Reflex Changes in Human Skeletal Muscle Blood Flow Associated with Intrathoracic Pressure Changes

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Rapid alternating intrathoracic pressure changes caused by rapid breathing with partial obstruction to airflow caused a three to four fold increase in forearm blood flow whereas following the Valsalva maneuver the blood flow was decreased. Evidence is presented that these changes are brought about reflexly through alterations in vasoconstrictor tone. It is demonstrated that the reflex changes are confined to skeletal muscle vessels, providing further evidence that the vasomotor centers controlling skin and muscle vessels can function independently.

THOUGH both the skin and muscle blood vessels in human limbs are innervated by sympathetic nerve fibers, recent evidence has demonstrated that the vasomotor centers controlling these vessels can function independently. In the reflex control of body temperature the skin vessels only are involved, whereas with alterations in posture the reflex changes are confined to the muscle vessels.

In the present study the effects of changes in intrathoracic pressure on the blood flow in human limbs has been investigated. Evidence is presented that the alterations in flow which result from these changes are reflexly mediated through sympathetic vasoconstrictor nerves and confined to the skeletal muscle.

METHODS

The experiments were carried out on healthy young adults in a room kept at a temperature of 24 to 26 C. Blood flows to the forearm, hand and calf were measured by venous occlusion plethysmography using temperature controlled plethysmographs. In some experiments deep and superficial veins in the forearm were catheterized and the oxygen saturation of blood sampled from these veins determined by a spectrophotometric technic. In other experiments the deep (motor) nerves or the deep and superficial (cutaneous) nerves to the forearm were blocked by infiltrating around them 2 per cent lidocaine (lignocaine, Xylocaine) solution containing epinephrine (1:

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grains during resisted breathing presented technical difficulties because of movement artefact. Trained subjects were used who had practiced the maneuver before the actual experiment. They lay recumbent with the arm semiabducted and the elbow slightly flexed since in this position they were best able to avoid movement. The float recorders used to measure the volume changes were filled with a heavy oil (castrol S.A.E. 140) instead of water so that the movements of the float were considerably damped. When these conditions were fulfilled readily interpretable plethysmograms were obtained (fig. 1).

Valsalva Maneuver. In this case the subject blew against a mercury column and supported it at about 60 mm. Hg for 5 to 10 sec.

RESULTS

Resisted Breathing. Alternating intrathoracic pressure transients of about +30 to -20 mm. Hg were produced by this procedure. The central venous pressure did not show similar changes but fell from about -1 to -3 mm. Hg (fig. 2). Presumably, therefore, the intrathoracic vascular transmural pressure transients were greatly augmented. The effect on arterial pressure depended on the phase relationships of the intrathoracic pressure changes and the pulse pressure changes. When inspiration and expiration coincided with diastole and systole respectively, there was a large increase in the magnitude of the arterial pressure transients; when they were out of phase the transients were sometimes smaller than during the control periods. The mean arterial pressure, however, was little altered throughout the procedure, a slight fall being the usual finding.

During resisted breathing the forearm blood flow was invariably increased, often three to fourfold (fig. 2), as was that through the calf. Though the increase occurred consistently in each of the 10 subjects examined, the size of the increase varied greatly from subject to subject and in the same subject from time to time. This was not surprising since it was almost impossible for the subject to make identical respiratory excursions each time resisted breathing was carried out. Similar increases in blood flow were observed in the forearm when resisted breathing was repeated with 5 per cent CO₂ in the inspired air. The increase in flow was not, therefore,
A. RESISTED BREATHING

B. VALSALVA MANOEUVRE

C. LEG RAISING

Fig. 3. Effects of (A) resisted breathing, (B) the Valsalva maneuver and (C) passively raising the legs of a recumbent subject on the following: blood flow through the nerve-blocked forearm (O), the normal forearm (D) and the normal hand (D), and on the oxygen saturation of superficial (D) and deep (D) forearm venous blood. The various procedures were carried out during the periods represented between the dotted lines.

...a consequence of washing out CO2 from the lungs, which can produce a vasodilatation in the forearm through a humoral mechanism.12

Role of Muscle and Skin Vessels. During resisted breathing, though the blood flow through the normal forearm increased, that through the nerve-blocked forearm showed no comparable change (fig. 3A, left panel). It was evident therefore that the increase in flow in the normal forearm was due to an active dilatation of the forearm vessels and not a passive change due to alteration in perfusion pressure. This was in keeping with the previous finding that there was no important change in the mean perfusion pressure during the resisted breathing. Further, as the dilatation was confined to the normal forearm it was mediated by vasomotor nerves and was not due to a humoral mechanism.

The oxygen saturation of blood from a superficial forearm vein draining skin did not increase during resisted breathing (fig. 3A, middle panel). On the assumption that resisted breathing did not affect the skin tissue metabolism, this result indicated that skin blood flow did not increase and that the vasodilation with resisted breathing occurred deep to skin, presumably in the skeletal muscle. The fact that the blood flow through the hand showed no important change (fig. 3A, right panel) indicated that the vessels of the hand, like those of the forearm skin, were not involved in the reflex vasodilatation.

