Reduced regional myocardial perfusion in the presence of pharmacologic vasodilator reserve

JOHN M. CANTY, JR., M.D., AND FRANCIS J. KLOCKE, M.D.

ABSTRACT To determine whether reductions in regional myocardial perfusion at reduced coronary arterial pressures reliably indicate maximal vasodilation of the distal vasculature, coronary autoregulation was studied in open-chest dogs at heart rates of ~60 beats/min, a level at which metabolic demand, time-averaged systolic compressive forces, and transmural vasodilator reserve approximate those found under usual resting conditions. Circumflex pressure was controlled with a programmable pressure source. Regional circumflex inflow was 0.56 ± 0.04(SEM) ml·min⁻¹·g⁻¹ when circumflex pressure equaled spontaneous aortic pressure and fell to 0.34 ± 0.02 ml·min⁻¹·g⁻¹ when circumflex pressure was reduced to 35 mm Hg. Reductions were similar in each myocardial layer, with endocardial flow falling from 0.68 ± 0.04 to 0.39 ± 0.03 ml·min⁻¹·g⁻¹. During adenosine-induced vasodilation at 35 mm Hg, full-thickness and endocardial flows rose to 0.92 ± 0.08 and 1.07 ± 0.10 ml·min⁻¹·g⁻¹, respectively. When coronary pressure was reduced to 25 mm Hg and autoregulation was again operative, full-thickness and endocardial flows fell to 0.28 ± 0.03 and 0.28 ± 0.04 ml·min⁻¹·g⁻¹. During adenosine vasodilation at 25 mm Hg endocardial flow did not increase significantly but epicardial reserve remained present. These results indicate that significant reductions in regional myocardial perfusion can occur before pharmacologic vasodilator reserve is exhausted. In the absence of tachycardia, endocardial vasodilator reserve can persist to coronary pressures less than 35 mm Hg, but is ordinarily exhausted before epicardial vasodilator reserve.


AUTOREGULATORY reductions in impedance to flow cause coronary flow to be held relatively constant as coronary arterial pressure is reduced at a constant level of myocardial metabolic demand.1–3 When vasodilator reserve has been exhausted, coronary flow becomes pressure-dependent and falls rapidly with pressure. Coronary flow in this situation also varies importantly with diastolic period, i.e., heart rate and systolic compressive forces. Because these vary transmurally, subendocardial perfusion is in particular jeopardy.4 An inherent transmural gradient in conductance favoring the subendocardium compensates in part for subendocardial vulnerability,5,6 but is not sufficient to maintain normal inner-outter flow ratios at higher heart rates.7

In recent years it has generally been held that a diminution in local flow accompanying a reduction in coronary pressure implies exhaustion of local vasodilator reserve. In animal preparations of coronary stenosis, interventions that increase full-thickness flow but decrease poststenotic pressure have been associated with reductions in subendocardial perfusion, with the latter attributed to a "transmural steal," i.e., the exhaustion of subendocardial vasodilator reserve while subepicardial reserve is still present.8,9 Although the concept of earlier exhaustion of subendocardial reserve has been supported by other experimental studies,10,11 reductions in resting flow in an animal preparation of a coronary muscle bridge have been difficult to reconcile, since all transmural myocardial layers showed substantial increases in flow when adenosine was infused into the "bridged" artery.12 Also, Bache and Schwartz13 have reported full-thickness flows during vasodilation at reduced coronary pressures that exceed usual resting flows at normal pressures.

Systematic studies of local vasodilator reserve at low pressures have not been performed, in part because of the difficulties involved in maintaining poststenotic pressure constant under control conditions and

From the Departments of Medicine and Physiology, State University of New York at Buffalo, and the Erie County Medical Center, Buffalo. Supported by a grant from the American Heart Association with funds contributed from the WNY affiliate, The Alexandrine and Alexander Sinsheimer Fund, and Clinical Investigator Award HLB-01168, and program-project grant HLB-15194 from the National Heart, Lung, and Blood Institute.

