Effect of Chronic Pressure and Volume Overload on Left Heart Volumes in Subjects with Congenital Heart Disease

By Graham A. H. Miller, B.M., B.Sc., and H. J. C. Swan, M.B., Ph.D.

Increase in chamber volume (and therefore increase in wall surface area) is an appropriate adaptation to an increased volume load. Conversely, a small thick-walled chamber is better suited to deal with a pressure load. That the human heart so adapts itself to chronic volume and chronic pressure loads is evident from clinical experience and post-mortem studies. However, actual measurements of chamber volume under these conditions are lacking. Detailed study of the adaptation to increased stress requires knowledge of chamber volumes during the different phases of the cardiac cycle and such measurements cannot be obtained post mortem. Technics that measure change in a single ventricular dimension have yielded valuable information. However, although applicable to unanesthetized subjects under varying conditions of rest and exercise, they are necessarily indirect measures of absolute volume.

The recent development, by Arvidsson, of a method for estimating left heart volumes from biplane angiocardiograms and its validation by Dodge and co-workers, has made possible measurement of absolute volume and change in volume of individual cardiac chambers.

The present study concerns the volume responses of the human heart to chronic pressure or volume overload imposed by congenital cardiac malformations. The method of Arvidsson was thought to measure absolute volumes and volume changes of the left atrium and the left ventricle during the cardiac cycle with a degree of accuracy sufficient for the purposes of this study. Since the normal range of volume of the left atrium and ventricle has not been established for subjects of all body sizes, an essential preliminary was the establishment of normal values for heart volumes in subjects of different body size.

Material and Methods

A total of 50 patients were studied at the time of diagnostic cardiac catheterization.

Group 1 comprised nine patients in whom no evidence of cardiac abnormality was found on complete right and left heart catheterization. Group 2 comprised nine patients with lesions causing pressure overload of the right ventricle of mild to moderate degree with no demonstrable abnormality of the left heart. Group 3 comprised 12 patients with lesions causing only pressure overload of the left ventricle (aortic stenosis or coarctation) and group 4 comprised 20 patients with lesions causing only volume overload of the left ventricle (group 4a, patent ductus arteriosus, 11 patients; or group 4b, congenital mitral insufficiency, nine patients) (tables 1, 2, and 3). Subjects in group 1 generally had been referred for study because they had minimal murmurs suggestive of either valvular stenosis or small left-to-right shunt. In the former case, measurement of pressures revealed no gradient. In the latter, no shunt was detected either by selective sampling of dye in the central circulation or by angiocardiography. For group 2 cases there was no evidence of abnormality of the left heart. While an enlarged right ventricle may have dis-

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* Patient no. 18 had cor triatriatum and the volume of the left atrium of this patient was excluded from data used in establishing the normal left atrial volume.
† Details of seven of these patients have been reported elsewhere (Miller, C. A. H., Brown, R., and Swan, H. J. C. Circulation 29: 356, 1964).
placed the left ventricle, it did not distort its ellipsoidal shape and, thus, measurement of volume by the Arvidsson method was still possible.

Cases of patent ductus arteriosus and of congenital mitral insufficiency were selected as examples of volume overload, since, in them, only the left side of the heart is opacified during angiocardiography. Cases with ventricular septal defect usually have simultaneous opacification of both ventricles, which prevents clear recognition and measurement of the limits of the cavity of the left ventricle. Cases of acquired heart disease were excluded, since it seldom was possible to be certain that stenosis or insufficiency existed as the sole lesion.

For patients in groups 1, 2, and 3 who had no intracardiac shunt or valvular insufficiency, the left ventricular stroke volume is forward flow. Data from these three groups were used to determine the relation between stroke volume determined angiocardiographically and by indicator dilution. Since there was no evidence of abnormality of the left heart in patients in groups 1 and 2, data from these groups were used to establish normal values for left heart volumes.

