Characteristics of Reactive Hyperemia in the Canine Intestine

By Ewald E. Selkurt, Ph.D., Carl F. Rothe, Ph.D., and Daniel Richardson, B.A.

Although many studies have dealt with postocclusion ("reactive") hyperemia in skeletal muscles,1-13 and a considerable number with such hyperemia in the coronary14-16 and renal circulations,17-19 little systematic study of this phenomenon appears to have been made on the intestinal circulation. Since this vascular bed has received considerable attention in relation to intestinal ischemic shock,20-23 endotoxic,24,25 and hemorrhagic shock,26-28 a detailed study of the response of the intestinal circulation to brief periods of ischemia appeared warranted as a help in understanding better the hemodynamic changes which occur in shock.

Methods

A total of 29 mongrel dogs, anesthetized with sodium pentobarbital, 30 mg/kg iv, was used in the study. Periods of ischemia had durations of 15, 30 seconds, 1, 3, and 5 minutes. A technique employed in a previous study27 was used to measure the intestinal circulation. A loop of ileum was isolated, with freeing of the major arterial and venous vessels, and dissection away of nerve fibers. Plexiglas cannulae were placed in the intestinal lumen to permit movement of the contents through the intestine. With minimal interruption of the circulation, catheterizations of artery and vein were performed with Clay-Adams animal-tested polyethylene tubing and cannulae. Inflow blood came from a femoral artery, and outflow was led back to a reservoir connected to an external jugular vein. When flow studies were begun, heparin sodium was used as the anticoagulant (3 mg/kg priming dose and 10 mg/hr sustaining dose).

The preparation was kept moist with gauze soaked in Ringer-Locke saline and kept between 35 to 38°C by means of a heat lamp and a plexiglas table through which water at 40°C was circulated. The temperature was monitored with banjo-shaped thermistor probes.*

In the first series (I), (nine animals, average gut weight, 87 g) inflows and outflows were measured simultaneously. In three preliminary experiments, flows were measured with Shipley-Wilson rotameters, and pressures with optical manometers. In six of the animals, flows were measured with an automatic 1-ml bubble flowmeter. In three of the latter preparations, intestinal intraluminal pressure was measured from a balloon inserted in the lumen. The inflow pressure was measured proximal to the cannula with a Statham P23D pressure transducer. The venous outflow level was kept at a constant height so that the outflow pressure, also recorded by transducer, averaged ca. 10 mm Hg during the control periods. Data for these and the succeeding series were recorded on an Offner type R direct-writing oscillograph.

In series II, (eight animals, average gut weight, 84 g) only venous outflow was measured, utilizing a flow-through electromagnetic flow probe in the venous return circuit. In these, phasic weight changes of the isolated segment were recorded by the method of Johnson and Hanson.29 In this group, rapid serial hematocrit samples were taken approximately every 15 seconds following release. These were spun at 2,000 rev/min for 15 minutes in Wintrobe hematocrit tubes. Arterial occlusions lasted one, three, and five minutes in this series.

Series III (twelve animals, average gut weight, 355 g) was concerned with an attempt to test the possible role of a myogenic mechanism vs. a metabolic type of reactive hyperemia. In these, arterial inflow and venous outflow circuits were both clamped for varying periods of time (0.5, 1, 2, and 3 minutes). During occlu-

* Yellow Springs Instrument Company.
sion, dextran solution,* warmed to body temperature but unoxygenated, was injected at varying rates into the arterial inflow circuit using a power-driven syringe injector, so that arterial pressure in the segment was restored by varying degrees up to, or beyond, the initial control arterial pressure. Upon release, the degree of reactive hyperemia in the "dextran-packed" segment of gut was compared to the hyperemic response observed in the control segment clamped for equal periods of time. In this series, arterial inflow was measured using either a flow-through electromagnetic probe, or in some experiments, a wrap-around probe placed about the arterial supply branch.

Results

SERIES I
Arterial Occlusion: Effects on Simultaneous Inflow and Outflow

In total, 93 individual observations were made. The number of tests distributed to each of the several durations of arterial occlusion differed somewhat (ranging from 21 observations with 30-second occlusion to 8 observations with the 5-minute occlusion). Results were averaged for each animal for grouping of data in the figures.