Address for correspondence: John M. Canty, Jr., M.D., SUNY/AB Clinical Center, Room CC-15, Erie County Medical Center, 462 Grider St., Buffalo, NY 14215.

Received Sept. 24, 1984; accepted Oct. 25, 1984.
at the same level during a vasodilative stimulus as before. Changes in heart rate and/or systolic compressive forces also require consideration, since they may result in alterations in metabolic demand, diastolic period, and/or subendocardial impedance to flow. In the present studies a coronary pressure control system was used in paced heart-blocked dogs to minimize these problems. The intent was to determine whether regional pressure reduction is an adequate stimulus for maximum vasodilation or whether reductions in flow can occur in the face of residual pharmacologic vasodilator reserve.

Methods

Fourteen adult mongrel dogs weighing 20 to 32 kg were anesthetized with sodium pentobarbital. The animals were ventilated through auffed endotracheal tube with use of a Harvard pump with room air supplemented with oxygen. Body temperature was measured with a vena cavalm thermistor and maintained at 37° to 39° C with heating pads. A left thoracotomy was performed on each dog and the heart suspended in a pericardial cradle. Complete heart block was produced by injecting formalin into the atrioventricular tract.13 and the animals were paced at a constant rate with electrodes placed on the right ventricular outflow tract.

The left circumflex artery was dissected free near its origin and cannulated; flow was usually restored within 90 sec and always within 120 sec. After cannulation, at least 30 min were allowed for systemic and coronary hemodynamics to stabilize. Perfusion to the cannulated circumflex artery was controlled by a programmable pressure control system.14 Side-ports in the perfusion cannula provided for the injection of radionuclide-labeled microspheres and for infusion of adenosine. Phasic and mean coronary flow were measured with an extracorporeal flow probe (Series 2000-C, Biotronex Laboratory, Kensington, MD) excited by a gated sine wave flowmeter (Biotronex Model BL 613). Mechanical zero was checked frequently by brief (<5 sec) cannula occlusions and was stable within ±2 ml/min after the initial adjustment. Coronary pressure within the circumflex artery was measured with a small Teflon catheter inserted into the epicardial artery distal to the cannula tip. Fluid-filled catheters were inserted into the aorta through the right carotid artery and into the left ventricle through the left atrial appendage. These and the catheter used to measure circumflex pressure were flushed with vacuum-degassed saline and connected to Statham P23dB transducers.

Regional flow measurements. Regional myocardial perfusion was measured with radionuclide-labeled microspheres 10 ± 1 μm in diameter (New England Nuclear, Boston). Since circumflex pressure control necessitated isolation from the systemic circulation, microspheres were injected directly into the coronary cannula with use of a 25-gauge needle directed upstream. Up to five measurements were made in each experiment with the use of 57Co, 51Cr, 103Ru, 113Sn, 99Nb, and 48Sc. Microspheres were suspended in 10% dextran with 0.01% Tween and dispersed in vials in an ultrasonicator for at least 5 min before injection. Vials were then shaken vigorously and 2 to 5 × 10⁶ microspheres were withdrawn into a 1 ml tuberculin syringe. The microsphere suspension (~0.05 ml) was mixed with warmed arterial blood and injected into the coronary cannula over 10 to 20 sec. There was no discernible effect of the injectate on coronary or systemic hemodynamics.

At the end of each experiment the perfused circumflex seg-

ment was identified by injecting India ink into the coronary cannula during perfusion at 35 mm Hg. The cannula was immediately occluded and the heart was arrested by injection of KCl. The entire heart, including the atria and great vessels, was excised and fixed in formalin for several days. Ink-stained atrial and ventricular regions and 1 to 2 cm borders of surrounding unstained tissue were assayed for radioactivity by standard techniques. A core segment of perfused ventricular tissue was defined as the homogenously stained central portion of the posterolateral free wall (excluding the apex and papillary muscles). This core segment averaged 23 ± 3(SEM) g and was cut into 2 to 4 g subsegments, with each of the latter then divided into three transmural layers.

