BIOPHYSICS OF PERICARDIUM, GREAT VESSELS AND CHAMBERS OF FROG HEART AND THEIR HAEMODYNAMIC INTERRELATIONSHIPS

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The biophysical parameters of the pericardium and different chambers of the frog heart (*Rana tigrina*) have been investigated in relation to the extracardiac, intracardiac and vascular pressures and their interrelationships. The volume-pressure distensibility curves of the sinus venosus, auricles and the ventricle were found to be linear while the pericardial distensibility curve had (*i*) an initial slow phase, and (*ii*) a steep phase due to the involvement of elastic and collagen components respectively. Mutual interaction between the intrasinus and pericardial pressures and the haemodynamic effect of pericardial distension on the sinus, the venous and the aortic pressures have also been investigated. It was observed that the adverse circulatory influence of pericardial tamponade is partly counteracted by concomitant rise in the intrasinus and the venous pressures due to which the patency of veins is maintained.

INTRODUCTION

The frog heart has been usefully employed for the investigation of the fundamental characteristics of the heart. Besides easy availability, the simplicity of its anatomy is largely responsible for its extensive use in biological and biomedical research. It is a four chambered organ : (*i*) the sinus venosus which receives the venous blood, (*ii*) right auricle, (*iii*) left auricle, and (*iv*) a common ventricle. The heart is enclosed in the pericardial sac. The junctions between the sinus venosus, auricles and ventricle are well demarcated and it is easy to handle each chamber for specific purpose. Because of the varying amount of fibroelastic tissue in the pericardium and in the myocardium of different chambers, their biophysical characteristics are likely to be different. The sinus venosus is of special importance as it is the pacemaker. Investigations have been in progress in this laboratory on the influence of intrasinus (Pathak 1957, 1958, 1972), extrasinus (pericaredial) (Pathak 1974) and transmural (Pathak, Jog and Goyal, 1974) pressures on pacemaker frequency of frog hearts. In this context it was considered necessary to study the distensibility characteristics of the pericardium, the sinus venosus and other chambers of the heart in relation to the haemodynamic effects of pericardial distension.

MATERIALS AND METHODS

Hearts of decapitated or pithed frogs (*Rana tigrina*) were exposed *in situ* and experiments were conducted both on unperfused hearts as well as on hearts perfused

with Ringer's solution (NaCl, 102 mM; KCl, 1 mM, $CaCl_2$, 1 mM; $NaHCO_3$, 1 mM; Glucose, 5 mM; *p*H 7.6) at room temperature. The sinus perfusion pressure was regulated by an overflow device and the velocity of flow was kept constant with the help of a specially designed perfusion cannula introduced into the posterior vena cava (Fig. 1A). A needle or polythene catheter was securely placed in the pericardial cavity and connected to a Statham pressure transducer and a 20 ml glass syringe filled with the same stock of Ringer's solution at room temperature. The extra sinus pressure was altered by pericardial distension in small graded steps. The intrasinus pressure was altered by changing the perfusion pressure. The transmural pressure across the wall of the sinus venosus was calculated as the difference between the intrasinus and pericardial pressures. The pericardial and intrasinus pressures and in some experiments the aortic pressure were monitored on an electronic pressure meter in parallel with reservoir type of sensitive Hg-manometers. The level of sinus venosus of the heart was the common reference zero level for the pressure recording and monitoring system. After setting the common zero, the response of the transducer and the Hg-manometers was matched so that there was a good correlation between the mean pressure given by the transducer and the Hg-manometers. The entire system was thoroughly checked for any possible leak several times during each experiment.

Haemodynamic effects of pericardial distension were investigated both in unperfused and perfused hearts. Changes in aortic pressure due to changes in the perfusion and pericardial pressures were investigated in perfused hearts. The effect of clamping the venacavae and aortae on intrasinus and pericardial pressuers was investigated in unperfused hearts in order to exclude the influence of perfusion pressure. The relation between intrasinus and pericardial pressures was investigated in dynamic as well as in asystolic hearts. The biophysical behavior of the pericardium and chambers of the heart was investigated through volume-pressure distensibility curves. The experimental set-up and reflections of the pericardium in relation to chambers of the frog heart and great vessels are shown in Fig. 1.

