Ventricular Elastic Modulus as a Function of Age in the Syrian Golden Hamster

RICHARD L. KANE, B.S., THOMAS A. McMAHON, PH.D., RICHARD L. WAGNER, B.E.E., AND WALTER H. ABELMANN, M.D.

SUMMARY Analysis of passive right and left ventricular pressure-volume curves for hearts of 72 Syrian golden hamsters studied in vitro showed increases in ventricular weight, volume, and compliance at mid-age. Both ventricles were filled by syringe pumps at a constant rate. Ventricular compliance ($dV/dP$) was determined by electronic differentiation of the intraventricular pressures and formation of the ratio $(dV/dt)/(dP/dt)$ as a continuous function of intraventricular pressure between 0 and 30 mm Hg. By relating, with justification, the left ventricle to a thin-walled elastic sphere, ventricular elastic moduli, $E$, for different ages were compared at constant levels of myocardial wall stress, $a$. The elastic modulus $E$ proved to be a linear function of $a$. The slope of the $E-a$ plot yielded a stiffness constant, $K$, for each age group. Body weight, heart weight, end-diastolic volume, and $dV/dP$ all varied by more than 200% up and then down as a function of age, but $K$ was not a significant function of age. These results suggest that the aging heart does not normally undergo substantial alterations in passive properties that affect the muscle cells and fibers themselves, but rather that the observed changes in compliance are primarily attributable to alterations in ventricular size.

VENTRICULAR compliance has become recognized with increasing frequency as a major determinant of cardiac function both in health and in disease. Now that it is possible to measure the compliance of the ventricles in human patients, there is great interest in interpreting these measurements. Diamond et al. found that the reciprocal of ventricular compliance ($dV/dP$) is a linear function of filling pressure so that, for any individual ventricle, $dP/dV = aP + \beta$. The constants $a$ and $\beta$ were found to be constant for a particular normal heart and independent of initial ventricular volume and filling pressures, but $a$ was different for different ventricles.

Mirsky and Parmley correctly identified the local slope of the stress-strain curve, $E = de/dx$, as the important intrinsic parameter in measurements of ventricular compliance. Here the stress, $\sigma$, is the force per unit of cross-sectional area which acts on the myocardial tissue and the strain, $\epsilon$, is the incremental change in length per unit of length. They demonstrated that the elastic tangent modulus $E$ is a linear function of $\sigma$ and related to it by the equation $E = K\sigma + C$, where $C$ is the intercept. They found that the stiffness constant, $K$, is nearly the same for normal canine hearts and isolated cat papillary muscles, but is lower for freshly infarcted canine hearts. When $E$ is a linear function of $\sigma$ the stress-strain curve is exponential; this relationship is found for many biological materials, including the series elastic components of cardiac muscle.

Recently, Mirsky and co-workers used their method to determine the stress-strain curve during diastole for 10 normal subjects, 34 subjects with coronary artery disease, and 22 subjects with cardiomyopathy. They found values for $K$ to be generally elevated for diseased hearts; this suggests that fibroed and scarred ventricles are made of a material that is intrinsically stiffer (higher $E$) at a given stress than is normal ventricular tissue. Parmley and associates examined resected human ventricular aneurysms and found consistently greater values for $K$ in fibrous, as opposed to muscular, aneurysms.

The curve $E$ vs. $\sigma$, and its slope $K$, thus appear to be excellent candidates for a new diagnostic test, but before one can ascertain the difference between a pathological and normal state, one must decide what the normal state is. The test most often will be applied to ventricles that have felt the effects of age. It is reasonable to expect that the progressive cross-linking of collagen, known to accompany aging, may promote an increased $E$ for a given level of stress, hence an increased $K$ for older patients. The evidence bearing on this question is incomplete. Band et al. found no significant difference in values for $E$ in the thoracic aorta of young and old rats. Korecky et al. observed generally increased compliance of the left ventricles of older, as opposed to younger, rats. Lenkiewicz et al., in studies on human hearts, found a small increase with age in the volume proportion of collagen gel in regions where muscle fibers were predominantly transverse, but no significant increase in the central myocardial zone. Sulkin and Sulkin reported no differences in cardiac mitochondria, sarcoplasmic reticulum, or Golgi apparatus between young and old rats. Singh and Kanugula found lactate dehydrogenase activity of cardiac muscle to peak in rats of mid-age. Romero et al., in their study of pressure-volume relations for sheep of different ages, found ventricular compliance to be highest in adult as opposed to newborn or fetal sheep. On the other hand, no significant age-related differences between young and adult pigs and cats were observed by Lee and Downing when left ventricular distensibility was normalized in terms of ventricular mass. There is abundant evidence that the contractile properties of the myocardium do change (Heller and Whitehorn showed a substantial...
increase with age in myosin ATPase activity and prolongation of time-to-peak tension development in rat ventricular muscle, but the issue of passive compliance changes with age seems to be less well understood.

