cannulated. The cannula was connected to a water manometer, and the sinus pressure and the specimen of coronary sinus blood were obtained. The circumflex branch of the left coronary artery was isolated at its origin and ligated. An incision was made in the artery just distal to the ligature, through which the distal artery was cannulated and specimens of retrograde coronary artery blood were obtained. Simultaneously, aortic and pulmonary arterial blood were also obtained. The minute volume of retrograde bleeding from the distal cut end of the circumflex artery was recorded. The oxygen content of all blood samples was determined according to the method of Van Slyke and Neill (3). Oxygen capacity and saturation were determined in the sample of aortic blood.

Group B consisted of ten mongrel dogs of similar weight on which other forms of cardiac surgery had been previously performed. In four of these dogs a previous attempt at arterialization of the coronary sinus had been made, but the grafts had been demonstrated to be thrombosed and non-functioning. In the remaining dogs the right atrium had previously been opened for a period of six to twelve minutes during hypothermia experiments conducted one to three months previously. In some of the dogs in this group, interatrial septal defects had been created and closed. In five of the dogs, the anterior descending branch of the left coronary artery was ligated at its origin, and in the remaining five, the circumflex

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branch of the left coronary artery was ligated. The distal segment of the ligated vessel was then cannulated, and samples were obtained similar to those in Group A.

Group C consisted of ten mongrel dogs which were first prepared with arterialization of the coronary sinus in a two stage operation. At a first stage, through a left-sided approach, a segment of an external jugular vein was used to anastomose the aorta to the coronary sinus. Three to four weeks later, through a right-sided approach, the coronary sinus was partially ligated, over a probe, to a residual diameter of two or three millimeters. Four to eight weeks following the second stage of the procedure, the animals were anesthetized with halatal, after which artificial respiration was maintained by using intermittent positive pressure through an endotracheal tube. The left chest was entered through the fourth intercostal space and all pleural and pericardial adhesions were divided. The vein graft was dissected and examined for patency. Only dogs with functioning grafts were used. An umbilical tape was passed around the graft to permit easy occlusion at the appropriate time during the procedure. A needle-tipped polythene catheter connected to a water manometer was inserted into the coronary sinus, after which sinus pressure and blood samples

were obtained. The circumflex branch of the left coronary artery was carefully dissected to its origin and ligated. The artery was cannulated distal to the ligature and a sample of the retrograde blood was obtained, simultaneous samples being obtained from the aorta and the pulmonary artery. The timed minute volume of retrograde bleeding was then immediately recorded (Figure 1). Then the graft was clamped, and the experiment was repeated (Figure 2). This was the method used for the first five dogs studied.

During the study of the sixth dog, following the clamping of the vein graft, the cannula inadvertently slipped out of the circumflex artery distal to the ligature. It was noted that the retrograde bleeding was dark prior to the clamping of the graft, and that it remained so immediately after clamping. Several minutes elapsed before the cannula was reinserted into the artery during all of which time the graft was clamped. It was noted that during the period of time necessary for the reinsertion of the cannula, the retrograde blood changed from blue to red. Consequently, in dogs 6 to 10, after the graft had been clamped, the circumflex artery was permitted to bleed freely for a period of two minutes prior to obtaining blood samples for oxygen content.