Results

The results of experiments on 27 frog hearts (15 dynamic and 12 asystolic) are considered here.

Distensibility of pericardium

The distensibility of the pericardium can be calculated from volume-pressure relationship using the equation :

$$\text{Volume distensibility} = \frac{\text{increase in volume}}{\text{increase in pressure}}$$

Fig. 2 shows the volume-pressure distensibility curve obtained by pericardial distension in graded steps and the release (suction) curve obtained by withdrawing the distending fluid from the pericardial cavity. The release curve was to the right of the distension curve and at a lower position, indicating that after distension the restoration of the visco-elastic property of the pericardium was not immediate. The difference between the distension and suction curves represented the "hysteresis loop"

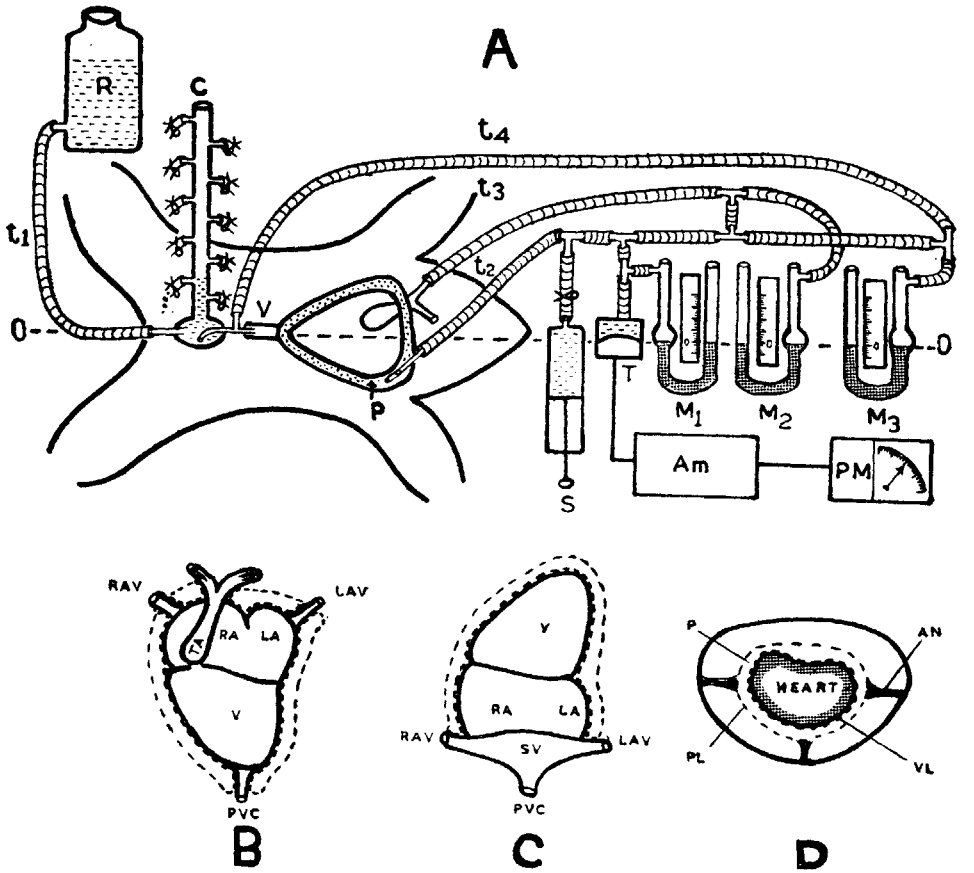
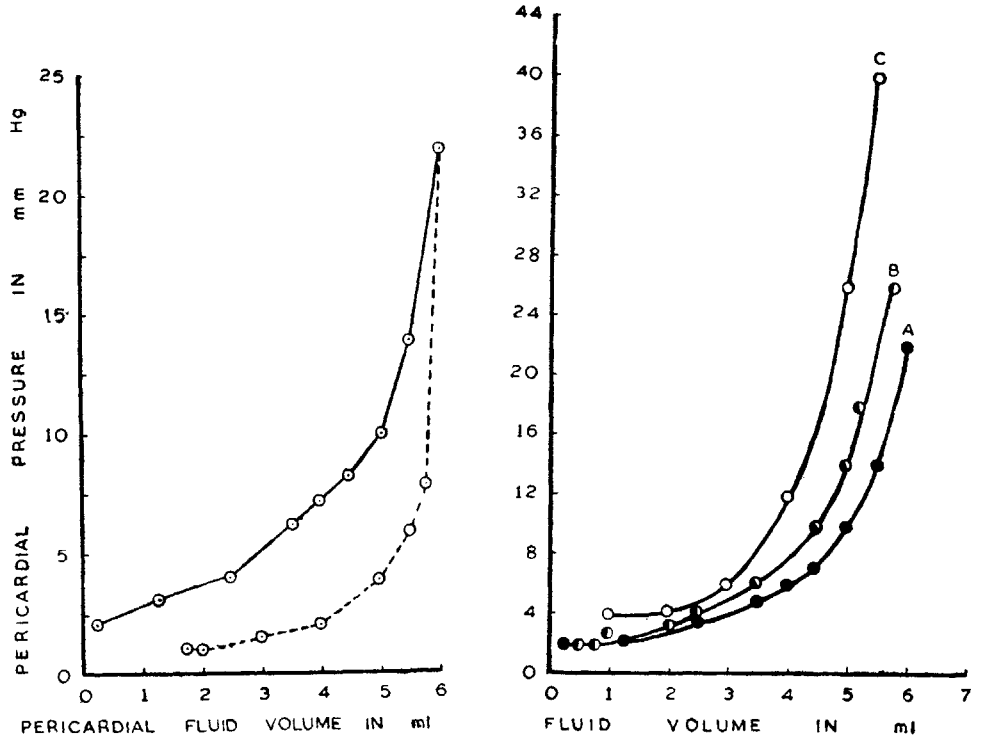


