Day-to-Day Changes in Coronary Hemodynamics Secondary to Constriction of Circumflex Branch of Left Coronary Artery In Conscious Dogs

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ABSTRACT
The studies were carried out in four dogs. The effects of applying ameroid constrictors to the circumflex branch were observed on the circumflex blood flow, circumflex and peripheral circumflex pressures, circumflex reactive hyperemia and aortic-circumflex pressure difference. Recordings were successfully made for periods of 16 to 64 days. During this time the circumflex branch became completely occluded in three of the dogs. The circumflex blood flow remained in the normal range until reactive hyperemia (following a 10- to 12-second occlusion of the circumflex branch) almost disappeared; the flow then decreased to zero in 5 to 10 days. Although there was some rise in mean peripheral circumflex pressure and aortic-circumflex pressure difference before circumflex blood flow decreased, the major rise in these variables occurred only when flow and reactive hyperemia became markedly decreased. The maximum rate of rise of mean peripheral circumflex pressure varied from 6 to 15 mm Hg/24 hours. The experiments indicate that a severe degree of coronary insufficiency precedes a rise in mean peripheral circumflex pressure to 60 to 70 mm Hg. We interpret such increments in mean peripheral circumflex pressure to mean that large collaterals must be open; the studies with injection of Schlesinger mass confirmed this interpretation.

ADDITIONAL KEY WORDS
- circumflex blood flow
- ameroid constrictors
- peripheral circumflex pressure
- aortic-circumflex pressure difference
- electromagnetic flow transducer
- coronary collateral circulation

The development of the coronary collateral circulation has been explored in dogs by Gregg et al. (1), Eckstein et al. (2), and Garamella et al. (3). The initial procedure in these experiments was acute ligation of either the anterior descending or circumflex branch of the left coronary artery. At various intervals thereafter, ranging from minutes to several months, the coronary hemodynamics were examined under open-chest conditions, by measuring peripheral coronary pressure or retrograde flow or both. The retrograde flow and peripheral coronary pressure, which are respectively the blood flow and pressure in these branches beyond the site of an occlusion, proved to be interdependent (1, 4). In the dogs whose peripheral coronary pressure was continuously followed for several hours after the initial ligation, the values remained essentially unchanged (2, 3). In the dogs whose peripheral coronary pressure was determined at a second operation, there was a significant rise by 1 week and a further rise by 3 weeks (2, 3).

A better understanding, however, of the effect of coronary occlusion on coronary hemodynamics might be obtained if it were possible to make appropriate measurements in a con-
scious dog and to repeat the measurements many times in the same dog. By using the Herd-Barger technique (5) for implanting a small tube, coronary phasic pressures can be measured for long periods.

This report is concerned with the day-to-day changes in circumflex flow and pressure, peripheral circumflex pressure and aortic-circumflex pressure difference, secondary to a progressive constriction of the circumflex branch in dogs. These data provide indirect evidence of the rate of development of coronary collateral circulation.

Methods and Materials

Large dogs1 (25 to 39 kg) were chosen to increase the probability that the circumflex branch would be approximately 3 mm in outer diameter and 2.5 to 3 cm long. After a routine quarantine period of several weeks, the four dogs studied were trained to lie still on a table.

Surgical techniques.—Clean surgical technique was used. The dogs were anesthetized by sodium pentobarbital, 30 mg/kg intravenously, with additional small doses as necessary. After preparation of the left chest and spinal area, the chest cavity was entered through the 5th interspace. The lungs were ventilated with air by a Harvard respiratory pump connected to an endotracheal cuffed tube. The pericardial sac was incised parallel to the phrenic nerve. The implantations on the vessels were arranged as illustrated in Figure 1. The vinyl tube in the aortic arch for recording pressure was implanted by the Herd-Barger method (5). The circumflex branch was dissected out, and the electromagnetic flow transducer (6), the pneumatic cuff (7), and the ameroid constrictor were placed around it. A special tube was implanted in the lumen of the artery.

