Pericardial Adaptations during Chronic Cardiac Dilation in Dogs

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SUMMARY. The manner in which the pericardium adapts to chronic cardiac dilation is not known. Recent work from our laboratory indirectly suggested that the size of the pericardium and/or its pressure-volume relation was altered by chronic cardiac enlargement. To examine this question further, we compared pericardial pressure-volume and stress-strain relations, surface area, mass, and average thickness in seven normal dogs and seven with chronic volume overload hypertrophy due to a systemic arteriovenous fistula. Dogs with significant cardiac hypertrophy had an increased pericardial volume at any pressure and a proportionality constant for the slope of the entire curve as determined by nonlinear regression analysis. This was associated with parallel increases in pericardial surface area and mass such that average thickness was unchanged. Stress-strain analysis of the data revealed that the mechanical properties of the pericardium were not significantly different in dogs with chronic cardiac dilation. These results indicate that during chronic cardiac dilation the pericardium enlarges in size and mass. The pericardial chamber is more compliant, although the intrinsic stiffness of the pericardium appears to be unchanged. Further, since pericardial mass is increased, the response to chronic dilation appears to also involve the addition of new pericardial tissue. (Circ Res 54: 294–300, 1984)

Experimental Protocol

Nineteen mongrel dogs weighing between 20 and 31 kg were studied. Seven were normal and 12 had had prior creation of a systemic arteriovenous fistula. The latter was produced through a midline abdominal incision after pentobarbital anesthesia (25 mg/kg) by constructing an approximately 1 cm² anastomosis between the aorta and inferior vena cava below the level of the renal vessels. These dogs were allowed to recover an average of 63 days (range 21–107).

On the day of the study, all dogs were premedicated with morphine sulfate (3 mg/kg) and then anesthetized with urethane (1000 mg/kg) and α-chloralose (100 mg/kg). After endotracheal intubation, respiration was maintained with a Harvard ventilator. The chest was opened through a median sternotomy and either a right or bilateral 5 interspace thoracotomy. The azygous vein was ligated and the caval veins, subclavian artery, brachiocephalic artery, and aorta were isolated. 2-0 Mersilene suture was looped around each of these vessels and left loosely in place. The hila were also isolated and looped with umbilical tape.

A length of 0.5-mm internal diameter Tygon microbore tubing with multiple side holes was placed in the posterior portion of the pericardial space at the level of the left atrium through a small puncture in the left lateral aspect of the pericardium, and secured with a pursestring suture. The tubing was attached to a Statham P23Db pressure transducer. 8F pigtail catheters with multiple side holes were introduced into the left and right ventricles from a femoral artery and jugular vein and the left ventricular catheter was also attached to a Statham P23Db pressure transducer.
transducer. Both the left ventricular and intrapericardial pressure transducers were referenced to the level of the midsternum. In 10 of the hearts (five from each group) a left ventricular sonomicrometer segment length gauge was implanted through a 1- to 2-cm incision in the anterior pericardium. The gauge was used to measure left ventricular dimensions as part of an unrelated in vivo protocol performed before KCl arrest of the heart as described below. The edges of this incision were closely approximated with 6-0 silk suture. This was usually sufficient to seal the intrapericardial space. In cases in which leaks were present, small dabs of cyanocrylate cement were applied over the suture line.

Baseline recordings of left ventricular and intrapericardial pressure were made at 200 mm/sec paper speed using a series 2000 eight-channel Brush-Clevite forced ink recorder. At this point, the venae cavae were ligated, followed by the hila, subclavian artery, brachiocephalic artery, and aorta. Forty milliliters of a solution of 2 mEq/ml of KCl then was injected via the left ventricular pigtail catheter to produce cardiac arrest. The cardiac catheters then were positioned so that side holes lay on either side of the atrioventricular (AV) valves. Placement was verified by direct visualization of both ventricular and atrial expansion upon the injection of saline, and subsequent collapse of the chambers upon removal of the fluid. When a precise volume of saline could be repeatedly injected and withdrawn, the right and left heart chambers were emptied by suction via their respective catheters, which were then occluded by means of a stopcock. Failure to obtain further fluid or air after the experiment confirmed that the chambers had remained collapsed. The pressure-volume relation of the pericardium was determined in all normal dogs and in 11 of the arteriovenous fistula animals. While keeping the pericardium moist with normal saline, all fat tissue was removed by gentle blunt dissection, and two or three sets of ink marks were made approximately 25 mm apart on the intact pericardial surface. The pericardium then was carefully dissected from the heart and spread onto a flat surface. All suture material and dried cement were removed. Radial cuts were made as needed along the edge of the tissue to allow complete flattening. To prevent overstretching the flattened pericardium, we aligned the ink marks made on the pericardial surface at the same distances as that present in situ. We then traced the outline of the pericardium and weighed the tissue on a triple balance scale accurate to 0.05 g. In one normal animal, the pericardial weight was inadvertently omitted. The area of the pericardial surface was determined by hand planimetry of the tracing. Average pericardial thickness was calculated by dividing the pericardial volume (mass/1.05) by the pericardial area. Total heart weight (including short aortic and pulmonary artery remnants and the periaortic fatpad) and left and right ventricular weights were recorded in all animals; the intraventricular septum was considered part of the left ventricle.

