The Effects of Surgical Abolition of Left-to-Right Shunts on the Pulmonary Vascular Dynamics of Patients with Pulmonary Hypertension

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A

N IMPORTANT deficiency in our knowledge of congenital heart disease is the lack of detailed information concerning the effects of corrective surgery on the pulmonary vascular bed in patients with pulmonary hypertension. It is now well established that operation in such patients is associated with a substantially higher mortality and morbidity than in patients with similar anatomic lesions but without pulmonary hypertension. On the other hand, little specific information is available concerning the effects of operation on the elevated pulmonary vascular pressure and resistance. Such data would be helpful in the rational selection of patients with pulmonary hypertension for operation. To provide this information the present study was undertaken in 29 patients with congenital heart disease and pulmonary hypertension in whom both preoperative and postoperative cardiac catheterizations were carried out.

Patient Material

At the time of their operations, the patients ranged in age from 17 months to 59 years, and the average age was 21 years. Nine patients were under 10 years, six were between 10 and 20 years of age, and 14 were over 20 years (tables 1 and 2). There were 16 males and 13 females. Of the 29 patients, nine had atrial septal defects (ostium secundum defects in seven patients, a sinus venosus defect in one patient, and an ostium primum defect in one patient). Eight patients had isolated ventricular septal defects, four aortopulmonary septal defects, and the remaining eight patients had patent ductus arteriosus. No patient was cyanotic. In every patient the systolic pulmonary artery pressure was at least 50 mm. Hg and the mean pulmonary artery pressure exceeded 30 mm. Hg. In 28 patients the left-to-right shunt was found at the postoperative catheterization to have been completely eliminated. In the remaining patient (J.S.) a trivial shunt persisted.

The time intervals between the preoperative catheterization and the operation were less than 2 months in 24 of the 29 patients; in the other five patients this interval ranged from 4 to 13 months. The time intervals between operation and the postoperative hemodynamic study ranged from 1 month to 38 months. In five patients this time interval was less than 6 months, in 16 it was between 6 months and 1 year, and in the remaining eight patients it was greater than 1 year.

Both the inhaled foreign gas test, with either nitrous oxide¹ or Krypton⁸⁵,² and the dye-dilution technique were employed to characterize the circulatory shunts at both the preoperative and postoperative catheterizations. The dye-dilution curves were used primarily to exclude the existence of large right-to-left shunts and to confirm the presence and to indicate the approximate magnitude of the left-to-right cardiac shunts.

The inhaled foreign gas tests were utilized to calculate the ratio of pulmonary to systemic blood flow, and this ratio was employed, together with the pressure in the systemic and pulmonary arterial beds, to calculate the ratio of pulmonary to systemic vascular resistance. The results of the inhaled foreign gas tests were expressed as percentages, as outlined elsewhere.²

The following formulae were employed:

\[
\frac{\text{Pulmonary flow}}{\text{Systemic flow}} = \frac{100\% - \text{R.A. } \text{Kr}^{85} \%}{100\% - \text{P.A. } \text{Kr}^{85} \%}
\]

where R.A. Kr⁸⁵ per cent and P.A. Kr⁸⁵ per cent represent the results of the foreign gas tests in the right atrium (a chamber proximal to the entry of the shunt) and the pulmonary artery (a chamber distal to the entry of the shunt), respectively. In patients with atrial septal defects the value of 4 per cent was used instead of the R.A. Kr⁸⁵ per cent, since this value was found to be the average value obtained in 162 patients without left-to-right shunts.³
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Systemic vascular resistance

where P.A., L.A., B.A., and R.A. represent the mean pressures in the pulmonary artery, left atrium, brachial artery, and right atrium respectively. P.F. = pulmonary flow, S.F. = systemic flow. A mean left atrial pressure of 8 mm. Hg was utilized in calculations when this chamber was not actually catheterized. This value was chosen because it was the average one recorded in 18 normal subjects.

The operations were carried out between 1956 and 1961 and, accordingly, a variety of operative technics was utilized. Total cardiopulmonary bypass, with use of a rotating disk oxygenator and roller pump, was employed in the closure of the intracardiac defects and aortopulmonary septal defects in the majority of patients. General hypothermia was used in several of the patients with atrial septal defects early in the series. During the cardiac catheterizations in three infants general anesthesia with sodium pentothal was employed. In older children the studies were performed after premedication with a mixture of demerol, pro-methazine, and phenergan.

