Editorial

Exercise and the Circulation

Recent interest in the response of the circulation to muscular exercise has stemmed from apparent discrepancies in the literature concerning the relative importance of changes in heart rate and stroke volume, from controversy as to whether conclusions drawn from the behavior of the Starling heart-lung preparation can be applied to the intact organism, and from studies that have attempted to define the coordinating role of the central nervous system.

It is now well established that in man different views concerning the contribution of stroke volume stem, not from faults in methodolagy, but from differences in the posture of the subjects in the various studies. Thus, when the subject is in the supine position, the stroke volume at most is only 10 to 20 per cent greater during leg exercise than at rest. When the subject is standing relaxed the heart rate is greater and the cardiac output less than in the supine position; hence, the stroke volume is considerably reduced, sometimes by as much as 50 per cent. With mild exercise in the upright position, such as marking time, the stroke volume increases to approach or to equal that in the resting supine position, but with increasingly severe exercise there is only a slight additional increase in stroke volume, even when the cardiac output exceeds 20 liters per minute and the oxygen consumption is about 3 liters per minute.

Few data are available concerning the response in trained athletes, despite the popular notion that their stroke volume greatly increases during severe exercise. Bock and colleagues, however, showed that the pattern of response in a marathon runner was qualitatively similar to that of untrained men, although values for stroke volume were considerably greater both at rest and during exercise. A recent study confirmed that, although athletes have a higher resting stroke volume, the pattern of response both to change of posture and to graded exercise is identical with that in sedentary subjects. The maximal cardiac output attained by the athletes, corresponding to an oxygen consumption of 3.5 to 4.5 liters per minute, did not exceed 30 liters. Although the athletes might have attained a slightly greater output during completely unrestrained activity, earlier estimates of a tenfold increase in output above resting values were too high.

A similar relationship of changes in heart rate and stroke volume may be seen even in patients who have complete atrioventricular dissociation. For example, in one such patient the resting cardiac output was 8.3 liters, the heart rate 36, and the stroke volume 230 ml. During leg exercise in the supine position the output attained 14.5 liters and the heart rate increased to 59; the stroke volume increased only to 248 ml.

Rushmer and colleagues from measurements of left ventricular diameter and thoracic aortic blood flow in dogs, found only relatively slight changes in stroke volume from rest to exercise, and this has been confirmed by the indicator-dilution technic. Not all workers agree with these findings. Although the left ventricular diameter decreases when the dog stands up from the prone position such postural changes have less influence on the stroke volume than they do in man.

Although these patterns of response are regularly observed in man and dog, under other circumstances stroke volume can readily change and even play the major role in the increased output during exercise. For example, in dogs before atropinization the cardiac output, heart rate, and stroke volume during exercise were increased by 95, 90, and 2 per cent over the resting values; after atro-
pinization corresponding increases were by 110, 7, and 100 per cent. Similar findings were observed by Warner and Toronto, who stimulated the ventricle at different rates during exercise in a dog with complete heart block and found that, within wide limits, cardiac output was independent of heart rate. Also, when epinephrine or norepinephrine was infused during exercise, stroke volume increased by 25 to 50 per cent. After cardiac denervation in the dog the increase in cardiac output under mild exercise is due to an increase in stroke volume; with maximal work, increases in heart rate and stroke volume make almost equal contributions.

In another study paired measurements of cardiac output were made in a man at different grades of exercise on an inclined treadmill. For the first of each pair, the circulation to the lower limbs was unimpaired. Forty-five seconds before the second observation pneumatic cuffs around the thighs were suddenly inflated to 250 mm. Hg to reduce venous return from the exercising muscles; although the cardiac output decreased sharply, the heart rate was maintained and the stroke volume decreased from 120 to 85 ml., a value less than that when the subject was at rest in the supine position (100 ml.). Thus it is easy to dissociate the normal relationship of changes in heart rate and cardiac output.

It will be recalled that Patterson, Piper, and Starling, using the heart-lung preparation, found a direct relationship between the diastolic volume of the ventricles and the energy liberated during the subsequent systole. They concluded that "the law of the heart is therefore the same as that of the skeletal muscle, namely that the mechanical energy set free on passage from the resting to the contracted state depends on the area of 'chemically active surfaces,' i.e., on the length of the muscle fibres." Starling was well aware that conclusions from the heart-lung preparation could not be indiscriminately applied to the behavior of the heart in the intact animal. Thus he stated "... we must remember, as Haldane has so often insisted, that no organ of the body works by itself or for itself ... we must always remember that the extraordinary powers with which the heart muscle is endowed represent but the central fortress of the system, and under normal conditions are protected and, to a large extent, prevented from coming into play by the activities of the defending positions and outposts provided by the central nervous system and its servants. It is only when these other defences fail that the heart is called upon to display those reactions which are at once brought to light in our study of the isolated organ."

Failure of the cardiac output to increase after large intravenous infusions has been cited as evidence that the Starling mechanism does not operate in intact animals. However, Frye and Braunwald have demonstrated that the autonomic nervous system buffers changes in cardiac activity during acute hypervolemia in normal man. After rapid infusion of 1.5 liters of blood there was little or no change in cardiac output or stroke volume; however, similar infusions after treatment by a ganglion-blocking agent resulted in substantial increases in output and stroke volume resembling those seen in the heart-lung preparation when venous inflow is augmented. Additional studies by Braunwald and his colleagues in man have confirmed that the end-diastolic pressure is an important determinant of the characteristics of ventricular contraction, and that the characteristics of left atrial contraction are a function of the atrial pressure at the onset of left atrial contraction. There can be little doubt, therefore, that Starling's law is applicable to the human heart.