**Data Analysis**

The initial volume of the intrapericardial space was considered to be the space occupied by the empty heart. To obtain this value, we divided the heart weight by a specific gravity of 1.05 g/cc. In plotting the pressure-volume relation, we considered the total intrapericardial volume to be this value, plus the volume of saline added.

In order to assess intrapericardial volume at a physiologic pressure, we compared the total intrapericardial volume at a pressure of 2 mm Hg in the two groups. This value was similar to the in vivo intrapericardial pressure at left ventricular end-diastole (see Results). The volume at a pressure of 2 mm Hg was normalized to each dog's body weight to allow comparison between the normal and arteriovenous fistula animals. For normal dogs, we used the body weight measured on the day of the study, and for arteriovenous fistula animals, the weight measured before the initial surgery. Preoperative weight was used to avoid falsely elevated weights due to fluid retention or changes in fat deposition. Because of the very small changes in pressure which occurred with each increment of volume at low intrapericardial pressures, a volume at a pressure of 2 mm Hg was available without the need for extrapolation in all animals but one. In the latter animal (number 3, normal group) the initial intrapericardial pressure was greater than 2 mm Hg without any added volume. Therefore, the volume at a pressure of 2 mm Hg was determined by linear extrapolation in this particular case.

Pericardial pressure-volume relations were analyzed in two ways. First, the data were fit to a monoeponential curve of the form: $P = \alpha \left(e^{\beta V} - 1\right)$, where $P$ is the intrapericardial pressure and $V$ is the intrapericardial volume. The data were analyzed by means of the BMDPAR (1981) nonlinear regression computer program. This package estimates parameters by a pseudo-Gauss-Newton algorithm (Ralston and Jennrich, 1977) and does not use the derivatives of the function. All data were fit with the same convergence criteria, a change in the absolute difference between the sum of the residuals squared at two consecutive iterations of less than 0.00001 for five successive iterations. Visual inspection of computer plots of the residuals revealed them to be randomly distributed in all cases; also, normal probability plots of the residuals indicated that the data were approximately normally distributed. The equation was solved for $\alpha$, and $\beta$, constants which
can be used to characterize the general shape of the curve. An equation of this form has been previously applied to the analysis of the isolated pericardium (Rabkin and Hsu, 1975). It should be noted that this equation assumes that the volume equals 0 ml at a pressure of 0 mm Hg, or that the unstressed volume (V₀) equals 0 ml. In an attempt to arrive at a more realistic V₀ value, we performed linear extrapolation of the data points at pressures less than 5 mm Hg to determine volume at zero pressure. We also applied nonlinear regression techniques to the equation \( P = a(e^{r-v}-1) \), solving for V₀ as well as \( \alpha \) and \( \beta \).

Both of these attempts yielded V₀ values that were negative, and, thus, nonsensical, in a majority of the cases. It is possible that the pericardial sac may not follow this monoeXponential function, but—like the left ventricle—may develop negative pressures at low volumes (Ross et al., 1966; Glantz, 1980). Another possibility is that catheter entrapment occurred at very low volumes, resulting in less accurate pressure measurement in this range of the curve. Whatever the cause, we were unable to determine an empiric V₀ for the pericardial space. Accordingly, rather than fit the data to a more complicated and arbitrary function, we chose to retain the relatively simple function described above to describe the general nature of each curve. Because of these difficulties, we have not reported the derived V₀ values.

