Infusion Rate Effects on Arterial Pressure, Vascular Conductance, and Muscle Weight[1] (34943)

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Immediately after a sudden increase in the rate of perfusion of blood into the arterial system of a muscle or a limb, recordings commonly show a triphasic response (2, 5) consisting of: (1) a sharp, brief rise in arterial pressure; (2) a rapid fall toward the control pressure value; and (3) a slow progressive increase in arterial pressure. Conversely, a sudden decrease in the rate of infusion of blood into the artery has been recorded as producing: (1) an initial sharp fall of pressure; (2) a tendency of the arterial pressure to rise toward the control value, and then (3) a gradual decrease of arterial pressure. The response to an increase in infusion rate is of greater magnitude than the response to decrease in infusion rate.

These arterial pressure changes have been attributed to myogenic and/or metabolic effects operating through the arterioles (2, 3, 5, 6).

Our analysis of factors which can affect vascular conductance (flow/perfusion pressure) suggests that some effects previously ascribed to active arteriolar responses may represent passive mechanical effects at the capillary level. We have, therefore, reexamined the mechanisms of the observed vascular responses in the isolated muscle preparation, and in a model of the vascular bed.

Muscle. Methods. Gracilis muscles from five dogs were used. Figure 1 shows the experimental arrangement. The weight (and volume) of the muscle was monitored with a strain-gage balance. A variable-speed pump (Masterflex Tubing Pump, Cole-Parmer, Chicago) perfused the muscle with the dog's own blood. The blood pressure proximal to the muscle, and the rate at which blood was pumped into the arterial system were continuously recorded. A sidearm in the arterial system between the pump and the muscle was connected to a U-tube mercury manometer. Opening of the sidearm to the manometer increased the compliance of the arterial system by a value which varied with half the cross-sectional area of the mercury column. By using manometer tubes of 0.2- to 1.0-cm diameter, the effects of compliances of 0.0016–0.04 ml/mm Hg were studied. Arterial pressure and changes in muscle weight were recorded continuously. After a control period in which the rate of input of blood into the artery, the weight of the muscle, and the arterial pressure were relatively constant, the rate of infusion of blood into the artery was suddenly altered. In our recording, an apparent delay in the increase in flow is due to an averaging circuit in the flowmeter.

Results. Approximately 10 tests were made on each muscle; the results were essentially identical for each set of experimental conditions. Figure 2 shows a typical record of a test in which the tube leading to the mercury manometer was clamped, thereby eliminating the compliance offered by the tube associated with the mercury column. When the arterial input rate was suddenly increased, an immediate and marked rise in arterial pressure was observed; this was followed by a rapid fall in pressure toward the control values; the arterial pressure then exhibited a progressive rise. The progressive rise in arterial pressure was associated with a simultaneous increase in muscle volume.

A sudden reduction in the arterial input

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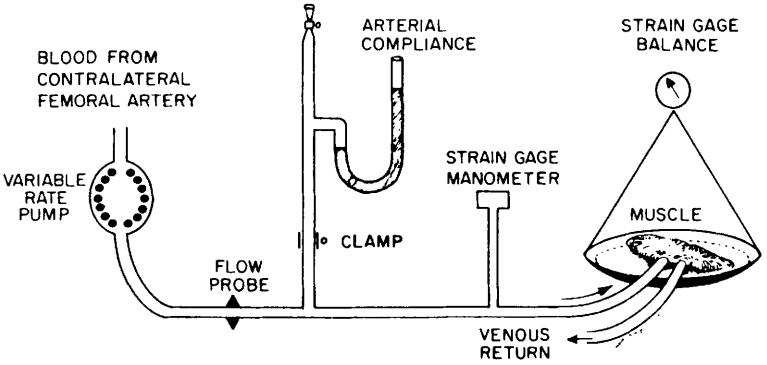

FIG. 1. Experimental arrangement for volume loading of an isolated dog gracilis muscle. Described in text.

rate (Fig. 3) was associated with an immediate transient fall in arterial pressure; this was followed by a small but real, transient pressure rise. A slowly progressive but persistent fall of arterial pressure was then observed in association with a simultaneously continuing decrease in muscle volume.

The addition of the compliance of the mercury manometer to the arterial system diminished the initial pressure changes in proportion to the arterial compliance. With a compliance of 0.04 ml/mm Hg the initial "vasoconstrictor" response to volume loading was completely eliminated (Fig. 4). However, the third phase of the progressive rise in arterial pressure and the progressive increase in muscle volume persisted.

Results with a sudden reduction of arterial input were in opposite direction to those with sudden increase in input but were less pronounced.

