Pressure Development in the Hyperthrophied Heart.* (31687)

BARBARA B. KRAMES, DAVID W. NORTHUP, AND EDWARD J. VAN LIERE
Department of Physiology, West Virginia University Medical Center, Morgantown

The myocardium may greatly increase its muscle mass in response to stress, but whether its relative effectiveness and performance also increase is still a matter of controversy. The earlier literature is reviewed by Grant(1). More recently, Beznak(2), working with rats, produced cardiac hypertrophy by narrowing the aorta just below the diaphragm. Within 3 weeks the heart was enlarged 45% of its original weight. The hypertrophy was due entirely to the enlargement of the left ventricle. The reserve force of the heart was determined by ascertaining the maximum to which the output could be raised. It was found that while the output of the hypertrophied heart was normal, its reserve force was greater. Alexander *et al*(3), using a heart-lung preparation (with flow limited to the coronary vessels), studied cardiac performance of rabbits 4-120 days after severe constriction of the abdominal aorta. Heart performance was evaluated by finding the maximum mean arterial pressure against which the heart could pump. By the second or third postoperative week cardiac performance began to exceed the normal range, and was well above normal after the first month. It was observed, moreover, that a high cardiac performance was not necessarily associated with marked ventricular hypertrophy.

We deemed it worthwhile to compare the degree of pressure produced by isovolumetric contraction in hearts in which hypertrophy had been produced physiologically, either by exercise or by hypoxia with that of the normal heart.

Methods and materials. A total of 177 rats of the Sprague-Dawley strain was used; 99 served as control and 78 as experimental animals. Male and female rats were studied separately; 92 females and 85 males. They were fed Purina Chow, and kept in an air-conditioned room at an approximate temperature of 78°F. Cardiac hypertrophy was produced by one of two methods, hypoxia or exercise.

In the hypoxia experiment 47 females (23 controls and 24 experimentals), and 54 males (32 controls and 22 experimentals) were used. The animals were placed in a decompression chamber and subjected to 303 mm Hg pressure, corresponding to a simulated altitude of approximately 24,000 feet and a partial pressure of approximately 63.5 mm Hg. They were kept in the chamber 8 hours daily, except Sundays, for 24 days.

The exercise experiment included 45 females (23 controls and 22 experimentals), and 31 males (21 controls and 10 experimentals). These animals were made to run on an electrically-driven treadmill at a rate of one mile per hour. They were exercised for 2 one-hour periods daily 6 days a week until a total of 60 hours was reached. The day after the last exposure to the stress condition, each rat was weighed, and given 40 mg/kg of sodium pentobarbital intraperitoneally. The rat was securely attached to an animal board and a 3 way tracheal tube inserted so that artificial respiration could be administered. The heart and aorta were exposed by a ventral incision to the left of the midline.

An 18 gauge needle, attached to a strain gauge transducer, was placed into the left ventricle and connected to a Sanborn Twin-Viso recorder. The transducer was calibrated, by attaching it by means of thick-walled rubber tubing to a sphygmomanometer; a record was made showing pressure rises in increments of 20 mm Hg. After a control reading, the aorta was occluded and the maximum amount of developed left ventricular isometric pressure measured. The aorta was occluded only for a few seconds at a time, and several measurements of pressure were made to assure attainment of the true maximum.

The animals were sacrificed, the hearts excised, washed with tap water and blotted dry. The vessels were cut flush with the surface of

* Suported by USPHS grants 2G-437, C2 and 5Ti-GM-437-04.

TABLE I. Effects of Exercise on Heart Weight, Left Ventricular Weight, and Pressure Development in Left Ventricle.

	Female control	Female exp	Difference	P	% increase
HW/BW*	3.02	3.32	.30	<.001	10
LV/BW	1.61	1.89	.28	<.001	17
Pressure (mm Hg)	296	290	−6	.323	−2
	Male control	Male exp	Difference	P	% increase
HW/BW	2.66	2.94	.28	<.001	11
LV/BW	1.46	1.66	.20	<.001	13
Pressure	280	287	7	.326	3

* Heart wt/body wt, g/kg.
Left ventricular wt/body wt, g/kg.

the heart and any remaining pericardium or fat removed. The heart was weighed and then placed in a 4% solution of formaldehyde. Prior to partitioning, each heart was weighed again, and since its weight changed during the fixation period, a correction factor was established. The method described by Keen(4) was used to partition the heart. Using a stereoscopic microscope and a fine pair of scissors, the heart was partitioned into 4 sections: right ventricle, left ventricle, ventricular septum and atria.

Since this paper is concerned with the left ventricle, only its weight will be given. Ratios of heart-weight/body-weight and left ventricle-weight/body-weights were determined, average of each calculated, and the mean percentage of increase tabulated. The t-test was performed to determine significance.

Results. Table I shows the effects of exercise on the heart-weight/left ventricle-weight, and isometric pressure development in the left ventricle. It will be noted that exercise produced a significant hypertrophy in both male and female rats, but isometric pressure development was not significantly increased in either sex. Table II shows that hypoxia also caused a significant hypertrophy in both sexes. As with the exercised group, the isometric pressure development was not significantly increased; indeed, in the hypoxic male rats it was significantly decreased.

