Effect of Respiration on Venous Return and Stroke Volume in Cardiac Tamponade

MECHANISM OF PULSUS PARADOXUS

By Warren G. Guntheroth, M.D., Beverly C. Morgan, M.D., and Gay L. Mullins, B.S.

With the Technical Assistance of George A. McGough and Donald G. Breazeale

ABSTRACT

In 40 lightly anesthetized dogs, 5 to 30 days after surgical preparation, flow was measured simultaneously in the venae cavae, pulmonary artery, pulmonary vein, and aorta with ultrasonic flowmeters. Intrapleural and pericardial pressures were measured via silastic cannulas. Pulmonary vein diameter was monitored by miniature mutual inductance coils. In the resting animal with sinus arrhythmia, inspiration increased heart rate and flow in the vena cava, and to a lesser extent, in the pulmonary vein. Left ventricular stroke volume (LVSV) varied directly with the right ventricular stroke volume (RVSV) in dogs with slow heart rates. Cardiac tamponade invariably caused tachycardia and a marked decrease in cardiac output, arterial pressure, pulse pressure, and stroke volume; venous pressure and diameter increased. Pericardial pressure, although markedly elevated, fell with inspiration paralleling the fall in intrapleural pressure. Flow in the pulmonary vein rose or remained constant with inspiration. Pulmonary vein diameter frequently increased with inspiration during tamponade, but only after the pulmonary artery diameter increased with the inspiratory surge. LVSV did not decline sharply with inspiration, and actually increased within 2 beats of the increase in RVSV. The sum of LVSV plus RVSV increased markedly with inspiration, contradicting the concept of fixed intrapericardial volume. Almost all of the changes of pulsus paradoxus reflect the normal respiratory effects on the RVSV, delayed by transit through the pulmonary bed and exaggerated by the small LVSV in a vasoconstricted state.

ADDITIONAL KEY WORDS

determinants of stroke volume
pericardial effusion
cardiac output
pericardial pressure
pulmonary vein flow
sinus arrhythmia
vena cava flow
ultrasonic flow studies
respiratory effect on blood pressure

dog

The mechanism of normal variation in blood pressure with respiration must be understood in order to understand the mechanism of pulsus paradoxus, an exaggerated fall in systolic blood pressure with inspiration found in cardiac tamponade. However, there are two major obstacles to a complete understanding of either the normal state or the abnormal state of cardiac tamponade. First, the large number of variables which influence the blood pressure make it difficult to measure these simultaneously in a preparation that is physiological. Secondly, the interrelationships of these variables are inconstant in different states in any given animal, and between animals there is even more variation in the determinants of systolic blood pressure.

From the Division of Pediatric Cardiology, Department of Pediatrics, University of Washington School of Medicine, Seattle, Washington.

This work was supported by U. S. Public Health Service Grants HE-03908 and HE-07158 from the National Heart Institute. Dr. Morgan is recipient of U. S. Public Health Service Research Career Program Award HE 7945-01.

This paper was presented in part at the Scientific Sessions, American Heart Association, October 22, 1966, in New York.

Accepted for publication February 20, 1967.
We have previously reported the variations in pericardial pressure with respiration and heart beat in the normal, and in tamponade (1). We found that changes in pericardial pressure followed pleural pressure closely, effectively ruling out Dock's (2) theory that pericardial pressure rises during inspiration with tamponade, due to traction on the pericardium. Our findings are also difficult to reconcile with the theory of Katz and Gauchat (3), who inferred that the inspiratory drop in pleural pressure was not transmitted to the pericardium and left heart chambers. Katz and Gauchat concluded that the increased capacity of the pulmonary veins with inspiration, in the face of an unchanged distending pressure for the left atrium and ventricle, caused a transient pooling of blood in the pulmonary veins. This concept has been challenged by Dornhorst, Howard, and Leathart (4) and by Lange and Tsagaris (5). Recently, Lange and others (6) have suggested that pulsus paradoxus is a simple reflection of events of the right heart delayed by transit through the pulmonary circulation. Dornhorst and his associates (7) accept this for the normal, but attribute a dominant role in pulsus paradoxus to competition by the right ventricle for a fixed, total diastolic volume, resulting in a reduction of left ventricular filling with inspiration. Shabetai and co-workers (8) also favor this theory.

