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THE TIME COURSE AND MAGNITUDE OF BLOOD FLOW CHANGES IN THE HUMAN QUADRICEPS MUSCLES FOLLOWING ISOMETRIC CONTRACTION

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SUMMARY

1. Blood velocities in the human femoral artery were measured using pulsed bidirectional Doppler-ultrasound equipment before, during and after single isometric contractions of the quadriceps muscle group.

2. After contraction periods lasting more than 20 s (long) and of tensions from 10 % up to 75 % of maximal voluntary contraction (m.v.c.), an increase in blood velocities of seven to eight times the resting level was observed. Estimated maximal volume flow to the whole leg during the post-contraction hyperaemic phase calculated from these blood velocity measurements and vessel diameter (measured with echo-ultrasound equipment) was in two of the subjects 2·4 l/min (female) and 4·4 l/min (male), respectively. In the latter, this estimate fitted very well with results obtained using a venous thermo-dilution method. When using computer tomography to estimate the volume of the quadriceps muscle group, the calculated maximum flow to this muscle group in the post-contraction hyperaemic phase was approximately 175 (female) and 185 (male) ml/min . 100 ml muscle, respectively. This was about forty times the estimated resting volume flow to this muscle of 4·7 (female) and 4·5 (male) ml/min . 100 ml muscle.

3. The length of the post-contraction hyperaemia after short (< 10 s) contraction periods was 12–13 s, by which time velocities had reached 25 % above the pre-contraction level. After long contractions, the corresponding values were 23–25 s. By contrast, previous plethysmographic observations by others indicate that post-contraction hyperaemias following long contractions last 10–15 min.

4. There was a marked difference between the times taken to reach maximal velocity in the hyperaemic phase when comparing short and long contractions. Maximal velocity was reached four to six cardiac cycles following short periods of contraction but during the very first heart beat after long periods of contractions.

5. The present observations are compatible with the hypothesis that locally released metabolites or hormones play a dominant role in the regulation of the post-contraction hyperaemia. Since during the short contraction periods maximal velocity was reached only after some seconds, whereas with the longer contraction periods it was reached during the first heart beat, it is suggested that these metabolites are released at some distance from the resistance vessels and that some time is needed for diffusion.

INTRODUCTION

Blood flow through skeletal muscle during and following contraction, and the nature of the mechanisms behind the regulation of this blood flow, has been a subject of great interest to physiologists since the early experiments of Gaskell on flow from cut muscle veins in dogs in 1877. Surprisingly many of the reports give conflicting and confusing results.

Only a few have been able to make recordings during the first few seconds of contraction (Gaskell, 1877; Anrep, Blalock & Samaan, 1934; Anrep & von Saalfeld, 1935). The Cairo group of Anrep used a constant-pressure perfusion set-up and a hot-wire anemometer. The good time resolution of their technique made it possible to observe in dogs a ' back thrust ' of arterial blood flow lasting less than 1 s at the very beginning of a strong contraction.

During the remainder of the contraction Grant (1938), Barcroft, Greenwood & Whelan (1963), Humphreys & Lind (1963), Lind, Taylor, Humphreys, Kennelly & Donald (1964) and Lind & McNicol (1967) have all observed an increase in blood flow. However, Gaskell (1877) observed first a cessation of venous blood flow followed by a steady increase exceeding resting levels while Anrep & von Saalfeld (1935) only found a cessation of venous flow. Anrep *et al.* (1934) observed a diminution or an arrest of arterial blood flow during this part of the contraction. Barcroft & Millen (1939) also deduced from their experiments an arrest of flow even during low-tension contractions. Some of these discrepancies may be explained by differences in experimental techniques.

Most investigators have observed a rapid and considerable increase in blood flow following relaxation of contraction. Anrep and coworkers (Anrep *et al.* 1934; Anrep & von Saalfeld, 1935) also observed a temporary increase in blood flow (a so-called ' overshoot '), before a further and greater increase.

But there is great controversy concerning the duration of the post-contraction hyperaemia. Grant (1938) found that blood-flow values declined to the former resting level in about 10 min after a strong contraction of 1·25 min duration while Lind *et al.* (1964) found that when measurements were terminated 10 min after contraction post-exercise hyperaemia was still clearly present. However, in 1967 Lind & McNicol found that the hyperaemia had subsided 5 min after a sustained hand-grip contraction. After short contractions lasting less than 5 s, Concordilas, Koroxenidis & Shepherd (1964) observed blood flow falling to pre-contraction values in about 20–25 s, while Lind & Williams (1979) using the same method found that the post-exercise hyperaemia lasted 2 min even after a short period of contraction.

In contrast to the discussion about the length of post-contraction hyperaemia, there has been little controversy about the magnitude of its maximum volume flow. Results given by investigators using plethysmography are all in the range of 20–40 ml/min . 100 ml muscle (Grant, 1938; Clarke & Hellon, 1959; Barcroft *et al.* 1963; Lind *et al.* 1964; Lind & McNicol, 1967; Lind & Williams, 1979).

However, precise information on the time course of blood flow through skeletal muscle in humans during and immediately following voluntary contraction is distinctly lacking. This is partly because the detailed time course of blood flow has been difficult to study due to lack of suitable methods with sufficient time resolution.

In consequence, several specific questions need to be answered. First, can the ' back

thrust' observed by Anrep and coworkers (Anrep *et al.* 1934; Anrep & von Saalfeld, 1935) during the first few seconds of contraction under rather unphysiological (e.g. constant pressure) conditions in dogs, be detected during voluntary contractions and normal pulsatile flow in humans? Secondly, is there an arrest, a diminution or an increase in flow during the remainder of the contractions? Thirdly, does maximal flow occur immediately after or only some time after relaxation? Further, how great is the maximal flow both in absolute terms and relative to resting levels, and for how long does the increase in flow last? Finally, do more modern methods show anything comparable to the 'overshoot' described by Anrep and coworkers (Anrep *et al.* 1934; Anrep & von Saalfeld, 1935)?

For this purpose, Doppler-ultrasound equipment was used to measure the blood velocities in the femoral artery before, during and after controlled isometric contractions of the quadriceps muscle group. The main advantage of this non-invasive and non-disturbing method is that it has an excellent time resolution, so that changes in the blood velocities can be followed through each cardiac cycle throughout the experiment. An attempt was also made to compare these velocity measurements to more absolute measurements of volume flow. A preliminary report of some of the results have been presented at a meeting of the Scandinavian Physiological Society (Wesche & Walløe, 1984).