Myocardial flow within the core segment was calculated with the microsphere data referenced to mean circumflex electromagnetic inflow16 as follows:

\[ Q_R = Q_{EMF} \times (A_S/A_F) \times (1/W_S) \]

where \( Q_R \) = regional flow (ml·min⁻¹·g⁻¹); \( Q_{EMF} \) = mean electromagnetic circumflex inflow (ml·min⁻¹); \( A_S \) = activity of tissue sample (cpm); \( A_F \) = summed activity of all tissue analyzed (cpm); \( W_S \) = weight of tissue sample (g). Data for subsegments within the perfused core were pooled for each transmural layer.

Experimental protocols. Regional flow was initially measured with coronary pressure kept constant at the corresponding mean aortic pressure level. Mean electromagnetic flow during constant-pressure perfusion was the same as during perfusion at the same mean pressure with the normal pulsatile aortic pressure wave form. In one animal microsphere injections were performed at two control pressures (with the pressure closer to spontaneous aortic pressure used in the tabulated results).

Protocol I: nominal circumflex pressure (35 mm Hg). After the control flow measurement, coronary pressure was abruptly reduced to 35 mm Hg (range 30 to 40 mm Hg). In each animal the transient flow response was characterized by an oscillatory flow adjustment with a period of 15 sec. A new steady-state flow level was reached in 1 to 3 min, after which a second microsphere injection was given. A third microsphere injection was subsequently given at the same reduced coronary pressure during intracoronary infusion of 2 μM adenosine at 0.5 ml·min⁻¹. Calculated plasma adenosine concentrations were in excess of 40 μM.

Protocol II: nominal circumflex pressure (25 mm Hg). In five animals additional regional flow measurements were performed at a pressure of ~25 mm Hg. After protocol I had been completed and the infusion of adenosine terminated, circumflex pressure was maintained at 35 mm Hg and flow was allowed to return to the prevasodilation level. Pressure was then reduced from 35 to 25 mm Hg. Flow oscillations were not observed during these further pressure reductions. The further reductions in flow were frequently associated with ventricular premature beats, for which lidocaine was sometimes given. After several minutes, when hemodynamics had stabilized, microsphere flows were measured before and during adenosine infusion at 0.05 μM·min⁻¹.

Collateral flow measurements. Since unmeasured collateral flow might have occurred at low circumflex (and normal aortic) pressures, two animals were studied with use of systemic as well as intracoronary microsphere injections at reduced circumflex pressures. After protocol I had been completed, ~3 × 10⁶ microspheres were injected into the left atrium and a standard reference sample was collected from the femoral artery for 90 sec. During this period the circumflex artery continued to be perfused from the servovalve reservoir at 35 mm Hg, but the reservoir inflow line was temporarily occluded. Thus, microspheres entered the perfused core segment only through inter-
coronary collaterals. A second systemic microsphere injection was subsequently given with the circumflex cannula occluded (and the interarterial gradient for collateral flow therefore maximized). In regional flow calculations for the systemic injections the reference sampling technique was used.18

Data analysis. All hemodynamic data were recorded on a Gould eight-channel forced-ink recorder. Data were digitized on-line in 13 animals and hemodynamic variables were determined by averaging 8 to 10 beats during each microsphere injection. In the remaining animal, data were taken from the chart record. Statistical analysis of each variable was performed by a one-way analysis of variance at the .05 level of significance. When significant differences were present, comparisons were made with two-tailed pairwise t tests with the Bonferroni correction for repeated measurements.

Results

Aortic mean pressures immediately before regional flow measurements averaged 84 ± 3(SEM) mm Hg. Heart rate was kept constant throughout each individual experiment and averaged 61 ± 1 beats/min. Arterial blood gases at the time of regional flow measurements were pH 7.36 ± 0.01, PCO2 33 ± 1 mm Hg, and PO2 149 ± 17 mm Hg. Hematocrit was 46 ± 1% and mean arterial oxygen saturation 99 ± 1%.

