Effect of Venous Pressure on Mean Capillary Pressure and Vascular Resistance in the Intestine

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It is well known that capillary pressure depends to a considerable degree upon venous pressure. Bayliss and Starling pointed out the importance of this relationship in 1894, but few studies have dealt with its quantitative aspects. Krogh et al. found that capillary filtration in the human forearm was influenced greatly by venous pressure, although changes of the latter were quantitatively less effective than an equivalent change of plasma colloid osmotic pressure. Pappenheimer and Soto-Rivera observed with the gravimetric technique applied to the hind limbs of dogs and cats that a pressure change applied from the venous side appeared to be five to ten times more effective in changing capillary pressure than was a similar change of pressure when applied from the arterial side. It appears from their data that approximately 80% of a venous pressure increment is transmitted to the capillaries. In studies of capillary filtration in skin and muscle it is generally assumed that the figure of 80% applies. Folkow et al. have assumed that 85% of the venous pressure increment is transmitted to the capillaries in the intestine.

The purpose of the present study was to examine the quantitative relationship between venous and capillary pressures in the dog intestine. For this purpose we utilized a modified isogravimetric technique. The results indicate that changes of venous pressure are not transmitted to the intestinal capillaries to the same extent as appears to be the case in the hind limb. Changes of arterial and venous resistance appear to be responsible for this attenuation.

Methods

The relationship between venous and capillary pressure was examined by means of two types of experiments. In the first series, mean capillary pressure was determined by the isogravimetric technique and the effects of altered venous pressure on mean capillary pressure, arterial and venous resistance were determined. In the second series, a pipette was placed in a small vein and the resistance of a segment of the venous vasculature was determined as a function of venous pressure.

A. Determination of Mean Capillary Pressure

Fifteen dogs anesthetized with sodium pentobarbital (30 mg/kg iv) were used in this study. A loop of intestine was completely isolated, covered with moist gauze and plastic film, and suspended from a recording beam balance. Blood was supplied to the intestinal loop from the femoral artery by way of polyethylene tubing. A plexiglas T connector was used for recording arterial pressure. The venous circuit was made of one-fourth inch silicone tubing with side branches for pressure measurement and for an orifice flowmeter. The exit orifice of the venous tubing was mounted above a reservoir connected to the jugular vein. Arterial and venous pressures were measured from side branches of the appropriate circuits with strain gauge transducers. Venous outflow was measured with an orifice flowmeter. All data were recorded on a multichannel direct-writing oscillograph (Offner type R). Details of the methods have been described previously.

Mean capillary pressure was determined by the zero-flow isogravimetric technique illustrated in figure 1. The preparation was initially isogravimetric at a venous pressure of approximately 1.0 mm Hg. At time A, the arterial inflow tubing and venous outflow tubing were occluded simul-
FIGURE 1
Record of weight and venous pressure during zero-flow isogravimetric technique. At A, arterial inflow was occluded and venous pressure adjusted by a reservoir. Weight was stabilized at a pressure of 13.0 mm Hg. At venous pressures of 10.7 and 12.2 mm Hg, weight decreased, at 13.9 mm Hg, weight increased.

Tubing leading from a saline-filled reservoir to the venous circuit was then opened. The hydrostatic pressure in the vasculature was thus controlled by the reservoir, the level of which was adjusted to achieve the isogravimetric state during zero flow. In the experiment shown, a venous pressure of 13.0 mm Hg was required to render the preparation isogravimetric. Ordinarily the procedure requires one to two minutes.

The venous pressure at which the preparation became isogravimetric during zero flow was taken as the mean capillary pressure which existed before flow was occluded. In practice several pressure levels near the expected isogravimetric level were chosen and the precise isogravimetric venous pressure was determined by examination of the weight record and interpolation.

In a previous study, it was shown that the intestine will become isogravimetric at any venous pressure between 0 and 18 mm Hg. This is apparently characteristic of the hind limb also, although the range of isogravimetric venous pressures is smaller there. Pappenheimer and Soto-Rivera found that if enough fluid was filtered across the capillary membrane to increase the extravascular volume by 15 grams, the isogravimetric range of venous pressures was reduced to a single point. The tendency for weight to stabilize over a range of venous pressures is due presumably to changes in colloidal osmotic pressure of the proteins in the interstitial fluid. In support of this interpretation we have observed that protein concentration of intestinal lymph decreases as venous pressure is increased (unpublished results). In the present studies the lymph vessels were tied off.

Since arterial and venous pressure and flow are also measured, postcapillary and precapillary resistance may be calculated. Precapillary resistance represents the resistance on either side of the midpoint of the capillaries, and include therefore a portion of the capillary network as well. Since the contribution of the capillary network may be of some importance, especially for the resistance of the postcapillary segment, we will refer to them as pre-midcapillary and post-midcapillary resistance respectively.