The second data analysis entailed derivation of a pericardial stress-strain relation as follows. The pericardium was assumed to be a thin-walled spherical shell. Stress was defined as \( P \times 1/r²h \), where \( P \) = intrapericardial pressure, \( r \) = midwall radius of the pericardium, and \( h \) = pericardial thickness. The internal pericardial radius was calculated from the intrapericardial volume. The volume of pericardial tissue, calculated from its mass, was added to the intrapericardial volume to allow determination of an external pericardial radius. Subtraction of these two values yielded pericardial thickness. Pericardial stress then was derived for each point on the pressure-volume curve. Pericardial strain was defined as \( (r - \lambda h)/r₀ \) (Langrangian), and expressed as a percent. The radius at a low stress value (50 mm Hg) was defined as \( r₀ \). We used this value, rather than a radius at zero transmural pressure, because of the aforementioned difficulties in extrapolating an unstressed pericardial volume. This analysis could not be performed on the normal dog in which the pericardial weight was not recorded. The stress-strain data were fit to an exponential curve of the form \( e = a(e^{\alpha r} - 1) \), using the previously defined convergence criteria, and the constants were compared between groups.

To determine whether the creation of the arteriovenous fistula had produced significant cardiac hypertrophy in individual animals, we calculated the heart weight:body weight ratio in the seven normals and an additional group of 20 normal dogs in which this ratio was determined in an identical fashion. The mean ± 1 SD for the total group of 27 normal animals was 6.6 ± 0.7 g/kg. We used a value of 9.0 g/kg (two standard deviations above the mean) as the upper limit of normal; all arteriovenous fistula animals with a heart weight:body weight ratio greater than this value were considered to have significant hypertrophy.

Statistical comparisons were performed on the anatomic data, including heart weight:body weight ratios and pericardial surface area and mass data using the unpaired t-test. Results are reported as mean ± 1 SEM. Comparison of the pressure-volume and stress-strain relations between groups was performed using a Mann-Whitney-Wilcoxon test (Gibbons, 1976).

Results

Seven of the 12 arteriovenous fistula dogs had significant cardiac hypertrophy by the criterion described above. Because the aim of this study was to examine the effects of cardiac enlargement on pericardial properties, statistical comparisons were confined to normal animals and the seven dogs with significant hypertrophy. All of the morphological data are shown in Table 1. Heart weight:body weight ratio was 6.36 ± 0.25 g/kg in normals and 9.67 ± 0.38 g/kg in hypertrophied animals (\( P < 0.001 \)). Left ventricle weight:body weight ratio was 4.01 ± 0.14 g/kg in normals and 6.04 ± 0.27 g/kg in hypertrophied animals (\( P < 0.001 \)), while right ventricle weight:body weight ratio was 1.63 ± 0.13 g/kg in normals and 2.25 ± 0.11 g/kg in hypertrophied animals (\( P < 0.001 \)). The mean intrapericardial pressure at left ventricular end-diastole measured before cardiac arrest was 2.3 ± 1.2 mm Hg in all animals and was not significantly different for the normal and hypertrophied groups.

Pressure-Volume Relations

Pressure-volume relations were determined in six normal and seven hypertrophied dogs. The plotted data for a representative dog from each group are shown in Figure 1. As demonstrated in the figure, the pressure-volume relation was shifted to the right in the hypertrophied animals; this was true in every case, whether or not the volume was normalized to body weight. At an intrapericardial pressure of 2 mm Hg, close to the mean intrapericardial end-diastolic pressure measured before cardiac arrest, the intrapericardial volume was 7.0 ± 1.4 ml/kg body weight in normals and 10.8 ± 0.7 ml/kg body weight in hypertrophied animals (\( P = 0.008 \)). Derived pericardial pressure-volume constants are shown in Table 2. The constant of proportionality for the slope of this relation (\( \beta \)) was significantly reduced in hypertrophied animals (0.001 < \( P < 0.01 \)). \( \alpha \) values were not significantly different between the groups.

Stress-Strain Relations

Representative stress-strain curves from one dog in each group are shown in Figure 2. The exponential constants of the stress-strain relation are shown in Table 2. There were no significant differences in \( \alpha \) or \( \beta \) between the groups.