In normal dogs at rest, with slow respiratory rate, slow heart rate and sinus arrhythmia, we found that the best predictor of left ventricular stroke volume (LVSV) was the duration of the preceding filling interval (9). The inspiratory surge was transmitted from the right heart in 1 to 2 beats, but had less effect on left ventricular stroke volume than did the diastolic interval. However, with tachycardia or simply absence of sinus arrhythmia, the best predictor of LVSV became the right ventricular stroke volume of the preceding 1 or 2 beats. We also showed that the pulmonary vein flow did not regularly fall during inspiration, but rose in more than one-half of our experiments (10).

We are now reporting our studies of the venous return and stroke volume of the two ventricles in intact dogs with cardiac tamponade to elucidate the mechanism of pulsus paradoxus.

Material and Methods
Forty dogs weighing 17 to 30 kg were subjected to left thoracotomy with aseptic technique under pentobarbital anesthesia (30 mg/kg). The pericardial sac was entered and ultrasonic flow transducers were implanted at the base of the aorta and pulmonary artery. A special silastic catheter was sutured into the pericardial sac (1) and the pericardial sac was tightly closed. Additional flow probes were placed on the superior or inferior vena cava near the right atrial junction and on a lobar pulmonary vein outside the pericardial sac; from 2 to 4 flow transducers were implanted in each animal. In 15 of the animals, a pair of miniature mutual inductance coils (11, 12) were sutured onto another pulmonary vein and onto a lobar artery to record dimension changes. A flat, silastic balloon, 20 x 25 mm, was placed in the pleural space. The pericardial sac was irrigated with saline containing hydrocortisone on the day of operation and daily for 3 days thereafter; integrity of the pericardial sac was confirmed by recovery of irrigating fluid.

Data were obtained from these dogs 5 days to 6 weeks postoperatively; the dogs were under light general anesthesia (morphine 1 to 1.5 mg/kg and pentobarbital 10 to 15 mg/kg) and were breathing spontaneously. The following 16 variables were measured in the course of the 40 experiments: electrocardiogram, intrathoracic pressure, pericardial pressure, vena caval pressure, right ventricular pressure, left ventricular pressure, arterial pressure, pulmonary vein pressure, superior vena caval flow, inferior vena caval flow, pulmonary artery flow, pulmonary vein flow, aortic root flow, descending thoracic aortic flow, and pulmonary artery and vein diameters. Not all variables were recorded in each animal; some experiments were designed to elucidate a particular aspect of the problem, and in some animals, incomplete data was a result of chewed wires and other vicissitudes of chronic animal studies. Arterial and venous pressures were measured by catheterizing appropriate vessels, and in 3 dogs, left ventricular pressure was measured by retrograde aortic catheterization. A single limb lead ECG was recorded in most animals. Pressures were recorded by means of Statham P23Db, P23bb, and Sanborn 276 transducers with zero level at the mid-right atrium. Flow records were not calibrated, since our interest was
MECHANISM OF PULSUS PARADOXUS

in relative changes rather than absolute values. Zero level for venous flows was determined by intravenous administration of acetylcholine in dosage sufficient to produce transient cardiac arrest. All animals appeared to be in good health at the time of study, and at autopsy the pericardium appeared normal. Tamponade was produced by infusion of 100 to 330 ml of sterile saline at 37 to 38° C into the pericardial sac.

