Evidence for a Metabolic Mechanism in Autoregulation of Blood Flow in Skeletal Muscle

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Autoregulation of blood flow in skeletal muscle is well documented but the mechanism for this phenomenon is still unsettled. Currently two theories, the myogenic and the metabolic, have received the strongest support. With myogenic regulation of blood flow it is suggested that the vascular smooth muscle of the precapillary vessels responds to stretch by enhanced tone following a sustained arterial pressure increase. This results in an augmentation of vascular resistance and restoration of blood flow toward or to control levels. A sustained reduction in arterial pressure elicits the opposite response. With metabolic regulation of blood flow an equilibrium between production and washout and/or destruction of vasodilator substances in the tissue is postulated. According to this hypothesis, the initial blood flow increase following a sustained arterial pressure increase would reduce the concentration of vasodilator material and allow greater expression of inherent vascular tone to reduce blood flow until equilibrium is re-established at an increased level of vascular resistance. A reduction of perfusion pressure promotes accumulation of vasodilator metabolite(s) and results in a reduction of vascular resistance.

Relatively simple criteria may be employed to discriminate between the metabolic and myogenic regulation of blood flow. For example, an increased transmural pressure produced by a sustained increase in venous pressure should elicit vasoconstriction if the regulatory mechanism is myogenic whereas a metabolic mechanism would produce vasodilation. If transmural pressure is increased by decreasing the atmospheric pressure surrounding an organ, a myogenic mechanism should produce vasoconstriction whereas if a metabolic mechanism were operative, vascular resistance should be unchanged. Additional evidence may be obtained by applying the discriminatory criteria to the changes in resistance observed during perfusion of the organ at constant rates of blood flow. Under these conditions a metabolic mechanism should be relatively unaffected by venous or atmospheric pressure changes whereas a myogenic mechanism should find full expression. The present study represents an attempt to distinguish between myogenic and metabolic mechanisms in the regulation of skeletal muscle blood flow by application of these criteria.

Methods

The muscle preparation used was one which has been shown to exhibit autoregulation following sustained changes in arterial pressure or pump controlled blood flow. Under pentobarbital anesthesia (30 mg/kg), the thigh muscles of the dog were detached from the pelvis and the lower portion of the limb was removed by disarticulation at the stifle joint. The skin of the thigh was removed and the muscle mass wrapped with saline-soaked gauze. At the time of cannulation of the iliac artery and vein the vessels were transected and the femur was disarticulated at the acetabulum so that the perfused tissue included only the...
thigh muscles and the femur. The weight of the muscles perfused ranged from 760 to 1200 g (average 850 g) and the weight of the bone averaged approximately 10% of the total thigh weight.

Following cannulation, the thigh was placed in an aluminum chamber provided with an air-tight Plexiglas cover. The aluminum chamber formed the top of an enclosed water bath through which warm water was circulated to maintain the muscle temperature at 36 to 38°C. In addition, the blood entering the muscle was prewarmed during passage through a silicone coated metal coil immersed in the water bath.

Perfusion of the isolated muscle was obtained from a reservoir (200 to 300 ml) supplied with arterial blood from the contralateral femoral artery. An electrically driven pump forced air into a balloon over the blood in the reservoir and perfusion pressure was regulated by varying the pressure in the balloon by means of an adjustable air escape valve. Alternatively, the muscle could be perfused at controlled rates of blood flow by means of a Sigmamotor pump. Venous blood outflow from the muscle was led through wide bore tubing to a funnel connected to the contralateral femoral vein of the dog. Venous pressure was adjusted by varying the height of the open end of the outflow tube relative to the level of the iliac artery and vein of the isolated muscle.

Air pressure in the chamber enclosing the isolated muscle was measured with a Statham P23Db strain gauge. Subatmospheric pressure within the chamber was produced by an electrically driven suction pump and was regulated by means of an adjustable bleeder valve. An air switch allowed rapid connection of the chamber to the vacuum pump or to a vent open to atmospheric pressure.

