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TIME COURSE AND MAGNITUDE OF BLOOD FLOW CHANGES IN THE HUMAN QUADRICEPS MUSCLES DURING AND FOLLOWING RHYTHMIC EXERCISE

BY LARS WALLØE AND JARLIS WESCHE
From the Departments of Physiology and Informatics, University of Oslo, Karl Johans gate 47, 0162 Oslo 1, Norway

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SUMMARY

1. Pulsed bidirectional Doppler-ultrasound equipment was used to measure changes in blood velocities in the femoral artery on a beat to beat basis for consecutive contraction and relaxation phases during voluntary rhythmic exercise of the quadriceps muscle group in man.

2. Rapid and large fluctuations of blood velocities were found, being high during relaxation and low during contraction phases. At the onset of contraction phase, negative velocities were present, indicating retrograde flow. During the rest of the contraction phase, forward flow occurred comparable to the resting flow level even at high loads.

3. Estimated maximal flow to the whole leg during relaxation phase, calculated from these blood velocity measurements and vessel diameter (measured with echo-ultrasound equipment with high resolution) was in two of the subjects 3·32 l min^{-1} (female) and 5·97 l min^{-1} (male). When using computer tomography to estimate the volume of the quadriceps muscle group, the calculated maximum flow to this muscle group was 243 (female) and 257 (male) ml min^{-1} 100 ml $muscle^{-1}$. The time-averaged flow during exercise to the whole leg was 1·51 l min^{-1} (female) and 2·47 l min^{-1} (male). The calculated time-averaged flow to the quadriceps muscle group was 101 (female) and 98 (male) ml min^{-1} 100 ml $muscle^{-1}$.

4. The duration of post-contraction hyperaemia following such rhythmic exercise of up to 6 min duration and up to 75% maximum voluntary contraction was never in excess of 150 s.

INTRODUCTION

The blood flow to voluntary contracting muscles during rhythmic exercise has been difficult to study in detail due to lack of suitable methods. However, since the early estimates of blood flow to a lip lifting muscle in a horse chewing oats by Chauveau & Kaufmann in 1887 several attempts have been made to make such investigations.

Anrep, Blalock & Samaan (1934) described rapid fluctuations of blood flow under rather unphysiological conditions in dogs. Barcroft & Dornhorst (1949) had difficulties with the plethysmographic method during rhythmic exercise in humans.

However, indirect estimates of flow during relaxation and contraction phases were found. Average values of blood flow to working muscles have been estimated using radiolabelled microspheres in rats (Laughlin & Armstrong, 1982), in ponies (Manohar, 1986) and in miniature swine (Armstrong, Delp, Goljan & Laughlin, 1987) and using thermodilution in humans (Andersen & Saltin, 1985). Quantitative measurements of blood flow on a beat to beat basis during rhythmic contractions in humans or experimental animals have not yet been performed. Consequently, the actual evidence available of what occurs in detail to blood flow in muscles during consecutive contraction and relaxation phases of rhythmic exercise is rather poor.

A bidirectional pulsed Doppler-ultrasound technique (Guldvog, Kjærnes, Thoresen & Walløe, 1980) has previously been used to measure changes in blood flow to the human quadriceps muscles during and following short isometric contractions (Wesche, 1986). In the present paper the same Doppler-ultrasound method and experimental set-up has been used to measure changes in blood velocities in the human femoral artery before, during, and after controlled rhythmic contractions of the quadriceps muscle group. An attempt has also been made to convert these velocity measurements to more absolute measurements of volume flow. A preliminary report of some of the results has been presented to The Physiological Society (Wesche & Walløe, 1985).

METHODS

Instruments and equipment

The instruments and experimental design were similar to those used and described in a previous investigation (Wesche, 1986). Two Doppler-ultrasound velocity-meters were used in the present investigation, UNIDOP and SD-100 (both Vingmed; Horten, Norway). The UNIDOP and the computer system for data analysis have been described in detail in previous publications (Wille, 1977; Hatteland & Eriksen, 1981; Guldvog *et al.* 1980; Pedersen, 1982; Wesche, 1986). The SD-100 is connected to a similar computer system (Apricot; Applied Computer Techniques, Birmingham). In the same subjects and with the same experimental procedure the two instruments give identical results.

The velocity-meters were used in the pulsed mode in the present experiments, the UNIDOP with an operating frequency of 1·5 MHz and the SD-100 of 3 MHz. The diameter of the transducer crystal was 13 mm, and the total cross-section of the femoral artery was isonicated with approximately constant intensity (Guldvog *et al.* 1980).

The back-scattered Doppler signal was in the kilohertz range and could therefore be listened to continuously through a loudspeaker system. By means of fourier transforms the velocity spectra and the mean of each spectrum were calculated every 10 ms. The velocity spectra together with the mean velocities were displayed in real time on a TV monitor. Examples of such velocity spectra from a recording on a normal femoral artery both in a resting subject and during and following isometric contractions have been shown in detail in the Figs 1, 3 and 4 in Wesche (1986), and are also shown in small scale to the left in Fig. 2*B* below. The computer calculates the time average of these mean velocities for each cardiac cycle, the length of the cardiac cycle being determined from the ECG signal.

Subjects and experimental design

The experiments were carried out on twelve subjects, six female and six male (age 22–48 years), who were not known to have any cardiovascular disease. Several experiments were performed on each subject, making 243 bouts of exercise altogether.

One of the males and one of the females were studied more extensively. There can be considerable differences in velocities between individuals due to different diameters of the femoral arteries. In one and the same subject, however, such velocity measurements show good reproducibility as shown in Wesche (1986). All the figures in the present paper therefore show results from one and

the same subject to obtain comparable velocity values. Normalized to resting velocity values, similar results were obtained in all the other subjects.

The subjects lay supine on a bench with their knees at one end of it, and with their heels supported on a bar slightly below the level of the bench. The quadriceps muscle group was contracted by extending the slightly flexed knee, while making sure the thigh remained resting on the bench. This manoeuvre resulted in the heels being lifted approximately 3–5 cm from the supporting bar. Blood velocities in the femoral artery were measured at a constant angle just proximal to the inguinal ligament, and recordings were made continuously before, during and after periods of rhythmic exercise. Since the Doppler-ultrasound method is susceptible to noise from the movement itself, it was only possible to obtain reliable recordings (omitting noise and still keeping the insonicated artery in focus) by measuring at some distance from the contracting muscles and making the movement of the leg slight. The short distance of the movement also explains why the load of this exercise is not easily expressed in units of effect (e.g. watts). By taking EMG recordings during some of the experiments we made sure that it was only the quadriceps muscles that were contracting. The tension generated in the muscle was increased by attaching weights to a strap around the ankle. Maximal voluntary contraction (MVC) was also measured using a strain-gauge dynamometer, and the percentage of MVC was calculated for each weight. The responses to tensions of 10, 20, 30, 50, 75 and 80 % MVC, were examined. In pilot experiments, the duration of each contraction and relaxation phase varied from 1 to 4 s. Of these, contraction and relaxation phases of 2 s duration were chosen to be studied more extensively. The subjects contracted their quadriceps muscles to the sound of a metronome, and the duration of the periods of exercise was usually 2 min, but periods of 1, 3 and 6 min (or for the higher tensions to fatigue) have also been investigated. An interval of a minimum of 5 min was allowed between the shorter exercise periods of low tension, and 10 min between the longer ones and those of high tension. By continuously observing the velocity spectra on the TV monitor we were certain that the artery was always in focus and that the blood velocities had returned to resting levels between tests.