In this study, we recorded pressure as a function of volume in a series of hamster hearts from an inbred strain at a variety of ages, and from a random-bred strain at older ages. We used a simple model based on the law of Laplace to calculate $E$ as a function of wall stress and thus determine $K$ as a function of age. The validity of the model in providing reliable calculations for $E$ is discussed.

**Methods**

We studied a total of 72 golden Syrian hamsters divided into nine groups. Fifty-five, comprising seven of the groups, were from Lakeview Hamster Colony, strain LSH-SSLAK. The remaining 17, comprising the two groups with the oldest hamsters, were from Lakeview Hamster Colony’s random-bred strain. Old animals from the LSH-SSLAK strain were not immediately available to us when we needed them, therefore inclusion of animals from a different breeding group was primarily a matter of expediency. We felt that we were justified in using the latter because their growth curves were similar to those of the LSH strain, as were their heart to body weight ratios. On the other hand, we do not feel justified in emphasizing the comparative data between the different strains, and include these data only for the sake of completeness. Hamsters reach full sexual maturity by the age of 2 months, middle age is considered to extend roughly from 4 to 10 months, and old age is reached within a year and a half.

The experimental arrangement used to study pressure-volume relationships and compliance is similar to that previously used in this laboratory in a study of ventricular compliance in mice with myocarditis associated with Chagas’ disease. The animals were anesthetized with intraperitoneal sodium pentobarbital, 50 mg/kg of body weight. Sodium heparin (100 units) was then injected into the femoral vein to prevent clot formation. After thoracotomy, all vessels leading to and from the heart were ligated and the isolated organ was removed from the body. The atrial appendages were opened and sponged dry, and double-lumen cannulas were inserted into the ventricles through the mitral and tricuspid valves. Ligatures were placed around the atrioventricular grooves, care being taken not to compromise the ventricles. The hearts were kept moist but were not submerged. The outer polyethylene tubings of the cannulas (PE 50, inside diameter, 0.03 inches, outside diameter, 0.05 inches) were connected to a duet, calibrated Harvard infusion pump operating at a rate of 0.206 ml/min. Neither halving nor doubling this rate had any noticeable effect on the pressure-volume relationship. Normal saline solution at room temperature (22 ± 1°C) was used as the filling fluid. The inner needles (o.d., 0.016 inches) were connected by a three-way stopcock to strain gauge manometers (Statham P23G). The zero reference point was the level of the atrioventricular valves. Before infusion, and with the stopcocks open to air, both ventricles were compressed dry in order to reduce residual fluid to a minimum. To better approximate physiological conditions, and because results have been shown to vary with univentricular vs. biventricular filling of the heart, pressure-volume relationships and their first derivatives, $dP/dV$, were recorded simultaneously for both ventricles on a direct-writing four-channel recorder (Sanborn 964). The differentiators were active devices with unity gain at 0.1 Hz, a gain slope of 6 db per octave to 2 Hz, rolling off 12 db per octave above 10 Hz. To calibrate them we manually generated a constant slope in the pressure-volume curve $P(V)$ and measured the deflection of the derivative channels $dP(V)/dt$. Since the differentiators were linear over the range of applied inputs, their deflections were linearly related to a constant by the slopes of the input signals.