The cables and tubes for these devices were brought out through the incision, and except for the coronary tube (see below), ran in a subcutaneous tunnel to the back. There, the external connector of the flow transducer together with the two valves (7) for the pneumatic cuff (no ball in this valve) and aortic pressure tubes were located in the skin just caudal to the scapulae. The chest cavity was closed and the pneumothorax evacuated. Penicillin and streptomycin were intramuscularly administered before, and for approximately 10 days after, operation.

Ameroid constrictors.—These were made from stock 6 mm in external diameter;2 they were slotted and encased in stainless steel slotted rings 3 mm long. The internal diameter varied from 2.5 to 3 mm. We used ameroid constrictors because they produce a gradual constriction (8), which has a lower mortality rate than acute occlusion (9). However, their application is not free of difficulties. If they fit too loosely, full occlusion may not occur; if too tightly, constriction may occur too soon. Further, we found that when soaked in normal saline at 37°C, 30% of the reduction of the internal diameter of the constrictor that occurred in 24 days took place in the first 2 days. Nevertheless, we considered it better to risk early constriction than incomplete occlusion, and so in 3 dogs we used constrictors that fitted snugly.

Special features and care of the coronary tube.—Approximately 0.8 cm of the tube was implanted into the circumflex branch. The tip was directed downstream except in dog 1 (see Results). Some modifications of the technique were necessary to use the tube to obtain phasic coronary pressures. A minimal length of 18 to 20 cm was required. The free end was expanded as in Figure 2, E to accommodate a 20-gauge needle; this prevented narrowing the bore when connected to the pressure transducer tubing (Fig. 2, B). The tube was supplementaliy fixed to the

Circulation Research, Vol. XXII, February 1968

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1The principles of laboratory animal care as promulgated by the National Society for Medical Research were observed.

2American Plastics Corporation, Bainbridge, New York, N. Y., 13733.
Diagram illustrating certain features of the coronary tube that varied from description given by Herd and Barger (5). Variations were mainly with minor stabilizing techniques of the tube and method for sealing off tube. (A) Coronary vinyl tube measured 0.025 mm i.d. and 0.079 mm o.d. Tapered portion at G used for implantation is not shown and was not changed from the Herd-Barger technique (5). (B) Connecting tube to strain gauge was approximately 10 cm long and 1.2 mm i.d. and 2 mm o.d. Inset at E shows a 20-gauge thin-walled stainless steel connection glued into B and fitting into dilated end of A, the object being not to narrow the bore of A. (C) Inset showing expanded cuff at one end, through which a suture could be passed to stabilize tube to myocardium as in Figure 1. Also shown in inset C is a 5-0 suture on needle glued to tube A and used to stabilize it to adventitia at its entry into circumflex branch. (D) Inset to show cuff cemented to A and suture cemented to cuff; suture was used to stabilize A to rib cage. (F) Upper part of inset shows needle (26 gauge) with fine vinyl tubing inside needle—represented by stippled area. Lower part shows needle cut across and vinyl tube inside the needle acting as a sealer.

The tube was filled with heparin solution (1000 USP units/ml) and sealed every 24 hours. The technique used was: Vinyl tubing, drawn out over heat, was threaded through 26-gauge needles and cut flush at the tip and bottom of the hub (Fig. 2, F). A 20-gauge needle, 0.65 cm long, was fitted into the free end of the coronary tube (not shown in Fig. 2) just allowing a 26-gauge needle to pass and fit tightly into the tube. Then, while heparin solution was being injected, the 26-gauge needle threaded with vinyl tubing was snipped across with wire cutters; this filled the tube with heparin solution to the tip and sealed it. Blood did not flow freely each time the 26-gauge needle was removed. However, free flow could be reestablished by injecting a solution of fibrinolysin (2500 to 3000 MSD units in 10 ml of isotonic saline or water) at the rate of 0.1 or 0.2 ml/minute for 5 to 15 minutes. No resistance to injection was ever experienced, even when there was not free blood flow. The intraluminal portion of the coronary tube offered some resistance to circumflex blood flow, but even with a vessel of just 1.5 mm internal diameter, the tube would occupy only 24% of the cross-sectional area. Since in experiments in which no constrictor was applied, reactive hyperemia was marked, resistance created by the tube in the lumen must have been small.