To avoid large fluctuations in the velocities due to temperature regulation of arteriovenous anastomoses (AVAs) in the skin of the foot (Burton, 1939; Thoresen & Walløe, 1980), we made certain that the subjects remained cool during the experiments and did not use a suprasystolic cuff inflation method. This was described in detail and discussed in Wesche (1986).

Estimation of volume flow

Our equipment measures velocities and not volume flow. In order to convert these velocity measurements to volume flow, a new echo-ultrasound technique with pre-filtered waveforms (Eriksen, 1987) was used to measure femoral artery diameter in two subjects, one male (48 years, weight 80 kg, height 1·85 m), and one female (25 years, weight 57 kg, height 1·74 m). These diameter measurements have an accuracy greater than 0·1 mm, and the volume flow Q was then calculated using the formula $Q = \pi r^2 v$ (r, radius; v, blood velocity) and assuming the insonication was performed at an angle of 45 deg. The position of the vessel in relation to the abdominal wall was checked from echo-ultrasound longitudinal sector scans, and the angle of insonication was estimated to be 45 deg. Since the instrument was a pulsed Doppler and a good signal was always obtained, the angle had to be constant.

To estimate the blood flow not only in absolute terms but also relative to quadriceps muscle volume, computer tomography was used in these two subjects to measure the area of the muscle at three different levels, and from these data the volume of the quadriceps muscle group was estimated.

The estimation of the relative distribution of the resting femoral artery blood flow has been described in detail in Wesche (1986). Of the total femoral artery blood flow going to the whole leg, one-quarter was estimated to go to the quadriceps muscle group and three-quarters to inactive muscles, skin and bone. Since there was no EMG activity recorded from the other muscles during rhythmic exercise, and no change of leg blood flow was found in contralateral femoral artery recordings in these cool environments, it is a reasonable assumption that blood flow to other parts of the leg did not alter during exercise.

To check the possible role of systemic effects during such exercise, blood pressure (BP; DINAMAP, 1846, Critikon, Jampa, FL, U.S.A.) and heart rate (HR, from the ECG signal) were also recorded in these two subjects. There was only a small increase of up to 10 mmHg in diastolic and systolic BP and up to 15 beats min^{-1} in HR during rhythmic exercise of up to 50 % maximum

voluntary contraction (MVC), and an equal duration of contraction and relaxation phases. Even during rhythmic exercise of 75% MVC (of which results are shown in Fig. 4), and consecutive contraction and relaxation phases lasting 2 s each, HR increased only by at most 25 beats min^{-1}, and diastolic and systolic BP up to 15 mmHg.

RESULTS

In Fig. 1 typical results from a series of rhythmic contractions lasting 6 min are shown. Each cross represents the time-averaged velocity for one cardiac cycle. Consecutive contraction and relaxation phases each lasted 2 s, and the tension was

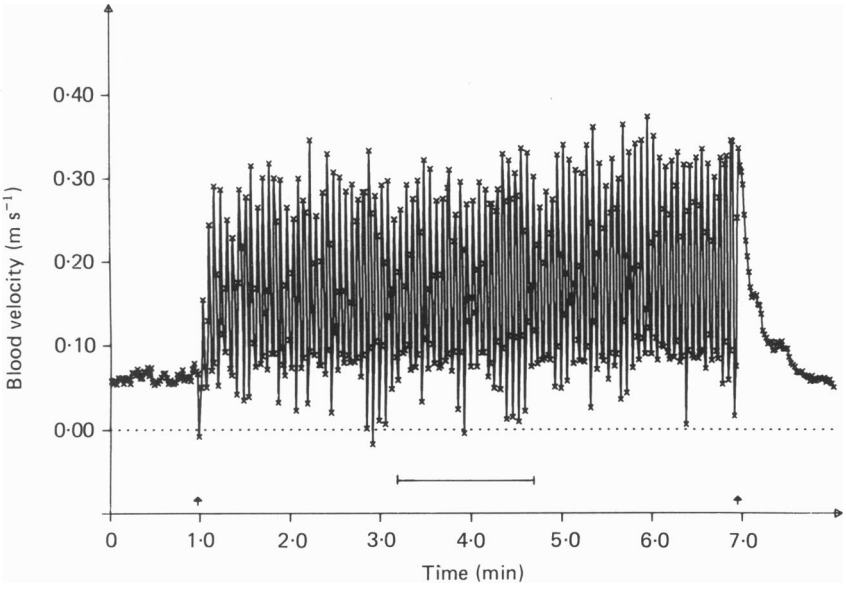

Fig. 1. Results from a 6 min exercise period with a tension of 10% MVC are shown. Each contraction and relaxation phase lasts 2 s. The arrows mark the beginning and the end of the exercise. Each cross represents the time average of the cross-sectional mean velocity for one cardiac cycle. The period underlined is shown in greater detail in Fig. 2*A*.

10% MVC. Prior to contraction resting velocities were steady. Following the initiation of the first contraction, there was a rapid decrease in average velocity, such that by the very first heart beat the velocity had become negative. Negative velocities represent net retrograde flow, that is blood flowing towards the heart.

Fig. 2. *A*, the period of the exercise underlined in Fig. 1 is shown with better time resolution. Velocity spectra from the period underlined is shown in *B*. The numbers in the figure mark relaxation phase 1, 2 and 3 during that particular period, corresponding to R1, R2 and R3 in *B*. *B*, velocity spectra of twenty-one complete cardiac cycles taken from the exercise in Figs 1 and 2*A* are shown. The lower tracing of the upper panel shows to the left two normal velocity spectra from the resting period, followed by eight consecutive cardiac cycles during the exercise, with the corresponding mean of each spectrum on top. The lower panel shows the consecutive eleven cycles in the same manner. Positive velocities above the baseline represent forward velocities, whereas negative velocities below the baseline represent retrograde velocities. The onset of contraction and relaxation phases is indicated by arrows. Consecutive contraction and relaxation phases are marked C1, C2, C3,...and R1, R2, R3,.... The relaxation phases marked R1, R2 and R3 correspond to the relaxation phases marked 1, 2 and 3 in *A*.

