Determinants of Impairment of Cardiac Filling During Progressive Pericardial Effusion

By William E. Nerlich, M.D.

The progressive reduction in cardiac output—and later in arterial pressures—that develops during advancing degrees of pericardial effusion is usually attributed to a steady decrease in the venoatrial pressure gradient. Evaluation of changes in instantaneous pressures in the right and left atria at the end of ventricular diastole (Z pressure) and systole (V pressure) indicates that as pericardial pressure rises other determinants enter in the following order: (1) reduction in diastolic capacities of the atrium and ventricles; (2) increase in venoatrial pressure gradient and preponderant rise of left atrial pressures due to the higher elasticity coefficient of this chamber; (3) blockage of atrial inflow during ventricular diastole; (4) impairment of atrial inflow during ventricular systole as its stroke volume diminishes to an extreme degree; and (5) inauguration of a vicious cycle in which a diminishing venopressure gradient decreases ventricular filling, while the consequent reduction in stroke volume attenuates the facilitating effect of ventricular ejection on the venoatrial gradient.

Since the initial work of Cohnheim, it has been known that the rapid introduction of fluid into the pericardial sac of experimental animals produces an increase of venous pressure and a fall of mean arterial pressure. The data later collected by Starling, Lewis, Kuno, and others demonstrated that the increased pericardial pressure acts as a barrier to the venous filling of the heart, resulting in a decrease in diastolic heart size when the gradient of pressure between the central veins and atrium is sufficiently diminished. The rise of central venous pressure results from pooling of venous blood which has failed to reach the right atrium, and the fall of mean arterial blood pressure is ascribed to the progressively decreasing cardiac output.

It was the purpose of this investigation to subject the accepted dynamics of pericardial effusion to closer scrutiny and, if possible, to evaluate the importance and incidence of other suspected and unsuspected determinants of reduced ventricular filling and output. Incidentally, it seemed important to determine whether the right and left sides of the heart react similarly and simultaneously to a common increase in pericardial pressure. For these purposes, right and left atrial and pericardial pressures were recorded by optical manometers during step-wise increases in pericardial fluid. "Open chest" preparations were employed so that the complicating effects of changing intrathoracic pressure would not be involved in the analysis of basic hemodynamic effects.

Methods

After the animals had been anesthetized with morphine and phenobarbital sodium, artificial respiration was given and the chest was opened through a midline sternum-splitting incision. Cannulas filled with saline and heparin were inserted (1) into the left atrium via the superior branch of the left pulmonary vein, (2) into the right atrium via the right jugular vein, and (3) into the aorta via the left subclavian artery. A cannula filled with saline was also inserted into the ventral surface of the pericardium without disturbing the pericardial diaphragmatic attachments or introducing air. The cannula was adjusted so as to cause minimal distortion of the pericardial sac and to avoid impacts of the contracting ventricles.

The various cannulas, rigidly fixed, were attached by lead tubing to Gregg-type manometers of adequate sensitivity and frequency for the optical registration of each pressure curve. The level of the animal board was used as a zero for all manometers. Changes in atrial levels such as are caused by lung inflation and deflation were controlled by recording...
these acts on the same record by means of a Frank segment capsule connected with the outlet tube of the respirator. The atrial and pericardial manometers were calibrated against a saline manometer, the aortic manometer against a mercury manometer. Pressure relations to a base line were checked after each record. After placement of cannulas was such that good records resulted, the cannulas were maintained in a fixed position and were not manipulated during the experiment, a point of considerable importance.

After the animal's blood pressure had stabilized, as evidenced in a series of control records, isotonic saline at 38 to 50 C. was introduced into the pericardium in 5 or 10 cc. increments at intervals of four minutes until the arterial pressure and/or heart rate had declined to precarious levels. After a short period of stabilization in this dynamic state, the pericardial fluid was slowly withdrawn in 5 cc. increments. Optical records were taken after each alteration in pericardial volume throughout the experiment.