Indicator-dilution curves were recorded 1 to 3 minutes before angiocardiography; indocyanine green* was injected through the same catheter and into the same chamber as used for the injection of contrast medium during angiocardiography. Cardiac output was calculated from these curves according to the method of Hamilton and the value obtained divided by the heart rate during inscription of the curve to give average stroke volume \( V_S \) under anesthesia immediately before angiocardiography.

Selective angiocardiography was performed with the patient in the supine position under light anesthesia (nitrous oxide and oxygen). Halothane in concentrations of less than 1 per cent had been used for brief periods in some cases. In all cases, 100 per cent oxygen was administered for at least 60 seconds prior to angiocardiography. Contrast medium† was injected into the left ventricle in 25 cases, the pulmonary artery in 15 cases, and the outflow portion of the right

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### Table 1

**Summary of Data for Normal Left Hearts**

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr.) and sex</th>
<th>BSA (M.²)</th>
<th>( V_{ED} )</th>
<th>( V_{ES} )</th>
<th>( V_{ED} - V_{ES} )</th>
<th>( V_S )</th>
<th>( V_{ED} - V_{ES} )</th>
<th>( V_L )</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1F</td>
<td>1.48</td>
<td>93</td>
<td>30</td>
<td>63</td>
<td>49</td>
<td>0.68</td>
<td>31</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>7M</td>
<td>0.98</td>
<td>79</td>
<td>23</td>
<td>56</td>
<td>45</td>
<td>0.71</td>
<td>31</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>6M</td>
<td>0.76</td>
<td>101</td>
<td>34</td>
<td>67</td>
<td>42</td>
<td>0.66</td>
<td>21</td>
<td>13</td>
</tr>
<tr>
<td>4</td>
<td>5F</td>
<td>0.75</td>
<td>83</td>
<td>36</td>
<td>47</td>
<td>36</td>
<td>0.57</td>
<td>23</td>
<td>8</td>
</tr>
<tr>
<td>5</td>
<td>5F</td>
<td>0.75</td>
<td>85</td>
<td>24</td>
<td>61</td>
<td>71</td>
<td>0.72</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>6</td>
<td>4F</td>
<td>0.65</td>
<td>108</td>
<td>46</td>
<td>62</td>
<td>78</td>
<td>0.57</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>7</td>
<td>1F</td>
<td>0.48</td>
<td>81</td>
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<td>53</td>
<td>46</td>
<td>0.65</td>
<td>33</td>
<td>21</td>
</tr>
<tr>
<td>8</td>
<td>1M</td>
<td>0.41</td>
<td>73</td>
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<td>41</td>
<td>25</td>
<td>0.56</td>
<td>29</td>
<td>17</td>
</tr>
<tr>
<td>9</td>
<td>9 wk. F</td>
<td>0.24</td>
<td>90</td>
<td>31</td>
<td>59</td>
<td>33</td>
<td>0.66</td>
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**Group 2**

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr.) and sex</th>
<th>BSA (M.²)</th>
<th>( V_{ED} )</th>
<th>( V_{ES} )</th>
<th>( V_{ED} - V_{ES} )</th>
<th>( V_S )</th>
<th>( V_{ED} - V_{ES} )</th>
<th>( V_L )</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
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<td>1.29</td>
<td>84</td>
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<td>41</td>
<td>35</td>
<td>0.49</td>
<td>19</td>
<td>13</td>
</tr>
<tr>
<td>11</td>
<td>8F</td>
<td>0.8</td>
<td>66</td>
<td>14</td>
<td>52</td>
<td>55</td>
<td>0.79</td>
<td>20</td>
<td>11</td>
</tr>
<tr>
<td>12</td>
<td>6M</td>
<td>0.79</td>
<td>94</td>
<td>22</td>
<td>72</td>
<td>47</td>
<td>0.77</td>
<td>24</td>
<td>11</td>
</tr>
<tr>
<td>13</td>
<td>8M</td>
<td>0.77</td>
<td>68</td>
<td>17</td>
<td>51</td>
<td>35</td>
<td>0.75</td>
<td>21</td>
<td>5</td>
</tr>
<tr>
<td>14</td>
<td>4M</td>
<td>0.76</td>
<td>91</td>
<td>21</td>
<td>70</td>
<td>46</td>
<td>0.77</td>
<td>28</td>
<td>16</td>
</tr>
<tr>
<td>15</td>
<td>5F</td>
<td>0.73</td>
<td>79</td>
<td>27</td>
<td>52</td>
<td>34</td>
<td>0.66</td>
<td>19</td>
<td>12</td>
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<td>76</td>
<td>17</td>
<td>49</td>
<td>31</td>
<td>0.74</td>
<td>28</td>
<td>6</td>
</tr>
<tr>
<td>17</td>
<td>4M</td>
<td>0.65</td>
<td>88</td>
<td>34</td>
<td>54</td>
<td>43</td>
<td>0.61</td>
<td>18</td>
<td>11</td>
</tr>
<tr>
<td>18</td>
<td>14Mo. F</td>
<td>0.3</td>
<td>93</td>
<td>33</td>
<td>60</td>
<td>37</td>
<td>0.65</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

