Local Postural Vasomotor Reflexes Arising from the Limb Veins

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Blood flow of the toes and fingers was studied plethysmographically with the level of the blood vessels below or above the heart, using the contralateral digit as control. The apparent flow is a maximum when the vessels are near the heart level. The decrease of flow when the vessels are raised is explained on the basis of narrowing and closure of vessels when the hydrostatic pressure within them falls. The decrease in flow when the limb is lowered is interpreted as evidence of a vasoconstriction elicited by distension of the local veins. This raises serious doubt about the classic flow method.

Since the discovery in 1926 by Heymans of the “buffer” reflexes from the carotid sinus and aortic regions, there has been little search for vasomotor reflexes concerned in adjustments to posture that might arise from other receptor areas. Yet it is hard to see how the classic carotid sinus reflexes could be adequate in all of the usual circumstances of postural changes. These reflexes are elicited by a change of the central blood pressure, so that only when change of posture is sufficient to produce this can they operate. Again their effector mechanism, since it is mediated mainly by the sympathetic vasconstrictor system, gives essentially a diffuse mass reaction, not adapted to produce compensatory changes in individual limbs according to the posture of that limb.

The experiments that have convinced us that additional local vasomotor reflexes exist in the limbs were originally undertaken with another object in view. In the last few years, research in this laboratory has shown that peripheral vascular beds when under vasomotor tone display an intrinsic instability. If the pressure within certain small vessels (probably the arterioles or precapillary sphincters) falls below a certain limiting level, called by us the “critical closing pressure” (c.c.p.), flow will cease altogether indicating that these vessels have closed. Under high vasomotor tone this c.c.p. can be as high or higher than the available blood pressure (the vessels are in “spasm”). By an indirect method, the same has been shown for the vessels of the human arm and for the finger (unpublished). Our attempt to show critical closure in the forearm by the seemingly more direct method of arterial catheterization and recording of the fall of pressure when the artery was suddenly cut off from above by an occlusion cuff failed for two reasons. First, without the use of local anesthetic, the artery often went into spasm extending above the point of the catheter, and with anesthetic the vasomotor tone we wished to measure was probably destroyed. Secondly, even the most rapid inflation of the cuff resulted in a rise of venous pressure to unexpected heights, and this was evidently influencing the results.

It occurred to one of us (P.G.) that simply by raising the level of a limb above the heart, and so lowering the pressures in all of the vessels within it, evidence of critical closure of these vessels might be obtained without these complications. Accordingly a study of the changes of blood flow with posture of the limb have been made. While the effects of raising the limb have indeed given the desired evidence of critical closure, those of lowering the limb have shown that there are important vasomotor reflexes (or at any rate, increases in peripheral resistance) elicited by distension of the local veins.
PREVIOUS EVIDENCE OF SUCH REFLEXES

Recently Girling found, in the hind limb of rabbits, that the c.c.p. of that limb increased when the venous pressure was raised, and that this effect was abolished if the anesthesia was sufficiently deep. This seems clear evidence of a local reflex, arising from distension of the veins and causing an increased tone in the arterioles or capillaries. However, a careful search of the relevant literature shows that though some authors hint at such a reflex, none seem to present definite evidence. The results on the change of blood flow of a limb or digit with posture are most contradictory and confusing, mostly because of the many different methods of measurement used as an index of flow. Abramson and colleagues specifically describe a reflex constriction in a dependent limb, but do not interpret it as elicited by distension of the veins. We conclude that there is still much need for clear evidence on the existence of local "veni-vasomotor reflexes," which are certainly suggested by the clinical findings of arterial spasm in phlebitis.

METHOD

Postural vasomotor reflexes might be expected to be more developed in man than in animals that do not assume the erect posture, and the depression of such reflexes by anesthesia can be more easily avoided in human experiments. For our purpose it was obviously better to change the level of one limb only, and to use simultaneous observations of flow and pulsation of the contralateral limb as a "control" that would indicate which of the changes seen were central in origin, which local. (It is well known that central vasomotor reflexes, in general, are widespread and diffuse in their effects, so that they are seen in both limbs.) As to the choice between the arms and the legs, the latter seemed to be likely on teleologic grounds, to show the anticipated reflexes more strongly, as well as allowing greater changes of level of the extremities. Of the blood vessels of the legs, those of the toes were the greatest vasomotor control. Plethysmography of the toes was therefore chosen, but a few experiments were similarly made on fingers.