METHODS

Instruments and equipment

The Doppler-ultrasound velocity-meter, UNIDOP (Vingmed, Horten, Norway), used in the present investigation and the computer system for data analysis have been described in detail in previous publications (Wille, 1977; Guldvog, Kjærnes, Thoresen & Walløe, 1980; Hatteland & Eriksen, 1981; Pedersen, 1982).

In the present experiments the UNIDOP was used in the pulsed mode with an operating frequency of 1·5 MHz. The depth range with this operating frequency is from 1 to 10 cm. The femoral arteries on which it was used in the present study were all within this depth range (2·5–4 cm). The diameter of the crystal was 13 mm, and the total cross-section of the femoral artery was insonicated with approximately constant intensity (Guldvog *et al.* 1980).

The back-scattered Doppler signal was filtered by sharp high- and low-pass filters. The remaining Doppler signal was in the kilohertz range and could therefore be listened to continuously through a loudspeaker system. The heterodyne Doppler signal was simultaneously stored on one channel of a stereo cassette tape-recorder (AKAI CXC-760D), and the electrocardiogram (e.c.g.) signal and verbal comments on the other.

The UNIDOP was also connected to a digital fast-fourier transform spectrum analyser (Pedersen, 1982), which calculated the velocity spectra each 10 ms and the mean of each spectrum. The output from the spectrum analyser was fed through a graphic processor and then to a grey-tone TV monitor on which the velocity spectra together with the mean velocities were continuously displayed in real time. An example of such a recording from a normal femoral artery in a resting subject is shown in Fig. 1 (lower and upper panels respectively). Note that negative (retrograde) blood velocities are present even during normal resting conditions in the femoral artery.

The spectrum analyser was also connected on-line to a microcomputer (ALTOS ACS 8000-2 with two floppy disk drives, running a UCSD-PASCAL system) which fed to the computer the mean of each Doppler spectrum. The computer calculates the time average of these mean velocities for each cardiac cycle, the length of the cardiac cycle being determined from the e.c.g. signal.

Subjects and experimental design

The experiments were carried out on eighteen subjects, nine male and nine female (aged 22–45 years), who were not known to have any cardiovascular disease. Several experiments were performed on each subject, making 549 single contraction periods altogether.

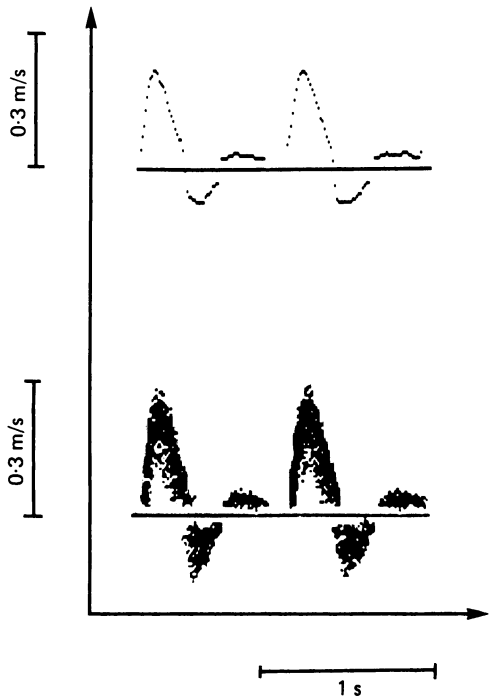

Fig. 1. The lower panel shows the velocity spectra from two consecutive cardiac cycles from measurements on the femoral artery in a supine resting subject. In the upper panel the corresponding mean of each spectrum is given. Positive velocities above the base line represent forward blood velocities, whereas negative velocities below base line represent retrograde velocities.

The subjects were asked to lie 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 manouevre resulted in the heels being lifted approximately 3–5 cm from the supporting bar, and although the contraction cannot be said to have been purely isometric, this was without consequence for the results of this study. By taking electromyogram (e.m.g.) 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 (m.v.c.) was also measured using a strain-gauge dynamometer, and the percentage of m.v.c. was calculated for each weight. The responses to tensions of 10, 20, 30, 50 and 75 % m.v.c. were examined. In pilot experiments the duration of the contractions varied from 1 s to 2 min. These divided naturally (based on the time course of the velocity changes) into two groups of short (< 10 s duration, $n = 338$) and long contractions (> 20 s duration but always less than 2 min, $n = 211$). Of these, contractions of 5 s and 30 s were chosen to be studied more extensively as they were representative of short and long contractions respectively. An interval of a minimum of 75 s was allowed for recovery between successive short contractions while a minimum of 3 min and 15 s was allowed between the long contractions. By continuously observing the velocity spectra on the TV monitor we were certain that the flow velocities had returned to resting levels between tests.

In order to avoid large fluctuations in the velocities due to temperature regulation of arterio-venous anastomoses in the skin of the foot (Burton, 1939; Thoresen & Walløe, 1980), we made certain that the subjects remained cool during the experiments. The subjects were, however, not allowed to

become so cold that shivering occurred, as this would cause hyperaemia in itself. This method of minimizing the problem of fluctuations in skin blood flow was chosen in preference to using the suprasystolic-pressure cuff-inflation method, because these inflations may, in themselves, influence velocities by either evoking sympathetic reflexes from skin receptors (Thoresen & Walløe, 1980) or causing alterations in the pulse wave form in the femoral artery due to retrogradely reflected pressure waves.

Blood velocities in the femoral artery were measured just proximal to the inguinal ligament. The Doppler signal was continuously recorded before, during and after contractions. A typical contraction is shown in Fig. 2*A* (onset and offset marked by the arrows). It lasted 60 s and the tension was 10% m.v.c. Each point represents the average velocity for consecutive cardiac cycles.

Fig. 2*B*, which shows results from nine single isometric contractions plotted on top of each other, illustrates that there was good reproducibility of such measurements. Each contraction lasted 5 s (from the arrow) and the tension was again 10% m.v.c.; the time interval between the contractions was 1·5 min. They were all performed by the same subject, and were remarkably similar both in shape, amplitude and duration. Some of the spread was due to the fact that the subject had some difficulty in maintaining the contraction for exactly 5 s each time.