B. SMALL VEIN PRESSURE

Eighteen dogs anesthetized with sodium pentobarbital (30 mg/kg iv) were used in studies of small vein pressure and its relation to large vein pressure. The surgical preparation of the intestine was similar to that used in the weight measurements. A piece of Tygon tubing somewhat longer than the intestinal segment itself was inserted through the intestine and tied in place. This tubing had numerous holes to permit drainage of secretions from the intestine. In addition, a smaller tube was placed inside. Water at 38°C was circulated through the smaller tube from a constant temperature bath. The intestinal loop was covered with moist gauze and plastic film and mounted on a stable platform. The arterial and venous circuits were of the same design described above for the weight experiments.

Small vein pressure was measured with a 0.2 mm glass pipette inserted by a micromanipulator approximately 2 mm into a vein (average inside diameter 0.3 mm). Every attempt was made to place the pipette in such a position so that it did not obstruct entirely the small vein into which it was inserted. However, from inspection alone, the presence of some interference with normal flow could not be excluded with certainty. The intestine is a more favorable organ than most for such a study because submucosal venous anastomoses are abundant.

The pipette was connected to a Statham P23B pressure transducer by no. 60 polyethylene tubing. The frequency response of this system was too low for satisfactory determination of small vein pressure during rapid change. For this reason, resistance of the venous segment was calculated only from steady state values of small vein pressure. Large vein pressure and blood flow were measured in the same manner as in the weight studies. Venous pressure was raised from zero to a final level of approximately 18 mm Hg in steps of 3 to 4 mm Hg. In most preparations small vein pressure was measured from two or three sites in consecutive experiments.
Results

A. Mean Capillary Pressure

With large vein pressure initially set at approximately 0 mm Hg, mean capillary pressure as determined by the zero-flow isogravimetric method averaged 9.7 mm Hg as shown in figure 2. When venous pressure was elevated the capillary pressure increased by 62% of the venous pressure increment. The relation between capillary and venous pressure appeared to be approximately linear over the venous pressure range of 0 to 18 mm Hg (fig. 2). This relationship may be expressed as $P_c = 9.7 + 0.62 P_v$, where $P_c$ = mean capillary pressure and $P_v$ = venous pressure (both in mm Hg).

Elevation of venous pressure increased capillary pressure less than would be expected in a rigid system. From figure 2, when venous pressure was initially 0 mm Hg, mean capillary pressure averaged 9.7 mm Hg while arterial pressure was 100 mm Hg. When venous pressure was elevated to 15 mm Hg, mean capillary pressure increased to 19.0 mm Hg. If arterial and venous resistance had remained constant, the increment of capillary pressure should have been 90% of the increase of venous pressure, giving a capillary pressure of 23.7. This can be calculated from equation 1, assuming $R_v$ to be 10% of total vascular resistance.

$$P_c = P_v + \frac{P_A - P_v}{R_A + R_v} \cdot R_v \quad (1)$$

The disproportionately small increase of mean capillary pressure which actually occurs could be due to changes in arterial resistance or venous resistance, or both. The contribution of each of these factors could be studied in these experiments.

B. Pre- and Post-Midcapillary Resistance

Figure 3 shows that post-midcapillary resistance $((P_c - P_v)/\text{flow})$ decreased consistently when venous pressure was elevated. This pattern was typical for the intestine and seen in all but one of the 15 experiments. By contrast, the pre-midcapillary resistance increased with elevation of venous pressure (fig. 3), a response which was seen in 12 of 15 or 80% of the experiments. It is apparent that the increase of pre-midcapillary resistance and the decrease of post-midcapillary resistance would both attenuate the rise of capillary pressure which follows elevation of venous pressure. The relative contributions of these two factors can be determined from equation 1 above by calculating...
the effect on capillary pressure of changing venous pressure when $R_A$ or $R_F$ is held constant. These calculations indicate that, typically, most of the attenuation (80%) is due to the reduction of post-midcapillary resistance while 20% is due to the increase of pre-midcapillary resistance.

C. LARGE VEIN RESISTANCE

To verify and extend the data on the behavior of the venous vessels obtained by the zero-flow isogravimetric technique, the resistance of a segment of the venous system was determined from measurements of small vein pressure. In 28 experiments on 18 preparations, large vein resistance decreased in every instance as venous pressure was elevated. Figure 4 shows results from a typical experiment. These findings agree fully with the changes of post-midcapillary resistance obtained by the zero-flow isogravimetric method as described above.

D. VENOUS PRESSURE VS. LARGE VEIN AND POST-MIDCAPILLARY RESISTANCE

The effect of venous pressure on post-midcapillary resistance and large vein resistance in preparations having similar total vascular resistance (between three and seven resistance units) is shown in figure 5. This figure presents pooled data from 28 experiments. It should be noted that the magnitude of the change of large vein resistance was very nearly the same as that of the change of post-midcapillary resistance. As a result, the difference between the two, which represents the sum of small vein and distal capillary resistance, is essentially unchanged. It should be noted also that when venous pressure is zero, large vein resistance is approximately half of post-midcapillary resistance.

Discussion

The zero flow modification of the isogravimetric technique used here has been applied previously to the intestine and the hind limb. In the latter the capillary pressure determined by actual occlusion of blood flow is the same as that obtained by extrapolation to zero flow, the method originally used by Pappenheimer. In the intestine the values obtained by occlusion of flow and by extrapolation to zero flow are similar when a local arteriovenous reflex has been disabled.