The plethysmographs were light cans of phosphor-bronze, enclosing the last phalanx of the big toe, to which they were sealed by a coating of thin rubber cement, applied under, as well as over, a wrapping of adhesive tape. The cans were supported freely by the toes, with their outlets connected by "Tigon" plastic tubing, the distensibility of which is desirable low, to the volume recorders. These were of the type already described, in which the deflection of a mirror on the edge of a thin rubber membrane was recorded on a photokymograph. For the venous occlusion, cuffs were made from surgical drainage tubing, backed with adhesive tape, exactly as described for the finger. These were wrapped round the adjacent phalanx of the toe, or finger. They were inflated suddenly from a large pressure bottle, with pressures usually from 20 to 70 mm. Hg. When one leg was above the other, the pressure used in the cuff was lowered by the equivalent hydrostatic head, but a variety of occlusion pressures was used in all cases to be sure that they were adequate.

Flow measurements on the toes proved to be no more difficult than on the fingers, though it became obvious that the pressures in the occluding cuff on the toe, below the plethysmograph, were in some cases not so well transmitted to the tissues as in the case of the fingers, where there is room for a wider cuff. The only other measurements of flow in the toes with which we are acquainted are those of Goetz, but since his "collecting cuff" was above the ankle, we felt that the changes in volume upon venous occlusion can hardly be interpreted as direct measures of flow in the toe. Flow measurements could be made in succession at intervals of about 10 seconds.

The experiments were made in an air-conditioned room of constant temperature, controlled between 70 and 85 F. The air movement was high so that with this range subjects could be kept in a cold, vasoconstricted, or a warm, vasodilated state. They lay on a special form of tilt-table which allowed each leg to be raised or lowered independently. The angle of the trunk could also be adjusted. Changes of posture could be effected rapidly and smoothly since the apparatus was controlled by ropes and pulleys rather than by the usual clamps and wheels of the conventional tilt-table. Observations were made on five normal subjects, and one patient (Buerger's disease) with unilateral sympathectomy.

RESULTS

Preliminary Experiments on Effects of Posture on Flow

Figure 1 shows the results of an experiment in which the flow in the toe was measured with that leg at different angles to the horizontal, with rapid changes of angle between each period in a given posture. The characteristic ex-
treme fluctuation of digital flow from moment to moment is seen. Such experiments showed clearly that the maximum flow occurred when the leg was near the horizontal, or, from records taken during the transitions of posture, when slightly above the horizontal. The flow decreased markedly when the leg was raised, and fell to values that were apparently negative when it was lowered. In the latter case the records of flow showed obvious differences from the normal changes of volume upon venous occlusion. These changes are discussed in the next section.

Because of the possibility that the changes in apparent flow seen were general rather than local and due to central vasomotor reflexes elicited by changes in blood pressure, the size of the volume pulsation of the toe in the contralateral leg was then simultaneously recorded, and a greater series of angles of posture were used (fig. 2). Again the experiments showed a maximum flow in the toe when the leg was raised slightly above the horizontal and a progressive decrease at angles above or below this optimum angle. The apparently "negative" flows when the leg was lowered were again recorded. The size of the pulsation on the control toe remained within normal limits, indicating only slight, if any, changes that could be attributed to central reflexes. The pulsation in the test toe, on the contrary, changed very markedly, and obviously the correlation between changes in flow and in volume pulsation seen in the horizontal position no longer held, for the maximum pulsation was at a different posture of the leg from the maximum flow. This lack of correlation between pulsation and flow is examined in more detail later. It was apparent, because of this, that we would have to make simultaneous measurements of flow on the toes of both legs, and this was done in all subsequent experiments. Figure 3 illustrates the change in flow in the control toe which could be attributed to carotid sinus reflexes or to incidental changes in the physiologic state of the subject during a long experiment (sensations of warmth or cold, etc.). However, a comparison of the flow in test and

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**Fig. 1.** Apparent blood flow (plethysmographically) of the big toe in different postures of the leg. The rest of the body remained horizontal. The open circles at −30 degrees tilt indicate corrected flows, as discussed in the text.

**Fig. 2.** (Upper graph) Blood flow of the toe in different postures of the test leg. (Lower graph) Simultaneous sizes of volume pulsation in the test toe (solid dots and continuous line) and in the control, level, toe (crosses and broken line). The open circles in upper graph represent corrected flows when the apparent flows were negative (see text).

