THE INFLUENCE OF RATE OF FILLING ON APPARENT VENOUS DISTENSIBILITY IN MAN

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ABSTRACT

The physical properties of the vessel walls which determine the response of the venous system to a distending force have been investigated in the human extremity. It has been found that there is a quantitatively significant time-related (viscous) component in the response of the veins to stretch. This means that one of the deterimants in the relation between venous volume and transmural pressure is the rate of rise of transmural pressure, which is a function of the blood flow to the segment. This time-related component in the response to stretch can serve as a local buffering mechanism, minimizing volume changes after sudden changes in local postcapillary pressure such as occur after changes in posture or in blood flow. Since blood flow and apparent venous distensibility are interrelated, flow changes must be taken into account in the interpretation of studies where venous distensibility curves are used as an index of venous tone.

It has also been demonstrated that the limb supported above heart level contains a minimal volume of blood, which is not altered by plethysmograph cuff pressures up to 40 mm Hg.

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There has recently been considerable interest in the contributions of the venous system to cardiovascular homeostasis in man, 1, 2 but investigation of the physical characteristics of the venous wall itself has been limited. Many tissues display a time-related or viscous component in their response to stretch, 3, 4 as has been demonstrated in the splanchnic venous system of the dog, where the slope of the distensibility curve relating venous pressure to volume is influenced by the rate of filling.4,5. A significant viscous component in the resistance of the venous system to distension would buffer the effect of a sudden increase in transmural pressure. The magnitude of this effect would increase with increasing rates of change, and thus could be of considerable importance.

In the case of the human extremity the rate of venous distension after proximal venous occlusion is a function of the blood flow. The method of venous occlusion plethysmography, classically used for measuring blood flow of the extremities in man, has also been used to obtain venous distensibility curves. Thus, the influence of rate of filling on the apparent distensibility of human veins can be evaluated by altering the rate of blood flow in a limb segment while keeping the transmural pressure of the venous system constant. This was accomplished by the use of airfilled rubber plethysmograph cuffs at varying pressures for the measurement of both blood flow and venous distensibility. Such a cuff can apply a pressure of variable magnitude which will modify the movement of blood into the limb segment under study. By keeping the pressure difference between the venous occlusion cuff and the plethysmograph cuff constant, it has been possible to measure the apparent venous distensibility at different flows but a constant transmural pressure.

METHODS

The plethysmograph. The air-filled, flexible rubber cuff plethysmograph described by Dohn (6) and employed in the studies of Graf and Westersten (7) was used throughout this study. The cuffs were 5 cm wide and in a range of circumferences to provide a good fit around the calf of all subjects. The plethysmograph was connected to the pressure transducer of a Vasograph (Electromedical Engineering Co.), and calibrated by displacement of 1.0 ml into the air system enclosed in the plethysmograph cuff, connecting tubing and transducer.

The system was tested on a model consisting of a glass beaker, around the circumference of which was wrapped a thin-walled rubber tube, closed at one end and connected to a motor-driven syringe at the other. The plethysmograph cuff was placed over the rubber tube and infusion of known volumes of water into the tubing mimicked volume increases in a limb segment. The temperature of the injected water and water filling the beaker was held constant. Figure 1 shows the deflections of the recording pen plotted against the deflections expected from the calibration of the Vasograph prior to and after the measurement. These were in good agreement over a wide range of temperatures and plethysmograph cuff pressures. The volume injected was up to 20 ml, which was greater than the largest volume change recorded in the human extremities.

The venous occlusion cuff and the distal cuff, to cut off the circulation of the foot, were rubber cuffs 8 cm wide, with nondistensible backing.

Procedure. The experiments were performed in a constant-temperature room at 20 ± 0.5° C. The subjects were lying comfortably on a bed with one leg supported so that the entire calf was above heartlevel.