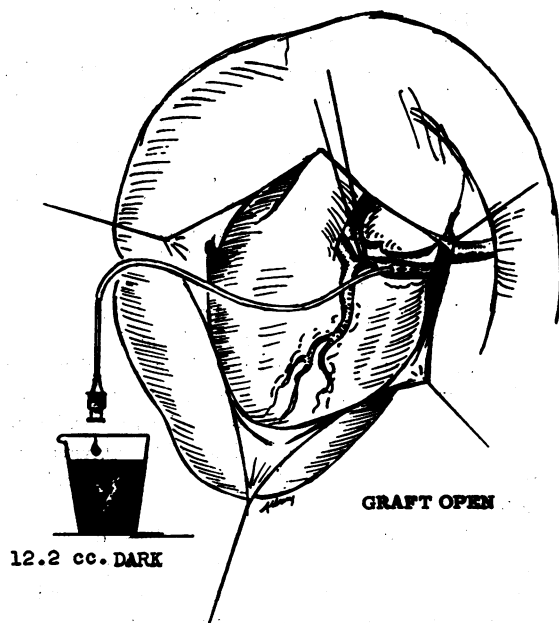


FIG. 1. CANNULATING THE DISTAL SEGMENT OF THE LIGATED LEFT CIRCUMFLEX CORONARY ARTERY

The circumflex branch of the left coronary artery is isolated at its origin, and ligated. An incision is made in the artery just distal to the ligature, through which the distal artery is cannulated. Retrograde minute blood flow, and blood samples for determination of oxygen content are obtained from the distal cut end of the circumflex branch of the left coronary artery in this fashion.

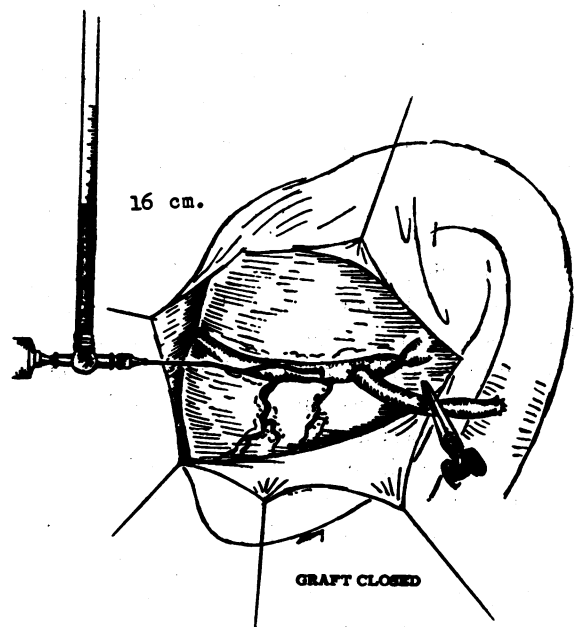


FIG. 2. MEASUREMENT OF CORONARY SINUS PRESSURES

A needle tipped polythene catheter is inserted into the coronary sinus proximal to its point of partial ligation, and is attached to a water manometer. The graft is clamped, and the fall in coronary sinus pressure is recorded. Following a two-minute interval, after clamping of the graft, a blood specimen is obtained for determination of oxygen content.

TABLE I

*Retrograde blood flow and oxygen content of blood from the distal cut end of the ligated left circumflex coronary artery in normal dogs **

Dog No.	Retrograde cor. art.		Aortic blood		Pul. art.	Coronary sinus		Survival time
	Flow cc./min.	O ₂ content vol. %	Content vol. %	Cap. vol. %	O ₂ content vol. %	Press. cm. water	O ₂ content vol. %	
1	2.2	17.3	18.8		10.2	12	9.2	30 min.
2	1.4	15.1	15.8	16.8	12.6	4	6.3	36 hours
3	4.4	17.5	18.2	18.2	12.2	2	6.7	18 min.
4	1.0	14.7	16.2	16.7	10.9	5	4.4	20 min.
5	0.4	15.8	16.9	17.8	14.5	8.6	2.9	3 min.
6	0.5	18.0	17.5	17.8	11.5	8.4	7.4	4 min.
7	0.6	15.4	16.3	17.1	11.6	4.6	3.6	15 min.
8	1.1	8.1	7.2	12.2	4.8	4.0	1.0	16 min.
9	1.0	11.6	11.5	17.4	8.6	7	2.4	5 min.
10	5.0	11.9	14.7	19.5	9.5	5	1.3	12 min.
Aver.	1.7	14.5	15.3		10.6	6.1	4.5	

* Death was by ventricular fibrillation in all except Dog 2.

RESULTS

A. Retrograde bleeding from the distal segment of the divided circumflex branch of the left coronary artery

1) *Group A*: The retrograde bleeding ranged from 0.4 to 5.0 cc. with an average of 1.7 cc. per minute (Table I).