FIG. 1. A, block diagram of experimental arrangement. *R*, Ringer reservior. The vertical limb of the specially designed perfusion cannula, *C*, had out-flow arms at 1 cm intervals; the outlet limb was introduced into the posterior venacava, *V*, and its curved end inside the bulb of the cannula controlled the velocity of fluid inflow into the heart. The perfusion pressure was monitored on a mercury manometer, M_3, through a side arm of the outlet limb. The perfusion fluid flowed out of the heart through the aortae one of which was connected to a mercury manometer, M_2. A needle or polythene tubing was securely placed in the pericardial cavity, *P*, and connected to a graduated 20 ml glass syringe, *S* and to the mercury manometer, M_1 through the transducer *T*. The response of M_1, M_2 and M_3 was matched with the transducer after setting a common reference 'O' at the level of the sinus venosus (horizontal interrupted line). Any of the three pressures could be monitored through the transducer and a pressure amplifier, *Am* on a pressure meter, *PM*; t_1, t_2, t_3 and t_4 are connecting polythene tubings. B, C and D : show the reflections of the pericardium in relation to various chambers of the frog heart and great vessels. *B*, ventral view as seen after exposure of the chest; *C*, view observed on lifting the ventricle upwards to expose the sinus venosus, *SV*; note that the pericardium does not cover the sinus venosus all round; *D*, diagrammatic transverse section of frog chest to show the location of the heart and suspensory anchorages (*AN*) of the pericardium to the front and sides of the chest wall. *RAV* and *LAV*, right and left anterior venacavae; *PVC*, posterior venacava. *RA* and *LA*, right and left auricle; *V*, ventricle; *TA*, truncus areriosus. *PL* and *VL*, parietal and visceral layers of the pericardium.



