SUMMARY  Instantaneous femoral artery pressure-flow (P/Q) relations were evaluated in consecutive 50-msec intervals of the pulseless flow changes during cardiac arrest in six anesthetized dogs and in two anesthetized dogs with α-adrenergic blockade. In all 245 P/Q graphs obtained under conditions of normal or elevated venous pressure, either with or without a blockade, the pressure-flow relations are linear, and the zero-flow intercept on the pressure axis—reached in less than 3 seconds after the onset of cardiac arrest—is markedly higher than the simultaneous venous pressure. We believe that the zero-flow intercept is the effective downstream pressure to arterial flow and that the reciprocal of the slope of the pressure-flow line indicates the arterial resistance. The elevation of femoral venous pressure raises the effective downstream pressure and the resistance to arterial flow in the same leg. The effective downstream pressure in the contralateral leg is raised also. α-Adrenergic blockade abolishes the reflex change in the contralateral leg, but a change in P/Q relations in the manipulated leg remains. We believe that the central reflex change could be triggered by stretch receptors in the wall of the small veins transmitted to the arterioles through α-adrenergic receptors. The encroachment on the smallest arterioles by distended small veins and by the rise in interstitial fluid pressure might be the local mechanism by which venous pressure elevation directly changes arterial P/Q relations in the manipulated leg.

IN 1933, Whittaker and Winton found in the isolated hindlimb of dogs linear pressure-flow relations with a positive zero-flow intercept on the pressure axis. In the intact hindlimb of dogs, Gomez and Veil (1936) observed that the femoral artery pressure fell during aortic occlusion to about 45 mm Hg. By increasing the sympathetic nervous tone, Pappenheimer and Maes (1942) shifted the projection of their straight femoral artery pressure-flow lines to higher pressures at zero-flow. Conversely, lowering sympathetic nervous tone shifted the projection of their lines to lower pressures at zero-flow values.

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The femoral artery pressure-flow lines obtained by Green et al. (1944) also led to markedly positive zero-flow intercepts on the pressure axis, but the pressure-flow lines were convex to the pressure axis. Levy and Share (1953), Doyle (1953), and Levy et al. (1954) also obtained convex pressure-flow lines. These lines, however, point to a zero-flow intercept of about zero pressure.

It is, of course, easy to dismiss the earlier reported linear pressure-flow relations and the positive zero-flow pressures with the argument that they were obtained with less advanced experimental technology than the convex pressure-flow relations with zero-flow intercepts at zero pressure obtained more recently. We believe, however, that the difference between the results of these two groups can be explained by the difference in experimental approach.

Whittaker and Winton (1933) and Gomez and Veil (1936) followed the instantaneous fall of the femoral arterial pressure from continuous direct
pressure recordings, and Whittaker and Winton (1933) judged the simultaneous flow decline from measurements of the femoral venous outflow. Both groups obtained their results from transient values. The authors of more recent publications, on the other hand, based their analysis of the peripheral circulation on steady state values. Flows were determined by differential pressure measurements (Green et al., 1944), by measuring the hydrostatic pressure in a vertical tube connected with venous flow (Levy and Share, 1953), or by use of the Fick principle (Levy et al., 1954). All these measurements were carried out many seconds or many minutes after each stepwise alteration of inflow pressure. Doyle (1953) altered the flow through the hindquarters of rats in steps by altering the speed of the rotary pump. The perfusion pressure was, however, not measured until it had reached a constant pressure level for the given flow. It seems evident that these latter studies are bound to test quite different qualities of the arterial bed than the earlier instantaneous studies. Investigation of steady state pressure-flow values provides information about the capability of a given arterial bed to compensate for a fall in perfusion pressure and thus maintain a flow adequate to the demands of the supplied tissue. In the present study, we will attempt to show that instantaneous pressure-flow relations, on the other hand, provide information about the fluid-dynamic characteristics of an arterial bed existing in a given moment or in a given steady state. This investigation elucidates the actual values of the effective pressure gradient that moves the blood through the arterial bed and the actual resistance to this flow. If these investigations are carried out in the same arterial bed under two different established steady state conditions, it becomes possible to elucidate the intrinsic, local, and reflex mechanisms which contribute to the change of one pressure-flow relation into another. These are mechanisms involved in blood flow regulation.

As the studies of Whittaker and Winton (1933) and Gomez and Veil (1936) were carried out in a time when flow in the intact arterial bed could not be measured, we decided to investigate with techniques available today whether or not instantaneous femoral artery pressure-flow relations are linear and whether or not the zero-flow intercept on the pressure axis is higher than venous pressure. We were also interested to learn how instantaneous pressure-flow relations are altered during peripheral vascular adaptation. Venous pressure elevation previously has been shown to decrease femoral arterial flow (Girling, 1952b; Phillips et al., 1955; Wright and Hobson, 1974; Conrad, 1976). Therefore, we decided to study the changes in the instantaneous pressure-flow relationship which might cause this fall in flow.