**Mean**

85 |

28

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* Cardio-green supplied by Hynson, Westcott & Dunning, Baltimore, Maryland.
† Sodium and methylglucamine diatrizoates (Renovist).
PRESSURE AND VOLUME OVERLOAD

Table 2

Summary of Data for Pressure Overload (Group 3)

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>BSA (m²)</th>
<th>V₁ED (ml/M²)</th>
<th>V₁ED – Vₛ (ml/M²)</th>
<th>Vₛ (ml/M²)</th>
<th>Vₛ – Vₛ (ml/M²)</th>
<th>Vₛ – Vₛ (ml/M²)</th>
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<td>0.96</td>
<td>0.86</td>
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<td>0.75</td>
<td>0.79</td>
<td>0.81</td>
<td>0.83</td>
</tr>
<tr>
<td>11M</td>
<td>2.5</td>
<td>0.91</td>
<td>0.79</td>
<td>0.75</td>
<td>0.75</td>
<td>0.81</td>
<td>0.81</td>
<td>0.83</td>
</tr>
<tr>
<td>8F</td>
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<td>0.91</td>
<td>0.79</td>
<td>0.75</td>
<td>0.75</td>
<td>0.81</td>
<td>0.81</td>
<td>0.83</td>
</tr>
<tr>
<td>5M</td>
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<td>0.91</td>
<td>0.79</td>
<td>0.75</td>
<td>0.75</td>
<td>0.81</td>
<td>0.81</td>
<td>0.83</td>
</tr>
</tbody>
</table>

ventricle in 10 cases. The left ventricle was entered by passing the catheter retrograde through the aortic valve. Simultaneous anteroposterior and lateral exposures were made at a rate of six per second during left heart opacification using a roll film or cut film changer. Simultaneous recording of the arterial pressure, electrocardiogram, and time of x-ray exposure permitted correlation of the radiographic appearances with the events of the cardiac cycle. Measurements of angiographic diagrams were made as indicated in figure 1 and read to the nearest 1 mm. Left atrial and ventricular volumes were calculated from the angiographic measurements according to the method of Arvidsson.

Only those films showing satisfactory opacification of the left heart were measured and, in general, three to four complete cardiac cycles were available for study during sinus rhythm. Composite left atrial (V₁LA) and ventricular (V₁LV) volume curves were constructed by plotting the volumes calculated from an angiographic pair against the time, expressed in fractions of a second after the “R” wave of the electrocardiogram, at which the exposures were made (fig. 2). Values for left ventricular end-diastolic (V₁ED) and end-systolic (V₁ES) volumes and maximal (V₁LA Max.) and minimal (V₁LA Min.) left atrial volumes were obtained from the composite volume curves so constructed. The total volume ejected by the left ventricle is given by V₁ED – V₁ES and this was also expressed as a percentage of end-diastolic volume to give a value for percentage ejection.

