The Electrocardiogram in Ventricular Septal Defect

By DENNIS J. VINCE, M.D., AND JOHN D. KEITH, M.D.

The prognosis and indications for treatment in children with ventricular septal defects are dependent on three fundamental factors: the size of the defect, the amount of blood flowing through it, and the response of the pulmonary vasculature to the increased blood flow. The electrocardiogram has proved a useful tool in estimating the severity of these factors by giving some indication of the dynamics in any individual case.

To assess this in detail, we have studied 119 cases of isolated ventricular septal defects with intracardiac catheterization and electrocardiogram, oximetry, and fluoroscopic and physical examination. They all had repeated electrocardiograms over months or years, and in a number of cases the cardiac catheterizations were repeated. The 12 commonly used electrocardiographic leads were obtained, including precordial leads V_{3R} to V_{6}. In many instances, additional leads to right or left were also recorded.

Since this study was begun, several articles have appeared in the literature on the electrocardiogram in ventricular septal defect.\textsuperscript{1-11} There is general agreement on the presence of various patterns of systolic and diastolic loading, but the incidence of these patterns and their significance for the dynamics of the heart have met with a difference of opinion.

We have therefore presented our own criteria, primarily in the identification of right and left ventricular loading. At the end of the study additional criteria have been set down to aid in the recognition of the hemodynamics of the pulmonary circulation in an infant or child with a ventricular septal defect.

Criteria for Identification of Ventricular Loading Patterns

The electrocardiograms taken at the time of cardiac catheterization were reviewed and divided into four patterns, normal, left ventricular loading, combined ventricular loading, and right ventricular loading, according to the criteria in table 1.

It was decided not to use the axis as a criterion for right or left ventricular loading in this study, but to note how the axis related to other criteria. Notching of the P wave and late inversion in V_{1} with broadening of the P wave will be referred to in the discussion as will the counterclockwise vector.

Results

A general summary of our findings is shown in table 2, which reveals that normal electrocardiographic patterns appeared in 14 per cent of the cases, left ventricular loading in 11 per cent, combined ventricular loading in 61 per cent, and right ventricular loading in 14 per cent. As might be expected, the majority of the cases fell into the group that had combined ventricular hypertrophy.

The normal pattern and the combined ventricular pattern were approximately equally divided between the cases over and under 1 year of age. The right and left ventricular loading patterns were much more commonly found after 1 year of age than under 1 year. This is to be expected, since the right ventricle is physiologically approximately equal to the left ventricle at the time of birth, and the dominance of one ventricle over the other usually requires many months or years to develop.

Details of Patterns

The P-R interval was 0.18 second or longer in 6 per cent of the cases. The average was that usually found in normal children. The P-wave duration was found to be slightly prolonged in 30 per cent of the cases (fig. 1).
in table 4. Approximately one third had a counterclockwise vector and 80 per cent of these had an axis less than 90°. There were 26 such cases, and all had other evidence of a relatively low pulmonary vascular resistance and good pulmonary blood flow. All but 2 satisfied the criteria of DuShane et al. they had other evidence of satisfactory pulmonary blood flow. Among the cases with counterclockwise vector and an axis of 90° or over, all satisfied the criteria of DuShane et al. for operability.

The height of the T wave in V6 was somewhat elevated in 5 per cent of cases (over 4 mm. under 1 year, over 5 mm. over 1 year).

In the children over 1 year of age the average height of the T wave in V6 was essentially the same in all 4 groups, averaging 3.1 mm. in the normal, 2.1 in those with left hypertrophy, 3.0 in those with combined hypertrophy, and 3.0 in those with right ventricular hypertrophy. The T wave tended to be slightly lower in the children under 1 year of age, averaging in the normal 2.3 mm., in the left hypertrophy group 3.1, the combined hypertrophy group 1.7, and the right ventricular hypertrophy group 1.7. The height of the T wave in V6 did not significantly aid in defining diastolic loading of the left ventricle (table 5).

DuShane et al. have paid a good deal of attention to the height and peaking of the T wave in leads II, III, or aVp. They have stated that a tall peaked T wave in these leads is indication of a sufficiently low pulmonary vascular resistance to permit successful surgery on the ventricular septal defect. They do not specify how tall the T wave needs to be. In our series a T wave of 4 mm. or more included a number of cases that had markedly increased pulmonary vascular resistance and reversal of flow. This was also true of 5 mm. or more. It was also true if 4 mm. or more in all 3 leads were taken as a basic criterion. The peaking appeared to be a function of the height.

Tall T waves in many cases appeared to be related to deep wide S waves, which were associated with right bundle-branch block or right ventricular loading and did not in any
VENTRICULAR SEPTAL DEFECT

Criteria of Loading* Patterns

Table 1

Right ventricular loading
1. Voltage of R in V₁ greater than maximum normal for age.
2. Voltage of S in V₂ greater than maximum normal for age.
3. R/S ratio in V₁ greater than maximum normal for age.
4. Positive T in V₂ after third day of life when R/S ratio greater than 1.0.
5. QR pattern in V₆.

Left ventricular loading
1. Voltage of R in V₆ greater than maximum normal for age.
2. Voltage of S in V₁ greater than maximum normal for age.
3. R/S ratio in V₁ less than minimum normal for age.
4. Secondary T inversion in V₂ and/or V₆.
5. Deep Q over the left precordium—4 mm. or greater.

Combined ventricular loading
1. Direct signs of right plus left ventricular loading (as above).
2. Direct signs of right ventricular hypertrophy with the following signs in the left chest leads:
   (a) q wave (1 mm. or more).
   (b) T₂ inversion, after a positive T in right chest leads.

