Serial Cardiac Catheterizations and Exercise Hemodynamics after Correction of Tetralogy of Fallot

Average Follow-Up 13 Months and 7 Years after Operation

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SUMMARY
Eleven patients had right heart catheterization an average of 13 mo after total correction of tetralogy of Fallot, and the procedures were then repeated an average of 7 years postoperatively. In the intervening time there was generally no important change in the pressure gradient between the right ventricle and pulmonary artery or in right ventricular systolic pressure. Mean right atrial pressure tended to fall with time. Arteriovenous oxygen difference at rest was lower at the second study, and the resting cardiac output was generally normal. One patient with a persistent ventricular septal defect had progressive hemodynamic deterioration between the two studies. Exercise performance up to 10 years postoperatively was also assessed. The relationship between oxygen consumption and cardiac output was usually normal, but exercise magnified the right heart's filling pressure abnormalities. In the absence of an easily demonstrable ventricular septal defect, right heart hemodynamics were either stable or improved up to 10 years postoperatively. The exercise response of cardiac output was usually normal at moderate work loads.

Additional Indexing Words:
- Pulmonic regurgitation
- Ventricular septal defect
- Infundibular stenosis
- Open heart surgery
- Cardiac output
- Exercise capabilities

TOTAL surgical correction is well established as successful treatment for tetralogy of Fallot, many reports having described the highly satisfactory results usually achieved.1-7 Postoperative cardiac catheterizations have demonstrated residual hemodynamic abnormalities, however, and these are a source of uncertainty in the long-range outlook for these children.2, 8-14 One concern is pulmonic valve regurgitation, especially likely to be of significant degree when a prosthetic or pericardial patch is employed to enlarge the right ventricular outflow tract or hypoplastic pulmonary artery. Because of this complication and its unknown long-term effects, the trend in recent years has been to avoid the use of an outflow patch whenever possible and to avoid cutting the pulmonic valve annulus.15, 16 A second problem is residual obstruction of the right ventricular outflow tract which is usually mild in the early years after correction but is the cause of a modest systolic pressure gradient between the ventricle and pulmonary artery. A third concern is the permanence of repair of the large ventricular septal defect seen in tetralogy. Finally, there is little information about
the hemodynamic response to exercise in patients who have had these residual abnormalities for several years.

It is essential to determine whether the postoperative hemodynamic findings remain stable or become progressively more abnormal as time passes and children grow. It is equally important to understand their capability to respond to the demands of exercise. This paper reports cardiac catheterization in the first few years after surgical correction which was then repeated up to 10 years postoperatively in the same patients, most of whom had outflow tract prostheses. Attention was especially directed to the levels of the right heart pressures, the pressure gradient between the right ventricle and pulmonary artery, and the presence of residual left-to-right ventricular shunts. Exercise capability was also appraised by cardiac catheterization up to 10 years postoperatively.