Results

The results of studies before and after operation are presented in tables 1 and 2 and figures 1 to 6. A decline in the mean pulmonary artery pressure and in the ratio of the mean pulmonary artery pressure to the mean systemic artery pressure occurred in all 29 patients (figs. 1, 2, 4, and 5). In 10 of the 12 patients with extracardiac shunts (patent ductus arteriosus or aortopulmonary septal defect) the mean pulmonary artery pressure was reduced to a normal value, i.e., to below 18 mm. Hg (fig. 1). The postoperative mean pulmonary artery pressures in these 12 patients averaged 28.9 per cent of the preoperative values. When the ratio of the mean pulmonary artery pressure to the mean systemic arterial pressure was calculated, it was found to be normal in all but two patients, the ratios being reduced from preoperative values ranging between 0.47 and 1.00 (Av. = 0.81) to postoperative values ranging between 0.12 and 0.51 (Av. = 0.23) (fig. 2). The pulmonary/systemic resistance ratios were abnormally elevated preoperatively (above 0.15) in six of the eight patients with extracardiac left-to-right shunts in whom they were measured. These ratios decreased to normal in all except one of these patients (fig. 3). In two patients with patent ductus arteriosus the pulmonary/systemic resistance ratios were below 0.15 before operation, the elevations of their pulmonary artery pressures being related to excessive pulmonary blood flow. In these patients the resistance ratios remained within normal limits after operation.

In the 17 patients with the intracardiac left-to-right shunts, the decline in pulmonary artery pressures and in the pulmonary/systemic arterial pressure ratios tended to be less striking than in the patients with the extracardiac shunts. The mean pulmonary artery pressures dropped to normal values (below 18 mm. Hg) in only two patients, both with atrial septal defects. Either slight or moderate elevation of pulmonary artery pressure persisted in the other 15 patients (fig. 4). The postoperative mean pulmonary artery pressures in the nine patients with atrial septal defect averaged 58.1 per cent of the preoperative values, while in the eight patients with ventricular septal defect they averaged 53.6 per cent. Similarly, the pulmonary/systemic pressure ratios declined to normal (below 0.20) in only two patients with intracardiac defects (fig. 5). Preoperatively the mean pulmonary artery/mean systemic artery pressure ratios ranged from 0.36 to 0.65 (Av. = 0.53) in the patients with atrial septal defects; postoperatively they declined to between 0.14 and 0.47 (Av. = 0.29). In the patients with ventricular septal defects the pulmonary/systemic pressure ratios ranged from 0.45 to 0.84 (Av. = 0.70) preoperatively, and postoperatively these ratios were between 0.27 and 0.52 (Av. = 0.38).

In the patients with atrial and ventricular septal defects there was little change in the pulmonary/systemic resistance ratios, with identical preoperative and postoperative values being found in two patients and either small increases or decreases in the others. In
contrast to the patients with extracardiac shunts, only one of the patients with an intracardiac shunt (a patient with an atrial septal defect) had a postoperative resistance ratio below 0.15 (fig. 6).

Discussion
In the past several years corrective surgery has been carried out on a considerable number of patients with pulmonary hypertension and left-to-right circulatory shunts. Preoperative catheterization has been carried out in the majority of these patients, and in view of the widespread interest in their hemodynamic abnormalities, it is perhaps surprising that relatively few data concerning the effects of operation on the pulmonary vascular pressures and pulmonary vascular resistance are available.

The calculation of pulmonary vascular resistance in the standard fashion is subject to considerable inaccuracy, primarily because of difficulties in the accurate estimation of pulmonary blood flow. The latter generally requires measurement of the oxygen consumption, which is dependent on the patient's metabolic and emotional state at the moment of study. In addition, the relative accuracy of the measurement of the arteriovenous oxygen difference, the other variable which must be determined in order to measure flow, declines sharply as pulmonary blood flow rises. In the present investigation these difficulties were, in large measure, circumvented by the utilization of the inhaled foreign gas method for calculation of the pulmonary/systemic blood pressure ratio.
flow ratio. The accuracy of this method has been established previously in dogs with left-to-right shunts of varying magnitudes and it has been shown not to decline with increasing values of pulmonary blood flow. Since the foreign gas technics were employed, oxygen consumption measurements were not utilized in the calculations, and pulmonary resistance was expressed as a fraction of systemic vascular resistance.

