Physical Training and Intrinsic Cardiac Adaptations

There is much evidence that physical training programs are beneficial to integrated cardiovascular function. It is also suggested that training may afford protection against some of the effects of coronary artery disease. Training results in the ability to achieve an increased maximum exercise performance. This is accomplished by a greater cardiac output, increased oxygen extraction by peripheral tissues, and greater total oxygen consumption that can be achieved with maximum exercise. Part of the cardiac adaptation to training is by a decrease in heart rate and an increase in stroke volume for any level of physical exertion. This presumably permits a lower myocardial energy expenditure for a given cardiac output. Patients who have had myocardial infarctions, and who undergo retraining programs, demonstrate the same types of cardiovascular adaptations as persons with normal hearts. Early reports also indicate that such patients may have a reduction in symptoms of myocardial ischemia and may have decreased recurrence rates from myocardial infarction. Although the apparent cardiovascular benefits of training might be ascribed in part to the effects of the training program on heart rate and stroke volume, this editorial addresses itself to evidence that training also leads to adaptations that are intrinsic to the myocardium, and proposes that these may be significant factors in the beneficial effects of training.

The first question that might be asked is whether physical training changes the intrinsic capacity of the myocardium to function as a muscle or of the heart to function externally as a pump. When rats were made to swim 6 hours daily for several weeks, heart rate was reduced, and isometric tension development by myocardial wall was increased. In other experiments hearts from rats made to swim only 150 min/day for 8 weeks were studied in an isolated working rat heart apparatus and compared with hearts from sedentary animals. At equal heart rates, hearts from trained rats had increased mechanical responses to rapid atrial pacing or to increasing the ventricular filling pressure. Cardiac output, left ventricular pressure, maximum rate of pressure rise, and external work responses all were increased by training. When the left ventricle was made to contract isovolumically from the same end-diastolic pressure, greater left ventricular pressures and maximum rates of pressure rise were achieved in the conditioned hearts. These dynamic changes were not dependent upon an increase in the cardiac weight. These studies in rats subjected to moderate and more severe training programs suggest that physical training enhances both the function of the myocardium as a muscle (increased contractility) and the heart as a pump (increased external cardiac work capacity). The possibility that all exercise programs may not yield improvements in myocardial performance are suggested by a preliminary report in which heavy training failed to lead to an increase in contractility in rat papillary muscles.

The mechanisms by which physical training can improve cardiac performance have been examined. Several studies demonstrate that physical training either with treadmill exercise or by swimming increases the vascularity of rat myocardium. In one report, an absolute increase in the number of capillaries was observed in hearts of very young rats, whereas in old rats the capillary-to-fiber ratio was increased due to the loss of myocardial fibers. The physiologic counterpart to these observations of increased vascularity was found when hearts of exercised rats were perfused in the isolated working rat heart apparatus. Hearts of trained rats achieved higher coronary flows and rates of oxygen delivery per gram of heart than hearts of sedentary animals.

Changes in oxygen transport, substrate stores, energy liberation, and high-energy phosphate stores might be responsible for the increased cardiac work capacity associated with training. The effects of training on skeletal muscle metabolism have been studied in some depth. In general, training was found to result in an increase in glycerolipids, enzymes for lipid metabolism, and a shift toward fatty acid metabolism. Levels of myoglobin, citric acid cycle components, and cytochrome compounds have also been found to become elevated. In hearts of physically trained animals...

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levels of cardiac glycogen and the activities of enzymes of glycogen and glycolytic metabolism were found to be increased.10-15 Cardiac triglyceride levels appeared to be reduced in physical training, but the turnover rate of triglycerides was increased.12,16 Despite evidence that training may alter mitochondrial structure in the heart27 and increase mitochondrial resistance to exhaustive exercise,18 most mitochondrial compounds were found to be normal14,19,20 suggesting that a primary change in the oxidative capacity of the mitochondria is not important in the cardiac adaptation to training.

Myocardial high-energy phosphate stores also were not altered by the training process.12 Therefore, there does not appear to be convincing evidence that enhanced energy-generating mechanisms are of sufficient quantitative importance to explain the improved myocardial performance in physical training.