### Table 1

**Ages and Time Intervals for All Patients**

<table>
<thead>
<tr>
<th>Repeat catheterizations</th>
<th>Age at operation (yr)</th>
<th>Time from operation</th>
<th>Age at last cath. (yr)</th>
<th>Outflow tract prosthesis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>To 1st cath. (yr-mo)</td>
<td>To 2nd cath. (yr-mo)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>18</td>
<td>1-5</td>
<td>7-4</td>
<td>25</td>
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<tr>
<td>2</td>
<td>8</td>
<td>2-0</td>
<td>7-6</td>
<td>16</td>
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<td>3</td>
<td>11</td>
<td>0-6</td>
<td>7-2</td>
<td>18</td>
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<td>4</td>
<td>7</td>
<td>0-9</td>
<td>7-11</td>
<td>15</td>
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<td>5</td>
<td>3</td>
<td>0-9</td>
<td>6-0</td>
<td>9</td>
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<td>6</td>
<td>4</td>
<td>0-10</td>
<td>9-7</td>
<td>14</td>
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<td>7</td>
<td>10</td>
<td>1-5</td>
<td>10-0</td>
<td>20</td>
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<td>8</td>
<td>7</td>
<td>0-10</td>
<td>5-8</td>
<td>13</td>
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<td>9</td>
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<td>0-5</td>
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<td>10</td>
<td>20</td>
<td>2-4</td>
<td>5-6</td>
<td>26</td>
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<tr>
<td>11</td>
<td>16</td>
<td>0-8</td>
<td>6-5</td>
<td>22</td>
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<td>12</td>
<td>37</td>
<td>1-10</td>
<td>-</td>
<td>38</td>
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<td>13</td>
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<td>9-6</td>
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<td>14</td>
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<td>5-10</td>
<td>-</td>
<td>12</td>
</tr>
<tr>
<td>15</td>
<td>9</td>
<td>5-9</td>
<td>-</td>
<td>15</td>
</tr>
<tr>
<td>Average, repeat caths. group</td>
<td>10</td>
<td>1-1</td>
<td>7-3</td>
<td>17</td>
</tr>
<tr>
<td>Average, exercise group</td>
<td>12</td>
<td>6-10</td>
<td>-</td>
<td>19</td>
</tr>
</tbody>
</table>

**Abbreviations:** PA = patch extended across pulmonic annulus into the artery; cath. = right heart catheterization.

### Methods

Fifteen patients were selected because of their availability and willingness to have the postoperative procedures done (table 1). The surgical findings had confirmed the diagnosis of tetralogy according to criteria published previously.\(^3\) Correction had been performed by closure of the ventricular septal defect with a polyvinyl patch. Outflow tract resection or pulmonic valvotomy, or both, were done, and 11 of the 15 patients had a Teflon outflow tract prosthesis placed to widen the outflow tract and proximal pulmonary artery.

Eleven had two cardiac catheterizations after surgery; their average age at the time of operation was 10 years, with a range from 3 to 20 years. The first catheterization was performed an average of 13 mo postoperatively and the second an average of 7 years and 3 mo after operation. The average age at the time of the second study was 17 years.

Six of the foregoing patients and four others had exercise studies performed an average of 6 years and 8 mo postoperatively. Nine of the 10 had operation more than 5 years previously, and
Table 2
Serial Catheterizations in 10 Patients Without Significant Left-to-Right Shunting

<table>
<thead>
<tr>
<th></th>
<th>Upper normal limit</th>
<th>Catherization</th>
<th>Probability of difference*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No. 1 (range)</td>
<td>No. 2 (range)</td>
</tr>
<tr>
<td>Mean right atrial</td>
<td>5</td>
<td>6.6</td>
<td>3.7</td>
</tr>
<tr>
<td>pressure (mm Hg)</td>
<td>(2-12)</td>
<td>(1-6)</td>
<td></td>
</tr>
<tr>
<td>Right ventricular</td>
<td>5</td>
<td>5.7</td>
<td>5.9</td>
</tr>
<tr>
<td>end-diastolic</td>
<td>(0-10)</td>
<td>(2-8)</td>
<td></td>
</tr>
<tr>
<td>pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right ventricular</td>
<td>30</td>
<td>44</td>
<td>44</td>
</tr>
<tr>
<td>systolic pressure</td>
<td>(30-67)</td>
<td>(29-65)</td>
<td></td>
</tr>
<tr>
<td>(mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary arterial</td>
<td>30</td>
<td>31</td>
<td>27</td>
</tr>
<tr>
<td>systolic pressure</td>
<td>(25-45)</td>
<td>(16-40)</td>
<td></td>
</tr>
<tr>
<td>(mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV-PA pressure</td>
<td>0</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>gradient (mm Hg)</td>
<td>(0-34)</td>
<td>(5-34)</td>
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</tr>
<tr>
<td>Pulmonary arterial</td>
<td>20</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>mean pressure (mm Hg)</td>
<td>(10-21)</td>
<td>(7-20)</td>
<td></td>
</tr>
<tr>
<td>Systemic arterial</td>
<td>93.9</td>
<td>95.2</td>
<td></td>
</tr>
<tr>
<td>oxygen saturation (%)</td>
<td>(88.0-95.9)</td>
<td>(89.3-98.5)</td>
<td></td>
</tr>
<tr>
<td>Arteriovenous</td>
<td>5.1</td>
<td>3.7</td>
<td></td>
</tr>
<tr>
<td>oxygen difference (vol %)</td>
<td>4.2-6.9</td>
<td>2.6-4.7</td>
<td></td>
</tr>
<tr>
<td>Cardiac index (L/min/m²)</td>
<td>3.10†</td>
<td>4.36</td>
<td>NS</td>
</tr>
<tr>
<td>(L/min/m²)</td>
<td>(2.80-3.41)</td>
<td>(2.25-7.00)</td>
<td></td>
</tr>
<tr>
<td>Oxygen consumption (ml/min/m²)</td>
<td>152†</td>
<td>153</td>
<td>NS</td>
</tr>
<tr>
<td>(128-195)</td>
<td>(106-182)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Student's t-test for difference between means.
†Six patients only.
Abbreviations: NS = not significant at 0.05 level; RV = right ventricular; PA = pulmonary arterial.