Physiologic data obtained by means of cardiac catheterization must be applied with considerable caution in the determination of the effects of the closure of an intracardiac defect on the status of the pulmonary vascular bed. The difficulties in the interpretation of calculations of pulmonary vascular resistance have been summarized by Fritts and Cournand. The pulmonary vascular bed must not be considered to be a system of rigid pipes but rather one in which the calculated resistance varies inversely with the blood flow and the pulmonary vascular pressures. Thus, when the blood perfusing the pulmonary vascular bed is increased by muscular exercise, by sudden occlusion of one branch of the pulmonary artery, or by pneumonectomy, the pulmonary artery pressure rises proportionately less than the pulmonary blood flow. In view of these considerations it is apparent

Table 1

Preoperative and Postoperative Hemodynamic Studies in Patients with Patent Ductus Arteriosus and Aortopulmonary Septal Defect

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr.)</th>
<th>Sex</th>
<th>Interval, months</th>
<th>Pul/ Sys. flow</th>
<th>Pul/Sys. resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>J.N.</td>
<td>1½</td>
<td>F</td>
<td>Preop</td>
<td>70/27, 50 .78</td>
<td>2.06 .36</td>
</tr>
<tr>
<td>02-37-41</td>
<td>F</td>
<td></td>
<td>13</td>
<td>23/6, 12 .20</td>
<td>1 .07</td>
</tr>
<tr>
<td>J.D.</td>
<td>1 3/4</td>
<td></td>
<td>Preop</td>
<td>106/81, 86 .84</td>
<td></td>
</tr>
<tr>
<td>01-60-13</td>
<td>M</td>
<td></td>
<td>2</td>
<td>11/6, 8 .13</td>
<td></td>
</tr>
<tr>
<td>C.M.</td>
<td>2</td>
<td></td>
<td>Postop</td>
<td>80/34, 52</td>
<td></td>
</tr>
<tr>
<td>01-05-64</td>
<td>F</td>
<td></td>
<td>48</td>
<td>23/11, 15</td>
<td></td>
</tr>
<tr>
<td>M.J.</td>
<td>7</td>
<td></td>
<td>Preop</td>
<td>84/48, 66 .92</td>
<td>1.72 .49</td>
</tr>
<tr>
<td>03-47-59</td>
<td>F</td>
<td></td>
<td>Postop</td>
<td>50/10, 207 .31</td>
<td>1 .22</td>
</tr>
<tr>
<td>W.M.</td>
<td>8</td>
<td></td>
<td>Postop</td>
<td>64/42, 48 .69</td>
<td>3.84 .13</td>
</tr>
<tr>
<td>01-84-86</td>
<td>M</td>
<td></td>
<td>Postop</td>
<td>35/8, 16 .23</td>
<td>1 .12</td>
</tr>
<tr>
<td>B.J.</td>
<td>15</td>
<td></td>
<td>Preop</td>
<td>85/45, 65 .59</td>
<td>3.96 .14</td>
</tr>
<tr>
<td>00-87-64</td>
<td>F</td>
<td></td>
<td>Postop</td>
<td>25/6, 13 .17</td>
<td>1 .06</td>
</tr>
<tr>
<td>L.B.</td>
<td>30</td>
<td></td>
<td>Preop</td>
<td>128/80, 100 1.00</td>
<td>2.7</td>
</tr>
<tr>
<td>01-07-01</td>
<td>F</td>
<td></td>
<td>Postop</td>
<td>78/54, 64 .64</td>
<td></td>
</tr>
<tr>
<td>A.G.</td>
<td>59</td>
<td></td>
<td>Preop</td>
<td>58/26, 37 .47</td>
<td></td>
</tr>
<tr>
<td>02-80-15</td>
<td>F</td>
<td></td>
<td>Postop</td>
<td>25/10, 18 .19</td>
<td></td>
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</tbody>
</table>