**Fig. 3.** Simultaneous apparent flows in test leg (solid line) in different postures and the control leg (broken line) always horizontal.
control toes at a given time and in a given posture clearly showed the same relative changes in the test leg as had the simpler experiments. While there was nothing in the records of flow when the leg was raised to cause doubts as to the validity of the method, the appearance of the records when the leg was down, and the apparently negative flows, raised grave doubts and suggested a careful examination.

Changes in the Flow Records When the Leg is Lowered

The form of the record of the volume of a digit, when the venous outflow is momentarily stopped by inflation of a cuff, is very well-known. The components are shown diagrammatically in figure 4A. These are (a) the "cuff artefact," a sudden rise of volume due to pushing of tissue into the plethysmograph, (b) the "collection phase," in which the volume increases at an initial rate which is the rate of arterial inflow into the digit (the outflow being zero initially), (c) the phase of diminished collection, in which the slope of the curve becomes progressively less. This is because the inflow decreases as the arterial-to-venous pressure gradient is now less, and also because as the venous pressure rises some blood begins to escape past the cuff. This leads to (d) the "steady state" in which the volume remains constant, since now the outflow past the cuff has become equal to the diminished inflow. Upon release of the cuff pressure, there is first an abrupt reversed artefact (e), followed by the "emptying phase" (f) as the blood dammed up in the digit rapidly empties into the veins. The curve of emptying is normally exponential-like, to the original level of volume. The various phases are nearly always distinguishable, though modified by the rate of blood-flow at the moment when the measurement is made. When flow is low the curve of collection decreases in slope only slowly, and it may take many heart-beats before the "venous reservoir" is filled and the steady state is reached. When the flow is high, or the venous reservoir is quickly filled because the venous pressure is higher, the curve of collection may become horizontal very quickly, and only one or two beats are required before the steady state is reached. In such cases it becomes very difficult to obtain the initial slope with any degree of accuracy, and this demands careful analysis of the shape of the cardiac pulse-volume changes at the moment of occlusion.

All this has been noted by the many workers who have measured the blood flow of the fingers. Our records of the flow in the toes or fingers when they were level with, or above the heart level, showed the usual features (lower records of the pairs in figure 5). However, when the toe was lowered below this level, a striking new feature of the curves appeared (fig. 4B and upper records of fig. 5) in the emptying phase. The drop in volume was very abrupt and the curve fell below the original baseline (f). This was followed by a slower rise of volume (g) to the baseline. Examples of this "after-drop" and subsequent increase in volume are shown in the upper records of the pairs of figure 5.

This after-drop and subsequent recovery appeared regularly when the test leg was at an angle of 15 degrees below the horizontal, after a lag of one or two minutes. At an angle of −30 degrees it occurred after a shorter lag, and was much more marked. The phenomenon was more marked when the subjects were warm, and the blood flow was higher, than when they...
were cold and constricted, in which case it did not appear until the leg was at -30 degrees.

The initial slope of the collecting phase was lower than that in the control toe, and often the curve of collection differed from the usual shape showing an initial low rate of rise which increased later. Where the flow, in both legs, was low because the subject was constricted, the initial slope in the curve for the test toe, in which the phenomenon of after-drop was present, was often actually downwards (fig. 5C). By the usual interpretation this would indicate a negative rate of arterial inflow. The astonishing fact is, that in these cases, the damming back of the venous outflow by the inflation of a cuff to pressures much less than diastolic (it can be seen with as little as 20 mm Hg cuff pressure) results in a net decrease in volume of the toe. We can see no explanation for these phenomena except that the inflation of the cuff caused a constriction of the vessels of the toe, and that the slope of the curve of collection in the measurements of flow, at least when the toe is below the level of the heart, represents the algebraic sum of the actual collection in the veins and the decrease of the blood vessels by this reflex constriction. (Many examples of these paradoxic negative flows are seen in figures 6 and 7.)

Dependence of the Phenomena upon Venous Distension

It is easy to show that the phenomena just described are elicited by the filling of the veins when outflow of the digit is prevented by the occlusion cuff, for exactly the same abnormal features of the flow curves are seen if, instead of lowering the leg, the venous pressure be raised by a pressure in a cuff at the ankle before the flow measurement, with the leg still horizontal. The slow development of the signs of reflex vasoconstriction during the flow.
measurement agrees with the time taken for the veins to become full. Again, instead of using a cuff to raise the level of the venous pressure, the subject may sit up (fig. 6), when identical changes are seen. When the subject lies down again the flow curves become normal, but often (as in fig. 6) not until the leg veins have been drained by raising the leg for a few moments and replacing it in the horizontal position. Using the finger instead of the toe, so that there was room for a second cuff behind that used for the flow measurement on the proximal phalanx, it could be shown that these changes could be elicited from the small veins in the finger (fig. 7). The changes in shape of the flow curves when the finger was raised or lowered could be exactly imitated by leaving it level and raising the venous pressure by means of the second cuff (fig. 7).

