Negative Ventricular Diastolic Pressure in Beating Heart Studied *in vitro* and *in vivo*.* (22785)

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Since the classic studies of Harvey(1) it has been generally accepted that diastolic filling of the heart resulted from venous return and auricular contraction. While the senior author(2) was studying the effects of anoxia and work on the glycogen content of the rat heart, it was necessary to make observations on the excised heart beating in saline. With each systole it was observed that fluid ejection from the aorta resulted in the jet propulsion of the heart in the solution and it was obvious that the heart must draw in fluid in each diastole to make possible subsequent systolic ejection; thus it was concluded that part of systolic energy was dissipated in diastole(2).

This paper presents the results of a study of pressure changes in intact and excised heart during systole and diastole.

Materials and methods. White rats weighing 300 to 450 g were anesthetized with pentobarbital 6 mg/100 g. The thorax was rapidly opened and the intact heart removed. A 20 gauge needle was inserted into the left ventricle and the needle connected to a three-way stop cock on a Statham strain gauge so that opening the stop cock recorded hydrostatic zero. The heart was placed in a pottery pie plate filled with saline. The three limb leads of the EKG were placed equidistant around the perimeter of the plate with the electrodes immersed in solution. Pressures and EKG were recorded with an Oscillograph. When desired the auricles were opened widely or excised with a pair of scissors. *In vivo* studies were performed on dogs anesthetized with pentobarbital. Artificial respiration was administered through an intratracheal tube and the chest was widely opened. Umbilical tape was placed around the superior vena cava and azygos veins. In other instances tape was placed around the pulmonary veins. The venous return to right or left ventricle could thus be diminished by tightening the ligatures. A 19 gauge needle with multiple openings in the end was located in the left or right ventricle. The atmospheric zero pressure at the needle tip could be measured by opening stop cock to the air at needle level. The distance between the needle and the highest level of the ventricle was measured to determine the hydrostatic pressure of the column of blood above the needle. The high and low pressures were then charted (Figs. 2 and 3). Electrocardiograms and pressures were recorded on the same record-

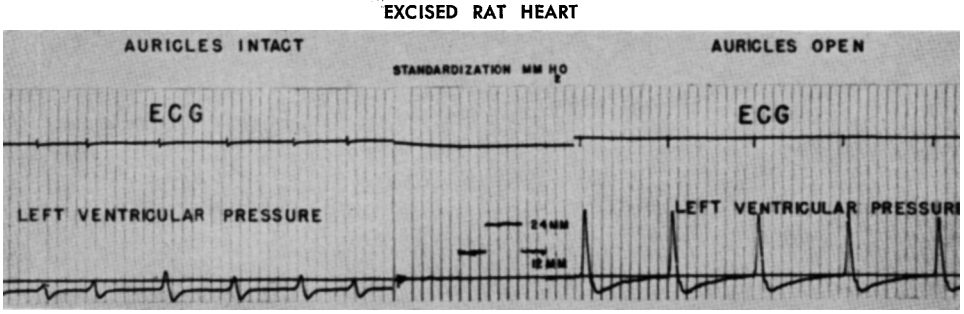

FIG. 1. Electrocardiogram and left ventricular pressure tracing on the excised beating rat heart. The continuous line in the pressure readings indicates hydrostatic zero.

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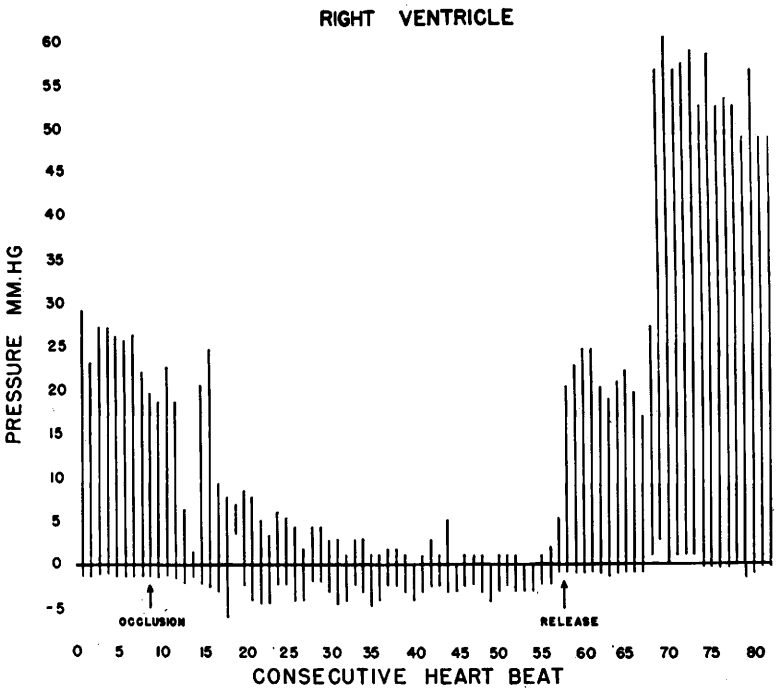

