evaluating numerous studies equating RES function with rates of particle phagocytosis.

Summary. Gelatin markedly inhibited the uptake of colloidal gold by rat liver slices incubated in heparinized rat plasma. In contrast, the phagocytosis of albumin aggregates was affected only at high gelatin doses. Gelatin had no inhibitory effect on gold particles previously incubated with heparinized plasma. Plasma of mice, dogs, and rats enhanced uptake by the respective liver slice. Rabbit plasma failed to support phagocytosis by rabbit or rat liver slices; however, rat plasma facilitated phagocytosis by rabbit liver. It is suggested that rabbit plasma is deficient in a factor essential for *in vitro* hepatic phagocytosis. It is also indicated that gelatin interacts with plasma opsonin in rat plasma and thereby induces reticuloendothelial depression.

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Effect of Hypertrophy on Myocardial Distensibility. (31085)

JOHN F. WILLIAMS, JR., EDMUND H. SONNENBLICK AND EUGENE BRAUNWALD
Cardiology Branch, National Heart Institute, Bethesda, Md.

The development of ventricular hypertrophy has long been recognized to be a fundamental adaptive mechanism utilized by the heart subjected to a chronically increased work load. However, only recently has detailed attention been given to the physiologic, biochemical and morphologic changes which are associated with the development of an increased myocardial mass. While distinct alterations at the cellular level have been demonstrated during and following the development of ventricular hypertrophy(1-4), the relations between these changes and the function of the myocardium remain to be elucidated. It has been reported that the development of hypertrophy permits the ventricle to attain a greater level of performance than normal, as reflected in the maximum pressure (5) or cardiac output it can achieve(6). Kerr *et al* found that hypertrophied papillary muscle was capable of developing greater than normal levels of active tension. This augmented tension was not due solely to an increase in the mass of the hypertrophied muscle, since the maximum developed tension per mg of hypertrophied myocardium also exceeded the normal(7). In contrast, Grimm and associates reported that hypertrophied and normal papillary muscles developed similar peak tensions when corrections were made for differences in muscle mass(8).

It is widely appreciated that cardiac hypertrophy decreases the apparent distensibility of the ventricle. A number of clinical studies have demonstrated marked elevations of left ventricular end-diastolic pressures with little or no increase of ventricular end-diastolic volumes in patients with marked ventricular hypertrophy(9-12). The problem of whether these changes are merely due to an increase in the ventricular muscle mass without a change in the distensibility of each unit of myocardium or to a change both in the mass of tissue as well as its elasticity has not been defined. Accordingly, the present study was performed to provide further information concerning the effect of hypertrophy on the distensibility of ventricular myocardium.

Methods. Ventricular hypertrophy was produced in Sprague-Dawley male rats by a modification of the method described by Beznak(13,14). Briefly, subdiaphragmatic suprarenal aortic constriction was produced in 170-180 g rats using a plastic clip (1.1 mm I.D.). Ten to 33 days (avg 14 days) after the constriction, the animals were anesthetized with ether, the hearts quickly removed and a longitudinal strip of the free left ventricular wall, extending from epicardium to endocardium and from apex to base, was placed in a muscle bath containing oxygenated buffered Krebs solution at 37°C. One end of the muscle strip was fixed to a stationary clamp at the base of the bath and the other was attached securely to a Statham G1-4-250 force transducer by means of a short braided silk ligature.

The force transducer was mounted in a fashion that allowed it to be moved in a vertical direction by known amounts, thus stretching the muscle segment by known lengths. The muscle strip was stimulated to produce a contraction rate of 6 per minute. The baseline length of the muscle (L_O) was defined as that length at which the resting tension was zero but at which an increase in length of 0.5 mm produced a detectable increase in resting tension. The resting tension was then determined following 0.5 mm increments in length to 35% above L_O. The effects of further extension of the muscle were not studied since they resulted in marked stress-relaxation. Three or 4 such length-resting tension curves were obtained over a 15- to 20-minute period from each left ventricular strip. The length and weight of the strip were then determined, allowing calculation of the cross-sectional area, and corrections for difference in muscle mass were made by expressing all tensions as g/mm^2.