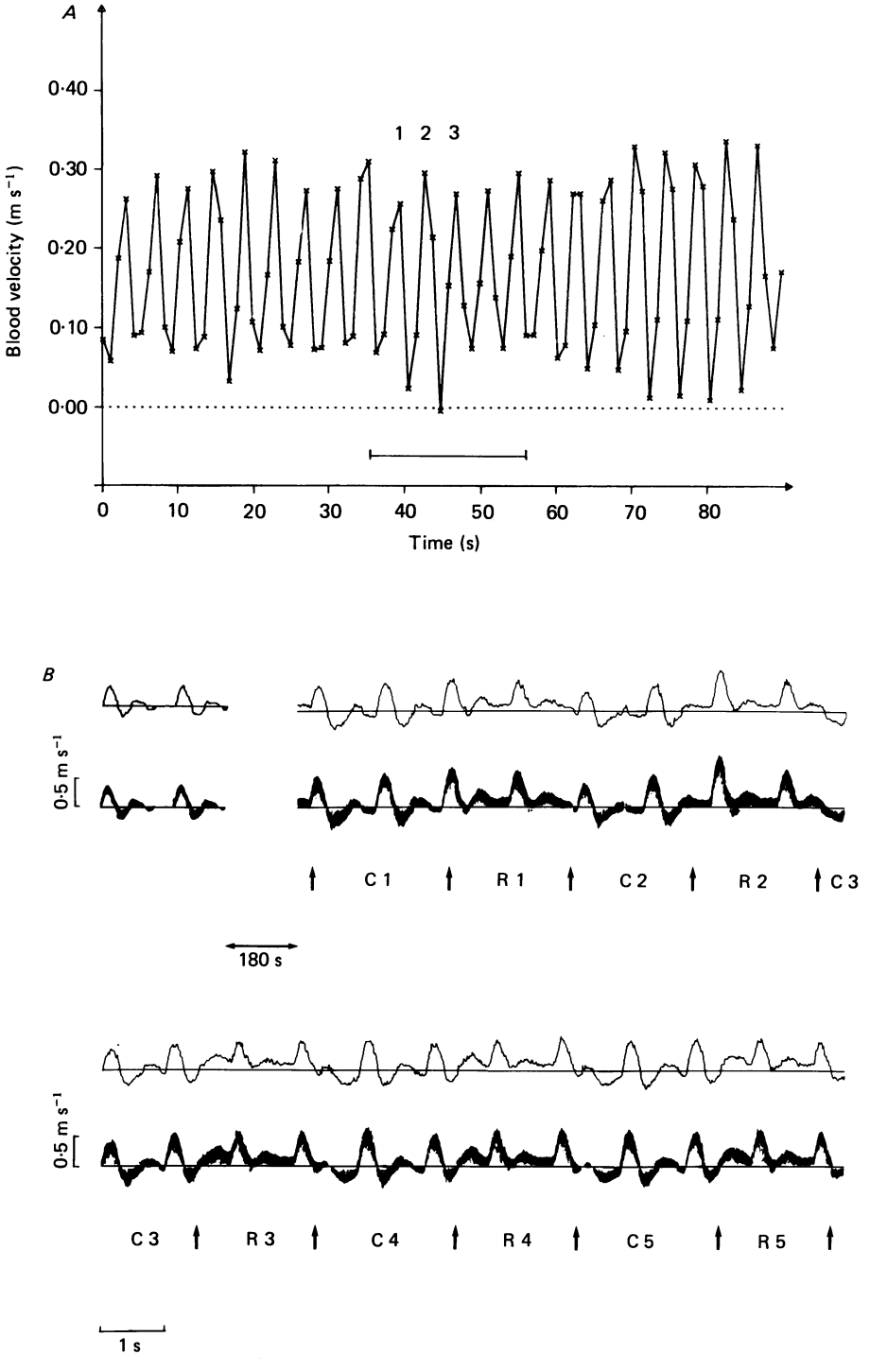

Fig. 2. For legend see opposite.

Immediately upon the first relaxation there was a dramatic increase in velocity with a maximum being reached within two cardiac cycles. Following the next few contractions the velocities of relaxation phase are even higher and soon reach a plateau of maximal velocity. The maximum velocities during relaxation were approximately 6 times the resting value. Velocities of post-exercise hyperaemia did not exceed these velocities of relaxation phases. During the contraction phases, velocities remained fairly steady and below the resting level. The median time-averaged velocity of contraction and relaxation phases during the last minute of sixteen similar exercise periods in the same subject is 0·17 m s^{-1}. The non-parametrical confidence interval of the median with confidence probability 0·95 is 0·16–0·19 m s^{-1}. The time taken for the velocity to return to pre-exercise resting level following rhythmic exercise was approximately half a minute in Fig. 1.

The period of blood velocity fluctuations underlined in Fig. 1 is shown in Fig. 2*A* for better time resolution. Figure 2*B* shows twenty-one velocity spectra taken from the same exercise illustrated in Fig. 2*A*, this particular period during exercise being underlined in Fig. 2*A*. The lower tracing of the upper panel of Fig. 2*B* shows to the left two normal velocity spectra from the resting pre-exercise period, followed by eight consecutive velocity spectra during exercise with the mean of each spectrum on top. The lower panel shows the following eleven cardiac cycles in the same manner. Start of contraction and relaxation phases (marked by the letters C and R, respectively) are indicated by arrows. Note that negative (retrograde) blood velocities are present even during normal resting conditions in the femoral artery. Initiation of contraction (C1) marked by the first arrow, caused an immediate and substantial increase in backflow (i.e.velocities below the baseline). Upon relaxation (R1) marked by the second arrow, there was a sudden increase in velocities which was seen most dramatically in diastole. Concomitantly the diastolic backflow more or less disappeared in these two cardiac cycles of relaxation phase (R1).

Maximum velocity during relaxation phase was reached within one or two heart beats depending on when during cardiac cycle the contraction was released. If relaxation starts just before the beginning of systole (R2 in Fig. 2*B*), the velocity increase will take place both during systole and diastole of the same cardiac cycle, the result being a high corresponding mean velocity value for that cardiac cycle (marked 2 in Fig. 2*A*). On the contrary, if relaxation is initiated just before the beginning of diastole (R1 in Fig. 2*B*), the velocity increase will be shared between this diastole and the systole of the next cardiac cycle, the resulting mean velocity value being lower (marked 1 in Fig. 2*A*). This explains the spread of maximum and minimum velocities seen during relaxation and contraction phases in Figs 1 and 2*A*. Consequently, the highest and lowest mean velocity values recorded during an exercise period probably represent the true velocity level of relaxation and contraction phases respectively.