Alteration of ambient pressure was a convenient method for producing an equal change in transmural pressure in all vessels of the muscle simultaneously. This procedure is considered to be the equivalent of an increase or decrease in both arterial and venous pressure with respect to atmospheric pressure.

In all experiments arterial and venous pressures were measured with Statham P23Db strain gauges with zero reference at the level of the iliac artery and vein of the isolated muscle. Arterial blood inflow to the isolated muscle was measured with a rotameter in all experiments and in several experiments venous blood outflow was measured simultaneously by an electromagnetic flowmeter. A standard 20 to 25 mm Hg stepwise pressure change in either arterial, venous or ambient pressure was used as a stimulus throughout the series of experiments. Pressure changes were made as rapidly as possible and were usually completed within one second. Vascular resistance was calculated as the ratio of effective perfusion pressure (arterial pressure minus venous pressure) to arterial blood inflow per 100 g wet weight of muscle. For each stimulus, resistance values were obtained during a control period, at the peak initial resistance change and 2 to 5 minutes following the initiation of the stimulus when resistance had reached a new steady state. In all experiments arterial pressure was between 60 and 200 mm Hg and venous pressure was within the range of 0 to 40 mm Hg. Following dissection and cannulation a 30- to 45-minute period of perfusion was maintained at constant, near normal levels of arterial and venous pressure in order to permit vascular tone to become relatively stable.

The level of metabolic activity of the isolated muscle was altered by stimulation of the muscle by a Grass stimulator with d-c pulses 1 to 3 msec in duration at a frequency of 2/second. The stimulation voltage was adjusted to induce muscle contractions sufficient to cause an increase in blood flow 2 to 3 times that observed during control periods in the resting muscle.

To insure that local reflex mechanisms did not play a role in the responses observed following venous pressure alteration, vascular regulation in muscle was studied following either acute or chronic denervation and during the infusion of procaine. Acute denervation was done at the time of dissection just prior to cannulation of the vessels. Chronic denervation was accomplished under aseptic conditions 5 to 20 days prior to the pressure-flow studies. Under pentobarbital anesthesia (30 mg/kg), three equally spaced longitudinal* skin incisions were made at the hip joint. All the muscles of the thigh were detached from the pelvis by sharp dissection. With the exception of the iliac artery and vein which were painted with 95% alcohol, all nerves were cut and all vessels were ligated and divided. The skin incisions were sutured with silk and the animal was given penicillin daily for the first postoperative week. In five acutely denervated preparations, 2% procaine was infused through a needle in the tubing at the arterial cannula of the isolated muscle by means of a motor driven syringe at a rate of 0.3 ml/min. This infusion rate introduced approximately 1 ml of procaine solution per 100 ml of perfusing blood.

*Transverse incisions were abandoned because of massive postoperative edema, presumably due to excessive interruption of lymphatic drainage pathways.
Vascular responses following increased transmural pressure from the arterial side of the circuit. A: sustained increase in arterial pressure (A.P.) during controlled pressure perfusion; B: sustained increase in blood flow from 25 ml/min to 34 ml/min during controlled flow perfusion. Venous pressure (V.P.) held constant in each instance. In this and all subsequent figures, 1: blood flow is depicted as arterial inflow; 2: derived resistance values (PRU/100 g) are indicated below the base line at control, initial and final points; 3: bars in pressure tracing during constant flow perfusion indicate mean arterial pressure.