It is essential for an investigation of instantaneous pressure-flow relations that the inflow pressure (and thus flow) is changed in such a short time interval that intrinsic, metabolic, and reflex adaptations triggered by the experimental procedure cannot interfere with the results. To minimize phase shifts between pressure and flow, it is desirable to use nonpulsatile flow. When, however, in the supine anesthetized dog the pressure in the abdominal aorta starts to fall from the peak systolic value, the flow into the femoral artery declines rapidly. At about 130 mm Hg, the femoral flow ceases and subsequently reverses itself. At the end of the diastolic pressure decline, a small amount of blood flows again into the femoral artery just before the next pulse wave moves blood into the femoral artery. In the supine anesthetized dog, therefore, practically all femoral artery flow takes place immediately before and during the phasic pressure rise in the abdominal aorta (Fig. 1). A similar description of femoral artery flow in anesthetized dogs was given by Milnor and Nichols (1975). To obtain a sector of pulseless flow, where the slope of successive pressure-flow points can be ascertained during diastole, we had to increase the femoral artery flow. To this purpose, we used standardized reactive hyperemia. This diminished the arteriolar tone somewhat, that is, it caused some vasodilation. It was, however, not our intention to abolish all arteriolar tone, to cause maximal vasodilation, as the characteristics of the femoral artery pressure-flow relations are, in our opinion, mainly determined by the existing degree of vascular tone. These considerations led us to study the transient fall of nonpulsatile femoral artery blood flow caused by cardiac arrest during a standardized degree of reactive hyperemia.

Figure 1  Recordings of pressure in the abdominal aorta (Pao) and of flow in the left (QLFA) and the right femoral artery (QRF) in a supine anesthetized dog. Broken line indicates Pao level when QFRA crosses the zero-flow line and starts to flow backward. Unbroken line indicates the same for QLFA. At the right of the flow tracings are occlusion zeros. In both flow tracings, one flow wave during aortic pulse pressure rise is shaded together with the forward flow preceding the flow wave and with the backward flow following it. A filter was used to prevent the grid lines of the recording paper from appearing on the reproduction. The tracings of the recorded function were reinforced with ink to make sure they were not damaged by the filtering. This applies also to Figures 2 and 4.
Methods

Mongrel dogs, weighing on the average about 25 kg were anesthetized with pentobarbital, 35 mg/kg. During the experiment, additional doses were given if and when needed. A flow transducer of 2.5 mm, i.d., was placed on the right femoral artery of all dogs. In six of the eight dogs, another transducer was placed also on the left femoral artery. Flow transducers with this diameter were used because, in these experiments, the flow transducers had to fit the vessels very tightly. The inner diameter should even occlude the vessel slightly to prevent movement of the flow transducer with respect to the vessel during cardiac arrest. We have convinced ourselves in appropriate experiments that there was no measurable difference between the arterial blood pressure upstream and the pressure downstream of the flow transducer during diastole and during the cardiac arrest. A 15-gauge polyvinyl catheter was introduced via the left axillary artery into the abdominal aorta. A 22-gauge polyvinyl catheter was threaded into the right femoral vein.

The flow transducers were connected to a two-channel Biotronex flowmeter type 610. The two P37 Statham pressure transducers were situated at the level of the femoral vessels. A Beckman R dynograph was used for recordings. Needle electrodes inserted in one or both uncut vagus nerves in the neck were connected with a Grass SD5 stimulator. The stimulus that caused a cardiac arrest of adequate length varied among dogs from 20 to 60 Hz and from 30 to 80 V.

At the onset of each trial, we occluded both femoral arteries for 30 seconds. During the ensuing hyperemia, we stopped the heart for about 3 seconds. After the heart activity had reappeared, we occluded the femoral arteries again to check zero flow. Only recordings for which before and after cardiac arrest zero-flow lines were identical were accepted for analysis. In trials in which we elevated venous pressure, we partially occluded the right femoral vein downstream from the venous catheter to the occlusion of both femoral arteries. Because we only elevated the venous pressure in the right leg, we call the right leg the “contralateral leg.” The pressure in the left femoral vein never was changed. We call the left leg the “manipulated leg.” From the recording of the nonpulsatile flow during cardiac arrest, we plotted the pressure values from the abdominal aorta against the flow in each femoral artery in consecutive 50-msec intervals. The least square regression line was computed to obtain the zero-flow intercept, the reciprocal of the slope, and the correlation coefficient. For the zero-flow intercept and for the slope, mean values ± 1 standard error were calculated for each dog and subsequently for all dogs under each condition. An analysis of covariance technique controlling for differences among dogs and for differences in the number of observations in dogs was used to compare the values obtained when the pressure in the manipulated leg was elevated with values obtained under control conditions. This evaluation was carried out for the first six dogs and separately for the last two dogs for which dibenzylene, 4 mg/kg, was infused into the brachial vein before starting the investigation. The limit for statistical significance was P < 0.02. Dr. Helen Abbey, Professor of Biostatistics at our school, chose the program for the statistical analysis and supervised its application. The number of dogs and the number of trials evaluated in each dog are given in the first two columns of Table 1. Even though the two conditions, the condition of unchanged venous pressure and the condition of elevated venous pressure in the right leg, were alternated during the experiment, the number of evaluated trials in the two conditions is different. This is so because we decided to discard all trials for which the zero-flow lines before and after the cardiac arrest were not identical.