Recording of arterial pressures, circumflex blood flow, and the electrocardiogram.—Aortic and circumflex phasic pressures were measured with P23Db and P23Ch Statham transducers, respectively. After equalizing the gains, the transducers were calibrated against a known pressure of mercury. The transducers and connections were then filled with boiled isotonic saline. The dogs lay with the left side up. The transducers were located just above the chest wall and arranged so that their diaphragms and zeroing stopcocks were at the same level; this was usually 14 to 15 cm above the level of the spinous processes, the reference point to which the pressures were corrected.

By applying Fry's method (10) for calculating the uniform response from the natural frequency and damping ratio, the uniform responses of the circumflex and aortic pressure tube systems were calculated to be 20 and 18 cps.

The circumflex blood flow was measured with a sine-wave electromagnetic flow transducer and calibrated as previously described (11). The internal diameter of the transducers varied from 2.5 to 3.5 mm. The flow transducer was connected to a 1000-cps, no. 310 Biotronex amplifier. Records of phasic pressures and flow and the electrocardiogram were obtained by an Electronics for Medicine DB-8 Recorder; from these records, values for the respective variables were determined by planimetry of the phasic curves. By holding the respective calibration factors essentially constant from day-to-day, gross comparison of the records was facilitated.

Lyovac Thrombolysin, Merck Sharp & Dohme.
The upper and lower records from dog 1 were taken 2 and 21 days, respectively, after operation. To accommodate the lower record, it was broken, and several seconds of record are missing during the 10- to 12-second period of cuff occlusion. The numerical values inset on the 2 records are mean values and were determined on the two cardiac cycles marked off by the vertical lines. The horizontal lines in this interval represent zero pressure and zero flow. Vertical time lines are 0.1 sec.

Procedure for obtaining data.—Figure 3 demonstrates the essential features of obtaining daily records. After the dog's heart rate and aortic pressure became stable, a continuous record was obtained before cuff occlusion, during cuff occlusion, and for several seconds after release. During the first few postoperative days, the cuff was occluded sometimes for only 4 to 7 seconds (upper record, Fig. 3); after several days it was occluded for 10 to 12 seconds. From this record, two cardiac cycles of the respective variables were analyzed as between the heavy vertical lines in Figure 3. Two cycles at peak reactive hyperemia were also analyzed, but this analysis is not shown in Figure 3 because the peak occurred approximately 6 seconds after cuff release.

Schlesinger mass injections.—After the completion of experimental studies, the animals were killed with an overdose of sodium pentobarbital, and the hearts were removed. The left anterior descending branch or the circumflex branch was cannulated, and a barium-gelatin mixture injected in accordance with Schlesinger's method (12). Representative sections of the left ventricular myocardium were taken for histologic examination. In 15 other dog hearts used as controls, Schlesinger's mass was injected into either branch; these hearts were subjected to no other operative procedure.

Results
The results are presented in Figures 3 through 10 and Tables 1 and 2. Satisfactory recordings were made in 4 dogs over a sufficient number of days to make evident the effects of constriction on circumflex blood flow and pressure (Figs. 4-7).

In three dogs, useful recordings were prematurely interrupted (cols. 6 and 7, Table 1). In dog 2, the tip of the coronary tube penetrated the wall of the circumflex branch. This also happened early postoperatively in dog 3, but the tube was replaced at a second operation 5 days after the first with the tube pointing upstream this time, and useful data were obtained until the tube was inadvertently severed at the skin level 28 days later. In dog 4, it was difficult to obtain data because the dog became unmanageable.