Model Experiments. Methods. We attempted to visualize the vascular responses to a sudden change in arterial input by using a mechanical model of the peripheral circulation.

An arrangement consisting of a perforated collapsible latex rubber tube ("capillary") enclosed with "extravascular" fluid in a compliant capsule ("extravascular space") was used (Fig. 5). This system, referred to as a "capillaron" reproduces a number of vascular responses, including autoregulation, reactive hyperemia, and muscle-contraction hyperemia, which are observed in muscle and other tissues (4). Responses in the capillaron model can be due only to the physical properties of the system.

Study of the components of the model assists in the analysis of the behavior of perfused muscles. In the model, the responses to a change in inflow rate are modified by the compliance of the vessel leading to the capsule ("arterial compliance"), by the permeability of the collapsible permeable tube (capillary), and by the compliance of the extravascular compartment (1, 4).

Results. The triphasic pressure response

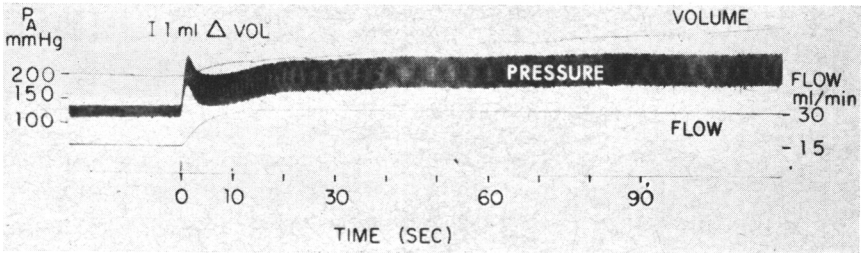

FIG. 2. Arterial pressure (P_A) and muscle-volume responses after a sudden increase in arterial inflow rate at time zero. The increase in inflow takes place within a second; the apparent delay in recording results from the averaging circuit of the flowmeter.

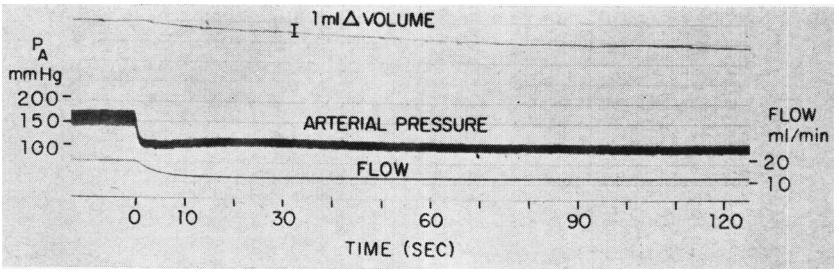

FIG. 3. Arterial pressure (P_A) and muscle-volume responses after a sudden decrease in arterial inflow rate at time zero.

observed in a dog's hindlimb was reproduced when the volume input into a capillaron system was changed suddenly (Fig. 6). The magnitude of the initial pressure rise after a sudden increase in input varied inversely with the compliance of the arterial system. The larger the compliance of the arterial system, the less pronounced the initial rise in arterial pressure and the less conspicuous the "vasodilatation" of the second phase. A large arterial compliance completely abolished the initial response and the second phase "vasodilatation," but the progressive rise in arterial pressure of the third phase persisted (Fig. 7).

