associated with interpretation of the $S_2$ vibratory complex in the conventional phonocardiogram. It provides clinically relevant information about the splitting interval at times when the phonocardiogram fails to do so, and is therefore offered as a supplement to phonocardiography.

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Influence of Age on Wall Thickness, Cavity Dimensions and Myocardial Contractility of the Left Ventricle in Simple Transposition of the Great Arteries

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AND ANDRE DAVIGNON, M.D.

with statistical analysis by Gilles Ducharme, M.Sc.

SUMMARY This study was carried out to establish a reference table of echocardiographic values for the left ventricle of simple d-transposition of the great arteries (d-TGA) and to determine at what age left ventricular dimensions in these patients become different from those of a normal population. Fifty-three patients with d-TGA and normal pulmonary pressure and 395 normal children ages 1 day to 10 years were studied by M-mode echocardiography. Results show that in d-TGA, left ventricular systolic and diastolic internal diameters are normal at birth. After 1 month, however, both diameters were below normal and despite a progressive increase with age, the mean values were always below normal. The mean posterior wall thickness of patients with d-TGA was also normal at birth but did not increase with age (2.3 mm in diastole and 4.3 mm in systole) and became significantly thinner than normal at 10 months of age in diastole and 7 months in systole. Septal thickness of patients with d-TGA did not differ from that of the control group. The shortening fraction and mean velocity of circumferential fiber shortening were significantly greater in d-TGA at all ages. Left ventricular measurements related to age are presented and should be of help in interpreting M-mode echocardiograms of patients with d-TGA.

MEASUREMENTS of anatomic specimens and by echocardiography have shown that patients with d-transposition of the great arteries (d-TGA) have a thinner left ventricular (LV) wall than subjects with normally related great arteries. This is expected because in transposition, the left ventricle is connected to the low-pressure pulmonary circulation. However, the influence of age on LV characteristics has only been studied in anatomic specimens and never, to our knowledge, in living patients with d-TGA. This information is important for at least three reasons. First, a reference table based on echocardiographic measurements related to age from patients with uncomplicated d-TGA is needed to interpret echocardiograms of patients with d-TGA, because comparison with normal subjects is obviously erroneous. Second, studies of fixed anatomic specimens cannot provide information about the dynamic characteristics of the LV wall. Third, with the increasing popularity of anatomic correction of d-TGA, it has become important to establish the age at

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which the anatomic and functional characteristics of
the left ventricle start to differ significantly from that of
the normal population. We therefore performed an
echocardiographic study to determine the influence of
age on LV wall thickness, cavity dimensions and in-
dexes of myocardial contractility in patients with sim-
ple d-TGA.

Materials and Methods

Subjects

The study group consisted of 53 patients with simple
d-TGA, ages 1 day to 10 years. To avoid undue influ-
ence of individual cases on the data of the group, each
patient was represented by only one echocardiographic
study. Only patients with normal pressure in the pul-
monary circulatory system were selected. Patients
older than 1 month who had an LV systolic pressure
higher than 40 mm Hg were excluded. In patients
younger than 1 month, pulmonary pressure was con-
considered normal if it was 50% of systemic or less and if
noninvasive criteria of normal pulmonary pressure
were noted on subsequent echocardiograms. Patients
with a gradient of 20 mm Hg or less in the LV
outflow tract were included in the study. Twenty-three
patients had undergone surgical correction by the Must-
ard procedure. The rest of the patients had an
interatrial balloon septostomy or a surgically created
atrial septal defect or both.

A control group was taken from an ongoing study of
normal echocardiographic data. This group consisted of
395 subjects matched for age. As in the d-TGA
group, each subject is represented by one echocardi-
ographic study.

Echocardiographic Technique

All echocardiograms were taken with an Ekoline
20A ultrasonoscope coupled with a Cambridge fiber-
optic recorder. An electrocardiographic lead showing
a well-identified Q wave was recorded simultane-
ously. Each value represents the average of at least five
measurements. In the few instances in which this was
not possible, the value for this variable was rejected.
Posterior wall and septal thickness as well as dimen-
sions of the LV cavity were measured at end-systole
and end-diastole according to the recommendations of
the American Echocardiographic Society. Ejection
time was measured from the pulmonary valve as pre-
viously described. From these data, the shortening
fraction (SF) (end-diastolic dimension - end systolic
dimension)/end-diastolic dimension) and the mean ve-
clocity of circumferential fiber shortening (Vcf) ((end-
diastolic dimension - end-systolic dimension)/end-
diastolic dimension x ejection time) of the left
ventricle were calculated. Septal motion was classi-
fied as normal, flat or paradoxical. The SF and the mean
Vcf were not calculated if the septal motion was para-
doxxical.