Results

Twenty-eight muscle preparations were studied; 23 following acute denervation and five following chronic denervation. To facilitate comparison of the responses obtained with those predicted by myogenic or metabolic mechanisms, the data have been divided into two groups; 1) stimuli which tended to produce vascular distention by an increased transmural pressure (arterial or venous pressure increase and application of subatmospheric pressure to the muscle), and 2) stimuli which tended to decrease vascular distention by decreased transmural pressure (arterial and venous pressure decrease and release of subatmospheric pressure).
1. INCREASED TRANSMURAL PRESSURE

a) Arterial Pressure

The muscle preparation used in these experiments demonstrated autoregulation equivalent to that reported previously following arterial pressure or blood flow alteration. The changes in peripheral resistance following a sustained 20 mm Hg elevation of arterial pressure during controlled pressure perfusion are illustrated in figure 1A. Distention of the vessels by the increased perfusion pressure produced an initial transient increase in blood flow followed by a return of blood flow toward the control level. Peripheral resistance was much reduced during the transient phase but reached a value greater than the control resistance when autoregulatory adjustment of equilibrium flow was completed one to three minutes later. During controlled flow perfusion of the

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**FIGURE 2**

Vascular responses following a sustained venous pressure increase during constant pressure perfusion, A, and constant flow perfusion, B. Blood flow in B = 28 ml/min. Flow: arterial blood inflow.
muscle, an increase in blood flow (fig. 1B) produced a similar transient decrease in resistance followed by a gradual increase in resistance to a value greater than the control level.

b) Venous Pressure

During perfusion at constant arterial pressure a sustained 20 mm Hg increase in venous pressure (fig. 2A) produced a transient decrease in blood flow followed by an autoregulatory adjustment of vessel caliber characterized by a decrease in resistance and return of blood flow toward the control value. A sustained 20 mm Hg increase in venous pressure during constant flow perfusion (fig. 2B) produced a corresponding transient increase in resistance followed by a return of resistance to the control value.

![Graph A](image)

![Graph B](image)

**FIGURE 3**

Vascular responses during a sustained reduction in atmospheric pressure (chamber pressure) surrounding the isolated muscle. Application of 20 mm Hg subatmospheric pressure during constant pressure perfusion, A, and during constant flow perfusion, B. Flow rate in B = 25 ml/min. Flow: arterial blood inflow.
Figure 4

Alteration of blood flow and peripheral resistance following, A, sustained 20 mm Hg decrease in arterial pressure during controlled pressure perfusion, B, sustained blood flow decrease from 32 ml/min to 22 ml/min. Flow: arterial blood inflow.

c) Subatmospheric Pressure

Negative pressures were applied to the chamber containing the isolated, acutely denervated muscles of 11 dogs. When the air pressure surrounding the isolated muscle was decreased 20 mm Hg, the pressure change was transmitted equally to the artery and vein within the chamber. This was demonstrated by recording a simultaneous 20 mm Hg pressure decrease in both artery and vein when the inflow and outflow tubes were clamped outside the airtight chamber. When subatmospheric pressure was applied to the muscle during perfusion, the distensible veins were filled in part by retrograde blood flow into the veins from the outflow tubing. To minimize transient venous pressure change during this time, blood or saline was added to the outflow tubing until forward flow from the vein resumed. The effectiveness of this procedure for controlling venous pressure upon application of subatmospheric pressure is illustrated in figure 3.

Distention of the vessels by application of subatmospheric pressure (−20 mm Hg) during constant pressure perfusion (fig. 3A)
produced a transient increase in arterial blood inflow (decreased resistance) followed by a return of resistance to the control level. During constant flow perfusion (fig. 3B) application of subatmospheric pressure produced initial arterial distention as indicated by the initial decrease in perfusion pressure and resistance. The initial resistance decrease was followed by a return of resistance to the control level.

2. DECREASED TRANSMURAL PRESSURE
   a) Arterial Pressure
   A sustained 20 mm Hg reduction of arterial pressure during controlled pressure perfusion (fig. 4A) produced an initial transient decrease in blood flow and an increase in resistance. In 9 to 15 seconds a gradual decrease in resistance produced a return of blood flow toward the control level. When equilibrium was attained, resistance was less than the control value despite the decreased intravascular distending pressure. During controlled flow perfusion a decrease in blood flow produced a transient increase in resistance followed by a return of resistance to below the control level (fig. 4B).