FIGS. 2–3. 2, Pericardial volume-pressure curves (mean values from 5 perfused dynamic hearts). Curve with continuous connecting line shows typical volume-pressure relation on raising the pericardial pressure in graded steps. The curve with interrupted connecting line was obtained when the steps of distension were reversed by graded withdrawal of fluid. Lower values of pericardial pressure, at corresponding intrapericardial fluid volumes, during withdrawal indicate that the restoration of viscoelastic properties of the pericardium was not immediate. 3, Pericardial distensibility curve in unperfused frog hearts : *A*, volume pressure relationship derived from mean values of 10 trials in 4 dynamic hearts; *B*, distensibility curve derived from mean values of 12 trials in 3 hypodynamic hearts; *C*, similar curve derived from mean values of 15 trials in 3 asystolic hearts. Note the shift in the distensibility curve with changes in the dynamic condition and tone of the heart.

which is characteristic of tissues containing large amount of fibroelastic component. The distension curve had a slow initial phase followed by a fast steep phase. The slow initial phase was due to the stretch of the elasitc fibres while the fast steep phase was due to the involvement of the inelastic collagen component of the pericardium. The shifted position of the release curve was due to the plastic yield of the collagen fibres which took time to recover. The plastic yield was clearly evident when fluid was injected into the pericardium in a sudden large step; the pericardial pressure increased to a certain value but later stabilized to a lower pressure. The pericardial distensibility curve was modified by the size of the heart and its dynamic condition. In case of the perfused heart, because of greater filling the heart was relatively large and the potential pericardial space was consequently smaller. Hence

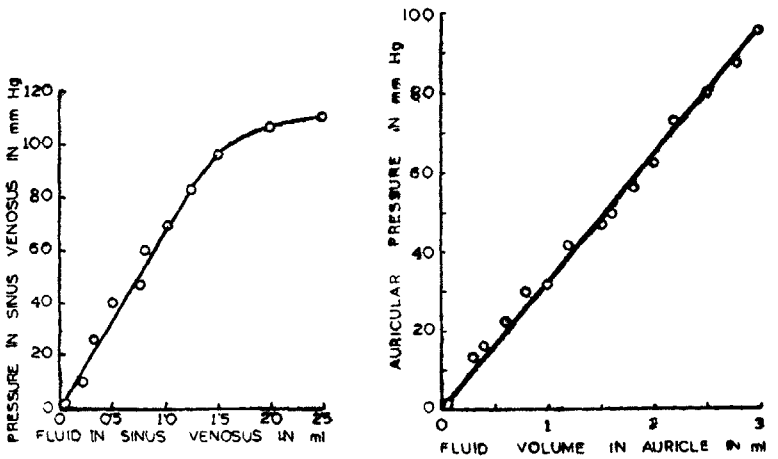
the takeoff of the distensibility curve was higher and the curve was shifted to the left. Similar shifts were observed when a dynamic heart became hypodynamic or asystolic (Fig. 3).

Distensibility of the sinus venosus

In comparison to the pericardium, the wall of the sinus venosus was quite unyielding and small increments in the fluid volume inside the closed cavity of the sinus venosus produced considerable rise in the intrasinus pressure (Fig. 4). The volume-pressure relationship was linear up to 1.5 ml fluid volume corresponding to about 95 mm Hg intrasinus pressure. The response, however, flattened off on further intrasinus distension.

Distensibility of the auricles and ventricle

The volume-pressure relationship in the case of the auricles was similar to that of the sinus venosus although double the amount of fluid was required to produce equivalent rise in the intra-auricular pressure. However, it is pertinent here to recall that normally the volume capacity of the auricles is much greater than that of the sinus venosus. The response of the two auricles was identical. Fig. 5 shows the distensibility curve of the right auricle. The response was linear without any indication of flattening off upto 100 mm Hg intraauricular pressure. A comparison of Figs. 4 and 5 shows that the distensibility curve of the sinus venosus was more steep as the intrasinus pressure was double of intraauricular pressure at corresponding fluid volumes.



FIGS. 4–5. 4. Distensibility curve of the sinus venosus (mean values from 3 hearts). Increase in the fluid volume in the sinus venosus (closed from all sides by tying the venacavae and sinoatrial groove) resulted in a steep rise in the intrasinus pressure in a linear manner. Only 1.5 ml of fluid raised the sinus pressure to 95 mm Hg. The response flattened off at greater fluid volumes. 5. Distensibility curve of the right auricle (mean values from 5 hearts). Distension of closed right auricle with 3 ml of fluid raised the intraauricular pressure to 100 mm Hg.

