Hemodynamics of Large and Small Vessels in Peripheral Vascular Disease

By Margaret C. Conrad, Ph.D., and Harold D. Green, M.D.

In this study, an attempt has been made to evaluate differentially the hemodynamics of the large artery, small artery, and venous segments of the peripheral circulation in normal persons and in patients with peripheral vascular disease. When only gross evaluations of flow are made, it is impossible to pinpoint the mechanism causing the observed deficiency. A more thorough knowledge of the basic mechanisms and their control is essential if the treatment of vascular disease is to be made more effective.

Method

The studies were carried out on 11 asymptomatic medical students; on 14 patients with vasospastic disease exhibiting intermittent color changes on exposure to cold; and on 24 patients with large-artery occlusion, as evidenced by intermittent claudication, absent pulsations, and arteriographic evidence of complete occlusion. Patients in whom only narrowing of the vessel had been observed have not been included. The report is confined to studies on lower extremities.

The subjects were placed supine in a constant-temperature room maintained at 20 ± 0.2 C., with humidity averaging 50 per cent and an airflow of 0.3 M./sec. The torso and proximal portions of the extremities were covered with a blanket and warmed with two 150-watt heating pads while the distal portions of the extremities were exposed to the room air.

Studies were made after the patient had equilibrated with the room temperature and were repeated at equilibration following vaso-

dilatation with two doses of 60 ml each of 86-proof alcohol orally. Emotional stimuli were reduced by allowing the patient to watch television during the period of study.

Digital flow was measured with an air-filled plethysmographic cup, sealed to the digit with plethysmoseal and connected to a venous-type Statham pressure transducer. The signal was amplified with a Honeywell carrier amplifier and recorded on a Visicorder; the system provided the high sensitivity and frequency response necessary for accurate reproduction of pulses. Venous occlusion was accomplished by means of a 1-cm. wide cuff of rubber tubing, which was backed with adhesive tape and secured around the digit just proximal to the cup by means of Velcro fastener tape. All studies were performed on the second toe. The volume included in the plethysmograph ranged from 2.5 to 5.0 ml; the flows are expressed on the basis of a digital volume of 5 ml. The accuracy of the plethysmographic method was evaluated earlier in this laboratory by comparison of flow rates obtained plethysmographically with those obtained with the electromagnetic flowmeter. The volume pulse was recorded at a high sensitivity, and the gain was lowered for recording flow. In each study several

![Figure 1](http://circ.ahajournals.org/content/29/3/847/F1.large.jpg)

**Figure 1**

a. Measurement of digital systolic arterial pressure by recording digital volume (ordinate) vs. declining cuff pressure (abscissa). Increase in digital volume indicates cuff pressure equals systolic pressure. b. Measurement of velocity of pulse transmission. Pulse velocity = time delay between leg and toe pulse (measured trough-to-trough) divided into distance between points of measurement.

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occlusion pressures were tried until a pressure that resulted in the greatest rate of volume increase was found; this pressure was used for the remainder of the study. Each recorded value for flow represents an average of several consecutive measurements.

The digital flow-to-pulse ratio was calculated by dividing the flow in ml./min. by the pulse amplitude in ml. In a preliminary study by the authors and in a previous study by Winsor, the magnitude of the flow/pulse ratio was found to reflect the extent of collateral circulation.

Digital artery systolic pressure was estimated by sudden inflation of the occlusion cuff to 200 mm. Hg followed by reduction of the pressure by 10 mm. Hg decrements until blood flowed beneath the cuff as evidenced by an increase in digital volume (fig. 1a); this technic is similar to that described by Winsor. In most cases an estimate of diastolic pressure also could be obtained by noting the pressure at which the maximal pulse amplitude was attained. The pressure drop in the large vessels was estimated by subtracting digital artery systolic pressure from brachial artery systolic pressure. Small-vessel resistance was estimated by dividing digital artery pressure by digital blood flow and was expressed as PRU.

The distensibility of the capacity vessels of the digit was evaluated by Burton's method of increasing the pressure in the occlusion cuff by increments and noting the resulting increment in volume (fig. 2). The slope of the early part of the curve was used rather than the total volume increase, since the resting volume upon which the plateau volume was superimposed was unknown. The intercept of the volume curve with the pressure axis was used as an estimate of venous pressure, i.e., the lowest pressure at which outflow was impeded. With dependency this intercept was found to move higher on the pressure axis in an amount equal to the change in length of the hydrostatic column.