![Figure 5](https://example.com/figure5.png)


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A large initial transient reduction of resistance was observed when venous pressure was lowered, during both constant pressure and constant flow perfusion (fig. 5). Following a sustained venous pressure reduction equilibrium resistance was greater than the control value during constant pressure perfusion (fig. 5A) or constant flow perfusion (fig. 5B). Damped oscillations of the type illustrated in figure 5A were occasionally seen following any of the pressure stimuli and were not peculiar to changes in venous pressure. The oscillations were similar to those reported previously following arterial pressure changes in skeletal muscle.

c) Subatmospheric Pressure

When ambient pressure in the chamber...
enclosing the muscle was suddenly changed from subatmospheric to atmospheric levels (fig. 6), the excess volume in the venous system emptied within 4 to 5 seconds. The transient changes in arterial blood inflow as ambient pressure was increased were multiphasic (fig. 6A and B). As ambient pressure rose during controlled pressure perfusion an abrupt (1 to 2 sec) increase in resistance was observed. This brief resistance increase was immediately followed by a decreased resistance which increased arterial inflow two- to threefold above control flow. Since the latter resistance change coincided in time with the transient resistance changes observed following all other pressure stimuli (peak at 9 to 15 seconds), the second, or dilator response was arbitrarily chosen as representative of the initial resistance value for purposes of comparison.

Following the transients, autoregulatory readjustment of vascular caliber restored blood flow to the control level within the next one to two minutes (fig. 6A). During constant flow perfusion the resistance alteration followed an identical pattern (fig. 6B).

3. COMPARISON OF RESPONSES TO PRESSURE STIMULI

The differences between control resistance and the initial (peak transient) and the final (equilibrium) resistance were analyzed statistically for each pressure stimulus during controlled pressure and controlled flow perfusion. There was no significant difference between acutely and chronically denervated preparations in the resting or contracting state with respect to the magnitude or direction of the change in equilibrium resistance as per cent of the control resistance for any given stimulus. Furthermore, infusion of procaine for periods of 5 to 20 minutes in acutely denervated preparations had no significant effect on either the patterns of response or the magnitude of the change in resistance as per cent of the control resistance. For these reasons all preparations were treated as a common group and the data were pooled.

The initial and final values for resistance expressed as per cent of the control resistance for each stimulus which increased transmural pressure are presented in figure 7. The transient flow responses during constant pressure perfusion were in the same direction as during constant flow perfusion for each stimulus. Values of resistance at equilibrium with increased transmural pressure were significantly different from the control resistance for all

![Graph](attachment:image.png)

**FIGURE 7**

Summary data for 28 isolated muscle preparations in which 20 mm Hg pressure changes increased vascular transmural pressure. All initial values of resistance were significantly different from the control value. Bars represent ± one standard error of the mean.

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stimuli except increased venous pressure during constant flow perfusion and during application of subatmospheric pressure with constant pressure perfusion. The summary data depicting the responses following pressure stimuli which decreased transmural pressure are presented in figure 8. With decreased transmural pressure, equilibrium resistance was not altered significantly by a change in ambient pressure or by reduction of venous pressure during controlled flow perfusion.

An imposed increase in blood flow (fig. 1B) evoked an autoregulatory response which developed more slowly than that observed following an imposed increase in arterial pressure (fig. 1A). When the pump flow rate greatly exceeded the flow observed during controlled pressure perfusion at approximately 100 mm Hg, the autoregulatory readjustment was even more prolonged and equilibrium resistance sometimes failed to exceed the control resistance. In some instances arterial pressure approached 300 mm Hg as vascular tone increased in the face of the excess blood flow. When blood flow was reduced from these high levels, a persistent increase in vascular tone and elevated resistance was observed as a consequence of the period of overperfusion preceding the flow reduction. When blood flow alterations were made within the range of flow observed during constant pressure perfusion near 100 mm Hg, the autoregulatory process was prompt and complete (fig. 4B).