Measurement of Atrial Pressure Curves. It has been stressed in several communications from this laboratory\(^5^-^7\) that measurements of instantaneous atrial pressures at definitive moments of the cardiac cycle are superior to mean pressure values in interpretations of dynamic problems. Accordingly, all measurements were made at the Z point, which expresses the state of atrial pressures at the onset of ventricular systole, and at the V point (at the moment of the second heart sound) which occurs at the end of ventricular systole. These points are marked on record C of figure 1. Since pericardial pressures also fluctuate during the cardiac cycle as soon as a layer of fluid surrounds the ventricles, pericardial pressures were measured at corresponding points.

RESULTS

Fifteen experiments were performed but the data of only nine were considered sufficiently reliable to be included in this survey; the others were vitiated by the necessity of changing the position of recording cannulas or by the development of leaks in the pericardial sac.

Actual pressure changes in the aorta, left atrium, right atrium, and pericardium during different stages of experimental pericardial effusion are shown in segments A, B, C, and D of figure 1. The effects of complete recovery are shown in segment E of the same figure. Figure 2 shows plots of data derived from similar curves in another experiment.

On the basis of trends in mean arterial pressure, the sequence of dynamic events following progressive increase and decrease in volumes of
pericardial fluid can be divided into four stages. These are indicated in the plot of figure 2.

Phase I starts with the introduction of saline solution into the pericardial sac and continues until approximately two-thirds of the maximal volume which can be introduced has been introduced. It continues as long as mean arterial pressure remains at the control level or declines only slowly. Frequently, as in the experiment plotted in figure 2—but not necessarily as shown in segment B of figure 1—the heart accelerates progressively. The reduction in diastolic size which accompanies such acceleration aids the heart in adapting its capacity to the diminishing pericardial space. The period of systolic ejection becomes shorter, even when the heart rate remains relatively constant, as in figure 1B and C. The pulse pressure diminishes and the contour of the pressure pulse (fig. 1B) shows a significant reduction in stroke volume. In fact, estimates of stroke volume and cardiac output by the pulse contour method of Hamilton and Remington, shown in the third curve of figure 2, indicate that cardiac output is diminishing steadily. The mechanism by which arterial pressure is sustained can be only inferred from the data, but an increase in total peripheral resistance was demonstrated in similar experiments by Post.8

Phase II is characterized by the precipitous decline of arterial pressure which follows additional small increments of pericardial fluid. Often, as in the experiment illustrated in figure 1, the heart slows abruptly to a rate well below normal. As shown in figure 1C, the pulse pressure diminishes progressively and the pressure pulse assumes a rounded configuration and flattened diastolic limb. Analyses by the pulse contour method indicate a continuing reduction in stroke volume and, owing to a pronounced slowing, a still greater decrease in cardiac output.

Phase III represents the interval during which arterial pressures reach a critically low level; indeed, small volumes of pericardial fluid may need to be withdrawn in order to maintain a barely minimal circulation. Ordinarily, the heart rate and arterial pressures are lowest during this period. The pulse pressure is small and, as seen in figure 1D, the contour of the aortic pressure pulse suggests a very small output.

Phase IV comprises the steady recovery of arterial pressure and heart rate following stepwise removal of pericardial fluid. The circulatory changes are essentially the reverse of those seen during addition of fluid; the heart promptly regains its control rate and the mean arterial pressure its control level, but the pulse

Fig. 2. Chart showing effects of increasing and decreasing pericardial fluid volumes (P.V.) on heart rate (H.R.), systolic and diastolic pressures (B.P.); cardiac index by pulse contour method (C.I.); Z and V pressures in left atrium (L.A.), and right atrium (R.A.), and in pericardial cavity (P.P.). I, II, III, IV indicate sequential phases discussed in text; 1, 2, 3, 4, 5, 6 indicate coordinate cross lines interrelating different curves.

pressure and cardiac output are not quite restored to normal.