A representative experiment from an animal in which intraluminal pressure was measured is illustrated in figures 1 and 2. Note that when the inflow circuit was clamped two minutes or more, venous outflow persisted for one to two minutes. When the clamp was released arterial inflow rose rapidly to about twice the control flow or greater. The peak of venous hyperemia, as recorded by the venous outflow meter, lagged behind the peak of arterial hyperemia by 10 to 15 seconds, and never reached the magnitude of arterial inflow. Integration of the area A (bottom, fig. 1) yielded the "outflow" volume; similarly, area B was integrated to yield an estimate of "inflow" volume. "Outflow" volume is taken as the volume of blood yielded by passive collapse of the vessels of the segment after occlusion of arterial inflow. "Inflow" volume is an estimate of the refilling volume following restitution of flow; it represents the excess of arterial flow over simultaneous venous outflow.

The tracing of figure 1 shows intraluminal pressure and gut motility. The motility increased during ischemia, with a rise of intraluminal pressure which became more prominent with greater duration of ischemia. These initial contractions subsided, to give way to a second phase of activity following the peak of the hyperemia. The changes of motility are reflected in the venous pressure (second tracing), and they influenced also the arterial inflow and venous outflow. This is indicated by retardation of flow, especially following the longer bouts of ischemia, with a slight tendency for the outflow to exceed the inflow during the initial portion of the phase of enhanced motility.

The average trends are summarized in figures 3 and 4, which include calculations of intestinal vascular resistance (P/F) during hyperemia and include calculations based on both venous (dotted line) and arterial (solid line) flows. Note that both the arterial and the venous flow patterns during reactive hyperemia were phasic in character. The curves show two peaks, especially noticeable following the two-, three-, and five-minute periods of ischemia. The heights of the initial flow peaks were constant, irrespective of the duration of blockade. Increase in total volume of blood supplied during reactive hyperemias after progressively longer occlusions was, therefore, brought about by broadening of the initial flow peaks and by greater prominence of the second phase of flow increase.

In figure 5 the data are plotted to show relations between the magnitude and duration of reactive hyperemic flow (RHF). The data here are based only on arterial flow measurements, and are calculated as that portion of the arterial hyperemic flow which was in excess of the control average flow. RHF

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* Dextran was prepared by the Cutter Laboratories. This was a 6% solution in saline (Na and Cl, 154 mEq/liter, respectively). The molecular weight of the median fraction ranged from 60,000 to 90,000. Intrinsich viscosity (ηsp) ranged from 0.220 to 0.290. Relative viscosity (ηrel) for the 6% solution would be approximately 3.8 at 37°C.

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was highest (as the average per minute) after the shorter periods of ischemia (panel A). The duration of RHF (B) rose linearly with the duration of ischemia but exhibited variability following the three- and five-minute occlusions. Total arterial RHF (panel C) showed a similar progressive increase through two minutes of occlusion, but then also became more variable after the three-minute and five-minute occlusion periods.

The bottom panel shows the percentage repayment by RHF of the arterial flow deficit during occlusion. This was greatest (58%) after occlusions lasting fifteen seconds and least (13%) after those lasting five minutes.

Table 1 compares calculated outflow or emptying volumes (A) and inflow or filling volumes (B). In the first comparison, volume B was calculated for a period of approximately 20 seconds after release of the clamp. Another comparison was made to include an average of 56 seconds after release. These comparisons are designated as phases a and b, respectively, of volume B (column 5) of table 1.

**FIGURE 1**
Representative experiment showing effects of occluding arterial inflow on simultaneous arterial and venous flow in isolated ileum. Top tracing: intestinal intraluminal pressure. Second: venous pressure. Third: arterial perfusion pressure. Fourth: solid line, arterial flow; dashed line, venous. Area A represents continued emptying by venous drainage during arterial occlusion. Area B is taken as the "filling volume" (arterial inflow in excess of venous outflow).

**SERIES II**
Arterial Occlusion: Effects on Venous Outflow and Phasic Changes of Tissue Weight

The previous series did not allow final conclusions bearing on the possibility of change in volume of blood vessels or of tissue occurring during the phase of reactive hyperemia. For this reason, a sensitive weight recording device was employed in this series. Figure 6 indicates that a phase of weight increase does in fact occur in association with the phase of increased (venous) blood flow following release of the arterial inflow clamp. The average peak increase of weight was 1.8, 1.3, and 2.3% following one-, three-, and five-minute periods of ischemia. Durations of weight increases were 4, 5, and 6.5 minutes, respectively.

