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Intestinal Blood Flow and Oxygen Consumption (41706)

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Abstract. In this study, we examined the effects of both pharmacologically and mechanically induced increases in intestinal blood flow on intestinal oxygen consumption. Intraarterial infusions of prostacyclin (1–20 $ng \cdot kg^{-1} \cdot min^{-1}$) significantly increased both blood flow and oxygen consumption under free flow conditions. However, the increase in oxygen consumption appears to be due to the corresponding increase in blood flow rather than a direct effect of prostacyclin on intestinal metabolism. This conclusion is supported by the finding that a mechanically induced increase in intestinal blood flow (60%) can also produce an increase in intestinal oxygen consumption (24%). These findings support the hypothesis that intestinal oxygen consumption is flow-dependent over a wide range of blood flows.

In a previous paper (1) we proposed that the intestinal circulation could be considered to consist of two components. In one component, which we termed the flow-independent component, oxygen delivery exceeds oxygen demand and oxygen consumption is independent of blood flow. In the second or flow-dependent component, oxygen delivery is not sufficient to meet demand so that the rate of tissue metabolism is below that of the flow-independent component.

It would appear that the majority of intestinal tissue falls within the flow-independent component as the resting arterial–venous oxygen content (AVO_2) difference is low and increased metabolic demand is met primarily by an increase in oxygen extraction (2, 3). In order to demonstrate the existence of the flow-dependent component of the intestinal circulation, it must be shown that an increase in intestinal blood flow alone can increase intestinal oxygen consumption. In this study we examined the effects of the vasodilator prostacyclin (PGI_2) on intestinal blood flow and oxygen consumption as well as the effects of mechanically induced increases in intestinal blood flow on intestinal oxygen consumption.

Methods and Materials. Fasted mongrel dogs of either sex (15–25 kg) were anesthetized with sodium pentobarbital (30 mg/kg) and ventilated with a positive pressure respirator. A femoral artery was cannulated with a saline-filled catheter which was attached to a force transducer (Hewlett–Packard) and systemic arterial pressure was recorded continuously on a direct-writing oscillograph (Hewlett–Packard). A midline laparotomy was performed and a loop of the small intestine which was perfused by a single artery and drained by a single vein was exteriorized.

Following the administration of heparin (10,000 units, iv), the artery perfusing the segment was cannulated with a polyethylene cannula which was connected to a catheter in the animal's femoral artery. By changing the location of clamps along the perfusion line, it was possible to perfuse the segment either at systemic arterial blood pressure or by means of a variable speed pump. The vein draining the segment was cannulated and the venous outflow was directed to a reservoir (200 ml of 6% dextran in normal saline). The contents of the reservoir were returned to the animal by way of a splenic vein at a rate equal to the venous outflow. The segment was then isolated by tying and cutting each end of the segment and by cutting the mesentery.

A portion of the venous outflow and an equal volume of arterial blood were pumped through the appropriate cuvettes of an arterial–venous oxygen content analyzer (AVOX Systems) and the output was recorded continuously (4). Blood flow to the intestinal segment was determined by measuring venous outflow with a graduated cylinder and stopwatch. Oxygen consumption was calculated as the product of blood flow and the AVO_2 difference.

Three series of experiments were performed. In the first series of experiments ($N = 9$), the effects of PGI_2 on intestinal blood flow and oxygen consumption were determined in seg-

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ments which were perfused at systemic arterial pressure. Prostacyclin was infused intraarterially (1–20 ng·kg^{-1}·min^{-1}) at a rate which did not directly alter intestinal blood flow (0.04–0.8 ml·min^{-1}). As the vascular sensitivity of the individual segments to PGI_2 varied, the initial dose was set as that dose which produced a 20% increase in intestinal blood flow. The dose–response curve was then generated by a successive doubling of the dose until either two doses produced the same blood flow or until systemic arterial blood pressure decreased 10 mm Hg.

