Distensibility and Water Content of Heart Muscle Before and After Injury

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WHEN we studied physiologic changes associated with overdistention of the left ventricle, the heart muscle appeared stiffer at the end of an experiment than at the beginning. We therefore arranged the procedure reported here in which the left ventricle was distended in a controlled manner at the beginning of the experimental period and at varying times thereafter while subjected to different hemodynamic conditions between observations. The data show that excessive stretch and other injury caused the left ventricle to become less distensible; injury also increased the water content of the myocardium.

Methods

Details of the experimental method and procedure have been described elsewhere.[1] Briefly, the systemic circulation was supported by a heart-lung machine; both atria were drained into the venous reservoir of the machine so that the left ventricle was virtually bloodless. The left ventricular pressure was registered through a semirigid polyethylene tube with the tip in the left ventricular cavity (Statham strain gage P23G) and was recorded at paper speeds of 1 mm./sec. and 50 mm./sec. About 90 minutes elapsed between the anesthesia of an animal and the first experimental observation.

A balloon was inserted into the left ventricle through a purse-string controlled stab wound at the apex. The balloon communicated with a 3-way stopcock and a syringe, so that known volumes of air could be injected into it. Before each standard observation of distensibility, the balloon was emptied and the systemic arterial flow (heart-lung machine) was set at a constant, known value. The syringe was then filled with a known volume of air at atmospheric pressure, which was rapidly injected into the balloon. Immediately after inflating the balloon, the contractions of the left ventricle became irregular and abnormal. However, it returned to a steady state and a coordinated, regular beat within minutes after distention (fig. 1). The data reported here refer to observations made during this steady state. Between observations, the left ventricle was inflated with volumes of air for periods of time which differed in each experiment; the systemic arterial pressure was raised or lowered by altering the flow of the heart-lung machine. Ventricular fibrillation developed in the instances indicated in table 1 and was terminated by electrical countershock.

The water content of "normal" hearts was measured on transmural samples from the left ventricle of donor dogs which had been rapidly exsanguinated under sodium pentobarbital anesthesia (control method "A"). Samples were also taken from the hearts of open-chest dogs in which the circulation had been carried on a heart-lung machine for 75 to 90 minutes, but which had not suffered other experimental interference (control method "B"). Similar samples of heart muscle were taken at the end of the distention experiments. They were blotted with gauze, placed in a glass dish, and weighed. The sample tissue was then minced with scissors and dried at 110 C. to constant weight.

Results

The left ventricle was distended with equal volumes of air at the beginning of an experiment when it had not been subjected to interference or handling (fig. 1) and at later stages of the same experiment (fig. 2). During the standard left ventricular distention, the systemic blood flow was the same in each dog; the heart rates, systemic arterial pressures, and left ventricular systolic pressures either did not vary significantly or showed no consistent directional variation (table 1). The data showed a significant increase of the diastolic pressure in the left ventricle when the standard observation was repeated after intervening periods of experimental interference.

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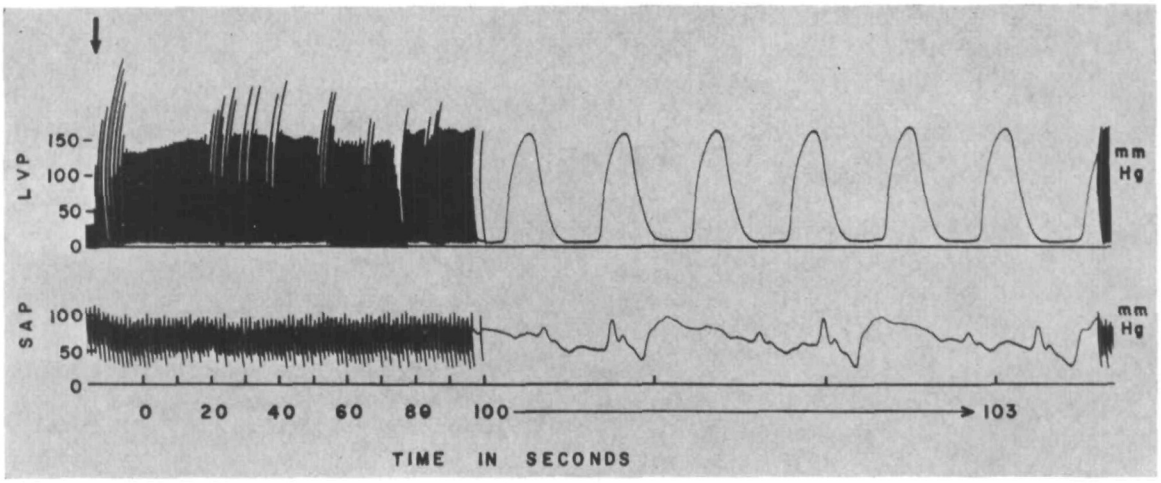

Figure 1

Balloon inflated with 35 ml. of air at arrow in left ventricle of dog (weight 10.9 Kg.). LVP = left ventricular pressure; SAP = systemic arterial pressure. Shape of SAP curve determined by characteristics of "Davol" pump. Note absence of LV ejection peaks in SAP tracing.