Despite the greater muscle mass in the ventricle, the ventricular volume-pressure relationship was not very different from that of the auricles. The pressures reached at corresponding fluid volumes were only slightly greater in the ventricles than in the auricles.

Influence of pericardial pressure on intrasinus pressure

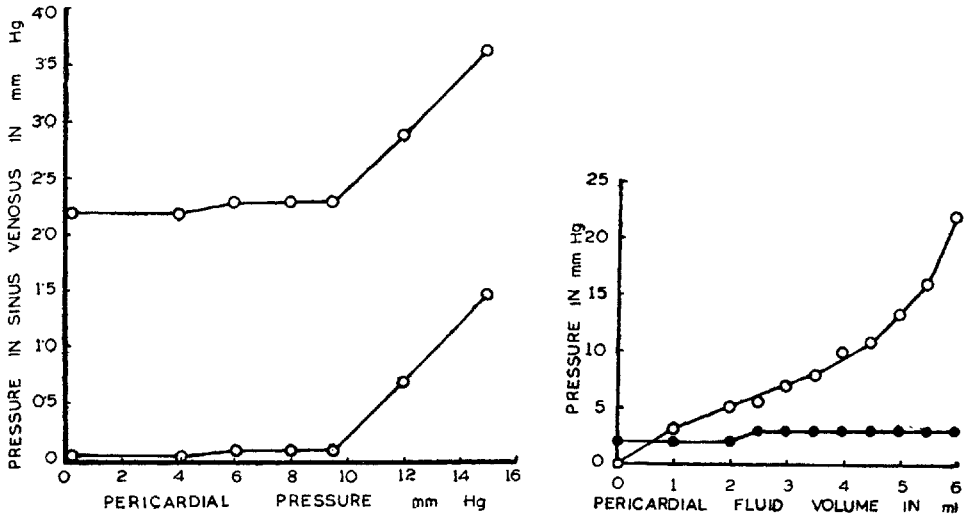
Fig. 6 illustrates the relationship between the pericardial pressure and intrasinus pressure in unperfused (lower curve) and perfused (upper curve) hearts. There was no change in the sinus pressure up to 4 mm Hg pericardial pressure and only a small rise in the intrasinus pressure on increasing the pericardial pressure upto 10 mm Hg. Further increase in the pericardial pressure, however, resulted in a steep rise in the intrasinus pressure, which could only be due to compression of the sinus venosus. Interference with venous return upto this degree of pericardial distension must have been negligible as substantial decrease in the venous return would have reduced the sinus pressure and thereby counteracted the rise in the intrasinus pressure caused by pericardial distension.

Influence of pericardial distension on venous pressure

The relationship between fluid volume in the pericardium and the influence of the resultant pericardial pressure (curve with open circle) on intraluminal pressure in the posterior venacava is shown in Fig. 7. Increase in the fluid volume by 2 ml corresponding to a pericardial pressure of 5 mm Hg had no effect on the venous pressure. Further increase in the fluid volume by 0.5 ml raised the intravenous pressure from 2 to a stabilised value of 3 mm Hg (1 mm increase). The intravenous pressure did not register any further rise even upto about 6 ml of pericardial fluid volume corresponding to about 22 mm Hg pericardial pressure. The rise in the inrtavenous pressure could be due to concomitant rise in the sinus pressure (compare with Fig. 6). It is important to note that the rise in the venous pressure during pericardial distension maintained the patency of veins and did not permit the great veins to collapse due to severe compression and the venous inflow was maintained, though at a reduced level specially in the case of unperfused hearts.