*The term loading has been used rather than hypertrophy, since it is a broader term, and hypertrophy may or may not be present.

way resemble the R and Q changes characteristic of diastolic loading of the left ventricle. A tall T in these particular leads is also dependent on the axis of T being +120 and +60°.

The most common characteristic feature of QRS patterns in V₁ is a relatively large R and S (table 6). With or without an original small R and S it occurred in 87 per cent. This is to be expected, since there is usually increased activity of both ventricles. The right bundle-branch block pattern of R' is a common finding in congenital heart defects with increased diastolic loading of the right ventricle, and was present in 40 per cent of our cases.

There were no instances of a QR pattern in V₁, although it was occasionally seen in RV₃ or leads farther to the right. This is usually associated with systolic or diastolic over-loading of RV and frequently is accompanied by an enlarged right atrium. Such a picture does not occur in the isolated ventricular septal defect in childhood in our experience.

Two cases showed a qRs pattern in V₁, and both were associated with enlarged hearts and a pressure in the right ventricle at systemic level.

A Q wave in V₆ was considered most significant, if it was 2 mm. or more; such was the case in 60 per cent. In 40 per cent it was 3 mm. or more. There is good evidence that this implies an active left ventricle with diastolic loading and correlates with the hemodynamic data in ventricular septal defect. A Q₆ of 1 or 2 mm. is of more significance in this regard when associated with evidence of right ventricular loading (table 7).

Pulmonary Blood Flow

The electrocardiographic patterns helped considerably in separating the various groups in relation to pulmonary blood flow (table 8). When the electrocardiogram was normal, the flow was invariably relatively low, never more than twice systemic whether the age group was over or under 1 year. When a left ventricular loading pattern was present, the flow through the pulmonary artery was usually not large but occasionally exceeded four times the systemic.

When a right ventricular loading pattern was found alone in the electrocardiogram, the pulmonary blood flow was not large, but in six cases was up to two or three times the systemic. In these cases there was no reversal.
of flow with exercise, while in the seven cases that had a flow of only one or two times systemic, all had reversal of flow with exercise. The greatest flows and greatest variations were found in the combined loading group. In this group more of the younger children had larger flows than the older children, as one would expect. Reversal of flow in these cases occurred almost entirely among those with a large flow and systemic pressure in the pulmonary artery. The hemodynamic findings in the group suggested that the majority were likely to respond satisfactorily to surgery.

Correlation between the Pressure in the Right Ventricle and Electrocardiogram

Table 9 shows that there is some correlation between the pressure in the right ventricle and the electrocardiographic pattern. When a normal electrocardiographic pattern was present, the pressure in the right ventricle rarely
Table 2

<table>
<thead>
<tr>
<th>Electrocardiographic Pattern</th>
<th>Age (yr.)</th>
<th>No. of cases</th>
<th>Per cent of total cases</th>
<th>Combined per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;1</td>
<td>7</td>
<td>5.9</td>
<td>14.3</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>10</td>
<td>8.4</td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>&lt;1</td>
<td>3</td>
<td>2.5</td>
<td>10.9</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>10</td>
<td>8.4</td>
<td></td>
</tr>
<tr>
<td>Combined</td>
<td>&lt;1</td>
<td>35</td>
<td>29.4</td>
<td>61.3</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>38</td>
<td>31.9</td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>&lt;1</td>
<td>2</td>
<td>1.7</td>
<td>13.5</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>14</td>
<td>11.8</td>
<td></td>
</tr>
</tbody>
</table>

*Total number of cases 119; 39.5 per cent under 1 year, 60.5 per cent over 1 year.

Table 3

<table>
<thead>
<tr>
<th>Electrocardiographic Pattern</th>
<th>Age (yr.)</th>
<th>No. with notching and broadening of P in lead I or II</th>
<th>Total cases reviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Left ventricular loading</td>
<td>&lt;1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>Combined ventricular loading</td>
<td>&lt;1</td>
<td>10</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>16</td>
<td>36</td>
</tr>
<tr>
<td>Right ventricular loading</td>
<td>&lt;1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>0</td>
<td>14</td>
</tr>
</tbody>
</table>

*There were 4 additional cases that showed broadening of P\textsubscript{2} and late inversion of P\textsubscript{1} in V\textsubscript{1} but without notching.

Ventricular Septal Defect exceeded 40 mm. Hg. When left ventricular hypertrophy was present, the majority had pressures in the right ventricle under 50 mm. Hg, and only rarely did it exceed 60 mm. Hg. The combined ventricular hypertrophy group showed the greatest variation, and again the pressures correlated with the predominant hypertrophy pattern; where it was predominantly right, it tended to be high.

When isolated right ventricular hypertrophy was present in the electrocardiograms, the pressure was rarely lower than 60 mm. Hg and was almost invariably at systemic level.

Oximetry

The information obtained by the ear oximeter correlated well with the electrocardiographic data. In Table 10 are shown the results following exercise. When a normal or left ventricular hypertrophy pattern was present, none showed a drop in arterial oxygen saturation with exercise. When combined ventricular hypertrophy was found in the electrocardiogram, approximately 17 per cent had a drop with exercise, a similar percentage being present whether over or under 1 year of age. When a pattern of isolated right ventricular hypertrophy was found in the electrocardiogram, 60 per cent showed a drop in oxygen saturation. As might be expected, the percentage with reversal of blood flow through the ventricular septal defect during exercise was much higher in those with right ventricular overloading alone, since they were associated with high pulmonary vascular resistances in most cases. In a few instances in this latter group, the pulmonary vascular resistance was only moderately increased, and no drop in arterial oxygen saturation occurred following exercise. In those with combined hypertrophy in which the right hypertrophy was markedly predominant, reversal of flow through the defect was more likely. This would appear to be due to the combination of a large volume flow through the lungs and increased pulmonary vascular resistance.