For the cases of mitral insufficiency, regurgitant flow is given by (V₁ED – V₁ES) – Vₛ, where Vₛ is the “forward” stroke volume calculated from indicator-dilution curves. Comparison of stroke volumes obtained angiographically (V₁ED – V₁ES) and by indicator dilution (Vₛ) (tables 1 and 2) indicates that the angiographic method gives a value for stroke volume which exceeds that obtained by the indicator-dilution method by approximately 15 per cent (fig. 3) as indicated by the regression equation

\[
V₁ED - V₁ES = 3.3 + 1.15 Vₛ; \text{m} = 0.92.
\]

The cause of this difference is not known but it may be due to a brief but real increase in stroke volume produced by the injection of a large volume of fluid into the central vascular system.

In the present study this difference could affect the calculation of valvular regurgitation. Therefore, the observed values for Vₛ were increased on the basis of the above regression equation to

Table 3

Summary of Data for Volume Overload (Group 4)

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr.) and sex</th>
<th>BSA (M²)</th>
<th>V₁ ED</th>
<th>V₁ ES</th>
<th>V₁ ED - V₁ ES</th>
<th>V₂ ED - V₂ ES</th>
<th>V LA max.</th>
<th>V LA min.</th>
<th>L-to-R shunt (%)</th>
<th>Diagnosis</th>
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<tr>
<td>31</td>
<td>4 mo. M</td>
<td>0.27</td>
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<td>89</td>
<td>0.48</td>
<td>56</td>
<td>25</td>
<td>77</td>
<td>PDA, ASD</td>
</tr>
<tr>
<td>32</td>
<td>1½F</td>
<td>0.33</td>
<td>185</td>
<td>67</td>
<td>118</td>
<td>0.64</td>
<td>57</td>
<td>22</td>
<td>?</td>
<td>PDA</td>
</tr>
<tr>
<td>33</td>
<td>6 mo. F</td>
<td>0.32</td>
<td>147</td>
<td>63</td>
<td>84</td>
<td>0.57</td>
<td>45</td>
<td>19</td>
<td>70</td>
<td>PDA, VSD</td>
</tr>
<tr>
<td>34</td>
<td>5½F</td>
<td>0.70</td>
<td>159</td>
<td>75</td>
<td>84</td>
<td>0.52</td>
<td>59</td>
<td>36</td>
<td>56</td>
<td>PDA, VSD, PS</td>
</tr>
<tr>
<td>35</td>
<td>6 mo. F</td>
<td>0.29</td>
<td>157</td>
<td>76</td>
<td>81</td>
<td>0.52</td>
<td>60</td>
<td>33</td>
<td>54</td>
<td>PDA</td>
</tr>
<tr>
<td>36</td>
<td>7 mo. M</td>
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<td>28</td>
<td>117</td>
<td>0.71</td>
<td>39</td>
<td>28</td>
<td>50</td>
<td>PDA</td>
</tr>
<tr>
<td>37</td>
<td>14F</td>
<td>1.23</td>
<td>149</td>
<td>62</td>
<td>87</td>
<td>0.58</td>
<td>34</td>
<td>9</td>
<td>41</td>
<td>PDA</td>
</tr>
<tr>
<td>38</td>
<td>58F</td>
<td>1.7</td>
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<td>101</td>
<td>0.71</td>
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<td>PDA</td>
</tr>
<tr>
<td>39</td>
<td>6½F</td>
<td>0.84</td>
<td>149</td>
<td>63</td>
<td>86</td>
<td>0.58</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>PDA</td>
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<tr>
<td>40</td>
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<td>147</td>
<td>60</td>
<td>87</td>
<td>0.59</td>
<td>—</td>
<td>—</td>
<td>—</td>
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</tr>
<tr>
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<td>9½F</td>
<td>1.1</td>
<td>141</td>
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<td>85</td>
<td>0.60</td>
<td>38</td>
<td>21</td>
<td>30</td>
<td>PDA, VSD</td>
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Group 4b