Vasconstrictor or Vasodilator Nerves? Passively raising the legs of a recumbent subject causes a reflex vasodilatation in forearm skeletal muscle8 (fig. 3C) similar to that seen during resisted breathing. It was found that with a combination of resisted breathing and leg raising the forearm vasodilatation was greater than when either maneuver was per-
formed separately (fig. 4). In this way increases in forearm blood flow of up to 14 ml./100 ml./min. were obtained.

Human skeletal muscle vessels are innervated with vasoconstrictor fibers and there is some evidence that they also have a vasodilator nerve supply. The experiments described below were designed to determine whether the large reflex dilatation of muscle vessels with resisted breathing and leg raising could be accounted for by release of vasoconstrictor tone.

Vasodilator nerves to skeletal muscle in dog and cat have been shown to act through a cholinergic mechanism which can be blocked by atropinization of the muscle. It was believed that if the vasodilatation with resisted breathing were brought about by vasodilator nerves, atropinization of the forearm tissues would abolish or at least reduce it. Infusions of 0.4 mg. atropine sulfate into the brachial artery abolished sweating and delayed the vasodilatation in the forearm during body heating, presumably by blocking the action of cholinergic fibers on forearm skin, but the drug did not affect the release of vasoconstrictor tone in the hand or forearm.

The infusion of a similar dose in 2 subjects was found to be without effect on the vasodilatation in the forearm during a combination of resisted breathing and leg raising (fig. 4). In one of these experiments the subject was subsequently heated and forearm sweating was found to be abolished and vasodilatation delayed on the infusion side, indicating that this forearm was effectively atropinized.

In another subject the deep nerves to the left forearm were blocked with local anesthetic solution. This abolished vasomotor activity in both the skin and the muscle of the forearm. As skin vessels are supplied with vasodilator as well as vasoconstrictor nerves the cutaneous nerves to skin vessels of the opposite forearm were also blocked to make the skin circulation similar on the two sides. Any difference in the level of flow on the two sides was then due to differences in vasomotor activity in muscle vessels. When a combination of leg raising and resisted breathing was performed, the flow in the right forearm increased to about the level of flow in the left forearm in which muscle vasoconstrictor tone was fully released (fig. 5). The results could therefore be accounted for solely by release of vasoconstrictor tone and did not require the postulation of vasodilator nerves.

**Resisted Breathing and Peripheral Blood Volume.** During resisted breathing, though there was a large increase in the blood flow through the forearm, there was no obvious change in the amount of blood contained in it, since its volume did not increase. Further, the amount of blood that could be accommodated in the capacity vessels of the forearm following application of a venous occlusion cuff at 60 mm. Hg to the upper arm was not increased. It was concluded that resisted breathing did not cause a dilatation of the capacity blood vessels in the forearm.

**Valsalva Maneuver.** During the Valsalva
maneuver there is an acute decrease in the venous return to the heart as blood is trapped in the peripheral veins. Vasodilatation occurs in the normally innervated forearm and persists for some seconds after release of the raised intrathoracic pressure. The characteristic arterial pressure and forearm flow changes are shown in figure 6. During the maneuver there was a tachycardia accompanied by a decrease in the arterial pulse pressure. On release of the raised intrathoracic pressure there was an arterial pressure overshoot with bradycardia and an increase in both mean arterial and pulse pressures. These changes gradually subsided and disappeared after about a minute. The central venous pressure, which was raised during the procedure, rapidly fell to normal within a few seconds of release, so that the perfusion pressure (mean arterial minus mean venous pressure) was initially increased.

Following the Valsalva maneuver, though the blood flow through the normal forearm decreased, the blood flow through the nerve-blocked forearm was found to be increased but it gradually returned to the resting level during the following minute (fig. 3B, left panel). The pattern of change in blood flow in the nerve-blocked forearm was roughly similar to the pattern of the mean arterial pressure overshoot and it is likely that the increase in flow in this forearm could be explained by the increase in the perfusion pressure. Since the perfusion pressure was increased, it was evident that the fall in flow in the normally innervated arm was due to vasoconstriction; since no fall occurred in the nerve-blocked arm it was clear that the vasoconstriction was mediated through vasomotor nerves. Following the maneuver, the oxygen saturation of forearm skin venous blood was increased (fig. 3B, middle panel) and the pattern of increase was similar to that of the blood flow in the nerve-blocked forearm, and the blood flow in the normal hand (fig. 3B, right panel). If the subject took a deep breath immediately before performing the maneuver, the hand blood flow often showed an initial decrease on release of the raised intrathoracic pressure. However, when he did not do so an increase in hand blood flow was invariably seen. It appeared therefore that the vasomotor fibers to the forearm and hand skin were not involved in the reflex peripheral vasoconstriction that followed the Valsalva maneuver. As with resisted breathing and postural change, the reflex effects appeared to be confined to the skeletal muscle vessels.

