Spontaneous Pressure Elevations in Small Veins and Effects of Norepinephrine and Cold

By John M. Wallace, M.D. and Eugene A. Stead, Jr., M.D.

This paper reports the occurrence of spontaneous pressure changes in human small veins recorded by retrograde venous catheterization and experiments on the effects of norepinephrine and cold.

Venous obstruction is known to increase capillary pressure in the obstructed area. Most observers have believed that in the normal subject pressure in the large veins draining a part gives a good indication of the pressure distal to the venous ends of the capillaries and that, if the pressure in large veins is not elevated, changes in the venous system are not important in causing change in the capillary pressure. Haddy and Kelly and their co-workers have reported that in dogs the pressure in small veins determined by retrograde catheterization can vary independently from that of the larger veins draining the part, and that the small vein pressure may rise enough to have a definite effect on capillary pressure.

There are at least two clinical states in which blood does not seem to drain easily from the skin, suggesting that local venous obstruction may be trapping blood. When a cold hand is elevated and the arterial inflow cut off, the hand pales very slowly as compared with a hot hand treated similarly. In some patients in profound shock who are receiving large amounts of norepinephrine, the extremities may be cold and livid. Elevation of the hand may have little effect on the color. Local pressure produces a white spot which slowly again becomes livid. In both of these situations venous pressures in the antecubital veins may be normal. With these facts in mind, retrograde catheterization of veins was attempted.

Method

The valves presented a great problem; catheters could never be passed below the first phalangeal joint. The external jugular system has fewer valves but enough to prevent satisfactory catheterization. No method was devised which allowed the observer to routinely determine whether or not the catheter plugged the lumen of the vein. In one instance satisfactory visualization by Diodrast showed that the catheter filled the venous lumen. The Diodrast passed retrogradely a short distance and then left the occluded vein by branches connecting with other veins. In general, the catheter was passed as far as possible and the pressures measured were compared with those of a large vein in the forearm.

The subjects were normal male university students. All were seated throughout the experiments, which lasted 2 to 4 hours. A 21-gage needle was inserted toward the fingers into a dorsal hand vein and a semi-stiff polyvinyl catheter less than 0.5 mm. in outer diameter was threaded through and worked as far distally as possible. The tip always lay in the web between any two fingers or over a proximal interphalangeal joint. It is assumed the veins entered were usually anatomically greater in diameter than the catheters; however, they are designated small veins. In the same extremity an identical catheter was placed in a large forearm vein, the point always resting at least 7 cm. above the wrist and 5 cm. below the volar elbow crease. In group I (6 subjects), arterial pressures were recorded in the opposite arm by cuff, mean pressures having been estimated by taking one third of the sum of the systolic and twice the diastolic pressure. In group II (5 subjects) the radial artery of the same arm was also catheterized and, in 3 of these subjects, satisfactory records of all 3 vessels were obtained under all test conditions. The elbows of all experimental arms were bent at 90°, the forearms and elbows resting in an open pan or plastic jacket requiring no water seal. The catheters, 10 cm. long, were joined to 30 to 40 cm. lengths of polyethylene no. 20 tubing and thence to Lilly capacitance manometers placed side by side at heart level. After catheterization, a slow intravenous saline infusion was begun in the other arm and norepinephrine (4 μg./ml in 5 per cent dextrose in water) turned in...
by stopcock when desired. The aim was to produce definite arterial pressure changes but only mild symptoms so the amount of drug used varied, depending on individual tolerance. It ranged from near 15 to near 22 μg./min. per subject, 1 subject having received 45 to 50 μg./min. Infusions lasted an average of 22 min. After a period of rest, tap water was then added to the arm jackets and cooled with ice within a 10 to 20 min. period to 8–12°C. Temperatures were recorded every 5 min. with a chemical thermometer, the bulb of which was pressed against the skin overlying each catheter tip. After the temperature fell to its lowest point, it did not vary more than 2°C. Average time in the cold was 48 min. All pressures are means and are given in mm. Hg. Hematocrit readings from capillary tubes were made in another group of persons subjected to local cold and warming. Samples were obtained by opening identical catheters placed as described above.