Sarnoff expanded the concept of the Starling hypothesis by his demonstration of a family of Starling curves; thus, failure to discern the mechanism at work in the intact heart may be hidden in the shift by the heart from one curve to another. "... the central nervous system has available to it both direct and indirect pathways by means of which it can continuously provide varying degrees of gain for the fundamental Frank-Starling relationship ... the exploitation of these avail-

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able pathways plays a most important role in the control of cardiac output.7,21 Thus at a constant heart rate, increased sympathetic stimulation of the myocardium causes the heart to do more work at a lower filling pressure22 and vice versa.23 Sarnoff and his co-workers24 have also demonstrated how the strength of atrial contraction is influenced by the cardiac nerves and that the relationship between mean left atrial pressure and ventricular stroke work is determined by the performance characteristics of the atrium as well as the ventricle.

Debate also has centered around a possible relationship between changes in pulmonary blood volume and in cardiac output. For example, it has been suggested that the pulmonary blood volume may increase during exercise to provide a ready reserve of blood for the left atrium.25 Progress in this field has been hampered by the difficulties inherent in attempts to measure the volume of blood in the lungs; deductions about changes in this volume based on measurements of "central" blood volume by the Stewart-Hamilton method are hazardous because of unknown but important changes in the extrathoracic component of this volume during exercise.26 In dogs there is no important increase in the volume of blood in the lungs and left heart chambers as between rest and severe exercise.26,27 Thus, there is no evidence of major shifts of blood from the systemic to the pulmonary circulation.

Lindgren and associates,28 working with cats and dogs, postulated the existence of a vasodilator pathway to skeletal muscles originating in the anterior sigmoid gyrus, and suggested that this was involved in the cardiovascular adjustments to muscular exercise. Abrahams and co-workers29 confirmed the occurrence of vasodilatation in muscle during stimulation of the brain stem, and concluded that it was one component of an integrated defense reaction involving autonomic and behavioral response. Rushmer, Smith, and Franklin30 have shown that stimulation of discrete areas in the diencephalon produced changes in left ventricular performance similar to those noted during exercise, and postulated that the cardiac response to exercise is initiated by impulses from the brain and modified by peripheral vascular reflex mechanisms such as arterial baroreceptors and chemoreceptors.

In man, as in animals, the complex interrelationship of all the receptor mechanisms concerned in the reflex regulation of the circulation makes precise analysis of the individual components difficult. However, it is now possible to distinguish different types of reflexes, each utilizing a different component of the sympathetic nervous system on the efferent side, presumably through activation of different centers in the brain. These include a center that receives impulses from the low-pressure vascular baroreceptors and causes reflex changes in vascular resistance in skeletal muscles via sympathetic vasoconstrictor fibers.31 Another center receives impulses from the arterial baroreceptors and causes reflex changes in blood pressure and heart rate, but does not affect resistance to the flow of blood in muscle or skin.32 A third center, activated by mental stress, causes reflex changes in the flow of blood through muscles via sympathetic cholinergic fibers.33,34 During leg exercise vasoconstrictor tone increases in the inactive arm muscles.35 Blair and colleagues36 found that in inexperienced subjects vasodilator fibers to the arm muscles may be excited during leg exercise, probably as a result of emotional stress; since this did not occur in experienced subjects, it is not an integral part of the general vasomotor response to exercise. A vasodilatation of the vessels in the forearm muscles can be detected within a second after a weak contraction of the forearm muscles lasting 0.3 second. The vasodilatation is locally mediated, since the same response is present in the sympathectomized forearm. The speed of onset of this dilatation makes it unnecessary to postulate a dilatation mediated from the brain to produce the immediate circulatory adjustments in muscles to exercise.37

The importance of these reflex adjustments is not always appreciated. However, it can
be demonstrated very effectively in two contrasting circumstances: first, in patients who have idiopathic orthostatic hypotension, and second, in patients who have severe mitral stenosis. In the former, during even mild leg exercise carried out in the head-down position, in which venous return to the heart is facilitated, there is a severe decrease in systemic arterial pressure which is caused by failure of compensatory vasoconstriction, as a consequence of the autonomic denervation, and not by failure of cardiac output to increase.\textsuperscript{38} In the latter, in whom severe obstruction exists to the inflow of blood to the left ventricle, during leg exercise the increase in cardiac output may be minimal; yet the blood pressure is maintained, because of an exaggerated vasoconstrictor response in non-exercising parts, such as the arms.\textsuperscript{35} Thus, compensatory vasoconstriction is a major factor in the maintenance of systemic arterial blood pressure in man, the total peripheral resistance being reflexly adjusted to maintain the pressure within reasonably normal limits, despite large changes in cardiac output.

ROBERT J. MARSHALL

JOHN T. SHEPHERD

References


The Effects of Artificial Electricity on Muscular Motion

I dissected and prepared a frog, and placed it on a table, on which was an electrical machine widely removed from its conductor and separated by no brief interval. When by chance one of those who were assisting me gently touched the point of a scalpel to the medial crural nerves of this frog, immediately all the muscles of the limbs seemed to be so contracted that they appeared to have fallen into violent tonic convulsions. But another of the assistants, who was on hand when I did electrical experiments, seemed to observe that the same thing occurred whenever a spark was discharged from the conductor of the machine.—LUIGI GALVANI. Commentary on the Effect of Electricity on Muscular Motion. Translated by Robert Montraville Green, M.D. Cambridge, Massachusetts, Elizabeth Licht, Publisher, 1953, p. 24.
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ROBERT J. MARSHALL and JOHN T. SHEPHERD

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