In Fig. 3 results from three exercise periods of 3 min duration each and a tension 30% MVC are shown. In the upper panel, contraction and relaxation phases lasted 2 s each. The plateau of maximum relaxation phase velocities was approximately 0·50 m s^{-1} which is higher than the 0·35 m s^{-1} in Fig. 1 where the tension was only 10% MVC. The time-averaged mean velocity during the last minute of exercise was also higher, being 0·20 compared to 0·17 m s^{-1} in Fig. 1. The median time-averaged velocity of contraction and relaxation phases during the last minute of twenty similar exercise periods shown in the upper panel in the same subject is 0·21 m s^{-1}.

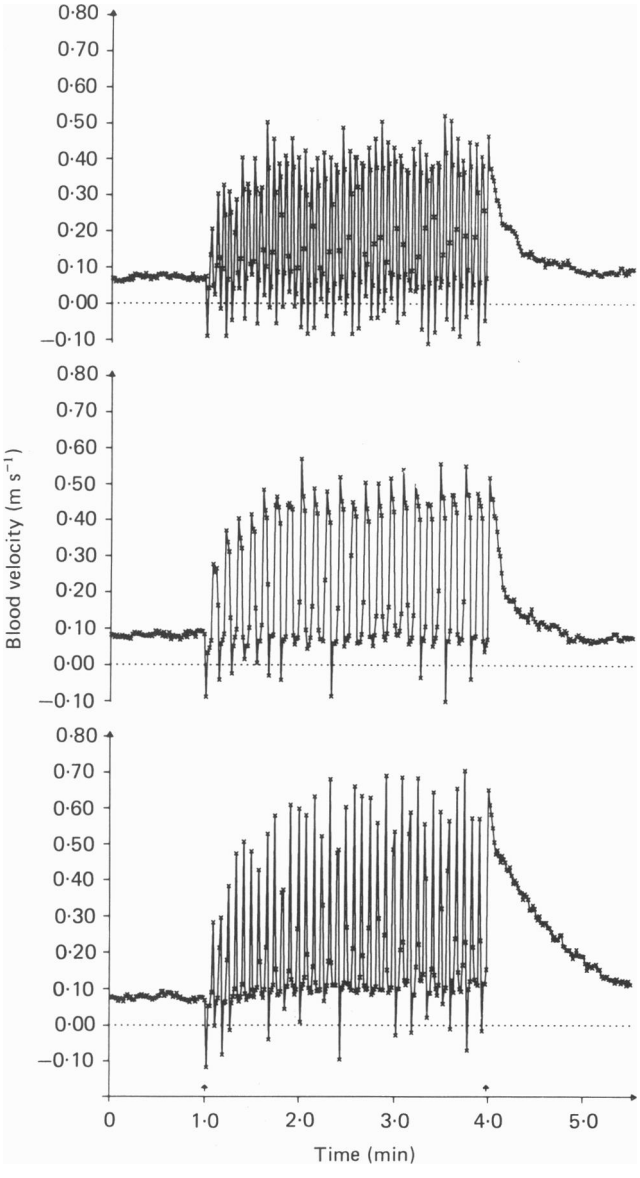

Fig. 3. Results from three exercise periods each of 3 min duration and a tension of 30% MVC are illustrated. The arrows mark the start and end of the exercise. Each cross represents the time-averaged velocity for one cardiac cycle. In the upper panel, each contraction and relaxation phase lasts 2 s. In the middle panel, each contraction and relaxation phase lasts 4 s. In the lower panel, each contraction phase lasts 4 s, while relaxation phase lasts only 1 s.

The non-parametrical confidence interval of the median with confidence probability 0·95 is 0·19–0·23. These results of exercise periods of 10 and 30% MVC are significantly different at a 5% level by the Wilcoxon two-sample test.

In the middle panel of Fig. 3, consecutive contraction and relaxation phases each lasted 4 s. The maximum velocities during exercise are on the same level as in the

upper panel, even at this lower frequency. The time taken to reach the plateau of maximal relaxation-phase velocity during the exercise periods shown in the upper and middle panel is about the same, and the duration of the post-exercise hyperaemia was about 1 min in both.

During relaxation phases which last 4 s each, several cardiac cycles take place. When the plateau of maximum relaxation phase velocities is reached, the shape and magnitude of the velocities of relaxation phase are the same as those first few cardiac cycles of the post-exércise hyperaemia. During contraction phase, minimum mean velocity will be reached during the first or second cardiac cycle depending on when during cardiac cycle contraction is initiated (as explained in detail above). When several cardiac cycles are allowed to take place during one and the same contraction phase as in the middle panel of Fig. 3, the mean velocity of the second, third and fourth cardiac cycles are somewhat higher than the minimum velocity and on the same level as the pre-exercise resting velocities.

In the lower panel, the contraction phases each lasted 4 s, while relaxation phases only 1 s. The plateau of maximum relaxation-phase velocities was higher (0·70 m s^{-1}) than in the upper and middle panel. The minimum velocities of contraction phases were on the same level of about $-0{\cdot}10$ m s^{-1} in all three panels.

The time-averaged velocity for the last minute of the exercise is also of the same order of magnitude being 0·20, 0·24 and 0·23 m s^{-1} in the upper, middle and lower panel respectively. The median time-averaged velocity of contraction and relaxation phases during the last minute of fifteen similar exercise periods as shown in the middle panel is 0·22 m s^{-1}. The non-parametrical confidence interval of the median with confidence probability of 0·95 is 0·21–0·25 m s^{-1}. The corresponding value of twenty-three similar exercise periods as shown in the lower panel is 0·20 ms^{-1}. The non-parametrical confidence interval of the median with confidence probability of 0·95 is 0·18–0·21 m s^{-1}. Although these exercise periods of 30% MVC have different exercise patterns, they show small differences in time-averaged velocity during exercise, but are all significantly different from the exercise periods of 10% MVC at a 5% level by the Wilcoxon two-sample test.

Figure 4 shows results from an exercise which was performed at a tension of 75% MVC and lasted 2 min, which was known from pilot experiments to be close to fatigue. Each contraction and relaxation phase lasted 2 s. The maximum velocities were 0·75 m s^{-1} which is considerably higher than in the exercise of 30% MVC shown in the upper panel of Fig. 3, but of the same level as the exercise shown in the lower panel of the same Fig. 3. However, the time-averaged velocity during the last minute of exercise was higher, 0·31 m s^{-1} compared to the 0·23 m s^{-1} in the lower panel of Fig. 3.