A plethysmograph cuff of suitable circumference was placed around the thickest part of the calf, connected to the recording system and inflated to either 10 or 40 mm Hg pressure. The proximal occlusion cuff was applied at a distance from the plethysmograph cuff such that only a very small cuff artifact was obtained when it was inflated, generally a distance of 5 to 8 cm. The distal cuff was applied around the ankle.

The subjects were allowed to adapt to the room temperature for 1 hour before the first measurement. In each test the distal cuff was inflated to suprasystolic pressure, the system calibrated and the occlusion cuff rapidly inflated by opening a valve to a large air reservoir preset at the desired pressure. Portions of at least three filling curves were recorded to measure blood flow and the next was followed until equilibrium at an increased volume was reached. In this way, both flow and maximum increase in venous volume in the segment were estimated for different combinations of pressures in the plethysmograph and venous occlusion cuffs.

For each subject, three such tests were made with occlusion cuff and plethysmograph pressures of 30 and 10 mm Hg, respectively, and three tests with pressures of 60 and 40 mm Hg. The pressure difference between the two cuffs, the transmural pressure applied to the veins under the plethysmograph, was 20 mm Hg for both combinations of pressures. However, the flow rate was always lower when the plethysmograph cuff pressure was 40 than when it was 10 mm Hg. Tests with the two pressure combinations were performed alternately on each subject, the pressures for the first test being selected in a random fashion. A period of at least five minutes was allowed between tests with the plethysmograph cuff pressure adjusted to the level appropriate for the next determination to allow the circulation in the segment to adjust to the applied external pressure.

The transmission of pressure from the plethysmograph and occlusion cuffs into the limb was checked in the forearm, where veins are more easily accessible for cannulation. The pressure in a vein under the plethysmograph cuff was recorded with an indwelling needle or intravenous catheter connected to a Statham pressure transducer and a Visicorder. In 2 such experiments, it was found that any increment in pressure in either of the cuffs individually gave a proportionate pressure increment in the vein under the plethysmograph cuff.

The possibility of a slow movement of tissue from the segment under the proximal occlusion cuff into the plethysmograph, so that the longer period of occlusion associated with lower flows would record from a larger volume of tissue than did a shorter period, was explored in the following way. A 10 cm-wide cuff was applied around the thigh, i.e., proximal to both the plethysmograph and collecting cuffs, and inflated to a suprasystolic pressure. After a few minutes equilibration, the occlusion cuff was inflated and the resulting effect on the volume under the plethysmograph recorded. No increase was found when the occlusion and plethysmograph cuffs were placed at a distance such that the cuff artifact was minimal. When the two cuffs were placed close together there was a large rapid increase in measured volume (cuff artifact) followed by a slower phase of volume increase. When present, the slow volume change was the same for both pressure combinations used in these experiments.

Since the estimations of the venous distension were made with two different pressures in the plethysmograph, the possibility had to be considered that the two measurements started at different baselines, i.e., that the veins were emptied more completely by the higher plethysmograph pressure. This possibility was assessed by experiments of the following type. The subject lay on a horizontal tilt-table with the plethysmograph cuff on a calf supported above heart level. No other cuffs were used. The table was tilted from the horizontal to head-up positions of approximately 10° and 20° and a head-down position of 10°, and the volume change of the calf segment recorded. The results of a typical experiment are shown in figure 2. The volume increase at each angle of head-up tilt was reproducible, and varied inversely with the pressure in the plethysmograph cuff. However, when the subject was tilted to a 10° head-down position, no volume change occurred at any of the cuff pressures. This indicated that the veins of a normal extremity held above heart level contain a minimal volume of blood, which is not altered by cuff pressures within the range employed in these experiments.

