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Effects of muscle contraction on skeletal muscle blood flow: when is there a muscle pump?

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Abstract

Effects of muscle contraction on skeletal muscle blood flow: when is there a muscle pump? *Med. Sci. Sports Exerc.,* Vol. 31, No. 7, pp. 1027-1035, 1999.

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Purpose:

The purpose of this study was to determine the effects of rhythmic muscle contraction on the dynamics of venous outflow in rat skeletal muscle.

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Methods:

The effects of frequency and duration of tetanic contraction on venous blood flow (BF) were examined with transonic flow probes placed on the femoral artery and vein.

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Results:

Results reveal that instrumentation of the venous system with cannulas or flow probes alters vascular mechanics so that the muscle pump effect is masked. Measurements conducted without instrumentation of the venous vasculature *in situ,* as well as experiments with conscious exercising animals, indicate that the muscle pump enhances BF during exercise. Also, recent *in vivo* studies of humans indicate an important role for the muscle pump. In contrast, results reported herein and recent results from *in situ* experiments, which allow control of more parameters, indicate that there is no measurable muscle pump effect on BF during rhythmic muscle contraction. Review of the literature indicates that many *in vitro/in situ* experiments used instrumented veins that may have altered venous vascular mechanics and the interactions of muscle contraction and venous vascular mechanics, thus minimizing or abolishing the muscle pump effect.

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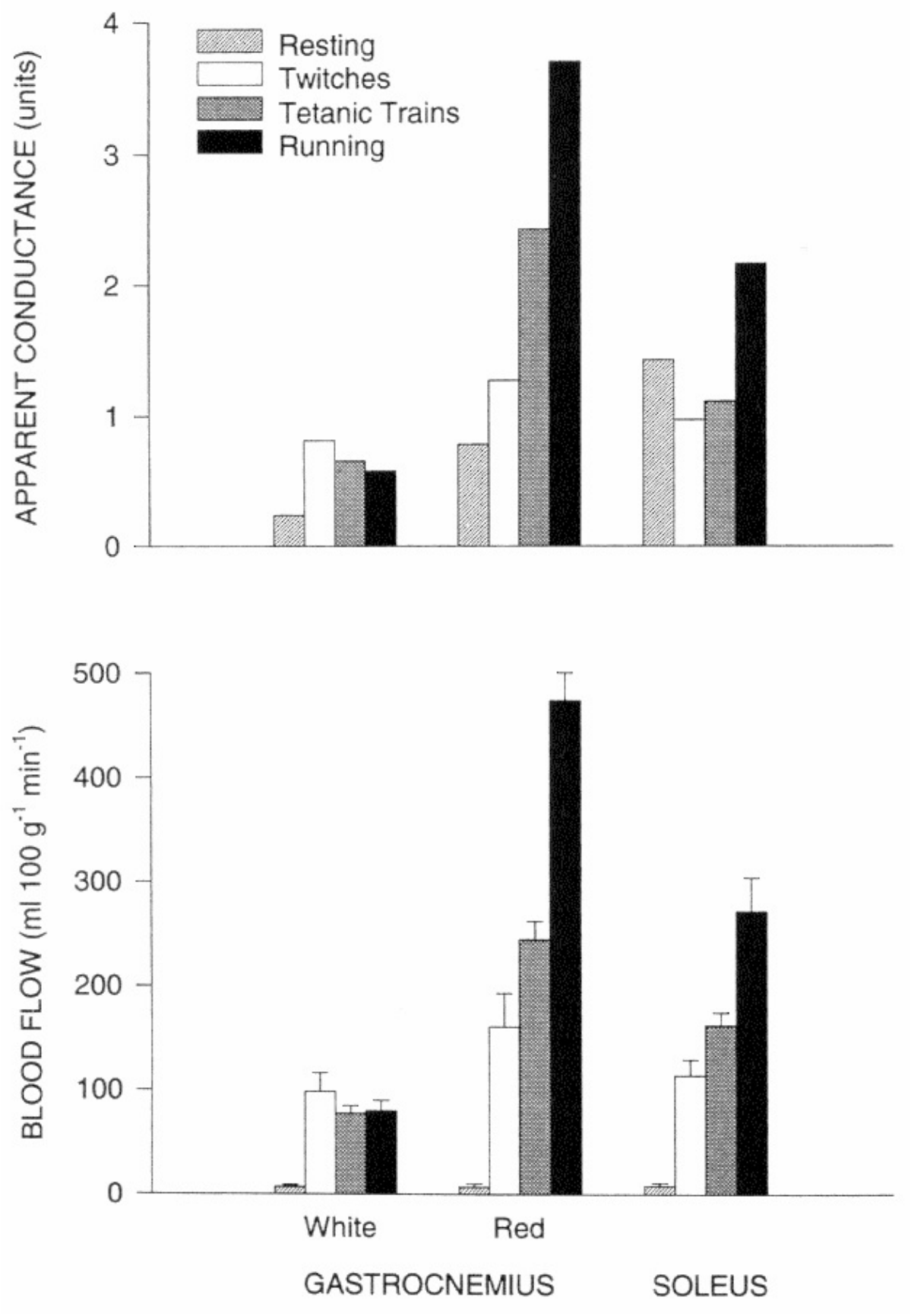
Conclusions:

The muscle pump contributes to the initial increase in BF at exercise onset and to maintenance of BF during exercise.

The cardiorespiratory effects of exercise are among the most interesting components of exercise science. One component of the cardiorespiratory response to exercise is the dramatic increase in blood flow to skeletal muscle (26). For exercise to be maintained for more than a few seconds it is essential that adequate blood flow be provided to skeletal muscle. As shown in Figure 1, only 5-10 mL of blood are distributed to 100 g of quiescent skeletal muscle. During high intensity exercise, skeletal muscle blood flow has been reported to increase to 150-500 $mL \cdot min^{-1} \cdot 100\ g^{-1}$(1,14,15,17,20,27,28,29). During exercise at various intensities, blood flow is greater in high oxidative skeletal muscles than in low oxidative skeletal muscles. Mechanisms responsible for the rapid increase in blood flow observed at the start of dynamic exercise remain poorly defined.


APPARENT CONDUCTANCE (units)
4
3
2
1
0
Resting
Twitches
Tetanic Trains
Running
BLOOD FLOW (ml 100 g-1 min-1)
500
400
300
200
100
0
White
Red
GASTROCNEMIUS
SOLEUS

pparent vascular conductance and blood flows of rat skeletal muscle(18). Vascular conductance was calculated for perfusion pressures of 130 mm Hg with equations derived from linear regression analysis of conductance (for each muscle) and perfusion pressure (corrected for effects of viscosity). Data for resting conditions are from (18), data for twitch and tetanic conditions are from (20), and data for running rats are from (4). Data for twitch contractions were collected after 10 min of contraction and for tetanic contractions after 1 min of contractions. Reference 17. Laughlin, M. H., R. J. Korthuis, D. J. Duncker, and R. J. Bache. Control of blood flow to cardiac and skeletal muscle during exercise. In: Handbook of Physiol. Sect. 12: Integration of Motor, Circulatory, Respiratory, and Metabolic Control During Exercise, Chap. 16, L. B. Rowell and J. T. Shepherd (Eds.). Bethesda, MD: Am. Physiol. Society, 1996, pp. 705-769 reprinted with permission. References: 18. Laughlin, M. H. and J. Ripperger. Vascular transport capacity of hind limb muscles of exercise-trained rats. J. Appl. Physiol. 62:438-443, 1987; 20. Mackie, B. and R. Terjung. Influence of training on blood flow to different skeletal muscle fiber types. J. Appl. Physiol. 55:1072-1078, 1983; 4. Armstrong, R. B. and M. H. Laughlin. Rat muscle blood flows during high speed locomotion. J. Appl. Physiol. 59:1322-1328, 1985.

