The Immediate Influence of Increased Venous Pressure Upon Resistance to Flow in the Dog's Hind Leg

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Variations in flow in the presence of a constant arteriovenous pressure difference can only occur when vascular dimensions have been altered, irrespective of the rheological properties of the liquid being perfused. When the vascular bed of the hind leg is subjected to parallel changes in arterial and venous pressures, higher absolute values of pressure result in an enhancement of flow. This constitutes convincing evidence to indicate that certain vessels which offer a significant resistance to blood flow are distensible.

A wide variety of opinions has been expressed concerning the influence of variations of intraluminal pressure upon the blood vessels which offer the principal resistance to blood flow. Indirect evidence has been adduced that the vascular bed of the hind leg behaves as a rigid hydraulic system. Data have been proffered by other investigators, however, to indicate that the vascular bed is passively dilated by elevated internal pressures. Finally, it has been postulated that augmented internal pressures induce vasocostriction as a myogenic reaction or as a local reflex.

The present series of experiments was designed to elucidate this problem by comparing the resistances to blood flow over a wide range of intraluminal pressures, while maintaining a constant pressure difference between the arterial and venous ends of the circuit.

Methods

Thirteen experiments were performed on mongrel dogs anesthetized with sodium pentobarbital, 30 mg. per Kg. body weight intravenously. In each animal, a hind leg was prepared for hemodynamic studies as illustrated in figure 1. The femoral artery (F.A.) and vein (F.V.) were exposed in the upper half of the thigh by means of a longitudinal incision. These vessels were dissected free over a length of 6 to 9 cm., and all side branches were ligated. Collateral circulation and conduction of nerve impulses were then precluded in one of two ways: In half of the experiments, a wire tourniquet was applied about the thigh by means of an érasur (E). In the remaining preparations, the thigh muscles were sectioned transversely, and the femur disarticulated. All sectioned surfaces were thoroughly cauterized. Heparin was administered to prevent blood coagulation, and T-cannulae were then inserted into the femoral vessels.

Figure 1 illustrates how a simple hydraulic system, when connected to the side arm of the arterial T-cannula (T1), makes it possible to obtain rapidly all the data necessary to construct an entire pressure-flow curve. Stopcocks S1, S2 and S4 are temporarily opened to permit about 200-300 cc. of blood to enter the reservoir (R). Stopcocks S1 and S4 are then closed and S1 and S2 opened to permit equilibration of pressures between the blood reservoir and a vertical glass column (V.C.) of constant internal diameter, which serves as the flowmeter. Any desired pressure can be exerted on this system by interposing a mercury escape valve (M.V.) between an air compressor outlet (A) and the blood reservoir (R).

To construct a pressure-flow curve, clamps C1 and C2 are applied to the femoral vessels proximal to the T-cannulae, and stopcocks S2 and S4 are opened. The venous pressure is set at any desired level by adjusting the height of the outflow tube, V.O. Blood is perfused through the extremity from the reservoir for approximately one minute at the constant pressure determined by the mercury valve. Stopcock S2 is then closed, so that the sole source of pressure for perfusing the limb is derived from the blood in the vertical glass cylinder (V.C.). The pressure head

* Heparin supplied through the courtesy of Dr. W. R. Kirtley, The Lilly Research Laboratories.
in this column declines progressively, and is recorded optically by means of a Gregg manometer ($M_A$). Since the cylinder has a virtually constant internal diameter, a proportionate relationship exists between volume and pressure. Since flow is the time rate of change of volume, the flow at any given moment can be ascertained by differentiating the recorded pressure-time curve at that point, as previously described by Nichol and coworkers. Therefore, an infinite number of points are available for constructing a pressure-flow curve from each registration of the decline of pressure with time.

In six experiments, the venous outflow level (V.O.) was maintained at a constant height during each recording of the arterial pressure decline. At least two curves were obtained with venous pressure set at the hydrostatic level of the femoral vessels, the zero reference level. Interposed between these “control” and “recovery” curves, records of pressure decline were registered with the venous pressure adjusted to varying degrees above this reference level.