Insertion of cannulas always was completed within 15 minutes after thoracotomy, and the entire experiment within 30 minutes. Previous studies in our laboratory have shown that the pressure-volume relationships do not change within 30 minutes after thoracotomy. The preparation was considered acceptable when the cannulas were open and lying freely within the ventricular cavities, and when there was no evidence of leakage from inspection of the heart and the pressure-volume curves. These criteria resulted in the rejection of several preparations. On completion of infusion, the hearts were weighed and examined grossly. Serial sections of representative specimens were examined histologically after staining with hematoxylin and eosin, Van Gieson, Masson trichrome, and also Congo red. The significance of differences in measurements between different groups of animals was determined by Student’s $t$-test.

In this study, compliance is defined as $dV/dP$, or the reciprocal of stiffness $(dP/dV)$, and was calculated at isobaric intervals of 0–30 mm Hg. This is a direct measure of the passive diastolic properties of the entire heart. To determine whether or not $dV/dP$ is an accurate reflection of the elastic properties of the myocardial muscle fibers, and to calculate the stress-strain curve for those fibers from the measured data, we need a mathematical model for the passive elastic heart. The model derived in Appendix I, and its application in Appendix II, justify the definition of $E$ as a function of $e$ for a wide range of hearts of differing sizes and conditions.

**Results**

A representative tracing of the simultaneously recorded right and left ventricular pressure-volume curves and their first derivatives is shown in Figure 1. Measured and derived values for each group are presented in Table 1.

There were significant increases in both the heart and body weight during adolescence. Both heart weight and body weight remained nearly constant during middle age, but exhibited a significant decrease in older age. These fluctuations in weight paralleled each other quite closely, as can be seen by the relatively constant value of the heart to body weight ratio.

Right and left ventricular volumes and compliances, as a function of age, determined isobarically at 10 mm Hg from the pressure-volume curves, are shown in Figure 2. Significant increases in volume were seen throughout adolescence and into middle age, whereas significant decreases were evident in older age.
Much as heart weight and ventricular volume, right and left ventricular compliance is characterized by an increase during adolescence, a leveling off in middle age, and a decrease in older age. Despite the geometrical dissimilarities between the right and left ventricles, the compliances are remarkably alike.

The results of the constant wall stress evaluation are shown in Table 2 and Figure 3. In Figure 3, the data for $E$ as a function of wall stress $\sigma$ are plotted and fitted to the best straight line (by least squares) for several ages. The data fall very close to a straight line for each age considered. The slope $K$ for all ages is shown in Table 3. $K$ appears to increase with age; however, the correlation coefficient ($r$) of $K$ vs. age is 0.5160, not significantly different from a correlation coefficient of $p = 0.05$.

Gross and microscopic examination of the selected hearts revealed no pathological changes. No consistent differences in the predominance of collagen were evident, and no deposits of amyloid were seen in the older hearts.

**Discussion**

**CALCULATING THE ELASTIC MODULUS**

The actual geometry of the mammalian heart is quite complicated. The ventricles are not spheres, nor are they thin-walled. Yet an equivalent spherical model of a ventricle, derived to be valid only for conditions normally found in thin-walled pressure vessels, may be appropriate for the task of determining the effective ventricular elastic modulus, $E$.

The model (derived in Appendix I) is based on the postulate that the mammalian heart is thick in regions where the radius of curvature is large, and thin in regions where it is small.