Blood flow is determined by the interaction of the total energy gradient driving blood flow and the impedance of the vascular network. The flow of blood to a vascular bed is governed by perfusion pressure gradient across the vascular bed (i.e., arterial minus venous pressure) and the resistance to blood flow. Thus, in most tissues since mean arterial and venous pressures are normally maintained within narrow limits, blood flow control is accomplished in large part by variations in vascular resistance. Alterations in vascular resistance result from changes in the caliber of resistance vessels which, in turn, are regulated by the contractile activity of vascular smooth muscle. The control of vascular resistance in skeletal muscle and its importance to providing blood flow during exercise has been discussed by other speakers in this symposium. In this paper we focus on mechanical effects of active skeletal muscle on perfusion and some considerations about approaches to the study of these effects.

Contraction of skeletal muscle produces dramatic effects on the vasculature within the muscle tissue, altering vascular compliance, resistance, transmural pressure across the vascular walls, and kinetic energy of the blood passing through the vascular bed. These dramatic changes in kinetic energy, compliance and impedance in skeletal muscle vascular beds associated with dynamic exercise, require a more careful analysis of the determinants of blood flow in active skeletal muscle than is required in quiescent tissues. Our interest in this area of investigation was kindled by observations of the magnitude of blood flow to the skeletal muscle of rats during normal exercise (15,16). We observed that blood flows to the red, high-oxidative muscle tissue deep in extensor muscles of rats often are in excess of 300 $mL \cdot min^{-1} \cdot 100\ g^{-1}$. In contrast, we were not able to reproduce flows of this magnitude in resting rat skeletal muscle with simple maximal vasodilation. Figure 1 summarizes these data suggesting that muscular contraction is important in exercise hyperemia. Further, the results of Mackie and Terjung (20) presented in Figure 1 indicate that rhythmic tetanic muscle contractions closely simulate the magnitude of blood flow observed in normal locomotory exercise. It is important to emphasize that

these data were collected with the microsphere technique which does not require instrumentation of the vasculature perfusing the skeletal muscle. We will return to this point later. First, we summarize the essence of the muscle pump theory.

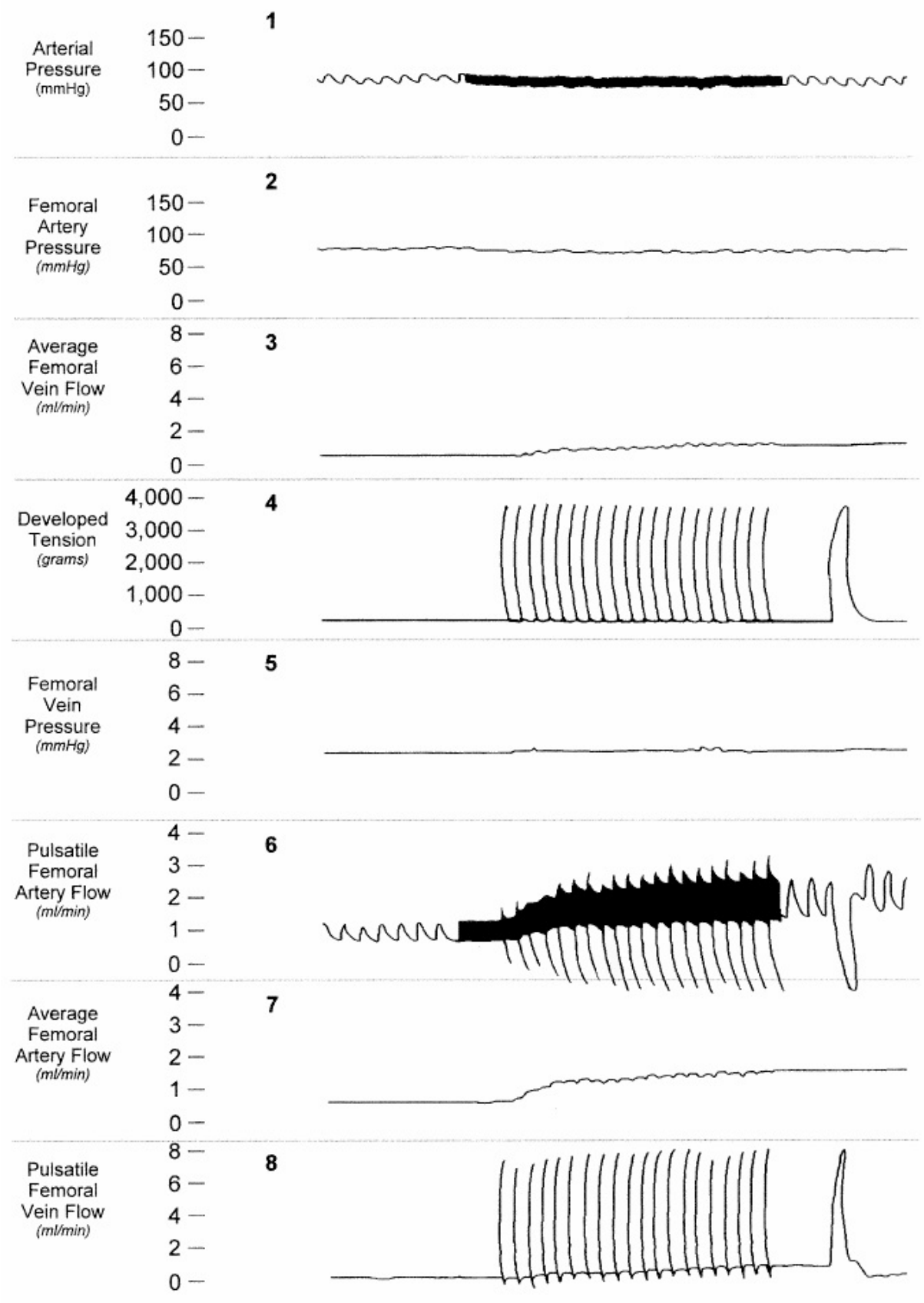
Important differences between the determinants of vascular conductance in striated muscle and nonmuscle tissues are the effects of muscle contraction and the associated effects of extravascular compression on calculated vascular conductance (14,17,27,32). Extravascular compression expels blood from the venous vasculature and impedes flow of blood into the arterial vasculature. The muscle pump hypothesis holds that in skeletal muscle the net effect of these forces is enhanced perfusion of the muscle. Thus the phrase "muscle pump" refers to contraction-induced, rhythmic propulsion of blood from skeletal muscle vasculature which facilitates venous return to the heart and perfusion of skeletal muscle. The orientation of venous valves causes blood to flow out of compressed segments toward the heart. If a tetanic contraction is maintained, the net effect is increased resistance to blood flow. Therefore, the muscle pump mechanism only exists during rhythmic contractions. Rhythmic contraction produces a pumping action on the venous circulation in skeletal muscle, imparting energy to the blood, ejecting it out of the veins. The venous segments of the circulation are refilled during muscle relaxation (6,10,11,14,17,19,24,25,30,31,32,35).