2) *Group B*: Retrograde bleeding from the distal segment of the divided circumflex branch of the left coronary artery ranged from 0.5 to 6.0 cc., with an average of 1.9 cc. per minute (Table II). Retrograde bleeding from the left anterior descending artery ranged from 1.8 to 11.0 cc. with an average of 5.1 cc. per minute (Table II). Two of the dogs in which the left anterior descending branch was ligated presented a large accessory anterior descending branch arising from the circumflex artery. This accessory branch may have accounted for the excessive retrograde bleeding by providing additional intercoronary communications.

3) *Group C*: With the graft open, retrograde bleeding from the left circumflex artery ranged from 9.0 to 18.0 cc. per minute with an average of 12.2 cc. per minute. After the vein graft was clamped, the sinus was to all intents and purposes no longer arterialized. At this point, the retrograde bleeding from the circumflex artery fell significantly in each dog. The retrograde bleeding with the graft closed ranged from 2.0 to 10.0 cc. with an average of 7.1 cc. per minute (Table III).

B. Oxygen content of the retrograde blood from the circumflex artery, obtained from the distal cut end of the vessel

1) *Group A*: Although blood from the aorta, pulmonary artery and distal segment of the coronary artery varied from dog to dog, the retrograde coronary arterial blood was always highly oxygenated, and its oxygen content usually approximated that of aortic blood, ranging from 8.1 to 18.0 volumes per cent, with an average of 14.5 volumes per cent. Concomitant samples of aortic blood ranged from 7.2 to 18.8 volumes per cent, with an average of 15.3 volumes per cent (Table I).

2) *Group B*: In this group, the findings were similar to those in Group A. Oxygen content varied from dog to dog, but the blood was always highly oxygenated, and except for animal No. 5, approximated that of aortic blood, ranging from 11.4 to 24.0 volumes per cent with an average of 16.6 volumes per cent. Concomitant samples of aortic blood ranged from 10.7 to 23.4 volumes per cent with an average of 16.5 volumes per cent (Table II).

3) *Group C*: The oxygen content of blood obtained from the distal cut end of the circumflex artery in this group again varied widely from dog to dog. The oxygen content of the retrograde blood ranged from 1.5 to 15.1 volumes per cent, with an average of 6.3 volumes per cent. Concomitant samples obtained from the aorta ranged from 12.1 to 22.5 volumes per cent, with an average

TABLE II

Retrograde blood flow and oxygen content of blood from the distal cut end of the ligated left coronary artery in dogs having had nondescript cardiac surgery

Dog No.	Retrograde cor. art.		Aortic blood	Pul. art.	Coronary sinus		Remarks
	Flow <i>cc./min.</i>	O ₂ content vol. %	O ₂ content vol. %	O ₂ content vol. %	Press. <i>cm. water</i>	O ₂ content vol. %	
Left circumflex coronary artery							
1	1.1	17.3	16.4	12.2	5.4		Thromb. Beck D. 6 wks.
2	1.2	24.0	23.4	20.6	6.0		Thromb. Beck D. Vent. Fib. 20 min.
3	1.2	11.4	10.7	4.6	23		I.A. septal defect under hypoth. cong. fail. D. card. arrest 17 min.
4	6.0	17.8	18.0	11.9	12		Thromb. Beck D. Vent. Fib. 20 min.
5	0.5	14.0	17.5	10.6	6.4	4.8	Hypoth. D. 14 min. Vent. Fib.
6	1.4	18.3	17.2	10.1	4.0	4.3	Thromb. Beck D. 48 hours
Aver.	1.9	17.1	17.2	11.6	6.7	4.5	
Left anterior descending coronary artery							
7	1.8	13.6	15.0	10.0			Rt. aur. open. under hypoth. D. 10 min. Vent. Fib.
8	1.5	14.9	14.9	10.1			I.A. septal defect under hypoth. D. 23 min. Vent. Fib.
9	11.0	18.0	17.1	13.0			I.A. septal defect under hypoth. large access. L.A.D. from cir- cum. Lived 30 days till sacrif.
10	6.2	17.2	14.5	10.5			I.A. septal defect under hypoth. access. L.A.D. Lived 30 days till sacrif.
Aver.	5.1	15.9	15.1	10.9			