In the model, the progressive rise in arteri-

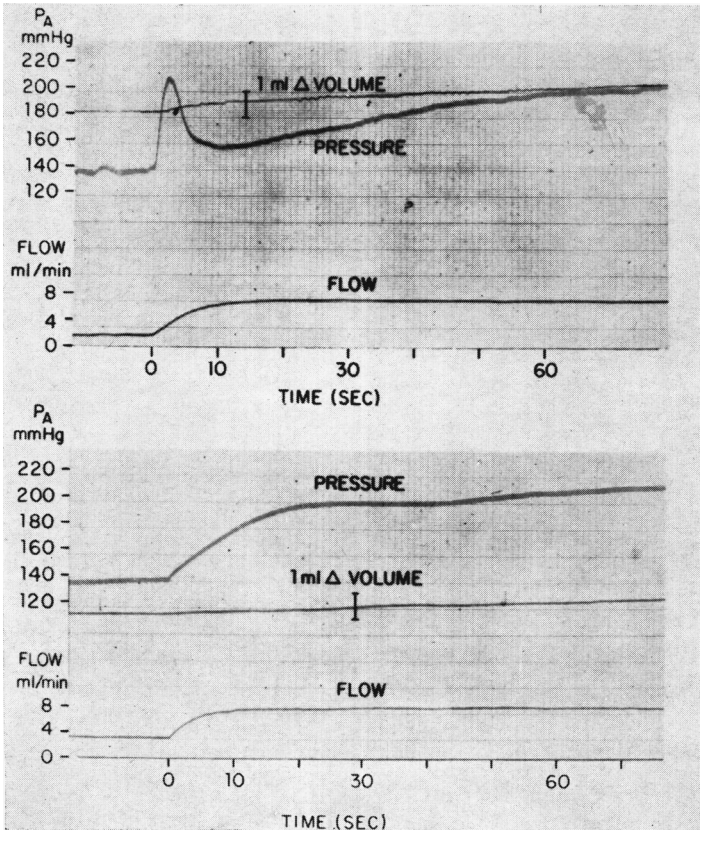

FIG. 4. Arterial pressure (P_A) and muscle-volume responses to a sudden increase in arterial inflow without an additional arterial compliance (upper record) and with an additional arterial compliance (lower record).

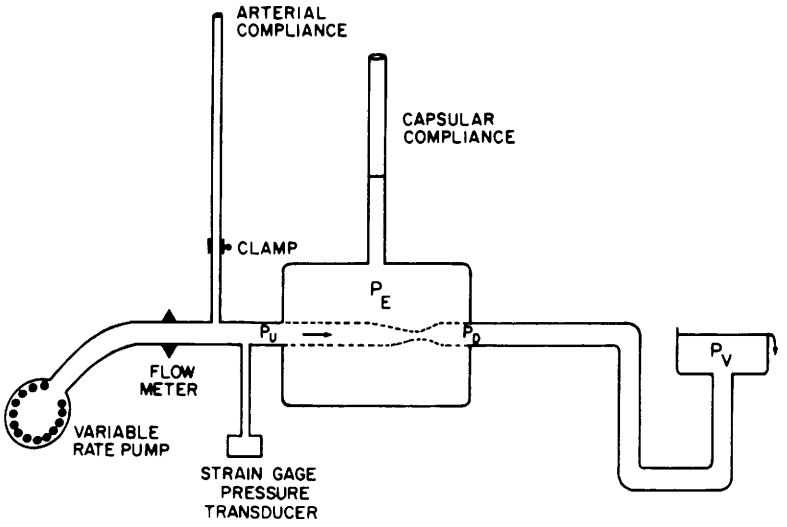

FIG. 5. Experimental arrangement for volume loading in the capillaron model. P_U = upstream pressure; P_E = capsular or extravascular pressure; P_D = downstream pressure; P_V = venous pressure.

al pressure of the third phase was associated with transudation of fluid out of the capillary into the capsule, thereby increasing extravascular fluid volume and pressure. The heightened extravascular pressure collapsed the downstream end of the capillary and decreased vascular conductance. The decrease in vascular conductance was accompanied by an increase in extravascular volume.

In the model, the mechanism of the initial rise in pressure differed from that which po-

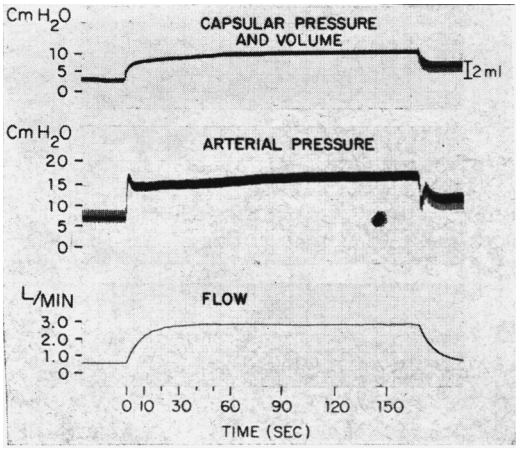

FIG. 6. Effects of a sudden change of volume input on pressure and volume responses in the capillaron model without an additional arterial compliance.

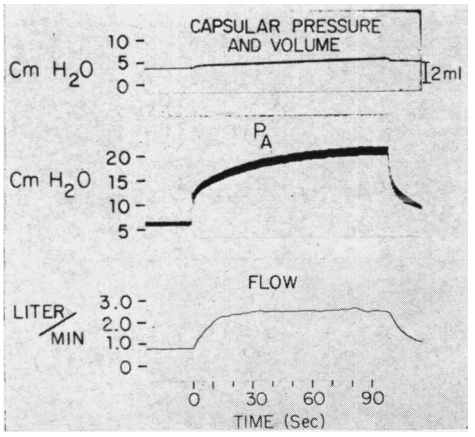

FIG. 7. Effects of a sudden change of volume input on pressure and volume responses in the capillaron model with an additional arterial compliance.

duced the progressive rise in pressure. The first-phase response was abolished by introduction of a larger arterial compliance, while the progressive rise in pressure of the third phase persisted.