Aortopulmonary Septal Defect

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr.)</th>
<th>Sex</th>
<th>Interval, months</th>
<th>Pul/ Sys. flow</th>
<th>Pul/Sys. resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>G.B.</td>
<td>7</td>
<td></td>
<td>Preop</td>
<td>82/40, 60 1.00</td>
<td>2.8 .36</td>
</tr>
<tr>
<td>03-2-65</td>
<td>M</td>
<td></td>
<td>7</td>
<td>37/6, 14 .18</td>
<td>1 .08</td>
</tr>
<tr>
<td>G.L.</td>
<td>7</td>
<td></td>
<td>Preop</td>
<td>82/40, 55 .85</td>
<td>2.8 .31</td>
</tr>
<tr>
<td>01-18-44</td>
<td>M</td>
<td></td>
<td>Postop</td>
<td>26/10, 17 .18</td>
<td>1 .10</td>
</tr>
<tr>
<td>S.S.</td>
<td>10</td>
<td></td>
<td>Preop</td>
<td>90/60, 70 .98</td>
<td>1.9 .43</td>
</tr>
<tr>
<td>02-29-81</td>
<td>M</td>
<td></td>
<td>Postop</td>
<td>35/5, 16 .22</td>
<td>1 .11</td>
</tr>
<tr>
<td>H.C.</td>
<td>14</td>
<td></td>
<td>Preop</td>
<td>75/50, 62 .76</td>
<td>1.7 .44</td>
</tr>
<tr>
<td>01-38-74</td>
<td>M</td>
<td></td>
<td>Postop</td>
<td>36/7, 17 .19</td>
<td>1 .10</td>
</tr>
</tbody>
</table>

PA = Pulmonary artery pressure; PAm = pulmonary artery mean pressure; Pul/Sys. flow = pulmonary/systemic flow ratio; Pul/Sys. Resistance = pulmonary resistance/systemic resistance ratio; S/D = systolic/diastolic pressure; BAm = brachial artery mean pressure; m = mean.

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Effects of closure of patent ductus arteriosus and of aortopulmonary septal defect on the ratio of pulmonary vascular resistance to systemic vascular resistance.

**Figure 3**

Effects of closure of atrial septal defects (ASD) and of ventricular septal defects (VSD) on the mean pulmonary artery pressure.

**Figure 4**

Effects of closure of atrial septal defects (ASD) and of ventricular septal defects (VSD) on the ratio of mean pulmonary artery to mean systemic artery pressure.

**Figure 5**

that pulmonary vascular resistance (or the pulmonary/systemic vascular resistance ratio) can be subnormal in the presence of a "normal" pulmonary vascular bed in a patient with a left-to-right shunt and elevated pulmonary blood flow. Abolition of the shunt in such a patient could be expected to raise the resistance (or the resistance ratio) to a normal level. Thus, it is possible that the state of the pulmonary vascular bed actually improved in those patients in whom the pulmonary/systemic resistance ratio remained essentially unchanged following operation. In spite of these acknowledged limitations in the accuracy of the measurement of pulmonary vascular resistance, and the difficulties in the interpretation of the calculated values for resistance, hemodynamic methods are the only

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practical ones that are currently available and that can be used to estimate the effects of operation on the pulmonary vascular bed in patients with congenital heart disease.

In 1949, Courmand, Baldwin, and Himmelstein\textsuperscript{14} reported observations in a patient with a patent ductus arteriosus in whom pulmonary hypertension was noted at catheterization 5 weeks postoperatively, but in whom measurements carried out 5 months postoperatively revealed that the pulmonary artery pressure had returned to normal levels. These data represent the first recorded demonstration of postoperative regression of an elevated

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Effects of closure of atrial and ventricular septal defects on the ratio of pulmonary to systemic vascular resistance.

likely that some regression of the abnormalities in the pulmonary vascular bed occurs when the shunt is eliminated in patients with pulmonary hypertension associated with patent ductus arteriosus or aortopulmonary septal defect.

