Effects of Increased Myocardial Oxygen Consumption on Coronary Reactive Hyperemia in the Awake Dog

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ABSTRACT

This study was undertaken to determine whether coronary reactive hyperemia is coupled to myocardial metabolic activity and thus proportional to myocardial oxygen consumption or whether it is mechanically determined, resulting from direct myogenic relaxation of coronary vascular smooth muscle in response to loss of the stretch stimulus provided by arterial blood pressure. In ten unanesthetized dogs, coronary artery occlusions 1—7 seconds in duration produced reactive hyperemia resulting in 260—410% repayment of the blood flow debt incurred during occlusion. When myocardial oxygen consumption and coronary blood flow were increased by paired ventricular stimulation, reactive hyperemia increased to a commensurate degree so that debt repayments remained unchanged at 270—420%. That this augmentation of reactive hyperemia was actually related to increased myocardial metabolic activity during the occlusion was demonstrated by a similar increase in the hyperemic response when paired ventricular stimulation was applied during the occlusion only. To demonstrate that augmented reactive hyperemia during paired ventricular stimulation did not merely represent direct myogenic relaxation imposed on a vascular bed more dilated from the onset, coronary blood flow was increased by infusion of adenosine with no increase in myocardial oxygen consumption. During adenosine infusion, the total volume of reactive hyperemic blood flow was similar to that observed during the control situation. Thus, in the coronary system reactive hyperemia is related to myocardial metabolic activity during the interval of arterial occlusion and not influenced by alterations in resting coronary blood flow which occur independently of myocardial oxygen consumption.

KEY WORDS coronary blood flow adenosine myogenic hypothesis coronary artery occlusion paired ventricular stimulation

Transient interruption of inflow of arterial blood to many organs and tissues effects vasodilation, causing a reactive hyperemic response. Freeman (1) has proposed that a cumulative local metabolic disturbance occurs as tissue metabolism continues in the absence of arterial inflow, resulting in a blood flow debt which is quantitatively repaid during the subsequent reactive hyperemia. Thus, the excess arterial inflow during the reactive hyperemia should equal the deficit incurred during the period of circulatory stasis. Reactive hyperemia has been demonstrated to occur in the coronary circulation following brief periods of coronary artery occlusion (2—4). However, the excess inflow of arterial blood during the reactive hyperemia generally far exceeds the deficit incurred during the occlusion, suggesting that the stimulus for vasodilation is poorly matched to the metabolic requirements of the myocardium (3, 4).

Bayliss (5) has postulated that the stimulus for maintenance of normal vascular tone is provided by the mechanical stretching effect of intra-arterial pressure on the vascular smooth muscle and that reactive hyperemia represents myogenic relaxation of vascular smooth muscle in response to loss of the arterial pressure stimulus during the arterial occlusion. Thus, the reactive hyperemic response would be mechanically determined and not directly dependent on the metabolic activity of the tissue under study during the period of occlusion. In addition, direct myogenic relaxation of vascular...
smooth muscle might account for the reactive hyperemia which occurs in the coronary circulation following exceedingly brief periods of arterial occlusion, which have been thought to be of inadequate duration to result in sufficient metabolic disturbance to produce the degree of vasodilation observed (6, 7).

To test this hypothesis, coronary reactive hyperemia was observed following brief periods of coronary artery occlusion. Myocardial oxygen consumption and coronary blood flow were then increased by paired ventricular stimulation to determine whether the reactive hyperemia responded to alterations in local tissue metabolic activity. If the reactive hyperemic response is a mechanically determined myogenic relaxation, then paired ventricular stimulation should not augment the reactive hyperemia because of increased myocardial metabolic activity during the occlusion but might augment the response merely because myogenic relaxation is imposed on a vascular bed more dilated at the outset. To evaluate this possibility, coronary blood flow was increased with no increase in myocardial oxygen consumption by infusing adenosine, and the reactive hyperemic response was again observed. Studies were carried out in unanesthetized dogs to eliminate possible interfering effects which might result from the use of general anesthesia or from acute surgical trauma.