The transient electromagnetic flow response to a step reduction in pressure to 35 mm Hg is illustrated in figure 1. In each animal the autoregulatory response was characterized by pronounced damped flow oscillations having a periodicity of ~15 sec. Flow initially approached zero and then frequently rose to (or even above) the control level. Steady-state data from all animals are summarized in table 1. Steady-state electromagnetic flow levels were reduced when compared with control (16 ± 2 vs 32 ± 2 ml·min⁻¹, p < .01). Mean flow increased in each animal during adenosine infusion and exceeded control values in 10 of 14 animals, averaging 43 ± 6 ml·min⁻¹ for all 14 animals (p < .05 vs control and p < .01 vs tone intact).

Steady-state electromagnetic flow responses to sequential step reductions in pressure were assessed in five animals. A representative mean pressure-flow relationship is shown in figure 2. As pressure was reduced sequentially, steady-state flow fell by ~40% despite the prominent transient flow adjustments that were observed during step pressure reduction.

Regional flows at circumflex pressure of 35 mm Hg. Regional myocardial flows in the perfused core segment are summarized for all 14 animals in table 2. Mean transmural flow fell from 0.56 ± 0.04 to 0.34 ± 0.02 ml·min⁻¹·g⁻¹ when pressure was reduced. During administration of adenosine vasodilation flow rose to 0.92 ± 0.08 ml·min⁻¹·g⁻¹. Directionally similar changes were observed in each of the three transmural layers. Figure 3 illustrates results for endocardium and epicardium in individual animals. Differences between flow with tone present and during adenosine infusion were significant at the .01 level. Thus, regional circumflex flow was reduced 40% below control when pressure was reduced to 35 mm Hg, despite the presence of a nearly threefold increase in flow during adenosine infusion.
Hemodynamics: control vs circumflex pressure ($P_{LC}$) of 35 mm Hg

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Tone</th>
<th>Vasodilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_{LC}$ (mm Hg)</td>
<td>88 ± 3</td>
<td>36 ± 1(^A)</td>
<td>35 ± 1(^A)</td>
</tr>
<tr>
<td>$Q_{LC}$ (ml min(^{-1}))</td>
<td>32 ± 3</td>
<td>16 ± 2(^A)</td>
<td>44 ± 6(^B),(^C)</td>
</tr>
<tr>
<td>$P_{LV sys}$ (mm Hg)</td>
<td>112 ± 3</td>
<td>107 ± 3</td>
<td>105 ± 3</td>
</tr>
<tr>
<td>$P_{LV end}$ (mm Hg)</td>
<td>8.4 ± 1</td>
<td>8.5 ± 1</td>
<td>8.1 ± 1</td>
</tr>
<tr>
<td>$P_{AO}$</td>
<td>84 ± 3</td>
<td>81 ± 3</td>
<td>79 ± 4</td>
</tr>
</tbody>
</table>

All values are mean ± 1 SEM.

$Q_{LC} = $ circumflex electromagnetic flow; $P_{LV sys} =$ left ventricular systolic pressure; $P_{LV end} =$ left ventricular end-diastolic pressure; $P_{AO} =$ mean aortic pressure.

\(^A\)p < .01 vs control; \(^B\)p < .05 vs control; \(^C\)p < .01 vs tone.

Adenosine vasodilation. The reduction in flow occurred on a transmural basis without significant changes in the inner-outlet (I/O) flow ratio.

Regional flows at circumflex pressure of 25 mm Hg. Except for left ventricular systolic pressure, which fell from 97 ± 1 to 91 ± 4 mm Hg (p < .05), systemic hemodynamics did not change from control or 35 mm Hg when pressure was lowered to a nominal value of 25 mm Hg. Mean electromagnetic flow was 11 ± 1 ml min\(^{-1}\) at 26 ± 1 mm Hg with tone present and increased to 17 ± 2 ml min\(^{-1}\) during adenosine infusion (while coronary pressure remained constant).

