Shrinkage of the Heart in Anesthetized, Thoracotomized Dogs

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Changes in heart size have been studied by means of intraventricular gages, serial roentgenography and cinefluorographic angiocardiography. Evidence is presented that the area of the cardiac silhouette and the area and diameter of the left ventricle all diminish in response to thoracotomy and during recovery return toward the pre-operative dimensions. Since fundamental concepts of cardiac function and control are based largely on investigation of exposed hearts, these concepts must be re-examined in intact, unanesthetized animals and man.

Little is known concerning changes in the absolute volume or linear dimensions of the individual ventricular chambers in intact, unanesthetized animals or man. Since the fundamental concepts of cardiac function and control are based principally on controlled experiments on anesthetized, thoracotomized animals, their application to man implies that cardiac function is essentially identical under the two conditions. For this reason, the response of the heart to anesthesia and thoracotomy assumes great importance in evaluating many basic concepts as applied to intact animals and man.

METHODS

Continuous measurements of the left ventricular diameter during recovery from operative procedures were obtained from variable inductance gages by methods described in a previous report. In the course of these experiments, serial roentgenograms were obtained before anesthesia, after anesthesia, after thoracotomy, immediately after surgical repair of the thoracotomy wound, and a few days after operation in 14 animals. The complete series was obtained in five animals and three or more roentgenograms in the remainder. The area of the cardiac silhouette on each roentgenogram was measured by a polar planimeter. No special efforts were directed toward making the exposure in either systole or diastole and it was impossible to distinguish the individual chambers of the heart. For this reason, a series of experiments was performed using cinefluorographic angiocardiography.

Preliminary experiments indicated that in dogs of 8 to 10 Kg., 50 cc. of Thorotrast, injected intravenously, rendered the blood relatively opaque to x-rays for periods up to 30 minutes. Significant changes in the area of the cardiac silhouette after the Thorotrast had been injected could not be demonstrated on serial cinefluorograms taken at frequent intervals over a period of 30 minutes in three animals. In each of nine animals, a series of cinefluorograms were taken under the following conditions: (a) while lying quietly in the left lateral position as a control, (b) after injection of 50 cc. of Thorotrast, (c) after surgical anesthesia had been induced with Nembutal, (d) after thoracotomy (either midsternal or through the right fourth intercostal space) with intratracheal artificial respiration, and (e) with a cardiometer in place in three of the animals. The rubber membrane which acted as a seal between the cardiometer and the atrioventricular groove was purposely made very loose to avoid constriction of the valve rings. Tracings of the cardiac silhouette and of the left ventricular chamber were made from 10 successive frames on the film, which included both diastole and systole in five experiments. In the remainder, the frames which contained extremes of diastolic and systolic excursions were selected by inspection. The projected area of the total cardiac silhouette (including atria) and the area of the left ventricular chamber were measured by means of a polar planimeter. Since the area of the right ventricular cavity could not be consistently traced with accuracy from these films for reasons which have been previously discussed, they are not included in this report.

In three additional experiments on two dogs, a similar sequence was followed except that, in lieu of thoracotomy, cinefluorograms were obtained (a) during pressure breathing (12 cm. water pressure), (b) after 200 cc. of air had been injected into the

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right pleural space, and (c) after withdrawal of as much of this air as possible (about 180 cc).

Since control of heart rate by atrial stimulation has been frequently employed in studies on exposed hearts, two experiments on a single dog from another series are included in this report. In this animal, two small metal markers, connected by resilient elastic, were installed on the epicardial and endocardial surface of the left ventricular wall by methods which have been previously described.4 Another pair of markers was installed on opposite sides of the interventricular septum. A polyethylene catheter was sutured to the external wall of the left atrium near the base of the atrial appendage, and was passed through the thoracic wall, with the external end of the catheter lying just beneath the skin. After complete recovery of the animal, cinefluorographic films were taken and the left ventricular diameter was measured on successive frames, enlarged eight times normal size. Ventricular depolarization was indicated by vectorcardiograms appearing in the corner of each frame of the film and by simultaneously-recorded electrocardiograms. A pair of wires was inserted through the catheter until they contacted the wall of the left atrium. Using an Electrodyne stimulator, the heart rate was controlled during cinefluorography while the dog was lying quietly on the table under light Pentothal anesthesia.