Methods

Ten adult mongrel dogs weighing 25—32 kg were anesthetized with sodium thiamylal (30—40 mg/kg, iv) and underwent left thoracotomy. The proximal 1.5 cm of the circumflex branch of the left coronary artery was dissected free, and a Statham type ST electromagnetic flowmeter probe was positioned around the vessel proximal to any branches. Care was taken to attain mechanical stability of the flow probe on the coronary artery to ensure a consistently stable base line during later coronary flow measurements (8). A pneumatic occluder constructed in our laboratory of polyvinyl chloride tubing with an outside diameter of 2.7 mm was placed around the circumflex coronary artery distal to the electromagnetic flow probe (9). In five dogs the ascending aorta was dissected free and a Statham type Q electromagnetic flow probe was placed on the ascending aorta as previously described (8). A polyvinyl chloride heparin-filled catheter 3 mm in outside diameter was introduced into the left internal mammary artery and advanced into the arch of the aorta. A polyvinyl chloride heparin-filled catheter 2.7 mm in outside diameter was introduced into the left atrial cavity through the left atrial appendage and secured in place with a purse-string suture. A bipolar epicardial pacing electrode was sutured to the region of the right ventricular outflow tract. The aortic and left atrial catheters, the electromagnetic flowmeter leads, the pneumatic occluder tubing, and the pacing wire were all tunneled dorsally into a subcutaneous pouch at the base of the neck but were not exteriorized to protect them from damage. The catheters, electromagnetic flowmeter leads, pneumatic occluder tube, and pacing wire were exteriorized through a 1-cm skin incision using 2% lidocaine infiltration anesthesia the morning prior to study.

Throughout this report the phrase "coronary blood flow" denotes measurements of flow through the circumflex branch of the left coronary artery. Computations of myocardial oxygen consumption were made using this flow measurement. Aortic and coronary flows were measured using Statham M-4000 electromagnetic flowmeters. Flowmeter calibrations were performed by passing measured flows of normal saline through the flowmeter probe. Calibration factors for all probes remained with a standard deviation of no more than ±5% during the period of study. Aortic blood pressure was measured with a Statham P23Db pressure transducer. Lead II of a standard electrocardiogram was obtained. Data were recorded using a Hewlett-Packard model 3917-A magnetic tape recorder and a Sanborn model 958-100 eight-channel direct-writing oscillograph.

Studies were carried out 12—28 days after the initial surgery. All dogs were active, fully recovered from surgery and without fever, anemia, or other evidence of ill health. The dogs were trained to lie quietly on their right sides during the period of study.

In four of these dogs a no. 7 French Sones cardiac catheter (U. S. Catheter and Instrument Company) was introduced through a 0.5-cm skin incision, using 2% lidocaine infiltration anesthesia into the left jugular vein, and positioned in the coronary sinus, using fluoroscopic control. Placement of the catheter 1—2 cm past the bend of the coronary sinus was confirmed by observing its position while the coronary sinus was opacified by injecting 34 ml of a 75% solution of sodium diatrizoate through the catheter at the beginning and the end of each study. This catheter position has been demonstrated to yield coronary venous blood uncontaminated by right atrial blood (10).

The laboratory was dimly illuminated and kept free of noise or other activity which might disturb the dogs. After all recording instruments were connected, 45—60 minutes was allowed for the dog to adjust to the laboratory conditions. To ensure a constant heart rate between interventions, studies were performed during ventricular pacing at a rate of 120 beats/min. Hemodynamic data were sampled continuously for the first 10 minutes of ventricular pacing to ensure that a hemodynamic steady state had been achieved before the study was begun. Coronary artery occlusions were performed by abruptly injecting and holding 3 ml of air in the occluder tubing with a hand-held syringe. Examination of recordings of coronary blood flow made at a paper speed of 100 mm/sec demonstrated that this technique allowed consistent complete occlusion or complete release of coronary blood flow within less than 0.1 second. The reactive hyperemic response was then
observed in duplicate following coronary artery occlusions 1, 2, 3, and 5 seconds in duration. In eight of the ten dogs, occlusions 7 seconds in duration were also performed. An interval of 2–3 minutes was allowed between each occlusion. Pacing was performed using a Grass model S-8 physiological stimulator delivering a 3-msec square-wave pulse 25% above threshold voltage through an isolation unit.