In the second series ($N = 5$), the effects of PGI_2 on intestinal vascular resistance and oxygen consumption were determined under constant flow conditions. Control blood flow was set by altering pump speed until perfusion pressure was equal to systemic arterial pressure. Perfusion pressure was measured just proximal to the arterial cannula with a saline-filled polyethylene cannula attached to a force transducer (Hewlett–Packard). Perfusion pressure was monitored continuously and used to calculate intestinal vascular resistance. Once control blood flow had been established, PGI_2 (1–10 ng·kg^{-1}·min^{-1}) was infused into the perfusion line proximal to the pump and its effects on perfusion pressure and AVO_2 were determined.

In the third series of experiments ($N = 5$), we examined the relationships among intestinal oxygen consumption, venous pressure, and blood flow when either blood flow or venous pressure were increased mechanically. Venous pressure was measured by means of a catheter in the venous outflow cannula. Control blood flow was established in the same manner as that used in Series 2.

After blood flow, AVO_2 difference and venous pressure had reached a steady state, flow was increased to a level 60% greater than control by increasing pump speed. Blood flow was maintained at this level until a new steady state had been established, whereupon, pump speed was decreased to return blood flow to the control level. After control blood flow had been reestablished, venous pressure and AVO_2 difference were determined and any animals in which these variables differed from control by more than 10% were rejected. Venous pressure was then increased to a level equal to or greater than that observed during the mechanically induced hyperemia by elevating the tip of the venous outflow cannula. Venous pressure was maintained at the new level until the intestinal AVO_2 difference had reached a new steady state.

In all series, the differences between treatments were taken as the differences between the appropriate steady state values. Blood flow and oxygen consumption were expressed as milliliters per minute per 100 g and resistance was expressed in PRU (mm Hg·ml^{-1}·min·100 g). AVO_2 difference was expressed as milliliters of oxygen per 100 ml blood. The data were analyzed using a two-way analysis of variance and differences between treatment levels were determined using Duncan's range test (5). Linear regressions were conducted using the method of least-squares. The level of significance was set at $P < 0.05$.

Results. In Series 1, resting blood flow and AVO_2 differences were 44.5 ± 3.9 ml·min^{-1}·100 g^{-1} and 4.5 ± 0.3 ml oxygen·100 ml^{-1} blood, respectively, yielding an oxygen consumption of 1.94 ± 0.15 ml·min^{-1}·100 g^{-1}. Mean vascular resistance in these segments was 2.82 ± 0.41 PRU. The intraarterial infusion of prostacyclin produced an increase in both intestinal blood flow and oxygen consumption. The mean maximum blood flow achieved in this series in response to PGI_2 infusion was 85.8 ± 7.3 ml·min^{-1}·100 g^{-1} (+98.7 ± 19.8%), and the mean oxygen consumption at that level of blood flow was 2.37 ± 0.19 ml·min^{-1}·100 g^{-1} (+25.7 ± 5.7%), which was significantly greater than control oxygen consumption.

This increase in intestinal oxygen consumption with increasing intestinal blood flow could be due to either a direct metabolic effect of PGI_2 or to an increase in blood flow through a flow-independent component of the intestinal circulation. If PGI_2 were stimulating intestinal metabolism, then one would expect a positive correlation between intestinal oxygen consumption and the increase in blood PGI_2 levels. However, there was no such correlation, although there was a significant correlation ($P < 0.05$) between intestinal blood flow and the change in blood PGI_2 levels. Furthermore, there is a significant positive correlation ($P < 0.05$) between intestinal oxygen consumption and intestinal blood flow (Fig. 1).