We proposed, based largely on results of Folkow et al. (10,11), that during relaxations of skeletal muscle pressures in the venules and deep small veins are negative (14). This hypothesis is also consistent with the fact that the muscles relax rapidly (50-100 ms) so that the compressive force is suddenly removed. Because the walls of small veins are fused to surrounding muscle tissue, it seems likely that negative pressure occurs when veins are pulled open by relaxing muscle. The extensive connective tissue fibers connecting the walls of microvessels to muscle tissue are easily observed in a high power dissecting microscope. The decrease in small vein pressure produced by the expansion of the small veins in the muscle during relaxation is key to our conception of the muscle pump. The magnitude of the proposed decrease in pressure in these veins and the duration of the decrease should be determined by the rapidity of blood flow from the arterial side through

the capillaries into the empty venous segments. Since Folkow et al. (10) observed that arterial inflow continued throughout the relaxation period and there was no femoral venous outflow during relaxation, their results suggest that the venous segments do not refill instantaneously. We conceive that after muscle contraction venous compartments are refilled in sequence from the first venous valves in the small veins to the systemic veins. If sufficient time is allowed before the next contraction, the venous compartments are completely refilled and the effect of the previous contraction is dissipated. On the other hand, if another contraction occurs before venous refilling is complete, then venous pressures will remain decreased.

The initiation of dynamic exercise produces immediate increases in blood flow to active skeletal muscle tissue. As described by others in this symposium, rhythmic isometric and/or dynamic contractions of various muscle groups produce increases in blood flow following the first contraction. Although time-averaged arterial inflow and venous outflow are generally equal, it is important to keep in mind that during dynamic exercise and/or rhythmic contraction of skeletal muscle, venous outflow occurs during contractions and most arterial inflow occurs during relaxation of the muscle (10). These time-dependent changes in blood flow are important because they mean that durations of contraction and relaxation as well as frequency of contraction have effects on muscle perfusion not apparent in time-averaged flow measurements.

The relationships among tension developed by the muscle, venous pressures, arterial pressures, venous outflow, arterial inflow, and time during rhythmic tetanic contraction are illustrated in Figure 2. These relationships are similar to those reported by Folkow et al. (10). Appreciation of the physical forces produced by alternating contraction and relaxation on muscle hemodynamics is essential to our understanding of the mechanisms that determine muscle blood flow during exercise. Many studies of muscle blood flow during dynamic exercise have only measured mean arterial flow so that pulsatile changes in arterial and venous blood flow that occur with each contraction/relaxation cycle are obscured.


Arterial Pressure (mmHg)
150
100
50
0
1
Femoral Artery Pressure (mmHg)
150
100
50
0
2
Average Femoral Vein Flow (ml/min)
8
6
4
2
0
3
Developed Tension (grams)
4,000
3,000
2,000
1,000
0
4
Femoral Vein Pressure (mmHg)
8
6
4
2
0
5
Pulsatile Femoral Artery Flow (ml/min)
4
3
2
1
0
6
Average Femoral Artery Flow (ml/min)
4
3
2
1
0
7
Pulsatile Femoral Vein Flow (ml/min)
8
6
4
2
0
8

Sample recording of measured parameters, calibration shown on the left. Resting conditions exist before stimulation of the sciatic nerve to produce 7.5 tetani·min−1, 100-ms duration. Resting muscle tension is 300 g to maintain the muscle at L0. Note that muscle stimulation had no effect on arterial pressures and only modest effects on femoral vein pressure. Average arterial and venous flow increased from 0.7 mL·min−1 at rest to about 1.7 mL·min−1 over the first minute of contraction. Venous outflow between contractions and peak venous outflow also increased over the first few contractions. The slow paper speed is 25 mm·min−1 and the fast paper speed is 25 mm·s−1 From reference 9. Crader, S. E. and M. H. Laughlin. Skeletal muscle venous outflow is phasic and correlated with muscle tension development (Abstract). Med. Sci. Sports Exerc. 28:S175, 1996.

Estimates indicate that the muscle pump provides substantial amounts of energy for muscle perfusion in exercising humans as well (14,19,27,28,35). It appears that the impact of the muscle pump on perfusion of active skeletal muscle is critically determined by the type of contractile activity (14). Figure 1 presents the apparent vascular conductance in skeletal muscle during maximal vasodilation and during different forms of contractile activity. Although vascular "conductances" are presented in Figure 1, it is important to emphasize that these data are apparent conductances, as labeled, because an Ohmic conductance or resistance does not exist across a pump. That is, if the differences among conductance values are the result of the muscle pump, the apparent increase in conductance produced by contraction is actually the result of increased energy imparted to the blood by the pump and not a result of relaxation of vascular smooth muscle and increased diameter of resistance vessels. The muscle pump may facilitate blood flow by at least two mechanisms: decreased venous pressures as described above and increased total kinetic energy in the system (i.e., the total energy gradient available to force blood through the muscle vascular bed is increased). Because of the assumptions used to calculate the vascular conductances presented in Figure 1, this increased energy is translated to increased apparent conductance.