Paired ventricular stimulation was then begun at 240 stimuli/min using the briefest interval between stimuli which resulted in two separate ventricular depolarizations (approximately 165 msec). Although hemodynamic parameters generally stabilized within the first minute of paired stimulation, pacing was continued for 10 minutes to ensure that a steady state had been achieved before studies were performed. The reactive hyperemic response was then observed in duplicate following coronary artery occlusions lasting 1, 2, 3, 5, and 7 seconds. A 2–3-minute interval was allowed between each coronary occlusion.

Paired stimulation was then discontinued, and ventricular pacing at 120 beats/min was resumed. After allowing 5 minutes for return to a steady state, the reactive hyperemic response to a 5-second coronary artery occlusion was observed in triplicate; 2–3 minutes was allowed between each occlusion. Subsequently, the reactive hyperemic response to a 5-second coronary artery occlusion was observed while the stimulator was switched from ventricular pacing to paired ventricular stimulation during the 5-second interval of arterial occlusion only. Ventricular pacing at 120 beats/min was performed prior to the occlusion and immediately following the occlusion during the reactive hyperemic response, and paired stimulation was performed only during the interval of coronary artery occlusion. The reactive hyperemic response to 5-second coronary artery occlusions performed in this way was observed in triplicate.

Ventricular pacing was reinstituted at 120 beats/min, and infusion of adenosine dissolved in normal saline (12.5 μmoles/ml) was begun through the left atrial catheter at a rate which increased coronary blood flow during ventricular pacing at 120 beats/min to the level previously observed during paired ventricular stimulation at 240 stimuli/min. The mean infusion rate of adenosine was 0.23 ± 0.07 μmoles/kg min⁻¹. After an infusion rate of adenosine was attained to establish the desired increase in coronary blood flow, the infusion was continued during 10 minutes of continuous data recording to ensure that a steady state had been achieved. The reactive hyperemic responses to coronary artery occlusions 1, 2, 3, 5, and 7 seconds in duration were then again observed in duplicate.

Studies were discarded in which arterial blood pressure or aortic blood flow differed by more than 5% from the control value during the occlusion and to the end of the reactive hyperemic response. The volume of flow occurring during the reactive hyperemia following a coronary artery occlusion was determined by electrical integration using a Donner-Systron model 3400 analog computer. The duration of the hyperemic period was taken as the time required for flow to fall within 5% of the control measurement. The maximum coronary blood flow rate during the hyperemic response was measured directly from the recording. Mean aortic and coronary blood flow and aortic blood pressure were measured directly from the recordings. Calculations of blood flow debt incurred during arterial occlusion, reactive hyperemic flow, and blood flow debt repayment were made as described by Freeman (1).

Blood flow debt (ml) = control flow rate (ml/sec) × duration of occlusion (sec).

Reactive hyperemic flow (ml) = [total flow during reactive hyperemia (ml)] - [control flow rate (ml/sec) × duration of reactive hyperemia (sec)].

Blood flow debt repayment (%) = (reactive hyperemic flow/blood flow debt) × 100.

Data were analyzed using Student's t-test for paired data. All computations were carried out on an IBM model 1130 digital computer.

In four dogs myocardial oxygen consumption was estimated using blood specimens drawn simultaneously from the aortic and coronary sinus catheters. During each intervention blood specimens were drawn after 10 minutes of steady-state pacing and at the end of each intervention 2 minutes after the last reactive hyperemic response had been observed. Hemoglobin content and oxygen saturation were determined in duplicate using an Instrumentation Laboratories model 182 oximeter previously calibrated using the Van Slyke manometric apparatus. This oximeter was capable of duplicating oxygen saturations measured with the Van Slyke apparatus within 95% confidence limits of ±3.6%.