of 17.1 volumes per cent. Despite the wide range of values in the oxygen content of the retrograde circumflex blood, the latter was constantly venous in nature, and its content was always lower than that of pulmonary arterial blood (Table III). Moreover, the oxygen content of the retrograde blood was within the limit of that normally ex-

pected for coronary sinus blood (Table I). In fact, the average oxygen content of the retrograde coronary arterial blood was 6.3 volumes per cent, which compared favorably with the average oxygen content of normal coronary sinus blood, which was 4.5 volumes per cent.

Following clamping of the graft, the values ob-

TABLE III

Retrograde blood flow and oxygen content of blood from the distal cut end of the ligated left circumflex coronary artery in sinus arterIALIZED dogs with the graft open and closed

Dog No.	Graft	Retrograde cor. art.		Coronary sinus		Aortic blood			Pul. art.	Remarks
		Flow cc./min.	O ₂ content vol. %	Press. cm. H ₂ O	O ₂ content vol. %	Cont. vol. %	Cap. vol. %	Sat. %	O ₂ content vol. %	
1	Open	9.6	9.0	45		15.2			10.3	8 wks. P. 2nd st. D. Tens. Pneumo. 24 hrs.
2	Open Clos.	9.0 7.0	1.9 5.3	80	17.2	18.8	20.6	91.3	11.4	12 wks. P. 2nd st. D. Tens. Pneumo. 10 hrs.
3	Open	11.0	11.8	60	12.5	19.2	20.7	92.8	15.9	4 wks. P. 2nd st. D. Hemor. 24 hr. PO.
4	Open Clos.	12.0 10.0	6.1 7.7	36	12.4	14.0	15.8	99.6	11.1	5 wks. P. 2nd st. D. 3 min. P. Graft Closed. Card. arrest
5	Open Clos.	12.0 7.0	1.5 4.6	60 20	9.7	12.1	13.0	93.1	10.2	5 wks. P. 2nd st. D. 5 min. P. Graft Closed. Vent. Fib.
6	Open Clos.	10.0 2.0	4.8 12.5	71 9	15.5	17.7	18.4	96.2	14.3	4 wks. P. 2nd st. D. 96 hrs. Pneumo. and Emp.
7	Open Clos.	18.0 8.0	4.0 13.2	64 19	11.9 7.1	14.3	14.0	100	9.2	4 wks. P. 2nd st. Lig. L.A.D. Vent. Fib.
8	Open Clos.	10.0 8.0	15.1 18.5	59 18	17.9	22.5	22.5	100	19.1	4 wks. P. 2nd st. No Ad'h'sn's. Surv. Lig.
9	Open Clos.	14.0 7.0	4.8 15.3	68 16	13.2 1.7	17.2	20.1	85.6	7.6	8 wks. P. 2nd st. D. 6 hrs. Tens. Pneumo.
10	Open Clos.	16.0 8.0	3.9 17.9	70 14	15.6 1.9	17.8	19.8	89.9	11.6	6 wks. P. 2nd st. D. 12 hrs. Tens. Pneumo.
Average: Open Clos.		12.2 7.1	6.3 15.5	61.3 16.0	14.0 3.6	17.1			12.1	

tained for the oxygen content of retrograde circumflex arterial blood divide themselves into two groups. The first group consists of those animals in which the blood was collected immediately after the clamping of the graft (dogs 1-5, Table III). The second group consists of those animals in which the ligated circumflex artery was permitted to bleed freely in retrograde fashion for a period of two minutes prior to the collection of the specimens (dogs 6-10, Table III). Inasmuch as these values are markedly different, and we believe this difference to be significant, we are reporting them separately. In the first group the oxygen content of the retrograde blood ranged from 4.6 to 7.7