Pericardial Surface Area, Mass, and Thickness

These data were available in all dogs, except for the one normal animal in which the pericardium was not weighed. The pericardial surface area, normalized to preoperative body weight, was 5.74 ± 0.21 cm²/kg in normals and 7.49 ± 0.25 cm²/kg in hypertrophied animals (\( P < 0.001 \)). The pericardial weight:body weight was 0.17 ± 0.02 g/kg in normals and 0.24 ± 0.02 g/kg in hypertrophied animals (\( P = 0.023 \)). Average pericardial thickness in normal
Morphological Comparisons between Normal and Chronic Volume Overload Animals

<table>
<thead>
<tr>
<th>Dog no</th>
<th>BW (kg)</th>
<th>HW (g)</th>
<th>HW/BW (g)</th>
<th>LVW (g)</th>
<th>LVW/BW (g)</th>
<th>RVW (g)</th>
<th>RVW/BW (g)</th>
<th>Peri A (cm²)</th>
<th>Peri A/BW (mm)</th>
<th>Peri Th (mm)</th>
<th>Peri vol at 2 mm Hg</th>
<th>Peri vol at 2 mm Hg</th>
<th>Days Post-Op</th>
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<td>134</td>
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<td>0.28</td>
<td>163</td>
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</tr>
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</table>

**SEM**

1 1.3 5.3 0.25 3.1 0.14 2.4 0.13 0.42 0.02 4.7 0.21 0.03 8.4 0.5

Chronic volume overload

1 22 249 11 31 149 6.79 63 2.86 6.8 0.30 178 8.09 0.36 244 11.1 57
2 27 243 8.99 148 5.50 58 2.13 7.4 0.27 186 6.89 0.38 291 10.8 68
3 31 276 9.03 171 5.59 61 1.99 7.1 0.23 209 6.83 0.32 403 13.0 95
4 28 246 8.91 158 5.38 61 2.19 5.1 0.19 190 6.88 0.26 234 8.4 49
5 26 283 10.82 190 7.24 58 2.21 5.2 0.20 216 8.23 0.23 350 13.5 46
6 25 243 9.64 145 5.73 58 2.28 5.6 0.22 207 8.21 0.26 251 10.0 47
7 30 274 9.00 184 6.05 64 2.10 7.6 0.25 222 7.30 0.33 269 9.0 107
Mean 27.0 259 9.67 163.6 6.04 64 2.25 6.4 0.24 201 7.49 0.31 292 10.8 67

**SEM**

1 1.2 6.6 0.38 6.9 0.27 1.0 0.11 0.40 0.02 6.2 0.25 0.02 23.7 0.7 9.3

*Pressure-volume relation not obtained, due to persistent leak.*

Definitions. BW = body weight; HW = heart weight; LVW = left ventricular weight; RVW = right ventricular weight; Peri W = pericardial weight; Peri A = pericardial area; Peri Th = average pericardial thickness; Peri vol = pericardial volume; P = P value comparing normals and chronic volume overload, unpaired t-test; NS = not significant (P > 0.05).

Discussion

Under normal conditions, the pericardium serves to limit acute distension of the heart, most notably at elevated cardiac volumes. This has been demonstrated in the setting of volume infusion (Bartle et al., 1967), and soon after creation of a systemic arteri-

FIGURE 1. Representative pericardial pressure-volume relations in one normal animal (closed circles) and one chronic volume overload animal (open circles), along with derived curve fits (solid lines).

FIGURE 2. Representative stress-strain relations for the same animals displayed in Figure 1, along with the derived curve fits (solid lines).
ovenous fistula (LeWinter and Pavelec, 1982). The latter work also demonstrated that—as the volume overload state progressed from the acute to the chronic phase—the apparent restraining effects of the pericardium were attenuated, indicating that some form of pericardial adaptation had occurred. In this study, the initial intrapericardial volume was defined as that occupied by the empty heart, and would thus be larger in chronic volume overload dogs. Thus, the magnitude of the overall rightward shift of the pressure-volume relation which we observed was considerable at physiological intrapericardial pressures. This rightward shift of the pericardial pressure-volume relation constitutes one aspect of pericardial adaptation to chronic enlargement of the intrapericardial contents.