Figure 3 illustrates measurements of peripheral circumflex pressure and some early findings of constriction. No signs of constriction were evident in the upper record, 2 days postoperatively. Aortic and circumflex pressures were essentially the same, and mean peripheral circumflex pressure was very low (2 mm Hg). When the cuff was released at 4 seconds, circumflex pressure rose immediately, and in 6 seconds there was a peak re-
active hyperemia of 100% increase in circumflex flow (not shown), i.e., the circumflex flow increased from 69 to 138 ml/min; the increase was more than 200% in a few days when the occlusions were held for 10 to 12 seconds. By 21 days after operation (lower record), there were signs of constriction. An obvious aortic-circumflex pressure difference
### Summary of Salient Data

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>Beats/min</th>
<th>Mean aortic pressure (mm Hg)</th>
<th>Circumflex blood flow (ml/min)</th>
<th>Mean peripheral circumflex pressure (mm Hg)</th>
<th>Postop. days before circumflex blood flow reached zero</th>
<th>Days useful data obtained after operation</th>
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<td>Col. 2</td>
<td>100-129</td>
<td>Col. 3</td>
<td>Col. 4</td>
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<td>Col. 6</td>
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<td></td>
<td>92-108</td>
<td>57-73</td>
<td>2 (2)</td>
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<td>64</td>
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<td>Col. 2</td>
<td>114-154</td>
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<td>Col. 4</td>
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<td></td>
<td>71-106</td>
<td>28-65</td>
<td>15 (1)</td>
<td>14</td>
<td>32*</td>
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<td>Col. 2</td>
<td>72-139</td>
<td>Col. 3</td>
<td>Col. 4</td>
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<td>Col. 6</td>
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<td>86-115</td>
<td>34-68</td>
<td>3 (1)</td>
<td>12-15</td>
<td>33*</td>
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<td>39-48</td>
<td>10 (1)</td>
<td>8 ml/min at 16 days</td>
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</tbody>
</table>

Numbers in parentheses in body of table denote days after operation.

*Explanation in second paragraph of Results. tD = died; K = killed.

### TABLE 1

Data from dog 3. Note that this dog had a second operation. Abbreviations are the same as in Figure 4.

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was present, especially in diastole. The amplitude of the circumflex flow trace was smaller and circumflex flow was reduced by 50%. There was a decrease in the slope of that portion of the flow curve which corresponded to the isometric relaxation phase of the cardiac cycle. Mean peripheral circumflex pressure was then 28 mm Hg. Following release of the cuff, the amplitude of the reactive hyperemia curve remained small and the peak increase in blood flow during reactive hyperemia was only 62% (not shown). Each of the graphs in Figures 4 through 8 present data from one of the four dogs and shows the day-to-day changes in mean values of circumflex and peripheral circumflex pressures. These, in conjunction with circumflex flow, constitute the focal determinations. Also
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<table>
<thead>
<tr>
<th>Postop. days at death</th>
<th>Mean max. aortic-circumflex pressure diff. (mm Hg)</th>
<th>Mean max. peripheral circumflex (mm Hg)</th>
<th>Mean aortic (mm Hg)</th>
<th>Max. circumflex peripheral pulse pressure (mm Hg)</th>
<th>Peripheral max. circumflex pressure rise-time mm Hg/24 hr</th>
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<td>55 (51)</td>
<td>108 (51)</td>
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<td>41 (D)*</td>
<td>21 (16)</td>
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<td>112 (19)</td>
<td>50 (16)</td>
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<tr>
<td>57 (K)*</td>
<td>56 (12)</td>
<td>75 (32)</td>
<td>90 (32)</td>
<td>50 (14)</td>
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<td>31 (13)</td>
<td>78 (16)</td>
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**FIGURE 7**

Data from dog 4. Abbreviations are the same as in Figure 4.

shown are the relationships among the other variables.

Figures 4 through 7 convey the over-all impression that circumflex flow started to fall from the time of operation. However, the values of circumflex flow remained within a normal range, so within the reservations outlined under Methods, an arbitrary interval of the first 4 to 5 postoperative days was used for a control period (Table 1, cols. 1 through 4). There was a point in the curves, however, after which the rate of fall in circumflex flow increased and the flow declined to zero within the next 5 to 10 days. The measurement of circumflex flow assisted in confirming the time of circumflex occlusion; this was quite variable (col. 5). The circumflex flow fell to zero in three dogs, and almost to zero in the fourth dog (Fig. 7). It eventually returned in dog 1 (Fig. 4); the explanation for this can probably be traced to the loose fit of the ameroid in this dog; complete occlusion may have resulted from a thrombus which later recanalized.