Interrelationship between pericardial and sinus pressures

Fig. 8 illustrates the mutual relationship between the pericardial pressure and intrasinus pressure. The curve with open circles indicates rise in the intrasinus pressure on increasing the pericardial pressure. There was no change in the sinus pressure upto about 4 mm Hg pericardial pressure. Further increase in the pericardial pressure increased the sinus pressure which, however, stabilised to a plateau level of 2 mm Hg at about 14 mm Hg pericardial pressure. This curve is very similar to those shown in Fig. 6. The curve with filled circles in Fig. 8 shows the influence of increasing the intrasinus pressure on the pericardial pressure. It is evident that increase in intrasinus pressure produced stepwise increase in the pericardial pressure which increased from 2 to 5 mm Hg on raising the intrasinus pressure from near 0 to 7 mm Hg. It is noteworthy that even with moderately severe intrasinus



FIGS. 6–7. 6, Influence of pericardial pressure on intrasinus pressure. Increase in the pericardial pressure from 0 to about 10 mm Hg produced only 0.1 mm increase in the intrasinus pressure. Further increase in the pericardial pressure raised the sinus pressure rather steeply. Upper curve, mean values from 6 hearts perfused at a pressure of 2.2 mm Hg (3 cm Ringer). Lower curve, mean values from 4 upnperfused hearts. 7, Relation between pericardial pressure (curve with open circles) and venous pressure (curve with solid circles) during progressive pericardial tamponade. Increase in the pericardial pressure up to 2 ml fluid volume corresponding to a pericardial pressure of 5 mm Hg, had no effect on the pressure in the posterior venacava. Further increase in the pericardial pressure up to 20 mm Hg raised the venous pressure by only 1 mm Hg.

distension, the intrasinus and intrapericardial pressures never equalized. Since the intrasinus pressure was always greater than the pericardial pressure, the transmural pressure remained positive.

Fig. 8 also shows that the influence of pericardial distension on intrasinus pressure was less marked then the influence of intrasinus distension on the pericardial pressure. This indicates that the sinus wall was more distensible from inside than from outside. This difference was perhaps due to the attachment and anchorage of the pericardium to the viscera and body-wall. The greater resistance (or relatively less compressibility) of sinus wall from the pericardial side could also be due to the adherence of the parietal layer of the pericardium with the external side of the wall of the sinus venosus as epicardium. The pericardium is not attached to all sides of the sinus venosus, the posterior side being free from pericardial covering. Further the pericardium is firmly attached to the chest wall, specially to the sternum. Due to these reasons the distensibility of the sinus venosus from inside and its compressibility from the outside may, therefore, differ. Also the increase in the sinus pressure increased the intracardiac pressure in general with resultant increase in the size of the heart and decrease in the pericardial space producing increase in the pericardial pressure. These considerations reasonably explain why the sinus pressure is communicated to a greater extent to the pericardium while the pericardial pressure is communicated to the sinus venosus to a much less extent. The resistance

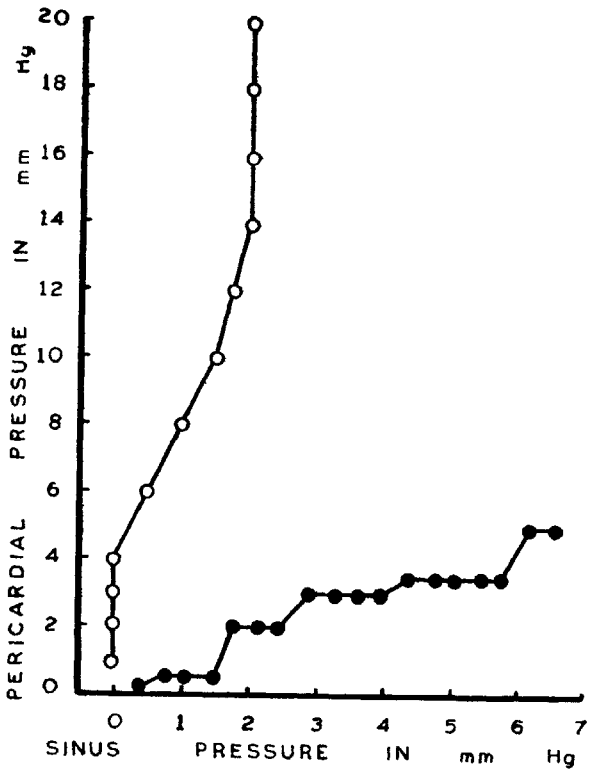


FIG. 8. Differential response of the wall of the sinus venosus to intrasinus and pericardial distension. Increase in the pericardial pressure (curve with open circles) initially had no effect on the sinus pressure but when the pericardial pressure was raised above 4 mm Hg, the sinus pressure increased progressively from 0 to attain a plateau at 2 mm Hg sinus pressure at about 14 mm Hg pericardial pressure, the pattern of effect being the same as in Fig. 6. Increase in the sinus pressure, however, raised the pericardial pressure slowly but progressively in a stepwise manner (curve with solid circles). It is clear that the intrasinus distension was more effective in raising the pericardial pressure i.e. the wall of the sinus venosus was more compressible from inside than from outside.