Figure 5 shows the averaged results of eleven exercise periods of 2 min duration and with a tension of 30% MVC. Each contraction and relaxation phase lasted 2 s. During exercise the curve is obtained by taking the averaged envelope of peak velocity values during relaxation phases. The vertical line shows the non-parametrical confidence interval of the mean with confidence probability of 0·95. There is both a very rapid increase of velocities following the start of exercise and a rapid decrease following the end of exercise. The slope of the curve is about the same following the start and stop of exercise, though there is a tendency towards a steeper velocity increase. Already by the third relaxation, that is 11 s, 75% of the maximal

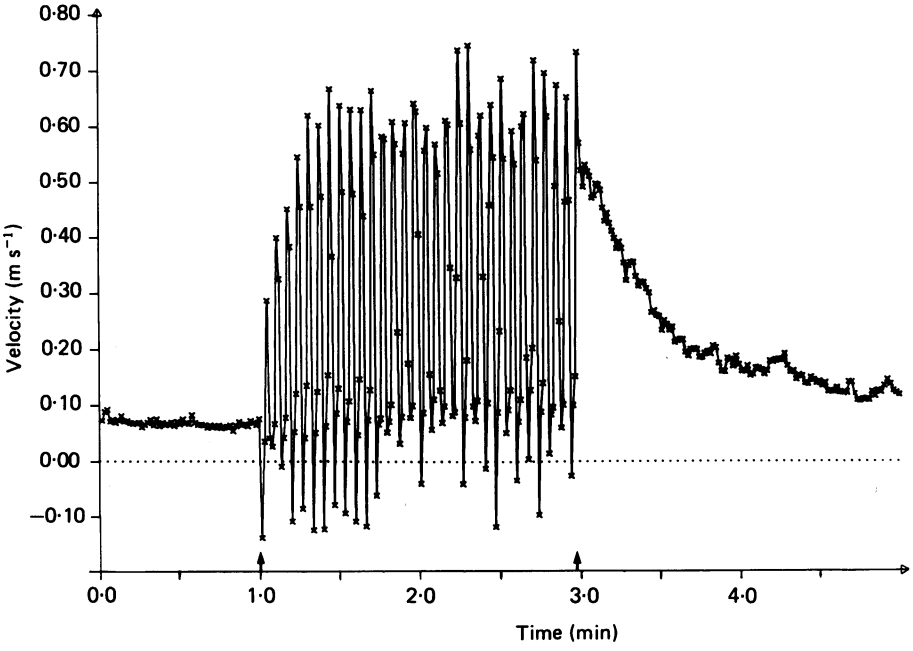

Fig. 4. Results from a 2 min exercise, marked by the arrows, and with a tension of 75% MVC is shown. Contraction and relaxation phase last 2 s each. Each cross represents the time-averaged velocity for one cardiac cycle.

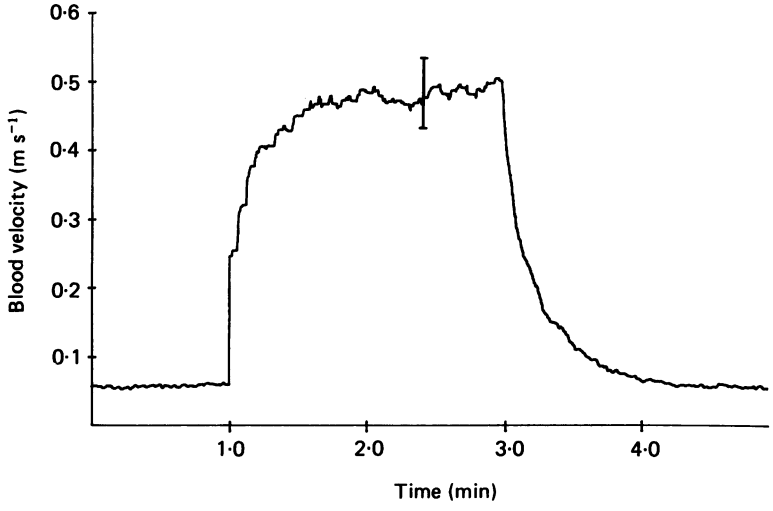

Fig. 5. Averaged results of eleven exercise periods, each of 2 min duration and with a tension of 30% MVC. consecutive contraction and relaxation phases lasted 2 s. During exercise the curve is obtained by taking the mean envelope of the peak velocity values during relaxation phases. The vertical line shows the non-parametrical confidence interval of the median envelope with confidence probability of 0·95.

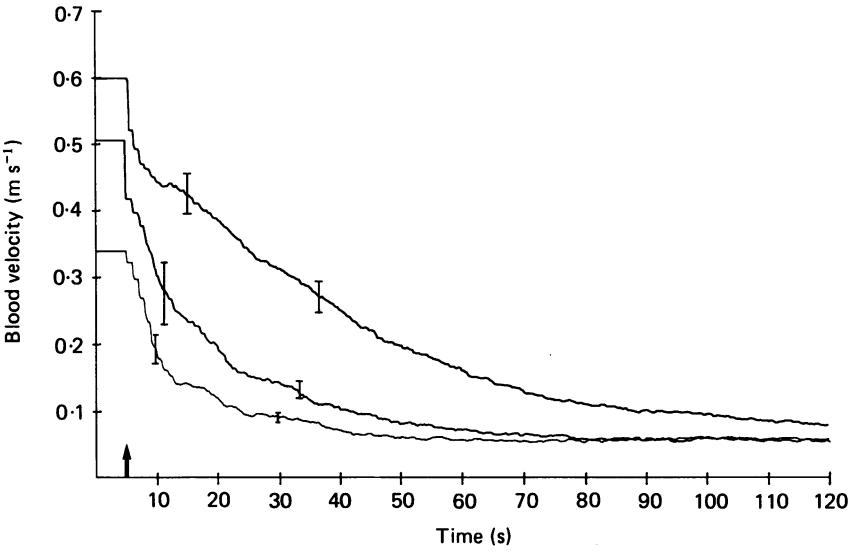

Fig. 6. Three curves showing averaged results of post-contraction hyperaemia, preceded by the mean of the last 5 s of the plateau of relaxation-phase velocities. The duration of each exercise period was 2 min. The lower curve shows the averaged results of eight exercise periods at a tension of 10% MVC and each contraction and relaxation phase lasted 2 s. The middle curve contains averaged results of eleven exercise periods with the same exercise frequency as in the lower curve, but at the higher tension of 30% MVC. The upper curve shows averaged results of seventeen exercise periods at the same tension of 30% MVC. Each contraction phase lasted 4 s, while each relaxation phase lasted only 1 s. The vertical lines show the non-parametrical confidence interval of the median with confidence probability of 0·95.

TABLE 1. Resting femoral blood velocities and maximal relaxation-phase velocities during rhythmic exercise. The exercise was performed at a tension of 10% MVC and lasted 2 min. Contraction and relaxation phases lasted 2 s each. The values shown are the median velocities of the number (n) of exercise periods performed by each subject. The third column gives the percentage increase of median maximal relative to median resting velocity.