Statistical Analysis

To make proper inference, normality of the data was
verified using Lilliefors’ test, at the 0.10 level, each
time theory required it.

In a preliminary study, linear and nonlinear multiple
regression analyses of the control group showed that an
excellent prediction of the wall thickness and cavity
dimensions was obtained by using the square root of
age as regressor ($R^2 > 70\%$). The same analyses were
also applied to the d-TGA group. Covariance analysis
was performed to evaluate the effect of the Mustard
procedure on the ventricular dimensions. For this anal-
ysis, an age range including both operated and nonop-
erated patients was chosen. The range of 30–54
months gave the greatest number of subjects.

As for shortening fraction and mean Vcf, significant
but nonlinear variations were noted with age in the
control group. For this reason, the results were sub-
divided into three subgroups, so that the within-group
variations were not significant: 0–6 months, 6 months
to 5 years and 5 years and older. Values for the d-TGA
group were similarly divided. Comparisons were car-
ried out between these three subgroups by analysis of

![Figure 1. Left ventricular internal dimensions in diastole (LVIDd) in normal subjects and in patients with d-transposition of the great arteries. In this and all other figures, patients 0–6
months old are presented separately (A) to better illustrate the changes during the postnatal period (B). Patients less than 1
month of age are excluded. Each patient with transposition is represented by a circle (before Mustard) or a dot (after Mus-
tard). The dashed lines are the mean and 95% tolerance limits. Regression equation for the control group: $y = 1.831 + 0.193\text{age}$, ($R^2 = 92\%$); for the d-TGA group: $y = 1.364 + 0.147\text{age}$ ($R^2 = 60\%$).]
variance, and with the normal group using the Bonferroni \( r \) statistic.\(^4\) The absence of correlation with age precluded the use of covariance analysis to evaluate the influence of Mustard correction on SF and mean Vcf. Therefore, this influence was tested by \( r \) test applied to data obtained in patients 6 months to 5 years old, since only this subgroup contained enough operated and nonoperated patients.

All 95% tolerance limits about mean values were estimated using the method outlined by Guttman.\(^5\) Ninety-five percent tolerance limits about regression line were also calculated.\(^6\) For clinical application, it was more useful to present the latter tolerance limits in table form.

## Results

### Left Ventricular Internal Dimensions

In diastole, the LVID of the transposition group was normal during the first days of life (fig. 1A). However, a rapid fall below the 95% tolerance limits of normal was observed in the following weeks. From 1–6 months, no change in LV dimensions was observed. Thereafter, LV dimensions increased progressively with age (fig. 1B). This increase followed the pattern of the normal population. Although patients with d-TGA occasionally fell within the 95% tolerance limits of normal, the regression curve for the group was always below these limits after 1 month of age.

The systolic LVID was normal at birth (fig. 2A), but dropped below the 95% tolerance limits a few weeks after birth. The cavity remained significantly smaller than normal throughout the first 10 years of life, although a progressive increase in size was noted during this period (fig. 2B). No significant difference was found between uncorrected patients and those corrected with the Mustard procedure. The mean values according to age for LVID in d-TGA and their upper tolerance limits are listed in table 1. The regression equations for weight and body surface are given in the Appendix.

### Left Ventricular Posterior Wall Thickness

Most values for LVPW were normal, in both diastole and systole, for subjects 1 day to 6 months old (figs. 3A and 4A). However, for subjects 1 month to 10 years old, wall thickness in the d-TGA group remained constant, while a significant increase with age was observed in the normal population (figs. 3B and 4B). The mean value for LVPW in d-TGA was 2.3 mm in diastole and 4.3 mm in systole. The upper tolerance limits are shown in table 1. Because of the difference in growth between d-TGA and normal subjects, mean...
TABLE 1. Means and Upper Tolerance Limits of Left Ventricular Parameters for Different Age Groups in Patients With Simple d-TGA