The heart muscle exhibited a stiffer consistency after injury; small hemorrhagic foci were often noted in scattered areas of the muscle. In some instances, the epicardial surface of hearts which were still beating in situ was covered with drops of clear liquid resembling beads of perspiration. These phenomena suggested edema of the myocardium and required the measurement of the water content of injured, as compared with normal, heart muscle. From the data in table 2 it is evident that the water content of left ventricular muscle taken from injured hearts was significantly increased ($p < 0.01$) when compared with the water content of either set of control specimens.

Discussion

There is now good evidence for changes of myocardial distensibility which can be induced by drugs or by "acute failure."[3-5] In these experiments on isolated hearts, "failure" was produced by elevating the aortic resistance and, presumably, the left ventricular systolic pressure to a level of 135 to 170 mm. Hg for 15 to 20 minutes, after which it was returned to the control value (70 to 90 mm. Hg). "Failure" of the ventricle was characterized not only by its decreased distensibility, but also by reduced work, rate of contraction, and rate of relaxation. Buckley and Zeig[4] suggest that the temporary elevation of aortic resistance to such relatively low levels might have caused structural damage or ischemia of the heart muscle. They also suggest that "failure," as produced by their method in isolated hearts, may be related to an alteration of the contractile proteins of failing hearts, but make no mention of the possibility of myocardial edema.

Distensibility refers to a change of volume of a hollow object with change in internal pressure.[6] We maintain that changes in distensibility can be detected even when the volume of the hollow object is not known: by measuring the internal pressure during the application of a standard, internal force. In a heart which pumps blood, the distending force can be measured only with a large error because of the sizable variation of inflow due to regurgitation through the heart valves. However, the left ventricle can be distended by a known, standardized force when an air-filled balloon is placed into it. In this system, the left ventricle compresses the balloon during systole. At the beginning of diastole, the ventricle is then dilated by 2 forces: the elastic recoil of its own wall and the expansion of

Table 1

*Changes of Left Ventricular Pressure (LVP) During Otherwise Comparable Conditions at Varying Times after Initial Distension**

Weight Kg.	Systemic flow ml./Kg./min.	Time in min.	SAP mm. Hg	HR	LVP mm. Hg	Remarks
10.4	96	0	70/20	52	200/20	
	95	5.5	105/75	76	220/60	
17.6	57	0	85/65	126	85/0	After defibrillation
	57	25	80/55	136	75/10	After defibrillation
	57	30	85/65	130	95/10	
17.6	57	0	85/60	117	75/0	After defibrillation
	57	20	75/50	115	100/10	After defibrillation
	57	25	75/50	130	100/10	
	57	30	85/65	126	110/10	
15.8	57	20	130/95	96	105/10	
	57	37	110/80	71	100/32	
	57	45	120/95	92	100/48	
11.8	85	0	95/70	62	240/10	Bilateral vagotomy and occlusion of both common carotid arteries
	85	40	175/130	126	150/90	
10.9	91	0	90/45	108	160/8	
	91	25	100/40	109	155/18	
11.8	85	0	130/110	154	225/10	Bilateral vagotomy and section of both common carotid arteries
	85	35	160/110	152	175/15	
10.0	100	0	185/150	72	240/0	After defibrillation
	100	40	80/40	136	85/20	After defibrillation
22.1	54	0	130/100	102	125/0	Pericardium intact in both observations
	54	20	120/105	96	105/12	

*Air content of balloon identical in each experiment.
SAP = Systemic arterial pressure.
HR = Heart rate.

the balloon. During mid-diastole and end-diastole the ventricle is dilated only by the expansile force of the balloon. Because, in our experiments, this did not vary during diastole, an observed increase of the intracavitary pressure (measured between the wall of the balloon and the endocardium of the left ventricle) could have been due only to decreased volume of the left ventricular cavity, other factors being constant. Decreased intracavitary volume with a constant distending force could only be due to decreased distensibility of the left ventricle.