Discussion. The results show that the initial pressure response to an increase in the rate of arterial input into a skeletal muscle is reduced or even abolished by introducing an arterial compliance between the pump and the muscle. The amplitude of the initial increase in pressure varies with the magnitude

of the sudden increase in input into the arterial system, and with the compliance of the arterial tree. This finding indicates that the first pressor effect may result from the arterial compliance rather than from a response to the volume loading of the peripheral vascular bed. Published data (2, 5) of the responses of tissues to volume loading may have depended on such differences in arterial compliance. The initial responses reported for the vascular system of an isolated gastrocnemius muscle (5) which had a small arterial compliance, were marked. The smaller initial response observed when an entire forelimb was perfused (2) may have been due to the larger compliance of the arterial system. The possible effects of attached compliances such as those of manometers can not be evaluated on the basis of published data.

The fall in pressure during the second phase is clearly related to an increase in conductance of the system. This increased conductance can be attributed to a heightened intravascular pressure which opens previously collapsed vessels and thereby permits a more rapid flow of blood out of the arterial system. Since the first phase can be adjusted by introducing an adequate compliance into the arterial system, the second-phase response will also vary with the compliance. Thus, elimination of the first phase by introduction of a large compliance into the arterial system also eliminates the pressure effects of the second phase.

The progressive decrease in vascular conductance of the third phase and the consequent rise in arterial pressure were associated with a simultaneous increase in the weight (and volume) of the muscle. This increase in muscle volume can be attributed to an increased filtration of fluid out of the capillaries and into the extravascular spaces.

The decrease in conductance associated with an increased rate of filtration out of the vascular system can be reconciled with the rising arterial pressure if the change in conductance is distal to the vascular segment in which the filtration takes place. Such a site of constriction could be the distal end of the capillary. A decreased capillary pressure would diminish the rate of filtration of fluid out of the capillaries, and the volume of the tissue would decrease. The similarities of the results obtained in the capillaron model to those obtained in the muscle indicate that these effects can result from the collapse of the downstream end of the capillary (4). Observation of the capillaron model (4) shows that collapse of the distal end of the capillary places the resistance distal to the locus of the filtration of fluid into the extravascular space. These observations appear to obviate the need for postulating arteriolar constriction in the third phase, though this possibility can not be excluded.

The findings on sudden reduction of the input into the arterial system can also be interpreted in terms of the capillaron concept. The sudden reduction in arterial input results in an arterial pressure change, depending on arterial compliance. If arterial compliance is large, the arterial pressure change is small, and little immediate effect is observed. If compliance is small, the arterial pressure will fall at once as flow drains out of the arterial system through the vascular bed. However, the falling arterial pressure lowers the capillary intravascular pressure and these vessels can collapse and reduce the vascular conductance. The pressure then tends to stabilize and may even rise toward the control level. As fluid drains from the extravascular compartment and peripheral conductance increases, the pressure falls and the volume of the tissue decreases.

The different rates of change in volume and resistance between increase and decrease of perfusion rate are also consistent with observations on the model with a uniformly distributed permeability of the capillary. The rate of return of fluid from the extravascular compartment when extravascular pressure exceeds the pressure in the capillary and this vessel is completely collapsed, is slower than the rate of outward filtration when the capillary tube is open for most of its length.

Summary. Vascular responses to sudden changes in perfusion rate were studied by continuous simultaneous measurements of blood pressure and muscle volume in isolated, de-

nervated gracilis muscles of dogs. The responses were also studied in a mechanical (capillaron) system (a permeable soft-walled capillary enclosed in a compliant capsule). In both systems an increase in arterial volume input was accompanied by: (1) a concordant rise in pressure, followed by (2) a transient vasodilation and fall in pressure and then by (3) a slow, progressive pressure rise. The initial pressure response to volume loading in both systems varied inversely with the compliance of the arterial system. Larger arterial compliances eliminated the first and second phases, but the tertiary phase pressure rise persisted. Thus, the initial responses, previously attributed to an active vascular response to volume loading may be due to an incidental change in perfusion pressure. The tertiary phase progressive rise in pressure in the muscle and in the capillaron system was associated with an increasing tissue volume. These results are more consistent with a decrease in vascular conductance resulting from a higher tissue pressure as the capillaron model suggests, than with an arteriolar constriction.

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