Results

Serial Catheterization
One patient had a large left-to-right shunt and is considered separately from the other 10 who had repeat catheterization.

Ten Patients Without Significant Residual Shunt
The right heart pressures are summarized in table 2 and figure 1. Peak right ventricular pressures were remarkably consistent. The greatest difference between the two procedures was a fall of 16 mm Hg, and the averages were identical at the two times at 44 mm Hg. The peak pressure gradient between the body of the right ventricle and the pulmonary artery was also nearly constant over the years, averaging 14 and 16 mm Hg. Mean pulmonary arterial pressure averaged 17

three were more than 9 years from surgery. Their mean age was 18% years when studied.

Right heart catheterization was usually performed from an antecubital vein cutdown and a brachial artery was cannulated. Cardiac output was measured by the Fick principle using analysis of expired air by the Scholander technic, and measurement of oxygen content of blood samples with the Van Slyke apparatus. At the time of the second studies dye-dilution curves were performed by pulmonary arterial injection of indocyanine green, and systemic arterial sampling, through a cuvette densitometer. Appearance times of inhaled hydrogen were used to detect left-to-right shunts, using a platinum-tipped catheter in the right heart chambers. Exercise was performed in the supine position by pedalling an electrically braked bicycle ergometer. Three patients performed during a single work load whereas the other seven had measurements made at two different loads.
Results from cardiac catheterization an average of 13 mo (no. 1) and 7 years (no. 2) after operation. (A) Mean right atrial pressures decreased from abnormal levels to the normal range in six subjects and rose to an abnormal level in one other. (B) Arteriovenous oxygen difference was lower in all subjects at the time of the second catheterization.

mm Hg at the first procedure and 15 mm Hg later.

Hemodynamic evidence of pulmonic regurgitation was judged by equality or near equality of end-diastolic pressures in the right ventricle and pulmonary artery. At the second catheterization the pressures in these two chambers were equal to or within 2 mm Hg of those at the first catheterization in eight of these 10 patients. Right ventricular end-diastolic pressure was abnormal in five patients at both times; the highest value in the more recent study was 8 mm Hg.

At the time of the first catheterization, mean right atrial pressure was greater than normal in six patients; when the second procedure was performed, only one patient had a slightly abnormal level. The average mean right atrial pressure fell from 6.6 to 3.7 mm Hg and some decreases were as great as from 12 to 2 mm Hg (fig. 1). Despite the individual changes, the difference of the means for the group was not statistically significant.