**Table 1**  

<table>
<thead>
<tr>
<th>Age (mo.)</th>
<th>N</th>
<th>BW (g)</th>
<th>HW (g)</th>
<th>HW/BW</th>
<th>$V_{ec}$ ($\mu l$)</th>
<th>$V_{lv}$ ($\mu l$)</th>
<th>$dV/dP_{ec}$ ($\mu l/mm Hg$)</th>
<th>$dV/dP_{lv}$ ($\mu l/mm Hg$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>9</td>
<td>49 ± 3</td>
<td>0.1806 ± 0.0076</td>
<td>0.0038 ± 0.0001</td>
<td>41.26 ± 5.39</td>
<td>27.94 ± 6.83</td>
<td>1.57 ± 0.25</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>95 ± 3</td>
<td>0.2967 ± 0.0121</td>
<td>0.0031 ± 0.0001</td>
<td>40.63 ± 5.95</td>
<td>17.31 ± 3.69</td>
<td>1.24 ± 0.18</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>19</td>
<td>96 ± 3</td>
<td>0.3180 ± 0.0115</td>
<td>0.0033 ± 0.0001</td>
<td>58.63 ± 4.82</td>
<td>36.63 ± 5.92</td>
<td>1.24 ± 0.18</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>122 ± 3</td>
<td>0.3951 ± 0.0114</td>
<td>0.0033 ± 0.0001</td>
<td>147.42 ± 15.81</td>
<td>119.14 ± 13.98</td>
<td>1.24 ± 0.18</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>124 ± 6</td>
<td>0.4054 ± 0.0224</td>
<td>0.0033 ± 0.0001</td>
<td>112.54 ± 10.45</td>
<td>86.81 ± 7.99</td>
<td>1.24 ± 0.18</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>6</td>
<td>99 ± 3</td>
<td>0.3025 ± 0.0125</td>
<td>0.0034 ± 0.0001</td>
<td>82.63 ± 12.77</td>
<td>51.68 ± 15.65</td>
<td>1.24 ± 0.18</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>4</td>
<td>69 ± 6</td>
<td>0.2292 ± 0.0162</td>
<td>0.0034 ± 0.0001</td>
<td>49.75 ± 5.58</td>
<td>28.48 ± 8.05</td>
<td>1.24 ± 0.18</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>8</td>
<td>155 ± 5</td>
<td>0.5622 ± 0.0171</td>
<td>0.0036 ± 0.0001</td>
<td>78.84 ± 9.33</td>
<td>72.29 ± 9.89</td>
<td>1.24 ± 0.18</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>9</td>
<td>160 ± 6</td>
<td>0.5690 ± 0.0285</td>
<td>0.0036 ± 0.0002</td>
<td>72.91 ± 4.67</td>
<td>70.80 ± 4.20</td>
<td>1.24 ± 0.18</td>
<td></td>
</tr>
</tbody>
</table>

$N =$ number of hamsters.  
Values are means ± SEM. Ventricular volumes and compliances all are expressed at an intraventricular pressure of 10 mm Hg.
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**Figure 2** Right (RV) and left (LV) ventricular volume and compliance as a function of age. The comparisons have been made at an intraventricular pressure of 10 mm Hg. Significance of the difference between groups: * P < 0.001; ** P < 0.005; *** P < 0.025.

is small, thus keeping the local stress applied to the ventricular wall material approximately constant. The law of Laplace, which assumes that no bending moments, only tensile forces, are applied to any little element of wall material and thus that the stress is constant across the thickness of the wall, may be applied to the dimensions of fixed mammalian hearts to calculate the principal stresses at a variety of points. This principle was first used by Woods in 1892 for canine hearts and was repeated recently by Martin and Haines for the hearts of rats, guinea pigs, rabbits, dogs, hogs, and calves. Woods measured the thickness, \( h \), and the principal radii of curvature, \( r_1 \) and \( r_2 \), for hearts inflated at end-diastolic pressure, and found that the ratio \( h(1/r_1 + 1/r_2) \) was constant to within ±5% over the surface of canine hearts. Martin and Haines found that the coefficient of variation for this product was only 22%, even though heart weight varied by a factor of 767 between their specimens. The result seems reasonable when we consider that, were it not true, the hearts of a particular species, or selected segments of the same heart, would have to be made of intrinsically stronger muscle. The ventricular wall is composed of both muscle and connective tissue, with the muscle fibers arranged in overlapping spiral patterns. During systole, the direction of the local stresses developed in the ventricular wall can be expected to be different in the several layers of muscle, but roughly of uniform average magnitude as demonstrated by the studies cited above because the intrinsic structure of the myofibrils does not change with location throughout the ventricle.

A number of authors has suggested thick-walled models of the ventricles. In these models, stress is allowed to vary across the wall thickness. These more complex models may indeed be an improvement over the law of Laplace for the calculation of wall stresses in diastole, if it is true that the ventricle changes shape enough during filling to produce significant bending stresses in the wall. There now is a sufficient number of calculations and experiments which compare thick-walled and Laplace law models. Mirsky compared the Laplace relation for a prolate spheroid, sphere, and general ellipsoid with calculations for a thick-walled model and concluded that a “modified Laplace’s law,” based on the internal radii of curvature, gave close agreement with the thick-walled theory. Hood et al., using thin- and thick-walled ellipsoidal models, compared calculations of left ventricular circumferential wall stress in human subjects and decided that thin-walled models of the type suggested by Sandler and Dodge overestimated mean stress, as determined from the thick-walled model of Wong and Rautaharju, by an average of less than 10%. McHale