Further evidence that PGI_2 does not have

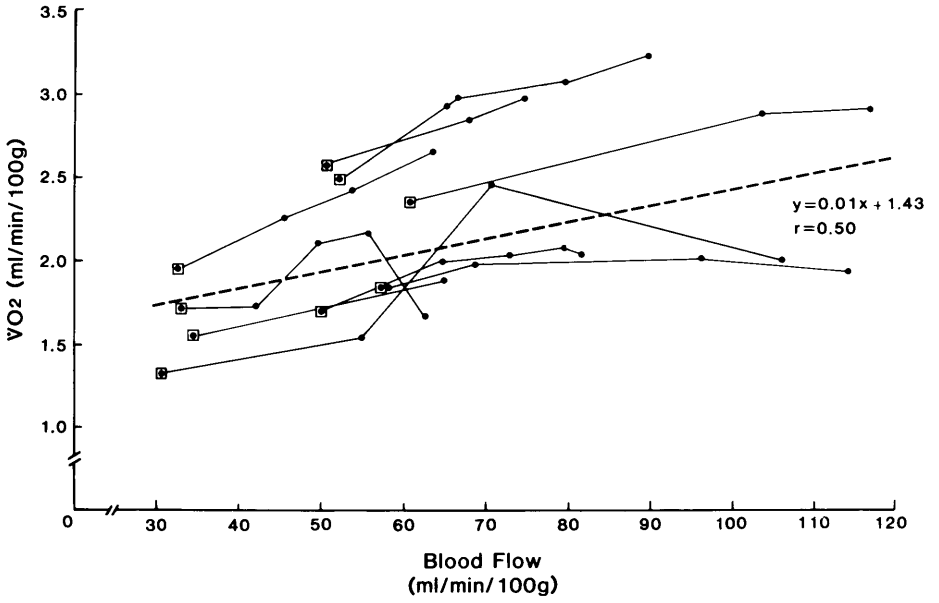

FIG. 1. The relationship between oxygen consumption ($\dot{V}O_2$) and blood flow in the small intestine as blood flow is increased by means of intraarterial infusion of prostacyclin. Solid lines represent the responses in individual animals; ⊡, control values. The dashed line is the plot of the linear regression equation.

a direct effect on intestinal metabolism is provided by Series 2. In this series, control blood flow was 40.8 ± 6.3 ml · min^{-1} · 100 g^{-1}, control AVO_2 difference was 4.8 ± 0.3 ml oxygen · 100 ml^{-1} blood, control oxygen consumption was 1.94 ± 0.24 ml · min^{-1} · 100 g^{-1} and control resistance was 3.80 ± 0.47 PRU. As seen in Fig. 2, although intraarterial PGI_2 significantly reduced intestinal vascular resistance at all doses studies, it had no significant effect on oxygen consumption when blood flow was held constant. The maximum increase in PGI_2 blood levels produced in this series (14.7 ± 1.1 ng · ml^{-1}) was three times that seen in Series 1. These findings lend further support to the conclusion that the increase

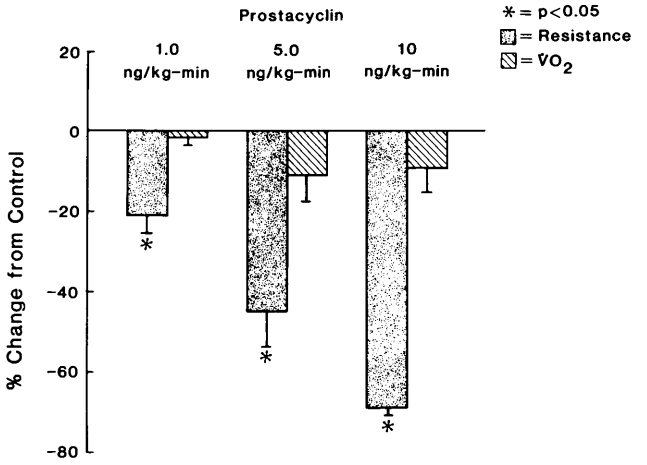

FIG. 2. The effects of intraarterial infusions of prostacyclin (PGI_2) on intestinal resistance and oxygen consumption ($\dot{V}O_2$) under constant flow conditions.

in oxygen consumption in Series 1 was due to the PGI_2-induced hyperemia rather than a direct effect of PGI_2 on intestinal metabolism.

We have previously reported that a mechanically induced increase in intestinal blood flow results in an increase in oxygen consumption; indicating that an increase in blood flow per se could produce an increase in oxygen consumption (1). It has been suggested that this method of increasing blood flow might also increase venous pressure, an event which itself has been shown to increase intestinal oxygen consumption. Therefore, in Series 3, we examined the effects of mechanically induced increases in either blood flow or venous pressure on intestinal oxygen consumption.