Comparison between short and long contraction periods

Of the total number of 549 contraction periods performed in these experiments, the statistical results from those short and long contractions with a tension of 20% m.v.c. are presented.

Sixty-seven contraction periods of 5 s duration and forty-eight of 30 s duration were performed by seven subjects, six male and one female. The following variables were determined for each of these 115 contraction periods: (1) time to maximal velocity, i.e. the time taken to reach maximal velocity from the end of contraction; (2) recovery time, i.e. the time it takes from the end of the contraction until the velocities are down to a level of 25% over the base-line (resting) level; (3) relative maximal velocity increase, i.e. the magnitude of the velocity increase in the post-contraction hyperaemia relative to the base-line value.

For these three variables there was no indication in the results of systematic differences between subjects. The results obtained for each of these sets of variables were therefore pooled and compared by the Wilcoxon two-sample test.

Estimation of volume flow

Our equipment measures velocities and not volume flow. In order to compare the velocity changes with measurements of volume flow, a venous thermo-dilution method (Wahren & Johrfeld, 1973; Andersen & Saltin, 1985) was used during similar isometric contractions in a single experimental series on one of our subjects (male: 45 years, weight = 80 kg, height = 1·85 m). Having determined from the Doppler measurements the timing of maximal hyperaemia following contractions, thermo-dilution measurements were carefully taken to include just this period. Measurements were also always made in the respiratory pause at the end of a normal expiration.

In a further attempt to check that the velocity measurements are a good reflexion of volume flow, echo-ultrasound sector-scan equipment (Technicare Auto-Sector, 5 MHz, mechanical) was used to measure femoral artery diameter in this subject and in one other (female: 22 years, weight = 57 kg, height = 1·74 m). These diameter measurements are subject to considerable inaccuracy, and the opportunity was taken to re-check them using a new echo-ultrasound technique with pre-filtered wave forms (Eriksen, 1986), which has an accuracy greater than 0·1 mm. There was in fact a good correlation between the two estimates of vessel diameter, 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 of this vessel was performed at an angle of 45 deg. The position of the vessel in relation to the abdominal wall was checked from echo-ultrasound sector-scans.

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

The relative distribution of the femoral artery blood flow was estimated as follows: the total blood flow to the lower leg was estimated to be one-quarter of that of the femoral artery, since the femoral artery velocities decreased by a quarter upon inflation of a suprasystolic cuff just beneath the knee in a cool environment. Of the remaining three-quarters, an equal volume flow to the hamstrings

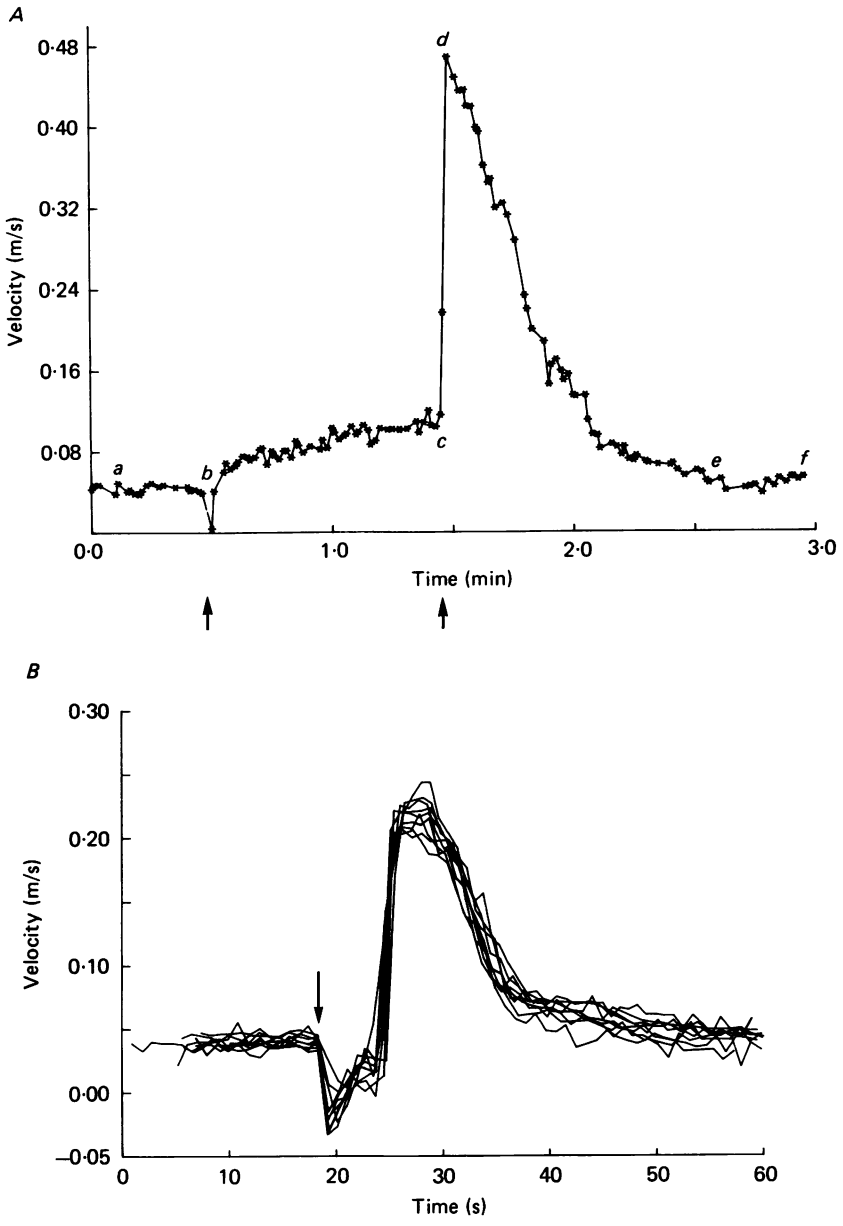

Fig. 2. *A*, results from one typical contraction lasting 60 s and with a tension of 10% of the maximal voluntary contraction (m.v.c.). Each point represents the average mean velocity for one cardiac cycle. The beginning and the end of the contraction are marked by arrows. From *a–b*, resting level; *b*, velocity decrease as the contraction starts; *b–c*, contraction with slowly increasing velocities; *c*, relaxation with rapidly increasing velocities; *d*, maximum velocity; *c–e*, post-contraction hyperaemia; *e–f*, resting level. *B*, results from nine single isometric contractions are plotted on top of each other. The points are not plotted for clarity. Each contraction lasts 5 s and the tension is 10% m.v.c. They were all performed by the same subject. Note that the rapid decline in velocities starts immediately muscle contraction is initiated, as indicated by the arrow.