Physical Findings

Normal Electrocardiographic Pattern

In this group a loud, harsh murmur and thrill were found in all; the cardiothoracic ratio varied between 52 and 68 per cent. The hilar shadows were increased and many were pulsating. The pulmonary second sound was increased slightly in about 30 per cent.

Left Ventricular Hypertrophy

A loud harsh murmur and thrill were present in all of these cases. In all, the pulmonary second sound appeared within normal limits, and intensity and normal splitting were noted. The cardiothoracic ratio varied between 50 and 69 per cent. Left atrial enlargement was demonstrated radiologically in 7 of the 10 children over 1 year of age.

Combined Ventricular Hypertrophy

All these cases had the usual murmur and thrill, approximately a quarter of those in
the first year of life showed signs of failure at some time, and many of the others had dyspnea at rest. All had evidence of increased pulmonary flow on fluoroscopic examination, although pulsations in the hilar shadows during the first year were hard to see. The second sound was increased in approximately half of them, and the cardiothoracic ratio varied from 50 to 70 per cent.

Right Ventricular Hypertrophy

The systolic murmur was frequently short and occasionally absent in this group. The thrill was the exception rather than the rule. Clinical cyanosis was observed in 6 of the 16 cases at rest. A precordial lift to the right ventricle was present in all over 1 year of age. The pulmonary artery bulged under the fluoroscope, and hilar shadows were increased. Pulsation of the hilar shadows was evidenced in the majority. One child at the age of 12 showed only very questionable pulsations. The second sound was uniformly loud and closely split; in 1 case it appeared to be single. The and 82 per cent of these had an axis of less heart size was slightly smaller than in the combined ventricular hypertrophy group.

Changing Electrocardiographic Pattern

From repeated electrocardiograms in 61 cases table 11 was drawn up to show the relationship of the four fundamental patterns to change over the years of follow-up. The time in follow-up varied from 7 months to 7 years, and the average between the first and the last electrocardiogram was 3 years.

Among the cases that did not have isolated right ventricular systolic loading to begin with, only one developed this pattern later during the period of observation. Our first
VENTRICULAR SEPTAL DEFECT

Table 6
Summary of the QRS Patterns in Precordial Lead V6.

<table>
<thead>
<tr>
<th>Number of cases</th>
<th>qR</th>
<th>qRs</th>
<th>rsR'</th>
<th>r's</th>
<th>rsR'S'</th>
<th>RS</th>
<th>R</th>
<th>rS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>10</td>
<td>30</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>&gt;1 year</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>0</td>
<td>27</td>
<td>37</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 7
Size of Q Wave in V6.

<table>
<thead>
<tr>
<th>Size of Q Wave in V6</th>
<th>0</th>
<th>1 mm.</th>
<th>1 mm.</th>
<th>2 mm.</th>
<th>3 mm.</th>
<th>4 mm.</th>
<th>5 mm.</th>
<th>6 mm.</th>
<th>7 mm.</th>
<th>8 mm.</th>
<th>9 mm.</th>
<th>10 mm.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>16%</td>
<td>4%</td>
<td>20%</td>
<td>15%</td>
<td>17.5%</td>
<td>11%</td>
<td>7%</td>
<td>2.5%</td>
<td>2.5%</td>
<td>2.5%</td>
<td>1%</td>
<td>1%</td>
</tr>
</tbody>
</table>

electrocardiogram was done at 4 months of age (fig. 3), and the last at 4 years. The combined ventricular loading was changed to pure right, with no evidence of left systolic or diastolic loading. Re-catheterization showed a relatively constant state over the childhood years. A gradual shift may occur from combined ventricular loading to isolated right. Those that have this latter pattern are chiefly in the age group from 6 to 13 years. Some of the cases with right loading showed deepening S in V6 over a period of a few years.

It would appear that evidence of left ventricular loading in a child over 2 or 3 years of age, or an isolated right ventricular loading pattern, is likely to be maintained for long periods.

In a few cases with combined loading, the right ventricular loading pattern has become increasingly dominant after 1 or 2 years of age. The most characteristic pattern was that of left loading. Of the 61 cases followed over several years, 43 remained unchanged (most had left loading at first observation); 11 developed signs of left loading when it was not present before. The new appearance of right loading was an uncommon event, since most of our cases were followed from infancy during the early years. These findings indicate that the presence or appearance of left diastolic loading after the fetal pulmonary vascular pattern recedes is a common event.