Nine animals had satisfactory simultaneous records of flow at the aortic and pulmonic roots in the normal state and during cardiac tamponade. The stroke volumes for the right and left ventricles were determined by planimetry, and the mean values for these two variables were equalized and the correction factor, if any, applied to all of the individual values. The amplification was not changed during the procedure, so that the values during tamponade could be compared with the normal values. These values, and data on pressure and interval, were entered on punch cards and computations were performed at the University of Washington Computer Center on the IBM 7094. "Plot 1" from XTAB Programs1 was used for generating scattergrams, and the BMD03R program was used to calculate the usual descriptive statistics in addition to regression coefficients, correlation coefficients, partial correlation coefficients, and multiple correlation coefficients (13). The data from the control state and tamponade were analyzed separately and as a pooled group.

Results

Although several general changes in circulatory function occurred in all instances with tamponade, there was considerable variability from one animal to another. Pulsus paradoxus was not invariably produced by tamponade, but was present in 70% of the animals. Pulsus alternans occurred in almost 20%. However, in all animals with tamponade, there was a marked tachycardia and a decrease in cardiac output, mean blood pressure, pulse pressure, and stroke volume. The venous pressure, the diameter of the pulmonary vein, and the pericardial pressure were elevated, although the inspiratory drop in the pericardial pressure was unchanged (1). The voltage of the limb lead electrocardiogram was reduced by over 50%, but there were no S-T segment or T-wave changes.

Flow patterns in the vena cava and pulmonary vein with respiration were not appreciably different in tamponade than in the normal. Inspiration in both the normal and in tamponade increased the caval flow by only 20% in these chronic animal preparations, much less than the 50 to 60% figure found by Shabetai et al. (8) in acute experiments. Although the pulmonary vein diameter frequently increased during inspiration, it usually increased 1 or more beats after the augmented right ventricular stroke volume (RVSV) and increased diameter of the pulmonary artery. Flow in the pulmonary vein increased simultaneously with or shortly after the increase in vein diameter (Fig. 1).

An important relationship observed in over one-half the experiments was a simultaneous increase in RVSV and caval flow with inspiration. The increased capacity of the thoracic cage with inspiration appeared to favor an increase in RVSV even before the venous return was augmented. In the remaining experiments, RVSV increased 1 beat after the increase in caval flow. The decline in LVSV and arterial systolic pressure with inspiration was rarely abrupt, appearing rather as a continued, gradual decline from the preceding peak flow (Fig. 2). The cycle of rising and falling stroke volume of the left ventricle was 1 to 2 beats delayed from the cycle of the RVSV.

A "smoothing function" of the pulmonary vascular bed has been described which reduces the variance in LVSV compared to the variance of RVSV (14). We indeed found a greater variance in RVSV in both normal and in cardiac tamponade, but in only six of nine experiments subjected to statistical analysis. The average of the standard deviations of nine experiments for the LVSV was 11% and 13% for the RVSV in the control state, and 27% and 31% respectively during tamponade. In absolute terms, the variance for LVSV was greater in tamponade than in normal for only three of nine experiments, whereas the variance expressed as a percentage of the mean stroke volume was greater in tamponade

---

Records from a normal animal. In this animal, the pericardium was not entered and the aortic flow probe was on the descending thoracic aorta. With inspiration, the systolic pressure in the pulmonary artery decreased by 6 to 7 mm Hg, but the intrathoracic pressure fell 8 to 9 mm Hg, producing a net increase in the distending pressure, reflected by a prompt increase in the pulmonary artery diameter. One beat later, the pulmonary vein diameter has increased in dimension. The pulmonary vein flow increased slowly with inspiration, peaking in late inspiration or early expiration. The major flow pulse in the pulmonary vein occurred in early ventricular diastole.

in six of nine. This reflects principally the marked reduction in stroke volume uniformly found with cardiac tamponade. This increase in deviation in relation to a smaller mean stroke volume accounts for the exaggerated variation in systolic blood pressure with respiration. The variation in systolic pressure was more than doubled; in the normal state standard deviation was ±4% of the average systolic pressure and ±10% during tamponade.