and adductor muscles together, on the one hand, and the quadricep muscle group on the other was assumed, since in all three cross-sections the c.t. area of these two muscle groups were of the same magnitude. There was some uncertainty in the estimation of the skin and bone blood flow of the thigh, but these were unlikely to amount to more than one-third of the total volume flow of the thigh. This gives an estimate of one-quarter of the total femoral artery blood flow to the quadriceps, one-quarter to the hamstrings and adductor muscles, one-quarter to skin and bone of the thigh and one-quarter to the total lower leg.

Blood pressure (Dinamap, 1846) and heart rate (from the e.c.g. signal) were also recorded, together with contralateral femoral artery Doppler recordings in these two subjects in a similar experimental series.

RESULTS

Short and long contractions show very characteristic responses of blood velocity which are described in detail below. Figs. 3 and 4, and Table 1 serve to illustrate these general findings.

Short contraction periods

Fig. 3*A* shows the velocity spectra of twenty-two consecutive cardiac cycles taken from a typical contraction lasting 5 s, with a tension of 50 % m.v.c. The lower tracing of the upper panel shows velocity spectra of the first eleven cardiac cycles with the corresponding mean of each spectrum above, while the lower panel shows the following eleven cycles in the same manner. The series starts with the last cycle from the preceding resting period, and the initiation of contraction is indicated by the first arrow. This caused an immediate and substantial increase in back flow (i.e. velocities below the base line), which was present even during early systole. There was also back flow in late diastole in all the heart beats during the contraction. The contraction was released during the diastole of the fifth heart beat after contraction (marked by the second arrow). The first cardiac cycle following relaxation is marked by an asterisk. Upon relaxation there was a marked increase in velocity mainly in systole, there still being some back flow in diastole. During the next seven cardiac cycles the back flow in diastole disappeared and concomitantly there was a great increase in diastolic forward velocity, resulting in higher mean velocities. This can be readily seen from the mean velocity tracings. During the following few heart beats the diastolic velocity diminished gradually, and from the sixteenth heart beat, back flow began to appear again. By the last cardiac cycle illustrated here, most of the hyperaemia had subsided and the spectrum was again similar to the first one of the series.

In Fig. 3*B* results from the computerized calculations of the same velocity spectra illustrated in Fig. 3*A* are plotted, giving the time-averaged velocity for each cardiac cycle. Immediately following the start of the contraction, there was a rapid decrease in average velocity within the first two heart beats, such that by the second heart beat the velocity had become negative. This was typical of these short contractions. Negative velocities represent net retrograde flow, i.e. blood flowing towards the heart. Following this sharp decline in velocities, they rapidly increased during the remainder of the contraction, though the values were almost always below the pre-exercise resting level.

Immediately following relaxation, the blood velocity increased quickly to an initial peak which lasted one heart beat, (marked by the asterisk in the Figure and