Discussion
There have been numerous studies on the electrocardiogram in ventricular septal defect. Several authors have dealt with the incidence and criteria of right and left ventricular hypertrophy patterns in this defect. A distinct advance in our understanding of the relationship of the electrocardiogram to the underlying physiology was made by Sodi-Pallares and co-workers when they outlined the criteria for systolic and diastolic loading of the heart chambers. The tall R in V1 with inverted or upright T waves as evidence of right ventricular systolic overload has stood the test of time. The tall broad R waves, the lengthened ventricular activation time, and the flat or inverted T waves in V6 are accepted as good evidence of left ventricular systolic overloading. The rsr pattern in V1, not uncommonly occurred with right ventricular diastolic loading, but frequently occurred in normal patients also, and is, therefore, much less specific than those mentioned above. The tall peaked upright T waves in standard leads II, III, and aVF and V6 are of little value in indicating left ventricular diastolic overload except when accompanied by tall R waves or a deep Q in V6. The latter criteria presented by Sodi-Pallares and co-workers have needed more accurate definition, and this has been provided lately, to some degree, by DuShane and associates in elucidating those cases with ventricular septal defect that show diastolic loading. Their criteria were as follows: a tall R in V6, a deep S in V1, a Q in V6 of 4 mm. or greater, an axis of 0 degrees (or less than 60 when the age is under 3), a counterclockwise direction of the vector under the age of 3, and tall peaked T waves in leads II, III, or aVF. They concluded that if any one of these criteria was present in patients undergoing

Circulation, Volume XXIII, February 1961
surgery, 96 per cent showed a satisfactory drop in pressure in the pulmonary artery postoperatively. These are helpful criteria, but on reviewing our data we find that a number of important modifications are needed. These relate to the axis of QRS, the counterclockwise vector, the tall peaked T wave in leads II, III, and aVF, and P-wave abnormalities such as notching, broadening in the standard leads, and late inversion in V1.

**Axis**

We find the axis to have a broader and more applicable significance than was noted by DuShane's group.\textsuperscript{12} Whenever the axis was less than 90° we found other evidence of a moderate or low pulmonary vascular resistance that would be expected to permit successful surgery. This axis occurred in approximately one half of our cases, appearing only in those that had an electrocardiographic pattern showing normal, left, or combined loading. It was not seen in those with a pure right loading configuration.

**Counterclockwise Vector**

As would be expected, the direction of the vector followed the direction of the axis as a rule. One third had a counterclockwise vector, and 82 per cent of these had an axis of less than 90°. Thus the axis is a more useful measurement than the direction of the vector. There were, however, 7 cases that had a counterclockwise vector with an axis 90° or more. On reviewing these separately it was obvious that they had other evidence of relatively good pulmonary blood flows and would, therefore, fall into the operative group.

**Tall Peaked T Waves**

DuShane and associates\textsuperscript{12} have stated that a tall peaked T wave in standard leads II, or III, or in aVF is indicative of sufficiently low pulmonary vascular resistance to permit successful surgery on the ventricular septal defect. They do not state how tall the T wave needs to be. If the T wave is 4 mm. or more, this includes a large number of cases that have marked pulmonary vascular resistance with

### Table 8

<table>
<thead>
<tr>
<th>Electrocardiographic Pattern</th>
<th>Age (yr.)</th>
<th>Total Cases</th>
<th>Ratio of Pulmonary Flow to Systemic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1-2 times</td>
</tr>
<tr>
<td>Normal</td>
<td>&lt;1</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Left loading</td>
<td>&lt;1</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Combined loading</td>
<td>&lt;1</td>
<td>34</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>35</td>
<td>11</td>
</tr>
<tr>
<td>Right ventricular loading</td>
<td>&lt;1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>13</td>
<td>7</td>
</tr>
</tbody>
</table>

### Table 9

<table>
<thead>
<tr>
<th>Electrocardiographic Pattern</th>
<th>Age (yr.)</th>
<th>Right Ventricular Pressure mm. Hg (systolic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;1</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>6</td>
</tr>
<tr>
<td>Left</td>
<td>&lt;1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>1</td>
</tr>
<tr>
<td>Combined loading</td>
<td>&lt;1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>1</td>
</tr>
<tr>
<td>Right</td>
<td>&lt;1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>1</td>
</tr>
</tbody>
</table>
VENTRICULAR SEPTAL DEFECT

Figure 3

Electrocardiogram at 4 months shows a tall R and deep Q in V₆. At 2½ years and at 4½ years one sees a diminishing R and Q in V₆, at the same time the R in V₁ is increasing in height. These findings are consistent with increasing pulmonary vascular resistance.

reversal of flow. If the measurements included only those 5 mm. or more, it still included a number of cases that should be eliminated. We have one case (a boy of 15 years) whose T wave in II is 9 mm., tall and peaked, whose oxygen saturation drops to 60 per cent with exercise, whose heart is not significantly enlarged, and whose hilar shadows are increased centrally, but cut off peripherally. The chances of successful surgery in him would appear slim. If only those with T waves in all 3 leads II, III, and aV₆ of 4 mm. or more are accepted, the above-mentioned boy is eliminated; but an analysis of our cases indicates that several of those included by this measurement would be bad risks.

If only those with T waves of 5 mm. or more in all 3 leads II, III, and aV₆ were included, there were usually other signs indicating operability: but again exceptions appeared.

The height of the T in II, III, and aV₆ appears to be related to the direction of T vector and the area of the QRS complex. This is particularly misleading when a deep S wave occurs with or without right bundle-branch block. There is no constant relation to the pulmonary flow or diastolic loading of left ventricle. We cannot demonstrate any significant help in selecting cases for surgery by this method.

Char and associates, studying surgically treated cases, found some correlation between the height of the T in V₆ and survival rate. The prognosis was better if the T in V₁ was inverted, and better if the T in V₆ was upright and tall. If the T in V₁ was upright and the T in V₆ down, the prognosis at the operation was poor, with survival of only 2 out of 10 cases.

Broad Notched P Waves

An analysis of the P wave in the electrocardiogram in the ventricular septal defect group is of interest, since it is associated with increased flow or pressure in the left atrium, and thus gives us another indication of pulmonary vascular resistance.