From the output of the BMD03R program, we ranked the measured variables as predictors of LVSV and aortic systolic pressure. The three statistics used to rank each variable were the correlation coefficient, the partial correlation coefficient, and the proportion of total explained variance. An example of the analysis for LVSV from 1 animal is
MECHANISM OF PULSUS PARADOXUS

given in Table 1. The correlation between these variables and LVSV ranged widely from animal to animal. Even when additional independent variables were used, the multiple correlation coefficient was not necessarily improved. Table 2 is from an experiment in a different animal in which left ventricular filling pressure (left ventricular diastolic — pericardial pressure, LV—PP) was measured in addition to the variables listed in Table 1. Although LV—PP in mid-diastole was the most successful predictor of LVSV, the multiple correlation coefficient was less than in the previous analysis in Table 1. Of additional interest is the lack of predictability of LVSV from end-diastolic LV—PP in this experiment, although in other experiments, this predictor was more successful.

In the nine control experiments, in order of their performance, intrathoracic pressure, preceding diastolic interval, and preceding aortic diastolic pressure were the three best predictors of LVSV, excluding left ventricle—pericardial pressure which was measured in only two of the nine. During tamponade, the right ventricular stroke volume of the preceding beat (RVSV, i-1) was the best predictor of LVSV, followed closely by RVSV (i-2) and intrathoracic pressure.

For aortic systolic pressure in the control animal and in tamponade, left ventricular peak ejection velocity was the major determinant in every animal, followed by intrathoracic pressure, preceding aortic diastolic pressure, and preceding diastolic interval.

If Dornhorst's theory is correct (4), that during inspiration left ventricular filling is reduced because of competition by increased right ventricular filling for a fixed intrapericardial volume, the sum of LVSV plus RVSV should be relatively unvarying. Figure 3 is a Cal-Comp plot of the stroke volumes and their sums during tamponade, indicating that the sums of LVSV and RVSV increase as

TABLE 1

Data from Dog G-39 During Cardiac Tamponade

<table>
<thead>
<tr>
<th>Variable</th>
<th>Regression coefficient</th>
<th>Correlation coefficient</th>
<th>Partial correl. coefficient</th>
<th>Proportion of variance added</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrathoracic pressure</td>
<td>8.7843</td>
<td>.5259</td>
<td>.5581</td>
<td>.2755</td>
</tr>
<tr>
<td>Preceding diastolic interval</td>
<td>— 6.3542</td>
<td>— .7243</td>
<td>— .5018</td>
<td>.2754</td>
</tr>
<tr>
<td>Preceding aortic diastolic pressure</td>
<td>4.2394</td>
<td>.2366</td>
<td>.6064</td>
<td>.0641</td>
</tr>
<tr>
<td>RVSV, (i — 1)*</td>
<td>0.3824</td>
<td>.3412</td>
<td>.7057</td>
<td>.2688</td>
</tr>
<tr>
<td>RVSV, (i — 2)</td>
<td>0.3741</td>
<td>.7122</td>
<td>.6922</td>
<td>.0879</td>
</tr>
</tbody>
</table>

Dependent variable, left ventricular stroke volume.
Multiple correlation coefficient, .9680.

*i — 1 Identifying the beat preceding the beat analyzed, the i th beat. Similarly, i — 2 is the RVSV for the second beat preceding the i th beat.

