phylactoid symptoms in the unsensitized animals. Whether the inherent toxic principle detected in two samples of house dust is responsible for non-specific positive cutaneous reactions in human subjects has not been determined. However, in associated clinical trials, house dust extract "E" has been found to possess skin whealing agents of unusual potency.

Specimen results appear in Table I.

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Aortic Pressure and the Diastolic Volume Law of Energy Output in Cardiac Contraction.

GORDON K. MOE, EARL H. WOOD AND MAURICE B. VISSCHER.

From the Department of Physiology, University of Minnesota, Minneapolis.

The conclusion of Starling and Visscher[1] that the oxygen consumption of the isolated heart under constant chemical and temperature conditions is determined solely by the initial length of its muscular fibers has been the subject of some disagreement. Stella[2] asserted that at constant initial fiber length, the energy output of the tortoise ventricle in contraction varied with the arterial resistance. It was shown, however, by Moldavsky and Visscher[3] that a systematic error in measurement of diastolic ventricular volume occurred in Stella's experimental procedure and that when this error was obviated by suitable means the energy output in contraction was found to depend only upon initial fiber length and was entirely unrelated to pressure or work conditions.

Kiese and Garan[4] have attacked this problem again with the mammalian heart-lung preparation. In a series of exact studies they have shown that the oxygen consumption of the heart is significantly greater when a diastolic ventricular volume increase is brought about by raising the inflow, and therefore the minute volume, at constant arterial pressure, than when the same diastolic volume is obtained by increasing the aortic pressure, keeping the inflow constant at a low level. Stated in numerical terms, they found in a typical experiment that in order to have identical oxygen consumptions the

1 Starling, E. H., and Visscher, M. B., *J. Physiol.*, 1927, **62**, 243.

2 Stella, G., *Ibid.*, 1931, **72**, 247.

3 Moldavsky, L. F., and Visscher, M. B., *J. Physiol.*, 1937, **91**, 23.

4 Kiese, M., and Garan, R. S., *Arch. f. Exp. Path. u. Pharmak.*, 1938, **188**, 226.

diastolic volume had to be about 5 cc greater when the arterial pressure was 200 mm of mercury, than when it was 100.

Kiese and Garan measured the ventricular volume with a Henderson cardiometer and did not take into account the obvious fact that the coronary vessels themselves, particularly the larger arteries on the surface of the heart, are elastic chambers and that the volume of blood within them depends upon the aortic pressure. Changes in the volume of blood in the coronary vessels influence the apparent volume of the ventricles but do not correspondingly change the length of the heart muscle fibers. In order to determine what rôle, if any, this factor plays in measurements of the external ventricular volume, it was necessary to have a quantitative measure of the volume of blood within these vessels at various perfusion pressures while the heart was beating. We have, therefore, made several hundred measurements on 6 separate hearts in which in effect the blood in the coronary system has been weighed. A cannula carried blood from a pressure reservoir to the brachiocephalic artery in which it was inserted. A length of 20 cm of thick-walled rubber tubing connected this cannula with a warming coil which was rigidly fixed, and through which the blood passed from the reservoir to the coronary system. The aorta was tied distal to the cannulated vessel. The heart was suspended by a rigid hook inserted in the musculature of the apex which was attached to the arm of a spring steel torsion lever. An extension of this lever, recording on a smoked drum, was used to record the changes in position of the torsion lever. By means of this device, the weight of the heart was continuously recorded. To permit free drainage of the coronary blood, the atrioventricular valves were cut and the venous blood was collected in a large funnel under the heart. The blood from the heart passed through an oxygenator and was pumped back mechanically to the reservoir. Hearts set up in this manner will beat spontaneously for periods up to 5 hours. In some experiments the heart rate was controlled by an artificial stimulating device. With each contraction of the heart, there is a swing of the lever which is sufficiently damped to come to rest during the diastolic pause. The torsion lever was calibrated by weights hung on the beating heart. The changes observed with alterations in perfusion pressure were found to be perfectly reversible. The sensitivity of the whole system was usually such that 10 g of added weight produced a lever deflection of 12 mm.