Dines and Parkin have reviewed P wave morphology in patients with increased left atrial pressure and left atrial enlargement. They point out that notching and broadening of the P wave in standard lead I or II is the best evidence of this pathology. Broadening of the P wave and late inversion of the P in V₁, associated with broadening, are also evidence of the same pathology. In the pediatric age group a P wave over 0.09 second was taken as significant broadening. The broadening of the P wave is an important accompaniment of late inversion of the P wave in pre-

Table 10

<table>
<thead>
<tr>
<th>Electrocardiographic loading pattern</th>
<th>Age (yr.)</th>
<th>Total done</th>
<th>Number showing drop with exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;1</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Left</td>
<td>&lt;1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Combined</td>
<td>&lt;1</td>
<td>28</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>23</td>
<td>4</td>
</tr>
<tr>
<td>Right</td>
<td>&lt;1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>14</td>
<td>8</td>
</tr>
</tbody>
</table>

Circulation, Volume XXIII, February 1961
cordial lead V₁. Late inversion alone may occur in normal persons.

There appears to be no close relationship between the anatomic type of ventricular septal defect and the electrocardiogram, except that the smaller defects are associated with normal patterns or left loading and the larger ones with combined or pure right loading.

Toscano-Barboza and DuShane¹⁰ suggested that when the electrocardiographic pattern of isolated left ventricular overload, such as seen in patent ductus, occurs in ventricular septal defect, it is associated with an opening between the right and left ventricles in the outflow tract of the right ventricle. On reviewing our electrocardiographic and pathologic material we were unable to substantiate this finding in any single case. Furthermore, on reviewing their paper, we note that one of their cases had such an electrocardiographic pattern and yet the ventricular septal defect was found at operation to be in the membranous portion of the septum.

The Q Wave in V₆

A special word is required regarding the Q wave in V₆. In a recent study Watson and Keith¹⁵ demonstrated that 74 out of 95 cases of tetralogy of Fallot had a Q wave in V₆ of less than 1 mm. All these cases were associated with a high pulmonary vascular resistance in the sense that they had obstruction at the entrance to the pulmonary artery. The other 26 per cent that had a Q wave of 1 mm. of more were those that had associated patent ductus, a Blalock operation, or a relatively high oxygen saturation of the arterial blood at rest and with exercise. All this latter group had a good volume flow through the lungs returning to the left ventricle, averaging twice the systemic flow. The presence of this good pulmonary flow was suggested by a significant Q in V₆. These findings may be compared with those of our group of 119 cases of ventricular septal defect. Eighty per cent of our series had a Q wave in V₆ of 1 mm. or more, and again this appears to be clear evidence of a considerable diastolic volume flow to the left ventricle, since those that did not show this Q wave were either those that had high pulmonary vascular resistance with reversal of flow through the defect, or very mild cases with a normal electrocardiogram that had normal flows, and, therefore, no diastolic overloading of the left ventricle. In spite of the fact that a Q wave in V₆ may occur frequently in the normal, a review of this data indicates that a Q wave bears a close relationship to the presence or absence of a diastolic overloading in the ventricular septal defect group, especially when the electrocardiogram shows a systolic loading of the right ventricle at the same time. Twenty-five per cent of our cases with ventricular septal defect showed a Q wave in V₆ of 4 mm. or more, 60 per cent had a Q of 2 mm. or more. A Q wave of 4 mm. was always associated with other evidence of left diastolic loading, such as a tall R in V₆, or deep S in V₁, or notching of P wave, a left axis or a pulmonary blood flow more than two times systemic. The same could be said of a Q in V₆ of 2 mm. or more. There

Table 11

<table>
<thead>
<tr>
<th>Electrocardiographic Pattern</th>
<th>Total</th>
<th>Remained unchanged</th>
<th>Became normal</th>
<th>Became left loading</th>
<th>Became combined loading</th>
<th>Became right loading</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>10</td>
<td>5</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Left ventricular loading</td>
<td>6</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Combined ventricular loading</td>
<td>34</td>
<td>25</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Right ventricular loading</td>
<td>11</td>
<td>7</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>
was less evidence in this direction when \( Q_6 \)
was 1 to 2 mm., but when associated with
right ventricular systolic loading it was suffi-
cient to indicate that a very high pulmonary
vascular resistance had not yet been reached.
A \( Q_6 \) of less than 1 mm. was of no signifi-
cance in this regard. Both the clinical, physiologic,
and operative findings all indicate that cases
with a good \( Q \) wave in \( V_6 \) have a significant
degree of diastolic loading of the left
ventricle.

**Hemodynamics and the Electrocardiogram**

The electrocardiogram is simply one of the
various clinical and hemodynamic techinie for
recognizing systolic and diastolic loading of
the heart chambers and in interpreting the
various degrees of physiologic and pathologic
change in the pulmonary arteries. Other meth-
ods include an estimation of the pulmonary
vascular resistance, pulmonary blood flow and
pressure, a study of the arterial oxygen sat-
uration, ear oximetry, or biopsy of lung tissue.
The effect of acetylcholine on the pulmonary
artery pressure should also be included as
well as the clinical examination including a
chest x-ray, murmur, thrusts, pulsating hilar
shadows, pulmonary second sound, systolic
click, activity of right and left ventricle, and
response to exercise. Finally, the age of the
child is important.