### Table 1: Mean Pressures and Flows at Onset of Nonpulsatile Flow

<table>
<thead>
<tr>
<th>Dog</th>
<th>No. of arrests</th>
<th>(P_{Ao}) (mm Hg)</th>
<th>(P_{Pv}) (mm Hg)</th>
<th>(Q_{Aoa}) (ml/min) manipulated side</th>
<th>(Q_{Aoa}) (ml/min) contralateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8</td>
<td>105 ± 1</td>
<td>103 ± 3</td>
<td>2.5 ± 0.5 *</td>
<td>38 ± 8</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>95 ± 1</td>
<td>92 ± 3</td>
<td>2.6 ± 0.4 *</td>
<td>37 ± 4</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>105 ± 1</td>
<td>109 ± 2</td>
<td>2.5 ± 0.3 *</td>
<td>48 ± 4</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>118 ± 2 *</td>
<td>114 ± 2</td>
<td>7.0 ± 0.4 *</td>
<td>36 ± 2</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>93 ± 5</td>
<td>97 ± 5</td>
<td>4.4 ± 0.2 *</td>
<td>37 ± 2</td>
</tr>
<tr>
<td>6</td>
<td>11</td>
<td>99 ± 4</td>
<td>105 ± 3</td>
<td>4.3 ± 0.5 *</td>
<td>37 ± 3</td>
</tr>
<tr>
<td>Mean of six dogs</td>
<td>46</td>
<td>101 ± 2</td>
<td>104 ± 2</td>
<td>4.1 ± 0.2 *</td>
<td>38 ± 1</td>
</tr>
<tr>
<td>7</td>
<td>10</td>
<td>70 ± 1</td>
<td>87 ± 1</td>
<td>7.8 ± 0.3 *</td>
<td>21 ± 2</td>
</tr>
<tr>
<td>8</td>
<td>10</td>
<td>84 ± 3</td>
<td>89 ± 4</td>
<td>7.8 ± 0.6 *</td>
<td>23 ± 1</td>
</tr>
<tr>
<td>Mean of two dogs with dibenzylene</td>
<td>20</td>
<td>77 ± 2</td>
<td>78 ± 2</td>
<td>7.8 ± 0.3 *</td>
<td>22 ± 1</td>
</tr>
</tbody>
</table>

Values are expressed as ± 1 se. Abbreviations and symbols: C = control, E = elevated venous pressure; * indicates statistically significant difference between the values obtained during E conditions and those obtained at C conditions; the limit for statistical significance is P < 0.02.
Results

Table 1 gives values for mean abdominal aortic pressure and femoral artery flow at the onset of the nonpulsatile flow decline during cardiac arrest, averaged across trials in each dog. The elevation of right femoral venous pressure did not significantly change aortic pressure. It lowered the femoral artery flow in the manipulated leg of all six unmedicated dogs and of both α-blocked dogs. The initial femoral artery flow in the contralateral leg was not consistently changed.

Figure 2 shows the recording during cardiac arrest. During the period of nonpulsatile flow, the pressure in the abdominal aorta and the flow in both femoral arteries fell. The pressure in the femoral vein was not markedly changed. The rate of change in aortic pressure and in femoral arterial flow decreased with time. When the aortic pressure reached about 45 mm Hg, the femoral arterial flow stopped. The aortic pressure proceeded to an asymptote of about 35 mm Hg. In this trial, the zero-flow in the femoral artery was reached about 2.6 seconds after the onset of nonpulsatile flow.

Figure 3 is the instantaneous pressure-flow graph drawn for the right femoral artery from the trial which is reproduced in Figure 2. The points represent the pressure-flow values from consecutive 50-msec intervals during cardiac arrest. The linear least square regression line drawn through these points intersects the pressure axis at 45 mm Hg. The reciprocal of the slope of this pressure-flow line is 0.96 mm Hg/ml per min. It can be seen that these points fit the least squares regression line well. In fact, in each of the 245 pressure-flow graphs obtained under conditions of normal or elevated venous pressure, either with or without α blockade, the consecutive pressure-flow values fit the linear regression lines as expressed by correlation coefficients that always exceed 0.98. Likewise, zero-flow intercept of these regression lines on the pressure axis is in all cases markedly higher than the simultaneous venous pressure (Table 2).