In another type of experiment the effect of filling rate on the distensibility of a superficial forearm vein was investigated by the isolated venous segment technique (8). A long venous segment without apparent tributaries was isolated between two clamps fitted around the arm. A 20-gauge needle was inserted into the isolated segment and heparinized saline infused. The vein segment was then emptied by stopping the infusion, releasing the proximal clamp, and stroking the vein proximally with the finger, following which the clamp was reapplied. The empty vein segment was then filled with heparinized saline by means of a motor-driven syringe and the concommitant pressure increase recorded with ~~of~~ a Statham P23AC transducer connected to a Visicorder. This procedure was repeated at different injection rates in random order, and the pressures obtained for equal injection volumes plotted after correction for pressure drop in the tubing, which was minimal.

<u>Subjects</u>. Twelve healthy subjects, eight males and four females ranging in age from 26 to 36 years, were used in these experiments. None

had signs of varicose veins, or of other cardiovascular disease.

RESULTS

A pressure of 40 mm Hg in the plethysmograph resulted in a lower blood flow in the calf segment than did a pressure of 10 mm Hg in all cases. Since the proximal occlusion cuff pressure was always 20 mm Hg higher than the plethysmograph pressure, the system made it possible to compare the venous distensibility at a constant transmural pressure but at different blood flows.

The results of experiments on the twelve subjects are shown in figure 3, where the mean volume increase is plotted against the mean blood flow for each subject and each combination of cuff pressures. It is apparent that the veins consistently accumulated larger volumes of blood at lower flows, although the transmural pressures were unaltered. The lower flow rates also were reflected in a slower approach to equilibrium.

Some conclusions about the visco-elastic properties of the veins in the calf may be drawn from these results. Since elasticity is a property which is unrelated to the rate of application of a force, the difference in venous volume at different blood flows must be due to a viscous component in the response of the vessel walls to stretch. It is apparent from the data presented in figure 3 that this time-related component made a large contribution to the total venous volume. A rough estimation of the parts played by elastic and viscous components can be made by plotting the collected blood volume at equilibrium against the time taken to reach this equilibrium. If a straight line drawn through these points for each subject is extrapolated to 0 time, its intercept on the volume axis should correspond to the contribution of nonviscous elements to the distension. Such a calculation involves the assumption that the contribution of the viscous component increases linearly with time, which may not be entirely correct. However, if this approximation is accepted, plots for ten subjects indicated a viscous component of 40 ± 11% (S.E.) of the total venous distension at control resting flows, and a much larger percentage at lower flows.

The effect of rate of filling on the apparent distensibility of human veins was also demonstrated in isolated segments of superficial forearm veins (figure 4). In order to demonstrate the phenomenon clearly at physiological pressures and volumes, a wide range of filling rates was used. The recorded pressure-volume curves were clearly affected by infusion rate even at minimal pressures and volumes, the pressure at any volume being a direct function of the rate of filling.

DISCUSSION

The properties of a material which affect its resistance to deformation can be divided into three components -- viscous, elastic, and inertial. The viscous component is that property which makes deformation a function of the rate at which force is applied. The elastic component is independent of time, or the rate of application of force, and the inertial component is a function of the acceleration of the material. Peterson *et al*. 9 have quantitated these factors for the aorta and large vessels of the dog. The elastic component was quantitatively the most important in that system, followed by the viscous component, which was much smaller. The inertial component was negligible. The present studies indicate that in the venous section of the peripheral vascular bed in man the viscous component of the resistance to deformation is an important factor determining the relationship between volume and transmural pressure; being involved in some 40% of the volume increase measured at normal resting blood flows and a higher percentage at lower flows.

The possible effect on circulatory homeostasis of such a marked viscous component in the response of the venous system to a change in pressure is of some interest. Postural change or arteriolar dilatation can increase the transmission of pressure to the postcapillary vessels of a given vascular bed. This increase in postcapillary pressure should increase local vascular volume and thus decrease the venous return to the heart. However, a large viscous component in the response of the postcapillary vessels to distension would tend to minimize this effect, acting in many ways as a postcapillary analogue of the autoregulatory mechanisms in precapillary vessels. 10 Conversely, in the hypodynamic shock state, which is associated with very low blood flows, any increase in flow following transfusion would tend to be dissipated in a slowly expanding venous space.