FIG. 2. Highest systolic and lowest diastolic pressure recorded from the right ventricle of the open chest dog. Pressures recorded in respect to atmospheric zero corrected for the hydrostatic column of blood above the needle. Occlusion produced by clamping superior and inferior vena cavae.

ing apparatus used in the rat studies.

Results. Simultaneous electrocardiogram and intraventricular pressure tracings of the excised, beating rat heart suspended in saline are presented in Fig. 1, first with the auricles intact and then with the auricles excised. With the auricles intact the intraventricular pressures were continuously negative, rising toward zero in systole and becoming more negative in diastole. There was no positive intraventricular pressure because there was no filling since the thin walled auricles were collapsed and fluid cannot be drawn through such a freely collapsible structure. With the auricles excised the systolic pressure in the ventricle was positive and the diastolic pressure in the ventricle slightly negative. In this preparation the maximum positive pressure during systole was similar to the maximum negative pressure in diastole with the inflow obstructed. It may be seen that the heart rate slows and the P waves of the EKG disappear when the auricles are excised.

Diastolic pressures recorded in the right ventricle of the intact dog's heart in the open chest were slightly negative and were found to become progressively more negative (–5.0 mm Hg) as the inflow (superior and inferior vena cava, coronary sinus and azygous veins) was occluded (Fig. 2). The systolic pressures also fell (from 27 mm to 2 mm) during this procedure. During each systole a positive pressure developed indicating that venous return was only partially occluded (Fig. 1). Other studies have shown that with further impairment of venous return systolic pressure was further reduced and the shape of the tracings approached that of the excised heart with intact auricles. Following release of venous occlusion the pressures in the right ventricle returned temporarily to pre-occlusion levels.

Left ventricular diastolic pressure was usually 1 to 3 mm Hg below atmospheric pressure (Fig. 3). Diminution of venous return by pulmonary venous occlusion resulted in more negative intraventricular pressures (–15 mm Hg). In other studies pressures as

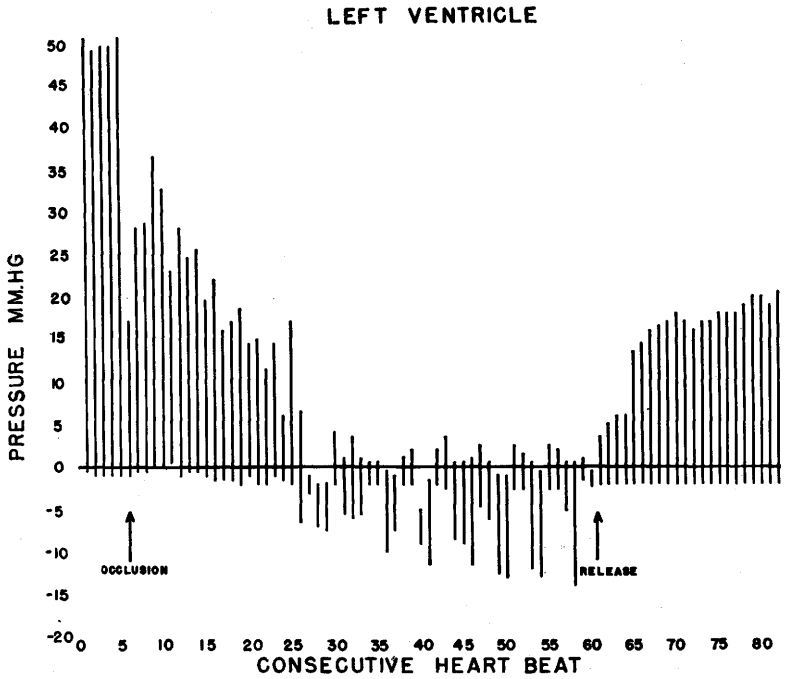

FIG. 3. Highest systolic and lowest diastolic pressure recorded from the left ventricle of the open chest dog. Pressures recorded in respect to atmospheric zero corrected for the hydrostatic column of blood above the needle. Occlusion produced by clamping pulmonary veins.

low as –25 mm Hg have been observed. Systolic pressures also fell (from 50 mm to 3 mm) following impairment of venous return to the ventricle. Following release of venous occlusion the pressures in the left ventricle returned toward normal (from 3 mm to 25 mm) and the diastolic pressures remained negative (–2 mm).