Figure 4 shows the recording of a cardiac arrest under conditions of elevated femoral venous pressure in the manipulated leg. The recording is from the same dog as the recording in Figure 2. During the arterial occlusion, the femoral venous pressure

\[ I = 35.8 \pm 0.9 \text{ mm Hg} \]
\[ RS = 1.24 \pm 0.04 \text{ mm Hg/ml per min} \]

\[ I = 35.7 \pm 1.1 \text{ mm Hg} \]
\[ RS = 1.14 \pm 0.04 \text{ mm Hg/ml per min} \]

**Table 2** Mean Zero-flow Intercept (I) and Reciprocal of Slope (RS) of Femoral Artery (P/Q) Lines

<table>
<thead>
<tr>
<th></th>
<th>Manipulated leg</th>
<th>Contralateral leg</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of</td>
<td>No. of arrests</td>
<td>I (mm Hg)</td>
</tr>
<tr>
<td>dogs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>46 C</td>
<td>35.8 ± 0.9</td>
</tr>
<tr>
<td></td>
<td>47 E</td>
<td>51.2 ± 1.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>20 C</td>
<td>26.9 ± 1.4</td>
</tr>
<tr>
<td></td>
<td>20 E</td>
<td>40.6 ± 1.6</td>
</tr>
</tbody>
</table>

* As in Table 1.
in this trial was elevated to about 30 mm Hg. In the brief period between the release of the arterial occlusion and the cardiac arrest, the venous pressure rose to about 45 mm Hg. Originally, we used three degrees of venous pressure elevation about 25, 35, and 50 mm Hg when measured at the onset of cardiac arrest. We pooled the data from the arterial pressure-flow relations ascertained under all degrees of right femoral venous pressure elevation. In Table 2, we compare these values with the values characterizing the pressure-flow relations under control conditions. A qualitative comparison of Figure 4 with Figure 2 indicates that the elevation of right femoral venous pressure decreases right femoral blood flow and shortens the time to the point where the flow in the right leg stops. Table 2 shows that the values for zero-flow intercept and for reciprocal of slope found in the two groups are quite consistent and that there are clearcut differences between the tested conditions. In the manipulated leg, the elevation of femoral venous pressure raised the zero-flow intercept by 15.4 mm Hg, i.e., by 43.0%. The reciprocal of the slope of the line was raised by 1.21 mm Hg/ml per min, i.e., by 100%. The changes in both parameters are statistically significant (Fig. 5A). In the contralateral leg, the elevation of the venous pressure did not change either the zero-flow intercept or the slope (Fig. 5B).

In the dogs with α-adrenergic blockade, the zero-flow intercepts and the reciprocal of the slopes were markedly smaller than in nonblocked animals. The mean zero-flow intercept was 10-25% lower, and the reciprocal of the slope was 46-48% smaller in the α-blocked dogs than in the nonblocked dogs. In the manipulated leg of the α-blocked animals, the elevation of venous pressure above 20 mm Hg raised the zero-flow intercept by 13.7 mm Hg i.e., by 50.9%. The reciprocal of the slope was raised by 0.3 mm Hg/ml per min, i.e., by 44%. The changes in both parameters are statistically significant (Fig. 6A). In the contralateral leg of the α-blocked animals, the elevation of the venous pressure did not change either the zero-flow intercept or the slope (Fig. 6B).

Discussion

Our results confirm the conclusion of earlier authors (Whittaker and Winton, 1933; Gomez and Veil, 1936) that instantaneous femoral artery pres-
Femoral artery pressure-flow relations in α-blocked animals. A: Manipulated leg. Unbroken line is mean regression line from 20 cardiac arrests in two α-blocked dogs under conditions of normal venous pressure (C). Broken line is mean regression line from 20 cardiac arrests in the same dogs under conditions of venous pressure >15 mm Hg (E). B: Contralateral leg. Unbroken line is mean regression line from 20 cardiac arrests in two α-blocked dogs under conditions of normal venous pressure (C). Broken line is mean regression line from 20 cardiac arrests in the same animals under conditions of elevated venous pressure (E).