volumes per cent with an average of 5.8 volumes per cent. This, it may be noted, is almost identical to the average oxygen content of retrograde blood with the graft open. However, the data from individual dogs indicate that in each case there was significant rise in the oxygen content of the circumflex retrograde arterial blood immediately after clamping of the graft. In dog 2, oxygen content of the retrograde blood with the graft open was 1.9 volumes per cent, and rose promptly to 5.3 volumes per cent. In dog 4, the value rose from 6.1 to 7.7 volumes per cent; in dog 5, from 1.5 to 4.6 volumes per cent. It is possible that had the artery been permitted to bleed

freely in retrograde fashion for a period of two minutes, the values obtained in dogs 1-5 would have risen further towards that of the content of systemic arterial blood, as occurred in animals 6-10.

In the second group of animals (6-10) the oxygen content of the blood ranged from 12.5 to 18.5 volumes per cent, with an average of 15.5 volumes per cent. Despite the wide range of values, the blood was compatible in oxygen content to the aortic blood. Concomitant samples of aortic blood in dogs 6-10 ranged from 14.3 to 22.5 volumes per cent, with an average of 17.9 volumes per cent. The blood oxygen content obtained from the retrograde flow of the left circumflex artery increased significantly from an average of 6.3 volumes per cent with the graft open, to an average of 15.5 volumes per cent with the graft closed, and changed in appearance from dark venous to bright arterial blood.

C. Mean coronary sinus pressure and oxygen content of coronary sinus blood

1) *Group A*: The mean coronary sinus pressure ranged from 2 to 12 cm. of water with an average of 6.1 cm. of water. The coronary sinus blood oxygen content ranged from 1.0 to 9.2 volumes per cent, with an average of 4.5 volumes per cent (Table I).

2) *Group B*: The mean coronary sinus pressure ranged from 4.0 to 12 cm. of water with an average of 6.7 cm. of water. The one dog with a mean coronary sinus pressure of 23 cm. of water is not included in this average since it was in severe right heart failure, and was included to determine the effect of elevated coronary sinus pressure without sinus occlusion upon retrograde coronary artery bleeding. Coronary sinus blood oxygen content determined in two dogs, was 4.8 and 4.3 volumes per cent, respectively (Table II).

3) *Group C*: With the graft open, coronary sinus pressure ranged from 36 to 80 cm. of water with an average of 61 cm. of water. The oxygen content of the blood obtained from the arterialized coronary sinus ranged from 9.7 to 17.9 volumes per cent with an average of 14.0 volumes per cent. There was no direct relationship between the quantity of retrograde bleeding and mean coronary sinus pressure (Figure 3).

Following the clamping of the graft, the coronary sinus pressure fell significantly towards, but not quite to normal sinus pressure, as established in the normal dogs. These pressures ranged from 9 to 20 cm. of water, with an average of 16 cm. of water. In a few dogs, specimens of coronary sinus blood were obtained two minutes after clamping of the graft. The oxygen content of these samples ranged from 1.7 to 7.1 volumes per cent, with an average of 3.6 volumes per cent. Thus, in these animals, the oxygen content of the coronary sinus blood fell from within arterial range with the graft open, to oxygen contents within normal sinus range following clamping of the graft.

DISCUSSION

The most striking result was the marked difference in the amount and nature of the retrograde bleeding from the distal cut end of the circumflex artery in normal and in sinus arterialized dogs. In all instances the retrograde blood approximated the oxygen content of blood simultaneously obtained from the aorta, and probably originates in the non-occluded coronary arteries by intercoronary arterial collateral flow.

We have demonstrated that nonspecific cardiac procedures *per se* alter neither the quantity nor the character of the blood flowing in retrograde fashion from the coronary artery of the normal animal. This change in the character and the quantity of the retrograde blood apparently only follows arterialization of the coronary sinus. These findings attest to the increase in the retrograde flow through the circumflex artery following aortico-coronary sinus anastomosis, and the venous nature of this blood is evidence that it has traversed the myocardial capillary bed, with the extraction of oxygen by the myocardium.

This increase in retrograde flow has been similarly demonstrated by Hahn, Kim, and Beck (4), and Eckstein and his associates (5-8). The latter have similarly demonstrated a retrograde perfusion of the capillary bed of the occluded circumflex artery, acutely, and for about one month after coronary sinus arterialization.