For purposes of comparison with other stimuli, the data in figures 7 and 8 exclude those trials for blood flow increase and blood flow decrease during overperfusion of the isolated muscle. Overperfusion was defined arbitrarily as controlled blood flow rates which exceeded 150% of average blood flow rates observed during constant pressure perfusion near 100 mm Hg in each preparation. Comparison of the final equilibrium resistance values obtained in the normally perfused group, overperfused group, and all trials is made in table 1. During overperfusion, equilibrium resistance values are in the direction opposite to those obtained during perfusion at lower blood flows. The data in figures 7 and 8 include all trials during alteration of venous pressure and ambient (chamber) pressure since only 7 of 110 of these stimuli were applied during overperfusion.

**FIGURE 8**

Summary of the responses to pressure stimuli which decreased transmural pressure. All initial values of resistance were significantly different from the control value. Bars represent ± one standard error of the mean.

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Discussion

EQUILIBRIUM RESISTANCE VALUES

The data presented satisfy the criteria for control of equilibrium vascular resistance by a metabolic mechanism. Increased transmural pressure produced by venous pressure elevation or application of subatmospheric pressure during constant pressure perfusion or constant flow perfusion failed to evoke vasoconstriction at equilibrium as predicted by the myogenic hypothesis (fig. 7). This failure to show myogenic regulation at equilibrium occurred despite the presence of true autoregulation following increased arterial pressure or increased arterial blood inflow. Similarly, transmural pressure reduction during decreased venous pressure or following release of subatmospheric pressure evoked equilibrium autoregulatory responses predicted by a metabolic rather than a myogenic mechanism (fig. 8). During constant flow perfusion there is no reason to expect a change in the level of tissue metabolism following relatively small pressure alterations and constancy of blood flow should maintain an unaltered rate of washout of vasodilator metabolite(s). Since metabolic regulation should be constant under these circumstances an unopposed myogenic response to transmural pressure alterations would be expected following venous or subatmospheric pressure stimuli. Alteration of venous pressure or chamber pressure during constant flow perfusion, however, failed to evoke a myogenic response at equilibrium. In point of fact, during constant flow perfusion, equilibrium resistance was less than control following transmural pressure elevation and greater than control following transmural pressure reduction, suggesting passive distention of the vessels.

The decrease in vascular tone during muscle contractions is attributed by many investigators to increased production of metabolic products. Both arterial and venous pressure alteration during rhythmic muscle contraction produced percentage alterations of equilibrium resistance which were not significantly different from the changes observed in resting muscle. Since it seems reasonable to expect that metabolic mechanisms should predominate over other mechanisms in the regulation of vascular caliber during increased metabolic activity, an equal change in resistance following transmural pressure changes at rest and during contraction, suggests that the same mechanism may be responsible for the autoregulatory adjustments observed. The fact that the autoregulatory adjustments were more rapidly initiated during contraction is consistent with the hypothesis that an equilibrium between vasodilator metabolite production and washout, forms the basis for metabolically linked autoregulation.

It is apparent from the data presented that the autoregulatory mechanism in skeletal muscle does not depend on the presence of central nervous system innervation. The extent of autoregulatory readjustment of vascular caliber in innervated muscle was not different from that observed in acutely or chronically denervated muscle following arterial or venous pressure alterations. These observations

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<td><strong>Comparison of Final Resistance Values Following Blood Flow Alterations During Controlled Flow Perfusion at Rates Above and Below 150% of Control Blood Flow During Constant Pressure Perfusion Near 100 mm Hg</strong></td>
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agree with those of other investigators\(^7,^8\) for arterial pressure changes. The presence of peripheral nerve nets or ganglion cells responsible for reflex activation of the vascular smooth muscle appears unlikely in the present experiments because prolonged periods of procaine infusion at a concentration of approximately 0.02 g of procaine per 100 ml of perfusing blood failed to affect the direction or magnitude of the initial or final resistance change. This is consonant with the observations of Folkow and Oberg\(^8\) that depletion of peripheral vasoconstrictor substance from sympathetic ganglia by reserpine did not affect the nature of the response to intravascular pressure alteration in skeletal muscle of the cat.