<table>
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<tr>
<th>Case</th>
<th>V₁ × 100</th>
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<tr>
<td>42</td>
<td>9 M</td>
</tr>
<tr>
<td>43</td>
<td>5 F</td>
</tr>
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<td>44</td>
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<td>5 F</td>
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<td>7 F</td>
</tr>
<tr>
<td>49</td>
<td>9 F</td>
</tr>
<tr>
<td>50</td>
<td>5 F</td>
</tr>
</tbody>
</table>

Mean |                                     | 0.61 |

Figure 1

Paired angiograms in diastole (anteroposterior and lateral projections). Calculations of left heart volumes are made from the dimensions indicated on the line drawings. Lowercase symbols refer to semiaxes and uppercase symbols, to axes. The volume of the left atrium (V LA) is

\[ V_{LA} = \frac{a}{f_1} \cdot \frac{b}{f_1} \cdot \frac{c}{f_2} \cdot \left( \frac{4}{3} \pi \right) \]

and of the left ventricle (V LV) is

\[ V_{LV} = \frac{L}{2} \cdot \frac{B}{2f_1} \cdot \frac{C}{2f_2} \cdot \left( \frac{4}{3} \pi \right), \]

where L, the true long axis of the ventricular ellipsoid, is

\[ L = \sqrt{\left( \frac{D \cos \alpha}{f_2} \right)^2 + \left( \frac{A}{f_1} \right)^2} \]

and f₁ and f₂ are the anteroposterior and lateral magnification factors, respectively, and are measured for each subject. Note that the left atrial appendage is not included in calculations of left atrial volume.
give the real forward stroke volume during the injection of contrast medium,

\[ V'_S = 3.3 + 1.15 V_S \]

and the regurgitant volume \( V_R \) was taken as \( (V_{ED} - V_{ES}) - V'_S \).

Volume overload is reported either as the volume of blood shunted left-to-right or regurgitated across the mitral valve, in either case expressed as a percentage of total left ventricular ejection. In the former instance, quantitation was based on the values for blood oxygen saturation; in the latter, it was calculated as shown in the preceding paragraph.

Body surface area was determined from nomograms constructed according to the formula of DuBois\(^{13}\) for subjects having body surface area greater than 0.8 M.\(^2\). For subjects of surface area less than 0.8 M.\(^2\), nomograms according to Crawford and co-workers\(^{14}\) were used.

**Results**

**Normal Left Heart (Groups 1 and 2)**

For each subject of groups 1 and 2, the values for left ventricular and left atrial volumes are given in table 1. There is a linear relationship between body surface area and left ventricular end-diastolic and end-systolic volumes, and a linear relationship also exists between body surface area and maximal and minimal left atrial volumes (fig. 4). The mean values for the volumes expressed in milliliters per square meter of body surface area together with the regression equations relating volumes to body surface area are given in table 4.

The change in volume of the left ventricle during the cardiac cycle is given by \( V_{ED} - V_{ES} \). The mean and standard deviation for the fraction \( \frac{V_{ED} - V_{ES}}{V_{ED}} \) for groups 1 and 2 is 0.67 ± 0.08.

Mean left atrial volume change is 50 ± 14.7 per cent and is of the order of one quarter of the left ventricular volume change.

**Pressure Overload of Left Heart (Group 3)**

In the presence of pressure overload of the
Relationship between stroke volume determined angiocardiographically ($V_{ED}$-$V_{ES}$) and mean stroke volume determined by indicator dilution ($V_d$) for the same subjects. Broken lines indicate one standard error of the estimating equation.

For all subjects in all groups there is a linear relationship between $V_{ED}$ and $V_{ES}$ (fig. 7) given by

$$V_{ED} = 8.25 + 2.51 V_{ES}; \ S.E.E. = 20.22; \ r = 0.94.$$

Within the range of volumes determined for the subjects reported here, the relationship between $V_{ED}$ and $V_{ES}$ remains constant and the total volume ejected by the ventricle ($V_{ED} - V_{ES}$) forms approximately the same fraction of end-diastolic volume independent of the absolute volumes at which the ventricle is working. The average value for the fraction $V_{ED} - V_{ES}$ for subjects with normal left hearts (groups 1 and 2) is $0.67 \pm 0.08$. With pressure overload the average value (group 3) is $0.66 \pm 0.13$ and for volume overload (group 4), it is $0.61 \pm 0.08$.

