Regional Flow Responses to Exercise*
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Both neural and humoral systems participate in the control of blood flow to various organs. Exercise places the greatest demands on the circulation. At rest, in humans, skeletal muscle receives somewhere between 15% and 20% of cardiac output, while during maximal exercise, this percentage reaches a value of 80% to 90%. The active human muscles have a high-flow capacity that exceeds the capacity of the heart to pump blood. Measurements in single human muscle have indicated that blood flow may be inhomogeneous, that is, probably depending on variations of the vasomotor tone of the muscle mediated by neural and regional factors. Exercise raises cardiac output and coronary blood flow, which rise linearly with increases in heart rate. In normal young men, coronary blood flow averages 280 ml/min/100 g of the left ventricle and reaches as high as 390 ml/min during moderately severe exercise, requiring about 85% of maximal heart rate. In nonexercising organs, the blood flow decreases at about 20% to 40% of the resting values, being the net result of competing vasoconstrictor and vasodilator drives.

Both neural and humoral systems participate in the control of blood flow to various organs. Exercise places the greatest demands on the circulation; virtually every organ of the body is involved. This presentation will provide some flashes on splanchnic and cutaneous districts, taking into account particularly the blood flow in the exercising muscles and in the heart. The main question is: how is blood flow to exercising and nonexercising regions regulated and what is the significance of this regulation to overall cardiovascular function? Muscular work can be performed at different levels and consequently, the blood flow response to exercise is evidently modulated by the work load.

Splanchnic and Cutaneous Blood Flow
In a supine, resting subject, cardiac output is distributed among the different vascular regions in a predictable manner. That is, the total blood flow and also the fraction of total cardiac output received by each organ appear to be essentially constant among different individuals of similar body size and composition. However, it is not possible to measure total blood flow to all organ systems. It is possible to measure total splanchnic, renal, cerebral, and coronary blood flows with reasonable precision; flows to regions such as skeletal muscle, skin, and other regions, which include adipose tissue, connective tissue, bone, etc., must be calculated from measurements of flow to some portion of the total tissue and an estimate of the total weight of that tissue. In a normal subject at maximal work load, with a cardiac output of 20 L/min, heart rate of 190 beats/min, stroke volume of 110 ml, A-V oxygen difference of 16 ml%, corresponding to a maximal oxygen consumption of 3.5 L/min, the splanchnic and renal flow decreases to 20% of the resting value. Concerning the cutaneous district, it can be said that of all organs, skin is the most accessible; nevertheless, the measurement of its blood flow is fraught with problems. Rough estimates of total skin blood flow in resting normothermic humans place the value between 200 and 500 ml/min or 100 to 300 ml/m² of body surface per minute. During mild dynamic exercise in animals, the skin blood flow decreases at about 60% of the resting value. As exercise continues and body temperature rises, the vasoconstriction gives way to vasodilation. The current concept is that skin blood flow during exercise is the net result of competing vasoconstrictor and vasodilator drives.

Skeletal Muscle
Skeletal muscle comprises approximately 40% of the total body mass, depending, of course, on different factors. The density of capillary networks varies greatly among the 2 basic muscle fiber types that are present in humans. The capillary surface area is estimated to be 7 sq m kg of muscle or 210 sq m in a 75-kg subject with 30 kg of skeletal muscle. Oxygen can be taken up by individual muscles at a rate approaching 300 to 400 ml/min/kg, which exceeds the resting value by about 50-fold. Skeletal muscle is another tissue to which the Fick principle cannot be easily applied to measure blood flow in intact animals. In resting humans, skeletal muscle receives somewhere between 15% and 20% of cardiac output and consumes about 60 ml of oxygen per minute; thus, muscle extracts only about 30% of the available oxygen at rest. Most subjects cannot supply the flow needed to perfuse 30 kg of maximally dilated skeletal muscle at normal pressure. Even when one exerts himself maximally by running, less than 50% of the total muscle mass is strongly engaged in the task and approximately 80% to 85% of the maximal cardiac output is distributed to the working muscle. The estimated total muscle blood flow in a normal young sedentary subject with a maximal cardiac output of 22 L/min and a maximal oxygen uptake of 3.5 L/min would be 18.6 L/min. If 50% of the muscle mass (15 kg) is uniformly engaged, then blood flow per 100 g of muscle would be 125 ml/100 g. This far exceeds the estimates for maximal muscle blood flow derived from isotope clearance in humans or studies in muscle isolated from laboratory animals. To put these numbers in perspective, there are endurance athletes weighing 75 kg who can pump 42 L of blood per minute, consuming oxygen at a rate of 6.3 L/min. If 85% of this cardiac output (36 L/min) perfuses 15 kg of muscle (ie, 50% of total muscle mass), then muscle blood flow would be 240

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ml/100 g.