Evidences of Reflex Vasoconstriction from Volume Changes

While the evidence so far cited shows that the reflex vasoconstriction is present during a flow measurement, when the veins are filled, study of the volume changes of the toe during change of the posture of the leg clearly indicated that the reflex vasoconstriction occurs, without the added venous occlusion of the collecting cuff.

It is well-known that when the whole foot, leg, hand or arm is included in a plethysmograph, lowering the limb results in a large permanent increase in volume, undoubtedly due to the filling of the veins by the increased local venous pressure. In the case of the toe we found that there were large transitory increases in volume when it was lowered, and decreases when it was raised, but that the volume returned to close to the original base line very quickly (fig. 8C and D). Examination of the records showed clear evidence of a compensatory vasoconstriction, when the leg was lowered, and a dilation when it was raised. Sometimes these reflex effects were clearly seen separate from the volume changes due to the filling or draining of the veins, sometimes they were deducible from changes in slope superimposed upon the latter. The evidence is complicated by the presence of the spontaneous waves of change of volume which are always present. Similar compensatory volume changes occurred when the ankle cuff was inflated (fig. 8A and B).

"Apparent" and "Corrected" Flows

Since it was obvious in the dependent digit (figs. 3 and 6) that a reflex decrease of volume had taken place during the measurement, the apparent flows could not represent the undisturbed flow that existed before the moment of venous occlusion. An attempt to calculate
response to the increased steady level of venous pressure in the dependent leg.

Changes in Volume Pulsation and in the Pulse Wave

It is well known that, when the measurements are confined to those made at one level of the digit, there is a very close correlation between the flow determined by the classic method and the size of volume pulsation at the moment before the measurement was made. This has been the basis of the use of the volume pulsation by Goetz and many others as an index of flow or of "vasomotor tone." However, it has been recognized that the pulsation of volume, which presumably comes mostly from the venules and capillaries, depends on a number of factors. First, there is the actual arterial pulse-pressure, secondly the tone of the arterioles determining how much pressure-pulse emerges from them, and thirdly the state of distensibility of the capillaries and veins, which will determine how much volume change occurs in response to the pressure fluctuations. The last factor, of distensibility, is greatly affected by the level of venous pressure. If our conclusions from the work here reported are right, the second factor, that is, the vasomotor tone, is also affected by venous pressure.

It is not surprising then to find that, though the size of volume-pulsation decreases as the digit is lowered, and increases greatly when it is raised above the horizontal, the changes do not parallel the changes in apparent flow, so that the ratio of flow to volume pulsation is very different at different levels of the digit (fig. 2). The maximum volume pulsation occurs usually at a higher level of the toe than the maximum apparent flow, probably because the distensibility continues to increase after the raising of the limb has produced a decrease in the flow.

There are also striking changes in the shape of the pulse curve. Lowering the digit accentuates the dicrotic notch and wave, and raising it causes it to disappear. Again the changes in distensibility and consequent damping of the waves are probably responsible. A change in the pulse-wave velocity is also obvious. When the toes are on the same level, the images from the two membranes on the camera "beat" synchronously. It is most astonishing to see how much that from the higher toe lags behind the other when they are at different levels. The lag is obvious in some of the records shown (fig. 10), though of course a fast camera speed would be necessary to make good measurements on this point.

Because of these changes due to the dependence of the distensibility of the venous vessels upon their fullness, we concluded that the changes in volume-pulsation with posture could not be taken as an index of the changes in vasomotor tone, but they give valuable additional evidence when combined with measurements of flow.

Effects of Raising the Limb

Figure 9 summarizes the experiments on three different subjects by showing the mean flows over three or four minutes at different levels of the toe. Though the flows are characteristically very fluctuating, the averages of so many flows (at least 20 for each) are statistically reliable, especially when compared with the simultaneous values for the control toe of the other foot. The very different levels of flow in the different experiments were produced by changing the temperature of the air-conditioned room, to produce general vasoconstriction or vasodilation.