<table>
<thead>
<tr>
<th>Age range</th>
<th>LVIDs (cm)</th>
<th>Age range</th>
<th>LVIDd (cm)</th>
<th>Age range</th>
<th>IVSd (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3 months</td>
<td>0.7 (1.4)</td>
<td>1-3 months</td>
<td>1.6 (2.3)</td>
<td>1-2 months</td>
<td>2.7 (4.6)</td>
</tr>
<tr>
<td>3-5 months</td>
<td>0.8 (1.5)</td>
<td>3-6 months</td>
<td>1.7 (2.4)</td>
<td>2-4 months</td>
<td>2.8 (4.7)</td>
</tr>
<tr>
<td>5-8 months</td>
<td>0.9 (1.6)</td>
<td>6-9 months</td>
<td>1.8 (2.5)</td>
<td>4-6 months</td>
<td>2.9 (4.8)</td>
</tr>
<tr>
<td>8-12 months</td>
<td>1.0 (1.7)</td>
<td>9-14 months</td>
<td>1.9 (2.6)</td>
<td>6-8 months</td>
<td>3.0 (4.9)</td>
</tr>
<tr>
<td>12-16 months</td>
<td>1.1 (1.8)</td>
<td>14-19 months</td>
<td>2.0 (2.7)</td>
<td>8-11 months</td>
<td>3.1 (5.0)</td>
</tr>
<tr>
<td>16-22 months</td>
<td>1.2 (1.9)</td>
<td>19-26 months</td>
<td>2.1 (2.8)</td>
<td>11-14 months</td>
<td>3.2 (5.1)</td>
</tr>
<tr>
<td>22-28 months</td>
<td>1.3 (2.0)</td>
<td>26-33 months</td>
<td>2.2 (2.9)</td>
<td>14-18 months</td>
<td>3.3 (5.2)</td>
</tr>
<tr>
<td>28-35 months</td>
<td>1.4 (2.1)</td>
<td>33-41 months</td>
<td>2.3 (3.0)</td>
<td>18-22 months</td>
<td>3.4 (5.3)</td>
</tr>
<tr>
<td>35-42 months</td>
<td>1.5 (2.2)</td>
<td>41-56 months</td>
<td>2.4 (3.1)</td>
<td>22-26 months</td>
<td>3.5 (5.4)</td>
</tr>
<tr>
<td>42-51 months</td>
<td>1.6 (2.3)</td>
<td>56-61 months</td>
<td>2.5 (3.2)</td>
<td>26-31 months</td>
<td>3.6 (5.5)</td>
</tr>
<tr>
<td>51-60 months</td>
<td>1.7 (2.4)</td>
<td>61-72 months</td>
<td>2.6 (3.3)</td>
<td>31-37 months</td>
<td>3.7 (5.6)</td>
</tr>
<tr>
<td>60-69 months</td>
<td>1.8 (2.5)</td>
<td>72-84 months</td>
<td>2.7 (3.4)</td>
<td>37-43 months</td>
<td>3.8 (5.7)</td>
</tr>
<tr>
<td>69-80 months</td>
<td>1.9 (2.6)</td>
<td>84-97 months</td>
<td>2.8 (3.5)</td>
<td>43-49 months</td>
<td>3.9 (5.8)</td>
</tr>
<tr>
<td>80-91 months</td>
<td>2.0 (2.7)</td>
<td>97-110 months</td>
<td>2.9 (3.6)</td>
<td>49-55 months</td>
<td>4.0 (5.9)</td>
</tr>
<tr>
<td>91-103 months</td>
<td>2.1 (2.8)</td>
<td>110-120 months</td>
<td>3.0 (3.7)</td>
<td>55-63 months</td>
<td>4.1 (6.0)</td>
</tr>
<tr>
<td>103-120 months</td>
<td>2.2 (2.9)</td>
<td></td>
<td></td>
<td>63-70 months</td>
<td>4.2 (6.1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>70-78 months</td>
<td>4.3 (6.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>78-86 months</td>
<td>4.4 (6.3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>86-95 months</td>
<td>4.5 (6.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>95-104 months</td>
<td>4.6 (6.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>104-114 months</td>
<td>4.7 (6.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>114-120 months</td>
<td>4.8 (6.7)</td>
</tr>
</tbody>
</table>

Values in parentheses represent the upper limit of normal.