Mean peripheral circumflex pressure 1 to 2 days postoperatively varied between 2 and 15 mm Hg (Table 1, col. 4). In the next 10 to 14 days, the curves of mean peripheral circumflex pressure showed a gradual rise; this was followed by a more rapid rise over approximately 10 to 14 days, when the curves started to level off. The maximum rate of rise in mean peripheral circumflex pressure was determined from the best-fit line of the respective curves in Figures 4 through 7, and these values varied between 6 mm Hg/24 hours and 15 mm Hg/24 hours (col. 12). During this interval of greatest rise, there was a lag in the rise of the diastolic peripheral circumflex pressure curves when compared with the corresponding systolic components, evident from Figures 4-7. The curves reached maximum mean values ranging from 75 to 99 mm Hg. The mean pressure rose to within about 20 mm Hg of the mean aortic pressure (cols. 9 and 10 and Figs. 4-7).
TABLE 2

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>Peak reactive hyperemia* (ml/min)</th>
<th>Mean peripheral circumflex pressure* (mm Hg)</th>
<th>Control circumflex blood flow (ml/min)†</th>
<th>Mean peripheral circumflex pressure at 50% control circumflex blood flow (mm Hg)</th>
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<td>4</td>
<td>102</td>
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</table>

*Values of peak reactive hyperemia and mean peripheral circumflex pressure are for point at which day-to-day curves cross each other.
†Values obtained from col. 3, Table 1.

![Graph](image)

**FIGURE 8**

Data from dog 1, first 36 postoperative days, show relationship between the day-to-day changes in peak circumflex reactive hyperemia and circumflex blood flow, mean peripheral circumflex pressure, aortic-circumflex pressure difference.

For several days after operation there was only a slight rise in mean peripheral circumflex pressure, the main rise appearing to occur only when the circumflex flow was severely reduced; for example, by the time there was a 50% reduction in circumflex flow from control, the mean values of peripheral circumflex pressure had risen to 36 to 52 mm Hg (Table 2). By the time of zero circumflex flow, the major rise in mean peripheral circumflex pressure had taken place (Figs. 4-7). Also, at this time the peripheral circumflex pressure became essentially equal to the circumflex pressure, thus providing another means to check on the time of circumflex occlusion; the small variations between the two pressures were due to an interval of 10 to 12 sec between the measurements. In dog 1 (Fig. 4) when the circumflex flow reappeared 60 days postoperatively, the values of mean peripheral circumflex pressure were lower than in the preceding interval of zero flow.

The mean aortic-circumflex pressure difference is shown by the lowermost pair of curves.
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FIGURE 9
Data from dog 3. The upper and lower records correspond respectively to phasic records at 5 representative intervals, just before, and 10 to 12 seconds after pneumatic cuff occlusion. In each set of records, e.g., at 9 days, from top down the traces are electrocardiogram lead II, aortic pressure, circumflex pressure (in the lower record peripheral circumflex pressure) and the bottom trace, the circumflex blood flow. The aortic and circumflex pressure traces are essentially superimposed at 1 day. Zero base lines for pressure are shown and have been corrected for the position of the pressure transducers 14 to 15 cm above the level of the spine. Circumflex flow traces were not recorded at 23 and 33 days but there was still zero flow. Time lines 0.2 seconds.

in Figures 4 through 7. A small gradient which usually existed at the time of operation increased gradually; the maximum values varied considerably (Table 1, col. 8). The major rise of the peripheral circumflex pressure occurred by the time these maximum differences had been reached, except in dog 3 whose mean peripheral circumflex pressure had risen to only 30 mm Hg (Fig. 6).

Figure 8 shows the changes in reactive hyperemia for dog 1. Only the first 36 postoperative days are included (compare Fig. 4). From 10 to 22 days postoperatively, the circumflex flow remained about 40 ml/minute and the values for peak reactive hyperemia steadily decreased. Toward the end of this interval, the major rise of the peripheral circumflex pressure began. By 20 to 22 days, the reactive hyperemia had almost disappeared. The same relationship between these three variables was observed in the other three dogs.