As the leg is raised above the horizontal with the subject constricted, the apparent flow decreases, until at +45 degrees, or higher for dilated vessels, it becomes zero or very low (fig. 9). There is no evidence here of a "reflex artefact" so that the apparent flows are probably true undisturbed flows, although it would be difficult to prove that, even here, the inflation of the cuff was not eliciting a vasoconstriction during the measurement. However the veins are completely empty before the measurement, so that if the reflex constriction occurs, it will be delayed until they have filled, and is not likely to affect the initial slope of the flow curves. These curves often show a very abrupt reaching of the steady state level in which the volume does not change further, and the presence of the later reflex constriction may be responsible for this. We consider that when the
leg is raised above 15 degrees the apparent flows can be taken as true undisturbed flows.

The eventual decrease in flow on elevation would be expected if the vessels which control the resistance to flow are distensible, for the pressure in all the vessels is reduced by the hydrostatic factor. However, the fact that, especially when the subjects were in vasoconstriction (cold), the flow becomes zero when the absolute pressure in the elevated toe is still far from zero, is confirmation of the existence of a critical closing pressure of considerable magnitude. The decrease in flow with elevation was more marked the lower the levels of flow, (the greater the vasomotor tone), and the decrease was then evident at much lower elevations. At elevation where the flow was zero or nearly so, the phenomena of negative flows were often seen. We believe their origin here is quite different from the negative apparent flows seen when the toe is lowered, which are due to the reflex constriction. Here they are probably evidence that the vessels which are closing are pushing blood back up the arteries as they close, when the arterial pressure is slightly lowered by the inflation of the venous occlusion cuff. The phenomena have been noted by us in the case of isolated perfused preparations (as in the frog’s leg) when the pressure is lowered below the critical closing pressure, and in the human arm when the transmural pressure is reduced below the critical value.

Dissociation of the Spontaneous Changes of Flow and Pulsation

Previous curves of the relation between pressure and flow in vascular beds obtained by us have shown that when the critical closing pressure is approached, the flow becomes very markedly dependent on the perfusion pressure (the slope of flow vs. pressure is very steep). Unexpected confirmation of this was seen in these experiments.

![Diagram of flow and pulsation](image-url)

FIG. 10. Simultaneous records of the volume of the big toes. A and B, both legs level, showing the close positive correlation of the spontaneous changes in volume and in volume-pulsation. In C and D the leg of the upper record was raised to +45 degrees and the correlation becomes negative. In E a flow determination made during a spontaneous vasoconstriction shows there is an increase in flow in the toe that is raised.

It is well known that the spontaneous changes in volume pulsation and in flow in the digits are very closely correlated, and in these general vasoconstrictions are accompanied by demonstrable transient rises of heart rate and of blood pressure. However it appears that this close correlation between changes in fingers and toes and between the two toes is not present when one digit is elevated sufficiently above the heart. Figures 8A and B show the close correlation of the volume and pulsation changes in the two big toes when both are level. Figures 8C and D, where one leg is elevated to near the critical level at which flow becomes small, show, in contrast, a com-
plete dissociation of these changes. When a spontaneous vasoconstriction occurs in the level toe, the volume and pulsation in the elevated toe increases, so that the two records are almost mirror images of each other. We were often fortunate enough to be measuring flow in the elevated toe at the moment when a spontaneous vasoconstriction occurred (fig. 10E), and the change of slope in the flow records showed that the flow in the elevated toe increased at this moment.

There can be no doubt that the mass discharge of the sympathetic nervous system which causes these spontaneous vasoconstrictions all over the body, is also sending constrictor impulses to the elevated toe, and increasing the tone of the vessels there. The paradoxical increase in volume pulsation and flow that follows can be explained in terms of critical closure. The vessels, in their critical condition, have become so sensitive to slight increases of blood pressure (due to general vasoconstriction in all the vessels elsewhere) that the effect of this can reverse the effect of the increased tone in these particular vessels. This dissociation of the spontaneous fluctuations is therefore confirmatory evidence that by elevation of the limb the blood vessels of the toe can be brought to the condition of critical closure, and that the decrease in flow in the elevated digit is due to this cause.

Phenomena in a Sympathectomized Limb

The experiment was made upon a patient who, 10 days previously, had had a unilateral lumbar sympathectomy (for the relief of intermittent claudication, presumably from thromboangiitis obliterans or Buerger’s disease. The temperature of the operated side was very high (36 C.) compared with the unoperated side (31 C.). When both legs were level with the heart, the flow of the toe on the sympathectomized side had a mean of 8.2 ml./minute/100 ml. of tissue, and on the unoperated side only 0.4 ml./minute/100 ml. (a very low value). There was therefore evidence that the interruption of the vasoconstrictor fibers was complete.