sure-flow investigations provide information different from the findings from steady state investigations, where arterial pressure is changed stepwise and flow is measured only many seconds or minutes later, at a time when it can be assumed that steady state pressure-flow values have been established. Steady state values are established when an adaptation of the arterial bed to the new perfusion conditions has been accomplished. For instance, Levy et al. (1954) maintained each inflow pressure value for 10 minutes. After eight minutes, they started to take blood samples for the flow measurements. Figures 1 and 2 of their publication illustrate that, at relatively higher arterial pressures, i.e., at pressures where adequate perfusion is likely in relation to the metabolic needs of the supplied tissue, the extrapolation of the lines connecting two or more neighboring pressure-flow points leads to zero-flow intercepts which are markedly higher than the concurrent venous pressure. As inflow pressure is decreased, the peripheral arterial bed adapts by intrinsic, local, and reflex mechanisms, and the line connecting the pressure-flow values becomes increasingly convex to the pressure axis. The convexity of the line characterizes the degree to which the vascular bed opens in response to a decreasing inflow pressure rather than characterizing a gradual closing of the vascular bed, a rising resistance. The experimental proof of the correctness of this interpretation of the results of steady state pressure-flow lines can be found in the work of Green et al. (1944). Figure 4 of their publication documents clearly that, if lower than normal femoral artery pressure values are maintained between 45 seconds and 1 minute before flow is measured, flow values are markedly larger than they are if flow values are measured after 5 seconds. The convex line connecting the five points at which pressure was maintained for 5 seconds might have been completed within 30 seconds. This line has a zero-flow intercept of about 35 mm Hg. The convex line connecting the five points where pressure was maintained between 45 seconds and 1 minute might have been completed within 4-5 minutes. This line has a zero-flow intercept of about 10 mm Hg. It appears, therefore, that the longer a low inflow pressure is maintained, the more the vascular bed will open. It is in total agreement with these findings that Levy et al. (1954), who maintained the flow at each of the low inflow pressures for 10 minutes, find their convex line points to zero pressure at zero-flow. Green et al. (1944) suggested that the most likely explanation for the convex shape of their curve is that, at perfusion pressures below mean aortic pressure, reactive vasodilation occurs. This interpretation is in total agreement with ours. Also, it is in agreement with the phenomenon of reactive hyperemia which most investigators have observed, but is not compatible with the current belief of many that the line connecting steady state values indicates resistance. If these lines were to be taken...
as an expression of resistance to flow, it would indicate relatively low resistance at normal and high inflow pressures and high resistance at low inflow pressures. The peripheral vessels would not compensate for the low inflow pressure, as we know that they do from compensatory hyperemia and from the results of Green et al. (1944); instead, the rising resistance would make an unfavorable situation for the supplied tissue still worse.

In our investigation, however, the interval of nonpulsatile flow is shorter than 3 seconds, and at the onset of this interval the flow values are not yet low. In our own experience and in the experience of others (Folkow, 1949; Shoukas and Sagawa, 1973), a change in arterial flow alters the downstream vascular bed only after a latency of at least 4 seconds. The stimulation of the vagus nerve does not affect the peripheral arteries directly, as no vagal fibers are known to lead to the peripheral vessels. A possible central reflex effect of the vagus stimulation also would have a latency of 4 seconds or more. However improbable it is that the central or local adaptations appear within the short time interval of our pulseless flow, if they did appear, they would only relax the arterial tone. Thus, in turn, would work against the linearity of our pressure-flow relations and diminish or even abolish the positive zero-flow intercept on the pressure axis.

The question might be asked whether our positive zero-flow intercepts are not the effect of the immediate change from more or less distended to totally closed vessels at a critical pressure as Burton’s (1972) concept of the instability of small vessels with tone would predict. If the positive zero-flow intercept on the pressure axis were to be the effect of a sudden total collapse of the unstable vessels, this intercept would have no function at all at higher flow values when the vessels are stable. The zero-flow intercept reached in our experiments, however, is the back pressure for the line connecting all pressure-flow values up to the one at the onset of cardiac arrest. The pressure and flow values that are established at the moment the heart is arrested determine the value for the zero-flow intercept at the pressure axis at a given functional and metabolic state of the supplied organs. The studies of small blood vessels in situ, innervated or denervated, and of isolated vessels, by Bayliss (1902), Folkow (1949), and many others, led to conclusions which are incompatible with Burton’s (1972) claim that the laws, which Laplace worked out for soap bubbles, apply in Burton’s modification to arteries with thick walls. Against Burton’s assumption that a critical fall of intravascular pressure leads to an immediate collapse of the vessels stand the findings of the above mentioned authors that 2-4 seconds after a fall in transmural pressure the arterial wall tension relaxes. Azuma and Oka (1971) came to the conclusion that the closure of the lumen of an arteriole or a precapillary sphincter is dependent only on whether the developed active tension exceeds a critical value and is not dependent on whether the intravascular pressure is less than a critical value.

Previous work from our laboratory also supports the conclusion that the positive zero-flow intercept in our present pressure-flow lines indicate the effective back pressure to flow during perfusion and not the closing pressure existing only at zero-flow. We enhanced the cardiac output of unanesthetized standing dogs by paced heart rate increase. We connected the control pressure-flow values with the values after 4 and 6 seconds of pacing, that is, with values from the transient steady state before the effect of vascular stretch receptor reflexes appears. The resulting pressure-flow line extrapolated to the pressure axis at an average of 49 mm Hg (Ehrlich et al., 1975). Similar lines with comparable zero-flow intercepts have been reported by other investigators using various methods for altering flow. Noble et al. (1986) elevated and reduced heart rate and therefore cardiac output. Wetterer and Pieper (1955), Early et al. (1974), and Dewey et al. (1974) injected and withdrew blood from the aorta, and Bellamy (1978) correlated pressure and coronary artery flow during long lasting diastoles. Especially in the case of enhancement of flow or of variations of flow in the vicinity of the control values, it is difficult to explain the extrapolation of the line to a markedly positive zero-flow intercept by suggesting that this intercept represents an abrupt closure of the vessels at low pressures. It is the reasonable alternative to accept the fact that there is a markedly positive back pressure to arterial flow which is determined by the equilibrium between the arterial flow and the metabolic and functional state of the supplied organs. In the present study, this positive back pressure was actually revealed when the inflow pressure into the femoral arteries was reduced relatively quickly.