An almost control situation has been obtained shortly after the graft has been occluded. The coronary sinus pressure falls significantly towards, but not quite to normal levels, whereas the retro-

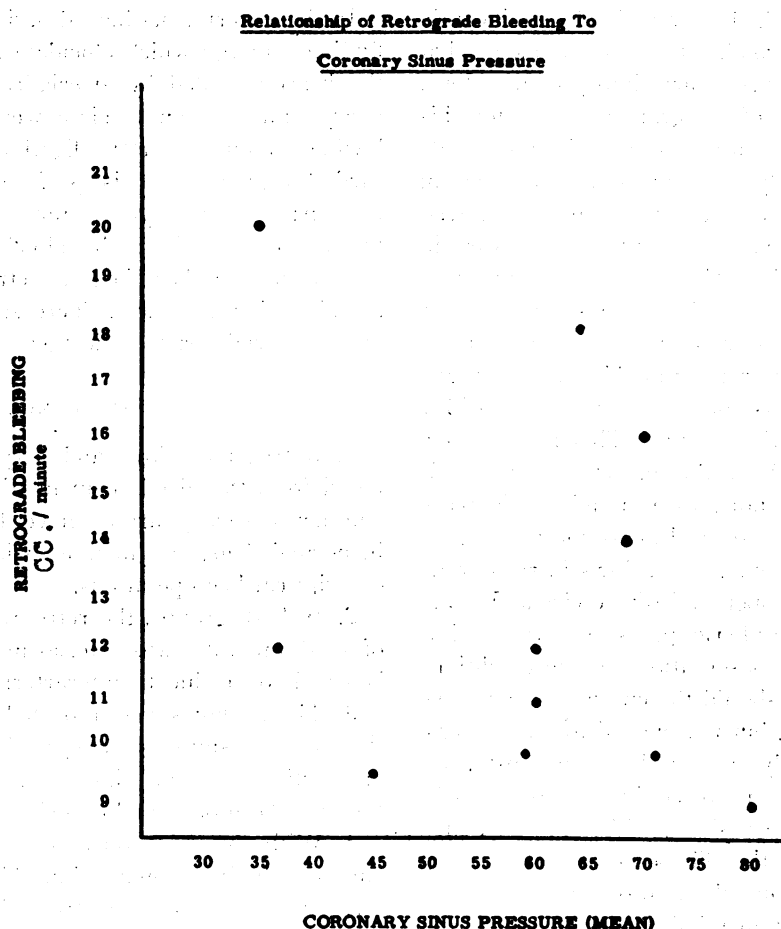


FIGURE 3

The graph shows no noticeable relationship between retrograde bleeding and mean coronary sinus pressure in dogs in which the sinus was chronically arterialized for four to eight weeks.

grade blood becomes arterial in nature, both simulating those values found in the normal dog. It may be of significance that the pressure in the coronary sinus does not fall to normal.

Gregg, Dewald, Thornton, and Mautz (9-12) have demonstrated that, following ligation of the coronary sinus, without preceding arterIALIZATION, retrograde bleeding from the distal cut end of the descending ramus of the left coronary artery increased in quantity up to 39 cc. per minute, and became venous in nature. It may be inferred that the increased residual coronary sinus pressure may be a factor in the increased retrograde bleeding from the circumflex artery following occlusion of the graft. Eckstein, Hornberger, and Sano (6) have shown that the retrograde bleed-

ing in dogs in which the coronary sinus was arterIALIZED acutely varied proportionately with the pressure in the coronary sinus. This relationship was not noted in dogs in which the sinus was chronically arterIALIZED for four to eight weeks (Figure 3). Moreover, in several animals in which the coronary sinus pressure was elevated to 48 to 58 cm. of water by complete occlusion of the coronary sinus proximal to its entrance into the right atrium, retrograde flow averaged approximately 2.5 cc. Though coronary sinus pressure was elevated 8 to 10 times above normal, the flow from the distal segment of the divided circumflex coronary artery was within normal range (13).