**Results**

Records of the left ventricular diameter obtained from variable inductance gages within the chamber characteristically consisted of small rounded deflections coincident with the QRS complex (fig. 1A, B, C). Such records indicated that the stylus remained pressed within the coil during all phases of the cardiac cycle except for the maximum expansion of this dimension at the transition between diastole and systole.1 Within 24 hours the diameter of the left ventricle expanded until both the systolic and diastolic dimensions were within the recording range of the gage. (In one dog this process required five days.) Thereafter

**Fig. 1.** (A, B, C) Changes in left ventricular diameter recorded from variable inductance gages installed within the cavity immediately after the operation and after recovery. Under some circumstances, such as sleeping, the left ventricular diameter spontaneously diminished to very low levels (D) but this was exceptional. (E) Intravenous administration of Nembutal produced a prompt reduction in both left ventricular diameter and intraventricular pressures and shortly thereafter, the animal expired.
the full pattern of the changing left ventricular diameter could be recorded for as long as 26 days (fig. 1A). If the left ventricular diameter had ever exceeded the combined length of the coil and stylus during that time, the stylus would have come out of the coil and recording would have ceased. On several occasions, the left ventricular diameter diminished markedly when the animal was completely relaxed and appeared to be sleeping (fig. 1D). In three animals, Nembutal was administered in the same dose as had previously been used for surgical anesthesia. In each case, the left ventricular diameter diminished promptly, the deflections disappeared completely and, shortly thereafter, the animal expired. In one animal, both the diameter and intraventricular pressure were recorded during this procedure (fig. 1E). A progressive drop in both systolic and diastolic pressure accompanied the reduction in left ventricular diameter. Note that systolic elevations of intraventricular pressure persisted even after the left ventricular diameter dropped below recording range of the gage (below 24 mm.). The apparent increase in the sensitivity of the animals to the administration of Nembutal is difficult to explain.

Roentgenograms taken before, during and after aseptic surgical operations on the hearts of 14 dogs provided evidence that the area of the cardiac silhouette diminished significantly during thoracotomy in every instance and, on the first postoperative day, approximated the control level. The average reduction in area was from 52 sq. cm. to 46.8 sq. cm. In some of the animals, the heart was even smaller just after completion of the operation: that is, when the lungs were re-expanded and the thoracic incision was closed. Since the measured areas included both ventricles and both atria, a more direct evaluation of the changes in the left ventricular size was considered essential.

Cinefluorographic films were traced and measured as indicated in figure 2. This experiment was performed on a dog which had been previously trained to lie recumbent during venapunctures for other experiments. The cardiac silhouette and the outline of the left ventricular chamber are indicated both in diastole and systole after injection of Thorotrast but before anesthesia (fig. 2A), after thoracotomy (fig. 2B), and after application of a radiolucent cardiometer (fig. 2C). The reduction in area of the heart and of the left ventricle are clearly visible (compare fig. 2A with fig. 2B). The shape of the heart was significantly altered when it was within the cardiometer in each of the experiments. Note that the left ventricular area diminished while the cardiac silhouette became slightly larger in the cardiometer, indicating that the right ventricle had become somewhat more distended. The apparent area of the left ventricle is probably misleading in figures 2B and 2C because the chamber was poorly outlined. Indeed, the projected frames seemed to show only very small quantities of opaque blood distributed in

Fig. 2. (A) Changes in the projected area of the cardiac silhouette and of the left ventricular chamber were measured from tracings of individual frames of cinefluorographic films during angiocardiography with Thorotrast. Changes in size and shape of these shadows during thoracotomy and cardiometry are illustrated in B and C respectively. (D) Planimetric measurements of the areas indicated on the tracings reveal a marked reduction in the area of both the cardiac silhouette and the left ventricular chamber in the thoracotomized animal. The shape of the cardiac silhouette was altered during cardiometry but the projected area remained about the same.
relatively narrow interstices between papillary muscles and heart wall. In other words, the left ventricle appeared virtually empty during each systolic ejection when the animal had been thoracotomized and when a cardiometer was applied.

Numerical values for the area of the cardiac silhouette and the left ventricular chamber are plotted in figure 2D. Similar data from five other animals are indicated in figure 3. The response to anesthesia was quite variable, but in every thoracotomized dog the area of the cardiac silhouette and the left ventricular chamber was significantly reduced, with one exception. In one animal, the size of the cardiac silhouette altered only slightly during these procedures (fig. 3D, lower record). Changes in the area of the left ventricle are not presented because the left ventricular chamber was not clearly outlined in this case and only fragmentary data could be obtained. In a number of experiments, the difference between diastolic and systolic areas was reduced. This is attributed to changes in heart rate. In our experience, anesthetized dogs generally have faster rates than unanesthetized dogs.

In three experiments, on two dogs, pressure breathing produced a slight increase in the projected area of the heart while pneumothorax produced little or no reduction in size. These preliminary experiments were not sufficiently informative to stimulate further investigation.