### Table 2 Left Ventricular Elastic Modulus (E) Evaluated for Each Group at Various Levels of Myocardial Wall Stress (\( \sigma \))

<table>
<thead>
<tr>
<th>Age (mo.)</th>
<th>( \sigma = 3.5 ) mm Hg</th>
<th>( \sigma = 5 ) mm Hg</th>
<th>( \sigma = 7 ) mm Hg</th>
<th>( \sigma = 10 ) mm Hg</th>
<th>( \sigma = 15 ) mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>31.44 ± 3.57</td>
<td>34.92 ± 5.55</td>
<td>37.12 ± 7.17</td>
<td>39.10 ± 11.55</td>
<td>152.59 ± 16.51</td>
</tr>
<tr>
<td>2</td>
<td>26.43 ± 1.74</td>
<td>36.00 ± 2.14</td>
<td>42.72 ± 2.72</td>
<td>51.86 ± 3.70</td>
<td>133.41 ± 5.04</td>
</tr>
<tr>
<td>4</td>
<td>28.70 ± 2.08</td>
<td>40.22 ± 2.17</td>
<td>57.31 ± 2.21</td>
<td>84.55 ± 2.37</td>
<td>136.19 ± 3.54</td>
</tr>
<tr>
<td>6</td>
<td>26.33 ± 3.14</td>
<td>43.04 ± 4.12</td>
<td>69.22 ± 4.62</td>
<td>108.72 ± 6.52</td>
<td>176.35 ± 9.46</td>
</tr>
<tr>
<td>8</td>
<td>26.25 ± 1.52</td>
<td>39.23 ± 2.00</td>
<td>59.69 ± 3.97</td>
<td>94.08 ± 6.66</td>
<td>156.36 ± 9.88</td>
</tr>
<tr>
<td>10</td>
<td>29.58 ± 5.31</td>
<td>43.01 ± 6.68</td>
<td>64.09 ± 8.35</td>
<td>98.22 ± 11.34</td>
<td>152.75 ± 18.63</td>
</tr>
<tr>
<td>11</td>
<td>26.29 ± 0.88</td>
<td>38.84 ± 0.79</td>
<td>56.42 ± 1.56</td>
<td>83.09 ± 3.86</td>
<td>129.41 ± 6.79</td>
</tr>
<tr>
<td>17</td>
<td>29.33 ± 1.52</td>
<td>45.34 ± 2.54</td>
<td>67.67 ± 4.27</td>
<td>101.74 ± 7.13</td>
<td>159.98 ± 11.94</td>
</tr>
<tr>
<td>24</td>
<td>33.44 ± 1.41</td>
<td>49.17 ± 2.25</td>
<td>72.53 ± 3.45</td>
<td>111.66 ± 4.88</td>
<td>183.76 ± 7.50</td>
</tr>
</tbody>
</table>

Values are means ± SEM.
and Greenfield used a force transducer and wall thickness transducer and measured circumferential wall stress directly in open-chest dogs. They also measured intraventricular pressure and chamber geometry, and calculated wall stress on the basis of thin-walled and thick-walled elliptical models. They concluded that both thin- and thick-walled elliptical models were generally accurate predictors of the measured wall stress. Burns et al. also measured left ventricular wall stress directly in dogs and compared these measurements with calculations based on ventricular pressure. Although they did not measure wall thickness directly, their conclusions were much the same as those of McHale and Greenfield.