RESULTS

The average pressure in the small vein, 11.8 mm. Hg, was significantly greater than the average pressure in the large vein, 9.2 mm. Hg (table 1). In 1 subject, large vein pressure was higher than the pressure in the small vein. Continuous recording of pressures on slowly moving paper provided good illustrations of normal pressure variations in both veins. While the pressure tended to vary in the same direction, spontaneous fluctuations in pressure were more common in the small vein. Figure 1 shows an unusual degree of spontaneous activity in a small vein without concomitant changes in the pressure in the large vein or radial artery. Pressure pulses were frequently present in the small vein and less commonly in the larger vein.

When blood pressure cuffs on the arm were inflated to a pressure of 40 to 50 mm. Hg, the venous pressures in both veins rose to approximately the level of the pressure in the cuffs. When the venous pressure distal to the cuff was lower than the cuff pressure, a column of blood did not connect the veins on either side of the cuff. During this period the pulse pressure waves persisted in all small and some large veins. When the venous pressure had risen to approximately cuff level, pulse pressure was increased in both veins. The Valsalva

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Number of subjects</th>
<th>Control</th>
<th>Norepinephrine</th>
<th>30 min. in the cold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radial artery</td>
<td>11</td>
<td>03.0</td>
<td>128.0*</td>
<td>107.0*</td>
</tr>
<tr>
<td>Small vein</td>
<td>11</td>
<td>11.8 ±3.1</td>
<td>16.0* ±5.2</td>
<td>32.6 ±6.5</td>
</tr>
<tr>
<td>Large vein</td>
<td>10</td>
<td>9.2 ±1.7</td>
<td>10.1* ±1.7</td>
<td>13.1 ±6.8</td>
</tr>
</tbody>
</table>

Difference between small and large veins,
control ................................................. 0.05
norepinephrine ................................. <0.01
cold ............................................... <0.01

Difference between small veins,
control and norepinephrine ............. 0.05
cold and norepinephrine ............... <0.01

Large vein differences not significant

All pressures are in mm. Hg.
* Indicates values for one less than the stated number of subjects.
† S.D.

![Fig. 1. Simultaneous pressure recordings in radial artery (upper), small vein (middle), and large vein (lower). Tips of arterial beats darkened to facilitate reproduction. Paper speed, 1 mm./sec. Pressures, mm. Hg. Small vein tracing marred by artifacts from motion of catheter outside vein.](http://circres.ahajournals.org/DownloadedFrom)
maneuver caused changes similar to those produced by a cuff obstructing venous return.

Effect of Norepinephrine. All subjects had an increase in arterial pressure and a fall in heart rate. The skin became pale and the veins less easily visible. The mean difference between small and large vein pressures increased from 2.6 to 5.9 mm. Hg. Pressure in the small veins rose an average of 4.2 mm. Hg in the 11 subjects, although no increase occurred in 3 subjects. Large vein pressures rose an average of 1 mm., the increases occurring in 5 of the 11 subjects. The greatest difference between small and large vein pressures was 7.0 mm. Hg. Pressure changes related to the arterial pressure appeared in both veins but most strikingly in the small ones (fig. 2). Peak venous pressures tended to decrease slightly as the infusion was continued and remained above the control level for a short period of time after the infusion. The norepinephrine markedly decreased the vasomotor fluctuations in arterial pressure but the fluctuations in small vein pressure either remained unchanged or increased. Raising the venous pressure in the arm by cuff and by the Valsalva maneuver produced changes similar to those present before the infusion. The post-Valsalva arterial overshoot was decreased or absent.

Effect of Cold. The first effect of the cold was to decrease the spontaneous variations in venous pressure and to eliminate the pulse pressure. Usually within 5 min. the pulse pressure reappeared in the small veins and to a lesser extent in the large veins. Within 5 to 10 min. all the immersed area was red and remained so. The venous pressure in the small veins began to rise in 5 to 10 min., reaching its peak in about 30 min. and showing no tendency to decrease thereafter. In 2 subjects the large vein pressure increased appreciably, but in the others the changes in large vein pressures were small in contrast to those in the small veins.
It was common for the small vein pressure at the end of 30 min. to be four times that present before cooling. In 3 subjects whose small vein pressures rose to 45 to 50 mm. Hg, a pulse pressure of 5 to 8 mm. Hg was present.