An impedance plethysmograph (Parks Electronics) was utilized for recording the volume pulse in the proximal part of the extremity. The trough-to-trough pulse velocity was measured from the distance between the impedance electrodes and the digital cup divided by the time delay between the simultaneously recorded proximal and digital pulse (fig. 1b) and was expressed in meters per second.

Results

Flows

In the normal persons in the control state, the flows varied widely between subjects (fig. 3a). The flows consistently increased after alcohol (average 250 per cent of control) though the results were still quite variable. With vasospasm, flows were decreased markedly in the control state; though there was an increase after alcohol to 650 per cent of control, normal values usually were not attained. The control flows with arterial occlusion were not so low as with vasospasm but on the average increased to only 190 per cent of control after ingestion of alcohol.

Pulse Amplitude

In the normal subjects the pulse amplitude varied considerably in the control state and almost doubled after ingesting alcohol (fig. 3b). The pulse amplitude was extremely low in vasospasm and increased six-fold with alco-
Flow/pulse ratio in the digit. Ordinate scale, ratio of flow in ml./min./5 ml. of digit to pulse amplitude expressed as ml./5 ml. of digit; Abscissal scale, flow in ml./min./5 ml. of digit. Circles indicate studies after alcohol and arrows show change with alcohol.

<table>
<thead>
<tr>
<th>Normal</th>
<th>Vasospasm</th>
<th>Art. Occ.</th>
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<tbody>
<tr>
<td>C</td>
<td>D</td>
<td>C</td>
</tr>
<tr>
<td>Mean ratio</td>
<td>128 184 115 140 396 550</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>12 17 10 30 73 91</td>
<td></td>
</tr>
<tr>
<td>Per cent of control</td>
<td>144 122 139</td>
<td></td>
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</tbody>
</table>

C, control; D, dilated state.

Flow/Pulse Ratios

The ratio of flow to pulse was essentially normal in patients with vasospasm but was markedly elevated in patients with arterial occlusion (fig. 4). In all three groups the flow/pulse ratio increased to 120 to 140 per cent of control following alcohol; the increase per unit increase in flow was greater in patients with occlusive disease (fig. 4).

Pulse Contours

The normal pulse rose rapidly to a peak at about 24 per cent of the cycle length after the trough and developed a dicrotic notch about the midpoint of the cycle (fig. 5). With vasospasm the peak was slightly but significantly delayed (28 per cent of the cycle length) and the notch occurred higher on the descending limb but stayed at about the midpoint in the cycle. In the presence of arterial occlusion the peak was greatly delayed (40 per cent of the cycle length) and rounded and the dicrotic notch was absent. There was no significant change in any of the above with alcohol.

Small-Vessel Resistance

In the normal subject the resistance was moderately high in the control state (600 PRU) and decreased to about one third of this value after alcohol (fig. 6). The resistance to flow in the small vessels was markedly elevated in patients with vasospasm in the control state and decreased with alcohol, though not to normal levels. Although with arterial occlusion the small-vessel resistance was also greater than normal, it was suspected that some of the increased resistance could be due to secondary occlusion of the digital vessels rather than to increased vascular tone.

Small-vessel resistance. Resistance expressed in PRU = mm. Hg/ml./min. calculated for 5 ml. digital volume. Numbers equal per cent of control.

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As a first approximation of the presence of small-vessel occlusion, the patients with ulcerations of the digits were separated from those without ulcers and the values for small-vessel resistance were compared in the two groups. The resistance of those with ulceration and probably small-vessel occlusion was quite variable and was greater than normal. The resistance of those without ulceration and probably minimal small-vessel occlusion was not significantly different from normal in the control state though it did not decrease as much as the normal with alcohol.

**Distensibility**

The distensibility of the capacity vessels did not change significantly following oral alcohol in the normal individuals (fig. 7). With vasospasm the distensibility was far below normal in the control state; following dilation with alcohol the distensibility rose but did not return to normal levels. The distensibility of the capacity vessels in general varied reciprocally with digital small-vessel resistance (fig. 8).

