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Cardiac Hypertrophy: Synergistic Effects of Pericardiectomy and Mild Exercise in Rats (38850)

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The functional significance of the pericardium has been debated for many years. Functions that various investigators have attributed to the pericardium include prevention of overdilatation of the heart, protection of the heart from infection and from adhesions to surrounding tissue, maintenance of the heart in a fixed geometric position within the chest, and prevention of right ventricular regurgitation when diastolic pressures are increased (1). Others have noted that humans with congenital absence of the pericardium (2) and pericardiectomized animals have a normal survival and appear to carry out their physiologic functions in a more or less normal manner. Acute experiments in dogs have shown that the pericardium will prevent excessive cardiac dilatation in response to the infusion of very large volumes of fluid (3). In the present study we evaluated the effect of pericardiectomy on the development of cardiac hypertrophy secondary to a mild exercise program.

Methods. Animals. Female rats of a Wistar strain (specific pathogen-free CFN rats), weighing 177 ± 20 g, were provided with Purina chow and water ad lib. They were randomly assigned to four groups. Groups 1 and 3 were restricted to their cages. Groups 2 and 4 were subjected to a program of swimming. In addition, a pericardiectomy was performed on the rats in groups 3 and 4.

Pericardiectomy. The rats in groups 3 and 4 were anesthetized with intraperitoneal sodium methohexital (Brevital), 100 mg per kg body wt. Oxygen was administered via a small plastic cannula inserted into the animal's mouth. The lungs were ventilated by temporarily occluding the nose and mouth. The chest was opened through the left fourth or fifth intercostal space and the ribs were spread with eyelid retractors. The entire pericardium was stripped from the heart. The lungs were reinflated and the chest was closed.

Swimming program. One week after the pericardiectomy on the animals in group 4, groups 2 and 4 were started on an exercise program consisting of swimming for 1 hr per day, 5 days per week, in steel barrels, 47 cm in diameter, filled to a depth of approximately 34 cm with water maintained between 33° and 35°. There were six animals per barrel. The program lasted 8 wk, during which the animals swam a total of 40 hr.

Tissue preparation. After the 8 wk of exercise, all animals were weighed and then sacrificed on the same day. The chest was opened, the heart was carefully dissected out, and the great vessels were trimmed off. The hearts were opened and washed in lactated Ringers solution, blotted dry on filter paper and weighed on a Mettler P136 balance. Myocardial water content was determined by drying portions of ventricular muscle to constant weight at 80° over $CaCl_2$.

Data analysis. All data were compared for statistical significance using Student's paired t test. Tabulated data are expressed as the mean ± standard error.

Results. As can be seen from a comparison of groups 1 and 3 in Table I, pericardiectomy alone had no effect on heart weight in the sedentary animals. Since body weight was the same in groups 1 and 3, the heart weight to body weight ratio was also unaffected. Similarly, 60 min of swimming per day did not, by itself, result in significant increases in either heart weight or heart weight to body weight ratio (Table I). However, as shown in Table I, when pericardiectomy and 60 min of daily swimming (group 4) were combined, both heart weight and heart weight to body weight ratio increased significantly ($P < 0.01$). The water content of myocardium in groups 2, 3, and 4 did not differ significantly.

TABLE I. EFFECT OF PERICARDIECTOMY AND EXERCISE ON BODY WEIGHT, HEART WEIGHT, AND HEART WEIGHT/BODY WEIGHT RATIO.[a]

Group[b]	Body weight (g)	Heart weight (wet) (mg)	Heart weight (dry) (% of wet weight)	Heart weight (mg)/ Body weight (g)
Group 1, Sedentary	261.9 ± 16.9	802.7 ± 51.5	—	3.12 ± .018
Group 2, 60-min swim	254.8 ± 13.2	814.2 ± 37.2	25.0 ± 0.4	3.16 ± .023
Group 3, Pericardiectomy and sedentary	257.0 ± 11.9	800.0 ± 63.3	24.1 ± 0.1	3.11 ± .014
Group 4, Pericardiectomy and 60-min swim	261.3 ± 13.4	887.6 ± 48.5[c]	25.0 ± 0.5	3.40 ± .018[c]

[a] Values are mean ± SE.
[b] Each group contained nine rats.
[c] Group 4 vs group 1, group 2, or group 3, $P < 0.01$.

Discussion. The only previous report of the combined effects of pericardiectomy and mild exercise we have been able to find is an article in the French literature by Ruchenbush and co-workers (4). They reported that exercise comparable to that used in the present study resulted in a 61% increase in heart weight in pericardiectomized rats (4). Although we have been unable to reproduce this remarkable increase, the present finding of a small (10%) but significant increase in heart weight of pericardiectomized rats subjected to exercise which, by itself, did not produce hypertrophy, confirms that the intact pericardium affects the cardiac response to exercise (4). Although it has been reported that the pericardium of the dog contains chemo- and mechanoreceptors which can produce bradycardia and hypotension (5), it is doubtful that removal of these factors played a role in the development of cardiac hypertrophy in our study, since the hearts of pericardiectomized animals that remained sedentary did not develop cardiac hypertrophy. Similarly, the mild exercise program of 5 hr per week was not an adequate stimulus, by itself, to induce cardiac hypertrophy.

It has been shown that an intact pericardium affects the maximal stroke volume and amount of cardiac work done by the ventricles (6). After the removal of the pericardium in cats, radiological and autopsy studies of heart size showed the volume of the pericardiectomized heart to be permanently enlarged (7). In recent studies in dogs subjected to volume expansion, Bartle presented evidence that removal of the pericardium resulted in an increase in left ventricular end diastolic volume (3).

Previous studies suggest that removal of the pericardium allows the heart to function at a larger end diastolic volume than when the pericardium is intact (6, 8). During the stress of exercise this difference in end diastolic volume of the ventricle may be even greater. According to a modification of Laplace's law relating to stress ($\sigma = P \cdot r/h$), the stress (σ) in the wall of a sphere is dependent upon the pressure (P) within the sphere, the radius (r) of the sphere, and the thickness (h) of the wall of the sphere. It appears that when the stress in the myocardial wall is increased by either a pressure or a volume overload, the heart adapts so as to return the stress on the myocardial fibers toward normal by hypertrophying and, thus, increasing wall thickness (9, 10). The mechanisms by which this adaptation is mediated are unknown.

The development of cardiac hypertrophy after pericardiectomy and mild stress has other experimental and clinical implications. This factor must be considered in experimental studies of cardiac hypertrophy produced by aortic constriction or pulmonary artery banding, since the pericardium is also frequently removed. Clinically, it is frequently noted that the heart size, heart mass, and electrocardiographic signs of ventricular hypertrophy do not significantly change in patients after corrective cardiac surgery (11). Although this may reflect the irreversibility of cardiac hypertrophy, it may also be secondary to removal of the pericardium.

Summary. Removal of the pericardium in combination with a mild exercise program of swimming resulted in a significant increase in heart weight and heart weight/body weight ratio of young rats. Either exercise or pericardiectomy alone did not significantly alter these parameters as compared to the control group of rats. This finding further substantiates the pericardium's physiologic effect on the heart. The effects of pericardiectomy should be considered in experimental studies of cardiac hypertrophy and in clinical studies involving cardiac surgery.

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