Mean full-thickness regional flow was 0.54 ± 0.05 ml min\(^{-1}\) g\(^{-1}\) under control conditions, 0.28 ± 0.03 ml min\(^{-1}\) g\(^{-1}\) with tone present at 25 mm Hg, and 0.39 ± 0.05 ml min\(^{-1}\) g\(^{-1}\) during adenosine infusion at 25 mm Hg. When pressure was reduced from 35 to 25 mm Hg, flow fell in each transmural layer, with the difference significant for the innermost two layers (p < .05). Endocardial and epicardial flows under control conditions and at 25 mm Hg are illustrated in figure 4. In four of five animals endocardial flow did not increase during adenosine infusion; the mean difference for all five animals was also not significant (p > .05). In contrast, epicardial flow increased in four of five animals; the mean increase was significant at the p < .01 level. The I/O ratio with tone present fell from 1.29 ± 0.04 at 35 mm Hg to 1.02 ± 0.12 at 25 mm Hg (p < .05). A further reduction in I/O ratio occurred during vasodilation (0.84 ± 0.08; NS). Thus, epicardial

![FIGURE 2. Steady-state mean pressure-flow relationship. The four measurements shown by the large symbols represent microsphere flow measurements obtained as described in the text. The smaller points represent flows derived from the electromagnetic flowmeter (EMF) reading and the weight of the total perfused segment. The latter was estimated by multiplying the core segment weight by the ratio of total/core radioactivity; values at 80 and 100 mm Hg were 53 and 54 g, respectively.](http://circ.ahajournals.org/)

Vol. 71, No. 2, February 1985

373
vasodilator reserve was still present at 25 mm Hg, even though the endocardium was usually maximally vasodilated.

Collateral flow measurements. Collateral flow measurements are summarized in table 3. Mean full-thickness collateral flows at a circumflex pressure of 35 mm Hg were 0.02 and 0.09 ml/min \cdot g^{-1}. These values constituted only 12% and 23%, respectively, of the measured reductions in full-thickness circumflex flow between control and 35 mm Hg. Endocardial collateral flows at 35 mm Hg were 0.02 and 0.11 ml/min \cdot g^{-1} and constituted 11% and 18% of the measured reductions in flow. During circumflex occlusion, circumflex pressures fell appreciably (to 18 and 15 mm Hg) and collateral flows were considerably higher than at 35 mm Hg.

Discussion

The results of this study indicate that coronary flow remains relatively, although not perfectly, constant as coronary pressure is initially reduced below a level of 90 mm Hg when heart rate is held constant at a relatively low rate. However, when a level of 35 mm Hg has been reached, regional myocardial perfusion is reduced by ~40% in all transmural layers despite the persistence of adenosine-recruitable vasodilator reserve. At 25 mm Hg reserve remains present, to a lesser degree, in the heart’s outer layers, but is frequently exhausted in the subendocardium. These results indicate that reductions in regional flow cannot always be taken to indicate maximal vasodilation of the distal vasculature.

The three following potential limitations of the present study require discussion:

1. Studies were conducted in open-chest anesthetized animals in which neural and neurohumoral effects no doubt differed from those in awake animals studied in the basal state. Since coronary autoregulation has not yet been studied systematically in animals in the conscious state, the influence of such effects under these conditions remains to be defined.

2. Collateral flow into the distal circumflex bed at reduced circumflex pressures would not have been included in measurements of circumflex inflow, causing regional flow to be underestimated. Earlier studies from other laboratories and our own current observations suggest that effects of collateral flow were small and insufficient to negate the conclusions that have been drawn. In 1964 Driscoll et al. reported that autoregulatory flow adjustments to changes in pressure in a cannulated canine circumflex arterial branch were similar in the presence and absence of 40 to 60 mm Hg pressure gradients between the cannulated artery and surrounding arteries. More recently, Messina et al. have studied a preparation in which the left main and circumflex arteries were perfused independently at several interarterial pressure gradients. Measurable