	Sex	Age	n	Resting Velocity (m s^{-1})	Maximal relaxation-phase velocity (m s^{-1})	Per cent increase
N.J.	M	24	4	0·22	0·71	222
H.C.	F	24	3	0·20	0·65	225
C.B.	M	24	2	0·17	0·63	271
T.S.	F	24	2	0·20	0·86	341
G.L.	M	25	4	0·18	0·81	350
B.W.	F	25	9	0·19	0·87	358
L.W.	M	48	12	0·06	0·30	400
W.N.	F	36	5	0·13	0·65	400
M.P.	F	22	3	0·15	0·87	480

velocity increase during exercise has taken place. The post-exercise hyperaemia lasted approximately 1 min.

Figure 6 shows three averaged curves of post-exercise hyperaemia, preceded by the last 5 s of the plateau of relaxation-phase velocities. This figure illustrates that the post-exercise hyperaemia is dependent both on the tension (the two lower curves), and the relative duration of contraction and relaxation phases of the rhythmic work (the two upper curves).

All the figures presented show results from one and the same subject. Normalized to resting velocity values, however, similar results were obtained in all subjects. As an illustration, velocity values observed during rhythmic exercise of 10% MVC are given in Table 1. Median values of resting velocity and maximal velocity during relaxation phases of rhythmic exercise and the relative increase are presented for nine subjects. The range of the resting velocity among these individuals is 0·06–0·22 m s^{-1}. The range of maximal relaxation-phase velocity is 0·30–0·87 m s^{-1}. The increase varies from 220 to 480%, and there is no difference between females and males.

Estimation of volume flow

In the male subject (L.W.) in whom diameter measurements were performed, the diameter of the femoral artery was found to be 13·0 mm using the echo-ultrasound technique with pre-filtered waveforms. The calculated resting volume flow to the whole leg was 400 ml min^{-1} from this diameter and the Doppler-ultrasound velocities. The maximum volume flow to the whole leg calculated in the same manner was 5·97 l min^{-1} (Fig. 4). The time-average flow during this rhythmic exercise of 75% MVC was 2·47 l min^{-1}. Of the 400 ml min^{-1} going to the leg at rest, approximately 100 ml min^{-1} goes to the quadriceps muscle group as discussed in the Methods. Subtracting the 300 ml min^{-1} going to inactive tissue from the maximum volume flow of 5·97 l min^{-1} leaves 5·67 l min^{-1} to the quadriceps muscle group. When divided by the estimated muscle volume of 2·21 l (from the computer tomography), the maximum volume flow during relaxation phases and following exercise to the quadriceps muscle group is approximately 257 ml min^{-1} 100 ml $muscle^{-1}$. However, the time-averaged blood flow (from the time-averaged velocity during the last minute of exercise) during the exercise is lower, being 98 ml min^{-1} 100 ml $muscle^{-1}$.

Computer tomography and diameter measurements were also performed on a young female (B.W.). The diameter of the femoral artery was found to be 8·0 mm and the total volume of the quadriceps muscle group was estimated to be 1·27 l. The resting and maximal volume flows to the leg calculated from this diameter and the Doppler-ultrasound velocities were 300 ml min^{-1} and 3·32 l min^{-1} respectively. Calculating in the same manner, the estimated maximum volume flow during and following exercise is 243 ml min^{-1} 100 ml $muscle^{-1}$, which is of the same magnitude as in the subject discussed above. The average flow to the whole leg during exercise was 1·51 l min^{-1} in the female subject, and 101 ml min^{-1} 100 ml $muscle^{-1}$ to the quadriceps muscles.

DISCUSSION

Our Doppler-ultrasound technique makes it possible to follow closely rapid and large fluctuations of the blood velocities on a beat to beat basis during rhythmic

exercise in man (Figs 1, 2, 3 and 4). These fluctuations have not been studied directly before, due to lack of methods with sufficient time resolution. However, such fluctuations of flow have been commonly believed to occur (Guyton, 1971) since Barcroft & Dornhorst (1949) suggested this on the basis of their indirect estimates.

Rhythmic variations in blood flow during rhythmic exercise have later been observed by Cronestrand (1970), Gault, Ross & Mason (1966) and Hall (1969) using electromagnetic flowmeters even if this part of their reports consists of rather unsystematical observations on blood flow during rhythmic arm or leg exercise in patients in a clinical setting. Folkow, Gaskell & Waaler (1970) observed a similar phenomenon in isolated cat calf muscle during nerve stimulation using the same technique.

Contraction phase

At the beginning of exercise, as the very first contraction phase is initiated, a constant observation was a sudden and conspicuous decrease in velocities which became negative, indicating backflow (blood flowing towards the heart for one or two cardiac cycles) as clearly shown in the Figs 1, 3 and 4. Retrograde flow was also found at the beginning of isometric contractions and was described in a previous paper (Wesche, 1986). During rhythmic exercise, however, the velocities show a similar decrease and reversal during consecutive contraction phases. This fits well with the observations of Anrep *et al.* (1934). A similar limitation of blood flow has also been reported by Gault *et al.* (1966), Anrep, Cerqua & Samaan (1934) and Bellamare, Whight, Lavigne & Grassino, 1983).

Barcroft & Dornhorst (1949) always observed forward flow during contraction phase exceeding that at rest. However, it is clear from their Fig. 2 that they missed the initial phase of arterial retrograde flow that we observe.

The retrograde velocities obtained during contraction phases of rhythmic exercise remained at the same negative level all through the exercise period (Figs 1, 3 and 4), the scatter of these velocities being due to the time during cardiac cycle at which contraction was initiated. The velocities during contractions are more negative during the exercises of 30% MVC (Fig. 3) than during that of 10% MVC (Fig. 1), which fits well with the observations of Anrep *et al.* (1934). We find no further change in these velocities when increasing the tension to above 30% MVC (compare Figs 3 and 4).

During contraction phases of more than 2 s duration (Fig. 4, middle and lower panel), the velocities of the second, third and fourth cardiac cycles are higher than the first, and of the same order of magnitude as the resting level. Consequently retrograde flow appears only during the first one or two cardiac cycles of each contraction phase. During the remaining part of contraction phase there is forward flow on the same level as the resting flow. Also when increasing the tension to above 75% MVC, there is forward flow and never a cessation during the later part of contraction phases. During longer-lasting (45–90 min) heavy rhythmic exercise with a mean blood pressure increase of 25 mmHg the velocities of the last part of contraction phase are no more than the double of resting flow. However, during exercise periods where contraction phases last 2 s or less, there is only time enough for the period of retrograde flow to appear in the vessel. Even if Barcroft & Dornhorst

(1949) missed the initial part of contraction phase, their values of contraction flow (5–15 times the resting flow) are much higher than our findings.

