Changing Hemodynamics in Patients with Transposition of the Great Arteries

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SUMMARY

Follow-up cardiac catheterizations were carried out on 65 patients with transposition of the great arteries. Patent ductus arteriosus (PDA) was a significant problem in this group only when closure resulted in a precipitous drop in arterial oxygen saturation. Spontaneous closure of ventricular septal defects (VSD) occurred in approximately 20% of patients while natural or surgically created atrial septal defects (ASD) tended to persist. Pulmonary stenosis (PS) was found in 28% of patients with an intact ventricular septum and 50% of those with VSD. Pulmonary artery hypertension (PAH) or pulmonary vascular obstruction (PVO) or both, were present in about half of the patients with an intact ventricular septum and all the infants with a large VSD without pulmonary artery banding or pulmonic stenosis (PS). PS, usually but not invariably, tended to protect the pulmonary vasculature.

Additional Indexing Words:
Patent ductus arteriosus Atrial septal defect Ventricular septal defect
Pulmonary artery hypertension Pulmonary artery banding
Pulmonary vascular obstruction

A DECADE AGO survival of an infant with transposition of the great arteries (TGA) beyond 6 months of age was unusual.1 Today, with earlier recognition and relatively low-risk surgical palliative procedures,2 the majority of infants with TGA survive infancy, and many live on into early childhood. Consequently, we are the first generation of cardiologists with the opportunity of observing and recording the "natural history" of a large number of survivors with TGA over a relatively long period of time.

These observations are more important now that a comparatively safe corrective procedure is available in the Mustard operation.3 The choice and timing of the initial palliative procedure, the frequency of subsequent clinical and hemodynamic studies, and, in selected patients, the timing of total surgical correction will depend on an appreciation of the natural history of TGA in survivors.

Several hemodynamic factors may influence the course of the patient with TGA: (1) a patent ductus arteriosus (PDA) which may transmit systemic pressure and systemic blood (unsaturated) to the pulmonary circulation; (2) a ventricular septal defect (VSD) that may aid in mixing of the systemic and pulmonary circulations and transmit systemic pressure to the left (pulmonary) ventricle; (3) an atrial septal defect (ASD) that may contribute to the mixing and lowering of left atrial and pulmonary venous pressures; (4) a pulmonic stenosis (PS) that might reduce pulmonary arterial pressure and possibly pulmonary blood flow as well, and (5) the presence of pulmonary artery hypertension.

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(PAH) and pulmonary vascular obstruction (PVO). To gain more insight into the role of these factors, we turned our attention to patients with TGA who have had follow-up cardiac catheterizations separated from the initial catheterization by an interval of not less than 2 months and usually longer.

**Methods**

Sixty-five patients form the basis for this study. All were admitted to the Children's Hospital Medical Center, Boston, with TGA with d-loop and situs solitus and all have had at least two cardiac catheterizations, separated by an interval of not less than 2 months. Patients with coarctation of the aorta, tricuspid atresia, dextrocardia, single ventricle, or transposition with l-loop are not included. Patients with PDA, VSD, and PS are included. Forty-four (68%) had their initial catheterization under the age of 3 months (table 1). Almost all of these (42 of 44) were critically ill and required prompt palliative procedures to permit survival. The average period between catheterizations for the entire group was 45 months. The diagnosis at the first catheterization and the palliative operations performed are presented in table 2.

Right heart catheterization was performed in all patients at least twice, usually through the femoral approach. The pulmonary artery was entered at the initial catheterization in 17 patients (26%) and at follow-up in 51 patients (78%). This improvement was due to the use of the flow-guided catheter technic of Carr and Wells and to the fact that the patients at follow-up catheterization were larger and less critically ill.

The left ventricular systolic pressure was used to estimate pulmonary artery systolic pressure in 12 patients in whom either (1) the left ventricular pressure was less than 50% of systemic arterial systolic pressure (seven patients); or (2) the left ventricular systolic pressure was greater than 75% of systemic pressure, but no PS could be demonstrated by selective left ventricular angiography, postmortem examination, or both (five patients).

The left atrium was entered at the initial study in all 29 patients catheterized before they were 1 month of age, in 12 of 18 patients (67%) between 1 and 6 months of age, and in 13 of 18 patients beyond that age. The left atrium was entered in 59 of the 65 patients (91%) at follow-up catheterization. The left ventricle was successfully entered in 68% of the patients at the first study and in 91% at follow-up catheterization.