**Large-Artery Pressure Drop**

In the large vessels of the normal lower extremity there was essentially no measurable pressure drop (fig. 9a). With arterial occlusion there was a marked pressure drop of the order reported by Winsor, who used a similar method of measurement but placed the occlusion cuff on the leg just proximal and distal to the site of occlusion. The change with alcohol was not statistically significant, but in individual cases the pressure differential increased as the digital flow rose and digital artery pressure fell. In patients with vasospastic disease a significant pressure drop was noted in the large vessels; however, this was smaller than that noted with occlusive disease. In contrast to the patients with occlusive disease, the patients with vasospasm demonstrated a decrease in the large-artery pressure drop and a rise in the digital artery pressure following alcohol.

**Pulse Velocity**

The velocity of pulse transmission in arterial occlusive disease was lower than normal and did not change significantly with alcohol (fig. 9b). With vasospasm, the velocity was less than the normal in the control state but rose to normal limits after dilation with oral alcohol.

**Discussion**

**The Normal Circulation**

The most striking observation in the normal medical students was the extreme variability of the results. Under controlled conditions of

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**Figure 7**

Distensibility of capacity vessels. Distensibility = tangent of plot of volume vs. cuff pressure as defined in figure 2. Numbers equal per cent of control.

**Figure 8**

Relationship between small-vessel resistance and distensibility. Arrows show change with alcohol.
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Figure 9

a. Pressure drop in the large vessels of lower extremity. Pressure drop = brachial artery systolic pressure minus digital artery systolic pressure. Numbers equal per cent of control. b. Effect of vascular disease on the velocity of pulse transmission (see legend for fig. 1). Pulse velocity = delay between leg and toe pulses divided into distance between points of measurement.

temperature and air velocity, and with at least an attempt to control emotional level, the control flows varied 27-fold between individuals in the control state and six-fold in the dilated state. Due to this variability, other factors were essential to determine if the circulation were actually "normal." The fact that the flow could increase in response to alcohol was one indication of a healthy vascular system. The lack of change in pulse velocity and pressure drop in the large vessels with alcohol suggests that the resulting increase in flow is not due to changes in the large arteries. Since the distensibility of the capacity vessels was unchanged, the differences in flow between the control and dilated states must have been primarily the result of changes in arteriolar tone.

Arterial Occlusive Disease

All the patients with arterial occlusion had complete blockage of the artery; therefore, the blood supply had to be through collateral channels, which resulted in a narrowing of the flow channel and an elongation of the flow path. This would present a higher resistance to the d.c. or steady state component of flow and account for the large brachial-to-digital artery pressure drop. These changes also would induce a damping effect on the a.c. or pulsatile component of the flow as evidenced by the decreased amplitude and rounded contour of the pulse. The elevated flow-to-pulse ratio suggests that the collateral vessels suppressed the pulsatile component of flow more than the steady-state component.

The decreased velocity of pulse transmission could be due to a passively increased distensibility of the vessels, such as might be expected to occur with the lower intraluminal pressure occurring below the site of occlusion, as well as to the longer path of the collateral channels.

The greater-than-normal small-vessel resistance observed in patients with arterial occlusion, particularly after the administration of alcohol, could be due to the presence of occlusive disease in the small vessels or to the relatively low head of pressure in the digital artery, which tends to result in a proportionally higher resistance at a given level of vasomotor tone. The higher resistance in the patients with ulceration than in those without suggests that at least some of this increased resistance is due to organic obstruction of small vessels.

The low flows present with occlusive disease appear to be mainly the result of the greatly increased large-vessel resistance. The small increase in flow with alcohol follows the changes in small-vessel resistance and distensibility. The absence of change in pulse velocity and large-vessel pressure drop following alcohol suggests that the collateral vessels do not dilate in response to the vasodilator stimulus.

Vasospasm

The most striking observations in vasospasm are (1) the extremely low control flows; (2) the excessively high small-vessel resistance, in both the control and dilated state as compared with both the normal subjects and those with occlusion without ulcers; (3) the low distensibility as compared with both normal subjects and patients with occlusive disease; (4) the relatively high pressure drop in the large arteries; and (5) the prolonged pulse transmission time, as compared with the normal subjects. Another striking difference was the

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marked change in all measured factors following alcohol.