To obtain a sector of pulseless flow we created conditions of reactive hyperemia. Thus, at a given aortic pressure, the flow is above that of normal resting conditions. The effect of this hyperemia has to be a shift of the pressure-flow line to a lower zero-flow intercept and to a steeper slope than we would obtain in the resting leg under normal conditions if we would know how to obtain a pressure-flow line under such conditions. Because it was found that the aortic pressure in dogs at the onset of exercise falls in spite of rising cardiac output (Ehrlich et al., 1972), we would expect a still lower zero-flow intercept and still steeper slope of the line in the femoral arterial bed of an exercising leg.

In the conventional circulatory analysis, it is assumed that blood is moved through the femoral artery by the pressure gradient between aortic pressure and femoral venous pressure. The energy loss of the blood flowing from the artery to the vein is assumed to be caused substantially by laminar vis-
cous friction. This friction is expressed as peripheral vascular resistance and is believed to be indicative of the state of peripheral vessels, especially of the arterioles which are, therefore, called resistance vessels. It is readily computed as pressure gradient divided by flow. If we apply this conventional analysis, for instance, to the trial whose recording is reproduced on Figure 2, we find that the fall of femoral artery flow with cardiac arrest raised the computed peripheral vascular resistance abruptly from \((108 - 5)\) mm Hg/66 ml per min = 1.56 mm Hg/ml per min, to \((45 - 5)\) mm Hg/0.0 = \(\infty\). Indeed, the resistance would have to become infinite if it would be the resistance which would prevent the flow in a continuous bed with a pressure gradient of 40 mm Hg. Figure 7 shows the graphical analysis of the results of this trial based on the conventional concept of peripheral vascular resistance. Each of the consecutive pressure-flow values during the nonpulsatile flow is connected by a line with the venous pressure value which is assumed to be the effective downstream pressure to flow through the vascular periphery. During the cardiac arrest, the lines become increasingly more inclined toward the pressure line and, at zero-flow, the line becomes identical with the pressure axis. The reciprocal of the slope of the peripheral resistance lines becomes bigger and bigger until it becomes infinite. As long as one bases the analysis of our data on the conventional concept of peripheral vascular resistance, one finds that each flow change, whatever its cause, is immediately accompanied by a change in peripheral vascular resistance. Under these conditions it is true, not only for our data but in general, that pressure changes that are caused by changes in flow, or vice versa, cannot be predicted with Poiseuille's law, because lines representing computed peripheral vascular resistance also change with each flow change. This is true for both instantaneous and steady state pressure flow lines. Take for instance Burton's (1972) analysis of Girling's (1952a) straight pressure-flow lines obtained in the artery of a rabbit's ear. Because Burton believes that the zero-flow intercepts on the pressure axis, to which Girling’s pressure-flow lines lead, are caused by critical closing pressure, he computes from the straight pressure-flow lines resistance curves of PRU values assuming that atmospheric pressure is the effective downstream pressure to arterial flow. These resistance curves turn abruptly to infinite values at low flows. The results of the application of the conventional analysis to our experimental results or to the results of Girling (Burton, 1972) are incompatible with our knowledge of arterial smooth muscle physiology (Bayliss, 1902; Folkow, 1949; Azuma and Oka, 1971) and the autoregulation of arterial flow (Green et al., 1944).

If one analyzes arterial flow on the basis of the experimentally found pressure-flow relations (Fig. 3) and assumes that the zero-flow intercept on the pressure axis is the effective downstream pressure to arterial flow, then Poiseuille's law retains in the arterial circulation the same predictive and analytic power it has in all dynamic systems. The pressure-flow line is by definition the resistance line for the system; the reciprocal of the slope of the pressure-flow line indicates the resistance to arterial flow. By analyzing the results from this point of view, one finds that during cardiac arrest the flow from the unreplenished arterial bed decreases arterial blood volume and, therefore, the arterial pressure. As the pressure in the abdominal aorta approaches the effective downstream pressure in the arterial bed, the pressure gradient for the flow through the femoral arteries becomes smaller and smaller. The flow, therefore, becomes smaller too. The continuously decreasing outflow from the aorta causes a continuously diminishing rate of fall in aortic volume, aortic pressure, and femoral flow, but the vascular resistance remains fixed during this short interval. When the pressure in the abdominal aorta becomes equal to the effective downstream pressure, the pressure gradient vanishes and the flow stops. The aortic pressure is the effective upstream pressure to flow. The effective downstream pressure to flow in the arterial bed, however, is equal to the zero-flow intercept on the pressure axis provided we have a linear instantaneous pressure-flow line. This is the value which is the proper subtrahend for the pressure gradient which moves the blood in the given arterial bed.