Following occlusion of the graft, the volume of retrograde bleeding from the distal cut end of

the circumflex fell, but remained significantly elevated above normal. It seems unlikely that the residual elevated coronary sinus pressure alone, following occlusion of the graft, accounts for this retrograde flow. Inasmuch as this retrograde bleeding was highly oxygenated and arterial in nature, it is probable that it represents blood arising from intercoronary anastomoses, as seen in the normal animals. However, this retrograde bleeding in sinus arterialized dogs was greater than the normal amount of intercoronary anastomotic flow. Normal retrograde bleeding averaged 1.7 cc. per minute, as opposed to an average of 7.1 cc. per minute in this group. This represents a fourfold increase above the expected normal values, and probably indicates a significant increase in the intercoronary arterial anastomotic flow.

In these experiments, blood flows in retrograde direction from the open end of the circumflex artery, against atmospheric pressure. It is difficult to relate these observations to the conditions which would exist should the circumflex coronary artery be occluded, but not opened to atmospheric pressure. Probably, under these circumstances, the capillary bed is perfused in retrograde fashion from the coronary sinus, with this blood then being drained *via* the Thebesian or other deep venous systems. Our observations must be qualified with this point in mind.

In the present experiments on dogs with arterialized coronary sinus, the heart continued to beat in vigorous, uninterrupted fashion, following coronary artery ligation. Whereas it was necessary to proceed rapidly to obtain data in the normal animals prior to the onset of ventricular fibrillation, we soon learned that we could proceed slowly in the sinus arterialized animals, provided the graft was left open. However, when the graft was occluded, it was necessary to obtain the data with dispatch lest the ventricles fibrillate with abrupt cessation of the retrograde arterial blood flow. In several sinus arterialized dogs in which the heart beat well for considerable periods of time following circumflex artery ligation, ventricular fibrillation ensued within 5 minutes of clamping of the graft. This finding further emphasized the value of the protection afforded by the aortico-coronary sinus anastomosis. These observations are in accord with those found by others (1, 4, 5, 14).

In the experiments here described, three salient findings emerge which elucidate the protection to the heart afforded by arterialization of the coronary sinus, of four to eight weeks duration, following circumflex artery ligation: 1) The myocardial capillary bed is perfused in retrograde fashion; 2) The myocardium is capable of extracting oxygen from the blood supplied to the myocardial capillary bed in retrograde fashion; 3) There is a significant increase in the intercoronary arterial anastomotic flow.

SUMMARY AND CONCLUSIONS

1. Retrograde flow and oxygen content of blood from the distal segment of the divided circumflex coronary artery have been determined in normal dogs, and in those with previous non-descript cardiac operations.

2. In both groups, the retrograde bleeding was of small quantity, was arterial in nature, and was believed to be due to interarterial collaterals.

3. These studies were repeated in dogs in which the coronary sinus was chronically arterialized by an aortico-coronary sinus communication, with the graft both open and closed.

4. With the graft open, coronary sinus pressure was high, coronary sinus blood was of high oxygen content, bleeding from the distal cut end of the circumflex coronary artery was greater in quantity than normal, and of low oxygen content. This demonstrated a reversal of blood flow through the capillary bed, with extraction of oxygen by the myocardium.

5. With the graft occluded, coronary sinus pressure fell significantly towards normal, and the blood oxygen content fell to control levels. Concomitantly, retrograde circumflex arterial blood oxygen content rose to arterial levels, and its flow fell significantly. This bleeding was still four times greater than the expected normal, and was believed to represent a significant increase in the interarterial coronary collateral anastomoses.

6. The physiologic explanation of the protection to the heart afforded by anastomosis of the aorta to the coronary sinus is believed to be threefold: (a) The myocardial capillary bed is perfused in retrograde fashion with arterial blood; (b) The myocardium is capable of extracting oxygen from the blood supplied to the myocardial capil-

lary bed in retrograde fashion; (c) There is a significant increase in the blood flow occurring *via* the intercoronary arterial anastomoses.

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