Controlling the heart rate by external stimulation of the left atrium affected the left ventricular diameter measured on cinefluorographic films, as indicated in figure 4. The diameter of the left ventricular chamber, and this diameter plus the thickness of the free wall, were both measured on each frame (fig. 4). The data were corrected for magnification so that the numerical values represent actual left ventricular dimensions. In the first experiment, cyclic changes in the left ventricular diameter were recorded during a control period. At the vertical arrow, left atrial stimulation was initiated at a rate faster than the control rate. In the first cycle, ventricular excitation occurred before there were any signs of diastolic increase in diameter. Following this abortive systole, the next diastolic interval revealed very rapid filling. The diastolic expansion and systolic reduction in diameter were very slight during alternate cycles for several beats. Gradually, this alternation disappeared so that at the end of the period of stimulation, the excursions were almost equal on successive cycles. Cessation of stimulation was associated with a prolonged diastolic interval and a marked increase in diastolic diameter followed by a few cycles with slightly shorter cycle lengths. Fifteen minutes later the same experiment was performed with similar results, but in this case termination of atrial stimulation was followed by coupled ventricular premature contractions which had little or no effect on the expanding diameter between normal complexes.

These experiments were initiated to explore the possibility of controlling the heart rate in intact, unanesthetized dogs, to stabilize this variable in studies on ventricular dimensions. Although it is quite possible that stimulation continued for longer periods would result in the disappearance of variation in the extent of diastolic expansion of this dimension, the fact...
that atrial stimulation can produce such changes may imply that cardiac response had been altered in some unknown way. Since the alterations in patterns produced during and after atrial stimulation could conceivably result from direct stimulation of receptors located in the atrial wall, this technic was abandoned. It is unwise to control variables by technics which may influence the basic function of the organ being studied.

**Discussion**

Two steps are required for the elucidation of the function and control of any organ system. In the first step, the characteristics of the system are investigated under rigidly controlled experiments so that the effects of each variable can be studied individually. Of necessity this involves inducing abnormal conditions in the experiments, because changes in a single variable rarely occur normally. Further, the technics for altering the variables are generally abnormal to some extent. From such investigations, the functional capabilities of the organ can be determined and the basic principles of its activity and control can be established.

The next crucial step involves direct measurement of these variables in intact animals and man to confirm the principles under "normal" conditions.

Cardiometer measurements on animals under surgical anesthesia with the thorax open have strongly influenced concepts of cardiac function and control, but they cannot be obtained under "normal" conditions. Evidence has been presented in this report that the heart becomes significantly smaller than normal in anesthetized, thoracotomized dogs. If the heart were already reduced in its dimensions at the beginning of cardiometer experiments, distension might be the only manner in which ventricular size is likely to change in response to an experimentally induced load. Considerable evidence has accumulated which indicates that relatively large volumes of residual blood remain in the ventricular chambers at the end of systole in intact animals3, 4 and in man.3, 6, 7

Cardiometry involves additional sources of error. The records indicate changes in the combined volume of right and left ventricles so that alterations in the baseline may represent variations in either chamber, or both. Functionally, anatomically, and architecturally, the right and left ventricles are very different and cannot be assumed to respond equally to any
specific change in conditions. Unless records are obtained with both ventricles completely emptied at some point during the experiments, the total quantity of blood in the ventricles cannot be assessed. During isometric contraction and isometric relaxation, the heart tends to move in and out of the cardiometer, producing uncontrollable artefacts during these phases in the cardiac cycle.

Anesthesia unquestionably alters the neural controlling mechanisms which may have important roles under "normal" conditions. Indeed, it is extremely doubtful if an accurate picture of cardiac function and control can be derived from experiments on anesthetized animals. The neural and hormonal mechanisms regulating ventricular capacity must ultimately be studied by directly measuring the size of the individual ventricular chambers in intact, unanesthetized animals and man using techniques which have minimal effects on cardiac function. Accomplishing this objective may prove exceedingly difficult, but it is of extreme importance, since the greatest advances in medical research come from direct measurement of those variables which elucidate function and control of the various organ systems.

Conclusions

1. Changes in the dimensions of the heart during and following thoracotomy have been measured by three techniques: (a) variable inductance gages continuously recording the diameter of the left ventricular cavity, (b) serial roentgenograms, and (c) cinefluorographic angiocardiography.

2. Data from these experiments consistently indicated a marked reduction in the size of the cardiac silhouette and of the left ventricle during and immediately after thoracotomy followed by re-expansion of the heart to approximate the preoperative size during a few hours or a few days after operation.

3. The left ventricle appeared to empty almost completely during systole when the thorax is open, although considerable residual blood is believed to be present in intact animals and man.

4. Controlling heart rate by external stimulation of the atra may affect basic cardiac function by producing changes in the filling and emptying patterns during the cardiac cycle.

5. Since several basic concepts of cardiac function and control are based on cardiometry performed on exposed hearts, these theories must be confirmed under more nearly "normal" conditions.

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