In 3 of the 5 subjects studied in group II there was a striking change in the behavior of the small vein pressure during the Valsalva maneuver. The large vein pressures followed the pattern seen with venous occlusion by a cuff, but the small vein pressure lost all its venous characteristics and closely mirrored the arterial pressure (fig. 3). The immediate rise in arterial pressure caused by the elevation in intrathoracic and intra-abdominal pressures, the gradual fall in arterial pressure as the Valsalva is maintained, and the gradual rise in arterial pressure as reflex vasoconstriction occurs are all accurately mirrored by the directional changes in the small vein pressure. The changes were greater in the arterial pressure. On release of the pressure, the overshoot and bradycardia are seen in both tracings.

In the cold the inflation of a venous cuff to 40 to 50 mm. Hg caused a relatively small rise in small vein pressure and no change in the venous pulse pressure (fig. 4).
**DISCUSSION**

Although we would have liked to have entered veins of 0.5 mm. or less, it made little difference to us whether the vein was actually occluded. It probably was not occluded with the hand at room temperature but probably was occluded when the vein was constricted by cold. If it were not occluded we measured the pressure in the open vein at the catheter tip. If it were occluded we recorded the pressure of the collateral system draining the occluded vein. These veins have such numerous anastomotic branches that a measurable rise in pressure would not be expected when the vein was occluded. The important point was to have the catheter tip in as small a vessel as possible.

The pressures in the small veins that we were able to catheterize behaved differently from those of the larger veins of the forearm. Norepinephrine causes arteriolar constriction. The finding of an increased small vein pressure in the presence of arteriolar constriction indicates active constriction of the small veins which must have an effect on capillary pressure. A rise in small vein pressure is produced by small vein constriction as well as by back pressure from the heart or by constriction of the larger veins.

A clear distinction must be made between a significant pulse pressure in a vein and a large expansile pulsation. When the pulse pressure is the greatest in the small vein, no expansile pulsation is present. As the change in volume is very small, the pressure recording device must record changes in pressure with a minimal change in volume.

**Table 2.—Large and Small Vein Hematocrits**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Large vein</th>
<th>Small vein</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Hot</td>
</tr>
<tr>
<td>R.H.</td>
<td>41.9</td>
<td>42.3</td>
</tr>
<tr>
<td>L.B.</td>
<td>39.4</td>
<td>40.8</td>
</tr>
<tr>
<td>E.D.</td>
<td>44.1</td>
<td>44.8</td>
</tr>
<tr>
<td>L.H.</td>
<td>38.3</td>
<td>38.3</td>
</tr>
<tr>
<td>C.B.</td>
<td>44.4</td>
<td>46.1</td>
</tr>
<tr>
<td>Avg.</td>
<td>41.8</td>
<td>42.7</td>
</tr>
</tbody>
</table>

Each individual value is the average of 3 or 4 microhematocrits.

The changes in small vein pressure in the cold resulted from the effects of cold on viscosity, arteriolar constriction and constriction of the small veins.

Viscosity of cold blood is greater than that of warm blood. This would raise the pressure. Hematocrit readings on blood taken from the cold hand indicated that hemoconcentration was not an important factor in the change in viscosity (table 2). Arteriolar and venous constrictions occurred during the first part of cooling as shown by the slight fall in venous pressure and by the absence of a pressure pulse in the veins, which could easily be seen to have constricted. As cooling continued, venous pulse pressure returned and later the venous pressure began to rise.

The decrease in venous pressure and the absence of pulse in the small veins during the first 5 min. of cold is the result of arteriolar constriction caused by the cold. As reported by others, constriction of arteries of the fingers becomes less intense on continued exposure to cold as blood flow increases. This is reflected in our subjects by a return of pulse pressure in the small vein. It is of interest that at this stage the pressure in the small vein has only begun to rise, although on inspection the veins are markedly constricted. It appears likely that the blood normally returning from the finger by way of the catheterized vein, or by superficial veins of the same size, no longer flows in such superficial veins because it is blocked by the intense vasoconstriction in them. The arterial inflow leaves the finger through deeper, less cool and less constricted veins and therefore high pressures cannot build up in the superficial vein. As the cold penetrates and the deep veins finally constrict, there is no way for blood entering the finger to leave it until the pressure is high enough to overcome the now generalized increase in small vein constriction. When this occurs, small vein pressures reach great heights.