In some subjects the fall in flow following the Valsalva maneuver was slight when the subject was recumbent and vasomotor tone relatively high. If, however, the subject's legs were raised and vasoconstrictor tone thus reduced, the fall in blood flow following the maneuver was much more dramatic (fig. 7).

DISCUSSION

It has been shown that the intrathoracic pressure changes associated with resisted breathing and the Valsalva maneuver cause reflex changes in the caliber of human skeletal muscle resistance vessels without causing comparable effects on skin vessels. In this
respect the results are similar to those seen during postural change and provide further evidence that the vasomotor centers controlling skin and muscle vessels can function independently. There is evidence that the reflex changes in muscle blood flow with postural change are due to stimulation of receptors in the vascular low pressure system in the thorax and are not a consequence of arterial baroreceptor stimulation. Indeed, there is now evidence that stimulation of the carotid artery stretch receptors in man does not produce reflex changes in resistance to blood flow in human limbs. It is unlikely therefore that the receptors concerned in the reflex changes with resisted breathing and the Valsalva maneuver are situated in the arterial system. It is more probable that they also lie in a low pressure area of the intrathoracic vascular bed.

The reflex changes in skeletal muscle blood flow can be explained by alterations in vasoconstrictor tone and provide no evidence for vasodilator nerves to skeletal muscle vessels. Vasodilator nerves to muscle have been described in various animals and in man, but no satisfactory explanation of the role they play in the normal economy of the body has yet been found. Lindgren and Uvnas have shown that these fibers play no part in the depressor reflexes and the present results suggest that the same is true in man.

The present experiments also demonstrate that large changes in muscle blood flow can be brought about by alterations in sympathetic vasoconstrictor tone. However since sympathetic tone in muscle is normally high, vasodilator reactions can be demonstrated more easily than vasoconstrictor ones and increases in forearm blood flow of the order of 10 to 15 ml./100 ml./min. can be obtained. If these changes in forearm muscle flow are representative of flow changes in muscle elsewhere in the body, it is clear that large changes in total peripheral resistance can occur in this way.

**Summary**

Intrathoracic pressure transient of +30 to —20 mm Hg with each respiratory cycle were produced by rapid shallow breathing with partial obstruction to airflow ("resisted breathing"). This procedure caused a three to fourfold increase in forearm blood flow. The blood flow through the nerve-blocked forearm did not increase demonstrating that the increase in the normal forearm was due to reflex vasodilation. Since the dilatation was unaffected by atropinization of the forearm and was not greater than could be obtained by full release of vasoconstrictor tone (produced by nerve block) it is suggested that the vasodilatation was due to release of vasoconstrictor tone.

The oxygen saturation of forearm skin venous blood and the hand blood flow were not increased during resisted breathing, indicating that the reflex changes in the limbs were confined to skeletal muscle vessels and that vasomotor fibers to skin were not involved in the response. Similar evidence was obtained that the peripheral vasoconstriction following the Valsalva maneuver is confined to muscle vessels.

The reflex changes in peripheral blood flow associated with intrathoracic pressure changes therefore seem to be brought about by alterations in vasoconstrictor tone in muscle and provide further evidence that the vasomotor centers controlling skin and muscle vessels can function independently.

**Summary in Interlingua**

Transientes de pression intrathoracic de +30 a —20 mm de Hg in omne cyclo respi- ratori esseva producite per rapide e non profunde respiration con obstruction partial del fluxo de aere ("respiration a resistantia"). Iste manovra causava un triple o quadruple augmento del fluxo de sanguine in le ante- brasio. Illo causava nullo tal augmento in antebracios subjecite a bocage de nervos. Assi il esseva demonstrate que le augmento que occurreva in le antebracio nonbloate esseva le effecto de un vasodilatation reflexe. Considerante que le dilatation non esseva afficite per atropinisation del antebracio e non ex- cedeva in magnitude le dilatation effectuabile per le complete relaxation del tono vasocon- strictori (per bocage de nervos), il pare plau- sible supponer que le vasodilatation esseva le
effecto de un relaxation del tono vasoconstrictor.

Le saturation oxygenic de sanguine venose del pelle antebrachal e le fluxo de sanguine in le mano non cresceva durante respiratio a resistentia. Isto indicava que le alterationes reflexe in le extremitates esseva limitate a vasos de musculo skeletic e que fibras vaso-motori ducente al pelle non partecipava in le responsa. Similemente il esseva demonstrate que le vasoconstriction post le manovra de Valsalva es restringite a vasos muscular.

Le alterationes reflexe occurrente in le fluxo de sanguine peripheric in association con alterationes del pression intrathoracic pare, per consequente, esser effectuate per alterationes in le tono vasoconstrictor del muscolo. Isto confirma additionalmente que le centros vaso-motori que governa le vasos cutanece e le vasos muscular es capace de functionar independentemente.

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