It is obvious that all these methods provide
useful information in their own way, but each
has its limitations. The pulmonary vascular
resistance is based on a formula involving
blood flow and pressure. A variety of factors
may influence these two measurements, such
as the type of sedation, anxiety, crying, or
activity on the part of the patient. The blood
pressure may be higher earlier in cardiac
catheterization and lower in the later stages.
Oxygen contents of heart chambers may vary
to some degree with the site of the catheter,
the time during the procedure that blood was
withdrawn, the systemic and pulmonary blood
pressures. Thus the figures presented as pul-
monary vascular resistance may be far from
accurate.

Ear oximetry gives us an opportunity to
study the oxygen content of arterial blood in
these patients at rest, with activity, and with
the administration of oxygen. Reversal of
blood flow through the defect at rest or with
exercise may be readily demonstrated by this
method, and provides useful information on
the state of the pulmonary arteries. There
was no evidence of reversal of flow through
the defect with exercise, in the group with

---

**Table 12**

<table>
<thead>
<tr>
<th>Electrocardiographic pattern</th>
<th>Age (yr)</th>
<th>Total cases</th>
<th>Total ( Q_6 )'s</th>
<th>Tall ( Q_6 ) or more</th>
<th>Deep ( Q_6 ) or more</th>
<th>Tall T or more</th>
<th>Deep T or more</th>
<th>( R/S ) ratio</th>
<th>Q in ( V_6 )</th>
<th>1-2</th>
<th>Broad P- and late inversion in ( V_1 )</th>
<th>Broad P- and late inversion in ( V_1 )</th>
<th>Axial less than 90°</th>
<th>Reversal of flow</th>
<th>Pulmonary to systemic blood flow ratio</th>
<th>Age 6 years or under</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( &lt;1 )</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>0</td>
<td>3</td>
<td>4</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>( \geq 1 )</td>
<td>10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>9</td>
<td>4</td>
<td>10</td>
<td>0</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Left loading</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( &lt;1 )</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \geq 1 )</td>
<td>10</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>6</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Combined loading</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( &lt;1 )</td>
<td>34</td>
<td>16</td>
<td>12</td>
<td>7</td>
<td>9</td>
<td>2</td>
<td>12</td>
<td>5</td>
<td>10</td>
<td>7</td>
<td>16</td>
<td>14</td>
<td>6</td>
<td>28</td>
<td>6</td>
<td>34</td>
</tr>
<tr>
<td>( \geq 1 )</td>
<td>36</td>
<td>16</td>
<td>12</td>
<td>7</td>
<td>4</td>
<td>1</td>
<td>7</td>
<td>15</td>
<td>16</td>
<td>16</td>
<td>18</td>
<td>13</td>
<td>11</td>
<td>25</td>
<td>3</td>
<td>29</td>
</tr>
<tr>
<td>Right loading</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( &lt;1 )</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>( \geq 1 )</td>
<td>13</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>7</td>
<td>6</td>
<td>7</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Totals</td>
<td>115</td>
<td>42</td>
<td>32</td>
<td>21</td>
<td>16</td>
<td>5</td>
<td>25</td>
<td>30</td>
<td>36</td>
<td>32</td>
<td>57</td>
<td>38</td>
<td>45</td>
<td>70</td>
<td>16</td>
<td>94</td>
</tr>
</tbody>
</table>

---

*Downloaded from http://circ.ahajournals.org/ by guest on November 16, 2017*
normal or left ventricular systolic loading in their electrocardiograms. A number demonstrated reversal in the combined ventricular loading group, the pulmonary vascular resistance appears not to be excessively great. The age in half this group was under 1 year. On the other hand, in the group with isolated right ventricular hypertrophy, oximetry almost invariably showed a reversal of flow with exercise, with a low flow to the lungs, and confirms the impression of high pulmonary vascular resistance. As one might expect, the age in this latter group was considerably older than the combined group, the average being 8 years, and most of them were 6 years.

Biopsy of the lung has been used occasionally to assess the pulmonary vasculature. This is a significant procedure, but the surgeon is limited to a small area (usually the lingula) in taking out a piece of lung, and while a study of such sections may permit one to place the case into one of the six categories described by Heath and Edwards, it has been shown on several occasions that certain patients having some of the most advanced intimal changes in the pulmonary arteries may occasionally respond successfully to closure of the septal defect with a satisfactory drop in pressure in the pulmonary artery.

The clinical examination is most helpful, since the murmur may be fainter and shorter with pulmonary hypertension and marked increase in pulmonary vascular resistance. The thrill may be absent. The hilar shadows show less pulsation, and the heart is smaller. These observations, while most useful, may be far from decisive in solving the problem at hand, but serve as corroborative evidence.

The resistance of the pulmonary vascular bed may be evaluated by injecting acetylcholine into the pulmonary artery. Adams found that approximately one third of a group of children with ventricular septal defects and pulmonary hypertension failed to respond to this drug, with a drop in pressure in the pulmonary artery. All those who were under 7 years of age responded, however.

Age is an important consideration in estimating the possible hemodynamic response to closure of a ventricular septal defect. The few cases with Eisenmenger's complex in childhood were usually in older children. We have seen several such cases over the age of 12 years. The only children that could legitimately be said to fall into this category in our series are those with reversal of flow coupled with high pulmonary vascular resistance. In table 12 one will see that there were 7 cases that might fit this description. Of these 7 cases all but 2 were over 6 years of age. Thus, in the under 7 age-group, our evidence suggests that only 2 per cent may be labeled as having the Eisenmenger's syndrome.