All the evidences of the venivasomotor reflex were present in the records for the operated side (fig. 9). Lowering the leg to −15 degrees decreased the apparent flow from the mean of 6.1 for the level to 1.1 ml./minute/100 ml., and the after-drop in the records was marked. Elevating this leg to +30 degrees decreased the flow from the level value of 6.1 to 3.6. We therefore conclude that the reflex vasoconstriction does not depend upon an intact sympathetic innervation of the leg.

Discussion

First Principles

It is essential to build upon the right foundation in thinking of the hemodynamic effects of posture. Too often physiologists have, implicitly, based their thinking on the fallacy that, even if we were dealing with a system of rigid tubes, the posture of a limb would affect the flow, so that, for instance, it is harder for the venous return from the legs to flow uphill, back to the heart. Yet it is fundamental, and to be found in the elementary textbooks of Physics, that in a nondistensible system the flow varies only with the pressure difference from the inlet of the system to the outlet, in this case, on the difference between arterial pressure at the heart and venous pressure at that level. This is the principle of the siphon, by which the flow in an oil pipe-line is the same for the same length of pipe, whether this be laid level throughout, over a hill, or down into and up out of a valley.

The first modification of this principle, when we apply it to the circulation, is that the blood vessels are not rigid and are distensible. Their diameter will increase if the hydrostatic pressure within them rises, and this will reduce the resistance to flow. When a leg is down, the pressure in all the vessels is increased; by the hydrostatic factor (gh), and if the vessels are distensible the resistance to flow must, if it changes at all, inevitably decrease in this posture, unless reflex effects supervene. Thus we would expect that, with a constant arterial to venous pressure (at heart level) the steady state blood flow of a leg must increase when the limb is dependent. Of course, there will be transitory changes in outflow during the change of posture, when the inflow will be
POSTURAL VASOMOTOR REFLEXES

absorbed in filling up the distending vessels, but when these are full the outflow will once more equal the inflow, and both should be greater than before, by reason of the decreased resistance of the distended vascular bed. There is no possibility, contrary to the implied suggestion of some authors, that on physical grounds alone the filling up of the veins could offer an increased resistance to flow. Such a view is a perversion of the concept of resistance.

If then, evidence is produced that there is a decrease in flow as the limb is lowered, or an increase as it is raised from the horizontal posture, this can only be explained in terms of reflex effects, either local or general. If, as in our experiments, the changes in flow are not parallel to those in the control, horizontal limb, these reflex effects must be local rather than the familiar central buffer reflexes from the carotid sinus and aortic arch.

Evidence for the Local Veni-vasomotor Reflex

In every case in the experiments here reported, the apparent flow in the digit decreased when the arm or leg was lowered, as compared with the flow in the control digit, which remained level with the heart. When the subjects were warm, the flow was less in the level position than when the limb was raised at an angle of 15 degrees. If, then, the flow measurements were to be relied upon as giving the undis turbed flow, this is unmistakable evidence of a local constrictor reflex. Since the same results are obtained whether the level of the digit be changed, or the subject sits up, or a distant venous occlusion cuff is inflated with a low pressure, the reflex must be elicited by the rise of venous pressure and distention of the veins. The experiments on the finger show that it can be elicited from distention even of the small veins in the proximal phalanx. The time relations of the appearance of the signs of the reflex constriction in the records, when for example, the subject sits up, agree with the hypothesis that filling of the veins, and distention of their walls, is the exciting stimulus.

Validity of the Flow Measurements

However, the startling changes in the form of the records of flow that appear when the veins are full, as when the level of the digit is lowered, clearly indicate that there is a vasoconstriction during the measurement, and that the initial slope of the collection phase cannot represent the undisturbed flow. This must be greater than the apparent flow. When the veins are comparatively empty, as when the digit is level with the heart, the signs of the reflex constriction are not usually obvious (after-drop and subsequent recovery of volume are not seen in the records). However, there is no doubt that the constriction during the measurement is present here also, since raising the level of the limb increases the flow, and this can only be explained as the removal of a constriction which existed in the level position. The curve in a flow measurement is then the resultant of a collection and a simultaneous vasoconstriction, and the curve of recovery after occlusion is the resultant of a sudden escape of the dammed-up blood from the veins and a simultaneous vasodilation. Obviously the resultant curve will not have to show an after-drop unless the time relations and relative magnitude of these opposing factors are favorable, and the lack of after-drop is not evidence that one factor was absent. Careful examination of the recovery phase of the flow records in the level and elevated positions reveals that there is a difference in shape in accordance with the above. We therefore have to conclude that all the flows in the fingers or toes that have been made by a host of workers, at least where the limb was horizontal or below, are under suspicion because the reflex artefact probably was present.