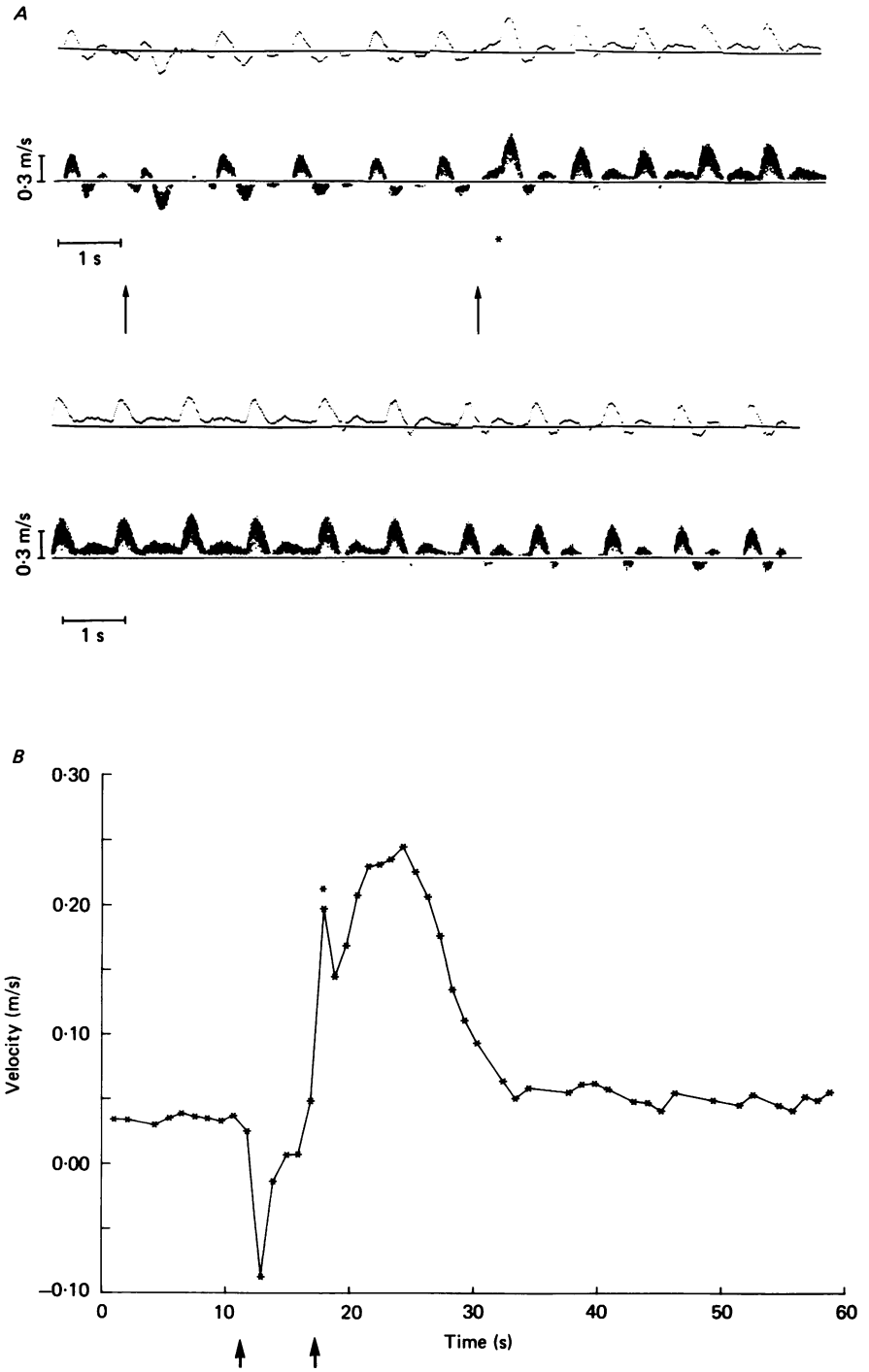

Fig. 3. For legend see opposite.

corresponding to the heart beat marked in the same way in Fig. 3*A*). Within the next cardiac cycle the mean velocity diminished again, but thereafter increased during the next six heart beats to reach a new maximum which was higher than the first peak.

The maximal velocity measured in the femoral artery after relaxation of the contraction was six times the resting value. The time taken for the velocities to return to resting pre-contraction values after relaxation was 25 s.

Long contraction periods

In Fig. 4*A*, the lower panel shows the velocity spectra of ten of the cardiac cycles taken from a contraction lasting 30 s and with a tension of 50 % m.v.c. Again the series starts with the last cycle from the preceding resting period. The corresponding mean of each spectrum is given in the upper panel. The contraction started during diastole of the second heart beat (as marked by the first arrow), and caused a large increase in diastolic back flow. After the fourth heart beat, the following velocity spectra from the next 25 s of the contraction are omitted for clarity. The next two cardiac cycles in Fig. 4*A* are the two last cardiac cycles of the contraction. During the omitted 25 s the shape of the spectra gradually changed from that shown in the fourth to that shown in the first after the break. Thus, during contraction, the systolic velocities increased gradually, while back flow remained prominent (compare heart beats three and four to heart beats one and two, just after the break). Relaxation was initiated during diastole at the time marked by the second arrow and caused a distinct increase in the diastolic velocities of the same cycle. During the next cycle, there was a sudden and substantial increase both in systolic and diastolic velocities, and the diastolic back flow disappeared. This gave high mean velocities, shown in the upper panel.

Fig. 4*B* shows the computerized calculations of the velocity spectra from the contraction illustrated in Fig. 4*A*, and gives the time-averaged velocities for each cardiac cycle. Following initiation of contraction, the velocities rapidly decreased and retrograde flow appeared in the vessel. During the remainder of the contraction, velocities increased gradually to just above the resting level. Immediately following relaxation there was a dramatic increase in velocities with a maximum being reached during the first cardiac cycle. Maximum velocity values after relaxation of this contraction were eleven times the resting value. The time taken for the velocities to return to resting pre-contraction levels after relaxation was 1·5 min.

Fig. 3. *A*, velocity spectra of twenty-two consecutive cardiac cycles taken from a contraction of 5 s duration and with a tension of 50 % m.v.c. They are fitted together from pictures taken from the TV monitor which explains why the base line is not always straight. The upper panel shows the first eleven heart beats with the corresponding mean of each spectrum on top, starting with the last cardiac cycle from the preceding resting period. The lower panel shows the following eleven cardiac cycles. The arrows mark the beginning and the end of the contraction lasting five cardiac cycles. The asterisk indicates the first cardiac cycle after the relaxation. *B*, results from the same contraction as in *A*, each point representing the average mean velocity for consecutive cardiac cycles. Negative velocities represent retrograde flow towards the heart. The arrows mark the beginning and the end of the contraction. The asterisk indicates the initial peak velocity after the relaxation of the contraction, corresponding to the cardiac cycle marked in the same way in *A*.