While the pulmonary vascular resistance is high at birth, and this may persist for some time, eventually all in this age group, with rare exceptions, show evidence of some degree of left ventricular loading, indicating a benign pulmonary vascular resistance that would permit corrective surgery. As indicated above we have only 2 cases under 7 years of age that have evidence clinically or hemodynamically that would suggest they would not respond favorably to surgery. DuShane and co-workers reported 10 cases operated on in spite of the fact that their electrocardiographic patterns did not have any of their operable criteria present. Two had a drop in pressure in pulmonary artery and right ventricle postoperatively. The age of this group was not stated, but one would expect it to be chiefly over 6 years of age.

Several observers have reported repeated cardiac catheterization measurements in ventricular septal defect. Very few children with this anomaly have shown any tendency for the pulmonary vascular resistance to change appreciably in childhood. The electrocardiogram may bear on this problem. From this source alone the evidence suggests that, while some cases have a much higher pulmonary vascular resistance in infancy and early childhood than others, it is not of sufficient magnitude to preclude successful surgical closure of the defect before the age of 7 years except in an occasional rare instance. For these vari-

Circulation, Volume XXIII, February 1961
ous reasons we have included age as one of the criteria of operability.

An examination of electrocardiographic patterns in cases followed for several years showed three types of response: 1. The great majority showed a remarkably constant electrocardiogram over the years each case was followed. 2. A modest number (6) showed a disappearance of the normally right dominant pattern in infancy, or a combined loading, and the appearance of a left loading configuration. Another 5 that were normal to begin with, developed evidence of left loading. This has always been a favorable sign, and such children have done well over the years and are good risks at surgery. Close to the first-mentioned cases are those patterns that have right loading when first seen but subsequently developed combined. This is also associated with the infant growing into the child, and the pulmonary vascular resistance apparently falling to a sufficient degree to produce signs of left diastolic loading. 3. Only 1 case developed a purely right loading pattern, while some of those with combined ventricular hypertrophy showed a progressively dominant R wave in V1 or a deeper S in V6, or both, but still retained some evidence of left ventricular loading. There are, therefore, signs of variation in the pulmonary vascular resistance with a gradual reduction in the first year sometimes proceeding into the second year. Only a rare exception is not operable between the ages of 2 and 5 regardless of what their electrocardiograms show.

The criteria of DuShane and his associates12 for selection of cases for surgery with ventricular septal defect are most helpful, in that they isolate a group that is most likely to survive operation providing the technique is adequate. Their criteria were not designed to provide detailed recognition of normal patterns, left loading, right loading, and combined, nor will they tell us which cases will survive surgery and be helped by it when their criteria are not satisfied.

We have found the criteria of DuShane and his associates useful as a baseline to check our own. By their standards our pure right ventricular loading group would be excluded from surgery as would our normal group. Our left loading group would be included. Approximately 70 per cent of our combined ventricular loading group would be included, but 30 per cent would be excluded from surgery. It is these minority groups that deserve special study.

In our pure right ventricular loading group of 14 cases, 2 have already been operated on successfully.

Broader criteria than those suggested by DuShane and co-workers12 are needed to permit a wider degree of grading of the pulmonary vascular flow and resistance, and thus enhance our ability to assess operability. The problem of the future lies not so much in identifying the groups that are sure to survive and be cured by surgery, as in identifying those that are operable but whose criteria are not so emphatic. The electrocardiogram is a great help in this, but must be used in conjunction with the cardiac catheter findings, oximetry, and age, as well as with the clinical signs.

In assessing a case of ventricular septal defect by the electrocardiogram two steps appear useful: first, an evaluation of the tracing to decide which of the four main groups it falls into, (a) normal, (b) left loading, (c) combined loading, and (d) pure right ventricular loading (table 12). If it is in group (a) or (b) the pulmonary vascular resistance is low and the child is suitable for surgery, provided the technic becomes adequately safe. When it falls into group (c) or (d), that is combined or pure right ventricular loading, the second form of evaluation is then most helpful. This consists of an itemized study of the factors that relate to pulmonary vascular resistance; the ones we consider the most important are listed in table 12; i.e., a tall R in V6, or a deep S in V1, a deep Q in V6, broadening and notching of the P wave in standard lead I coupled with late inversion of the P in V1, an axis of less than 90°, counterclockwise vector, a pulmonary systemic flow ratio of more than 2, absence or reversal.
of flow through the defect, an age under 7 years.

The application of these criteria to the group of combined loading has been discussed previously. Most cases that have one or more of these criteria in the combined group have shown only moderately raised pulmonary vascular resistance. The cases with the least favorable criteria were those that had neither a tall \( R_a \) nor deep \( S \) in \( V_1 \), nor a deep \( Q \) in \( V_6 \), but had a pulmonary/systemic flow ratio of less than 2 and an absence of notching and broadening of the P wave. There were only three under 1 year of age that fell into this category, and none of them had reversal of flow. The Q wave in \( V_6 \) varied from 1 to 3 mm. and was the only electrocardiographic evidence in favor of surgical correction.

Among those over 1 year of age in the combined loading group that had no tall \( R_a \) or deep \( S \) in \( V_1 \), or deep \( Q \) in \( V_6 \), and a flow ratio of less than 2, there were only 3 cases. One of these had notching and broadening of the P wave, one was operated on successfully, and the other had clinical signs indicative of an adequate pulmonary blood flow. None of the 3 cases had reversal of flow through the defect. Again a q wave in \( V_6 \) of 1 to 3 mm. was helpful in recognizing the potentialities of a favorable result.