In contrast to the decrease in vascular resistance at equilibrium following elevation of venous pressure observed in the present experiments, previous investigators have reported increased arteriolar resistance with venous pressure elevation in the isolated perfused forelimb,\(^9\) kidney,\(^10\) and intestine.\(^11\) Each of these vascular beds is characterized by a low resistance to blood flow when compared with that for isolated skeletal muscle in our experiments\(^1,^3\) and with skeletal muscle in unanesthetized human beings.\(^12\) Increased equilibrium resistance in skeletal muscle following elevation of venous pressure has been reported by Folkow and Oberg.\(^8\) However, it is evident from their records that the pattern of blood flow response following venous pressure elevation is the same as that observed by us, that is, an initial increase in resistance followed by a secondary readjustment of resistance such that blood flow returned toward the control value. The difference is that the return of blood flow in the experiments of Folkow and Oberg was not sufficient to reduce resistance to the control value at equilibrium, whereas a significant reduction of equilibrium resistance to values below the control level was observed in our experiments. An explanation of the conflicting results may lie in the difference in basal vascular tone since blood flow in resting muscle in the present series of experiments averaged one-half that in the experiments of Folkow and Oberg, 3 to 4 ml/min/100 g muscle compared with 6 to 8 ml/min/100 g tissue respectively. We, too, observed incomplete autoregulation of blood flow following arterial pressure\(^1\) or venous pressure alteration when vascular tone in resting muscle was low. More recently, Folkow\(^13\) has stated that, generally, the net response to elevated venous pressure is a vasodilation. Hanson\(^14\) has also reported that in one-half of his experiments on isolated muscle, venous pressure elevation produced a decreased equilibrium resistance whereas there was no change or slight elevation of resistance in the other experiments. The conflicting results in skeletal muscle seem to reflect a difference in degree rather than direction of the autoregulatory response.

During application of subatmospheric pressure the slight decrease in equilibrium resistance observed in the present experiments is in agreement with the results of Coles\(^15\) and Coles and Greenfield\(^16\) in the human extremity. These investigators concluded that blood flow remained unchanged or was elevated slightly during application of subatmospheric pressures up to 50 mm Hg.
peak. Measurement of forearm blood flow in human beings immediately after release of subatmospheric pressure indicates that in many instances blood flow was markedly increased during the first 10 to 15 seconds. The initial dilation was followed by a secondary constriction which usually persisted for less than one minute. A similar initial transient dilation was observed immediately following release of venous congestion in the human forearm. The responses observed in the present experiments are identical with those observed in the human forearm following release of subatmospheric pressure or release of venous congestion as illustrated in figures 5A and 6A.

The interval between application of any pressure stimulus and the peak transient resistance change was from 9 to 12 seconds at which time autoregulatory readjustment began to return resistance toward the equilibrium value. An exception to this time interval was noted following increases in venous pressure during constant arterial pressure perfusion (fig. 2A) where the interval to peak transient resistance change was prolonged to 15 to 30 seconds. The delay was attributed to the fact that valves in the veins prevented rapid backflow into the smaller venous vessels. Consequently the pressure change was effected gradually at the small vessel level by filling from the inflow side of the circuit. The delay was not encountered after decreases of venous pressure because the veins emptied freely and rapidly.

The transient changes in vascular resistance observed immediately following changes of transmural pressure appear to be compatible with a myogenic response of the vessels to an alteration in the degree of stretch of the vascular smooth muscle. Examination of the time course of the transient responses discloses discrepancies which suggest the possibility that an alternative mechanism may be responsible for some of the immediate resistance changes. If the relaxation of the vessels which begins 1 to 2 seconds after reduction of venous pressure (fig. 5A and B) is myogenic in nature, myogenic relaxation of the resistance vessels following decreased arterial pressure would be expected to occur with a similar latency, not at 9 to 12 seconds as was observed (fig. 4). Conversely, the autoregulatory constriction that accompanies arterial pressure elevation follows a primary vasodilation and the constriction is delayed 9 to 12 seconds after application of the stimulus (fig. 1). However, the constriction following venous pressure elevation begins immediately (fig. 2A and B) despite the fact that effective pressure changes at the resistance vessels are delayed by the restriction to rapid backflow offered by the venous valves. It does not seem reasonable to reconcile these discrepancies by suggesting that venous pressure changes are transmitted more rapidly to the smooth muscle of the resistance vessels than equivalent arterial pressure changes.