TABLE 2

Data from Dog G-40 During Cardiac Tamponade

<table>
<thead>
<tr>
<th>Variable</th>
<th>Regression coefficient</th>
<th>Correlation coefficient</th>
<th>Partial correl. coefficient</th>
<th>Proportion of variance added</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrathoracic pressure</td>
<td>13.8259</td>
<td>.2751</td>
<td>.7987</td>
<td>.0757</td>
</tr>
<tr>
<td>Preceding diastolic interval</td>
<td>2.7364</td>
<td>— .3417</td>
<td>.3502</td>
<td>.0923</td>
</tr>
<tr>
<td>Preceding aortic diastolic pressure</td>
<td>0.1083</td>
<td>.3598</td>
<td>.6372</td>
<td>.0340</td>
</tr>
<tr>
<td>LV — pericardial p., mid-diastolic</td>
<td>39.0833</td>
<td>.5967</td>
<td>.8353</td>
<td>.4705</td>
</tr>
<tr>
<td>LV — pericardial p., end-diastolic</td>
<td>5.3076</td>
<td>.3831</td>
<td>.2987</td>
<td>.0347</td>
</tr>
<tr>
<td>RVSV, (i — 1)</td>
<td>0.2896</td>
<td>.3967</td>
<td>.6750</td>
<td>.0885</td>
</tr>
<tr>
<td>RVSV, (i — 2)</td>
<td>0.2581</td>
<td>.4777</td>
<td>.4828</td>
<td>.0481</td>
</tr>
</tbody>
</table>

Dependent variable, left ventricular stroke volume.
Multiple correlation coefficient, .9175.

Circulation Research, Vol. XX, April 1967
A Cal-Comp plot from data from an animal with cardiac tamponade. The stroke volumes of the right and left ventricle and the sums of the 2 stroke volumes are plotted for 39 successive beats. The ordinate represents the reading of planimeter, not milliliters of blood. Gray bars indicate the duration of inspiration. In this animal, the LVSV lags the RVSV by only 1 beat. During inspiration the sum of RVSV plus LVSV increases to over 200% of the sum during expiration, in contrast to the prediction by Dornhorst (4) that the intrapericardial volume is relatively fixed.

Discussion

The cyclical events of the cardiopulmonary system with respiration which we observed in our normal, intact dogs were in substantial agreement with previous reports. The major difference was the pronounced effect of sinus arrhythmia which was present in the great majority of our animals at rest (9). With sinus arrhythmia, the preceding diastolic interval becomes the most important determinant of left ventricular stroke volume and may obscure the effects of the inspiratory enhancement of venous return from the venae cavae. With inspiration in a subject at rest there is an increased heart rate; the diminished diastolic interval results in less complete ventricular filling and a relative decrease in stroke volume. On the other hand, the systolic pressure in the aorta may actually rise in some subjects because the shortened diastole permits less runoff from the aorta, causing a higher diastolic pressure (Fig. 4).

With expiration, heart rate slows and there is increased ventricular filling time. However,
there is obviously a limit to ventricular filling, causing a curvilinear relationship between the interval and stroke volume, previously reported by Hoffman and co-workers (15). However, the relationship is reasonably linear for the first 1 sec of filling time, and the linear correlation coefficient was quite high with sinus arrhythmia. Figure 4 shows the reciprocal nature of caval flow and pericardial pressure with a long diastole, with leveling off of both after approximately 1 sec.

The variations in systolic pressure with respiration are influenced by almost all the determinants of LVSV. In addition to LVSV, there are several factors which influence the aortic systolic pressure in both the normal and in tamponade. Variation in intrathoracic pressure will be directly transmitted to the aorta (16). The preceding diastolic interval will influence the runoff time as well as the left ventricular filling period. This will determine the distension of the aorta, and its dia-

FIGURE 4

Records from a healthy animal with sinus arrhythmia. Note covariance of the stroke volumes of right and left ventricles. The systolic pressure in this animal actually rises with inspiration despite a decline in left ventricular stroke volume due to cardioacceleration, with resulting shortening of filling interval and aortic runoff time. A full inspiration occurs twice in this record, indicated by a substantial fall in pericardial pressure. With longer intervals between beats occurring in early expiration, caval flow—and to a lesser extent, the pulmonary vein flow—ceases and the following atrial systole produces a large, regurgitant pulse.

Circulation Research, Vol. XX, April 1967
stolic pressure, which also has a consistently high correlation with the systolic pressure. Cyclical changes in peripheral resistance and in heart rate emanating from the central nervous system may be major factors in systolic pressure fluctuations. Figure 5 was obtained after a period of forced hyperventilation with a Palmer respirator. The respirator was then turned off, and there was a period of apnea, accompanied by blood pressure oscillations unassociated with even slight respiratory movements. These are frequently referred to as Traube waves, and are ascribed to spill-over from the respiratory center to the cardiovascular center (7).

