Editorial

Capacity for Exercise after Denervation of the Heart

The complete disruption of autonomic nervous inflow which attends transplantation of an organ may interfere with the function of the organ itself and with the inclusion of that function in the coordinated response of the total organism to a stimulus. Since the behavior of the heart is abruptly and profoundly affected by stimulation of the cardiac autonomic nerves, it might be supposed that their loss in transplantation of this organ would be attended by serious consequences. Early experimental work in cats and dogs suggested that section of the extrinsic cardiac nerves results in severe limitation of capacity for exercise, but the denervation included the lungs and certain abdominal viscera. Autonomic denervation confined to the heart is now accomplished by excision and reimplantation of this organ or by regional neural ablation. These techniques have afforded an excellent opportunity to study in experimental animals the effects of disruption of the extrinsic cardiac nerves on cardiac function and morphology, sensitivity to drugs, integration of the heart into reflex cardiovascular responses, and the possibility and time course of reinnervation. Catecholamines are virtually absent in the denervated heart, but there is no depression of fundamental properties of the myocardium.

Dogs exercising freely on a treadmill under laboratory conditions sustain graded exercise up to a ten-fold increase in oxygen consumption and a four-fold increase in cardiac output. The capacity for exercise to these levels is not altered by denervation of the heart. Studies of trained and highly motivated greyhounds racing under field conditions show that, after denervation, the time required to run 5/16 mile is increased from an average of 32.1 to 33.6 seconds, an increment of approximately 5%. Greyhounds finish the race in a vigorous fashion with heart rates increasing to around 300 beats/min in both denervated and control animals.

Catecholamine contribution to maintaining work capacity is surmised since the denervated heart is particularly sensitive to noradrenaline. Beta-adrenergic receptor-blocking agents are without effect on work capacity of normal dogs under laboratory conditions but, when they are administered to dogs with denervated hearts, the animals fail to complete the previously attained top level of exercise in 85% of tests. Normal greyhounds treated with propranolol show only 3% increase in time required to complete a race, and they run vigorously. Propranolol-treated greyhounds with denervated hearts slow almost to a walk in the last third of the race and finish in an exhausted condition, and their heart rates do not exceed 180 beats/min.

The action of cardiac nerves and of catecholamines seems necessary for maximal performance, but this performance is little reduced if one or the other is absent. When
both are withdrawn and the heart must increase its output solely through the Frank-Starling mechanism of greater fiber length, the capacity for exercise is considerably reduced. Even in these circumstances, however, the heart is able to increase its output two to three times over the resting level, largely through an increase in stroke volume. After denervation the acceleration in heart rate is linearly related to work load, but the magnitude of increase is about one third of that found in the normal dog. This is effected through some mechanism intrinsic to the heart.6

Dogs with denervated hearts also require, on the average, 25 seconds longer than the normal dog to reach steady-state values of cardiac output. Oxygen saturation of pulmonary arterial blood and oxygen consumption during exercise and recovery are similar to those in normal dogs. Systemic arterial blood pressure is maintained during exercise equally as well in the denervated as in the normal dog, although a temporary decrease of 10 to 15 mm Hg in mean aortic blood pressure occurs as the animal goes from standing to running.

Tsakiris and Wood (personal communication) have found other changes in cardiac function after denervation. With induced systemic hypertension, both groups of dogs maintain cardiac output equally well, but during drug-induced hypotension there is a much smaller increase in cardiac output with work stress in dogs with cardiac denervation.

In summary, removal of the extrinsic cardiac nerves alters decidedly the manner in which the heart responds to the stress of exercise, but cardiac output is still augmented sufficiently so that capacity for exercise is not greatly curtailed. It is postulated that at lower work loads the denervated heart acts as a force-fed pump responding to an increase in venous return by increasing stroke volume; this is mediated through the basic Frank-Starling mechanism of increased contraction force from increased fiber length. The increase in heart rate is proportional to work load and is mediated through an unknown mechanism intrinsic to the heart itself. At higher work loads, work stress results in release of norepinephrine into the blood, to which the highly sensitive, denervated heart responds with tachycardia, increased force of contraction, and an increase in cardiac output adequate for the metabolic demand.

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References
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