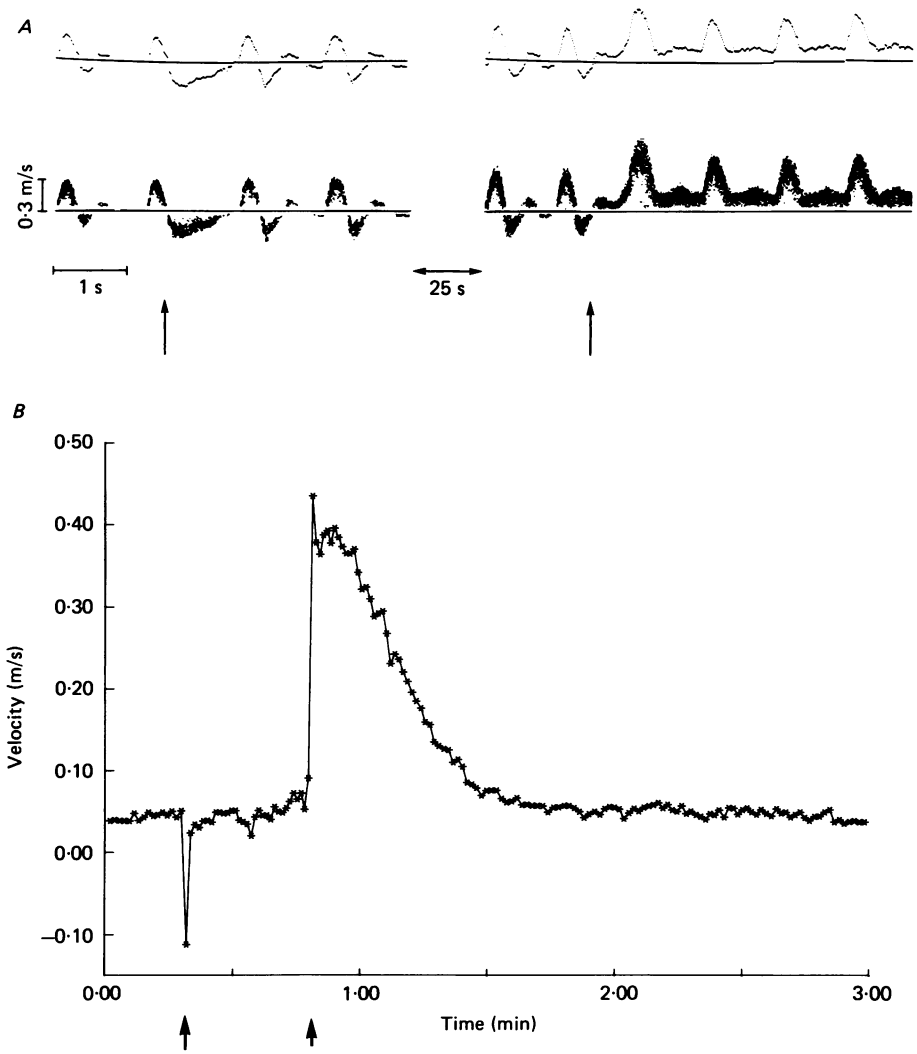

Fig. 4. *A*, the lower panel shows the velocity spectra from ten cardiac cycles from a contraction of 30 s duration and with a tension of 50 % m.v.c., starting with the last heart beat in the resting period. The mean of each spectrum is given in the upper panel. The arrows mark the beginning and the end of the contraction. After the fourth cycle shown here, velocity spectra from the following 25 s of the contraction are omitted for clarity as marked by the horizontal arrow in the Figure. *B*, results from the same contraction as given in *A*, each point representing the average mean velocity for consecutive cardiac cycles. Negative velocities represents blood flowing towards the heart. The arrows mark the beginning and the end of the contraction.

Upon initiation of contraction, the velocity spectra altered differently depending on when during the cardiac cycle the contraction was initiated. In Fig. 3*A* contraction started during early systole, while it started during diastole in Fig. 4*A*. In the former instance, back flow appeared during early systole followed by an exaggeration of back flow during diastole, while in the latter there was an aggravation in diastole only.

TABLE 1. Values of time to maximal velocity, recovery time and the relative maximal velocity increase are shown for short contractions of 5 s duration ($n = 67$) and long contractions of 30 s duration ($n = 48$), each with a tension of 20% m.v.c. The '95% interval' is the non-parametrical confidence interval of the median with confidence probability 0·95

	Time to maximal velocity (s)	
	Short contractions	Long contractions
Mean	4·35	1·34
S.D.	0·15	0·56
Median	4·30	1·32
95% interval	4·00–4·40	1·14–1·50
	$P < 0·0001$	
	Recovery time (s)	
	Short contractions	Long contractions
Mean	13·25	24·08
S.D.	3·22	4·80
Median	12·48	23·97
95% interval	12·00–13·20	22·98–25·14
	$P < 0·0001$	
	Relative maximal velocity increase	
	Short contractions	Long contractions
Mean	4·69	7·76
S.D.	1·19	2·61
Median	4·44	7·70
95% interval	4·24–4·74	6·74–8·36
	$P < 0·0001$	

In Fig. 4*B*, the maximum velocity was reached during the first cardiac cycle upon relaxation which took place just at the start of systole. In contrast, in Fig. 2*A* the maximum velocity was actually reached during the second heart beat after the end of a contraction which was released during early diastole of one cardiac cycle, such that the following velocity increase was shared between two heart beats. To release a contraction just at the beginning of a systole was not of course always easy for the subjects to manage.

Comparison of short and long contraction periods

Values of time to maximal velocity, recovery time and the relative maximal velocity increase characterizing the short and long contraction periods each with a tension of 20% m.v.c. are presented in Table 1.

On comparing long and short contractions, the maximal velocity was reached sooner, the recovery time was approximately twice as long, and the relative velocity increase was twice as great following a contraction of 30 s duration. These differences were statistically significant. Similar results were obtained with other tensions.

In the experiments, from which results are shown in Figs. 3 and 4, the velocity responses are somewhat larger than average.

Estimation of volume flow

In the single experimental series using venous thermo-dilution, the resting blood flow values for the whole leg were approximately 400 ml/min. Maximal volume flow to the leg measured after a contraction of 30 s duration and with a tension of 20 % m.v.c, was approximately 4·0 l/min. This is ten times the resting value and is similar to the increase in the Doppler-ultrasound velocity measurements.

In the subject just discussed, the diameter of the femoral artery was found to be 13·0 mm using echo-ultrasound equipment. The calculated resting volume flow and maximum volume flow from this diameter and the Doppler-ultrasound velocities (0·55 m/s) were almost identical to the volume flow measured by venous thermo-dilution, being 440 ml/min and 4·4 l/min respectively. From the c.t., the volume of the quadriceps muscle group was estimated to be 2·21 l in this subject.

C.t. and diameter measurements were also performed on a young female. 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 was 240 ml/min and 2·4 l/min respectively, again a 10-fold increase.

DISCUSSION

Contraction

At the beginning of contraction, a constant observation was the sudden and conspicuous increase in back flow clearly shown in Figs. 3*A* and 4*A*. The average velocities were almost always negative in the first one or two cardiac cycles and then increased during the rest of the contraction. Negative velocities represent net retrograde flow, i.e. blood was flowing towards the heart for one or two cardiac cycles. This finding is most likely due to the contracted muscles creating high intramuscular pressures (Gray, Carlsson & Staub, 1967; Sejersted, Hargens, Kardel, Blom, Jensen & Hermansen, 1984), thereby compressing the vessels inside the contracted muscle, so that an intra-arterial pressure was transiently created that was high enough to overcome even the systolic systemic pressure. As a result, there was retrograde flow great enough to be detected at quite some distance from the contracting muscle, in this case the femoral artery just proximal to the inguinal ligament.

This phenomenon of retrograde flow is probably comparable to what Anrep *et al.* (1934) described as a ' back thrust ' of blood lasting 0·1–0·3 s. They observed blood flow in the arterial system of the dogs ' muscle being reversed at the start of strong tetanic contractions. Gaskell (1877) had already observed an outspurt of blood from the veins at the onset of a tetanic contraction, which he thought was ' dependent upon the contents of the vessels of the muscle in consequence of the change of form in the muscle '. This was later confirmed by Anrep & von Saalfeld (1935). Even Grant (1938) using water-plethysmography observed a fall in limb volume upon initiation of a strong contraction, but he was not able to detect any fall in blood flow in the first 3–5 s because of artifacts from oscillations of the recorder produced by the contraction itself. Yet he interpreted this fall in volume as ' due to blood being squeezed out of the forearm by the contracting muscles'.