With cardiac tamponade, there is invariably tachycardia, and very little variation in diastolic interval. The fluctuations in left ventricular stroke volume in tamponade then are largely correlated with events of the right ventricle 1 or 2 beats prior to a given LVSV. In this context, it is instructive to review the experiments of Katz and Gauchat relative to their conclusions that inspiration caused a reduction in venous return to the left atrium and a fall in LVSV (3). They found in dogs with open chest, that pinching the inferior vena cava resulted in a change in the peripheral arterial pulse after 3 or 4 beats, whereas obstructing the pulmonary veins produced...
MECHANISM OF PULSUS PARADOXUS

arterial changes in the first or second beat thereafter. They concluded that the event which conditioned arterial pulse changes with respiration must be pulmonary vein “pooling.” However, they did not comment on their observation that clamping the pulmonary artery involved the same delay as clamping the pulmonary vein. Their observations are then in agreement with our correlation of LVSV with RVSV of the preceding first or second beats. In addition, our measurements indicate that the pulmonary vein flow is relatively constant or increases with inspiration, 1 beat after pulmonary artery flow increases. These observations are also consistent with the results of Shabetai et al. (8), who found that marked variations in systemic blood pressure did not occur with cardiac tamponade if the right heart was bypassed and the pulmonary artery inflow was held constant.

Shabetai and co-workers (8) agreed with Dornhorst and his associates (4) that successful competition of right ventricular filling for a fixed intrapericardial volume was a major cause of reduction of LVSV, resulting in pulsus paradoxus. We did not usually find an abrupt reduction in left ventricular stroke volume with inspiration simultaneous with augmentation of the RVSV, nor did we find that the intrapericardial volume was fixed. On the contrary, the sum of RVSV plus LVSV increased considerably with inspiration simultaneous with augmentation of the RVSV, nor did we find that the intrapericardial volume was fixed. As is evident from Figure 2, the increase in pressure in the pericardium during tamponade is much more rapid in diastole than in the normal, and the instant at which one measures the transpericardial pressure will permit variations of more than 50% (1).

In conclusion, in the normal, resting animal with sinus arrhythmia, inspiration produces cardioacceleration, increased flow in the vena cava, and to a lesser extent, increased flow in the pulmonary vein. When it is not fixed, the filling interval is the single best predictor of the left ventricular stroke volume. In cardiac tamponade, there is tachycardia; the inspiratory surge into the pulmonary artery is the dominant event, and its appearance in the left ventricular output 1 or 2 beats later accounts for most of the changes of pulsus paradoxus. The respiratory variations of stroke volume during tamponade are unchanged from the normal in absolute terms but are increased when expressed as a percentage of the respective means. The exaggerated respiratory variations in blood pressure during tamponade are a result of normal fluctuation of a markedly reduced stroke volume in a vasoconstricted state.

Acknowledgment

Several individuals participated in some of the studies and have co-authored papers with us on other aspects of the problem, particularly Dr. Francis Abel, now at Indiana University, and Dr. David Dillard, who developed the operative techniques. Dr. Richard Kronmal of our Department of Preventive Medicine generously provided access to the computer techniques employed in this report and advice in the choice of programs and in interpretation of the output. Dr. Allen Scher was particularly helpful through many discussions and suggestions during the course of the experiments and preparation of the manuscript.

References

Effect of Respiration on Venous Return and Stroke Volume in Cardiac Tamponade: 
Mechanism Of Pulsus Paradoxus
WARREN G. GUNTEROTH, BEVERLY C. MORGAN, GAY L. MULLINS, George A. 
McGough and Donald G. Breazeale

Circ Res. 1967;20:381-390
doi: 10.1161/01.RES.20.4.381

The online version of this article, along with updated information and services, is located on the 
World Wide Web at:
http://circres.ahajournals.org/content/20/4/381