A glance at the lower group of pressure curves in figure 1 clearly shows that the general level of both right and left atrial pressures elevates with that of the pericardium. It is also noticeable that whereas the pressure curves from the pericardial sac exhibit only random vibrations when no fluid is present (A), the curves assume more and more the form of changes within the atrium as fluid accumulates.
The surprising feature of such records is the small reduction in pressure that occurs when the massive ventricles empty during systole and the relatively large pressure wave that accompanies atrial contractions (fig. 1B and C). This stresses the fact that, in studying the effect of increasing pericardial pressure, we need to consider two oppositely directed forces, namely, the reciprocal effects of increasing pericardial upon atrial pressures and the dynamic effects of intraatrial pressure changes upon phasic pericardial variations. To judge from the amplitudes of the conspicuous atrial waves in records such as these, increased pericardial pressure does not seem to diminish the vigor of atrial contractions until the third phase is approached (D). However, it is impossible to exclude a depressant vagal effect on atrial contraction coincident with the slowing, for the vagus exerts similar effects on atrial pressure curves.9

Careful measurements of atrial pressure curves are required to determine the relative effects of increasing pericardial pressure on the instantaneous Z and V pressures in the two atria, and caution is required in their interpretation. As analyzed by Opdyke and his associates,6 under natural conditions the instantaneous Z and V pressures allow inferences regarding inflow-outflow equilibria in the atriums at the ends of diastole and systole respectively. During varying degrees of pericardial tamponade such interpretations must be tempered by the reciprocal reactions between pericardial and intraatrial pressures. Nevertheless, gross differences in the trends of Z or V pressures in the two atriums become significant since they are subject to identical pericardial pressures.

In the chart of figure 2, it is observed that the initial increase in pericardial pressure (PP), caused by injection of five 10 cc. units of saline (PV), has only slight effect on the Z and V pressures (lines 1 and 2). The Z pressure in the right atrium rises first and to a greater extent than in the left; but in some other experiments the Z pressures increased in both atria. Such precedent elevation of Z pressure—at the end of ventricular diastole—is understandable, for increasing volumes of pericardial fluid will tend to restrict the diastolic but not the systolic size of the heart. Wiggers9 also found that pericardial volumes of similar magnitude cause a recognizable elevation of initial tension in the left ventricle which corresponds to Z pressure in the left atrium. Such precedence in elevation of Z pressure allows the inferences (a) that these pressures give an idea of the extent to which pericardial fluid encroaches upon the capacity of the atria, and (b) that the primary decrease in cardiac output is due to the reduced diastolic capacities of the atria and ventricles.