The hemodynamic effects of repair of an intracardiac left-to-right shunt are less clear cut than those following repair of an extra-cardiac communication. Burchell,19 reported little change in the pulmonary vascular resistances in four patients with atrial septal defect catheterized before and after operation. In the fifth patient, who was recatheterized 2 weeks postoperatively, an increase in the calculated pulmonary vascular resistance occurred. Beck and collaborators,20 reviewed the studies carried out in four of these patients and added data on seven other patients with atrial septal defect and pulmonary hypertension; a marked fall in pulmonary vascular resistance occurred in three of the seven patients, while little change was noted in the other four. A moderate decline in the absolute level of the pulmonary artery pressure and in the pulmonary artery/systemic artery pressure ratio occurred in the nine patients with atrial septal defect reported herein. However, the pulmonary/systemic resistance ratio exhibited no tendency to fall. Indeed, the largest change in this ratio that occurred in any patient with atrial septal defect was an elevation from 0.17 to 0.31 in J.G., a 39-year-old man, in whom the second catheterization was carried out 9 months after operation.

Burchell,19 reported a moderate postoperative decline in pulmonary vascular resistance in one patient with ventricular septal defect and a moderate fall in pulmonary artery pressure in the other patient whom he studied. The pulmonary artery pressure fell significantly, but little change in pulmonary vascular resistance occurred after closure of the defect in the nine patients with ventricular septal defect recently reported by Lucas et al.21 Although a moderate decline in mean pulmonary artery pressure occurred in all eight patients with ventricular septal defect
reported herein, a normal pulmonary artery pressure was noted postoperatively in only one of them. However, as in the patients with atrial septal defect, the pulmonary/systemic resistance ratio showed no consistent change. The largest alteration that occurred was a decline from 0.29 to 0.17 in a 19-year-old boy studied 3 months after operation. On the basis of the data presented, it appears that surgical closure of atrial or ventricular septal defects associated with pulmonary hypertension and left-to-right shunts consistently results in a lowering of the pulmonary artery pressure. However, the physiologic evidence suggests that little, if any, change in the pulmonary vascular bed occurs, at least during the first postoperative year.

It is the policy at this institution to carry out postoperative hemodynamic studies in all patients who survive operation. Thus the patients described in the present report were unselected except that all had pulmonary hypertension before operation. Although the number of patients in each of the three groups studied is small, there was no evidence that the age of the patient influenced the effect of operation on the pulmonary vascular resistance. A much larger number of patients with each lesion will have to be studied, however, before a firm conclusion regarding this important point can be reached. Finally, it will be of great interest to determine if further changes in pulmonary artery pressure and resistances will occur as the time interval following operation increases.

Summary

The preoperative and postoperative pulmonary artery pressures, the ratios of pulmonary to systemic arterial pressure, and of pulmonary to systemic vascular resistance were compared in 29 patients with congenital heart disease, left-to-right shunts, and pulmonary hypertension. These patients averaged 21 years of age and the time interval between operation and the postoperative catheterization averaged 11 months. The mean pulmonary artery pressure and the pulmonary artery to systemic artery pressure ratio fell significantly in all 12 patients with extracardiac left-to-right shunts (patent ductus arteriosus and aortopulmonary septal defect) and fell to normal in 10 of them. The pulmonary vascular/systemic vascular resistance ratio was abnormally elevated in only one patient postoperatively. In the 17 patients with atrial and ventricular septal defects the decline in pulmonary artery pressure and in the pulmonary/systemic arterial pressure ratio was less striking than in the patients with extracardiac shunts. These indices were normal postoperatively in only two of the nine patients with atrial septal defects and in none of the eight patients with ventricular septal defects. No significant changes were noted after operation in the pulmonary/systemic vascular resistance ratios in any of the 17 patients with intracardiac left-to-right shunts. From these observations it appears likely that some regression of the abnormalities in the pulmonary vascular bed occurs during the first year after closure of an extracardiac left-to-right shunt. On the other hand, there was little physiologic evidence that such favorable changes followed operation in the patients with atrial or ventricular septal defects.

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Modern medicine is a product of the Greek intellect, and had its origin when that wonderful people created positive or rational science.—Sir William Osler. Aphorisms From His Bedside Teachings and Writings. Edited by William Bennett Bean, M.D. New York, Henry Schuman, Inc., 1950, p. 78.
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