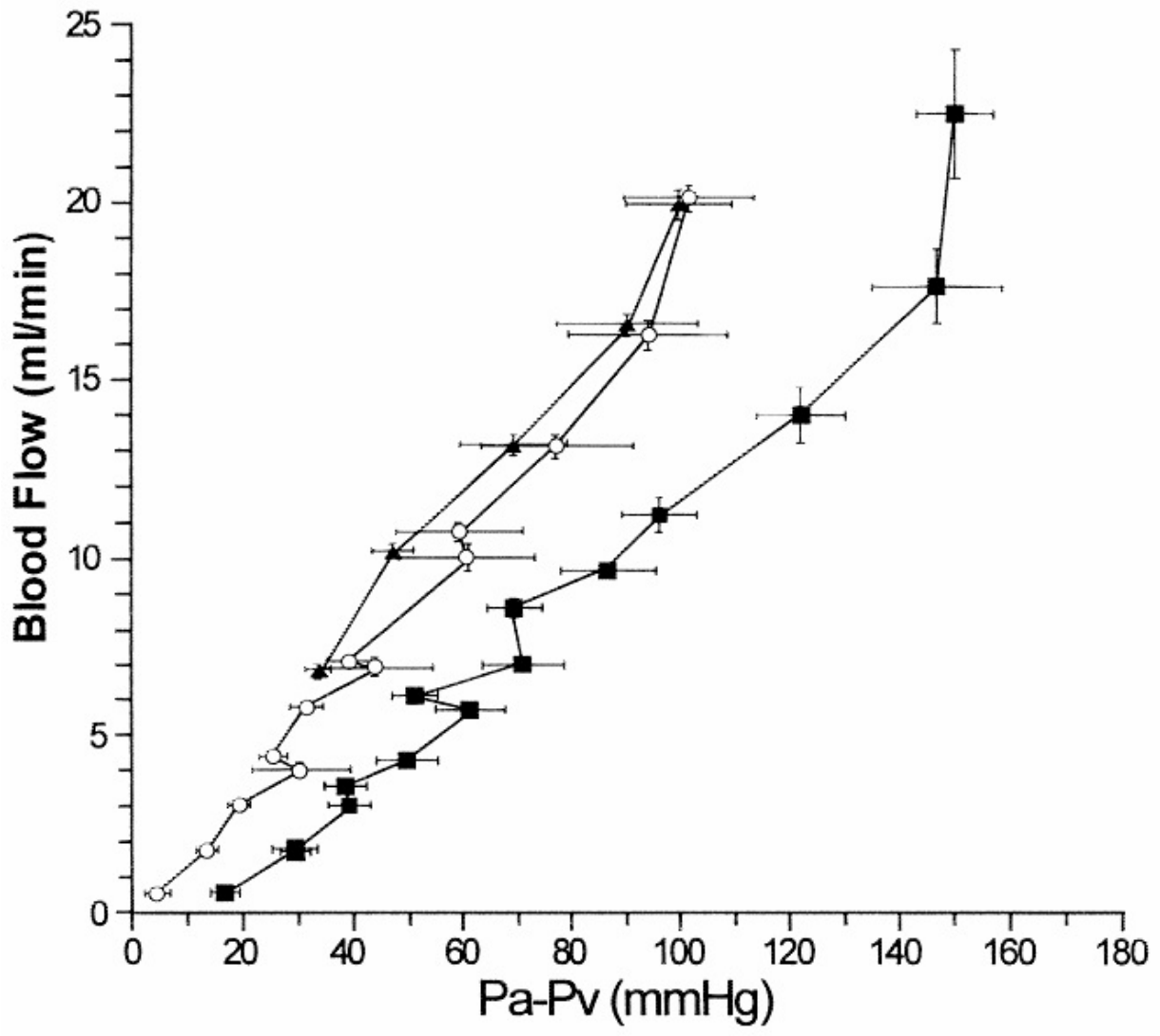
The comparison of maximal blood flows measured during normal locomotory exercise, models of exercise, and during maximal pharmacological vasodilation presented in Figure 1 supports the hypothesis that the muscle pump is important in sustaining muscle blood flow during exercise. Figure 1 also depicts the apparent vascular conductances of rat muscle determined under four different conditions: 1) isolated, perfused hindquarters maximally vasodilated with papaverine; 2) performing isometric twitch-type contractions; 3) performing trains of isometric, tetanic contractions; and 4) running on a motor-driven treadmill. It is possible that apparent vascular conductance in high-oxidative muscle tissue (soleus and red gastrocnemius muscles) is higher during normal exercise than during twitch and tetanic contraction because the type of muscle activity associated with voluntary exercise produces a more efficient pumping action. Also,

trains of tetanic contractions appear to be less effective for increasing perfusion of white gastrocnemius muscle than of red gastrocnemius muscle perhaps because the white muscle is located superficially in the leg and has less vascularization than red muscle (13,14,17). This may explain why apparent vascular conductance is about the same during all three types of rhythmic muscle contraction in white, fast-twitch muscle (Fig. 1). In contrast, in the red gastrocnemius muscle, apparent vascular conductance is much higher than in white gastrocnemius, and conductance during resting conditions < during twitches < during tetanic trains < during running in red muscle as shown in Figure 1. Thus, locomotory exercise produces the greatest value for apparent vascular conductance in the soleus and red gastrocnemius muscles. The data summarized in Figure 1 are consistent with the hypothesis that the muscle pump is an important determinant of apparent vascular conductance (or blood flow) during locomotory exercise.

It seems possible that the muscle pump is more effective in locomotory exercise than in various models of exercise such as twitch contractions and trains of tetanic contractions because of the sequence of muscle fiber activation and type of contraction associated with normal exercise activity. Important components of normal muscle activation relative to the muscle pump include the following: 1) The time at which muscles are active during the stride cycle varies so that each muscle has a unique period of activity within each stride cycle (5,8,12,15,37). 2) Muscle fiber recruitment is sequential, not simultaneous during locomotory exercise (12) (Thus, the efficacy of the muscle pump is not only determined by the maximal pressure developed but also by the spatial and temporal sequence of pressure development and precontraction vascular volume (10,11)). 3) In different phases of the stride cycle during locomotory exercise, muscle contractions consist of active lengthening and shortening as well as passive lengthening (8,12,14,15). Rhythmic isometric contractions may produce lower peak vascular conductances than locomotory exercise because the muscle pump mechanism is less effective in the absence of muscle length changes (compare tetanic trains to Running in Fig. 1) (14). Other factors that are believed to influence the efficacy of the muscle pump include: skeletal muscle fiber type and location within muscles or muscle groups, arrangement of the vasculature in the muscle (14), function of venous

valves (7,24), and the effects of gravity and/or venous filling pressures (10,11).

The muscle pump hypothesis predicts that if a skeletal muscle is stimulated to contract while it is already maximally vasodilated, then blood flow should be increased by the mechanical effects of muscle contraction. That is, blood flow should be greater during rhythmic contractions plus maximal vasodilation than that measured during maximal vasodilation alone (10). We tested this prediction using the single leg preparation of McAllister and Terjung (22). Once the preparation had attained steady-state conditions, we induced maximal vasodilation and examined the relation-ship between perfusion pressure and blood flow. We then stimulated the muscle to contract with tetanic trains and compared the pressure-flow curves. As shown in Figure 3, maximal vasodilation with sodium nitroprusside (SNP) shifted the pressure flow curve to the left. However, trains of 100-ms duration, tetanic contractions (15/min) superimposed on the SNP dilation did not increase blood flow significantly. We also observed that this preparation showed no evidence of autoregulation of blood flow. Therefore, we became concerned about the use of this preparation as an approach to study mechanisms of exercise hyperemia.



Relationship between perfusion pressure and blood flow in perfused rat hindlimb. Results represent means ± SE for seven rats. ▪, control limb, with no treatment; □, data obtained in resting muscle during maximal vasodilation with SNP; ▲, data obtained during maximal vasodilation with SNP and muscle contraction at 15 tetanic contractions per minute, each contraction of 100-ms duration. Maximal vasodilation was defined as the point at which further no vasodilation occurred with increased dose of SNP and when no reactive dilation occurred following 10-min occlusion of blood flow.

The results presented in Figure 3 do not support a muscle pump effect on blood flow. These results confirm results of recent studies (21,23,34) that examined blood flow in various *in situ* preparations of contracting skeletal muscle and report no evidence of a significant muscle pump effect. In contrast, other recent studies with conscious animals performing exercise on treadmills and in conscious human subjects described by others in this symposium provide evidence that the muscle pump is an important mechanism for providing blood flow during exercise (33,36). So why do results obtained from *in situ* preparations of experimental animal models of exercise indicate that the muscle pump has little or no effect on muscle

perfusion while results from studies of locomotion with normal muscle recruitment patterns indicate that the muscle pump is important to maintenance of normal blood flow to active muscle? This dilemma led us to propose that the muscle pump effect is abolished in *in situ* preparations where vascular mechanics of the veins are altered because of cannulation and/or instrumentation (9) of the veins.