Table 3: Slope \( (K = dE/d\sigma) \), Intercept, and Correlation Coefficient \( (r) \) of the Regression Line for the Left Ventricular Elastic Modulus as a Function of Myocardial Wall Stress at Different Ages

<table>
<thead>
<tr>
<th>Age (mo.)</th>
<th>Slope ( K )</th>
<th>Intercept (mm Hg)</th>
<th>( r )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10.62</td>
<td>-8.90</td>
<td>0.9985</td>
</tr>
<tr>
<td>2</td>
<td>9.33</td>
<td>-8.68</td>
<td>0.9985</td>
</tr>
<tr>
<td>4</td>
<td>9.38</td>
<td>-6.60</td>
<td>0.9986</td>
</tr>
<tr>
<td>6</td>
<td>13.13</td>
<td>-21.65</td>
<td>0.9997</td>
</tr>
<tr>
<td>8</td>
<td>11.41</td>
<td>-17.33</td>
<td>0.9984</td>
</tr>
<tr>
<td>10</td>
<td>10.83</td>
<td>-10.16</td>
<td>0.9996</td>
</tr>
<tr>
<td>11</td>
<td>8.98</td>
<td>-5.95</td>
<td>0.9999</td>
</tr>
<tr>
<td>17</td>
<td>11.39</td>
<td>-11.41</td>
<td>0.9999</td>
</tr>
<tr>
<td>24</td>
<td>13.15</td>
<td>-16.40</td>
<td>0.9985</td>
</tr>
</tbody>
</table>

All of the above evidence supports the conclusion that a thin-walled (Laplace) ellipsoid model of the left ventricle permits a wall stress calculation for both systole and diastole which is within 10% of the value given by thick-walled theory. A spherical model of the heart provides a lower estimate of the wall stress, but as Mirsky et al. have shown recently, the elastic modulus calculated on the basis of ellipsoidal geometry is always directly proportional to the modulus based on spherical geometry. Hence we may determine changes in \( E \) with age on the basis of a spherical model and be confident that the true elastic modulus undergoes these same changes.

Measurements of compliance, and particularly measurements giving an index of intrinsic stiffness, are of interest because they are a determinant of cardiac performance and have been shown to correlate with pathology. Simultaneous measurements of intraventricular pressure and volume alone do not provide enough information to determine the intrinsic stiffness of the myocardium. To calculate the elastic modulus \( E \) as a function of wall stress \( \sigma \), one must additionally know the thickness and curvature of the ventricle in one spot, or assume a geometric model and measure the ratio wall volume to ventricular volume. It makes little difference whether a thick- or thin-walled geometric model is chosen, primarily because the geometry of the ventricle is such as to induce nearly a uniform level of stress throughout the ventricular wall. The fact that the stress-strain curve for passive ventricular tissue is exponential, as it is for many biological materials, allows expression of the results in the particularly simple form \( d\sigma/d\epsilon = E = Ka + C \).
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In a total of 55 inbred golden Syrian hamsters of the LSH strain, we found that body weight, hence ventricular weight and end-diastolic volume, varied by more than 200% up and then down as a function of age. As a consequence of this variation, we found ventricular compliance \( dV/dP \) also varied more than 200% with age. When elastic modulus \( E \) was computed, it proved to be a linear function of the wall stress \( \sigma \). The constant of proportionality \( K \) was independent of age.

We conclude that the aging heart does not normally undergo substantial internal alterations that affect the physical characteristics of the muscle cells and fibers themselves. There are, however, marked changes in ventricular compliance throughout life. The observed decrease in compliance would appear to be due to alterations in size rather than substantial alterations in intrinsic structure of the ventricle.

Appendix I

EQUIVALENT HOLLOW SPHERE

Since the mean wall stress \( \sigma \) is approximately constant throughout any ventricle at a given pressure, let us propose an equivalent hollow sphere model of that ventricle. For the left ventricle, the mean radius, \( r \), and thickness, \( h \), of the model will be determined by the volume enclosed in the actual ventricle, \( V \) (known from pressure-volume curves)

\[
V = (4/3)\pi(r - h/2)^3
\]

and the weight of the empty ventricle, \( W \),

\[
h = W/(4\pi r^2 \rho)
\]

where \( \rho \) is the weight density of the ventricle. In the case of the right ventricle, \( W \) and \( V \) must be multiplied by the fraction of the total body of revolution actually represented by the tissues.

