Systolic and Diastolic Pressure Relationships in the Isolated Rat Heart

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This report deals with variations in intraventricular pressure in the excised, beating rat heart. A negative early diastolic pressure developed, the magnitude of which correlated with the vigor of contraction.

In 1956, Bloom observed that the excised beating rat heart with atria removed was capable of filling and emptying itself repeatedly and was able to propel itself in liquid. Somewhat later, Bloom and Ferris showed that there develops during systole a positive pressure in the left ventricle of the excised heart beating in liquid and that there is produced a negative intraventricular pressure during diastolic filling by suction. They also demonstrated strong negative pressures in the intact dogs' ventricles when inflow was impeded. In the same year, Brecher showed that upon temporary occlusion of the mitral orifice, negative intraventricular diastolic pressure of 13 to 108 mm. of water develops. Brecher concluded that the mammalian ventricle was capable of sucking blood into its cavity during diastole. He avoided the implication that the normally filled ventricle without obstruction to inflow exerted a negative diastolic pressure or suction effect in the intact animal. Kraner and Ogden also found that the turtle ventricle exerts diastolic suction.

In the course of our observations upon systolic and diastolic pressures in the excised beating heart it appeared that, in general, high systolic pressures were associated with more negative diastolic pressures and that if systolic pressures were weakened, either because of irregularity of cardiac action or by spontaneous decay, the diastolic pressures tended to diminish in negativity. Conversely, it appeared that when the systolic pressure in the excised heart was increased by sympathomimetic drugs, there tended to be an increase in diastolic negativity. The purpose of the present study is to observe systolic-diastolic pressure relationships in the isolated beating heart of the rat under three circumstances: (1) spontaneous deterioration of the excised beating heart, (2) weakening of systole because of alternans of the heart or because of prematurity of systolic contraction, (3) increase of systolic pressure by means of drugs having cardiac effect such as epinephrine or norepinephrine.

METHODS

Thirty-three white rats of the Sprague-Dawley strain were anesthetized with intraperitoneal Nembutal, 6 mg./100 Gm. The beating heart was quickly cut free of the great vessels and placed in a shallow open dish containing 500 ml. of lactate-Ringer solution at room temperature. Left ventricular pressures were recorded through a no. 19 hypodermic needle inserted into the left ventricular cavity. The fact that the left ventricle was impaled upon the needle prevented motion of the heart in the bath. Zero pressure levels were obtained by means of a three-way stopcock connected to the hypodermic needle and strain gage. The stopcock lay at the same level below the surface of the bath as did the needle tip within the heart; thus zero reference could be obtained by turning the stopcock so as to expose the gage to the hydrostatic bath pressure at this level. After the beating heart was excised and placed inside the bath, a period of approximately 15 to 60 sec. was required for balancing the strain gage and observing the pressure tracing on the oscilloscopic screen. The Statham transducer was carefully balanced and calibrated before and after each pressure record. The tracing was carefully checked for electrical drift.

In the drug studies, after a control record, 5 γ of epinephrine or 1-norepinephrine were introduced into the bath near the heart so that the drug could be aspirated into the heart by the force of diastole. Cardiac pressure was recorded continuously at this
time and the moment of drug introduction was indicated by a marker. The pressure record was continued until the drug effect began to subside. After this the gage was balanced and calibrated and the needle was checked for patency. Observations of drug effect upon systolic and diastolic pressures were made in 16 hearts.

The effect of deterioration of cardiac contractile force upon systolic-diastolic pressure relationships was observed in 16 hearts. The pressures were observed upon the oscilloscopic screen continuously and records were taken intermittently as the systolic pressure fell over a period of 5 to 10 min.

In 17 hearts observations were made of pressure records for the development of alternans of ventricular contraction. Alternans not infrequently developed in the isolated beating heart as ventricular force weakened. Observations were made also of irregularity of cardiac contraction due to premature beats or varying atrioventricular block. These observations were made on 17 rat hearts in which drug effects were not tested.

In comparing the relationships between systole and diastole, measurements were made of peak pressure deviations from the base line. The possibility of comparing systolic and diastolic relationships by means of analyzing the area of the ventricular pulse wave was seriously considered. However, this was not done because of the small area which would limit the accuracy of the measurements and because of the fact that agreement could not be reached upon which aspect of the systolic or diastolic area should be considered.

**RESULTS**

**Decay Records with Deterioration of Strength of Ventricular Contraction.** Although studies were made of this situation in 16 hearts, records were satisfactory for comparison of systolic and diastolic pressures in only 7 hearts. In the other nine, the negative pressure developed in diastole was not great enough to allow accurate measurement. Since the amount of negative pressure in diastole depends in part upon the amount of obstruction of inflow at the mitral orifice it may be that the obstruction to inflow was less in these hearts. Since the amount of pressure depends also on speed of diastolic filling it may be that the speed of filling was slower in these hearts, resulting from either alteration of elasticity of the ventricular muscle or alteration in the metabolism of the ventricular muscle. Presumably the volume of diastolic filling was not a factor since these hearts pumped the customary volume of liquid in systole and therefore must have been filling in diastole. In the 7 hearts in which satisfactory decay records were obtained, a comparison of systolic and diastolic relationships was made by plotting systolic pressure during each period against diastolic pressure over the 5 to 10 min. period of observation. A regression coefficient was calculated for each. In each instance, the association between systolic and diastolic pressure was highly significant ($p < 0.001$). Figure 1 shows excerpts of the decay curves of 1 heart.