Attempts to correct the flow, where after-drop is seen on the records, are only a first approximation. Upon venous occlusion, the apparent flow may be actually negative, that is, the digit decreases in volume as the direct result of damming-back the venous outflow. We may, if we wish, consider that blood was still flowing from arterioles and capillaries into the veins, but that the decrease in volume by constriction of the arterioles overshadowed this. By adding an estimate of the latter, from the magnitude of the after-drop, we may obtain a rough estimate of the flow into the veins.
(this corrected value was always positive), but obviously the correction is inaccurate.

In view of the unreliability of the apparent and even of the corrected flows in the dependent posture, the question may be asked whether we have any real evidence that the flow in the digit does actually decrease when the level is lowered. The answer is that if the evidence for reflex vasoconstriction due to the distention of the veins, during a flow measurement, or from an increased steady level of venous pressure, be accepted, logic forces us to conclude that the reflex will continuously operate when the limb is lowered. We could find no sign that the reflex was transitory, as the after-drop was just as great after some minutes of venous occlusion as after a few seconds. The undisturbed flows must be greater than the apparent flow, and probably greater than the corrected flows, but we deduce that they will still be less than in the level position. To determine with confidence their actual magnitude, other methods for flow determination (possibly the calorimetric) will have to be used.

**Nature of the Reflex**

It might be suggested that the decrease in volume upon venous occlusion was simply a direct reaction of the veins concerned, in that they responded to a rise of pressure by constricting their lumens. This would be a most paradoxical reflex, though not of course impossible in biology. Observation of superficial veins when the blood flow is dammed-back by the inflation of a cuff certainly does not suggest this. The veins always are seen to become distended. In any case, in our opinion such a constriction of the veins would not produce a marked decrease in flow, since the resistance to flow of the veins is so small a part of the total resistance, which is mainly that of the arterioles. The shape of some of the curves of flow, with an initial decrease followed by the normal increase of collection in the veins, suggests that the two processes are taking place in different parts of the vascular bed. We suggest that the constriction is that of the arterioles, or possibly the capillaries, through nervous connection with receptors in the walls of the veins. The finding by Girling that the critical closing pressure rises would support this view. We might speculate that such receptors are of the stretch receptor type present in the carotid sinus, that have been so well studied recently by Landgren and co-workers, and that they are stimulated by stretch of the venous wall when the vessel is full.

Prof. H. Barcroft has suggested to us (personal communication) that the phenomenon of after-drop might be explained on the basis of the persistence of the increased tone of the veins that have been filled for a few seconds after they have been allowed to empty. This is true, but it would not explain the phenomena of negative flows, in which the volume decreases during the period of venous occlusion.

There is an apparent inconsistency in the observations. The phenomena indicating the reflex constriction are very easily demonstrated when flow measurements are superimposed on veins which are full because of only a slight rise of the level of venous pressure (20 mm. is ample). Yet, if the veins are comparatively empty before a flow measurement, the use of even high pressures of venous occlusion (70 or 80 mm.) does not usually show the characteristic features of after-drop and subsequent vasodilation. We suggest that this is explicable in terms of the known volume-pressure relation in veins. When they are full to begin with, it requires only a little further filling, when the outflow is stopped, to distend them fully so that they strongly resist further distention. Stretch of receptors in the wall would require the addition of only a small volume of blood in the vein. If on the other hand, the veins are comparatively empty, a considerable volume must be collected before this occurs. The time-relations of the collection and the constriction would then be very different in the two cases. Similarly, if upon release of occlusion, the dammed-up venous blood is flowing into veins which are comparatively full, only a small volume will flow out before the level of venous pressure is reached, and the subsequent dilation, in recovery from vasoconstriction, will be obvious. If the venous pressure is low, the outflow will continue longer and be of greater volume, so that it may obscure the vasodilation. We believe, therefore, that the
reflex effects are present, and greater with greater values of venous occlusion pressures in the measurement, even when the veins are originally empty, but that these considerations explain the lack of obvious signs of the reflex in the records. The reflex is a local one. It can be elicited from veins in the digit itself; it is present after sympathectomy, and the latent period of the development of the vasoconstriction and its reversal after release of occlusion is certainly, from study of the records, a fraction of a second. Our guess would be that it must be mediated by nerves in a plexus in the walls of the vessel, but on this we have no evidence.