Discussion. The authors believe that cardiac hypertrophy produced either by exercise or hypoxia is a more physiologic approach than that of constricting large vessels such as the aorta. The increase in heart weight produced by exercise is caused by enlargement of myocardial fibers associated with increased cardiac work. In the experiments we are reporting on exercise, practically all the increase in total heart weight in both males and females can be accounted for by the hypertrophied left ventricle. While the other portions of the heart enlarged somewhat the increases were not statistically significant.

Cardiac hypertrophy produced by hypoxia is also associated with increased cardiac work due largely to the accompanying pulmonary hypertension. While both ventricles enlarge during hypoxia, the right ventricle enlarges relatively more than the left(5). Van Liere and Fedor(6) observed a 24% increase in the total heart weight of rats following exposure to a simulated atmospheric pressure of 303 mm Hg 4 hours daily for 41 days. The left ventricle of the hypoxic rats reported in this paper increased 36% in the females and 22% in the males.

Frank(7) formulated the length-tension relationships in the myocardium of the frog. Recording isometric contractions, and preventing outflow during systole, he observed that the pressure, within limits, increased directly with the degree of diastolic filling.

There is a question whether the relation between resting tension and resting length is a single curve which would imply a direct relationship between diastolic volume and effective filling pressure. Sarnoff and Berglund(8) report that there is more likely a series of curves depending on different

TABLE II. Effects of Hypoxia on Heart Weight, Left Ventricular Weight, and Pressure Development in Left Ventricle.

	Female control	Female exp	Difference	P	% increase
HW/BW	2.80	3.89	1.09	<.001	39
LV/BW	1.49	2.02	.53	<.001	36
Pressure	289	293	4	.430	1
	Male control	Male exp	Difference	P	% increase
HW/BW	2.87	3.42	.55	<.001	19
LV/BW	1.49	1.82	.33	<.001	22
Pressure	293	274	−19	.005	−7

physiological states of the myocardium since it has been found, for example, that epinephrine could increase the distensibility of the ventricle, thus changing its volume without altering the effective filling pressure.

Comparatively few studies have been made on the hypertrophied myocardium using precise isometric measurements, and these, for the main part, were performed on isolated papillary muscles. Kelly and Hoffman(9), using papillary muscles and muscle bundles from the posterior columns of rat hearts, found that as the muscles got larger the tension developed per unit weight of muscle decreased, but the increased weight of the muscles was brought about by increasing age and size of the rat, and not by cadiac hypertrophy. Kerr *et al*(10) reported that the maximum tension developed by a hypertrophied rat papillary muscle was greater than that from a normal papillary muscle. Recent work by Grimm and his associates(11) does not support the concept that the hypertrophied papillary muscles are stronger.

Our records indicate that isometric pressure development in the hypertrophied left ventricle was not significantly greater than the control values. In one instance, the male hypoxic animals, the pressure development was significantly less. On the whole, the data suggest that there is actually a decreased pressure development in the hypertrophied heart on a per gram of heart muscle basis when compared to control animals. Furthermore, when the experimental and controlled pressures were compared on a per gram of left ventricle basis, the hypertrophied chamber performed less effectively than the control chamber. There was no valvular leakage of blood as could be evidenced by the smooth, rounded tension peaks on the records. If the valves had not remained closed, the peaks would have exhibited a notched effect.

The results of our study indicate, therefore, that the hypertrophied rat heart is incapable of better performance than the normal rat heart, and is at times unable to match the performance of the normal heart.

Summary. The degree of pressure produced by isovolumetric contraction in the left ventricle of rat hearts hypertrophied either by exercise or hypoxia was measured. The rats were anesthetized and artificial respiration administered. Following thoracotomy an 18 gauge needle, attached to a transducer, was placed into the left ventricle. The aorta was occluded and the maximum pressure between the control and experimental animals was not significant, except in the male hypoxic group, which group showed a signficantly lower value. The data suggest that hearts hypertrophied by exercise or by hypoxia have a decreased isometric pressure development on a per gram of heart muscle basis when compared to control animals.

1. Grant, R. P., Am. Heart J., 1953, v46, 154.
2. Beznak, M., Circulation Res., 1958, v6, 207.
3. Alexander, N., Goldfarb, T., Drury, D. R., ibid., 1962, v10, 11.
4. Keen, E. N., J. Anat., 1955, v89, 484.
5. Van Liere, E. J., Baugh, B., Northrup, D. W., Circulation Res., 1965, v16, 244.
6. Van Liere, E. J., Fedor, E. J., Proc. Soc. Exp. Biol. and Med., 1955, v88, 676.
7. Frank, O., Z. Biol., 1895, v32, 370.
8. Sarnoff, S. J., Berglund, E., Circulation, 1954, v9, 706.
9. Kelly, J. J., Hoffman, B. F., Am. J. Physiol., 1960, v199, 157.
10. Kerr, A., Jr., Winterberger, A. R., Giambattista, M., Circulation Res., 1961, v9, 103.
11. Grimm, A. F., Kubota, R., Whitehorn, W. V., ibid., 1963, v12, 188.

Received September 29, 1966. P.S.E.B.M., 1967, v124.