**Results**

During ventricular pacing at 120 beats/min mean arterial blood pressure was 95 ± 4 mm Hg. Mean arterial blood pressure was not significantly different from this value during paired ventricular stimulation (99 ± 3 mm Hg, P > 0.05) or during ventricular pacing at 120 beats/min with adenosine infusion (94 ± 2 mm Hg, P > 0.5). Mean arterial blood pressure during paired ventricular stimulation was not significantly different from that during ventricular pacing at 120 beats/min with adenosine infusion (P > 0.05). Mean aortic blood flow in five dogs having electromagnetic aortic flowmeter probes was 2,100 ± 480 ml/min during ventricular pacing at 120 beats/min, 2,150 ± 440 ml/min during paired ventricular stimulation, and 2,050 ± 460 ml/min during ventricular pacing at 120 beats/min with adenosine infusion. There was no significant difference between mean aortic blood flows during any of these three interventions (P > 0.3).

In four dogs in whom myocardial oxygen consumption was estimated, mean coronary blood flow was 44.0 ± 7.5 ml/min with a coronary arteriovenous oxygen difference of 11.67 ± 0.52.
CORONARY REACTIVE HYPEREMIA

ml/100 ml blood, yielding a myocardial oxygen consumption of 5.13±0.91 ml/min (Table 1). During paired ventricular stimulation, coronary blood flow was increased 35% (P<0.02) with no significant change in coronary arteriovenous oxygen difference. Thus, myocardial oxygen consumption was increased 28% during paired ventricular stimulation. During infusion of adenosine with ventricular pacing at 120 beats/min, coronary blood flow was increased to a value similar to that during paired ventricular stimulation (57.0±9.6 ml/min). However, the coronary arteriovenous oxygen difference was reduced 25% below the control level during adenosine infusion so that myocardial oxygen consumption was identical with that during ventricular pacing at 120 beats/min without adenosine infusion (Table 1).

During ventricular pacing at 120 beats/min, coronary artery occlusions 1–7 seconds in duration resulted in reactive hyperemic responses 11.5–42.2 seconds in duration; the duration of reactive hyperemia increased regularly with the length of occlusion (Table 2). Debt repayments after occlusions 1, 2, and 3 seconds in duration were statistically similar (27%, 26%, and 29%, respectively), but debt repayment after occlusions 5 and 7 seconds in duration were significantly greater (39% and 41%, respectively, P<0.05).

During paired ventricular stimulation, occlusions 1–7 seconds in duration resulted in reactive hyperemic responses significantly longer than those during ventricular pacing at 120 beats/min (mean durations 13.4–60.4 seconds) (Table 2). Since resting coronary blood flow rates were greater during paired ventricular stimulation, blood flow debts incurred during occlusion were significantly larger than those incurred during ventricular pacing at 120 beats/min. However, reactive hyperemia during paired stimulation was increased in proportion to the increased blood flow debt, so that debt repayment was maintained at a level during paired stimulation the same as that during ventricular pacing (Table 2, Fig. 1).

During adenosine infusion, coronary blood flow was similar to that observed during ventricular paired stimulation, but myocardial oxygen consumption remained at the level observed during ventricular pacing without adenosine infusion (Tables 1 and 2). Excess reactive hyperemic flows during adenosine infusion were in every case significantly less than those observed during ventricular pacing without adenosine infusion so that blood flow debt repayments were significantly
TABLE 2
Left Circumflex Coronary Artery Occlusions in Ten Dogs during Ventricular Pacing at 120 beats/min (VP), Paired Ventricular Stimulation at 240 stimuli/min (VPS), and Ventricular Pacing at 120 beats/min with Infusion of Adenosine (ADEN)