The proportionality constant for the slope of the entire curve ($\beta_i$), was smaller in volume-overloaded dogs. This finding indicates that the pericardium is more compliant as a chamber after adaptation to the chronic volume overload state and constitutes a second form of adaptation. A given increment in intrapericardial volume will cause a smaller pressure rise in the hypertrophied animal. Despite these highly significant alterations in the pressure-volume relation of the pericardium, the exponential constants of the stress-strain relation were not significantly different in the normal and chronic volume overload animals, suggesting that these adaptations occur without a substantial change in the intrinsic stiffness of the pericardium. The fundamental response of the pericardium to an increase in heart size would therefore appear to be an increase in surface area and chamber compliance without a significant change in its thickness or material properties. Despite the previously discussed difficulties in extrapolating a meaningful unstressed pericardial volume from our curve fits, it is nonetheless highly likely that $V_0$ increased markedly in the animals with enlarged hearts, based on the considerable increase in pericardial surface area and substantial rightward shift of the curve. This increase in $V_0$ is

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**TABLE 2**

Derived Constants for Pressure-Volume and Stress-Strain Data

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>Pressure-volume</th>
<th>Stress-strain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\alpha_i$ (SD, mm Hg)</td>
<td>$\beta_i$ (SD)</td>
</tr>
<tr>
<td>Normals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.2541 (0.02088)</td>
<td>0.0125 (0.00027)</td>
</tr>
<tr>
<td>2*</td>
<td>0.1730 (0.01989)</td>
<td>0.0317 (0.00307)</td>
</tr>
<tr>
<td>3*</td>
<td>0.1603 (0.3288)</td>
<td>0.0201 (0.00088)</td>
</tr>
<tr>
<td>4*</td>
<td>0.0371 (0.00740)</td>
<td>0.0220 (0.00074)</td>
</tr>
<tr>
<td>6</td>
<td>0.0154 (0.00624)</td>
<td>0.0226 (0.00132)</td>
</tr>
<tr>
<td>7</td>
<td>0.7425 (0.24794)</td>
<td>0.0087 (0.00095)</td>
</tr>
<tr>
<td>Chronic volume overload</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.6124 (0.20231)</td>
<td>0.0051 (0.00025)</td>
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<tr>
<td>2*</td>
<td>0.0903 (0.03246)</td>
<td>0.0090 (0.00072)</td>
</tr>
<tr>
<td>3</td>
<td>0.0642 (0.2303)</td>
<td>0.0076 (0.00058)</td>
</tr>
<tr>
<td>4*</td>
<td>0.2002 (0.05954)</td>
<td>0.0104 (0.00070)</td>
</tr>
<tr>
<td>5*</td>
<td>0.0546 (0.00815)</td>
<td>0.0097 (0.00026)</td>
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<tr>
<td>6</td>
<td>1.0150 (0.12692)</td>
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</tr>
<tr>
<td>7</td>
<td>0.4506 (0.03770)</td>
<td>0.0074 (0.00018)</td>
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</table>

Definitions: VMSE = The square root of the mean squared error of the observed and predicted values of the exponential curve; SD = standard deviation; NS = not significant.
* Small pericardial incision made.
† Cyanoacrylate cement used.
almost certainly the major cause of our findings in regard to the shape and position of the pericardial pressure-volume relation, since such an increase would, in and of itself, both shift the curve to the right and result in a smaller change in pressure for a given change in volume. In this regard, normal dog no. 7 is of interest. In this animal, the constant for the pressure-volume relation was low, falling within the range of values found in the volume overload group. This was the largest animal in the normal group, so that the empty intrapericardial space (derived from the heart weight) would have been large, compared with the other animals, lending support to our conclusion that the differences in pressure-volume relations between the groups is largely a result of the overall size of the unfilled pericardial space.

Review of the stress-strain data shows that the constants from two of the chronic volume overload animals fell below the range of values found in normal dogs. Although our statistical analysis did not reveal a significant difference between the groups, it should be pointed out that large variations are present. Thus, we cannot conclude that the stress-strain relations are precisely the same in the groups. However, if changes are present, they are not consistent, and not of major proportions.

We found that the pericardial surface area increases during chronic cardiac dilation. Interestingly, Hort and Braun (1962) have demonstrated a relation between heart weight and pericardial size in a variety of species. One mechanism for this increase in area could be the occurrence of creep, which has been demonstrated in pericardial strips (Rabkin et al., 1974). Three factors make it difficult to invoke this mechanism as the sole explanation for our results. First, the average normalized surface area in arteriovenous fistula animals was 23% larger than the mean values for normals and, at its extreme, was 68% larger (see Fig. 2). In the previously cited studies, creep resulted in dimensional changes of a much smaller magnitude. Although creep was necessarily examined over a short period of time in these studies, the creep rate declines with time, and it is difficult to envision this phenomenon occurring indefinitely, and resulting in changes in size of the tissue that are an order of magnitude larger than those observed during short-term creep tests. Second, whereas the surface area of the pericardium increased in size, we also found that pericardial mass increased, resulting in a pericardium with the same average thickness. Creep alone should produce a pericardium with a larger surface area but a smaller average thickness. Third, we found the stress-strain relation of the pericardium in chronic volume overload to be unchanged. Experiments on isolated pericardium have shown that, after the occurrence of creep, the modulus of elasticity of the pericardium is increased (Rabkin et al., 1974). These factors strongly suggest that pericardial adaptation entails more than creep alone.