The purpose of the experiments described below was to examine the effects of muscle contraction on the dynamics of venous outflow in rat skeletal muscle *in vivo.* We examined the effects of different frequencies and durations of contraction of rat hindlimb muscle on characteristics of venous blood flow dynamics measured with transonic flow probes implanted on the intact femoral artery and vein. These results revealed the characteristics of rhythmic muscle contractions that produce the greatest venous outflow in this preparation. Second, we present data obtained with a modification of this preparation to test the hypothesis that instrumentation of the venous system, such as cannulation of the veins or application of a flow probe on the veins, alters vascular mechanics so that the muscle pump effect is abolished.

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METHODS

Adult, male Sprague-Dawley rats (*N,* 6; body wt., 337 ± 15 g) were anesthetized with pentobarbital sodium (60 $mg \cdot kg^{-1}$) and instrumented as described by Mackie and Terjung (20). Polyethylene catheters were placed in the left carotid artery and in branches of the left femoral artery and vein. The left gastrocnemius-plantaris-soleus muscle group was prepared for *in situ* stimulation. Briefly, the muscle group was exposed preserving the blood supply. The limb was secured at the distal end of the femur and the Achilles tendon was attached to a force transducer. The sciatic nerve was tied and cut, and the distal end was placed over a platinum bipolar electrode connected to a Grass Model S48 (Quincy, MA) stimulator. Flow was measured with a Transonic AT206 (Ithaca, NY) small animal blood flow meter. Flow probes (APO0.5VB or APO0.7VB) were placed on the femoral artery and vein.

Protocol 1: effects of muscle contraction on venous outflow dynamics. With the muscle at its optimum tension-producing length, the nerve was stimulated with supra-maximal square waves (6 V, 0.1-ms duration) producing tetanic contractions with 100 Hz stimulation for 100-, 200-, or 300-ms duration. The muscle group was stimulated to produce 7.5, 15, 30, 60 and 120 tetanic contractions per minute with each contraction duration.

During rest and muscle contraction the following parameters were measured: 1) Central arterial pressure (measured in the carotid artery), 2) Femoral artery pressure, 3) Femoral vein pressure, 4) Average and pulsatile femoral artery flow, 5) Average and pulsatile femoral vein flow, and 6) Developed tension.

Protocol 2: effects of tilt on muscle blood flow during contraction. The results of Protocol 1 demonstrated that the highest blood flows and calculated vascular conductances were observed during contraction at 15 tetanic contractions·min^{-1}, 300-ms duration and 30 tetanic contractions·min^{-1}, 100-ms duration. We used the experimental preparation outlined above except that the left femoral artery and vein were not cannulated and a flow probe was not placed on the left femoral vein. We then compared blood flow during muscle contraction at 15 tetanic contractions·min^{-1}, 300-ms duration and 30 tetanic contractions·min^{-1}, 100-ms duration with the rat supine and tilted to nearly upright (to increase venous pressure). We reasoned that if there is a muscle pump effect in this preparation, the blood flow during tilt should exceed that during supine exercise at the same intensities because of the increased venous pressure (11,14,17).

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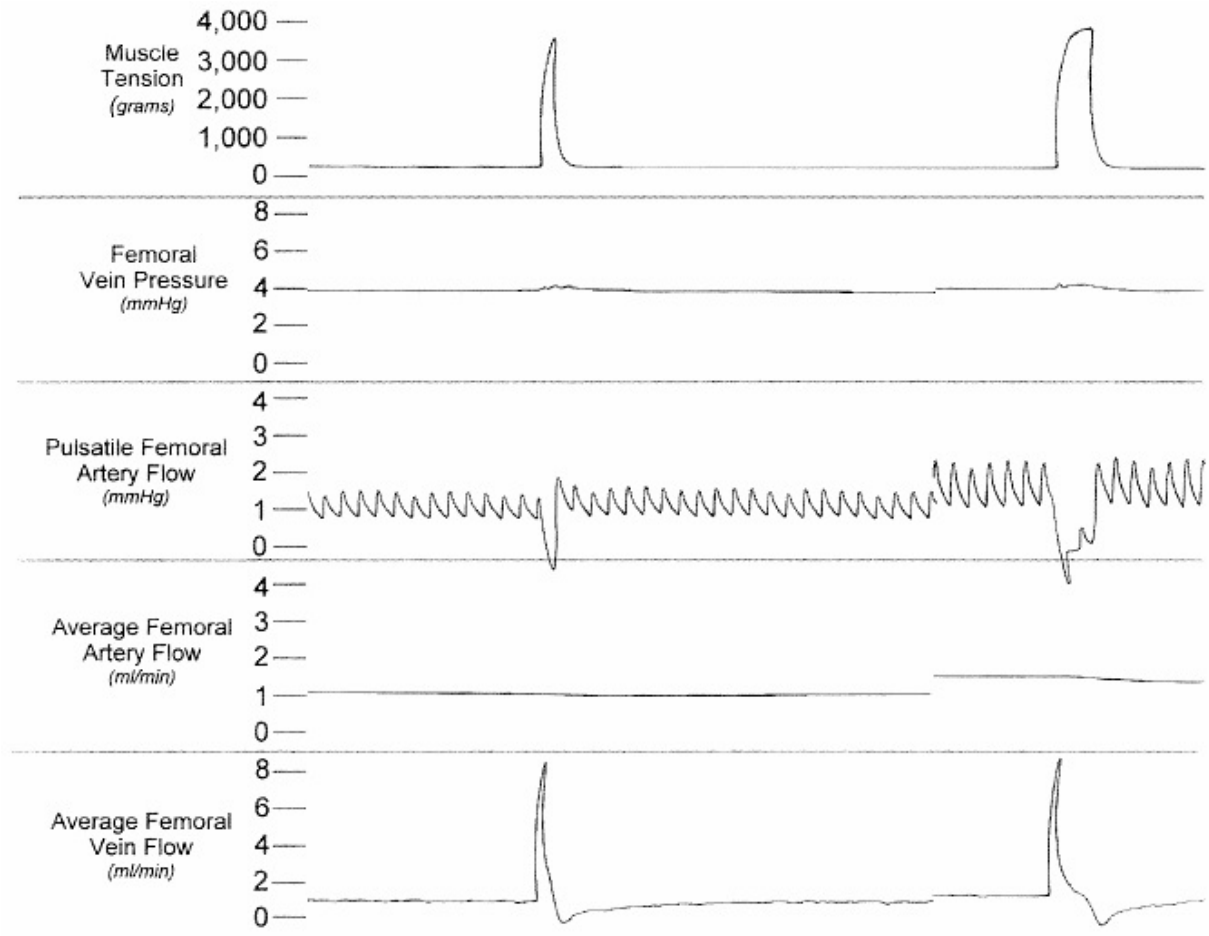
RESULTS

Figure 2 illustrates the effects of muscle contraction at 7.5 tetani·min^{-1}, 100-ms duration on the measured parameters. Note that muscle stimulation had no effect on arterial pressures and only modest effects on femoral vein pressure. Average arterial and venous flow increased from 0.7 mL·min^{-1} at rest to about 1.7 mL·min^{-1} over the first minute of contraction. Venous

outflow between contractions and peak venous outflow also increased over the first few contractions (Fig. 2).