Control blood flow, AVO_2 difference, oxygen consumption and venous pressure are shown in Table 1; control vascular resistance was 3.78 ± 0.42 PRU. As seen in Table 1, a 60% increase in blood flow resulted in a significant increase in intestinal oxygen consumption (+0.37 ± 0.07 ml · min^{-1} · 100 g^{-1}) and a slight, but significant increase in venous pressure (1.3 ± 0.2 mm Hg). When blood flow was returned to control levels and venous pressure was elevated to a level equal to or greater than that seen during the mechanically induced hyperemia, intestinal oxygen consumption was not significantly different from control (Table 1). Thus, the increase in intestinal oxygen consumption induced by mechanically increasing blood flow was not due to the corresponding increase in intestinal venous pressure.

Discussion. The data from this study indicate that an increase in intestinal blood flow, whether pharmacologically or mechanically induced, can produce an increase in intestinal oxygen consumption. In the case of the PGI_2-induced hyperemia, it appears that the increase in oxygen consumption is not due to a direct effect of PGI_2 on intestinal metabolism as oxygen consumption did not correlate with PGI_2 blood levels. Furthermore, PGI_2 had no affect on intestinal oxygen consumption when blood flow was held constant, even at blood levels which were three times those seen under free flow conditions.

As seen in Fig. 1, the correlation coefficient for the relationship between oxygen consumption and blood flow, although significant, is rather low (r = 0.50). One factor which contributes to this low correlation is the variation in control levels of blood flow and oxygen consumption among the animals. If this relationship is examined within each animal, the mean correlation coefficient is 0.83 ± 0.09 and the mean slope is 0.012 ± 0.002 (N = 8). This would indicate that although resting blood flow and oxygen consumption do not show a consistant relationship, changes in blood flow produce a fairly consistent change in oxygen consumption within the individual animals.

The data from this study support the hypothesis that a portion of the intestinal circulation is flow-dependent with respect to oxygen consumption over a wide range of blood flows, although this may not be the case at very high rates of flow (80 ml · min^{-1} · 100 g^{-1}; Fig. 1). Similar data have been reported by Shepherd *et al.* (6) in segments in which blood flow was increased by increasing the pressure in a perfusion reservoir. Kvietys and Granger (7), however, reported a similar relationship between blood flow and oxygen uptake in the small intestine only when flow was relatively low (<30 ml · min^{-1} · 100 g^{-1}). At higher levels

TABLE I. THE EFFECTS OF INCREASED BLOOD FLOW AND VENOUS PRESSURE ON INTESTINAL OXYGEN CONSUMPTION AND AVO_2 DIFFERENCE

	Control	Increased blood flow	Increased venous pressure
Blood flow[a] (ml · min^{-1} · 100 g^{-1})	34.1 ± 5.1	54.6 ± 8.2[b]	34.1 ± 5.1
AVO_2 difference[a] (ml · 100 ml^{-1})	4.5 ± 0.4	3.4 ± 0.3[b]	4.3 ± 0.3
Oxygen consumption[a] (ml · min^{-1} · 100 g^{-1})	1.50 ± 0.24	1.87 ± 0.31[b]	1.44 ± 0.22
Venous pressure[a] (mm Hg)	4.6 ± 0.7	5.9 ± 0.9[b]	7.4 ± 1.0[b]

[a] All values are means ± SEM.
[b] $P < 0.05$ relative to control.

of blood flow the authors found intestinal oxygen uptake to be independent of blood flow.

A similar disparity in results has been reported in skeletal muscle by Duran and Renkin (8). In experiments conducted within their laboratory using a common preparation they found two populations of skeletal muscle—one in which oxygen consumption was flow-independent and one in which oxygen consumption was flow-dependent. The reasons for the different relationships between oxygen consumption and blood flow in either skeletal muscle or the intestine is not clear.

It is not possible to determine either the extent or location of the flow-dependent component of the intestinal circulation, nor is it certain that these areas are anatomically fixed. It may be that they are generated by transient decreases in blood flow as a part of a normal cycle of vascular autoregulation. In our preparations, it appears that there is still a portion of the circulation in which oxygen consumption can be described as flow-dependent even at fairly high values of blood flow. As a consequence small changes in oxygen consumption associated with comparatively larger changes in blood flow do not necessarily indicate a direct metabolic effect of the agent under study. It seems useful in such cases to study the direct effects of the agent in question on oxygen consumption under constant flow conditions.

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