In studies performed with isolated pericardial strips, Lee and Boughner (1981) subjected the pericardium to a sustained load for periods up to 4 hours. This sustained load shifted the pericardial stress-strain relation, which was attributed to rearrangement of collagen fibers. Further, under these conditions, the pericardium lacked plasticity, i.e., the stress-strain relation changed in the absence of tissue deformation. In contrast to the effects of a sustained but short-term load, our data indicate that chronic loading does not significantly alter the stress-strain relation, but does result in permanent tissue deformation, as manifested by the increase in pericardial surface area.

Whether our stress-strain data can be compared to results obtained from isolated tissue is unclear. Our analysis was based on a spherical, thin-walled shell model. Although the thin-walled assumption is certainly a reasonable one for the pericardium, it remains uncertain whether a sphere is an appropriate geometric model. Further, it is also possible that the geometric shape assumed by the pericardial sac could change as a function of the volume of its contents. Thus, for instance, the pericardium could have assumed some asymmetric, partially collapsed shape when there was no fluid inside it, and could have changed to a more spherical shape after large amounts of fluid had been added. Another problem is the determination of an unstressed radius or volume, which has inherent difficulties with both isolated tissue experiments and in the setting of an intact pericardium. Also, uniaxial strain behavior of the pericardium is dependent on the orientation of the tissue, as well as on the site of tissue harvest (Bing and Wiegner, 1982). Furthermore, isolated tissue techniques commonly use a preconditioning phase prior to the data acquisition. This is not possible, when the pericardium is left intact. These factors, taken together, suggest caution in comparing data from the two techniques.

The parallel increase in pericardial mass and area that we observed implies that new pericardial tissue is produced in response to chronic cardiac enlargement. However, since we did not measure dry weights of the pericardial specimens, we cannot exclude the possibility that tissue edema is wholly or in part responsible for the increased mass. In general, an increase in the salt and water content of tissue interstitium over and above that which would normally accompany any new structural constituents should result in increased stiffness (Granger, 1981). Therefore, our findings of increased compliance and unchanged stress-strain constants in animals with cardiac dilation would suggest that tissue edema is not the cause of increased pericardial mass in these animals.

If it is assumed that new tissue is indeed present and that the stimulus for its production is enlargement of the cardiac chambers and the subsequent increased load to which the pericardium is exposed, one would hypothesize that any cause of increased
intrapercardial volume—for instance, a large, chronic effusion—would result in similar alterations in pericardial pressure-volume relations in association with an increase in the amount of pericardial tissue. The clinical observation that slowly accumulating pericardial effusions can become quite large without causing hemodynamic embarrassment (Shabetai, 1982) is consistent with this hypothesis.

The significance of our findings in relation to clinical cardiac dilation is at present uncertain. The arteriovenous fistula model results in global cardiac enlargement, and therefore might differ from common clinical situations in which dilation is frequently confined to one chamber or one side of the heart. However, it is interesting to note that—whereas acute cardiac dilation in humans may result in hemodynamic alterations resembling constrictive pericardial disease (Bartle and Hermann, 1967)—in the setting of chronic four chamber cardiac dilation, such hemodynamic features are not usually encountered. Another possible difference is that, in humans, the assumption of the upright posture could result in variations in the stress to which the pericardium is exposed, both by virtue of changes in intracardiac volume, and in external stresses imposed by the attachments of the pericardium to adjoining structures such as the diaphragm. Presumably, the stimulus to adaptation would be maximal during the prolonged recumbency of sleeping.

A further point of clinical relevance has to do with diastolic ventricular interaction. The role of the pericardium in modulating ventricular interaction has been well described, and it has been shown that coupling of the ventricles is diminished when the pericardium has been removed (Bemis et al., 1974; Grant SA, Misbach GA, Moores WY, Mathey DG, LeKven J, Stowe DF, Parmley WW, Tyberg JV (1978) The pericardium substantially affects the left ventricular pressure-volume relationship in the dog. Circ Res 42: 422–441


INDEX TERMS: Pericardium • Cardiac dilation • Hypertrophy

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