The time course of venous outflow during contraction, as reflected in the recording of venous flow versus time, was influenced by the duration of contraction. Figure 4 illustrates venous outflow produced during single contractions of two different durations. The first was a 100-ms duration contraction and the second 300 ms. Note that peak tension is greater with 300-ms duration (4,100 vs 3,800 g). Also, note that during contraction, venous outflow occurs in two phases with 100-ms duration. In contrast, the 300-ms duration produced venous outflow that exhibited a plateau phase during contraction. These changes in the pattern of phasic flow produced by increases in duration of contraction were similar across all stimulation frequencies.

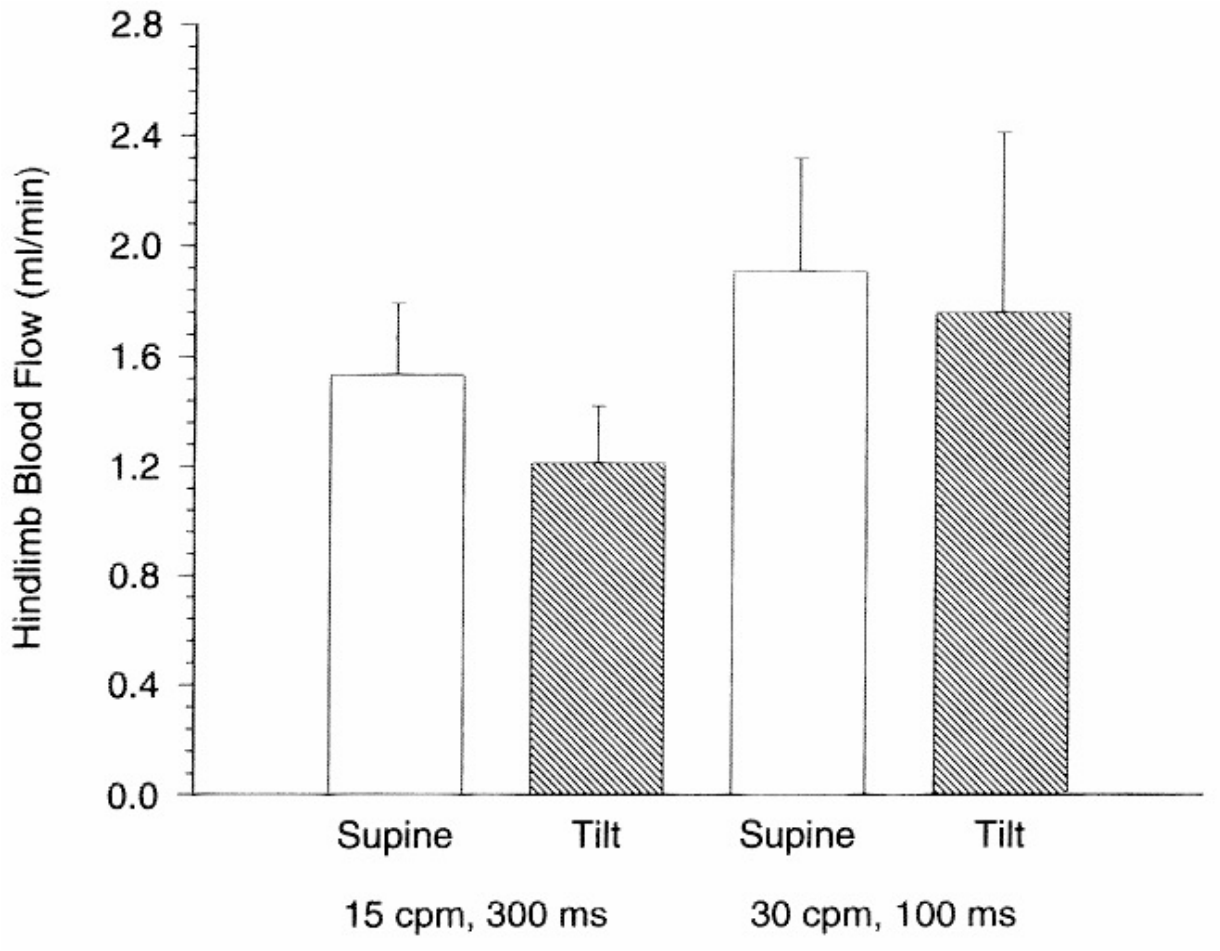


Recording of venous outflow produced during contractions of two different durations. The contraction shown on the left was a 100-ms duration stimulation and the contraction on the right was produced by a 300-ms duration stimulation. Paper speed is 25 mm·s−1. Peak tension is greater with 300-ms duration (4,100 vs 3,800 g). Also, during the 100-ms duration contraction, venous outflow increased rapidly to a peak of 8.3 mL·min−1 and then decreased to negative values at the end of contraction. Flow

slowly returned to precontraction levels following the negative flow period after contraction. In contrast, the 300-ms duration produced venous outflow that exhibited a rapid increase in flow to 8.4 mL·min−1 followed by a rapid decrease in flow to a plateau phase during contraction. Immediately after contraction, flow was transiently negative then increased to precontraction levels. These changes in the pattern of phasic flow produced by increases in duration.

The highest blood flows and calculated vascular conductances were observed during contraction at 15 tetanic contractions·min^{-1}, 300-ms duration and 30 tetanic contractions·min^{-1}, 100-ms duration. In general, across all contraction parameters, Pearson analysis of the results indicates that peak venous outflow is correlated with peak tension development (r = 0.77).

As shown in Figure 5, tilt had no effect on the blood flow measured during contraction with either set of stimulation parameters. Venous pressures were increased as expected. However, tilt often produced small decreases in arterial pressure at heart level. Calculated conductance values were also similar during contractions supine and during upright tilt.



lood flows measured with the rats supine or tilted with hindlimb stimulations as described in the methods. Cpm, contractions per minute; Ms, milliseconds duration of each contraction. There were no differences in blood flow between supine and tilt.

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DISCUSSION

The results of this study reveal that peak venous outflow is directly related to total tension produced during skeletal muscle contraction. Also, the duration of muscle contraction is an important determinant of venous outflow dynamics in that both the amount of venous outflow per contraction and the time course of outflow during contraction are altered by changes in stimulation patterns. Finally, the classic muscle pump hypothesis (11) predicts that increased venous pressure caused by head-up-tilt would produce increased blood flow. When we examined the effects of head-up-tilt on muscle perfusion, no increases in blood flow were observed. It is important that this was true in a preparation in which we did not instrument the skeletal muscle veins. However, it is possible that the muscle pump effect cannot be demonstrated in this preparation because placing the flow probe on the femoral artery of the rat also alters the vascular mechanics of the venous system sufficiently to interfere with the muscle pump effect.