In order to determine what fraction of the weight increase was the result of increase in local blood volume, and how much resulted from increased formation and volume of interstitial fluid, rapid serial hematocrit determinations were made on venous effluent blood, and averaged in relation to the weight changes. Figure 6 shows that the hematocrit
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FIGURE 2

Same experiment as in figure 1, showing effects of three- and five-minute periods of ischemia.

ratio decreased during occlusion (return of interstitial fluid into the capillaries when hydrostatic filtering pressure was lowered). After release of occlusion, a phase of increased hematocrit was observed in each instance, signifying enhanced capillary filtration. The phasic changes of hematocrit ratio were applied to the integrated volume of flow during hyperemia, based on the premise that the increase of hematocrit value resulted

TABLE 1

Comparison of Emptying Volume (during occlusion) with Refilling (after release) with Varying Durations of Ischemia

<table>
<thead>
<tr>
<th>Duration of occlusion</th>
<th>N *</th>
<th>Emptying vol (volume A) Avg ± SE ml/100 g</th>
<th>Time after release</th>
<th>Filling vol § (volume B) Avg ± SE ml/100 g</th>
<th>Ratio: Emptying vol (A) Emptying vol (B) Avg ± SE</th>
<th>P</th>
<th>Ratio: Filling vol (A) Emptying vol (B) Avg (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 min</td>
<td>11</td>
<td>4.4 ± 0.4</td>
<td>18 (11-22)</td>
<td>3.1 ± 0.2</td>
<td>0.71 (0.55-0.82)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>40 (15-60)</td>
<td>4.5 ± 0.9</td>
<td>0.99 (0.70-1.41)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>0.50 min</td>
<td>21</td>
<td>5.1 ± 0.5</td>
<td>16 (10-30)</td>
<td>4.1 ± 0.4</td>
<td>0.82 (0.68-0.98)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>49 (22-60)</td>
<td>4.7 ± 0.5</td>
<td>0.91 (0.57-1.14)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>1.0 min</td>
<td>20</td>
<td>7.3 ± 0.6</td>
<td>19 (12-28)</td>
<td>6.2 ± 0.5</td>
<td>0.86 (0.72-1.00)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>57 (40-60)</td>
<td>6.7 ± 0.8</td>
<td>0.94 (0.72-1.12)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>2.0 min</td>
<td>18</td>
<td>7.1 ± 0.6</td>
<td>24 (11-38)</td>
<td>6.0 ± 0.5</td>
<td>0.87 (0.77-1.14)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>53 (22-60)</td>
<td>7.3 ± 0.6</td>
<td>1.04 (0.77-1.32)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>3.0 min</td>
<td>15</td>
<td>7.4 ± 0.6</td>
<td>21 (11-30)</td>
<td>6.4 ± 0.6</td>
<td>0.86 (0.74-1.02)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>60 —</td>
<td>7.1 ± 0.8</td>
<td>0.94 (0.71-1.29)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>5.0 min</td>
<td>8</td>
<td>8.0 ± 1.6</td>
<td>21 (15-30)</td>
<td>7.5 ± 1.4</td>
<td>0.96 (0.83-1.28)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>60 —</td>
<td>8.1 ± 1.3</td>
<td>1.08 (0.75-1.70)</td>
<td>0.05</td>
<td></td>
</tr>
</tbody>
</table>

* Number of observations.
† Calculated as the average venous outflow period of arterial occlusion.
‡ First reading (a) taken at end of phase B (fig. 1); second (b) at end of phase of reactive hyperemia, or arbitrarily at 60 seconds, if hyperemia was longer than one minute.
§ Calculated as difference between arterial and venous flow.

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from enhanced filtration of fluid into the interstitium. By difference from the total weight change, the actual volume of the filtrate could be quantitated and, by difference, the increase in blood volume determined. A typical calculation is shown in Table 2 for ischemia lasting one minute.