The paper speed was 5 mm./sec. The relationship between systolic and diastolic pressures is shown during 5 different periods of observation as the force of systolic contraction gradually weakened. In the section to the extreme left, systolic pressures were 22 mm. of water; negative diastolic pressures were approximately 7 mm. water. In the second section, systolic pressures were 14 mm. of water and diastolic pressures were 4 mm. of water; in the third section systolic pressures were 12 mm. of water and diastolic pressures were 3.5 mm. of water; in the fourth section, systolic pressures were 7 mm. of water and diastolic pressures were 2 mm. of water. In the fifth section, sensitivity was increased. Systolic pressures were 6 mm. of water and diastolic pressures were 1.5 mm. of water.

Because of the previously discussed variation from heart to heart in the amount of diastolic negative pressure developed, no attempt was made to compare systolic and diastolic pressures in the group as a whole. Comparisons were thus limited to the individual hearts.

**Effect of Epinephrine and L-Norepinephrine Upon Systolic-Diastolic Pressure Relationships.** These observations were made in 16 hearts. In no instance was an increase in systolic pressure observed with a decrease in negative diastolic pressure. In no instance was an increase in one with a decrease in the other seen. A regression
of the change in diastolic pressure on change in systolic pressure in millimeters of water for each drug study was calculated in the 16 hearts. The results, $b = 0.2377, sb = 0.075, p < 0.01$, indicated a significant relation between change in diastolic and systolic pressure under these circumstances. The regression of per cent change in diastolic pressure on per cent change in systolic pressure was also calculated. The results, $b = 0.72; sb = 0.185, p < 0.01$, also indicated a significant regression of diastolic pressure change on systolic pressure change under these circumstances. Relation between diastolic and systolic pressure was, however, by no means linear. The variability of the hearts with regard to degree of obstruction to inflow of fluid produced a wide range of systolic and diastolic pressure relationships in the control period. Thus, no attempt was made to compare systolic and diastolic pressures in different hearts in this portion of the study.

In almost every instance, the appearance of alternans of ventricular contraction or of prematurity of ventricular contraction resulting in a weak beat was followed by a lowering of the negative pressure in the succeeding diastolic interval. Examples of this are shown in figures 2 and 3. Figure 2 shows excerpts of records from 2 hearts. On the left is shown an excerpt from the record of heart number 4, recorded at a paper speed of 25 mm./sec. In this heart, alternans of the ventricle developed. It may be seen from the record that the strong beats of ventricular contraction developed a pressure of about 25 mm. of water and a peak negative diastolic pressure of about 8 mm. water. The weak ventricular beats developed a pressure of approximately 5 mm. of water in systole and a negative pressure of about 1 or 2 mm. of water in diastole. On the right in figure 2 is shown an excerpt from the record of heart no. 6 recorded at a paper speed of 25 mm./sec. It may be seen here that irregularity of ventricular contraction was present. It is of interest to note again that the premature beats have a lower systolic pressure and less diastolic negative pressure. It is also of interest to note in this preparation that during long diastolic pauses pressure returned to the zero base line before systole. When there was a premature beat, however, diastolic pressure was still negative at the time of the premature beat, implying that complete filling of the ventricle had not occurred. In contrast, in the example of alternans shown to the left in figure 2, the time allowed for diastolic filling between weak and strong beats was the same. Another example of alternans of the ventricle is shown in figure 3. In this figure, the pressure pulses from the left ventricle are recorded at a paper speed of 75 mm./sec. It may be seen that the systolic pressure of the strong beats was followed by a more negative diastolic pressure than in the weak beats. Following the weak beats, the diastolic pressure is definitely lower both in peak pressure and in area than is the diastolic pressure wave following the strong systolic contractions.

SUMMARY

Systolic-diastolic pressure relationships in the left ventricle of the excised beating rat heart were studied under three circumstances: (1) spontaneous weakening of contraction; (2) ventricular alternans; (3) during increase of systolic pressure resulting from epinephrine and l-norepinephrine. A significant relation between positive systolic and negative diastolic pressure was found under these circumstances. The observations are consistent with the concept that
negative pressure change due to elastic diastolic recoil is inversely proportional to the ventricular volume following the preceding systole.

**SUMMARIO IN INTERLINGUA**

Le relationes pression systolo-diastolic in le ventriculo sinistre del excidite corde de ratto esseva studiate sub tres conditiones: (1) Attenuation spontanea del contraction, (2) pulso alternante ventricular, e (3) augmento del pression systolic effectuate per epinephrina e l-norepinephrina. Un significative relation inter positive pression systolic e negative pression diastolic esseva trovate sub iste conditiones. Le observationes esseva compatibile con le conception que un negative alteration del pression debite al elastic resalto diastolic es inversemente proportional al volumine ventricular post le precedente systole.

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