Relaxation phase

Immediately upon relaxation, there was a dramatic and substantial increase in velocities. As a result, blood flow was increased to more than 2 times the resting flow in the vessel already during the first relaxation phase as seen in the Figs 1, 3, 4 and 5. The velocities increased further following each consecutive contraction phase till a plateau of maximal relaxation-phase velocity was reached. This is in accordance with previous observations (Gaskell, 1877; Grant, 1938; Anrep *et al.* 1934; Lind & Williams, 1979).

For one and the same load of exercise, there is a considerable spread of maximal velocity among the subjects (Table 1). When normalized to resting velocity, however, the spread is reduced. This must be due to different femoral artery diameters of the individuals. The remaining differences are mainly due to problems with the determination of the resting velocity (keeping the subjects at rest and the muscles relaxed).

The level of maximal velocity during relaxation phases is dependent on the load of the exercise. As tension is increased from 10% MVC, to 30% MVC and to 75% MVC the level of maximal relaxation-phase velocity increases (Fig. 1, upper panel of Fig. 3, and Fig. 4). The time-averaged velocity during exercise also increases with the load. This fits very well with the observations of other investigators both in animals (Anrep *et al.* 1934; Bellamare *et al.* 1983) and in humans (Tønnessen, 1964; Lind & Williams, 1979).

The level of maximal velocity during exercise relaxation phases is also suggested to depend upon the frequency of the exercise (Lind & Williams, 1979) and of the relative duration of relaxation and contraction phases (Buchler, Magder & Roussos, 1985). We find no difference in the maximal velocity during relaxation phase between exercises where contraction and relaxation phase each last 2 s and those which last 4 s each (upper and middle panel of Fig. 3), as long as the tension is the same. The time-averaged velocity during exercise is also at the same level, indicating equal average flow during exercise.

We have not investigated exercises of higher frequency, as the subjects then have some difficulty in keeping the correct rhythm when using such a large muscle group. In addition, heart rate turned out to interfere with an exercise frequency of contraction every other second in pilot experiments creating 'beat' phenomena. However, if contraction phase lasts longer than the relaxation phase, maximal velocity during exercise increases even further (compare the lower and middle panel of Fig. 3).

Barcroft & Dornhorst (1949) measured the interpolated relaxation flow by omitting the first part of the curve. In this way they missed the period of high flow, which has a short duration as best seen in the middle panel of Fig. 3.

Post-exercise hyperaemia

In all our experiments, we never find post-exercise values exceeding those during exercise as long as the subjects relax their muscles completely during the relaxation phase (see Figs 1, 3 and 4). This is in agreement with the observations of Tønnessen (1964), Hall (1969) and Cronestrand (1970) but in contrast to those of Barcroft & Dornhorst (1949) who almost always found post-exercise flow exceeding relaxation flow.

In Fig. 6 showing averaged results, the two lower curves illustrate that the post-contraction hyperaemia is dependent on the tension of the exercise. The blood flow was greater and lasted longer following an exercise of a higher tension. This can also be seen when comparing Fig. 1, upper panel of Fig. 3, and Fig. 4. The two upper curves of Fig. 6 illustrate that the post-contraction hyperaemia is also dependent on the exercise pattern. The hyperaemia was greater and lasted longer following an exercise where the contraction phase lasted much longer than relaxation (upper curve), compared to an equal duration of the phases (middle curve). This can also be seen when comparing the middle and lower panels of Fig. 3.

The duration of post-exercise hyperaemia (Fig. 1 and two upper panels of Fig. 3) is much shorter than has previously been reported for comparable hyperaemias by other investigators who found values from 3 to 15 min (Grant, 1938; Barcroft & Dornhorst, 1949; Tønnessen, 1964). Even after exercise periods when the subject is near the point of fatigue at the end of exercise, we only find the duration of post-exercise hyperaemia to be moderately increased (Fig. 4 and Fig. 3, lower panel).

These findings, that blood flow during and following exercise is dependent on the load and the relative duration of contraction and relaxation phases support the hypothesis that locally released substances (metabolites or local hormones) play a dominant part in evoking and controlling the hyperaemic response during and following rhythmic exercise.

Estimation of volume flow

In the two subjects in whom volume flow was calculated, a maximum flow during relaxation phase and following exercise of 243 and 257 ml min^{-1} 100 ml $muscle^{-1}$ (female and male subjects respectively) was found to go to the quadriceps muscle group. The time-averaged flow to the muscle group during exercise was, however, approximately 100 ml min^{-1} 100 ml $muscle^{-1}$ (101, female and 98, male) in both these subjects. The greatest increase in flow has taken place up to 50% MVC, and we therefore expect hardly any increase in flow during exercise periods of tensions exceeding 75% MVC, even if it had been possible to obtain reliable recordings at such high work loads. Since the blood pressure increase is small, it can only account for a small fraction of these large blood flow responses to rhythmic exercise in the present investigation.

These values of both maximal flow and time-averaged flow during exercise are 3–4 times higher than those of Barcroft & Dornhorst (1949), which are very much quoted. They tried to estimate exercise flow taking into account both the collateral inflow and the escape of venous blood. Their estimates of exercise flow are 28–30 ml min^{-1} 100 ml $muscle^{-1}$, and maximum flows during relaxation phase are 45–77 ml min^{-1} 100 ml $muscle^{-1}$. The corresponding maximal flow values of

relaxation phase obtained using plethysmography by Grant (1938) and Lind & Williams (1979) are 30 and 20 ml min^{-1} 100 ml $muscle^{-1}$ respectively, both measured in the forearm. These lower flow values obtained are, in our opinion, probably due to difficulties with the plethysmographic method itself.

By contrast, recent reports on animal and human experiments have given values far exceeding those of Barcroft & Dornhorst (1949). Laughlin & Armstrong (1982) using a microsphere technique have reported mean volume flows during exercise of 2–300 ml min^{-1} 100 ml $muscle^{-1}$ in swimming and running rats at maximum speed. Manohar (1986) using the same technique during maximal exertion in ponies, measured flow values of 230 ml min^{-1} 100 ml $muscle^{-1}$ in propulsion muscles.

Andersen & Saltin (1985) found similar mean flow values during rhythmic exercise even in human skeletal muscle using their venous thermodilution technique of constant infusion. Their experimental set-up has some similarity to ours in that the subjects perform one-legged exercise of the quadriceps muscles. The maximal flow measured in the femoral vein was 5·7 l min^{-1}. Subtracting flow to skin and inactive muscles and dividing by the quadriceps muscle volume (estimated from surface measurements of thigh length and circumferences) they obtained flow values of the order of 200 ml min^{-1} 100 ml $muscle^{-1}$. This is approximately the double of our time-averaged flow values. Part of the discrepancy could possibly be explained by the thermodilution method overestimating blood flow at high levels of flow due to incomplete mixing in the vein. Their subjects obtain a greater increase in HR and BP during the exercise periods, and this greater increase in BP might explain part of their greater increase of blood flow.