Evidence of Critical Closing Pressure

While the decrease in flow on lowering the limb is not in accordance with hemodynamic first principles, and requires the postulation of a reflex to explain it, the eventual decrease of flow when the limb is raised high enough, is predicted from the distensibility of the vessels. The absolute, and transmural pressures of all the vessels in the limb will be lowered by the hydrostatic factor, and the tendency will therefore be for them to become smaller in diameter and for the resistance to flow to increase. The cessation of flow when the limb is raised sufficiently represents a closure of the vessels when pressure within them has reached the critical closing pressure. From the level of the toe, the equivalent hydrostatic factor to be subtracted from the blood-pressure (measured at heart level) could be calculated. Even with dilated vessels (subjects warm), a positive pressure remained when flow had ceased, and in constriction, the critical closing pressure so indicated was higher than in dilation. As an example of the calculation, in one experiment on a subject who was moderately warm, the flow in the toe was reduced to zero when the leg was raised at an angle of 45 degrees. The toe was then 72 cm. above the heart, which gives a hydrostatic factor of 53 mm. Hg. The arterial blood pressure was 100/70 at heart level, so that at the toe it must have been 47/17. Yet the vessels closed completely against this pressure, and flow ceased.

When the pressure approaches the critical value, the vessels become very sensitive to changes of blood pressure, as shown by the dissociation of the spontaneous changes in flow between the toe that is level and the one that is elevated. The same paradoxical effect of a general constriction would be expected to occur in a limb where the vasomotor tone was high, even when this was at the level of the heart. The practical implication is that in such a case, where vessels are in the critical condition, the giving of a sympathetic blocking agent may, in certain doses, result in the opposite of what was intended. The dilation of the other vascular beds may lower the blood pressure enough, actually to reduce the flow in a limb that has high vasomotor tone, even though that tone be reduced by the agent.

A previous study (Burton and Yamada) of the critical closing pressure in the human arm, was made by the study of the flow when tissue pressure was raised, so that the transmural pressure of the vessels was reduced. It might be thought that the doubt raised by the present paper as to the validity of the classic methods of measurement of flow would invalidate the conclusions of that work. This is not the case, if, as we conclude, the constrictor reflex is elicited by stretch of the walls of the veins. For the application of a tissue pressure, while it raises the absolute pressure in the veins, actually reduces slightly the transmural pressure, and the veins are under less stretch than normally. While the actual results for flow may be in error, because of the reflex-artefact, the conclusions as to the critical closing pressure should stand.

Conclusions

1. The apparent blood flow of the toe, measured by the classic method of the venous occlusion plethysmograph, decreases as the leg is lowered below heart level, as compared with that of a control toe on the other leg, which is left at heart level. The same is true for the fingers. When the leg is raised to 15 degrees, and the subject is warm the flow increases, but at greater heights the flow decreases. When the subject is in vasoconstriction the maximal apparent flow is at the level of the heart or below.
2. The flow measurements, when the digit is below the heart, are obviously complicated by a vasoconstriction elicited by the inflation of the venous occlusion cuff. The signs of this reflex are obvious whenever the veins are full before the flow measurement. There is no doubt that the reflex exists, and is an artefact when flow measurements are made at heart level, even though the signs of it are not as obvious. The validity of the classic method is seriously in doubt.

3. This veno-vasomotor reflex is local in origin and we think it represents a constriction of the arterioles, or capillaries, of a vascular bed elicited by the distention of the walls of the local veins. The possibility that the effect is entirely due to constriction of the veins when the pressure in them is raised (a myogenic reflex), has not been excluded, but this appears unlikely to explain the observed decreases in flow nor some of the other phenomena observed. The reflex is present after sympathectomy.

4. When the digit is raised to greater levels above the heart, the flow decreases and reaches zero at a level where the hydrostatic factor is still insufficient to reduce the mean arterial blood pressure in the toe to zero; that is, the critical closing pressure can be estimated in this way. The critical closing pressure is higher when the subject is cold.

5. The interaction between this local veno-vasomotor reflex and the effects of absolute hydrostatic pressure in the vessels (critical closure) is responsible for the maximum flow when the digit is at or above heart level. The local veno-vasomotor reflex supplements the central buffer reflexes in controlling the blood flow, in changes of posture of individual limbs of the body.

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Local Postural Vasomotor Reflexes Arising from the Limb Veins
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