The existence of a quantitatively significant viscous component in the response of veins to stretch also is important to the interpretation of the results of studies of venous tone. The method used most commonly for obtaining an index of venous tone in man is construction of a curve relating volume of a limb segment, measured plethysmographically, to either the pressure in a proximal inflated cuff, or to the pressure measured in a venous segment in the plethysmograph. Venoconstriction (increased venomotor tone) is reflected in a shift of the curve to the right and venodilatation in a shift to the left. However, in all cases where the effects of pharmacological agents or reflex stimuli have been investigated, concommitant flow changes have occurred, and these often have not been considered in the interpretation of the pressure-volume curves.

Several previously reported and apparently anomalous responses of the veins in man may be reinterpreted in the light of the present findings. The observation that α adrenergic blockade with phenoxybenzamine did not appear to inhibit forearm venoconstriction in response to adrenaline was interpreted as suggesting either that there are no α receptors in veins, or that phenoxybenzamine is fixed by the arterioles so rapidly that it does not reach the veins. 11 A more plausible interpretation is that blockade of venomotor tone was obscured by the reduced apparent distensibility due to the increased forearm blood flow induced by adrenaline after phenoxybenzamine. The postural hypotension generally seen after phenoxybenzamine suggests that, in fact, it does induce a prominent venomotor blockade. Angiotensin has been repeatedly demonstrated to cause little or no venoconstriction in animals, 12, 13, 14 and in man, 15, 16 using techniques not affected by the rate of venous filling. An isolated observation that angiotension appeared to cause venoconstriction in the human forearm 17 may have been primarily a reflection of the increase in forearm blood flow induced by this agent 18. An area where recognition of the contribution of viscous factors to venous distensibility is of great importance is in the assessment of venous tone during shock. The very low flows seen in shock can cause the veins to appear dilated, irrespective of the actual venous tone, with consequent misinterpretation of the cause of the hypotension.

Another topic meriting discussion is the finding that the limb held above heart level is truly at a minimal volume. While this positioning of a limb has been widely used as a method for obtaining a constant baseline, 19 and seems a priori to be acceptable, there has been relatively little direct evidence that this is so. The experiments presented above suggest very strongly that the "phlebostatic level" does approximate a minimal volume state.

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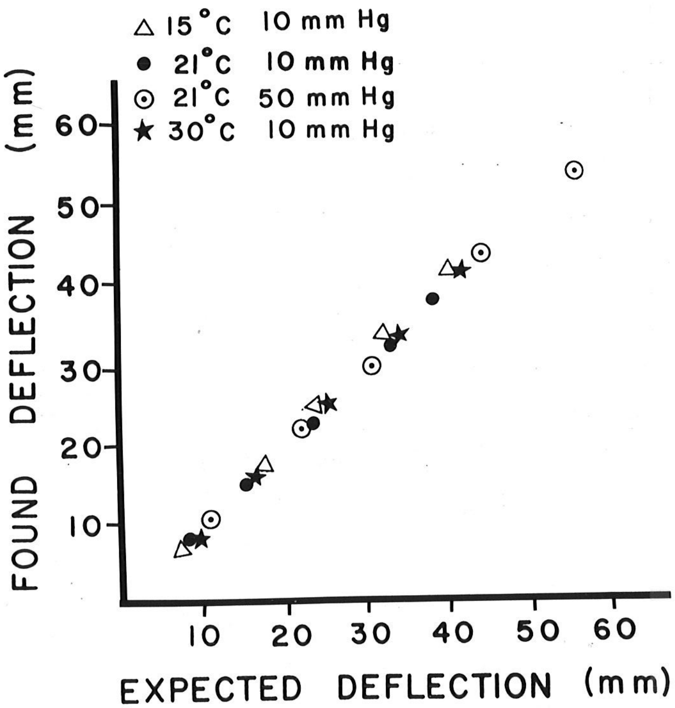
LEGENDS TO FIGURES