Because of the nonlinearity of the regressions for LVID and IVS, variable age intervals were obtained to minimize the error that occurs when a whole region bounded by two curve segments is condensed into a single interval. This was done in such a way that the difference between the minimum and maximum value on the upper tolerance limit within an age interval did not exceed 0.1 unit (cm or mm), ensuring that the reported bounds are not farther away from any point on the curves delimiting the tolerance limits for the age group by more than 0.05 unit.

Abbreviations: LVIDd and LVIDs = left ventricular internal dimensions in diastole and systole; IVSd = interventricular septal thickness in diastole; LVPWd and LVPWs = left ventricular posterior wall thickness in diastole and systole.

Values for LVPW were below the lower tolerance limit of the control group at about 10 months of age in diastole and 7 months in systole.

Interventricular Septum

During the first 6 months of life, values for diastolic septal thickness in d-TGA were all normal (fig. 5A). From 1 month to 10 years, a progressive thickening was observed (fig. 5B), following the trend in the normal population. However, the regression line of the d-TGA group remained at the lower limit of normal. The mean values and their upper tolerance limits are shown in table 1. The septal motion was flat in 13 patients and paradoxical in two. All 15 children with abnormal septal motion were older than 3 years of age (fig. 5B).

Shortening Fraction and Mean Vcf

The values in the normal subjects and the d-TGA patients for SF and mean Vcf are shown in table 2. For both variables, the values in the d-TGA patients were constantly higher than those in the control group (p < 0.005). Patients who had undergone the Mustard operation had lower values for both SF and mean Vcf, but this difference was not significant (table 3).

Discussion

M-mode echocardiography is a well-established noninvasive technique for measuring LV size, wall thickness and wall motion velocities. Our study shows that although LV transverse diameter is normal at birth in patients with simple d-TGA, both systolic and diastolic measurements decrease in the very first weeks of life below the 95% tolerance limits of normal. Using angiographic measurements, Graham and co-workers showed that patients with uncomplicated transposition had a normal end-diastolic volume before 6 months of age, whereas those older than 6 months had elevated volumes and outputs. Keesens et al., using the same technique, found the same trend, although the difference was present at age 2 months. The increase in end-diastolic volume in the older in-
Figs 4 and 5. Left ventricular wall thickness in systole (LVPWs) in normal subjects and in patients with d-transposition. Regression equation for the control group: \( y = 4.633 + 0.568 \times \text{age} \) (\( R^2 = 83\% \)); for the d-TGA group: \( y = 3.822 + 0.005 \times \text{age} \) (\( R^2 = 4\% \)). However, looking at table 1, a diastolic LVPW thickness of 5 mm in d-TGA means LV hypertrophy.

Similarly, assessment of LV contractility in patients with TGA should not be based on values of SF and mean Vcf for the normal population. Indeed, in the present study, the values of these two widely used echocardiographic indexes of myocardial contractility have been significantly higher in transposition patients at all ages. The reasons for this difference cannot be inferred from the present data, but are probably related to the peculiar hemodynamics of d-TGA and the changes in LV geometry.

Anatomic reports showed that LVPW thickness starts to differ significantly from that of the normal population at 5 months \(^3\) or 8 months \(^1\) of age. These figures are closer to those found during systole in our study, confirming that measurements of fixed specimens correspond to systolic LV thickness measured by echocardiography.\(^2\)

The time at which the left ventricle of patients with d-TGA becomes thinner than normal could have some effect on the choice of the safest age for anatomic correction of TGA in patients with an intact ventricular septum and normal pulmonary pressure. Despite a
consensus that an underdeveloped left ventricle cannot withstand the sudden increase in afterload created by the arterial switch operation,1,3,23 the exact time at which the left ventricle can no longer function as a systemic ventricle has not been determined. Other factors, such as changes in septal position and structure,24 marked hypertrophy and dilatation of the right ventricle and myocardial hypoxia, must also be considered. The left ventricle in patients with d-TGA is probably inadequate for systemic work some time before the regression line of the measurements of wall thickness crosses the 95% tolerance limits of normal.

The increase in septal thickness in the d-TGA group was similar to that of normal subjects. This increase is probably due to the progressive hypertrophy of the right side of the septum. Asymmetric hypertrophy of the septum in relation to the posterior wall is thus created. Similar observations have been reported.5,25

In d-TGA, LV dimensions could be used to assess pressures in the pulmonary circulatory system indirectly. For instance, an absence of a decrease in systolic and diastolic LVID after the first weeks of life strongly suggests persistence of a high LV pressure. The same conclusion should be drawn from any increase in LVPW.