Returning to figure 6, the peak increase in volume (or weight in g/100 g of tissue) averaged 1.6, 1.0, and 1.8 ml, respectively, for occlusions of one, three, and five minutes. The average increases of blood volume for the duration of the hyperemic response (shaded areas at bottom of fig. 6) were 0.82 ml for two minutes, 0.78 ml for three minutes, and 0.92 ml for four minutes following the one-, three-, and five-minute periods of ischemia. The increases have greater signifi-

**TABLE 2**

<table>
<thead>
<tr>
<th>Illustrative Summary of Method of Calculation from Data of a One-Minute Period of Ischemia</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Control</th>
<th>Postocclusion</th>
<th>Seconds after release of occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>Flow, ml/min/100 g</td>
<td>39</td>
<td>64</td>
</tr>
<tr>
<td>Wt change, %</td>
<td>-</td>
<td>-0.15</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>0.484</td>
<td>0.455</td>
</tr>
<tr>
<td>Vol of efflux</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cumulative vol of efflux</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Wt inc. due to blood</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* Volume of efflux = flow/sec × (hemat_{esp} - hemat_{post}) × t (seconds).
† Wt increase due to blood = total wt increase (g) - cumulative vol of efflux (1 ml = 1 g).

*Downloaded from http://circres.ahajournals.org/ by guest on July 10, 2017*
cance when considered in terms of the blood volume of the intestine. Taking the figure of 12% established by P. C. Johnson (personal communication) for average volume of blood in the intestine, these figures represent peak increases ranging from 8 to 15% for blood volume, and a range of 6.5 to 8% for the integrated increases in blood volume.

The peak of the volume increase during hyperemia came considerably after the peak of the venous flow during the same phase of hyperemia (22, 38, and 60 seconds, respectively). This lag supports the possibility that increase in volume of the capacitance vessels accounts in major degree for the observed small increase of the volume of blood in the segment of intestine under study.

SERIES III

Effect on Postocclusion Flow of Restoring Arterial Pressure During Intestinal Ischemia

Figure 7 compares the hyperemia which follows arterial occlusion only (control A) with the hyperemia which follows simultaneous occlusion of both artery and vein (control B). The hyperemia after simple arterial occlusion was greater than that after arterial and venous occlusion probably because of drainage of erythrocytes during A, whereas during B, erythrocytes were retained in the segment because of venous occlusion. These erythrocytes supplied a greater oxygen reserve for utilization during the period of ischemia.

Following control B, dextran solution was infused intra-arterially throughout the 0.5- and one-minute occlusion periods, but only during the final minute of the two- and three-minute clampings. Fixed volumes of 4, 9.5, 18, and 38 ml of dextran solution were given (columns 1, 2, 3, and 4, fig. 7), averaging 1.3, 2.7, 5.1, and 11 ml/100 g of intestine. With the larger injection volumes, pressure was restored approximately to the control range (column 3), or exceeded it (column 4). Despite this, the hyperemic response was not significantly reduced below control; to the contrary, in most cases, the hyperemia observed after filling the blood vessels with dextran tended to exceed the hyperemia of control B in which the blood vessels were filled with blood.
Reactive hyperemia blood flow (RHF) in panel A, duration in panel B, and total RHF in panel C. Panel D gives per cent of repayment of the blood flow debt which was produced by the period of ischemia. Equations for the regression lines for each set of data appear in the respective panels. All four sets of data have a significant regression with respect to duration of occlusion. The data were tested for deviation from linear regression (Snedecor, G. W., Statistical Methods, ed. 5, Ames, Iowa State University Press. 1956, pp. 455-57) and were found to be highly significant for the three- and five-minute points in panels B and C. Therefore, the regression equations presented in the figure were fitted over the 0.25- through two-minute periods only and extrapolated (dashed line) to five minutes.

Discussion

In the intestine, a phasic type of reactive hyperemia was commonly observed. The total response included an initial peak, a decline, and a secondary peak seen most often after the three- and five-minute periods of occlusion. A portion of the initial peak of arterial inflow during reactive hyperemia must be related to the filling of vessels partially drained by continued venous outflow during the prior arterial occlusion. The finding, that the initial peak of venous outflow was considerably lower than the peak arterial flow, favored this explanation. Following the initial peak, increased intestinal motility and intraluminal pressure affected the circulation by depressing flow after the initial rise. Flow then tended to increase again as the intensity of intestinal motility subsided. Sidky and Bean have shown clearly that contraction

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of intestinal smooth muscle reduces arterial inflow and tends simultaneously to increase venous outflow, by milking action on the venous channels. Such a mechanism is very evident in figures 1 to 4.