Our results, which indicate that the muscle pump effect is not important in providing skeletal muscle blood flow, confirm results of Naamani et al. (23). They examined blood flow in diaphragm muscle and limb skeletal muscle of mongrel dogs. Skeletal muscle was perfused with controlled arterial pressures at several levels generating pressure-flow curves. The pressure-flow relationships were compared under control conditions, after maximal vasodilation with the combination of sodium nitroprusside (SNP), adenosine (ADO), and acetylcholine (ACH), and during muscle contractions during maximal vasodilation with these agents. The muscle pump hypothesis predicts that when muscle contractions are superimposed on maximal vasodilation, blood flow will be increased. Figure 6 presents phrenic pressure-flow results from this study (23). The open symbols represent control data, closed circles maximal vasodilation data, and closed squares maximal vasodilation plus muscle contraction. The trains were 12 tetanic contractions·min^{-1}. It is apparent from the data in Figure 6 that only spontaneous muscle contractions produced enhanced blood flows. Figure 7 presents similar data from dog gastrocnemius muscle experiments. Here, the data provide no evidence of enhanced blood flow produced by muscle

contraction. Finally, Naamani et al. (23) examined the effects of increased venous pressure on the role of the muscle pump in dog gastrocnemius muscle and found that increases in venous pressure produced little or no change in blood flow. The muscle pump hypothesis predicts that such increases in venous pressure would result in increased venous filling, greater stroke volume per muscle contraction, and increased blood flows (10,14). This was not observed. However, evidence of the muscle pump effect is still evident in these data since the decrease in perfusion pressure related to increased venous pressures did not decrease blood flow.

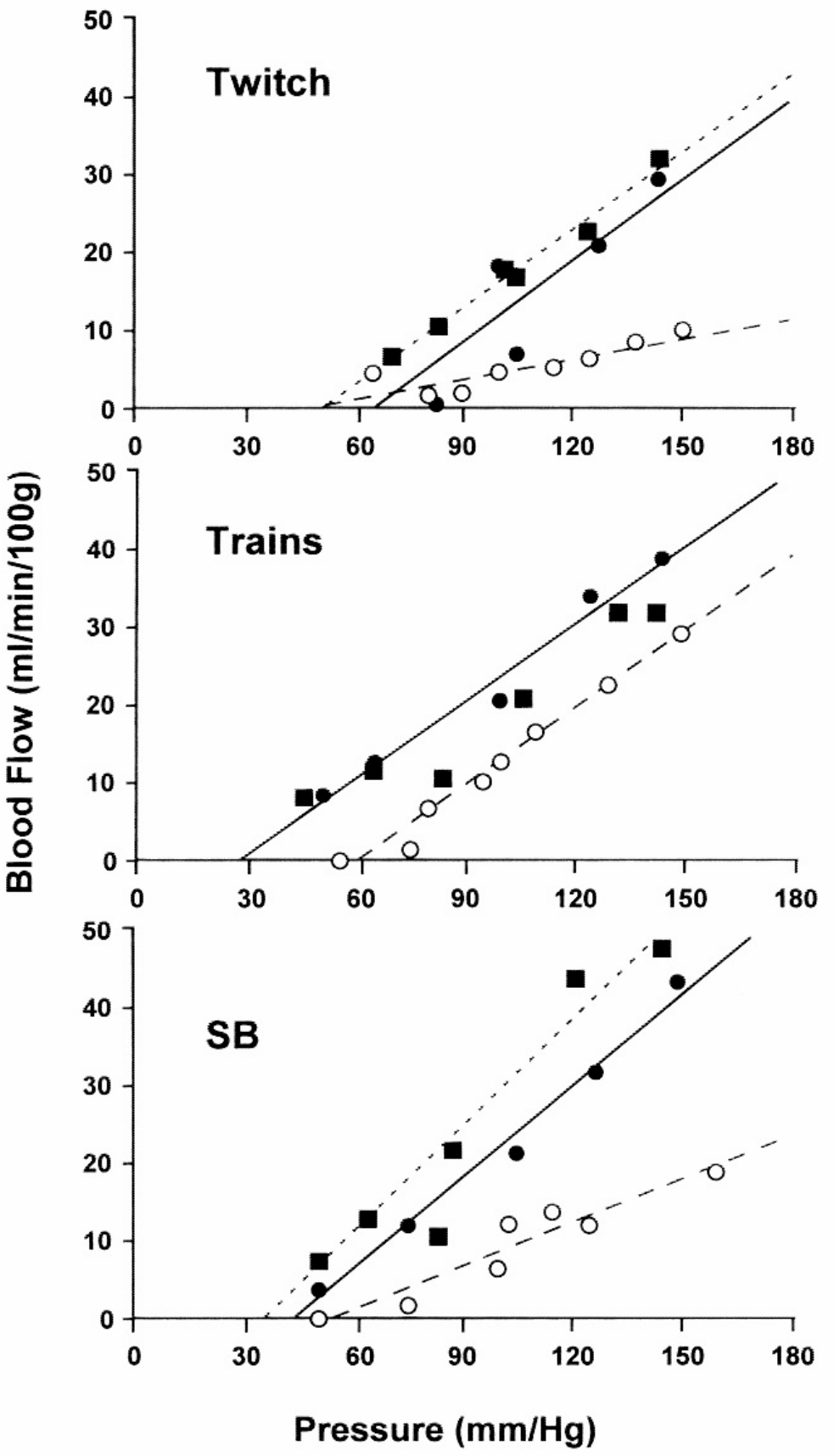
Twitch
Trains
SB
Blood Flow (ml/min/100g)
Pressure (mm/Hg)
0
10
20
30
40
50
0
30
60
90
120
150
180

Figure 4 redrawn from (23) with permission. Phrenic artery pressure-flow relations from three experiments. ○, control conditions (resting muscle no vasodilators); •, maximal vasodilation (resting muscle); ▪, maximal vasodilation during muscle contraction; SB, spontaneous breathing. Reference 23. Naamani, R., S. N. A. Hussain, and S. Magder. The mechanical effects of contractions on blood flow to the muscle. Eur. J. Appl. Physiol. 71:102-112, 1995. See text for further information.