The arteriovenous oxygen difference decreased with time in all patients (fig. 1). The average value was 5.1 vol% initially, the upper limit of normal, and fell to 3.7 vol% at the second study. No one then had an abnormal value. At the first postoperative procedure six of the 10 patients had determinations of cardiac output. The average value was higher at the second catheterization in the six, but no definite trend of increase or decrease occurred. At the second catheterization, the cardiac index was normal (greater than 2.5 L/min/m²) in nine of the 10 patients.

Measurements of pulmonary vascular resistance were within normal limits.

Three patients had systemic arterial saturation below 94% initially. In one it was below this value at the second catheterization. Although unexplained, it is assumed to be ventilatory in origin.

At the second study, the presence of left-to-right shunting was evaluated by three methods: oximetry of right heart blood samples, use of systemic arterial indocyanine green-dilution curves, and the detecting of single breaths of inhaled hydrogen by a platinum-tipped catheter in the right heart chambers and pulmonary artery. Hydrogen curves were recorded for nine of the 10 subjects. For the tenth, dye-dilution curves were normal. Four patients had early appearance of inhaled hydrogen in the right heart or pulmonary artery. In all four, sampling of blood for oxygen saturation during a single pass through the right heart failed to detect a significant step-up. A definite diagnosis of a small ventricular shunt was made in two of these patients. In the other two, hydrogen appeared early in the right atrium (appearance time 4 and 2 sec). The presence of an undiscovered atrial defect is an unlikely explanation, and two other possibilities remain. A small ventricular septal defect with tricuspid insufficiency could produce this finding but seems improbable on clinical grounds and in the presence of normal right atrial pressure. Early return of coronary circulation, however, could explain the short appearance time in these two subjects. In summary, two patients have
persistent small ventricular septal defects, and this possibility is unlikely but not completely excluded in two others. None of the four has had a significant change in right heart pressures between the two catheterizations.

**Patient with a Large Left-to-Right Shunt**

This patient, an 18-year-old man, had evidence of an open ventricular septal defect at catheterization 18 mo postoperatively. The pulmonary-to-systemic flow ratio was 1.5, right ventricular pressure was 48/9 mm Hg, and mean pulmonary arterial pressure was 22. No operation was advised. Restudy 6 years later, 7% years postoperatively, showed severe right heart failure with a right ventricular pressure of 95/24 and mean right atrial pressure of 17. Right ventricular blood had a 20% increase in oxygen saturation compared to that in the right atrium. The pulmonary-to-systemic flow ratio was 1.7. Both systemic and pulmonary flows, however, were lower than at the previous catheterization, and right-to-left shunting was present. The resulting systemic arterial saturation was 84%. He was reoperated upon and only a small remnant of Ivalon was present around the margin of the ventricular septal defect.

This is the one patient of the 11 whose serial catheterizations documented a marked increase in right heart pressures over the years and the one of 11 whose values were in a seriously abnormal range.

**Effects of Exercise Late After Correction**

The magnitude of the work load was judged in terms of total body oxygen consumption. The average resting value was tripled at the highest work level, changing from 150 to 453 ml/min/m²; the cardiac index rose about 50%. The heart rate increased 10 to 50 beats/min, with an average increase of 29. The relationship between oxygen consumption and cardiac index in these patients is shown in figure 2. The slope of the lines is an expression of the exercise factor, namely milliliter increase in cardiac output per 100-ml increase in oxygen consumption. Estimates of the lower limit of

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**Figure 2**

The relationship between oxygen consumption, corrected for body surface area, and cardiac index at rest and during one or more levels of exercise.