A comparison between the calculated "outflow (emptying) volume" (area A) and the "inflow (filling) volume" (area B) appears in table 1. In the present series, inflow volume averaged 85% of volume A (range, 72 to 96%) during the approximate time interval of 20 seconds (range, 18 to 24 seconds) during which the arterial inflow clearly exceeded the venous flow. This obtained up to, or slightly beyond, the peak of the venous hyperemic responses. However, over an average time of 56 seconds after release, volume B averaged 98% of volume A (range, 91 to 108%). This could imply that the incomplete inflow volume observed at 20 seconds, when the arterial hyperemia was maximal, was caused by a rapid increase in caliber of resistance vessels, with greater lag in refilling of the capacitance vessels. This might result from dilatation of preferential low-resistance "thoroughfare channels" (nonmetabolic or bypass flow), accounting for the early phase of hyperemia, with more gradual filling of other vascular circuits.

The observation (table 1) that the calculated refilling volumes after release did not systematically exceed the emptying volumes at any time during the hyperemia argued against any large increase in volume of the several segments of the intestinal vasculature (resistance, exchange, or capacitance). Thus, although it was hoped by this method to detect gross changes in volume of the capac-
FIGURE 7
Experiments in which warmed, unoxygenated dextran solution was infused into the arterial segment during combined arterial and venous occlusion. Injection was preceded by control arterial ischemia alone (A), followed by a combined arterial and venous occlusion (B) prior to dextran infusion. The volume of hyperemic flow (average increase x duration) is on the ordinate, and the per cent of restoration of control pressure by progressive increments of injection volume, appears on the abscissa. Columns 1, 2, 3, and 4 represent successive increments of 4, 9.5, 18, and 39 ml in the volume injected. Injection was made throughout the 0.5- and 1-minute occlusions, but only during the final minute of the two- and three-minute occlusions. Data represent means and SE of twelve experiments, with an average of seven experimental observations entering into the mean of each group.

<table>
<thead>
<tr>
<th>Volume (ml)</th>
<th>0.5 Minute</th>
<th>1 Minute</th>
<th>2 Minutes</th>
<th>3 Minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>B</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0.5</td>
<td>1.0</td>
<td>1.5</td>
</tr>
</tbody>
</table>

The experiments in which dextran solution was used to expand the vessels during occlusion appeared to rule out the myogenic re-
response as an important factor in postocclusion hyperemia, because restoration of arterial intramural pressure during occlusion did not obliterate the hyperemia. The occurrence of blood flows which were greater than those during control hyperemias may have resulted in part from reduction in viscosity of the blood in the clamped segment by the dextran solution. Serial hematocrit determinations of the venous effluent made in several experiments indicated the possible contribution of this factor especially when larger volumes (18 and 38 ml) were injected. A typical experiment showed a reduction of venous hematocrit from 57 to 48% with injection of 18 ml of dextran, and from 58 to 36% with 38 ml (gut weight, 278 g).

Distention of the vessels of the occluded limb with red blood cells during occlusion has been reported to diminish the subsequent reactive hyperemia. We have hesitated to employ this procedure in the intestine because of the probability that supplying additional oxygen with the added cells might attenuate or even abolish a hyperemia of metabolic origin. The present experiments with dextran do not rule out entirely the participation of a myogenic response in a minor degree, however. The spread of the data is such that minor contributions of a myogenic response type would not be detectable by this method of analysis, though a major role seems unlikely.

The characteristics of the intestinal RHF as shown in figure 5 are such that the total RHF (panel C) increases linearly with the duration of ischemia up to two minutes; then irregularities develop, with flows higher and lower than the expected trend at three and five minutes, respectively. In the coronary circulation, following occlusions beyond 90 seconds, a tendency to reach a plateau of maximal RHF for the coronary arterial supply is indicated in the work of Coffman and Gregg. Katz and Linder, studying reactive hyperemia in the isolated fibrillating dog heart, found that the increase of reactive hyperemia correlated only slightly, and that the duration of reactive hyperemia increased very little, with increasing periods of total ischemia. In skeletal muscle (human forearm and calf), Eichna and Wilkins found that reactive hyperemia was only slightly increased by prolonging the period of ischemia from five, to ten or fifteen minutes.