During contractions, after the immediate effects (lasting one to three cardiac cycles) had subsided, velocities were mostly below resting levels during short contraction periods, but generally and steadily increased to above resting levels during the long contraction periods even when held until fatigue (1–2 min) with tensions exceeding 50 % m.v.c. In previous studies, velocities have not been shown to be below resting levels during short contraction periods. For the long contractions, our results are in agreement with the findings of Grant (1938), Lind *et al.* (1964) and Lind & McNicol (1967). However, Barcroft & Millen (1939) observed a cessation of blood flow of the calf muscles in humans during isometric contraction when the tension exceeded 20 % m.v.c. Humphreys & Lind (1963) also suggested this occurred on the basis of their experiments on the human forearm when the tension of the contraction exceeded 70 % m.v.c.; they came to this conclusion by extrapolating the results obtained using lower tensions.

Relaxation

In Fig. 3*B*, which shows the responses to a short contraction, there was a small peak velocity (marked with an asterisk) on the first heart beat after relaxation which lasted only one heart beat. The velocities during the following two cardiac cycles were lower. This first peak in velocity was probably due to the fact that contraction of skeletal muscle causes high intramuscular pressures as mentioned above. Thus when contraction ceases there may be a transient pressure fall within the intramuscular vessels such that the pressure becomes lower than the intravascular pressure in the vessels just outside the muscle. This causes a temporary increase in blood velocities, lasting for as long as it takes for the vessels to refill. This phenomenon was observed consistently only during contractions at tensions of 50 % m.v.c. or more, whether long or short. In Fig. 4*B*, for instance, maximum velocity for the first heart beat after the relaxation was clearly higher than the velocities of the next few heart beats.

The initial small peak in velocity described above (Fig. 3*A*) probably corresponds to what Anrep *et al.* (1934) described as an ' overshoot ' lasting less than 0·2 s. They observed this phenomenon under rather unphysiological conditions: using a constant-pressure perfusion set-up in dogs when tetanic contractions were evoked by direct muscle or nerve stimulation. Our results confirm this finding of Anrep *et al.* (1934) and show that the phenomenon can be observed even under physiological conditions with pulsatile blood flow.

The finding of maximum velocity values four times the resting value after short contractions is in accordance with the results of Concordilas *et al.* (1964) and Lind & Williams (1979). For long contractions, maximum velocity values were eight times the resting value. Such an increase is only slightly greater than that observed by Grant (1938), Lind *et al.* (1964) and Lind & Williams (1979). However, the measurements of velocity were taken from the femoral artery, and blood flow increase relative to control in the quadriceps muscle group might be expected to be even greater than the increases actually recorded. When increasing the duration up to 90 s and tension up to 75 % m.v.c., there was only a small further increase in velocity (the greater part taking place between 20 and 50 % m.v.c.), but a larger increase in heart rate and blood pressure. During contractions of 3 min duration, Lind & McNicol (1967) observed an increase only during contraction and no hyperaemia exceeding the contraction values

with tensions of up to 15 % m.v.c. With 20 % m.v.c., they found an increase in blood flow up to eight times the resting level by the end of the contraction, but only a small increase upon relaxation. Only when the tension was increased to 30 % m.v.c. was there a marked hyperaemia of approximately ten times the resting value following relaxation, while the hyperaemia during the contraction was nine times pre-contraction levels. In the present study the hyperaemic phase was quite short (Table 1 and Figs. 2*A*, 3*B* and 4*B*), and since it seems from the Figures of Lind & McNicol (1967) that they were only able to obtain reliable recordings from 15 s after the relaxation, this may explain why they did not detect post-contraction hyperaemia following low-tension contractions.

Estimation of volume flow

In one of the subjects (male), the resting blood flow to the whole leg was estimated to be 400 ml/min both using venous thermo-dilution and from the diameter and the Doppler-ultrasound velocities.

Of the 400 ml/min going to the whole leg in the resting state, 100 ml/min goes to the quadriceps muscle group (see Methods). When divided by the quadriceps muscle volume of 2·21 l, the estimated resting blood flow to this muscle group is of the order of 4·5 ml/min . 100 ml muscle. The maximal volume flow was 4·0 l/min following a contraction of 30 s duration and 20 % m.v.c. In this subject, after a contraction of 45 s duration (by which time fatigue occurred) and 75 % m.v.c., the estimated (from the velocity increase) maximal volume flow increased only by 400 ml/min to 4·4 l/min.

It is a fairly reasonable assumption that blood flow to other parts of the leg does not alter, i.e. remains at 300 ml/min, since there is no e.m.g. activity recorded from the other muscles and no increase in skin blood flow could be measured in contralateral recordings in these cool environments. Subtracting the 300 ml/min going to inactive tissue from the maximum volume flow of 4·4 l/min leaves 4·1 l/min to the quadriceps muscle group. This, when divided by the muscle volume of 2·21 l, gives a maximum volume flow during post-contraction hyperaemia to the quadriceps muscle group of approximately 185 ml/min . 100 ml muscle, a 40-fold increase over resting values.

Calculating in the same manner for the female subject on whom vessel diameter measurements and c.t. were performed, the maximum volume flow of post-contraction hyperaemia to the quadriceps muscle group is approximately 175 ml/min . 100 ml muscle, which is of the same magnitude as in the subject discussed above.

To check the possible role of systemic effects during these contractions, blood pressure (B.P.) and heart rate (H.R.) were measured together with contralateral femoral artery Doppler recordings in the same two subjects. Neither H.R. nor B.P. altered significantly as a result of a 5 s contraction at a tension of 20 % m.v.c. With a 30 s contraction at the same tension, H.R. increased by 10 % but B.P. again remained unaltered. Even during contraction periods of 60 s duration and a tension of 75 % m.v.c., the rise in both systolic and diastolic B.P. was 30 mmHg at the most, and the H.R. increased maximally by 50 %. The contralateral Doppler recordings on the femoral artery during such contractions showed very small changes of velocity. Since the systemic effects were small, they could only account for a small fraction of the large velocity responses to isometric contractions in the present investigation.