The observed pressure changes did not indicate a change of the rate of relaxation of the ventricle. As is evident from figures 1 and 2, the diastolic pressures reported here represent a virtual plateau at a heart rate which left ample time for complete relaxation. It is, therefore, unlikely that the elevated diastolic pressures were caused by incomplete relaxation, or by abnormally slow relaxation. The constant heart rate rules out the explanation of the distensibility change as secondary to a "staircase phenomenon." The observations reported here could be interpreted as reflecting the compliance of heart muscle;[6] since we did not measure dimensions, the term "distensibility" seems to be more appropriate. In our system, changes of left ventricular diastolic pressure after injury were not related to changes of the heart rate. As is evident from table 1, the heart rate either remained constant or varied independently. In some experiments, not reported here, the left ventricle made a definite contribution to the systemic arterial pressure, registered in the arch of the aorta; the blood ejected by the contracting ventricle could only have entered it by regurgitation through the aortic valve. In the experiments reported here, a contribution of the left ventricle to the aortic pressure was

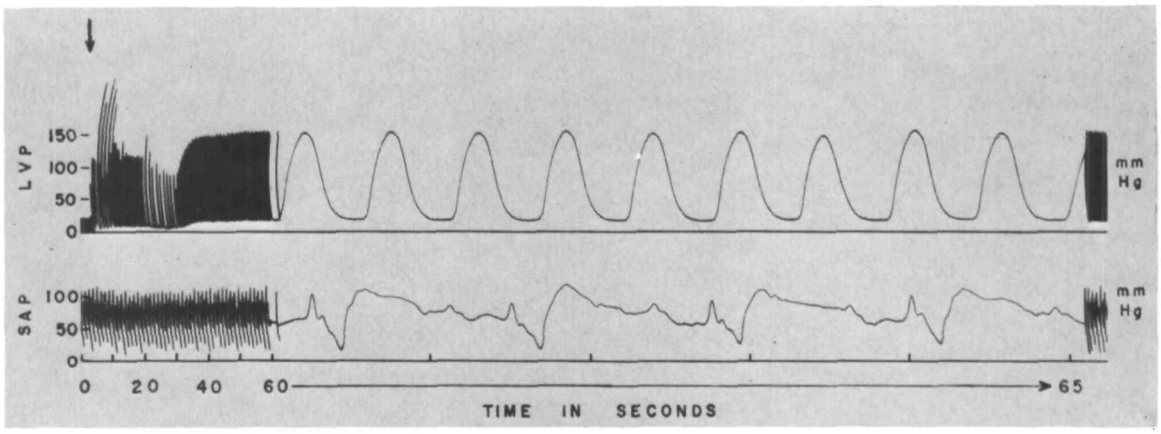

Figure 2

Same experiment as figure 1, 25 minutes later; 35 ml. of air injected into LV balloon at arrow. Note elevation of LV diastolic pressure under otherwise similar conditions.

not evident; since the aortic valve was competent, small amounts of thebesian drainage would have been ejected before contributing to the force distending the left ventricle in diastole. We can, therefore, exclude intracavity accumulation of blood as a cause of the elevated diastolic pressure observed here after injury.

We interpret the data reported here as evidence for decreased distensibility in heart muscle, overstretched or otherwise injured by experimental manipulation. Our experiments in innervated hearts, in situ, confirm the conclusions drawn by Buckley and Zeig[4] from studies on isolated hearts. Our data appear to have added significance because of the relatively brief periods of experimental interference preceding the distensibility change and because the change was observed (in one experiment) even when the pericardium was intact, so that the left ventricle could not be distended beyond the pericardial restraint. As indicated in table 1, the left ventricular diastolic pressure was the only parameter showing consistent, directional changes after injury. When the distensibility of the left ventricle had decreased in the course of our experiments, it did not thereafter return to normal. The relatively short duration of the observation periods did not permit us to test the reversibility of the phenomenon.

Myocardial edema associated with injury of the heart or with cardiac failure has been mentioned by a number of authors.[7-22] Our data demonstrate also that the water content of injured heart muscle is increased, while the water content of our control specimens was similar to data for "normal" heart muscle reported by other laboratories. The relatively modest changes of myocardial water content after injury do not reflect the partition of tissue water between intracellular and extracellular compartments. Whether the increased myocardial water content caused the distensibility change observed here is not certain. We believe, however, that the role of myocardial edema as a pathogenic mechanism in heart failure should be clarified before metabolic or biochemical derangements are invoked as explanations of functional change in the injured or incompetent heart muscle.