The introduction of additional 10 cc. of increments of saline solution has a different effect on atrial pressures (lines 2 and 3). Right atrial V pressure now increases steadily, while left atrial V pressure is elevated only slightly. Since the steadily rising pericardial pressure acts equally at the two atriums, and since the accompanying acceleration of the heart in this experiment would in itself tend to lower both atrial V pressures, the possibility must be considered that the systolic inflow into the left atrium is reduced relatively more than that of the right. The following reasoning could be applied. The progressive reduction of pulse pressure and cardiac output obviously denotes impairment of left ventricular filling. This is now due to diminishing capacity of the left heart plus a diminishing pressure gradient between the pulmonary veins and the left atrium. Since filling and output of the right heart are simultaneously reduced the pressure in the pulmonary veins never rises as much as in the venae cavae. For this reason the right atrial pressure at the end of systole (V pressure) rises earlier, more rapidly, and to a higher level than the V pressure in the left atrium. In other words, the pressure in the systemic venous reservoir is more effective for maintaining atrial filling than that in the pulmonary venous reservoir, because the latter depends on the diminishing output of the right ventricle. Such an interpretation is weakened by the fact that under such conditions inequality of the stroke volumes of the two ventricles must exist for some time and such disparity between the minute outputs of the two ventricles, even for a few beats, would cause an elevation of pulmonary venous pressure perhaps equal to that in the systemic venous reservoir.
The different effects of rising pericardial pressures on the V and Z pressures are more probably related to the higher elasticity coefficient of the left atrium. Thus, assuming as a first approximation that the elasticity coefficients \( \frac{dp}{dv} \) of the respective atria do not change as pericardial pressure rises, it can be postulated that the pressure at the end of systole (V pressures) is determined by \( \text{net systolic inflow} \times \frac{dp}{dv} + \text{pericardial pressure} \). By giving \( \frac{dp}{dv} \) for the left atrium any larger value than that for the right, a little calculation reveals that right atrial V pressure rises faster than left atrial pressure with equally diminishing inflow volumes. An example is shown in table 1. Similarly, the more rapid elevation of right atrial filling period incident to cardiac slowing. This slowing is at least partly of cardiac origin, for it persists after vagotomy. A study of pressure pulses during this period suggests that atrial inflow may be blocked during diastole and occurs solely during ventricular systole. As shown in figure 1C, systolic emptying of the ventricles causes a significant reduction in pericardial pressure, which aids the diminishing venoatrial pressure difference to fill the atrial chambers during systole. This facilitating hemodynamic force is greatly attenuated as pericardial pressures reach still higher levels (lines 4 and 5, fig. 2), for, with further impairment of ventricular filling, ventricular contractions reduce pericardial pressures very little, as illustrated in figure 1D. Thus, a vicious cycle is established which eventuates in a pronounced reduction of cardiac output and a decline of arterial pressures to critically low levels (fig. 2, line 4). This may be expressed diagrammatically as follows:

\[
\begin{align*}
\text{Diminishing veno-atrial gradient} \quad & \downarrow \\
\text{Attenuated facilitating effect} \quad & \downarrow \\
\text{Decreased systolic discharge} \quad &
\end{align*}
\]

In summary, development of the critical stage of pericardial effusion is hastened by the reciprocating effects of diminishing venoatrial pressure differentials on ventricular filling, and the progressive attenuation of the facilitating effect that contraction of the ventricles exerts on atrial inflow through systolic reduction in pericardial pressure.

The question of whether reduction in coronary flow contributes to the default of ventricular contraction must be left unanswered.
The writer has found no experimental studies of the problem, and Gregg mentions no such work in his recent monograph. Electrocardiographic studies cannot differentiate between myocardial effects caused by ischemia and those produced by other agencies. The volume of coronary flow during states of high pericardial pressure would be the result of many factors, among them lowering of arterial pressure, the elevation of diastolic and reduction of systolic pressures but no marked immediate effect on cardiac output or arterial pressure. Gradually (lines 5 and 6) a recovery of cardiac output, arterial pressures, and the heart rate occurs which corresponds rather well with conditions when similar pericardial volumes existed during introduction of saline (cf. curves at lines 3 and 6). The greater reduction of pericardial pressure at apparently equivalent volumes (lines 3 and 6) may have been due to (a) stretching of the plastic pericardium or (b) absorption of some of the saline solution. The presence of leaks was meticulous excluded. Similar factors may account for the common observation illustrated in figure 1C and D, that pericardial pressures often decline when excessive volumes of fluid are introduced.

The rate at which cardiac output decreases with progressive elevation of pericardial pressure depends upon the volume of circulating blood and the magnitude of the pressure elevation that can take place extrapericardial veins. To determine the importance of this factor, two animals with extremely large pericardial effusions were given intravenous infusions of 100 cc. saline solution over a period of four or five minutes. The effects were rather surprising, as indicated by data of one experiment in figure 3. It can be easily seen that such an infusion induces a prompt elevation of Z and V pressures in both atrium. As in normal dogs (Opdyke), these pressures rose higher in the left than those in the right atrium. The abrupt increase in cardiac output is evidence that a marked improvement in cardiac filling had taken place and that this occurred despite a further rise of pericardial pressure—probably as a result of the greater filling of the heart. The most interesting feature, however, was the fact that the effects of such a temporary infusion extend far beyond the period of infusion. As shown in figure 3, intraatrial Z and V pressures decline shortly after termination of the infusion, but they are maintained at a much higher level than before the infusion. The initial improvement in cardiac output is also maintained; arterial pressures remain higher and the pulse pressures larger. More favorable venoatrial gradients are obviously responsible for the improvement. The fact that the Z pressure equals or exceeds the V pressures was determined in figure 3, where it is seen that Z pressure equals or exceeds the V pressure.