<table>
<thead>
<tr>
<th>TABLE 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collateral flow measurements in core segments (ml \cdot min^{-1} \cdot g^{-1})</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Mean</td>
</tr>
<tr>
<td>Mean</td>
</tr>
<tr>
<td>Endocardium</td>
</tr>
<tr>
<td>Endocardium</td>
</tr>
</tbody>
</table>

P_{LC} = circumflex pressure; IC = intracoronary.
collateral flow in the circumflex region was not present until a pressure gradient of 40 to 60 mm Hg was reached. Absolute levels of collateral flow remained less than 0.1 ml·min⁻¹·g⁻¹ until the interarterial pressure gradient exceeded 70 mm Hg. When interarterial gradients are maximized by total coronary occlusion in dogs with an undeveloped collateral circulation, collateral flow has usually been reported to be only 0.1 to 0.2 ml·min⁻¹·g⁻¹. The collateral flows measured in the present study by systemic injection of microspheres while the circumflex artery was being perfused with microsphere-free blood are similar. At a circumflex pressure of 35 mm Hg (and interarterial pressure gradient of ~45 mm Hg), the addition of mean collateral flow to measured circumflex inflow increased total circumflex perfusion by only 3% and 13%, respectively (table 3).

(3) Although oxygen extraction is near maximal at rest in the coronary circulation, small increases are possible and can potentially minimize effects of flow reductions on oxygen supply. Assuming a venous oxygen saturation during pentobarbital anesthesia of as high as 40%, a decrease to 25% during reduced pressure perfusion would have allowed a 20% reduction in flow with constant oxygen delivery. It seems unlikely that the observed reductions in regional flow (~40%) could be explained entirely by increases in oxygen extraction.

Reactivity of the coronary bed has previously been assessed in three ways. (1) The first is by evaluation of the constancy of flow within the autoregulatory range. Mosher et al.¹ found steady-state flow to vary by ~15% between pressures of ~70 and ~145 mm Hg. Others have reported greater variations within this pressure range.² ³ ⁸ ¹⁸ ¹⁹ Below 70 mm Hg more pronounced reductions in flow with pressure occur consistently. Interpretations in this lower pressure range need to consider potential effects of collateral flow as outlined above. (2) Driscoll et al.² ³ have proposed that the transient response to a step change in pressure is more representative of autoregulation. Changes in pressure in a passive or nonreactive bed are not accompanied by flow adjustments after the initial transient. In the present study, flow adjustments after step changes in pressure were prominent (figure 1). (3) The ratio of vasodilated to resting flow at systemic arterial pressure is usually greater than 4, with smaller values suggesting partial vasodilation under basal conditions. Since coronary flow during adenosine vasodilation at a heart rate of 100 beats/min has been reported to be ~5.5

---

*Messina LM: Personal communication.
sures near 40 mm Hg and found vasodilator reserve to intracoronary nitroglycerin at a time when resting flow was reduced. Gould et al. \(^8\) employed a fixed stenosis of \(\sim 90\%\) and found resting flow to be reduced 25% at a distal coronary pressure of 53 mm Hg. During vasodilation after intracoronary Hypaque injection, mean flow rose toward control levels despite a further reduction in coronary pressure to 38 mm Hg. Under similar experimental conditions, Gallagher et al. \(^9\) observed a transmural redistribution of microsphere flow from endocardium to epicardium after administration of an adenosine bolus. In the latter two studies the reductions in resting inflow before the vasodilative stimulus were interpreted to indicate that the endocardium was maximally dilated. One difficulty in such an interpretation is the decrease in distal coronary pressure that occurs during vasodilation as a result of the increased transstenotic pressure gradient. Even though endocardial flow falls in such a setting, it is unclear whether this would be the case if the distal pressure before vasodilation were maintained. The presumed exhaustion of endocardial reserve at the prevasodilation pressure is difficult to reconcile with recent microsphere measurements by Bache and Schwartz\(^{11}\) of transmural vasodilator reserve at heart rates of 120 to 130 beats/min. During adenosine infusion mean full-thickness flows averaged 2.24 ml/min\(^{-1}\)g\(^{-1}\) with an I/O ratio of 0.55 when distal coronary pressure was 40 mm Hg, and 1.11 ml/min\(^{-1}\)g\(^{-1}\) with an I/O ratio of 0.44 when distal pressure was 27 mm Hg. The higher vasodilated flows at any given pressure in this latter study probably reflect both diminished compressive effects and a stronger vasodilative stimulus, i.e., adenosine infusion. The persistent endocardial and epicardial flow reserve to a pressure as low as 35 mm Hg in the present investigation is notable, and probably reflects effects of the relatively low heart rate on both myocardial oxygen demand and supply.