In the four dogs, if the same scales were used in each graph, the curves for reactive hyperemia and mean peripheral circumflex pressure crossed each other within the narrow range of circumflex flow values of 89 to 105 ml/minute (Table 2).

Phasic records selected at representative intervals from dog 3 (Fig. 6) are presented in Figure 9. The upper and lower records at the five intervals are paired and represent two cardiac cycles before, and 10 to 12 sec after, cuff occlusion. In the upper panel, a marked change in the circumflex flow pattern occurred between 1 and 9 days postoperatively. This illustrates a finding seen in Figure 3, namely, that as the circumflex flow became reduced and the amplitude smaller, a decrease in the slope of the upstroke corresponded to the period of isometric relaxation. The aortic-circumflex pressure difference which was very apparent 14 days postoperatively, narrowed again by 23 days. In the lower panel, a striking change in the phasic curves of the peripheral
circumflex pressure occurred at 1 and 9 days, and an even larger change at 14 days. This was characterized by large increases in pulse pressure. By 14 days, the systolic pressure had almost reached a maximum, rising only slightly higher by 23 and 33 days. The lag in rise of the diastolic compared to the rise in systolic peripheral circumflex pressure is again evident by comparing the phasic records at 14 and 23 days. The peripheral circumflex pressure trace exhibited a diastolic run-off by 33 days.

A wave appeared in the end-diastolic portion of the circumflex pressure curves which seemed to occur simultaneously with atrial contraction and can be observed in the records at 9, 23, and 33 days postoperatively. There was also another wave just after the period of isometric relaxation at 23 and 33 days postoperatively. In the absence of sinus rhythm, for example at 14 days, a constant finding was that the foot of the ascending limb of the pressure pulse began earlier. All of these features typify the phasic records observed in the other dogs.

Electrocardiograms were routinely done only in dog 3. Recurrent arrhythmias were noted on most tracings 5 to 24 days postoperatively, and consisted predominantly of short runs of bigeminy and short runs of paroxysmal ventricular tachycardia lasting several days. Five days postoperatively, while circumflex flow was still in the normal range, the electrocardiogram showed abnormal Q waves and progressive T wave inversions in leads II, III and aVF consistent with infarction of the inferoposterior wall, and similar changes in leads I and aVL consistent with anterolateral wall damage. The findings in leads I and aVL are often seen following implantation procedures on the circumflex branch. Transient ST depressions and further T wave inversions were noted in leads II, III and aVF at 23 postoperative days, compatible with inferoposterior subendocardial ischemic injury.

Despite the small variation in the early postoperative values of mean peripheral circumflex pressure, e. g., 2 to 15 mm Hg (Table 1, col. 4), there appeared to be a direct correlation between these values and the values for the maximum mean rise time of the peripheral circumflex pressure (col. 12). On the other hand, the values of maximum pressure difference resulting from the constriction (col. 8) appeared to vary inversely with the early values of mean peripheral circumflex pressure (col. 4).

An inverse relationship appeared between the maximum mean aortic-circumflex pressure difference and the maximum mean rise time of the peripheral circumflex pressure (cols. 8 and 12). This is especially evident by comparing the respective curves in Figures 5 and 6. In Figure 5, there was a steep rise in the mean peripheral circumflex pressure curve with only a small mean aortic-circumflex pressure difference, whereas in Figure 6 there was a gradual rise in the mean peripheral circumflex pressure curve with a large mean aortic-circumflex pressure difference. In these two dogs, the rates of reduction in circumflex flow were comparable.

As the circumflex blood flow decreased, the aortic-circumflex pressure difference increased across the developing constriction, the correlation between the two variables being \( r = 0.79 \) in 26 observations from the four dogs. The slope of the upstroke of the isometric relaxation phase of the circumflex blood flow trace became less as the circumflex blood flow was reduced. This is evident in Figure 3 and the 1- and 9-day postoperative records of Figure 9. In 26 observations from the four dogs, there was a correlation of \( r = 0.57 \) between the values for the slope of the upstroke and the circumflex flow. In the same 26 observations, the logio aortic-circumflex pressure difference versus the slope of the upstroke gave a correlation of \( r = 0.9 \).