As far as experimental "heart failure" is concerned, it is tempting to relate the changes observed here with the classical metabolic explanation. The experiments of Peters and Visscher,[15] recently confirmed by Lorber,[23] have made it clear that in experiments with "failing" hearts cardiac output and external work fall, while cardiac oxygen consumption, inflow pressure and diastolic volume can remain stable. Decreased ventricular distensibility per se would suffice to explain the low mechanical efficiency characteristic of experi-

Table 2

*Water Content of Transmural Specimens from Left Ventricle of Controls and of Overdistended Hearts (Expressed as Per Cent Wet Weight)**

Other authors	Control group A	Control group B	Experimental group
77.4	79.2	77.3	84.2
78.6	78.8	78.3	81.0
78.3	79.0	78.9	82.1
77.3	77.4	78.5	82.2
78.3	80.0	79.2	80.8
78.8	77.0	77.5	84.0
78.5	76.9	77.6	82.5
78.3	77.9	78.0	80.6
Mean ± S.E.	78.3 ± 0.4	78.1 ± 0.4	82.2 ± 0.5

*Water content of canine left ventricular myocardium measured elsewhere shown here for comparison. Note significant increase of water content of injured heart muscle. First column is derived from reference 2; control A represents dogs bled; control B represents dogs maintained by heart-lung machine.

mental heart failure. Lower distensibility without any other changes would tend to decrease inflow, stroke volume, external work, and mechanical efficiency under otherwise comparable conditions.

Our experiments are beset by the same perplexities applying to all similar investigations. Preparations analyzing circulatory failure states should reproduce the hemodynamic patterns found in definite clinical entities; furthermore, they should imitate the pathogenetic mechanism of comparable human lesions. Few experimental methods fulfill these criteria while permitting measurement of all significant parameters. In our experiments, the left ventricle was distended, while a normal systemic pressure was maintained by a heart-lung machine; the overstretched left ventricle usually generated a fairly high systolic pressure. In the clinical syndrome of acute heart failure, systemic arterial and left ventricular systolic pressures would be expected to fall when the failing ventricle dilates. For this reason, we cannot claim that "acute failure of the left ventricle" was created here in a manner analogous with disease processes in humans and prefer the term "injury" to the term "failure" when discussing our experiments. We cannot know from these data whether the changed distensibility was caused by structural damage to the heart muscle, or by other mechanisms such as myocardial edema, local myocardial ischemia, or by excess pressure in the small coronary veins. However, in spite of the limitations imposed by experimental methods, we believe to have shown here that injury such as was caused by stretch reduced the distensibility of heart muscle and caused myocardial edema, results which are of potential clinical significance.

Summary

In open-chest dogs the circulation was carried on a heart-lung machine. The right heart and the left atrium were drained. A balloon was placed in the virtually bloodless left ventricle and filled with a known volume of air at the beginning of an experiment; left ventricular pressure was recorded after a steady state had become established. After this control observation, the preparation was exposed to experimental maneuvers, such as variation of the systemic flow rate or changes of the air volume in the balloon. At one or more later stages of the same experiment, the balloon was emptied, the heart was allowed to beat empty for several minutes, and the standard observation was again repeated. Comparison of left ventricular pressures from the initial and later observations showed that the diastolic pressure in the left ventricle increased in the course of the experiment even though other conditions were comparable. From this we conclude that experimental maneuvers injuring the heart muscle reduce its distensibility. The water content of injured hearts was abnormally elevated; myocardial edema is therefore not excluded as one of the mechanisms explaining the reduced distensibility of injured heart muscle.

Summario in Interlingua

In canes a thorace aperte le circulation esseva transferite a un machina cardio-pulmonar. Le corde dextere e le atrio sinistre esseva drainate. Un ballon esseva inserite in le virtualmente exsangue ventriculo sinistre e plenate con un cognoscite volumine de aere al comenciamento del experimento. Le pression sinistro-ventricular esseva registrate post que un stato

stabile se habeva establite. Post iste observation de controlo, le systema esseva subjicite a varie manovras experimental, incluse per exemplo le variation del fluxo in le circulation systemic o le alteration del volumine de aere in le ballon. A un o plure stadios subsequente in le mesme experimento, le ballon esseva deflate completemente, de maniera que le corde poteva batter vacuemente durante plure minutas, e alora le observation standard esseva repetite. Un comparation del pressiones sinistro-ventricular in le prime e le subsequente observationes monstrava que le pression diastolic in le ventriculo sinistre cresceva in le curso del experimento, ben que altere conditiones remaneva comparabile. Ab iste constatation nos conclude que manovras experimental que resulta i un vulneration del musculo cardiac reduce su distensibilitate. Le contento aquose de vulnerate cordes esseva anormalmente elevate. Edema myocardial, per consequente, non pote esser excludite como un mechanismo que explica possibilemente le reducite distensibilitate de vulnerate musculos cardiac.

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