The low isogravimetric capillary pressure so evident in these experiments is apparently a normal feature of the small intestine. The protein concentration of intestinal lymph is approximately 60% of the plasma protein concentration. This suggests that interstitial fluid also has a high protein concentration. This would allow hydrostatic and colloid osmotic forces to be in balance across the capillary wall in accordance with the Starling hypothesis, at a low capillary hydrostatic pressure. This would also explain our observation that the intestine can become isogravimetric through a wide range of venous pressures. For example, an increase of capillary pressure would cause filtration of protein-free fluid into the interstitial compartment with dilution of extravascular protein and reduction of colloid osmotic pressure.

As noted previously, the data of Pappenheimer and Soto-Rivera indicate that 80% of an increase of venous pressure would reach the midpoint of the capillaries in the hind limb. Our results indicate that the influence
A. Effect of venous pressure on segments of the venous system and capillary bed. Open circles represent resistance of the large vein segment ($R_{vt}$) as a function of venous pressure. Open circles with dot represent resistance from the midpoint of the capillaries to the venous outflow point (post-midcapillary resistance). This segment is composed of total venous resistance ($R_{vt}$) and the resistance of the distal portion of the capillary bed ($R_{c,d}$). The difference between the two curves is represented by solid circles and composed of small vein resistance ($R_{v,s}$) and distal capillary resistance ($R_{c,d}$). Values represent averages for all experiments. B. Schematic diagram of the peripheral blood vessels, showing segments of the vasculature whose resistance is given in figure 5A.

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of venous pressure on the intestinal capillaries is considerably less, with 62% of the increment reaching the midpoint of the capillaries. This difference is especially noteworthy because the capillary and venous pressures are far closer to each other in the intestine than in the hind limb and the increment should, on this basis, be larger in the intestine. The primary reason for the smaller effect in the intestine is a notable reduction in venous resistance, although an increase in arterial resistance also contributes.

The effect of venous pressure on venous resistance has not been studied extensively. Haddy et al.\textsuperscript{12} noted a significant reduction of venous segment resistance in the foreleg of the dog in studies involving simultaneous elevation of arterial and venous pressure. Greenwood et al.\textsuperscript{18} found by the plethysmographic technique that small grades of venous congestion in the forearm did not appear to reduce blood flow. They suggested that these small elevations of venous pressure caused a proportionate decrease of venous resistance. Coles et al.\textsuperscript{14} obtained similar results in human subjects in the calf region.

In contrast to the reduction of large vein resistance, the resistance of the segment consisting of small vein and distal capillary seems to remain relatively unchanged. This suggests rigidity of these vessels, a condition which might seem tenable for the capillaries,\textsuperscript{4} but appears unlikely for the small veins. It is perhaps more likely that the observed constancy of resistance and apparent rigidity is due to opposite changes of diameter or of number of open channels in the two segments. Studies of capillary filtration coefficient and capillary blood volume in the intestine demonstrate that circulating capillary blood volume and capillary filtering surface decrease at higher venous pressures (unpublished results). This may be the result of closure of part of the capillary bed, which would increase resistance to flow there. Therefore dilation of the small veins and venules may be obscured by concomitant constriction and stasis in a portion of the arteriocapillary bed.

In view of the present findings it is surprising that post-midcapillary resistance did not decrease measurably when venous pressure was elevated in the course of an isogravimetric procedure. In the intestine no evidence of such a decrease was found after the arteriovenous reflex was eliminated.\textsuperscript{9} This may be ascribed to incomplete blocking of the reflex with pharmacologic agents or incomplete nerve degeneration after chronic denervation.

It has been shown previously that elevation of venous pressure increases total vascular resistance in the intestine.\textsuperscript{15} This was ascribed to a constriction of the precapillary vessels on the basis of indirect evidence. The present studies provide direct evidence which verifies this conclusion.

The vascular responses to elevation of venous pressure as described here are undoubtedly of some importance in homeostasis. When venous pressure is elevated, the arterial resistance increases while the venous resistance decreases; both of these responses tend to attenuate the increase in capillary pressure. Also, when arterial pressure is increased, the arteries constrict and the veins dilate.\textsuperscript{6} These responses tend to keep capillary pressure constant. Thus, the primary homeostatic significance of these active and passive responses of the intestinal vessels to changes of intravascular pressure may be to keep capillary pressure within given limits which would, in turn, help to regulate the volume of interstitial fluid.

\textbf{Summary}

Elevation of venous pressure in the intestine increases capillary pressure by amounts that average 62% of the venous pressure increment. The relation may be expressed as $P_c = 9.7 + 0.62 \times P_v$, where $P_c$ represents the mean capillary pressure and $P_v$ represents venous pressure (both expressed in mm Hg). The increase of capillary pressure is less than expected for a rigid system and less than reported for skeletal muscle. This attenuation of the effect of increments of venous pressure on capillary blood pressure is due to precapillary constriction and postcapillary dilation, with the latter playing the dominant role.
role. Measurement of resistance in a segment of the venous vasculature confirmed this and also demonstrated that most of the reduction of resistance occurs in venous vessels with diameters greater than 0.5 mm.

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