The presence of myocardial infarcts of varying sizes was confirmed by histologic section. The extent of the lesions and the stage of healing observed were related to the elapsed time from the onset of coronary constriction, similar to the findings of Karsner and Dwyer (13). For example, dog 4, killed within 2 weeks of the onset of circumflex constriction, had many regions of extensive fibroelastic
Injections of Schlesinger mass in control and experimental hearts. Barium-gelatin mass was injected into the anterior descending branch of the left coronary artery. (A) Control heart, lateral view. Boundaries of the bed of the anterior descending branch are sharply outlined (arrows). No barium-gelatin is present in the region of the bed of the circumflex branch. (B) Dog 3, lateral view. Both beds of anterior descending and circumflex branches have been filled with Schlesinger’s mass. Many anastomoses between the two beds range up to 400 µ (arrow) in diameter. The circumflex branch is filled with barium-gelatin up to site of occlusion by the ameroid constrictor (A). (C) Dog 3, posterior view. Complete filling of the circumflex bed from the anterior descending branch is demonstrated. One anastomosis (arrow) between the 2 beds was 1000 µ in diameter. Other anastomoses (R) were present in branches of the right coronary artery.

Discussion

The high mortality rate in dogs after occlusion of the anterior descending branch led Beck (14) to try gradual occlusion of this branch, which reduced mortality rate and permitted study of the period of incomplete occlusion. Our experiments with ameroid constrictors on the circumflex branch demonstrate that important changes in coronary hemodynamics occur before complete occlusion.

Based on the values of circumflex blood flow, the preocclusive period can be roughly divided into an early interval in which the proliferation and necrotic muscle fibers in sections obtained from the posterior left ventricular wall. The presence of polymorphonuclear and mononuclear cellular infiltrates in these regions indicated that acute inflammatory changes were still occurring with later stages of resolution. In contrast, dog 1, which died 1½ months after the onset of circumflex constriction, had only small condensations of fibrous connective tissue scattered diffusely in the sections of posterior myocardium. Necrotic muscle fibers and cellular infiltrations were absent, indicating that organization of the lesion was complete.

In the control hearts, Schlesinger’s mass did not pass from the anterior descending bed to the circumflex bed (Fig. 10A), indicating that any communications present were less than 40 µ in diameter (12). In the experimental animals, the barium-gelatin mixture passed readily from one vascular bed to another (Figs. 10B and 10C). Many connections were present between the terminal branches of anterior descending and circumflex branches and between the circumflex branch and right coronary artery (Fig. 10C). The largest of these anastomoses ranged from 400 µ to 1000 µ in diameter.
flows remained in the normal range and a later interval in which the flows progressively decreased to zero. It is evident from Figures 4-7 that although some of the rise in mean peripheral circumflex pressure and aortic-circumflex pressure difference occurred in the early interval, the greatest changes in both variables appeared later. This suggests that the circumflex branch must be severely narrowed before a large rise in peripheral circumflex pressure occurs, and corroborates Eckstein's findings (15) that "Substantial reductions in lumen size are required to depress coronary flow, to create sizeable pressure drops and to stimulate collateral growth in dogs at rest."

After complete occlusion of the circumflex branch, there was a more gradual and much smaller increase of peripheral circumflex pressure. The values of mean peripheral circumflex pressure never reached the values of mean aortic pressure even after 2 months (dog 1, Fig. 4). This finding agrees with other reports which describe comparable differences between the two pressures in dogs examined months to a year after occlusion (3, 16).

In our dogs, measurements were made when they were lying quietly on a table for periods of 30 to 120 minutes. At other times, their activity varied from moving about in the cage, to walking and occasionally running when taken outside; in these circumstances, with extra demands on the heart, the pressure gradient may have been higher than under resting conditions of the experiment. Eckstein (15) showed that vigorous exercise had a greater effect on retrograde blood flow in dogs with partial occlusion of the circumflex branch than in dogs restricted to cages. The effect to which the mild exercise of our dogs influenced the peripheral circumflex pressure is not known.