In the remaining seven experiments, flow was measured while a constant pressure difference was maintained across the vascular bed, but the absolute values of arterial and venous pressures were continually changing. This was accomplished in the following manner. The initial arterial perfusion pressure was exerted upon the blood reservoir as described above. The desired arterio-venous pressure difference was pre-determined by suspending the end of the venous outflow tube (V.O.) by means of a heavy string at the required distance below the meniscus in the arterial inflow cylinder (V.C.). The hind limb was perfused from the reservoir for 1–2 minutes to permit flow to become stabilized at the desired initial arterial and venous pressure values. The reservoir was then disconnected from the system by closing stopcock $S_6$. Immediately, the hydrostatic level of blood in the vertical cylinder began to fall. The upper end of the heavy string was made to follow the miniscus during its descent. Since the venous outflow tubing was attached to the other end of this string, the venous pressure diminished at an equivalent rate. No difficulty was experienced in maintaining the arterio-venous pressure difference constant to within ±1 cm. of blood.

In the six experiments where venous pressure ($P_v$) was maintained at a constant level throughout each registration of the decline of arterial pressure ($P_A$), the results were somewhat variable. Three of these experiments, especially in the earlier phases, disclosed evidence of a reduction in resistance ($R$) when $P_v$ was elevated, and figure 2 illustrates the most exaggerated response observed in this group. In curve A, the open circles represent the “control” relationships between flow ($Q$) and $P_A$, while $P_v = 0$. The convexity toward the pressure axis was evinced in four of the six control curves in this group, and conforms with the configuration described for the hind leg.

![Fig. 1. Principal components of the hydraulic system employed for temporary perfusion of the leg.](image)

![Fig. 2. Relationship between pressure, in mm. Hg (abscissa), and flow, in cc/min. (ordinate), for the hind leg when venous pressure is maintained at a constant value during each registration of pressure against time.](image)
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In previous reports, \( P_v \) was then elevated to 59 mm Hg, and curve B illustrates the \( P_A:Q \) relationship under these conditions. The curve lies to the right of the control plot, indicating that \( Q \) is diminished for any given value of \( P_A \) as a result of the augmented \( P_v \).

In curve C, the data of curve B are replotted in terms of \( Q \) as a function of \( P_A - P_v \). Since \( R = (P_A - P_v)/Q \) by definition, and since curve C falls considerably to the left of the control graph, it follows that \( R \) is appreciably reduced as a consequence of the increased \( P_v \).

Finally, the solid circles in curve A represent the “recovery” data, at \( P_v = 0 \), secured shortly after the values in curves B and C. It is obvious that, in this experiment, the recovery values are virtually identical with the control data.

In five of the six experiments in this group, however, a definite tendency was manifest for \( R \) to increase in serial recordings at \( P_v = 0 \). Under these conditions, the intervening curves representing \( Q \) as a function of \( P_A - P_v \) at the elevated values of \( P_v \) frequently fell between the control and recovery graphs. Therefore, it was not possible to draw valid conclusions concerning the effect of increased \( P_v \) on \( R \) with any degree of certainty in such cases.

It must be emphasized, however, that in not a single instance did a curve of \( Q \) as a function of \( P_A - P_v \) at elevated \( P_v \) fall to the right of both the control and recovery graphs at \( P_v = 0 \). Therefore, the results have militated consistently against the concept that increased \( P_v \) augments \( R \).

The second group of experiments was designed to eliminate the necessity of comparing \( Q \) at equivalent \( P_A - P_v \) in separate pressure-flow curves. Instead, it was rendered possible to assess \( Q \) over a wide range of \( P_A \) and \( P_v \), while maintaining a constant value of \( P_A - P_v \), from data acquired within the span of a relatively few seconds.

The results of the seven experiments in this group are much more uniform. Data from a typical experiment are presented in figure 3, where \( Q \) is plotted as a function of \( P_A \). In this experiment, the rate of \( P_A \) decline was recorded at four different, constant values of \( P_A - P_v \). These were acquired in the following sequence: 