**Acknowledgment**

The authors gratefully acknowledge the skillful technical assistance of Marguerite Poirier-Mégnélas and Jean Boileau and the excellent work of Micheline Raymond in typing this manuscript.

**References**


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**Table 2. Shortening Fraction and Mean Velocity of Circumferential Fiber Shortening in Normal Subjects (Controls) and Patients with Transposition of the Great Arteries**

<table>
<thead>
<tr>
<th>Age</th>
<th>Controls</th>
<th>d-TGA</th>
<th>t test</th>
<th>Controls</th>
<th>d-TGA</th>
<th>t test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 day to 6 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>200</td>
<td>16</td>
<td></td>
<td>195</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>0.30</td>
<td>0.47</td>
<td>(p &lt; 0.005)</td>
<td>1.6</td>
<td>2.6</td>
<td>(p &lt; 0.005)</td>
</tr>
<tr>
<td>SD</td>
<td>0.061</td>
<td>0.134</td>
<td></td>
<td>0.34</td>
<td>0.64</td>
<td></td>
</tr>
<tr>
<td>6 months to 5 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>115</td>
<td>19</td>
<td></td>
<td>109</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>0.34</td>
<td>0.56</td>
<td>(p &lt; 0.005)</td>
<td>1.5</td>
<td>2.2</td>
<td>(p &lt; 0.005)</td>
</tr>
<tr>
<td>SD</td>
<td>0.045</td>
<td>0.112</td>
<td></td>
<td>0.27</td>
<td>0.49</td>
<td></td>
</tr>
<tr>
<td>5 to 10 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>67</td>
<td>16</td>
<td></td>
<td>58</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>0.33</td>
<td>0.47</td>
<td>(p &lt; 0.005)</td>
<td>1.2</td>
<td>1.8</td>
<td>(p &lt; 0.005)</td>
</tr>
<tr>
<td>SD</td>
<td>0.043</td>
<td>0.109</td>
<td></td>
<td>0.19</td>
<td>0.64</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: d-TGA = d-transposition of the great arteries; Vcf = velocity of circumferential fiber shortening.

**Table 3. Effect of the Mustard Procedure on the Shortening Fraction and Mean Velocity of Circumferential Fiber Shortening in Patients with Transposition, Ages 6 Months to 5 Years**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mustard</th>
<th>Unoperated</th>
<th>t test</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>5</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>0.54</td>
<td>0.57</td>
<td>(p &gt; 0.4)</td>
</tr>
<tr>
<td>SD</td>
<td>0.12</td>
<td>0.11</td>
<td></td>
</tr>
<tr>
<td>Mean Vcf</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>4</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>2.06</td>
<td>2.29</td>
<td>(p &gt; 0.5)</td>
</tr>
<tr>
<td>SD</td>
<td>0.34</td>
<td>0.55</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: SF = shortening fraction; Vcf = velocity of circumferential fiber shortening.

### Appendix

#### Table A1. Regression Equations for Weight and Body Surface Area

<table>
<thead>
<tr>
<th></th>
<th>$R^2$</th>
<th>SEE</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVIDd</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.30 + 1.68 (BSA)</td>
<td>0.64</td>
<td>0.33</td>
</tr>
<tr>
<td>1.54 + 0.05 (weight)</td>
<td>0.61</td>
<td>0.35</td>
</tr>
<tr>
<td>LVIDs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.58 + 1.02 (BSA)</td>
<td>0.40</td>
<td>0.33</td>
</tr>
<tr>
<td>0.70 + 0.03 (weight)</td>
<td>0.41</td>
<td>0.33</td>
</tr>
<tr>
<td>Septum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.41 + 2.40 (BSA)</td>
<td>0.35</td>
<td>0.84</td>
</tr>
<tr>
<td>2.71 + 0.08 (weight)</td>
<td>0.34</td>
<td>0.84</td>
</tr>
</tbody>
</table>

Abbreviations: LVIDd = left ventricular internal diameter in diastole; LVIDs = left ventricular internal diameter in systole; BSA = body surface area.
Influence of age on wall thickness, cavity dimensions and myocardial contractility of the left ventricle in simple transposition of the great arteries.
E Maroto, J C Fouron, M Y Douste-Blazy, A M Carceller, N van Doesburg, C Kratz and A Davignon

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