Changes in reactive hyperemia appeared to be more sensitive to constriction than the changes in circumflex flow. From Figure 8, in the period 10 to 22 days after operation, it can be observed that while the peak reactive hyperemia declined steeply until it practically disappeared, the flow during this time remained essentially in the low range (40 ml/minute). However, by 23 days not even a flow of 40 ml/minute was attained, and in the next several days the flow regressed to zero. A critical degree of constriction seems to have been reached, therefore, about 20 to 22 days postoperatively; it may be significant that it was just at this time that the reactive hyperemia almost disappeared.

The changes in phasic circumflex pressure were striking, especially during the phase of rapid rise of the peripheral circumflex pressure (Fig. 9). At this time, the peripheral pressure curve resembled that of the usual left ventricular pressure curve. A possible mechanism might have been that the blood in the underfilled bed became trapped during isometric contraction—reverse flow by the cuff could not occur—while myocardial tension minimized forward flow. The rise in diastolic peripheral circumflex pressure, which developed more slowly, may have been dependent on blood flow arising from the development of larger collaterals; the injections of Schlesinger mass demonstrated that these were present (Fig. 10).

Electrocardiographic evidence of myocardial infarction was present as early as 6 days in dog 3, even though circumflex flow appeared adequate (Fig. 6). It is noteworthy that at 6 days the reactive hyperemia had almost disappeared (results not shown). In this dog, because there was a second operation and extra trauma to the circumflex branch from implanting another tube, the presence of a thrombus cannot be excluded. However, in the absence of thrombosis, it would be an interesting paradox if infarction occurs in the presence of seemingly adequate coronary flow. Lumb et al. (17) showed in dogs that myocardial infarction could develop without complete occlusion. The ventricular arrhythmias, which were adequately followed only in dog 3, can be a dominant finding after acute myocardial insufficiency both in humans and experimental animals (17-19).

The snug fit of the ameroid constrictor as well as the fact that the dog was just recovering from the operation detract from the value...
of the first 4 to 5 postoperative days as a control period. Despite this, there appeared to be a dependence of the maximum rise time of the mean peripheral circumflex pressure (Table 1, col. 12) on the early postoperative values of mean peripheral circumflex pressure (col. 4), for example, in the dogs in which the early peripheral circumflex pressure was small (2 to 3 mm Hg), the maximum rise time of the mean peripheral circumflex pressure was only one-half that in dog 2, whose early mean peripheral circumflex pressure was 15 mm Hg (compare Figs. 5 and 6). In addition, there was an inverse relationship between the maximum aortic-circumflex pressure difference and the early mean peripheral circumflex pressure (cols. 4 and 8). The variation in early values of mean peripheral circumflex pressure might have been due to different degrees of inherent collateral circulation. If this were so, it might have affected the rate of collateral development following constriction. No attempt was made to select dogs by the electrocardiographic response to occlusion as Eckstein (15) did.

In the four dogs studied, the slope of the isometric relaxation portion of the circumflex flow trace was reduced as the circumflex flow decreased after constriction. Although the start of the abruptly rising portion of the circumflex trace coincided with the onset of the dicrotic notch, it is only an assumption that the subsequent rising portion of the trace corresponded exactly to the duration of the isometric relaxation period. If this relationship did exist, a prolongation of the isometric relaxation period could affect the slope, but the measurements to clarify this possibility were not made in our dogs. A simpler explanation is that the reduction in slope was a consequence of the reduced amplitude of the circumflex flow trace following reduction in circumflex flow. This is evident by comparing the appropriate traces in Figures 3 and 9.

It is believed that the change in peripheral coronary pressure following sustained coronary insufficiency is an important index of the development of coronary collaterals, but the rise in peripheral coronary pressure does not give a measurement of coronary collateral circulation. The relationship between collateral flow increase and rise in peripheral coronary pressure awaits further examination.

Acknowledgments

The authors are indebted to Charles Massengill, David Bostrom, and Herbert Johnson for their technical assistance.

References


Day-to-Day Changes in Coronary Hemodynamics Secondary to Constriction of Circumflex Branch of Left Coronary Artery in Conscious Dogs
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doi: 10.1161/01.RES.22.2.237
Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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