<table>
<thead>
<tr>
<th>Control flow (ml/min)</th>
<th>Duration of occlusion (seconds)</th>
<th>1.0 ± 0.03</th>
<th>2.0 ± 0.05</th>
<th>3.0 ± 0.05</th>
<th>5.0 ± 0.10</th>
<th>7.0 ± 0.07</th>
</tr>
</thead>
<tbody>
<tr>
<td>VP</td>
<td>38.5 ± 3.9</td>
<td>38.5 ± 3.9</td>
<td>38.5 ± 4.2</td>
<td>37.5 ± 3.7</td>
<td>42.0 ± 5.0</td>
<td></td>
</tr>
<tr>
<td>VPS</td>
<td>53.5 ± 4.9*</td>
<td>53.0 ± 4.9*</td>
<td>53.0 ± 5.2*</td>
<td>53.0 ± 4.6*</td>
<td>54.5 ± 5.8*</td>
<td></td>
</tr>
<tr>
<td>ADEN</td>
<td>52.5 ± 5.2*</td>
<td>52.0 ± 5.2*</td>
<td>52.0 ± 5.5*</td>
<td>52.5 ± 5.0*</td>
<td>39.0 ± 7.1*</td>
<td></td>
</tr>
</tbody>
</table>

Blood flow deficit (ml)

| VP                   | 0.65 ± 0.07                     | 1.28 ± 0.20  | 1.93 ± 0.22 | 3.19 ± 0.33 | 4.90 ± 0.55 |
| VPS                  | 0.90 ± 0.10*                    | 1.77 ± 0.25* | 2.66 ± 0.21*| 4.50 ± 0.49*| 6.36 ± 0.55*|
| ADEN                 | 0.88 ± 0.10*                    | 1.73 ± 0.30* | 2.61 ± 0.37*| 4.45 ± 0.43*| 6.86 ± 0.87*|

Duration of reactive hyperemia (seconds)

| VP                   | 11.5 ± 1.2                      | 15.3 ± 1.2   | 22.4 ± 1.8  | 33.9 ± 3.8  | 42.2 ± 5.3  |
| VPS                  | 13.4 ± 0.5†                     | 23.5 ± 2.5†  | 27.3 ± 1.5  | 41.4 ± 3.8  | 60.4 ± 11.4 |
| ADEN                 | 5.3 ± 0.5*                      | 9.7 ± 1.6†   | 15.0 ± 1.5† | 27.0 ± 1.6  | 37.1 ± 3.5  |

Total flow during reactive hyperemia (ml)

| VP                   | 9.2 ± 1.7                       | 13.2 ± 2.0   | 20.1 ± 3.2  | 33.8 ± 5.1  | 49.6 ± 8.2  |
| VPS                  | 14.2 ± 2.5*                     | 25.7 ± 2.5*  | 32.6 ± 5.2* | 51.4 ± 7.5* | 81.6 ± 8.5* |
| ADEN                 | 10.9 ± 1.8                      | 15.0 ± 2.3   | 22.7 ± 3.3  | 37.4 ± 6.1  | 54.4 ± 8.9  |

Excess flow during reactive hyperemia (ml)

| VP                   | 1.86 ± 0.20                     | 3.33 ± 0.60  | 5.69 ± 1.01 | 12.60 ± 1.70| 20.09 ± 2.90|
| VPS                  | 2.48 ± 0.53*                    | 4.87 ± 0.60* | 8.38 ± 1.33*| 14.83 ± 2.42| 26.71 ± 2.50†|
| ADEN                 | 0.77 ± 0.15*                    | 1.73 ± 0.30* | 3.26 ± 0.33*| 7.79 ± 1.3* | 13.03 ± 2.4†|

Debt repayment (%)

| VP                   | 273 ± 25                        | 260 ± 9      | 265 ± 19    | 395 ± 26    | 410 ± 44    |
| VPS                  | 270 ± 15                        | 273 ± 15     | 315 ± 23    | 330 ± 29    | 420 ± 56    |
| ADEN                 | 85 ± 14*                        | 100 ± 15*    | 125 ± 15*   | 175 ± 17*   | 190 ± 25*   |

*P values indicate difference from VP.
†P < 0.03.