![Figure 3](http://circ.ahajournals.org/)

**Figure 3.** Plot of dynamic events showing the effect of 100 cc. intravenous saline solution during period indicated by arrows, on hemodynamic events. Symbols in figure 2. Discussion in text.

within the ventricles, the extracardial tension and uncertain effects of anoxia and metabolites on the tone of intramural arterioles. Speculation as to resultant effects on coronary flow and its adequacy for the reduced work and abnormal mode of performance is obviously hazardous. That any such effect was not lasting in these acute experiments is indicated by the observation that removal of only a small volume of pericardial fluid promptly improves cardiac action. In the experiment illustrated in figure 2, removal of 30 cc. of saline (lines 4 and 5) reveals a significant reduction in pericardial and atrial pressures but no marked immediate effect on cardiac output or arterial pressure. Gradually (lines 5 and 6) a recovery of cardiac output, arterial pressures, and the heart rate occurs which corresponds rather well with conditions when similar pericardial volumes existed during introduction of saline (cf. curves at lines 3 and 6). The greater reduction of pericardial pressure at apparently equivalent volumes (lines 3 and 6) may have been due to (a) stretching of the plastic pericardium or (b) absorption of some of the saline solution. The presence of leaks was meticulous excluded. Similar factors may account for the common observation illustrated in figure 1C and D, that pericardial pressures often decline when excessive volumes of fluid are introduced.

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pressure in the atria supports the view that atrial inflow takes place throughout the cardiac cycle.

**Summary and Conclusions**

An experimental attempt was made to evaluate the dynamic factors that operate to reduce cardiac output during progressive stages of pericardial effusion and to determine whether the right and left hearts are affected similarly and simultaneously when submitted to a common increase in pericardial pressure. For this purpose, a special study was made of the changes in instantaneous atrial pressures measured at the end of diastole (Z pressure) and at the termination of systole (V pressure). The contemplated analysis failed to identify the dominant factors at certain stages of pericardial tamponade, but they proved informative in the following ways:

1. The characteristic precedent elevation of Z pressure, particularly in the right atrium, strongly suggests that reduction in diastolic capacities of the atria and ventricles is the first factor that reduces systolic discharge.

2. The steady rise of right atrial V pressure and the small rise of left atrial V pressure following the progressive increase in pericardial fluid suggests that the venoatrial pressure gradient diminishes more rapidly on the left side. Such an interpretation is untenable, however, since it involves a disparity between the outputs of the two ventricles, a condition that cannot be maintained for more than a few beats. The higher elasticity coefficient of the left atrium seems to account for these differences.

3. During the phase when arterial pressures decline abruptly, other determinants enter, but their nature cannot be detected by analysis of atrial pressure pulses.

4. A study of pericardial pulsations reveals that the reduction in pericardial pressure during ventricular ejection facilitates atrial filling by creating a more favorable venoatrial pressure gradient. It is probable that with increasing pericardial pressures atrial inflow is blocked, first during the period of ventricular diastole and only later during the period of ventricular systole.

5. It is believed that development of the critical stage is hastened through establishment of a vicious cycle: diminishing venoatrial gradient → decreased systolic discharge → attenuated facilitation effect of ventricular systole → further reduction of venoatrial gradient and repetition of the cycle.

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WILLIAM E. NERLICH

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