**Discussion**

Angiocardiographic measurement of models and contrast medium-filled necropsy specimens has shown that the technic measures a known volume with an error of less than 10 per cent and that large and small volumes are measured with equal accuracy. While the angiographic technic employed has several important limitations, it should provide an approximate measurement of average end-diastolic and end-systolic chamber volume in a given subject. Therefore, it should be possible to compare values among different patient populations. Geometric and other considerations suggest that errors of overestimation of volume are more likely to occur than are errors of underestimation. The technic does not permit accurate measurement of small beat-to-beat changes in volume; however, more refined (and more time-consuming) technics do not indicate major changes in volume on a beat-to-beat basis during the time of chamber opacification, and this is also our experience (fig. 2). The required average values for end-diastolic and end-systolic volumes are best achieved by the construction of a composite volume curve through one hypothetical cycle.

It has been suggested that injection of large volumes of pharmacologically active contrast...
Normal left hearts. Left ventricular end-diastolic (VED) and end-systolic (VES) volumes and maximal and minimal left atrial volumes (VLA) for group 1 (solid circles) and group 2 (open circles) plotted against body surface area in square meters. Broken lines indicate one standard error of the estimating equation.

Table 4

Mean Values for Normal Left Heart Volumes Related to Body Size (Combined Groups 1 and 2)

<table>
<thead>
<tr>
<th></th>
<th>Mean (ml./M²)</th>
<th>S.D.</th>
<th>Regression equation*</th>
<th>S.E.E.</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>VED</td>
<td>85 ± 11.65</td>
<td></td>
<td>-2.98 + 88.6 BSA</td>
<td>8.7</td>
<td>0.95</td>
</tr>
<tr>
<td>VES</td>
<td>28 ± 8.75</td>
<td></td>
<td>-3.7 + 33.6 BSA</td>
<td>6.62</td>
<td>0.85</td>
</tr>
<tr>
<td>Max.</td>
<td>VLA</td>
<td></td>
<td>-1.5 + 26.15 BSA</td>
<td>4.28</td>
<td>0.89</td>
</tr>
<tr>
<td>Min.</td>
<td>VLA</td>
<td>24 ± 4.71</td>
<td>-1.47 + 13.9 BSA</td>
<td>2.84</td>
<td>0.84</td>
</tr>
</tbody>
</table>

* BSA, body surface area.

medium causes changes in circulatory dynamics such as to render volume measurements by this method of limited value. Such determinations are affected, but probably to a small degree, by the added volume of injectate resulting in an immediate increase in stroke volume of approximately 15 per cent. The major changes in cardiac dynamics associated with injection of contrast medium occur 20 to 40 seconds later, long after filming for volume determination has been completed.

Comparisons between stroke volume ob-
tained by the indicator-dilution technic before angiocardiography and by the angiocardiographic technic itself are open to criticisms that cannot be resolved until a suitable independent method of determining stroke volume during angiocardiography becomes available. Nonetheless, the relationship between values for stroke volume determined by the two methods (fig. 3) or determined by Fick methods and angiocardiography indicates that the angiographic technic can measure volume change over a wide range of volumes and should therefore indicate directional changes in volume in vivo. With the recognized limitations of the angiographic technic in mind, the data are presented to indicate (1) the order of absolute chamber volumes; (2) the interrelationship between chamber volumes; and (3) the similarities (or differences) between groups of patients with different left ventricular stress.

Interpretation of abnormal values requires knowledge of normal values under the same circumstances and over a wide range of body size. Available data are scanty but tend to confirm the values found by us for subjects with normal hearts. Thus Bunnell and associates studied seven children before and after operation for coarctation and obtained values for left heart volumes and for the fraction $\frac{V_{ED} - V_{ES}}{V_{ED}}$ similar to those obtained by us for normal children and dissimilar to values obtained by us for subjects with a volume overload. Sandler and associates reported end-diastolic volumes of $100 \pm 25$ ml. for 23 normal adults; these values were not related to surface area but are of the same order as predicted from the relationship $V_{ED} = -2.98 + 88.6$ BSA determined here.