These values of maximum volume flow are four to six times higher than results given by other investigators using plethysmography (Grant, 1938; Clarke & Hellon, 1959; Barcroft *et al.* 1963; Lind *et al.* 1964; Lind & McNicol, 1967; Lind & Williams, 1979). A problem when comparing these results with each other is that some investigators give blood flow per 100 ml limb volume, some per 100 ml muscle volume and some per 100 g muscle, but all have the difficulty of not knowing exactly the weight or volume of the muscle which is actually contracting during the experiment. Even when compared to blood flow values given per 100 ml limb volume (forearm, with all muscles contracting), the present estimates are two to three times higher than those previously given.

The most probable explanation for the considerable discrepancy in volume flow obtained using plethysmography and the estimates given above is the poor time resolution of plethysmographic methods (which may well miss the period of marked hyperaemia).

Duration of post-contraction hyperaemia

The duration of the hyperaemia following isometric contractions seems to have caused little interest, at least as judged by observations available in the literature so far. The results presented here indicate that post-contraction hyperaemia is shorter than suggested by previous reports, though all these experiments are not always directly comparable. After short contractions of less than 5 s duration and with tensions of up to 20 % m.v.c., the recovery time is 12–13 s (Table 1). This is less than a quarter of the time indicated by Lind & Williams (1979). Concordilas *et al.* (1964), using a strain-gauge method, found recovery times only slightly longer than ours (approximately 15 s estimated from their Fig. 4) following brief contractions. For the long contractions with tensions of up to 50 % m.v.c. the difference between the results presented here and those of others is more pronounced. In the present study, the recovery time following a 30 s contraction is 23–25 s (Table 1). Even after contractions of 2 min duration and a tension of 30 % m.v.c., the recovery time was at most 1·5 min whereas 10 min or more has been reported by those using plethysmographic methods (Grant, 1938; Lind *et al.* 1964). The only experiments showing that the hyperaemia lasts a shorter time than this were done by Lind & McNicol in 1967. Following a sustained hand-grip contraction of 30 % m.v.c. tension and a duration of 3 min, they found that the hyperaemia had subsided by 5 min.

This difference in the duration of the hyperaemia may be due to the use of blood pressure cuffs with plethysmographic methods. Such cuffs, both arterial and venous, are inflated quite frequently during an experiment. The consequent sensory stimuli may cause reflex changes in the skin blood flow (Thoresen & Walløe, 1980). Since plethysmography measures the total blood flow to the limb, this may explain some of this discrepancy. By keeping the subjects cool during the measurements of this study, skin blood flow was minimized and was therefore only a small fraction of the total blood flow to the limbs.

Early phase of post-contraction hyperaemia

Even if Concordilas *et al.* (1964) and Lind & Williams (1979) found a rapid increase in flow that was detectable within 1 s following short contractions, they always found this to be the maximum. This is in contrast to our results showing maximal flow after

4 s (Table 1, and Fig. 3*B*). Other authors suggest a large and immediate increase in blood flow following relaxation (Grant, 1938; Lind *et al.* 1964), but they do not give any details concerning the time taken to reach maximal flow, since they were only able to measure for 3–15 s after relaxation.

In contrast, Anrep and co-workers (Anrep *et al.* 1934; Anrep & von Saalfeld, 1935) had an excellent time resolution in their measurements. They were able to detect both the transient increase following relaxation described above, then a decrease and a further increase which reached a maximum after 0·5–3·0 s following short tetanic contractions. The increase was observed independently of whether the 'overshoot' was present or not. Despite the fact that their experiment is not directly comparable to those presented here, it still gives a surprisingly detailed time course that is remarkably similar. There is only some disagreement of the magnitude of maximal flow in the hyperaemic phase. This may be due to their tetanic contractions being much shorter than those isometric contractions described here.

The most interesting finding in the present investigation is, in my opinion, the difference in time course of the post-contraction hyperaemia following short and long contractions. Following relaxation of short contractions, maximal blood velocity is reached after 4·3 s (Table 1), whereas after long contractions it is reached during the very first heart beat (1·3 s, Table 1). Figs. 3*B* and 4*B* illustrate these phenomena. This is a consistent finding also in contractions of low tension where the initial peak (marked with an asterisk in Fig. 3*B*) is absent. This difference has not been observed before, probably because the shortest sampling interval possible using plethysmography is approximately 6 s, while our Doppler equipment can measure velocity changes occurring in a fraction of a cardiac cycle.

Even though the regulation of post-contraction hyperaemia has been a subject of considerable interest in physiology, it is still uncertain how the hyperaemic response to exercise is evoked or controlled. Numerous vasodilator substances or mediators have been suggested, the most interesting ones probably being potassium, inorganic phosphate and partial pressure of oxygen. Nervous regulation has also been suggested to at least partly control the response. The difference in the time taken to reach maximal velocity after short and long contractions may contain information about the mechanism involved. Hypothetically, during long contractions enough time has passed for 'metabolites' to have accumulated outside the resistance vessels and as a result maximal dilatation has taken place by the end of contraction. During short contractions, released 'metabolites' may not have had time to reach the smooth muscle of the resistance vessels, because they are released at some distance from them. Another explanation consistent with our findings, though less probable, is that the vasodilatation is partly due to a nervous reflex to the smooth muscle in the resistance vessels, and that this reflex takes some time to develop.

In keeping with our findings, Marshall & Tandon (1984) using an *in vivo* microscopy technique, recently observed quick responses of terminal arterioles to contractions of the skeletal muscle fibres in experiments on the rat spinotrapezius muscle. 8–10 s after twitch contractions evoked by a micro-electrode inserted into the muscle, terminal arterioles started to dilate. There was an even faster response to tetanic contractions. There was vasodilatation not only in all sections of the arteriolar tree

in the region of muscle contraction but also of the venules which crossed or ran alongside the muscle fibres. Despite quite different physiological conditions, it is interesting to note that there was a similar time lag of 8–10 s (see their Figs. 3*A* and 4*A*) before the post-contraction hyperaemic response as compared to the 4·0–4·4 s in these experiments (Table 1).

The present study thus supports the hypothesis that locally released substances (metabolites or local hormones) play a dominant part in the regulation of post-contraction hyperaemia, and provides evidence that these substances are released at some distance from the resistance vessels with some time needed for diffusion.

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