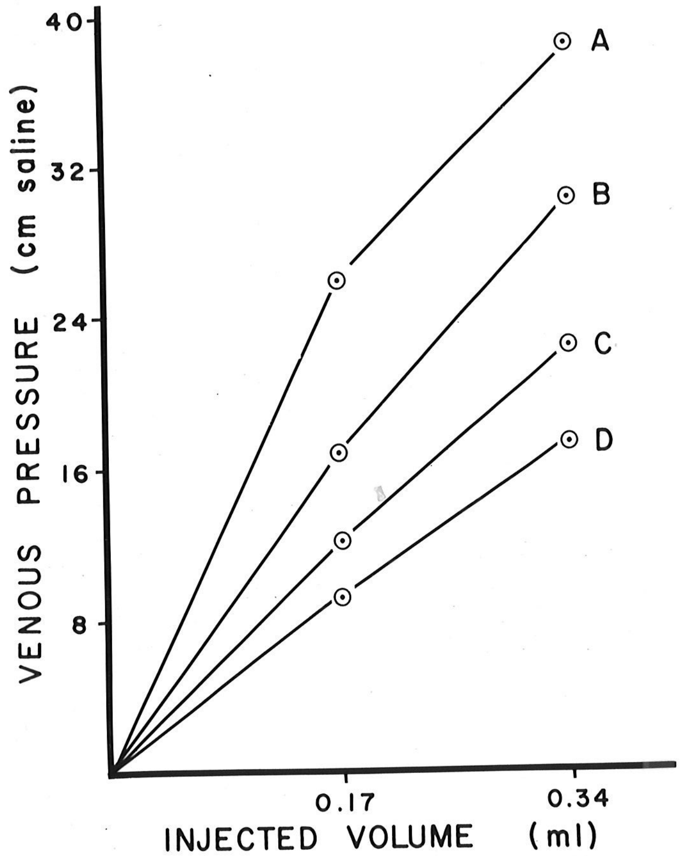
Fig. 1. Test of the Plethysmograph System. Water was infused into a rubber tube under the plethysmograph cuff on limb model at indicated temperatures and cuff pressures. The recorded pen deflection at injected volumes of 4, 8, 12, 16 and 20 ml. is plotted against the deflection expected from calibration prior to the injection.

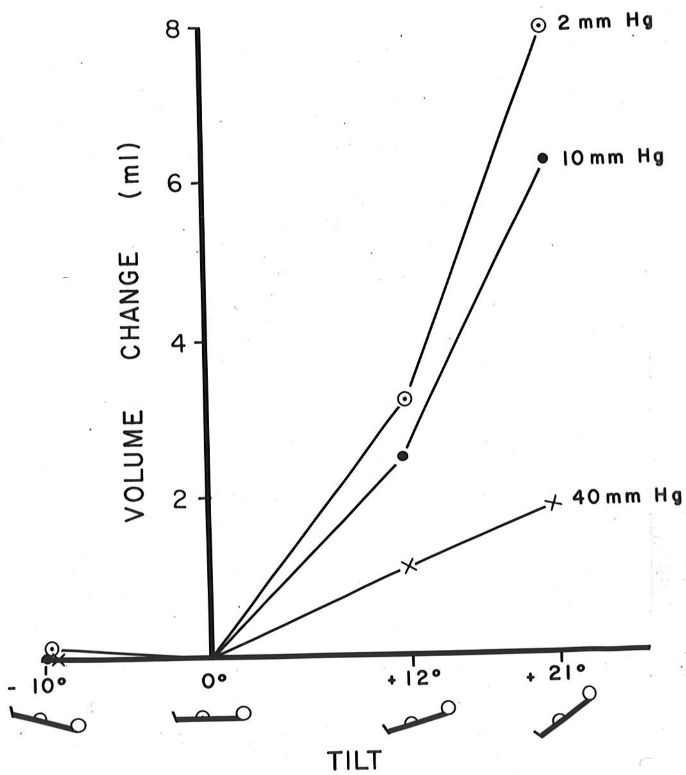
Fig. 2. Venous Volume of the Calf with the Limb above heart level. From the supine position with the calf supported above heart level, the subject was tilted to both head-up and head-down positions. The head-down position induced no further decrease in limb volume. The designated pressures are those in the plethysmograph cuff.