For the subjects in groups 1 and 2, a linear relationship was demonstrated between left

![Figure 5](http://circ.ahajournals.org/)

*Figure 5*

Pressure overload of left heart. Left ventricular end-diastolic ($V_{ED}$) and end-systolic ($V_{ES}$) volumes and maximal and minimal left atrial ($V_{LA}$) volumes plotted against body surface area in square meters. The regression lines shown are those established for the relationship between the same volumes and body surface area for normal left hearts (groups 1 and 2). The broken lines indicate two standard errors of the estimating equations for the normal values.
Figure 6

Volume overload of left heart. Left ventricular end-diastolic ($V_{ED}$) and end-systolic ($V_{ES}$) volumes and maximal and minimal left atrial ($V_{LA}$) volumes plotted against body surface area in square meters. $\Delta$ = patent ductus arteriosus; $\blacksquare$ = congenital mitral insufficiency. The regression lines (solid) and range of two standard errors (broken lines) shown are those for normal left hearts.

heart volume and body surface area. The relationship between volume and body weight was found to be no better than the relationship to surface area.

The results reported here show that, for all subjects studied, as left ventricular stroke volume increases in response to a chronic volume overload there is an increase in both end-diastolic and end-systolic volume so that stroke volume remains a constant fraction of end-diastolic volume. This is similar to the findings of Sarnoff and co-workers$^{21}$ who studied the response of the canine heart to an acute increase in stroke volume and found that the resulting increase in work was accomplished from an increased end-diastolic myocardial segment length. They also showed that, when work was increased acutely by increasing aortic pressure while keeping stroke volume constant, there was a slight decrease in end-diastolic segment length; since more external work was being performed from a smaller end-diastolic fiber length, an increase in myocardial contractility had occurred. Similar conclusions can be drawn from the data reported here for the cases of chronic pressure overload. Thus, for the same stroke volume, subjects with pressure overload had the same end-diastolic and end-systolic volumes as normal subjects and as subjects...
with volume overload but were performing more external work (pressure volume work) from these end-diastolic volumes.

This series of patients with pressure overload due to congenital aortic stenosis includes only five in whom the transvalvular gradient exceeded 50 mm. Hg under the conditions of the study. One of these (case 29) deviates from the group response in that only 30 per cent of end-diastolic volume was ejected during systole. He had clinical evidence suggesting endocardial fibroblastosis and was in severe cardiac failure at the time of study. While in the majority of these cases the degree of aortic valve narrowing was mild, as is usual in children, there was no tendency for these cases to deviate from the established pattern of normal left heart volumes.

The constant relationship between end-diastolic (VED) and end-systolic (VES) volumes among this heterogeneous group—patients with volume or pressure overload and normal subjects—suggests that there is an optimal dimension at which the ventricle ejects a given stroke volume. Burch and co-workers,22 in an analysis of the mechanical factors affecting cardiac performance, demonstrated that the normal left ventricle performs at essentially ideal end-diastolic and end-systolic volumes when these are taken as 85 ml. and 25 ml., respectively; the results reported here would predict virtually identical values for a normal subject of 1 M.2 body surface area.

If, under the circumstances of this study, the degree of myocardial fiber shortening is constant irrespective of the initial fiber length, the constant relationship between end-diastolic volume and end-systolic volume reported here would hold. A limited degree of fiber shortening implies that an increase in stroke volume can only be achieved from an increased end-diastolic volume; the resulting ventricular dilation permits an increase in stroke volume for a given degree of shortening at the expense, however, of increased ventricular wall tension and stress.22, 23

That this relationship between end-diastolic and end-systolic volume is not dependent on the relatively young age of the patients is suggested by the inclusion of a 58-year-old woman with a patent ductus arteriosus (case 38). However, in certain patients with acquired heart disease, there is a disproportionate increase in end-systolic volume so that the total stroke volume forms a smaller fraction of end-diastolic than normal. We have encountered this situation among those patients in whom myocardial function may be depressed due to coronary and intrinsic myocardial disease (case 29).