offered by the epicardial side of the sinus venosus can be calculated from the change in the pericardial pressure and the resultant change in the sinus pressure.

Influence of sinus pressure on aortic pressure

Fig. 9 illustrates the relationship between the intrasinus pressure and the aortic pressure. Increase in the sinus pressure (perfusion pressure) from 1 to 7 mm Hg increased the aortic pressure in a linear fashion. The two pressures did not equilibrate as the aortic pressure was always greater than the sinus pressure. The change in the aortic pressure is determined by the ventricular output and distensibility characteristics of the aorta. The sinus venosus communicates with the right auricle which in turn communicates with the ventricle through unidirectional valves. Increase or decrease in the sinus pressure increased or decreased the output in accordance with the Starling's Law (1918). At very high intrasinus pressures the

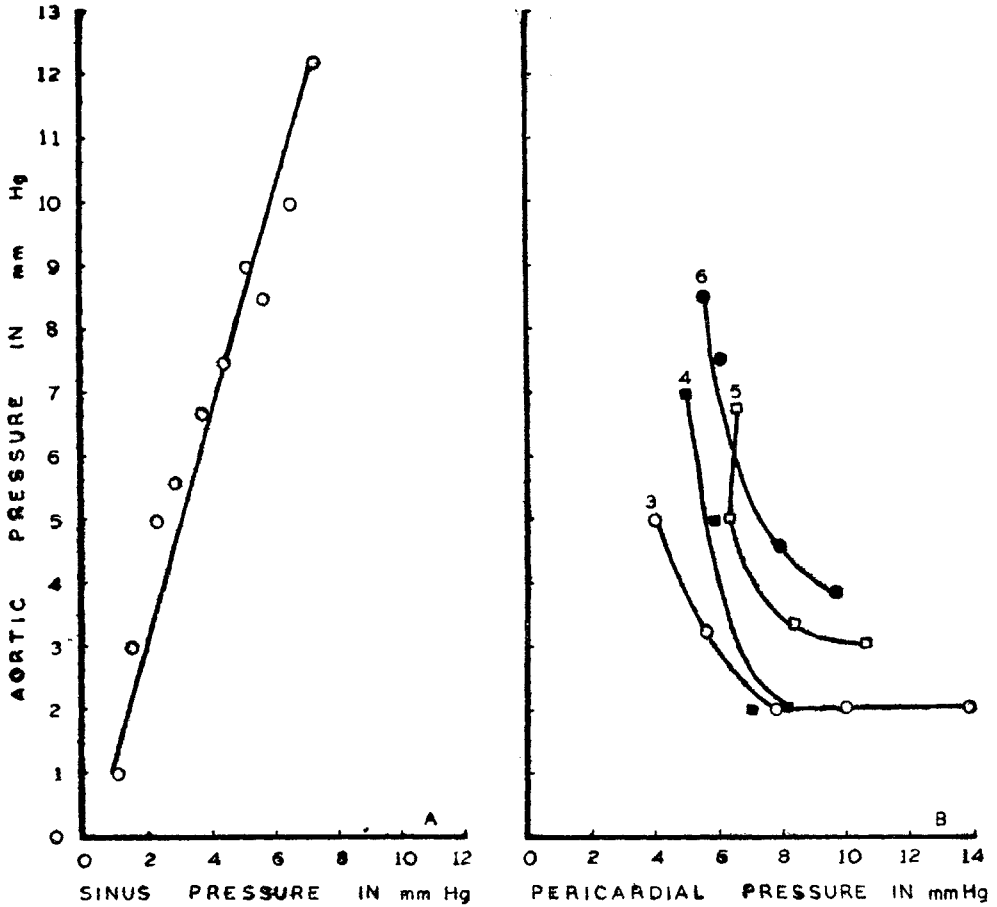


FIG. 9. A, relation between sinus pressure and aortic pressure. The aortic pressure increased in a linear manner with increase in the intrasinus (perfusion) pressure, and was always greater than the sinus pressure. B, relation between pericardial and aortic pressures at different perfusion prassures. The aortic pressure decreased with increase in the pericardial pressure but there was a tendency for the aortic pressure to stabilize at a plateau at high pericardial pressures. This plateau was higher at greater intrasinus pressures. Numerals on curves indicate perfusion pressure in cm Ringer.

sinoauricular and auriculoventricular valves were continually opened up; the three chambers, thus, became a continuous cavity and the intrasinus pressure was directly communicated to the aortae. However, this did not happen within the physiological range of changes in the sinus pressure, i.e. from 0 to +4 mm Hg.

Influence of aortic pressure on sinus pressure

The effect of aortic distension was investigated in unperfused hearts. One aorta was connected to a high level Ringer reservoir while the other was connected to a Hg-manometer. The aortic pressure was not communicated to the auricles or sinus venosus unless it rose above 40 mm Hg. Aortic pressures greater than 40 mm Hg

distended the truncus arteriosus, the right auricle and the ventricle and interfered with ventricular emptying. The end-diastolic ventricular pressure increased and the auriculoventricular valves were rendered incompetent. Finally, the back pressure was communicated to the sinus venosus due to the imcompetency developing in the sinoauricular valve also. Similar results were obtained due to accumulation of fluid when the two aortae were simultaneously clamped in both unperfused and perfused hearts.

Interrelationship of pericardial, aortic and sinus pressures