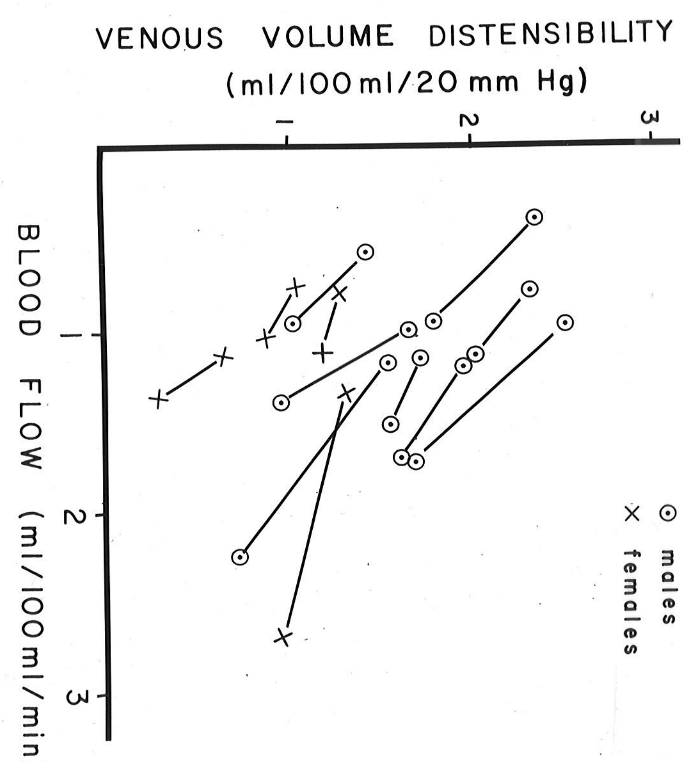
Fig. 3. Blood Flow and Apparent Venous Distensibility in the Calf.
Each of 12 subjects is represented by two symbols, joined by a straight line. Each symbol on the left is the mean of 3 complete tests with a plethysmograph cuff pressure of 40 mm Hg; that on the right, a similar mean at 10 mm Hg. The occlusion cuff pressure was always 20 mm Hg higher than the plethysmograph pressure.

Fig. 4. Relation of Rate of Filling to Pressure in an Isolated Segment of a Superficial Forearm Vein.
Saline was infused into an isolated segment of a superficial forearm vein at different rates with a motor-driven syringe, and the resultant pressures monitored. Infusion rates: (A) 1.94 ml/min (B) 0.97 ml/min (C) 0.39 ml/min (D) 0.19 ml/min.
All volumes plotted are well below maximal distention of the vein.


△ 15°C 10 mm Hg
● 21°C 10 mm Hg
⊙ 21°C 50 mm Hg
★ 30°C 10 mm Hg
FOUND DEFLECTION (mm)
10
20
30
40
50
60
EXPECTED DEFLECTION (mm)


VENOUS PRESSURE (cm saline)
8
16
24
32
40
A
B
C
D
0.17
0.34
INJECTED VOLUME (ml)


VOLUME CHANGE (ml)
2
4
6
8
2 mm Hg
10 mm Hg
40 mm Hg
-10°
0°
+12°
+21°
TILT


VENOUS VOLUME DISTENSIBILITY
(ml/100 ml/20 mm Hg)
1
2
3
BLOOD FLOW (ml/100ml/min)
1
2
3
⊙ males
× females