Decreased (mean blood flow debt repayments 85–190%) (Table 2). However, during adenosine infusion the total volume of arterial inflow during an interval equal to the duration of reactive hyperemia observed during control ventricular pacing at 120 beats/min was similar to the control reactive hyperemic flow (Fig. 1). Thus, the low debt repayments observed during adenosine infusion occurred because (1) the computed blood flow debt during adenosine infusion was artificially increased since resting coronary blood flow had been increased with no alteration in myocardial oxygen consumption and (2) the control rate of coronary blood flow which was subtracted from the total reactive hyperemic flow was also artificially increased during adenosine infusion. Thus, increasing coronary blood flow without increasing myocardial oxygen consumption did not significantly alter the total flow following a brief period of coronary artery occlusion. The computed blood flow debt repayment following coronary artery occlusion during adenosine infusion was decreased in proportion to the degree to which arterial inflow to the myocardium was increased above its metabolic requirements.

In six dogs a 5-second coronary artery occlusion during ventricular pacing at 120 beats/min resulted in a mean blood flow debt of 3.4 ml with excess flow during the subsequent reactive hyperemia of 12.8 ml, resulting in 370% repayment of the blood flow debt (Table 3). When the pacer was switched to paired ventricular stimulation during the interval of arterial occlusion only, the excess flow during the subsequent reactive hyperemic response was significantly increased (mean excess flow 16.0 ml, P < 0.01, Table 4). When the blood flow debt was computed by multiplying the duration of occlusion by the coronary blood flow rate observed during ventricular pacing at 120 beats/min, debt repayment was 475%, significantly higher than that observed when paired ventricular stimulation was not used during the period of occlusion (P < 0.01). However, when the blood flow debt was assumed to be equal to the period of occlusion times the

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coronary blood flow rate observed during paired ventricular stimulation, mean repayment of the blood flow debt was 355%, not significantly different from that observed during the control situation. Thus, the excess flow during reactive hyperemia increased in proportion to the increase in coronary blood flow which would have been predicted to result from paired ventricular stimulation.

**Discussion**

Over a wide range of myocardial contractile (and thus metabolic) activity, coronary blood flow is closely matched to myocardial oxygen consumption to maintain a nearly constant, very high level of arteriovenous oxygen extraction (11). The mechanisms responsible for this precise metering of arterial inflow in response to myocardial oxygen requirements appear to be entirely local in nature. Thus, pharmacologic autonomic nervous system blockade or denervation of the heart do not alter the ability of the coronary vasculature to perform autoregulation (12). The close correlation of coronary blood flow with myocardial oxygen consumption suggests that coronary autoregulation is intimately coupled to myocardial metabolic activity.

However, reactive hyperemia in the coronary vascular system appears to be poorly matched to the metabolic requirements of the myocardium.
Thus, the excess arterial inflow during coronary reactive hyperemia is far in excess of the deficit incurred during the period of arterial occlusion. Olsson and Gregg (4) found that during the course of the reactive hyperemia coronary sinus blood oxygen content rose far above the resting level, indicating that arterial inflow during the reactive hyperemia was in excess of myocardial oxygen requirements. In addition, it has been suggested that interruption of arterial inflow for only a few seconds does not result in sufficient metabolic disturbance to produce the degree of vasodilation seen during the subsequent reactive hyperemia (6, 7). Data from other vascular beds suggest that direct myogenic relaxation of vascular smooth muscle in response to loss of the mechanical stimulus of intraluminal blood pressure may contribute to the reactive hyperemic response. Wood et al. (13) maintained high intravascular pressure in human forearms during arterial occlusion by congesting the limbs with a pneumatic cuff at 70-80 mm Hg for 5 minutes before applying the arterial occlusion. The resultant reactive hyperemia was 21-51% less than that observed without prior congestion. It was concluded that decreased intravascular pressure during arterial occlusion did contribute to the vasodilatation which resulted in reactive hyperemia. Patterson (14), also in studies performed on human forearms, maintained elevated intravascular pressure during arterial occlusion by applying suction around the forearm before application of arterial occlusion. At a negative pressure of 100 mm Hg, the reactive hyperemic blood flow debt repayment was reduced to 39% of the control response. The greater the suction applied, the quicker the blood flow returned to the control level after release of the occlusion and the greater the reduction of the debt repayment.