The low flows in the control state and the failure of the flows to rise to normal in the dilated state appear to be due to elevated large- and small-artery resistances as compared to the normal. The decreased distensibility of the capacity vessels in vasospasm suggests that these vessels also contribute to the reduction in flow and can be relaxed with dilator procedures in a magnitude comparable to the decrease in small-vessel resistance. The distensibility did not rise to that of the normal following alcohol. If it can be assumed that the distensibility measurement reflects the behavior of the small vessels downstream from the arterioles, it could be considered that at least part of the persistently high small-vessel resistance is due to enhanced tone of these capacitance vessels.

The greater-than-normal large-vessel pressure drop could be due either to a component of occlusive disease or to persistent spasm of the large vessels. The pulse amplitude, the pulse contour, and changes in pulse velocity appear to us to be more compatible with spasm of the large arteries than with the occurrence of organic occlusive disease. Evidence that intermediate artery spasm can occur is provided by the studies of Davis and Hamilton and Kelly and Visscher. Thus, patients with vasospasm appear to have constriction of large vessels, arterioles, and capacitance vessels all of which can be partially but not completely relieved by alcohol. The "Moens-Korteweg equation" indicates that velocity is proportional to \( \left( \frac{E \cdot a}{2n\rho} \right)^{\frac{1}{2}} \). If our data on large-artery pressure drop are correct, it would seem probable that the larger arteries are in a state of partial contraction. Under these circumstances it would be anticipated that the radius (r) would be decreased and the wall thickness (a) would be increased, both of which should lead to an increased velocity of pulse transmission. Since the trough-to-trough velocity decreased, it must be concluded that the elastic coefficient (E) has decreased or that the position of the trough of one pulse has been shifted relative to that in the other pulse owing to some change in the reflected wave.

**Predictability of Flow from Pulse Amplitude**

In view of the frequent use of pulse amplitude as an indicator of flow, we compared the flow predicted from the pulse with the actual flow (fig. 10). These data indicate that even in normal subjects and patients with vasospasm the pulse is not a completely reliable index of flow. In patients with arterial occlusion the predicted flow was less than half of the actual in the control state and only about 30 per cent of the actual after alcohol. Pulse amplitude should be used therefore with caution in assessing the deficit in circulation especially in patients with occlusive peripheral vascular disease.

**Summary**

To evaluate the hemodynamics of large and small vessels in patients with complete arterial occlusion and patients with vasospasm, digital flow, digital pulse contour, small-vessel resistance, flow-to-pulse ratio, large-vessel pressure drop, pulse velocity, and distensibility were compared to values found in normal subjects.

![Figure 10](image_url)

**Figure 10**

Relationship of flow predicted from pulse amplitude to actual flow. In normal control (constricted) subjects the average of the flow/pulse ratios was 128. This value was multiplied by the pulse amplitude for each subject to obtain a predicted value for each digital flow. Data expressed as per cent actual flow and tabulated as average ± one standard error (S). Predicted flows in ml./min. are shown by each bar.
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In the normal subject following orally administered alcohol, small-vessel resistance decreased but large-artery pressure drop, pulse velocity, and distensibility of the capacity vessels were not altered significantly.

In arterial occlusive disease, small-vessel resistance was essentially normal in the absence of small-vessel occlusion; a high large-artery pressure drop, rounded pulse contour, and decreased pulse amplitude were observed. These are interpreted as being due to the damping effect of the narrowed, elongated collateral flow pathway that develops around the site of the occlusion. Pulse velocity also was decreased whereas flow-to-pulse ratio was increased in patients with occlusive disease. Large-vessel hemodynamics were unchanged after alcohol, suggesting lack of effect of the dilator on the collateral vessels.

In vasospasm there was evidence of increased large-artery and small-vessel resistance and decreased distensibility of the capacity vessels, all of which returned toward but not completely to normal following alcohol.

Digital pulse amplitude was found not to correlate well with flow, particularly in patients with arterial occlusive disease.

References

Of Surgery

The province of surgery is totally separated from the physician; some little acquaintance with the modern practice of it is all he needs desire. It may perhaps be of use to the surgeon to look back into the ancient writers (tho' it is probable that the common practice & the modern books preserve all their useful inventions and knowledge) but to physicians, at least to a beginner it can hardly be worth while to enquire after what were written a century or two ago.—WILLIAM HEBERDEN. An Introduction to the Study of Physic. New York, Paul B. Hoeber, Inc., 1929, p. 114.
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