The pulse pressure in the small veins and in the large veins cannot be reflected back from the large veins because it is present when the veins in the arm are obstructed by a venous cuff. As the arm fills below the ob-
structing venous cuff, the pressure waves increase in size. The venous pressure waves must be related to the arterial pressure waves either by direct transmission through the capillaries or by transmission through the tissues. Haddy et al.1 were unable to demonstrate transmission through tissues by placing catheters covered with thin rubber diaphragms in the tissue near the small vein. While it might be possible for transient, sharp pulses to be registered in the veins through the tissues, a sustained rise or fall in pressure in the small veins which did not occur in the large veins must be transmitted through the blood vessels. If the arterial pressure initially increased, the veins might show the very initial rise but would then empty and reflect no sustained alteration. Figure 3 shows a sustained rise in radial arterial and small vein pressures during a 25-sec. Valsalva maneuver. The large vein pressure is at all times less than the small vein pressure. Each directional change of arterial pressure is mirrored in the small vein. The pressure appears to be transmitted directly from artery through blood vessels to the vein.

The extent of pulse pressure present in a vein depends upon the state of the vessels between artery and recording vein and upon the rigidity of the venous system when the arterial pulse wave arrives. When the elasticity of the system is reduced by a venous cuff, by norepinephrine, or by cold, the arterial pressure wave is better transmitted to the vein. With a sensitive recording system, the arterial pressure wave is usually detectable in most small veins and in many forearm veins. These normal venous pulse waves are probably also conducted through blood vessels, there being no reason to believe that their origin is different from those seen in the cold.

Summary

Pressure recordings were made from catheters placed in a small vein near the web of the fingers, in a large forearm vein, and in the radial artery.

In normal seated subjects, the small vein pressure averaged 2.6 mm. greater than the large vein pressure. Norepinephrine infusions raised the average small vein pressure from 11.8 to 16.0 mm. Hg and the large vein pressure from 9.2 to 10.1 mm. Hg. Placing the hand and forearm in cold water (8 to 12 C) caused a striking rise in pressure in the small vein (up to 50 mm. Hg) and a small rise in large vein pressure. The small vein pulse pressure reached a level of 5 to 8 mm. Hg and during the Valsalva maneuver the small vein pressure followed that in the artery instead of the large vein pressure which retained its venous character.

These studies show that change in small vein pressure occurring without corresponding changes in large vein pressure may be of sufficient magnitude to affect capillary pressure and the drainage of blood from the skin. They extend the observations of Haddy and Visscher in the dog to the veins of man.

Summario in Interlingua

Registrationes de pression esseva obtenite ab catheteres placitate in un vena minor presso al membrana interdigital, in un grande vena del antebrazio, e in le arteria radial.

In subjectos normal in position sedente, le pression del vena minor excedeva le pression del vena major per un valor medie de 2,6 mm. Infusiones de norepinephrina augmentava le pression in le vena minor ab un valor medie de 11,8 a un valor medie de 16,0 mm de Hg e le pression in le vena major ab un valor medie de 9,2 a un valor medie de 10,1 mm de Hg. Le immersion del mano e del antebrazio in aqua frigide (8 a 12 C) causava un augmento frappante del pression in le vena minor (amontante a usque a 50 mm de Hg) e solmente un parve augmento del pression in le vena major. Le pression de pulso in le parve vena attingeva un nivello de 5 a 8 mm de Hg, e durante le manovra de Valsalva illo sequava le reaction trovate in le arteria e non le reaction trovate in le grande vena que reteneva su character venose.

Iste studios monstra que alterationes del pression in venas minor, occurrente sin alteraciones correspondente in le pression del venas major, pote esser sufficientemente grande pro afficer le pression capillari e assi le drainage de sanguine ab le pelle. Le studios extende le
observationes de Haddy e Visscher, qui laborava con canes, al venas del homine.

REFERENCES


Spontaneous Pressure Elevations in Small Veins and Effects of Norepinephrine and Cold
JOHN M. WALLACE and EUGENE A. STEAD, JR.

Circ Res. 1957;5:650-656
doi: 10.1161/01.RES.5.6.650

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1957 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/5/6/650

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/