The fluid dynamic mechanisms which explain the existence of an effective downstream pressure
to arterial flow in the small arterioles have been analyzed. Permutt and Riley (1963) postulated that the flow through the precapillary arterioles has the characteristic of a waterfall in the sense that the flow is determined by the fluid-dynamic conditions in the arterial bed (the bed upstream from the precapillary arterioles) and by the lumen of the precapillary arterioles rather than by the pressure gradient between the arterioles and the veins. In accordance with the model of Dawson and Elliot (1977), the precapillary arterioles can be considered as constricted hydraulic channels. To reach the flow value adequate to the existing pressure gradient, the fluid would have to surpass the highest speed possible for the given fluid in channels with given characteristics. Under these circumstances, the fluid will move with its maximal possible speed, and the flow will be determined by the area of the luminal cross-section of the limiting sector. The flow limitation is caused by the tone of the thick walls of the smallest arterioles together with the pressure of the surrounding tissue. The effective downstream pressure to arterial flow is also called the pressure at the onset of the vascular waterfall (Permutt and Riley, 1963) or the pressure at the choking point (Dawson and Elliot, 1977). The application of the analysis of Dawson and Elliot (1977) makes it clear that even though the difference between aortic and venous pressure does not indicate the driving pressure for arterial flow, it indicates the loss of energy between the arterial and the venous flow.

Only if the arterial pressure is higher than the pressure caused by the tonus of the arterial wall plus the surrounding pressure is the given arteriole perfused and hemodynamically active. The pressure in the smallest arterioles is the effective downstream pressure of the flow to this arteriole. The more precapillary arterioles are recruited and perfused, the more arterial blood is directed to the organs supplied by the given arterial bed. The tension of the arteriolar wall seems to depend on the metabolic needs of the organs, especially in the muscles (Krogh, 1918-1919; Guyton et al., 1964), on the given state of the nervous functions (Barcroft and Swan, 1953), and on the interstitial pressure.

Differently from the steady state inflow into an arterial bed, where one can assume that the inflow into the arterial bed is equal to the flow through the arterioles, continuously decreasing inflow and decreasing distending pressure may cause the flow through the arterioles and into the capillaries (if it could be measured) to be larger than the inflow measured with the flowmeter. It has been argued that this difference might be important and that it may cause "arteriolar flow" and flow into the capillaries after the inflow in the arterial bed has ceased. It is fortunate that the compliance of the arterial bed in dog limbs has been studied so that we are able to analyze the consequences of the arterial compliance for our data. Zingher and Grodius (1964) found in the nonisolated forelimbs of 20- to 40-kg dogs an arterial compliance of 0.62 \( \cdot 10^{-3} \text{cm}^3 \cdot \text{mm Hg}^{-1} \). Attinger et al. (1966) found in dogs weighing between 12.5 and 30 kg a femoral artery compliance of 0.56e\( ^{.0045 x} \cdot 10^{-3} \text{cm}^3 \cdot \text{dyn}^{-1} \), where \( x \) = the distance from the bifurcation of the iliac arteries.

If we use Zingher and Grodius (1964) findings to analyze the results of one of our trials where the femoral artery flow ceased after 2.5 seconds of cardiac arrest, we find that the compliance flow during the total fall of aortic pressure from 106 to 52 mm Hg would be 0.8 ml/min. The compliance flow for each of the consecutive half-second intervals of the cardiac arrest up to zero femoral artery flow is 1.33, 0.89, 0.89, 0.44, 0.44 ml/min. That means the compliance-flow is very small at the onset of the cardiac arrest, but it falls to a third of this small value before the flow ceases. Figure 8 demonstrates graphically the implications of values of this magnitude for the evaluation of our trial. The filled circles are femoral artery P/Q values taken in consecutive 0.5-second intervals. The open circles represent P/Q values from the first half of each 0.5-second interval. To these measured P/Q values, we added the computed compliance flow for the given 0.5-second interval in ml/min indicated by crosses over the circles. The crosses, therefore, indicate the presumed "arteriolar flow," the flow from the arterioles into the capillaries. The crosses are situated