The presence and degree of ventricular hypertrophy were determined by dissecting the atria and great vessel from the heart and re-

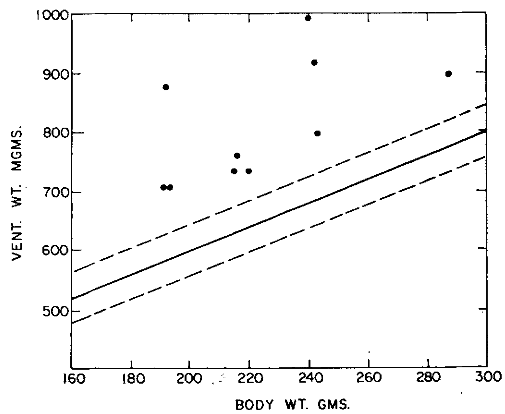

FIG. 1. Each point represents relation between ventricular weight and body weight in an aortic-constricted rat with myocardial hypertrophy. Regression line (± 1 S.D.) of this relation derived from 50 normal rats is also known.

lating the weight of the ventricles to the body weight of the rats at time of sacrifice. The normal ventricular weight was obtained from the regression line constructed from the relationship between ventricular weights and body weights of 50 normal rats determined in a previous investigation(14). Only those ventricles which exceeded the normal ventricular weight by more than 2 standard deviations were considered to be hypertrophied. To compare the distensibility of normal and hypertrophied myocardium, length-resting tension curves were obtained in an identical manner from the left ventricle of 10 normal rats, 10 rats with left ventricular hypertrophy, and 8 aortic-constricted rats in which hypertrophy did not develop; the latter served as sham-operated controls.

Results. The relations between ventricular weights and body weights of the 10 rats in which hypertrophy developed, as well as the regression line of ventricular weight on body weight derived from the normal rats, are shown in Fig. 1. The body and ventricular weights of the 50 normal rats averaged 271 g (range 182-430) and 685 mg (range 464-985), respectively. The body and ventricular weights of the 10 rats with myocardial hypertrophy averaged 224 g (range 193-287) and 809 mg (range 705-983), respectively. The increases in ventricular weight above normal ranged from 12 to 45%. None of these rats had pathologic evidence of heart failure at

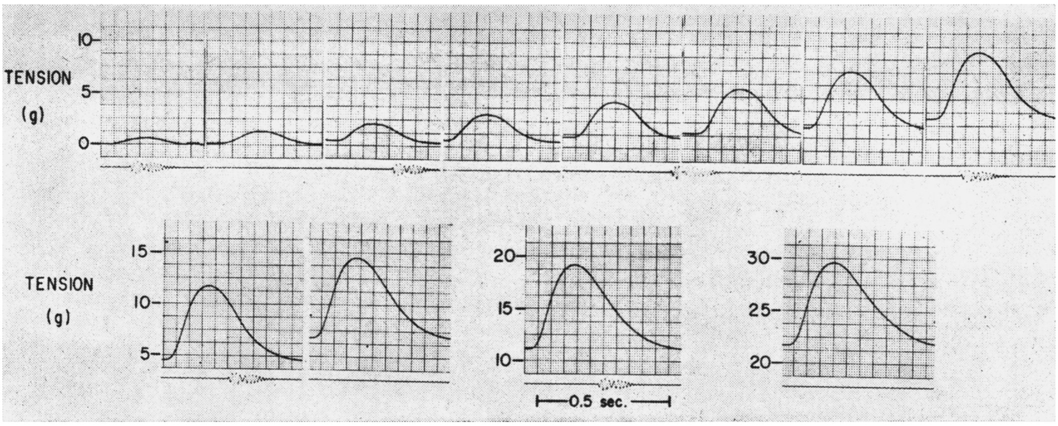

FIG. 2. Recording of resting and active tensions of a contracting segment of myocardium as muscle lengths were increased by 0.5 mm increments, proceeding from left to right and from top to bottom. Muscle length at L_O (top left) equaled 10 mm, muscle weight = 105 mg.

necropsy. The body weights of the 8 aortic-constricted rats in which hypertrophy did not occur averaged 215 g (range 117-406) and their ventricular weights averaged 664 mg (range 404-1098).