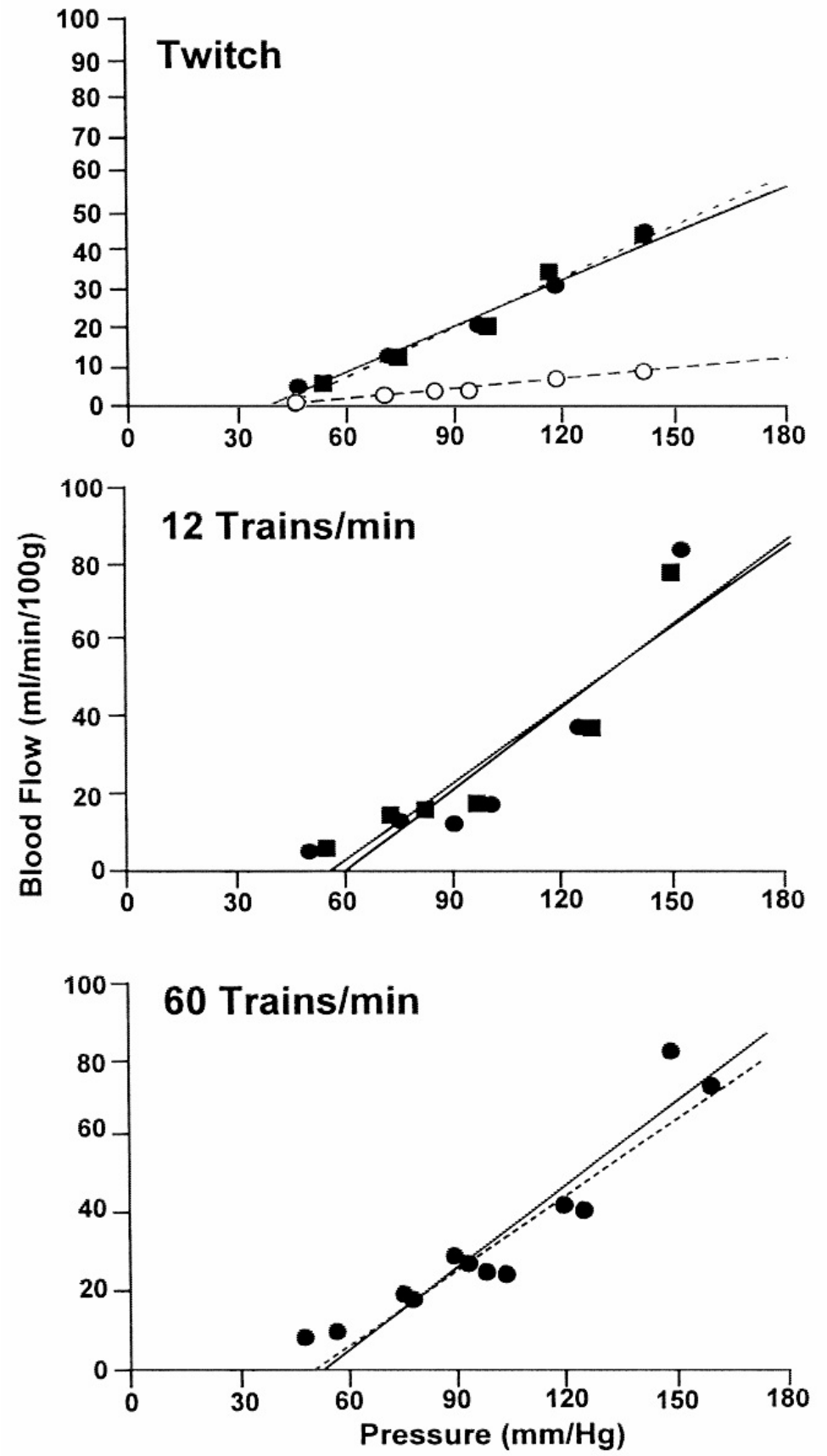
Twitch
12 Trains/min
60 Trains/min
Blood Flow (ml/min/100g)
Pressure (mm/Hg)
0
10
20
30
40
50
60
70
80
90
100
0
30
60
90
120
150
180

Figure 6 redrawn from (23) with permission. Popliteal artery pressure-flow relations from three experiments. ○, control conditions (resting muscle no vasodilators); •, maximal vasodilation (resting muscle); ▪, maximal vasodilation during muscle contraction. Reference 23. Naamani, R., S. N. A. Hussain, and S. Magder. The mechanical effects of contractions on blood flow to the muscle. Eur. J. Appl. Physiol. 71:102-112, 1995. See text for further information.

In summary, results available at this time indicate that simulated exercise *in situ* without instrumentation of the muscle vasculature (20) provides data that suggest a contribution of the muscle pump (Fig. 1). Also, blood flow data obtained from conscious rats performing locomotory exercise indicate that the muscle pump enhances blood flow during such exercise (Fig. 1). Recent *in vivo* studies of humans (28,36) and animals (2,3,14,16,33) indicate an important role for the muscle pump as well. In contrast, results reported herein and recent results from *in situ* experiments (21,23,34), which allow control of more parameters, indicate that there is no measurable muscle pump effect on blood flow during rhythmic muscle contraction. So we are left with the question: does the muscle pump contribute to active hyperemia in skeletal muscle? All available information considered, we conclude that the muscle pump is important in exercise hyperemia. The strongest support for this conclusion comes from the comparison of maximal *in vitro/in situ* results with those during normal exercise and recent *in vivo* results with spontaneous contractions in human subjects as discussed by others in this symposium.

However, it is important to emphasize that our laboratory has not been able to demonstrate clearly the muscle pump effect and the well-designed study of Naamani et al. (23) provides evidence of no muscle pump effect in dog gastrocnemius muscle. Naamani et al. (23) report that spontaneous contractions of the diaphragm did result in small increases in blood flow during maximal vasodilation (Fig. 6). There seem to be at least two possible explanations for the conflicting results. First, as discussed above, spontaneous contractions produce the muscle pump effect but artificial stimulation of muscle contraction does not. And second, the muscle pump effect is abolished by instrumentation of the veins associated with *in vitro/in situ* preparations that have been used to date. In reference to the first explanation, the fact that the results of Mackie and Terjung (20)(Fig. 1) indicate that muscle contractions stimulated by artificial means can produce greater blood flow than maximal vasodilation argues against this notion.

A relatively consistent difference between studies that report a muscle pump effect and those that do not is that the studies that report a muscle

pump effect had not instrumented the skeletal muscle veins. In experiments that did not observe a muscle pump effect, the veins were either cannulated with large bore, noncompliant catheters and/or instrumented with noncompliant flow probes. It is also possible that the vascular mechanics of the skeletal muscle veins and the muscle pump effect are coupled to the characteristics of the central veins and the abdominal thoracic pump in intact subjects to optimize the muscle pump effect. As a result, instrumentation of the veins, especially in small mammals, interferes with the muscle pump effect. An important exception to this notion is the classic study of Folkow et al. (10) in which cat triceps surae muscles were isolated from the cat and perfused during electrical stimulation. A muscle pump effect was demonstrated upon increased venous pressure by lowering the contracting muscles below heart level. Perhaps Folkow et al. produced a perfusion system that matched normal venous mechanics, a possible but unlikely occurrence?

It appears that the key to understanding the effects of muscle contraction on blood flow in skeletal muscle is understanding the effects of muscle contraction on vascular mechanics of the veins. We must determine whether a Starling resistor exists at the arteriolar level which produces a vascular waterfall during rhythmic muscle contraction (21,23,34). It seems quite clear that a vascular waterfall exists during muscle contraction; thus, arterial flow stops during maximal contractions (Fig. 2). However, between muscle contractions is the waterfall gone and is pressure in the small veins negative, drawing blood in from the arterial side? The recent work of Saupe et al. (30) suggests that the waterfall is gone in resting skeletal muscle because increased diastolic time associated with bradycardia produced increased external iliac artery blood flow. Also, it seems to be agreed that muscle contractions transiently decrease venous and capillary pressures thereby reducing capillary filtration during exercise (14,21). Are these changes sufficient to facilitate blood flow into the venous segments? If instrumentation of the veins abolishes the muscle pump by altering vascular mechanics, acquiring the needed data will be a challenge. A major problem with this hypothesis, as an explanation of this continuing controversy, is that we have not found a way to test it directly.

In conclusion, evidence indicates that several independent mechanisms contribute, in parallel, to exercise hyperemia and the maintenance of adequate blood flow to skeletal muscle during exercise. The muscle pump hypothesis remains a possible factor. Thus, it remains possible that integration of neurohumoral influences, metabolic vasodilation, endothelial vasodilator mechanisms, and the muscle pump mechanism will allow definitive identification of the determinants of blood flow in skeletal muscle in the near future. However, because the muscle pump effect may represent simply the effects of muscle contraction on vascular mechanics of the veins, it will be necessary to conduct experiments in a manner in which these characteristics are not altered by the experimenter.

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