![Femoral artery pressure-flow graph from one trial. Closed circles indicate P/Q values for each of the consecutive 0.5 seconds. The unfilled circles indicate the P/Q values after the first half of each 0.5-second interval. The compliance flow for each 0.5-second interval computed after Zingher and Grodius (1964) and added to each half interval P/Q value is indicated by X for "arteriolar" flow. The x values plotted to the inflow pressures and the same values plotted to the effective downstream pressures are connected by straight lines indicating that the pressure value to the arteriolar flow value would be between the two extremes, dependent on the points where we imagine that the arteriolar flow would be "measured."](image-url)
over the circles to demonstrate the difference between the measured arterial inflow value and the presumed "arteriolar flow." We realize, of course, that the pressure belonging to this flow would not be inflow pressure. The straight line connecting each cross with an equally high cross over the effective downstream pressure indicates that the pressure for the imagined "arteriolar flow" would be situated somewhere on this line dependent on the point of the imagined measurement. If this flow measurement could be carried out in all precapillary arterioles, the appropriate pressure for the arteriolar flows of all intervals would be the effective downstream pressure.

If we use the findings of Attinger et al. (1966) to analyze the results of the same trial, we obtain a compliance flow for the total cardiac arrest of 1.34 ml/min. The computed compliance flow values for the consecutive 0.5-second intervals are 2.24, 1.49, 1.49, 0.74, and 0.74 ml/min. Even though the actual numbers are different, the order of magnitude of the values for compliance-flow in our trial obtained with the equation of Attinger et al. (1966) is identical with the order of magnitude of the values arrived at with the equation of Zingher and Grodins (1964). The application of the available findings about the compliance of the arterial bed in dog extremities, gained in two different laboratories, to the analysis of our instantaneous femoral artery pressure-flow investigations shows that the difference between the inflow and the presumed "arteriolar flow" is very small, and it vanishes altogether during the investigation. It proves convincingly that the zero-flow intercept of the straight pressure-flow line indicates the pressure value where the flow in the total arterial bed ceases, the inflow as well as the flow through the arterioles.

Girling (1952b), Phillips et al. (1955), Wright and Hobson (1974), and Conrad (1976) showed that the elevation of the femoral venous pressure decreases femoral artery flow. The authors differ in their explanation of the mechanisms involved in this flow decrease. Only Girling (1952b) used the experimental investigation of pressure-flow relations for the analysis of these mechanisms. The curves he obtained with normal and with elevated venous pressure show zero-flow intercepts on the pressure axis which are higher than venous pressure. We believe that his results, as well as ours, show that the elevated venous pressure raises the effective downstream pressure to the arterial flow and diminishes, therefore, the effective perfusion pressure. Girling published results for individual trials, and this might be the reason why he failed to detect the change in slope of the pressure-flow line, i.e., an elevated arterial resistance, together with higher effective downstream pressure, when the venous pressure was elevated. Conrad (1976) demonstrated that an elevated venous pressure in one leg influences the conditions of arterial flow in the contralateral leg as well. Our results confirm this. Our results and our interpretation are also compatible with, and complimentary to, the findings of Baez et al. (1974), who found that the elevation of ileocolic vein pressure in rats resulted in a lumen expansion of venular microvessels and in a lumen reduction in arterioles, metarterioles, and precapillary sphincters by 17.9, 43.6, and 96%, respectively. The drastic changes in the precapillary arterioles correspond most probably to the rise in effective downstream pressure, whereas the changes in the arterioles and metarterioles affect probably the arterial resistance. The expansion of the venular microvessels is, of course, a direct consequence of the rise in venous pressure.

From our finding of concomitant changes in the arterial bed of the contralateral leg, it can be inferred that a central nervous reflex is involved in the adaptation of the pressure-flow relations to elevated venous pressure. It is conceivable that this reflex is triggered by stretch receptors in the wall of the distended small veins. Its effect is mediated by \( \alpha \)-adrenergic receptors. The findings that the changes in the manipulated leg are more extensive than in the contralateral leg and that changes in the manipulated leg are maintained during \( \alpha \)-adrenergic blockade indicate the involvement of local non-neural mechanisms. The encroachment of the small arterioles by the distended small veins and by the rise in interstitial fluid pressure might be such direct acting local mechanisms.

The theoretical implication of our findings that instantaneous pressure-flow relations are linear and have a positive zero-flow intercept on the pressure axis seems to be important. According to the conventional concept, the heart pushes the blood through the total peripheral circulation, and all vascular adaptations, autoregulation, nervous and humoral regulations, etc. act in the form of resistance to laminar flow. According to our concept, the pumping heart fills the arterial bed; the cardiac output is the inflow into the arterial bed. The number of perfused precapillary arterioles and the pressure in these precapillary arterioles determine the outflow from the arterial bed. The pressure gradient moving the blood in the arterial bed is the difference between the aortic pressure, caused by the degree of filling of the arterial bed, and the effective downstream pressure to arterial flow, caused by the tone of the precapillary arterioles and the surrounding pressure. The pressure gradient returning the blood to the heart is the difference between the peripheral venous pressure caused by the degree of filling of the bed of small veins and the right atrial pressure which is the effective downstream pressure for venous return.

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