A typical recording of the resting and active tensions of a segment of normal ventricle as muscle length was progressively increased is reproduced in Fig. 2, while Fig. 3 illustrates the average levels of resting tension of the segments of normal and hypertrophied myocardium at various increments of length

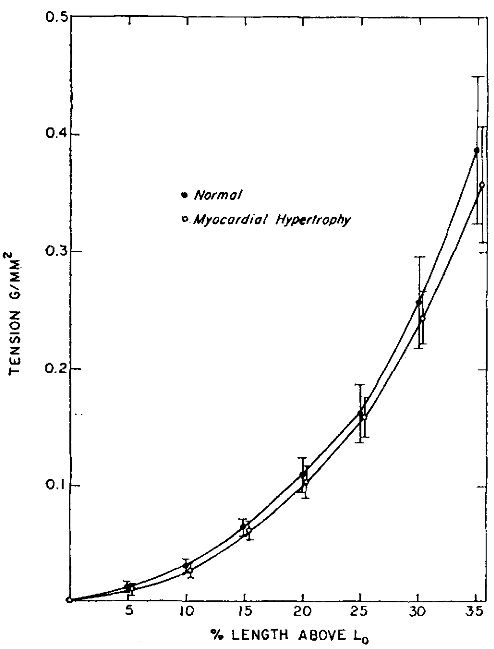

FIG. 3. Comparison of average length-resting tension curves (± S.E.) of the segments of normal myocardium, and of hypertrophied myocardium.

above L_O. No essential differences were observed between the two curves. The distensibility of the myocardium also was unaffected by aortic constriction *per se* since the resting tension of the ventricular strips obtained from 8 aortic constricted rats without hypertrophy was similar, averaging 0.12 ± 0.017 (S.E.) g/mm^2 and 0.39 ± 0.014 g/mm^2 at lengths exceeding L_O by 20% and 35%. These values are essentially identical to those observed in the ventricular strips removed from normal rats (Fig. 3).

Discussion. These results indicate that the resting length-tension curve of hypertrophied myocardium is quite similar to that of normal myocardium when corrections are made for differences in muscle mass and cross-sectional area. These findings are in agreement with the conclusions of Grimm *et al* that papillary muscles obtained from hypertrophied rat hearts had normal distensibilities(8). However, these authors did not study the hypertrophied ventricular wall itself.

Although the myocardial preparations utilized in this investigation were relatively thick, possibly interfering with the diffusion of oxygen and substrates, this factor would not appear to have affected the results since no changes in successive length-resting tension curves were observed. However, impairment of diffusion may have affected the contractile mechanism and therefore it was elected not to analyze quantitatively the length-active tension curves.

Meerson has described 3 stages of cardiac hypertrophy following aortic constriction, and has observed distinct biochemical and physiological differences between these states(15). The second stage, which commences 5-10 days after operation has been termed the stage of stable hyperfunction, and is characterized by hyperfunction of the organ as a whole due to an increase in muscle mass but without hyperfunction of the cellular elements. The animals in the present study were studied in this state and the finding of normal distensibility of the hypertrophied myocardium correlates with Meerson's view that the unit structure is qualitatively grossly normal despite an increase in mass. Although no obvious abnormality of one fundamental mechanical property of the hypertrophied myocardium was observed, these findings must not be interpreted to indicate that no biochemical or ultrastructural changes are present in hypertrophied tissue. Such changes do occur and are currently under investigation, but it appears that they do not affect the muscle's distensibility.

If the type of experimental hypertrophy utilized in this investigation is similar to that observed clinically, then it is likely that the marked decrease in the apparent distensibility of hypertrophied human ventricles(9-12) results primarily from an increase in muscle mass, rather than from a fundamental change in the properties of a given unit of tissue. Although the basic process of hypertrophy in the rat with aortic constriction may be similar to that occurring in patients with arterial hypertension, coarctation of the aorta and aortic stenosis, other factors such as the duration of the systolic overload and the presence of myocardial ischemia which might induce fibrosis could also influence the distensibility of the hypertrophied ventricle.

Summary. Length-resting tension curves were recorded from strips of left ventricle obtained from 10 rats with myocardial hypertrophy produced by subdiaphragmatic suprarenal aortic constriction, and 8 rats subjected to aortic constriction in which hypertrophy did not develop. No differences were noted between the distensibility of the normal and hypertrophied myocardium after corrections were made for differences in muscle mass and cross-sectional area.

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Effect of Estrogen and Progesterone on Mammary Gland DNA and Feed Intake in Hypophysectomized Female Rats.* (31086)

D. W. HAHN AND C. W. TURNER
(With technical assistance of Mary E. Powell)
Department of Dairy Husbandry, University of Missouri, Columbia

The determination of DNA has been used extensively in this laboratory as a quantitative index of mammary gland growth under normal and experimental conditions(1,2,3). It has been recognized for many years that hypophysectomy depresses lobule-alveolar growth in rats(4). Although the recent studies have established the fact that ovarian hormones fail to stimulate lobule-alveolar growth of the mammary gland in hypophysectomized rats(5,6,7,8), these studies had

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