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**Figure 3**

The relationship between oxygen consumption and cardiac index for normal subjects at rest and exercise is shown by the solid dots. These values were taken from other publications. Seventeen points shown by the stars are values during exercise from our 10 patients studied after correction of tetralogy. The line is the calculated regression for the normal data, with a slope equivalent to an exercise factor of 620.
normal for exercise factor vary between 550 and 800 ml.\textsuperscript{19–22} The average exercise factor determined from a large number of published results by others is about 620, as shown by the calculated line in figure 3.\textsuperscript{23–30} Harvey and her colleagues,\textsuperscript{21} however, have suggested that a higher value (800) is closer to the true lower limit of normal if one is completely assured of a basal resting state (in other words, judged by a cardiac index less than 3.5). The higher the cardiac output at rest, the less the increase in output expected with exercise, at least at moderate levels of oxygen consumption. In our young group in this paper, half of the patients had an index at rest above 3.5, and we chose to use 550 as the lower normal limit.
for exercise factor. Comparing the oxygen consumption and cardiac output at rest with that of maximum exercise, the average in our patients was 715, although five had values below 550.

The cardiac output response can also be appraised by judging individual values of cardiac index during exercise in relation to the actual oxygen consumption, rather than the change from rest to a level of exercise. This is shown in figure 3 in which are plotted normal results from several reports in the literature. Seventeen points obtained during exercise in the present study are also shown (seven patients with two levels of exercise and three with one level). Two points appear abnormally low.

Stroke volume rose with exercise in six of the 10 patients, was unchanged in one, and fell in three. Averages were 50.7 ml/beat/m² at rest and 53.6 with exercise, a statistically insignificant change. There was no correlation between the change in stroke volume and the exercise factor.

Pressures are shown in figure 4. Right ventricular systolic pressure was measured in both states in nine of the patients and increased an average of 11 mm Hg with exercise, reaching 47. The peak pressure gradient between the right ventricle and pulmonary artery did not change in a consistent way with exercise, however, and the increase in right ventricular pressure was usually translated into increased pulmonary arterial pressure. Decreases in the gradient in two subjects are of interest but are not explained. Mean pulmonary arterial pressure rose an average of 6 mm Hg but remained in the normal range in all but one patient. In nine patients right ventricular end-diastolic pressure was measured at rest and exercise and was found to rise in six. Values above 5 mm Hg were found in five of these, and the highest was 11 mm Hg. Eight subjects had right atrial pressure measured at rest and with exercise, and slight increases occurred in four. One rose to an abnormal level.

Systemic arterial oxygen saturation was normal in both states in all but one patient, who had a value of 93.4% with exercise.

Discussion
The results of the repeat catheterizations allow an optimistic outlook as to the assessment of the long-term course of the 10 patients without marked left-to-right shunting. In general, over the average span of 6 years between procedures, the right ventricular systolic pressure remained the same and the systolic pressure gradient between the ventricle and the pulmonary artery did not change appreciably. Similar results were reported recently in seven patients who were restudied 5 years after an earlier postoperative catheterization, showing stability of the hemodynamic findings.31 It appears that as patients grow, inadequacy of outflow tract dimensions will not be a problem. Most of our patients were of adult or near adult size at the time of the second procedure.

Evidence of pulmonic regurgitation remained obvious in many, however. It was not possible to measure the amount of regurgitant flow in our studies, but the influence of this valvular defect is reflected by the resulting right heart filling pressures and the cardiac output. The average right ventricular end-diastolic pressure was slightly above normal limits on both occasions and presumably is associated with an elevated ventricular end-diastolic volume due to valve incompetence.32, 33 A decrease in mean right atrial pressure over the years was associated, however, due to falls from distinctly abnormal levels in several patients. Since right ventricular end-diastolic pressure did not change for the group and right atrial pressure tended to fall, it may be that improved atrial or tricuspid valve function occurred. In any event, right atrial pressure is now normal in most of the subjects, and ventricular diastolic pressure, although persistently abnormal in several, has not changed in a consistent way.

Concern about postoperative pulmonic valve function has been expressed in several papers that recommend avoidance of prosthetic or pericardial widening of the outflow tract whenever possible, to prevent pulmonic regur-
gitation. This attitude is maintained, even to the point of acceptance of a substantial pressure gradient by some surgeons. Others have employed aortic valve homograft replacement of the pulmonic valve as part of correction of tetralogy.\textsuperscript{4} The extent to which this new approach with its own problems is explored surely should be influenced by catheterization findings over the years in those operated upon by established technics. The present work is not intended to make recommendations about surgical technics. We have shown, however, that pulmonic regurgitation has been tolerated well up to 10 years postoperatively, and this permits some confidence in managing those patients who require widening of the outflow tract with a patch.