74, 64, 56 and 70 mm Hg. The figure reveals that the greater the value of \( P_A - P_v \), the further the curve lies to the left, indicating that for any given \( P_A \), \( Q \) varies concordantly with \( P_A - P_v \). It is also evident that, in each individual curve, \( Q \) varies directly with \( P_A \), despite the fact that \( P_A - P_v \) is constant. Thus, increased values of \( P_A \) and \( P_v \), which enhance intraluminal pressure throughout the entire vascular bed, result in an augmentation of \( Q \). Since \( R = (P_A - P_v)/Q \), and since \( P_A - P_v = k \), increased values of \( P_A \) and \( P_v \) elicit a reduction of \( R \). It should be noted also that as a consequence of the alterations in \( R \) contingent upon changes in intraluminal pressure, it is possible for \( Q \) at one level of \( P_A - P_v \) to exceed \( Q \) at a lower value of \( P_A - P_v \). Referring to figure 3, for example, \( Q = 76 \) cc. per min. when \( P_A = 135 \) mm Hg, at \( P_A - P_v = 56 \) mm Hg. At the next higher pressure difference employed (64 mm Hg), however, \( Q \) is only 61 cc. per min. at \( P_A = 85 \) mm Hg.

The results illustrated in figure 3 are quite typical of those observed in the other experiments in this group. The range of arteriovenous pressure differences extended between

![Figure 3](http://circres.ahajournals.org/)

**Fig. 3.** Relationship between arterial pressure, in mm Hg (abscissa), and flow, in cc/min. (ordinate), for the hind leg when the arterio-venous pressure difference is held constant. Figures to the right of each curve represent the arterio-venous pressure difference, in mm Hg.
the limits of 48 and 97 mm Hg for the entire series of experiments, but the directional changes were quite uniform throughout. In six of the seven preparations, parallel augmentations of $P_A$ and $P_v$ engendered significant reductions of $R$. In more than half of these instances, the relationships between $P_A$ and $Q$ were essentially linear; in most of the remainder, the graphs were somewhat convex to the $P_A$ axis.

**DISCUSSION**

In a rigid hydraulic system, the rate of flow is constant for any given pressure drop, irrespective of the absolute levels of pressure at the inflow and outflow ends of such a circuit. As defined by Poiseuille's law, $Q = (P_A - P_v)/R$, where $Q =$ flow, $P_A =$ inflow pressure, $P_v =$ outflow pressure, and $R =$ resistance, the reciprocal of the constant of proportionality. In a distensible system, however, this proportionality no longer obtains. For any given value of $P_A - P_v$, the greater the absolute values of $P_A$ and $P_v$, the greater will be the cross sectional dimensions of the component tubes. This will result in a disproportionate reduction of $R$, and hence an augmentation of $Q$. If for any reason, elevated intraluminal pressure instituted a narrowing of the constituent conduits, then a parallel increase of $P_A$ and $P_v$ would result in a diminution of $Q$.

In the first group of the present series of experiments, comparison of data derived from successive pressure-flow curves indicated that increased intraluminal pressures reduced $R$ in some cases, and had no discernible effect in others. In those instances where no perceptible effect was manifest, the recovery $R$ was almost invariably greater than the control $R$. It is plausible that the elevated $P_v$ maintained during the registration of the experimental pressure-time curve might have augmented tissue pressure. This would account for the increased $R$ evident in the recovery data, and would tend to neutralize the vasodilating influence of increased $P_v$ during the experimental periods. It must be admitted, however, that this group of experiments did not furnish decisive evidence in support of the concept that increased intraluminal pressures distend vessels which offer an appreciable resistance to blood flow.

On the other hand, this same group of experiments was extremely valuable in eliminating from consideration the operation of a mechanism by means of which increased intraluminal pressures elicit vasoconstriction. Folkow has recently adduced considerable evidence to support Bayliss' contention that the smooth muscles of the vascular walls possess the inherent capacity to respond to variations in internal pressure. Vasodilatation was reported to be the myogenic response to reduced intraluminal pressures, and vasoconstriction to augmented pressures. In the present experiments on the denervated hind legs of dogs, the data consistently failed to disclose any evidence whatsoever of vasoconstriction in response to elevated intraluminal pressures. This first group of experiments was more suitable for attempting to reveal such a myogenic reaction than was the second group, because in the initial series $P_A$ and $P_v$ were maintained at high constant values for about one minute prior to recording the "experimental" pressure-time curves, and $P_v$ remained elevated throughout the entire registration. This would allow adequate time for a maximum response to be elicited, according to the results of Folkow. Vasoconstriction in response to elevated $P_v$ mediated by a local reflex has been postulated on the basis of experiments on rabbits and man. The operation of such a reflex in the denervated hind limb of the dog has not been verified in this study, for the reason outlined above; namely, that concordant changes in intraluminal pressure and $R$ were never observed.