Although atrial volumes were increased for most cases in group 4, no exact relationship exists between the volume load and atrial dimensions; for the patients in groups 1 and 2, atrial volume change was always less than left ventricular and stroke volumes. These findings are consistent with the view that the atrium is never a closed chamber but acts as a conduit for much of the cardiac cycle. The marked increase in left atrial volumes in patients with mitral insufficiency presumably results from the increased pressure during atrial diastole, a different situation from systolic pressure load on the left ventricle which did not result in chamber dilation.

The data presented here suggest that, for

**Figure 7**

*Relationship between V<sub>ED</sub> and V<sub>ES</sub>*. Left ventricular end-diastolic volume (V<sub>ED</sub>) plotted against left ventricular end-systolic volume (V<sub>ES</sub>) for all cases. Group 1 = ○; group 2 = O; group 3 = △; group 4a = ▲; and group 4b = ■. The relating regression line (solid) and one standard deviation (broken lines) are shown.
the nonfailing heart under a chronic volume load, as stroke volume increases there is a proportionate increase in end-diastolic volume and end-systolic volume so that end-systolic volume, and therefore stroke volume, remains a constant fraction of the end-diastolic volume. In response to a chronic pressure load, end-diastolic volume continues to bear the same relationship to end-systolic volume and stroke volume as in normal subjects and in subjects with a volume overload. Since the stroke volume is normal, the extra work imposed by the pressure load is performed from a normal end-diastolic volume. For all groups it thus appears that the end-diastolic volume of the nonfailing ventricle is related to the total volume load and may be relatively independent of the pressure load.

Summary

Left heart volumes were determined angiographically in 50 subjects of whom 18 had no abnormality of the left heart, 12 had lesions causing pressure overload of the left ventricle, and 20 had lesions causing volume overload of the left ventricle. The left heart volumes were in the normal range in the presence of pressure overload, but, with volume overload, end-diastolic, end-systolic, and atrial volumes were in excess of normal. A linear relationship was demonstrated between end-diastolic and end-systolic volumes, regardless of the pressure load on the ventricle. Thus, for all but one of the cases studied, total left ventricular ejection volume formed a nearly constant proportion of end-diastolic volume.

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References

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Sphygmomanometry

The history of blood pressure really begins with Stephen Hales (1677-1761), minister of Teddington, who with a sound training in Newtonian physics applied this knowledge to biology and physiology. Before 1723 he tied tubes into the arteries and veins of animals and estimated the pressure in the capillaries, thus being far in advance of his time. In a mare he found that the blood pressure was equal to a column of blood of eight to nine feet. Nearly a century passed before the subject was further investigated, and then Poiseuille (1828) employed a U-shaped mercurial manometer (haemodynometer) which, as van Leersum points out, was but a step from the mercurial column used by Hales to estimate the pressure of the sap in a pruned vine. To this, in 1847, Carl Ludwig added a float with a pen to record the variations of the blood pressure on a revolving cylinder (kymograph) . . . .

The clinical estimation of blood pressure by instrumental means was first attempted by Vierordt in 1855 by measuring the weight necessary to stop the arterial pulsation; but von Basch in 1880 invented a sphygmanometer on this principle which was applied locally over an artery and was widely used . . .

The present sphygmanometric methods became generally available as a result of Riva-Rocci's modification of von Basch's instrument with a piece of rubber tubing to surround the arm in 1897, and by Hill and Barnard's independent description of a somewhat similar instrument in the same year.—SIR HUMPHRY DAVY ROLLESTON. The Harveian Oration. Great Britain, Cambridge University Press, 1928, p. 101.
Effect of Chronic Pressure and Volume Overload on Left Heart Volumes in Subjects with Congenital Heart Disease

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