Andersen and Saltin measured the changes in blood flow during exercise to the quadriceps. Exercise was accompanied by marked increase of the blood flow that reached a value of 6 L/min at peak exercise, giving a flow per 100 g of muscle of up to 240 ml/min, and an oxygen uptake of 0.8 L/min, while oxygen extraction tended to remain constant. These data reveal the high-flow capacity of active human muscles. Taking into account that to perfuse 15 to 20 kg of muscle at this rate during maximal whole-body exercise, 36 to 48 L/min should be necessary from the heart; an unconditioned subject would never be able to do this, so it is possible to conclude that the capacity of active muscle to receive flow at a given pressure exceeds the capacity of the heart to pump blood. Repeated measurements of blood flow on human biceps have indicated that within a given muscle it may be inhomogeneous.

Piiper et al and Pendergast et al have studied the regional blood flow in isolated muscle and in the limbs of intact running animals (dogs). They found an inhomogeneity of blood flow in the muscle that is greater during spontaneous submaximal exercise if compared with resting conditions. Also, measurements on human biceps have indicated that blood flow within a given muscle may be inhomogeneous.

In a group of patients with heart transplants, we measured by xenon technique the quadriceps blood flow at rest and during dynamic exercise (75 W on a bicycle ergometer in sitting position during 5 min) compared with a control group of healthy, age- and sex-matched volunteers (Table 1). The difference is not statistically significant either at rest or during exercise also if the latter for patients seems to be a little higher than for control group. That could be due to the relative higher work load for patients, the maximum oxygen consumption being higher in control group compared with patients. The work load of 75 W was certainly maximal for patients with heart transplant and submaximal for the control group. In a group of 12 patients with heart failure (NYHA class 2 and 3) the flow we measured in the exercising legs at peak supine effort on a bicycle ergometer was on average 92% of the cardiac output, ranging respectively from 5 to 15 L/min and from 8 to 18 L/min (Table 2). This value is, in fact, not different from normal subjects, obviously taking into account the different level of physical working capacity.

The Coronary Circulation

The more blood the heart provides to other organs, the more it must provide for itself as its own metabolic costs rise with increased pumping. Like skeletal muscle, the heart depends heavily on metabolic vasodilation for its arterial supply. Normal human hearts contain approximately 3,000 to 4,000 capillaries per square millimeter in contrast to approximately 300 to 400 per square millimeter in skeletal muscle. Because the heart is always beating, it is not appropriate to compare the "resting" state of the heart with that of other organs. At rest, with a heart rate of 70 beats/min, coronary blood flow is 60 to 80 ml/min/100 g of left ventricle; total coronary blood flow is approximately 250 ml/min or about 5% of cardiac output. Most of this blood flow and oxygen uptake meets the costs of contraction; when the heart beat is stopped and perfused with oxygenated blood at a normal pressure, the basic living costs are about the 20% of the total in a beating heart; Coronary blood flow (CBF) rises linearly with increases in heart rate.

Data from exercising dogs show that CBF can reach very high values. For example, when sled dogs were severely exercised with heart rates of 300 beats/min, the CBF that at rest was 60 to 80 ml/min/100 g of left ventricle reached a value of 300 to 400 ml/min/100 g. In different studies, measurement of total CBF by the radioactive microspheres in heavily exercised animals has yielded CBF of 390, 400, and 424 ml/min/100 g. Barnard et al infused diprydamole in dogs during severe exercise, with a heart rate of 270 beats/min, and raised CBF from 424 to 618 ml/min/100 g; this means that coronary vasodilator reserve was far from exhausted in these animals despite the high demand of the myocardium. In an important series of experiments carried out on normal young men, CBF averaged 280 ml/min/100 g of left ventricle and reached as high as 390 ml/min during moderately severe exercise requiring heart rates of 165 beats/min that were about 85% of maximal heart rate.

Conclusions

To answer the question made in the introduction of this article, it must be said that the regional blood flow during exercise increases or decreases depending on the metabolic level required by the organ involved or not in the exercise; this mechanism is modulated by the interaction of local and central activations that must automatically take into account the solution of the following equation: Flow = Pressure/Resistance. It is evident that no single, dominant exercise stimulus can explain the control of regional blood flow; in fact: (1) chemical and mechanical reflexes originating in active skeletal muscle might trigger responses that could provide the necessary regulatory feedback; (2) centrally

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Table 2 — Cardiac Output and Leg Blood Flow at Peak Exercise in 12 Patients with Heart Failure

<table>
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<th>Patient</th>
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<th>Leg p</th>
<th>NYHA</th>
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*COp = cardiac output peak exercise (in L/min); Leg p = leg blood flow at peak exercise (in L/min); NYHA = NYHA class.
generated motor signals from the cerebral cortex and spinal cord might provide the necessary feed-forward control.

REFERENCES