The second group of experiments in the present series also has failed consistently to reveal any evidence of vasoconstriction in response to increased intraluminal pressures. Furthermore, the practicability of comparing the effects of a wide range of parallel variations in $P_A$ and $P_v$ occurring within a few seconds has rendered it possible to analyze the influence of variations in intraluminal pressures with greater precision and reliability. On the basis of this group of experiments, it has been
demonstrated that augmented intraluminal pressures actually distended vessels which offer appreciable resistance to blood flow. Numerous observations in each of seven experiments have demonstrated almost invariably that \( Q \) is appreciably augmented as intraluminal pressures are enhanced. On the basis of their studies, Pappenheimer and his colleagues\(^1\)\(^,\)\(^2\) have observed a reduction in \( R \), localized to the precapillary portion of the vascular bed, as perfusion pressure is raised in the hind legs of dogs and cats. These investigators postulated that the principal, and probably the sole factor responsible for these variations in \( R \) is the anomalous rheological nature of blood. It has been demonstrated that the apparent viscosity of blood may vary appreciably with changes in tubular dimensions and rate of flow, both in vitro and in vivo. In a perfectly rigid hydraulic system, however, even when filled with a non-homogeneous liquid, \( R \) will remain constant as long as \( P_A - P_V \) is constant, regardless of the absolute values of \( P_A \) and \( P_V \). When a change in \( R \) is observed in the face of a constant value of \( P_A - P_V \), therefore, it must be concluded that the initiating factor, at least, is a modification of vascular dimensions. This in turn may then induce profound alterations in the apparent viscosity of the blood.\(^1\)\(^,\)\(^2\)\(^,\)\(^16\) This would, of course, tend to increase \( R \) as intraluminal pressures rise, thus acting in opposition to the actual changes in \( R \) which were observed. Since the effects of vascular distention were evidently of greater magnitude than those of increased apparent viscosity upon \( R \), the overall consequence was an augmentation of \( Q \). Increased \( Q \), in turn, affects the apparent viscosity of blood, this time in the direction of diminishing the apparent viscosity.\(^1\)\(^,\)\(^2\)\(^,\)\(^16\) The experimental procedures in the present study, therefore, result in a dichotomy of effects upon the apparent viscosity of the blood, one tending to neutralize the other.

Finally, it should be emphasized that the present study has concerned itself only with the immediate effects of elevated intraluminal pressures. It is very probable that vascular distention contingent upon increased intraluminal pressures may be only a transitory phenomenon. Augmented internal pressures, especially when produced by elevating \( P_V \), accelerate the rate of capillary filtration, and ultimately lead to a rise in tissue pressure.\(^4\) Since the cross-sectional dimensions of a distensible tube are dependent upon the difference in pressures across its walls, as the external pressure increases the cross-sectional diameter will diminish. Therefore, the effects observed in the present study would probably abate or disappear if \( P_V \) were maintained at an elevated level for an extended period of time.

**Summary**

The influence of elevated intraluminal pressures upon the resistance to flow was studied in the vascular bed of the denervated hind leg of the anesthetized dog. When parallel changes in arterial and venous pressures were effected, it was found that in the majority of cases, higher absolute values of arterial and venous pressures resulted in an augmentation of flow, despite a constant arteriovenous pressure difference. Therefore, the immediate influence of elevated intraluminal pressure is to reduce the resistance to blood flow. Increased intraluminal pressure never produced an augmented resistance.

Variations in flow in the presence of a constant arteriovenous pressure difference can only occur when alterations in vascular dimensions are elicited, irrespective of the rheological properties of the liquid being perfused. Since increased intraluminal pressures engendered a diminution in vascular resistance even when
the arterio-venous pressure difference was maintained constant, certain of the vessels which offer significant resistance to blood flow must be distensible. Passive dilatation of these vessels resulting from elevated internal pressures is the initial and essential factor in reducing resistance. These alterations in vascular dimensions will result in secondary modifications of the apparent viscosity of the blood, which will contribute to the variations in resistance to an unknown degree.

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