With respect to repayment of flow deficit by RHF, Coffman and Gregg found that in the beating canine heart, this was grossly "overpaid" (average of ca. 200%), whereas in the fibrillating heart, the repayment averaged only 60%. The reports on skeletal muscle differ considerably. Although Freeman, and Yonce and Hamilton found approximately equal repayment, others found considerable variation (50% to 150-200%). and Wood et al. found generally that RHF overpaid the ischemic debt. In the human digit (mostly skin), repayment averaged 51%, while the dog paw (skin) showed no reactive hyperemia. In the intestine, as revealed by the present study, the repayment of deficit of flow averaged only about 35%. This was greatest (58%) after fifteen seconds of occlusion, decreasing to 13% after five minutes of occlusion (fig. 5).

It should be emphasized, however, that this classical approach to the consideration of repayment of flow deficit by reactive hyperemia may not be too useful in metabolic considerations. The work of Blair et al. in the human forearm emphasizes this point. They demonstrated that after five minutes of ischemia, controlled re-entry of blood at the preocclusion flow rate was enough to abolish reactive hyperemia, i. e., the "overshoot" was not necessary for repayment of debt. There are better studies which examine the total oxygen debt, and its subsequent repayment as was done in skeletal muscle by Abramson et al., Yonce and Hamilton, and Crawford et al., and in the heart by Coffman and Gregg.

This has not been studied systematically in the intestine, but based upon available data from this laboratory, an estimate of re-
payment of O$_2$ debt can readily be made.* This calculation shows that even after the five-minute period of ischemia, when flow repayment is only 13%, this flow plus the baseline flow is more than adequate to repay the oxygen debt of the intestine with its rather low requirement of 0.82 ml of O$_2$/100 g of tissue/min. 30

The cause of reactive hyperemia in skeletal muscle has been attributed classically to the production and accumulation of vasoactive metabolites, for which considerable cogent evidence exists. 2' 6 30 Despite much speculation, final identification of such substances has not been accomplished for skeletal muscle. However, for other tissues, strong evidence has been brought forward that the polypeptide bradykinin plays an important role in the production of hyperemia in the salivary glands, 87 and that adenine nucleotide derivatives play an important role in the coronary circulation. 38

For the intestine, evidence also favors participation of a humoral substance(s). 20, 23, 28, 80 The studies of Kobold and Thai 23 point strongly to the importance of a polypeptide resembling kallikrein as an important dilator substance. Serotonin 20-23 and possibly histamine may also play a role.

That the myogenic response of Bayliss 40 may be involved to some extent in the postocclusion response of muscle has been put forward by Folkow, 6 and supported by others. 5, 8, 9, 11, 12 According to this concept, the lowered arterial pressure during occlusion triggers the myogenic response, which then becomes evident upon release. The dextran packing experiments of the present study appear to rule out this mechanism as a major factor in the response of the isolated perfused intestine.

**Summary**

The isolated ileum of the dog shows a characteristic hyperemia following brief periods of arterial occlusion. The magnitude of this reactive hyperemia depends more upon prolongation of flow related to duration of ischemia, than upon increases of maximal or peak blood flow. Repayment of flow deficit, by the added flow of reactive hyperemia, averaged only 35% in the intestine, far below that found by others in skeletal muscle and in the coronary circulation. Nevertheless, estimates of oxygen debt indicated that this debt was overpaid, even after five minutes of ischemia.

A small but consistent increase in weight of the isolated segment was observed during the postocclusion phase. It was found that this weight increase was due largely to increase of the volume of blood in the ileum. The peak of the volume increment appeared slightly later than the peak of flow increase, and for this reason was ascribed to increase in volume of the capacity vessels.

In an attempt to assess the respective roles of myogenic vs. metabolic mechanisms in causation of reactive hyperemia, arterial pressure was restored during occlusion by injecting dextran solution into the arterial segment. Pressures in excess of control values did not abolish the hyperemic response. It was concluded that the reactive hyperemia observed in the ileum was chiefly metabolic in origin.
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