Fig. 9B illustrates the relationship between the pericardial and aortic pressures at 3, 4, 5 and 6 cm Ringer perfusion (intrasinus) pressures. In this connection two points are noteworthy : (*i*) the aortic pressure dropped promptly and progressively as the pericardial pressure rose above 4 mm Hg and (*ii*) with increase in the intrasinus (perfusion) pressure, the position of the curve relating the pericardial pressure with the aortic pressure, moved upwards and to the right, indicating that the cardiac performance (as judged from the aortic pressure) was more efficient at corresponding degree of pericardial distension when the intrasinus pressure was greater. Distension of aortae at high pressure in unperfused hearts and clamping of aortae both in perfused and unperfused hearts increased the intrasinus pressure due to back pressure and accumulation of fluid in all chambers caused enlargement of the whole heart. Both these factors increased the pericardial pressure.

Discussion

The results demonstrate that distensibility curves of the sinus venosus, auricles and ventricle are straight lines but the pericardial distensibility curve has to phases : (*i*) an initial slow phase followed by (*ii*) a steep fast phase. The slow initial phase was due to the involvement of the elastic fibres, while the later fast phase was due to the involvement of the inelastic collagen fibres present in abundance in the pericardium and which came into action at moderate pericardial distension. The 'hysteresis loop' observed in the pericardial distensibility curve represented the plastic yield by the collagen tissue which took time to recover after distension-stretch.

Observations on the interrelationship between the pericardial and intrasinus pressures indicate that pericardial distension was less effective in increasing the sinus pressure while the sinus pressure was more effective in increasing the pericardial pressure. Despite the tendency of the two pressures to equalise, they in fact never did so within the reasonable physiological limits of these two pressures. During intrasinus distension the intrasinus pressure was always greater than the pericardial pressure and therefore a positive transmural pressure was maintained. During pericardial distension the pericardial pressure was consistently greater than the intrasinus pressure and a negative transmural pressure was created.

The interrelationship between the pericardial pressure, aortic pressure and intrasinus pressure indicates that cardiac activity in the presence of pericardial tamponade may be effectively supported by raising the venous pressure through volume infusion. This appears to be the basis why infusion of fluid volume in patients with pericardial tamponade have been reported to be beneficial (Cooper, Stead and Warren 1944).

The present observations are very pertinent for the understaing of circulatory dynamics and mechanism of changes in heart rate under different conditions.

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