Finally, alteration of ambient pressure in either direction produces a primary vasodilation although in one instance transmural pressure is increased (fig. 3) whereas in the other, transmural pressure is decreased (fig. 6). The immediate, brief decrease in arterial blood inflow which precedes the transient dilation following release of subatmospheric pressure (fig. 6A) may be considered to represent passive recoil of the arterial vessels. Support for this view is derived from the responses observed when arterial pressure alone was decreased. As shown in figure 4A, arterial inflow decreased immediately and had the same time course and magnitude as when ambient pressure was increased. Furthermore, immediate brief changes of resistance in the opposite direction are observed upon distention of the arterial vessels (figs. 1 and 3) suggesting a passive effect on vessel caliber.

It is not clear why a reduction in transmural pressure produced by decreased venous pressure or by release of subatmospheric pressure should elicit vasodilation, because one would expect to observe passive recoil of the vessels and increased resistance to arterial blood inflow. A myogenic mechanism does not appear to fit the observed data, as noted above, and local neural reflex responses seem...
unlikely because the transient changes of resistance were present in chronically denervated muscle and during procaine infusion in acutely denervated muscle. Purely passive effects may play a role in the anomalous transient responses as has been suggested previously. Rapid emptying of the distensible venous system accompanies reduction of venous pressure and return of chamber pressure from subatmospheric to atmospheric. If the distended venous vessels supplied a portion of the equilibrium forces which maintain arterial resistance during the control period, rapid release of venous distention would disturb the equilibrium in such a way that arterial caliber could increase transiently until metabolic autoregulation restored vessel tone to a new equilibrium point. The venous vessels of skeletal muscle are parallel with the arterial supply to the arteriolar level and it is conceivable that lateral pressure exerted by distended veins may be transmitted to the arterial walls, particularly if these parallel vessels are contained within a common sheath or bounded by muscle fasiculi. A mechanism of this nature might explain how a 20 mm Hg reduction of venous pressure during constant flow perfusion produces a reduction of arterial pressure exceeding 70 mm Hg (fig. 5B).

The transient responses to transmural pressure changes may thus be passive effects consequent to perturbation of the equilibrium state of the arterial resistance vessels. The transient blood flow disturbances are then rectified by an autoregulatory mechanism closely linked to the metabolism of the tissues which adjusts blood flow on the basis of tissue requirements.

Summary

Simple criteria have been used in an isolated, perfused skeletal muscle preparation to determine whether autoregulation of blood flow in this tissue is the consequence of a metabolic or a myogenic mechanism. Elevation of venous pressure significantly increased equilibrium vascular resistance and reduction of venous pressure significantly increased vascular resistance during controlled pressure perfusion whereas alteration of ambient pressure had no significant effect on equilibrium resistance. These responses repudiate a myogenic mechanism for autoregulation of equilibrium blood flow since the myogenic hypothesis predicts increased resistance following increased transmural pressure and decreased resistance following decreased transmural pressure. Moreover, during perfusion at constant blood flow, metabolic regulation should be constant and myogenic responses would be permitted full expression. Alteration of venous pressure or ambient pressure during constant flow perfusion, however, failed to evoke myogenic responses at equilibrium. Rather, a passive distention was observed at equilibrium after increased transmural pressure, and passive recoil of the vessels followed decreased transmural pressure during constant flow perfusion. All pressure alterations were accompanied by transient resistance changes of undetermined origin. With the criteria employed, however, the results indicate that the regulation of equilibrium vascular resistance in skeletal muscle is based primarily on a metabolic mechanism.

References


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