Discussion. The persistence of negative intraventricular pressure during both phases of the cardiac cycle in the excised heart with auricles intact indicated that after the heart empties inflow was impeded by the auricles and fluid cannot be drawn into the ventricles. This results in a continued negative pressure with systole only increasing pressure to zero as a result of contraction. Opening the auricles allows fluid to be drawn through the mitral valve producing a temporary negative diastolic pressure and filling of the ventricle. Systolic contraction of the filled ventricle resulted in a positive intraventricular pressure and systolic ejection of fluid. These pressure changes confirm the observation that the excised heart was capable of drawing fluid into the ventricles during diastole.

The pressure changes in the intact heart of the open chest dog indicated that the *in vitro* findings apply in the intact circulation. The diastolic negative pressures which develop during obstruction of venous return indicated that part of the energy of systole was dissipated during diastole. The left ventricle produced more negative pressures than the right ventricle which might be explained by the differences of thickness and elasticity in the ventricular walls. The slight negativity of pressure in the heart with normal venous return does not indicate absence of a force drawing fluid into the ventricle, but showed that the venous pool was adequate to satisfy the filling force.

The findings suggest that the heart functions as a pump, drawing fluid in during diastole and ejecting fluid in septole. The early rapid diastolic filling observed during cineangiocardiography(3) can be explained by these observations and a mechanism is provided to explain the fact that ventricular volume increases in diastole

when intraventricular pressure decreases(4). Although the concept of the heart drawing fluid in during diastole is old(5,6,7) the magnitude of the negative pressure which can build up in diastole indicates that this mechanism is more important in cardiac filling than has been considered in the past.

We wish to thank Dr. Noble O. Fowler and Dr. E. Ronald Duschesne for their assistance.

Following the preparation of this paper, a communication with Dr. Gerhard Brecher of Department of Physiology, University of Ohio indicates that he has also obtained negative intraventricular pressures in the dog.

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Effect of Steroid Administration on Excretion of α-Ketolic Steroids and Sulfur in Cats. (22786)

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In the course of treating cats with 9α-fluorohydrocortisone and Δ^1-cortisone (prednisone), the changes in the chromatographic pattern of urinary steroids were measured. Two principal changes from the normal were encountered. (a) The α-ketols which were excreted increased only slightly, but there were changes in the proportions of several steroid metabolites. (b) It was unexpectedly found that elemental sulfur was present in large amounts in the chloroform extracts of these urines and that this interfered with the determination of α-ketols by the blue tetrazolium (B.T.) method, since elemental sulfur was found to give a positive B.T. reaction. After the separation of sulfur and steroids a significant increase in the urinary excretion of sulfur-containing compounds during steroid treatment was observed.

Methods. 9α-Fluorohydrocortisone and Δ^1-cortisone were administered subcutaneously in daily doses of 10 and 50 mg respectively.† The animals were fed diets of fresh meat which were constant during control and treatment periods. After 5 days or more of treatment, all urine was collected for 4 to 7 day periods and pooled. The pooled urine was then incubated with β-glucuronidase at pH 4.5 for 48 hours, extracted with chloroform at pH 1.0, and the chloroform extract washed briefly with 0.1 N NaOH and water. The B.T.-reacting materials were measured as described by Touchstone and Hsu(1). After the determination of total B.T.-reacting substances the remainder of the extract was subjected to paper chromatography.

Results. Fig. 1 shows three representative chromatograms. It appears that the principal metabolites in the normal cat occur in the region where H_4B, allo-H_4B, H_4A and H_4DOC appear (see legend for key to abbreviations). During the administration of 9α-fluorohydrocortisone and Δ^1-cortisone peaks can be found in the regions of H_4F, H_4E, B, A, and H_4DOC. Δ^1-Cortisone also caused excretion of three metabolites which were not found during administration of 9α-fluorohydrocortisone, and it seems that a large portion

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