The greater cardiac responses to atrial pacing and to preload or afterload in hearts from trained animals might conceivably be related to altered catecholamine levels. However, catecholamine stores21 and uptake of norepinephrine per gram of tissue by hearts of trained animals are reported to be reduced.22

The possibility must be considered that fundamental alterations occur in the pathways of energy utilization. Recently it has been discovered that physical training in rats results in an increase in adenosine triphosphate (ATPase) activities of cardiac actomyosin, crude myosin, and purified myosin.23-25 These contractile protein enzymatic activities probably correlate to the potential contractility of the myocardium. The increase in ATPase activity was found to be related to the severity and the duration of the training program.24 These changes preceded the onset of myocardial hypertrophy, but were accentuated during the hypertrophic phase of cardiac adaptation. Coincident with the increase in ATPase activity is a greater speed of interaction of actomyosin upon the addition of adenosine triphosphate (superprecipitation). Further preliminary studies indicate that training may induce a chemical change at the locus of enzymatic activity on myosin and at its site for interaction with actin.25 These findings with contractile proteins correlate well with the suggestion of increased contractility in the hearts of conditioned animals. They suggest that physical training induces a fundamental alteration in the structure or control of the myosin molecule. Such a change could be responsible for important alterations in myocardial performance.

There is little evidence that good physical condition protects against the development of coronary atherosclerosis. Therefore, the intrinsic changes observed in myocardial and cardiac function, vasularity, and biochemical changes in hearts of experimental animals may be relevant to the apparent beneficial effects of physical training in normal humans and in patients with coronary artery disease.

The effects of training on the response of the heart to ischemia or hypoxia is particularly important. It has been proposed that physical training might improve collateral vessel formation, particularly in areas of borderline perfusion. In one study, an exercise program was begun after the circumflex coronary artery was narrowed in dogs.26 Retrograde coronary flow in the ischemic bed was significantly greater in those animals made to exercise than in sedentary controls. Although collateral vessel formation in dogs is probably more abundant than in humans, it is possible that training in humans with ischemic heart disease has similar effects on the coronary vasculature.

There may be other mechanisms by which the trained heart can respond to hypoxia. Studies in the isolated, perfused working hearts of trained rats demonstrated an increased resistance to hypoxia.27 During hypoxia, external work performance was maintained at higher levels than in hearts from sedentary rats, although all hearts lost their ability to respond to increased filling pressure or to a greater afterload. There was no evidence that coronary flow, oxygen delivery, energy formation, or energy stores were responsible for the improved performance during hypoxia of hearts of trained animals. There was improved external efficiency of the hearts from trained animals (external work expressed as calories per energy input, expressed as calories). By inference, therefore, mechanisms of energy utilization were relatively more efficient during hypoxia in the conditioned hearts. This would provide an energy-saving mechanism for continued external cardiac work in situations where energy delivery may be borderline.

Thus, in addition to the improved heart rate-stroke volume relationships, the alterations in peripheral oxygen extraction, and biochemical changes in skeletal muscles, there appear to be important changes that occur in cardiac vascularity and biochemistry that may contribute significantly to the cardiovascular effects of physical training.
The studies cited on the heart have mostly been conducted in rodents under artificial conditions. Therefore, extrapolation to humans with ischemic coronary artery disease is speculative.

Although structural and biochemical alterations can be induced by physical training, it cannot be claimed at this time that all of these are beneficial to the heart. For example, it is conceivable that an increase in myosin ATPase activity and an increase in myosin. There may also be differences in the way hearts of males and females adapt to chronic training upon mechanical and metabolic performance of the rat heart. J Clin Invest 49: 1859, 1970

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Corrections

Legato MJ: Circulation 47: 178, 1973. On page 182, in table 1, and on page 187, line 3, capacitance of the Purkinje cell is shown as 1.28 \( \mu \)faradays/cm\(^2\); it should read “12.8 \( \mu \)faradays/cm\(^2\).”

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