Flow reductions in the face of adenosine-recruitable vasodilator reserve have also been observed in an animal preparation of a coronary “muscle bridge.”\(^{12}\) When the bridged artery was occluded during systole and a portion of diastole, resting coronary flow was reduced by 10% to 40%, but was increased above control values during adenosine infusion. In addition, Gorman and Sparks\(^{20}\) have reported adenosine-recruitable vasodilator reserve during prolonged myocardial ischemia in a preparation of stenosis in which distal coronary pressure was held constant by readjustment of the stenosis. The present study emphasizes the limitations associated with interpreting reductions in coronary flow to indicate maximal vasodilation of the distal vasculature in studies of spontaneous autoregulation and experimental ischemia.

The finding of reductions in regional myocardial flow in the face of residual vasodilator reserve is of interest in relation to clinical findings that have seemed in some respects paradoxical. Some clinical studies have reported reduced levels of resting myocardial perfusion distal to severe coronary stenoses and in collateral-dependent myocardium distal to an occluded source vessel.\(^{21-23}\) These reductions have been noted to occur in the absence of subjective or objective evidence of myocardial ischemia and are not readily attributable to myocardial necrosis. Recent human measurements of coronary pressure distal to occluded source vessels have shown mean pressures in collateral-dependent tissue of 35 mm Hg or less.\(^{24}\) The present findings are consistent with the concept of a chronic reduction in resting flow at reduced coronary pressure, with flow and oxygen supply being able to increase modestly during periods of increased demand. At relatively slow heart rates, subendocardial vasodilator reserve may conceivably persist until coronary pressure falls below 35 mm Hg.

Our findings are consistent with preliminary reports in dogs and swine from other laboratories. Aversano et al.\(^ {25}\) noted reduced endocardial flows that increased during adenosine vasodilation at circumflex pressures of 35 to 40 mm Hg in dogs. Findings by Pantley et al.\(^ {26}\) in swine were similar, showing substantial adenosine-recruitable reserve in a species in which native intercoronary collaterals are sparse. Gratton et al.\(^ {27}\) perfused the left main coronary arteries of dogs, thus minimizing collateral flow, and also reported flow reductions at reduced pressures in the presence of vasodilator reserve recruited by adenosine and chromonar. The latter study reported no level of perfusion pressure at which hypoperfusion resulted in maximal vasodilation. Data from the present study differ in that maximal endocardial vasodilation usually occurred at a coronary pressure of 25 mm Hg when epicardial reserve was still present.

Mechanisms underlying reductions in flow in the presence of vasodilator reserve remain to be elucidated. Possibilities deserving further study include reduced washout of a vasoconstrictor metabolite, altered interactions between metabolic and adrenergic vasoregulatory stimuli,\(^ {28}\) the so-called garden hose effect,\(^ {29}\) and reduced regional myocardial contractile activity (with or without concomitant regional myocardial ischemia).\(^ {25, 30}\)

The technical assistance of Mrs. Kathleen Harris, Mr. Rich-

CIRCULATION
and Kohlmeier, and Miss Amy Johnson and the secretarial assistance of Miss Kyle Doran are greatly appreciated.

References
Reduced regional myocardial perfusion in the presence of pharmacologic vasodilator reserve.

J M Canty, Jr and F J Klocke

Circulation. 1985;71:370-377
doi: 10.1161/01.CIR.71.2.370

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1985 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/71/2/370

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/