If myogenic mechanisms stimulated by loss of the direct mechanical stimulus provided by intravascular pressure are responsible for reactive hyperemia, alterations in tissue metabolic activity should not affect the reactive hyperemic response or only modify it partially. In the present study, paired ventricular stimulation was used to increase myocardial oxygen consumption. The 28% increase in myocardial oxygen consumption observed in the present study during paired ventricular stimulation was similar to that previously reported from this and other laboratories (15, 16). The mechanical effect of paired ventricular stimulation utilizing the briefest interval between stimuli which results in two depolarizations is principally expressed as an augmentation of contractility of the effective ejected beats. The second depolarization of each pair is not accompanied by a discrete mechanical contraction and is represented by only a barely perceptible slowing of the terminal downslope of the left ventricular pressure contour of the effective beat (16). Thus, paired ventricular stimulation with the shortest possible interval between stimulus pairs appears to result in no significant throttling of diastolic coronary blood flow (16).

When oxygen consumption and coronary blood flow were augmented by paired ventricular stimulation, the reactive hyperemic response was augmented to a similar degree so that the reactive hyperemia maintained a remarkably close proportionality to the rate of coronary flow and the debt repayments remained essentially constant. Reactive hyperemia increased with the increase in coronary blood flow even for occlusions as brief as 1 second. Thus, even for the briefest intervals of arterial occlusion studied, the reactive hyperemic response appeared to be related to the metabolic activity of the myocardium. These data quantitatively explain...
the findings of Pauly et al. (17) that in the open-chest dog paired ventricular stimulation increased reactive hyperemia following 30-60 second coronary artery occlusions.

It was possible that the increased reactive hyperemic response accompanying paired ventricular stimulation did not represent an increase in reactive hyperemia secondary to increased myocardial metabolism but merely a myogenic relaxation superimposed on a vascular bed more dilated from the outset. To test this hypothesis, coronary blood flow was increased independently of myocardial oxygen consumption by infusion of adenosine to increase coronary flow to a level similar to that observed during paired stimulation. In agreement with previous studies in anesthetized dogs, adenosine infusion caused no significant increase in myocardial oxygen consumption (18, 19). Total reactive hyperemic blood flow did not increase significantly with increased coronary blood flow produced by adenosine infusion but remained essentially the same as it was during the control situation (Fig. 1). Because the control rate of flow was increased during adenosine infusion, the excess flow during the reactive hyperemia was actually decreased. As the magnitude of the reactive hyperemia increased with occlusions of longer duration, progressively more of the reactive hyperemic flow became "excess," that is, emerged above the artifactually elevated control rate of flow to participate in the debt repayment. Thus, during adenosine infusion computed debt repayments increased progressively as occlusions increased from 1 to 7 seconds in duration, although they did not approach the control values.

The proportional increases in reactive hyperemia which accompanied increases in coronary blood flow secondary to increased myocardial metabolic activity and the failure of reactive hyperemia to increase with increases in coronary blood flow produced independently of myocardial oxygen consumption strongly link the reactive hyperemic response to the metabolic activity of the myocardium. To further determine the extent to which reactive hyperemia is responsive to myocardial metabolic activity during the interval of occlusion and to eliminate any possible influence of alterations in myocardial oxygen consumption immediately prior to and following the occlusion, paired ventricular stimulation was performed during the interval of coronary artery occlusion only. Again, the reactive hyperemia increased in direct proportion to the predicted increase in myocardial oxygen consumption produced by paired ventricular stimulation. Thus, the reactive hyperemia was related to the level of myocardial metabolic activity during the interval of occlusion and was not influenced by the control level of coronary blood flow prior to occlusion.

The data reported in this study document the close relationship between reactive hyperemic blood flow debt repayment and myocardial metabolic activity during the period of arterial occlusion. Unfortunately, however, these data do not permit speculation concerning the mechanism of the marked overpayment of the blood flow debt which is peculiar to the reactive hyperemic response of the coronary vascular system.

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References

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