Fig. 1 presents the results of a typical experiment in which variations in perfusion pressure were made. It will be noted that the weight of the whole heart increases steadily as the perfusion pressure is raised. The effect is completely reversible, and in view of the con-

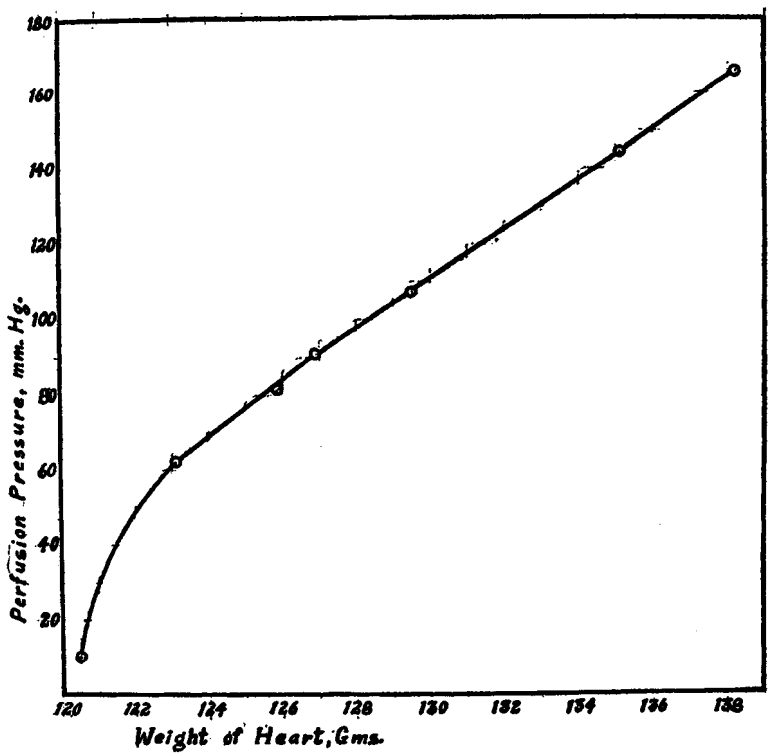

FIG. 1.

Effect of perfusion pressure upon the volume of blood contained in the coronary vessels.

ditions of the experiment it can be concluded that the change in weight is probably an exact measure of the change in the volume of blood within the coronary vessels under the several perfusion pressures. Comparable results were obtained in each one of the experiments.

In order to substantiate the conclusion that the weight change measurements are actually a reflection of volume changes within the coronary vessels, a known coronary constrictor drug was introduced. 1/10 cc of Parke-Davis Pitressin was introduced into the blood flowing into the coronaries which produced a decrease in weight of 4.7 g.

Further studies were made of the effect of rate changes, ventricular fibrillation and adrenaline injections. It was found that the coronary volume was less at higher heart rates and that it was considerably greater in the fibrillating heart. During the latter state, adrenaline still further increased the capacity of the coronary vessels.

It is of interest to employ these data in the interpretation of the findings of Kiese and Garan. The latter workers noted an unex-

pectedly small oxygen consumption at the higher aortic pressures. In the light of the present results, it will be obvious that this is exactly what might be predicted from the fact that the measured external diastolic volume is not a true measure of muscle fiber length when the coronary perfusion pressure is altered. The large coronary vessels on the surface of the heart stretch under the influence of internal pressure without any concomitant increase in fiber length. Likewise, in the case of arterioles, capillaries and veins, only those nearest the endocardium could cause muscle fiber extension comparable to their volume increase. As noted above, for a difference in perfusion pressure of 100 mm of mercury, Kiese and Garan found a disparity of about 3 to 5 cc in the diastolic ventricular volumes necessary to produce equal oxygen consumptions. Reducing our average results to hearts of the size used by the previous workers, we find that a rise in perfusion pressure of 100 mm of mercury increases the volume of blood within the coronary vessels by 8 cc. Since some of this increase in weight is due to blood within the walls of the heart, in which situation it would result in some increased fiber length, we interpret our observations to indicate that the discrepancies found by Kiese and Garan can be completely accounted for on the basis of the error introduced in external diastolic volume measurements by neglecting the volume of blood in the coronary vessels having little or no influence upon fiber length.

Conclusions. When very small changes in diastolic ventricular volume are measured one cannot disregard the coronary perfusion pressure as a factor in determining the volume of blood in the coronary vessels. Since the volume of blood in the superficial vessels has no influence upon the fiber length, and the quantity in the deeper vessels has a lesser influence than does the volume within the ventricles, it is obvious that corrections in the measured external diastolic ventricular volume must be made in order to compare energetic conditions at various perfusion pressures. The quantitative results obtained here are of the right order of magnitude to account completely for the small discrepancies found by Kiese and Garan in energy liberation at various aortic pressures. It is believed that the present results invalidate the conclusion that the aortic pressure is a determining factor in the energy liberation by heart muscle. The best evidence therefore indicates that the conditions of loading, other than those determining the initial fiber length, or diastolic ventricular volume, have no influence upon the energy liberated in cardiac contraction. This conclusion is most fully substantiated by the fact that in the tortoise ventricle, where there is no coronary system, the diastolic volume law obtains irrespective of the type of loading.