In summary, one can conclude that in the combined loading group there was good evidence that the overwhelming majority are operable and would respond favorably to closure of the ventricular septal defect.

The group that is least likely to respond is that with pure right ventricular loading. None of these satisfied the criteria of DusShane and co-workers, but 2 of the 14 have already been operated on successfully. Such cases may be picked out of this group by the finding of a pulmonary/systemic blood flow ratio of more than 2, or a counterclockwise vector, or an age that is under 7 years, or an absence of reversal of flow through the defect. If one or more of such items are present, the patient may well survive corrective surgery in spite of the unfavorable electrocardiogram. If none of these items is found, the chances of cure or survival are slim indeed.

A rare case of ventricular septal defect with complete right bundle-branch block will show a pattern indicative of right ventricular hypertrophy or loading when such is either not present or the loading is of a minor degree. The electrocardiogram may then be misleading. This was true of a case in our pure right group. This case was classified by cardiac catheterization, which revealed relatively low pressures and low flows in the pulmonary circuit.

Another case with an electrocardiogram indicating right ventricular hypertrophy and complete right bundle-branch block was found, on cardiac catheterization, to have dynamic evidence of high pulmonary vascular resistance. Such cases are less likely to be missed, since the unfavorable electrocardiogram will lead to further investigation.

We have concluded, therefore, that when complete right bundle-branch block is present it is important to investigate the child fully with adequate blood flow studies.

Summary

One hundred and nineteen cases of ventricular septal defect in infancy and childhood have been reviewed, with special reference to the electrocardiogram. The changes in the electrocardiogram were related to the hemodynamics found at cardiac catheterization, and particularly the pulmonary to systemic blood flow ratios, pulmonary artery pressures, and oximetry. They were also studied in relation to the groups of cases that obviously had a low pulmonary vascular resistance with or without diastolic loading of the left ventricle. Survival of a patient following closure of the defect with a drop in pulmonary artery pressure was also taken as a sign that the pulmonary vascular resistance was not excessive. The patients with clinical and hemodynamic evidence of a high pulmonary vascular resistance were also evaluated in relation to the electrocardiogram.

The information obtained from the electrocardiogram may be graded according to degree of severity: (a) normal electrocardiogram, (b) left ventricular loading, (c) combined loading, (d) isolated right ventricular
VENTRICULAR SEPTAL DEFECT

loading. These groups may be further graded depending on the diminishing number of signs listed below.1-7 A detailed review of these four groups in relation to the following criteria may allow one to identify a low or only moderately raised pulmonary vascular resistance, or one that is sufficiently moderate to permit successful corrective surgery in the pediatric age group:

1. An R in V₆ over 20 mm.
2. A Q in V₆ of 4 mm. or over.
3. An S in V₁ over 25 mm.
4. A Q in V₆ of 2 mm. or more when associated with evidence of right ventricular loading.
5. An axis of less than 90°.
6. Counterclockwise vector.
7. Broad notched P waves in standard leads I or II, with late inversion in V₁.

As a rule, several of these criteria occur together, but even if only one of them is present, one may conclude that the pulmonary vascular resistance is not excessive. Further support to this conclusion is evident if any of the above 7 items are accompanied by one or more of the following: (x) a pulmonary blood flow that is twice systemic, (y) an absence of reversal of flow through the defect either at rest or with exercise, (z) an age under 7 years.

Among the 119 infants and children with ventricular septal defect, over 90 per cent appeared to have a sufficiently low pulmonary vascular resistance to be operable provided the surgical technic is adequate and provided complete heart block does not occur.

Age appears to be an important factor in assessing the likelihood of success at surgery. Only an exceptional case shows hemodynamic findings indicating inoperability before the age of 7 years.

During the first year of life many cases of ventricular septal defect have signs of left ventricular loading appear or increase, suggesting a favorable trend in the pulmonary vascular resistance. Until surgical technic makes operation more readily feasible in infancy, the optimum age of correction would appear to be between 2 and 7 years.

Acknowledgment

The authors would like to express their appreciation to Dr. Richard Rowe, for the use of many of his cases in this study, and for his helpful criticism at various stages. They are also indebted to Dr. John Fay, who helped in the preparation of some of the data. The authors would particularly like to indicate their appreciation to Mrs. Tischler and Miss Laidlaw for their assistance in typing and arranging the details of the manuscript and charts.

References


Circulation, Volume XXIII, February 1961


15. WATSON, D. G., AND KEITH, J. D.: To be published.


Please do not conclude that I argue for medical protection and care as the summum bonum of existence. Man cannot live by bread alone, even when it is whole wheat and reinforced with minerals and all the known vitamins. There are greater ends in living than health. These ends can be attained by those who are not even in perfect health. The same is true of food, housing, and clothing—not particularly rewarding as ends in themselves, but, like health, of considerable importance as means to whatever ends you may deem worthy of living for. In claiming that health is as important as food, shelter, and clothing, I do not imply that it is more important, nor even that health is as important as truth, beauty, or love. But I like to imagine that at the end of a year's prosaic labors in a hookworm campaign in, say, South America, a public health officer encountered a seller of musical instruments who said, "Senhor Doutor, I thank you for your work, because now the people are well enough to sing." Though different races find each other's because I have sold this year more violins and guitars in this village than ever before, arts, philosophies, and religions not always acceptable, there is a notable amount of agreement everywhere that health wherewith to follow and practice them is good.—ALAN GREGG, M.D. Challenges to Contemporary Medicine. New York, Columbia University Press, 1956, p. 79.