The cardiac output at rest was normal up to 10 years after surgery and comparison of the arteriovenous oxygen differences over the years shows a consistently improved state of oxygen delivery to the body.\textsuperscript{39} Although left-to-right shunting would raise the pulmonary arterial oxygen content, this is not believed to be a significant factor in the diminution of arteriovenous oxygen difference with time. With one exception, residual shunts were not detectable by step-ups in oxygen levels in the right heart chambers and most of the patients had no evidence of shunting at all.

The exercise results demonstrate cardiac output increments which were slightly subnormal in some patients, as evaluated by the exercise factor. This may be accounted for by the relatively high values at rest in this young population. When judged with the large number of such measurements taken from the literature, the actual cardiac output levels at a given oxygen consumption were usually comparable with normals. Our conclusion that the cardiac output response is usually normal is similar to that reached by Gotsman\textsuperscript{38} in a previous study of six patients after operation.

The pressure changes with exercise, however, magnified the abnormalities found at rest. Abnormalities of right ventricular function were shown by increases in right ventricular end-diastolic pressure with exercise to abnormal levels in several patients\textsuperscript{21} and may be largely the result of pulmonic regurgitation. The lack of appreciable increase in pressure gradient between the right ventricle and pulmonary artery with exercise is encouraging.

The fate of repair of ventricular septal defect is another consideration of importance. Two of our patients who had repeat catheterizations had definite evidence of small left-to-right shunts. The more delicate means for detecting them were not employed at the time of the first catheterization and thus it is not certain whether they are of long-standing or recent development. Since they were not detectable by oximetry on either occasion, there is no sign of progressive enlargement. Similarly, there were no important changes in right heart pressures in these patients. The presence of a larger residual ventricular septal defect was evident early in one other patient's course, however, and culminated in severe heart failure. Although broad generalizations cannot be made from experience with this individual, it is clear that patients with an obvious left-to-right shunt after operation should be followed more closely than others.

Conclusions

Our study, which was intended to help define the hemodynamic course after total correction of tetralogy of Fallot, shows that the course of the original lesion is grossly altered by operation, with a very favorable clinical outcome. During the first 10 years after correction of the lesion the residual abnormalities of pulmonic valve function and right heart filling pressure were tolerated well and, if anything, right heart filling pressures decrease with time. Further evidence of accommodation to the new dynamics is shown by improvement in oxygen delivery to the body, as judged by the arteriovenous oxygen difference. The ultimate results of this procedure still remain to be defined, but the present study does demonstrate stability of hemodynamics during the first 10 years after correction and an acceptable response to the demands of moderate exercise. Exceptions to this evolution may be found in those with
significant left-to-right shunt postoperatively.

References

17. Clark LC Jr, Bargeron LM Jr: Detection and direct recording of left to right shunts with the hydrogen electrode catheter. Surgery 46: 797, 1959

Eulogy to Physicians

For these friends of ours who have gone before, there is now no more toil; they start from their slumbers no more at the cry of pain; they sally forth no more into the storms; they ride no longer over the lonely roads that knew them so well; their wheels are rusting on their axles or rolling with other burdens; their watchful eyes are closed to all the sorrows they lived to soothe. Not one of these was famous in the great world; some were almost unknown beyond their own immediate circle. But they have left behind them that loving remembrance which is better than fame, and if their epitaphs are chiselled briefly in stone, they are written at full length on living tablets in a thousand homes to which they carried their ever-welcome aid and sympathy —Oliver Wendell Holmes: Currents and Counter-Currents in Medical Science. Boston, Ticknow and Fields, 1861, p. 3.
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