The values for maximal flow to one single working muscle group found by Andersen & Saltin (1985) and presently by us are of such a high magnitude that they cannot possibly prevail during hard exercise performed with many muscle groups. One would expect then some regulatory flow reduction to occur in such exercise so that total muscle flow is kept within the pumping capacity of the heart. Some evidence for such regulatory mechanisms was presented by Secher, Clausen, Klausen, Noer & Trap-Jensen (1977).

It is interesting though that the estimates of Chauveau & Kaufmann (1887) on average flow during exercise obtained by weighing the outflowing venous blood from the small upper lip muscle in horses chewing oats were considerably higher than those later found and most quoted by Barcroft & Dornhorst (1949) and seem later to have been forgotten. They found flow values during exercise from 60 to 120 ml min^{-1} 100 ml $muscle^{-1}$ which are in good accordance with our corresponding estimates of average flow in the present paper of 100 ml min^{-1} 100 ml $muscle^{-1}$.

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REFERENCES

ANDERSEN, P. & SALTIN, B. (1985). Maximal perfusion of skeletal muscle in man. *Journal of Physiology* **366**, 233–249.

ANREP, G. V., BLALOCK, A. & SAMAAN, A. (1934). The effect of muscular contraction upon the blood flow in the skeletal muscle. *Proceedings of the Royal Society* B **114**, 223–245.

ANREP, G. V., CERQUA, S. & SAMAAN, A. (1934). The effect of muscular contraction upon the blood flow in the skeletal muscle, in the diaphragm, and in the small intestine. *Proceedings of the Royal Society* B **114**, 245–257.

ARMSTRONG, R. B., DELP, M. D., GOLJAN, E. F. & LAUGHLIN, M. H. (1987). Distribution of blood flow in muscles of miniature swine during exercise. *Journal of Applied Physiology* **62**, 1285–1298.

BARCROFT, H. & DORNHORST, A. C. (1949). The blood flow through the human calf during rhythmic exercise. *Journal of Physiology* **109**, 403–411.

BELLAMARE, F., WHIGHT, D., LAVIGNE, C. M. & GRASSINO, A. (1983). Effect of tension and timing of contraction on the blood flow of the diaphragm. *Journal of Applied Physiology* **54**, 265–273.

BUCHLER, B., MAGDER, S. & ROUSSOS, C. (1985). Effect of contraction frequency and duty cycle on diaphragmatic blood flow. *Journal of Applied Physiology* **58**, 265–273.

BURTON, A. C. (1939). The range and variability of the blood flow in the human fingers and the vasomotor regulation of the body temperature. *American Journal of Physiology* **127**, 437–453.

CHAUVEAU, A. & KAUFMANN, M. (1887). Experiences pour la determination du coefficient de l'activite nutritive et respiratoire des muscles en repos et en travail. *Comptes rendus hebdomadaires des séances de l'Académie des sciences* **104**, 1126–1132.

CRONESTRAND, R. (1970). Leg blood flow at rest and during exercise after reconstruction for occlusive disease. *Scandinavian Journal of Thoracic and Cardiovascular Surgery*, suppl. 4, 1–24.

ERIKSEN, M. (1987). Noninvasive measurement of arterial diameters in humans using ultrasound echoes with prefiltered waveforms. *Medical and Biological Engineering and Computing* **25**, 189–194.

FOLKOW, B., GASKELL, P. & WAALER, B. A. (1970). Blood flow through limb muscles during heavy rhythmic exercise. *Acta physiologica scandinavica* **80**, 61–72.

GASKELL, W. H. (1877). On the changes of the blood-stream in muscles through stimulation of their nerves. *Journal of Anatomy and Physiology* **11**, 360–402.

GAULT, J. H., ROSS, J. & MASON, D. T. (1966). Patterns of brachial arterial blood flow in conscious human subjects with and without cardiac dysfunction. *Circulation* **34**, 833–848.

GRANT, R. T. (1938). Observations on the blood circulation in voluntary muscle in man. *Clinical Science* **3**, 157–173.

GULDVOG, I., KJÆRNES, M., THORESEN, M. & WALLØE, L. (1980). Blood flow in arteries determined transcutaneously by an ultrasonic doppler velocitymeter as compared to electromagnetic measurements on the exposed vessels. *Acta physiologica scandinavica* **109**, 211–216.

GUYTON, A. C. (1971). *Textbook of Medical Physiology*, p. 373. Philadelphia, London, Toronto: W. B. Saunders Company.

HALL, K. V. (1969). Postoperative blood flow measurements in man by the use of implanted electromagnetic probes. *Scandinavian Journal of Thoracic and Cardiovascular Surgery* **3**, 135–144.

HATTELAND, K. & ERIKSEN, M. (1981). A heterodyne ultrasound blood velocitymeter. *Medical and Biological Engineering and Computing* **19**, 91–96.

LAUGHLIN, M. H. & ARMSTRONG, R. B. (1982). Muscular blood flow distribution patterns as a function of running speed in rats. *American Journal of Physiology* **243**, H296–306.

LIND, A. R. & WILLIAMS, C. A. (1979). The control of blood flow through human forearm muscles following brief isometric contractions. *Journal of Physiology* **288**, 529–547.

MANOHAR, M. (1986). Blood flow to the respiratory and limb muscles and to abdominal organs during maximal exertion in ponies. *Journal of Physiology* **377**, 25–35.

PEDERSEN, J. E. (1982). A fast dedicated microprocessor for real time frequency analysis of ultrasonic blood velocity measurements. *Medical and Biological Engineering and Computing* **20**, 681–686.

SECHER, N. H., CLAUSEN, J. P., KLAUSEN, K., NOER, I. & TRAP-JENSEN, J. (1977). Central and regional circulatory effects of adding arm exercise to leg exercise. *Acta physiologica scandinavica* **100**, 288–297.

THORESEN, M. & WALLØE, L. (1980). Skin blood flow in humans as a function of environmental temperature measured by ultrasound. *Acta physiologica scandinavica* **109**, 333–341.

TØNNESSEN, K. H. (1964). Blood flow through muscle during rhythmic contraction measured by xenon. *Scandinavian Journal of Clinical Laboratory Investigation* **16**, 646–654.

WESCHE, J. (1986). The time course and magnitude of blood flow changes in the human quadriceps muscles following isometric contraction. *Journal of Physiology* **377**, 445–463.

WESCHE, J. & WALLØE, L. (1985). Time course of blood flow in the human femoral artery during and following rhythmic contractions of the quadriceps muscle group. *Journal of Physiology* **361**, 72*P*.

WILLE, S. (1977). A computer system for on-line decoding of ultrasonic Doppler signals from blood flow measurements. *Ultrasonics* **15**, 226–230.

Time course and magnitude of blood flow changes in the human quadriceps muscles during and following rhythmic exercise.

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