ELASTIC STABILITY

Beginning with the Laplace result for a sphere,

\[
\sigma = Pr/2h
\]

we use the chain rule to calculate the increment in pressure \( dP \) necessary to dilate the model an amount \( dr \).

\[
dP = (2h/r)\sigma + (2\sigma/r)dh - (2h\sigma/r^2)dr.
\]

If the wall material is incompressible (i.e., Poisson’s ratio = 0.5),

\[
4\pi r^2 h = \text{constant} \quad \text{(from Eq. 2)}
\]

and

\[
(8\pi rh)dr + (4\pi r^2)dh = 0
\]

so that

\[
dh = -(2h/r)dr.
\]

Substituting Eq. 5 in Eq. 4

\[
dP = (2h/r)\sigma - (6h\sigma/r^2)dr.
\]

The increment in stress \( d\sigma = E \ dr/r \), where \( E \) is the elastic modulus of the wall (in general a function of \( \sigma \)). Incorporating this into Eq. 6,

\[
dP = (2Eh/r^3 - 3P/r)dr,
\]

or finally

\[
dr/dP = r/(2Eh/r - 3P).
\]

The significance of this result has been commented on. If a constant-pressure reservoir is attached to such an elastic sphere, a small positive change in reservoir pressure \( dP \) will be accompanied by a small positive change, \( dr \), in sphere radius only if \( P < 2Eh/3r \). This condition is described as statically stable, since every value of reservoir pressure \( P \) corresponds to a unique \( r \). When \( P = 2Eh/3r \), the sphere is neutrally stable, since no change in pressure is necessary to change the radius. For \( P > 2Eh/3r \), the sphere is unstable; in this condition the sphere either collapses or “blows out” given the slightest disturbance.

VENTRICULAR ELASTIC MODULUS

Let us introduce the parameter \( V = (4/3)\pi r^3 \), which is approximately the left ventricular volume when \( h/2 \) is small compared to \( r \). Substituting in Eq. 7

\[
(1/4\pi r^3) dV/dP = r/(2Eh/r - 3P),
\]

dividing by \( V \),

\[
(1/V) dV/dP = 3/(2Eh/r - 3P),
\]

and finally solving for \( E \),

\[
E = (3rV/2h)dP/dV + 3P/2h
\]

DISCUSSION

The expression given in Eq. 8 for the elastic modulus uniquely specifies \( E \) as a function of the wall stress \( \sigma = Pr/2h \). It should be possible to compare \( E \) measured this way between hearts of varying size and pathological state, provided care is taken to maintain the same value for \( \sigma \) between specimens to be compared.

Appendix II

CALCULATION OF THE VENTRICULAR ELASTIC MODULUS

A polynomial regression analysis was utilized in the determination of the elastic modulus \( E \). (This analysis was performed on PROPHET, sponsored by the Chemical/Biological Information Handling Program, National Institutes of Health.) The equation for \( E \) required that one first determine the values for \( P \), \( dP/dV \), and \( V \) at the particular level of stress that is chosen. Thus, stress was evaluated at various pressures from 0 to 30 mm Hg, and the resulting data points were plotted. A polynomial was fitted to these points (usually a quadratic) from which the exact ventricular pressure at any level of stress could be calculated. Knowing this pressure, the exact \( dP/dV \) could be determined by plotting \( dP/dV \) vs. pressure and fitting a polynomial to these points. In a similar manner, the exact volume was determined from a plot of volume vs. \( dP/dV \). Once these
variables were known, the elastic modulus (in mm Hg) could be calculated from

\[ E = \frac{3(a + b)/4(a - b)(VdP/dV + P)}{V} \]

where \( V \) is ventricular volume (in microliters) and the inner radius \( a \) (in millimeters) was derived from

\[ a = \left(\frac{3V}{4\pi}\right)^{1/3}. \]

It was assumed that the left ventricular weight was 80% of the entire heart weight. Thus, knowing the weight \( m \) (in grams) and density \((1.07 \text{ g/ml})\) of the myocardium, the external radius of the spherical ventricular shell (in millimeters) was

\[ b = \frac{a^2 + 3(0.8)(1000)m/(4\pi(1.07))^{1/3}}{a} = \frac{(a^2 + 2400m)/(4.28\pi)^{1/3}}{a}. \]

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References

22. Weng AYK, Rautaharju PM: Stress distribution within the left ventricular wall approximated as a thick ellipsoidal shell. Am Heart J 75: 649-662, 1968
Ventricular elastic modulus as a function of age in the Syrian golden hamster.
R L Kane, T A McMahon, R L Wagner and W H Abelmann

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