The presence or absence of a PDA was established by angiography in 42 patients (65%) at the first study and in 18 of the remaining 23 at

**Table 1**

<table>
<thead>
<tr>
<th>Age at 1st cath.</th>
<th>No.</th>
<th>Palliative procedure</th>
<th>Average</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3/12</td>
<td>44</td>
<td>42</td>
<td>30</td>
<td>2-108</td>
</tr>
<tr>
<td>&gt;3/12</td>
<td>21</td>
<td>9</td>
<td>76</td>
<td>7-138</td>
</tr>
<tr>
<td>Total</td>
<td>65</td>
<td>51 (78%)</td>
<td>45</td>
<td>2-138</td>
</tr>
</tbody>
</table>

**Table 2**

<table>
<thead>
<tr>
<th>Operation</th>
<th>ASD creation</th>
<th>Shunt</th>
</tr>
</thead>
<tbody>
<tr>
<td>No VSD; no PS</td>
<td>22</td>
<td>2 (1)</td>
</tr>
<tr>
<td>VSD</td>
<td>43</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Total</td>
<td>65</td>
<td>14 (6)</td>
</tr>
</tbody>
</table>

*One of the 43 patients with a VSD at the initial study underwent balloon atrial septostomy which proved inadequate. At restudy, just prior to surgical creation of atrial septal defect, spontaneous closure of the ventricular septal defect was documented. This patient has been included among the 43 patients with a ventricular septal defect at the time of the initial catheterization in the present table but has also been added to the 18 patients with an intact ventricular septum undergoing surgical atrial septal defect creation in the discussion of the outcome of this intervention in the text and as presented in table 3.

Abbreviations: TGA = transposition of the great arteries; ASD = atrial septal defect; band = pulmonary artery banding; shunt = systemic-to-pulmonary artery shunting procedure; VSD = ventricular septal defect; PS = pulmonary stenosis; () = patients in whom balloon septostomy produced a temporary improvement but surgical ASD creation was necessary later.

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second study. The presence of a VSD was documented by catheter passage, selective ventricular angiography, or both. PS was defined as a peak systolic pressure gradient of 20 mm Hg or more between the main pulmonary artery and left ventricle. PAH was considered to be present when either (1) the pulmonary artery systolic pressure was 50% or more of the systemic arterial pressure, or (2) the left ventricular systolic pressure was greater than 75% of the systemic pressure and no PS was evident on selective left ventricular angiography, postmortem examination, or both. PVO was defined as a calculated pulmonary vascular resistance of greater than 3 units/m² or a pulmonary-to-systemic vascular resistance ratio (R̅p/R̅s) of 0.30 or more. Pulmonary and systemic blood flows were calculated by using the Fick formula with the oxygen consumption estimated in infants and younger children and measured in the older children. No calculations of pulmonary blood flow or pulmonary vascular resistance were made without a pulmonary arterial blood sample and pressure.

Results

General Trends

A considerable change in hemodynamics took place in many of the patients between the initial and final catheterizations (fig. 1). Of 22 patients with an intact ventricular septum without PS at the original study, 16 were essentially unchanged at the time of the final examination, but six had developed PS.

Among 28 patients with a VSD, without PS at the original study, only eight remained unchanged, while seven had undergone spontaneous closure of the VSD, five appeared to develop PS, and the pulmonary artery was banded in eight.

Of the 15 patients with VSD and PS at initial study, two appeared to lose their PS, and the condition of the remaining 13 was unchanged.

Due to the changes presented in figure 1, and to be detailed later, the total number of patients with an intact ventricular septum without PS was about the same at the first and last study. Eight patients were found to have an intact ventricular septum with PS at the last study. The size of the group with solitary VSD had become appreciably smaller whereas there were about the same number with VSD and PS initially and finally.

Patent Ductus Arteriosus

A functioning PDA was demonstrated at the initial study in seven of the 42 patients with appropriate selective angiography. In three of these, studied first between 10 days and 3 months of age, the ductus appeared small and had closed at the time of the second study without influencing the clinical course significantly. In a fourth patient a small ductus was demonstrated at 12 days of age and again at 1½ years of age with normal pulmonary artery pressure. In the remaining three patients the ductus appeared large. In one of these closure of the PDA occurred within the first month, and in a second between 1 and 8 months. Closure in both instances was accompanied by a marked drop in systemic oxygen saturation necessitating surgical ASD creation. In the third patient, a similar fall in systemic saturation had taken place by 8 months of age, but instead of ductal closure, spontaneous closure of a VSD was found. The ductus was playing a supportive role in these three instances.

One may say then from our patients that (1) most PDAs close within the first weeks or months of life, (2) persistence of the ductus may contribute to maintenance of a satisfactory systemic arterial saturation beyond the first few weeks of life, and (3) that closure of the ductus may result in a precipitous drop in that saturation. A PDA did not seem to be responsible for PAH in the majority of patients at either the initial or final study. We must emphasize though that this may be true only for the particular patients discussed here who lived long enough to be catheterized a second time after an appreciable time interval. Many patients with TGA and a large PDA may not live long enough to be included in a natural history study.

Closure of Ventricular Septal Defect

Forty-three of the 65 patients in this study had a VSD at the time of the initial catheterization (fig. 1). Spontaneous closure was documented in seven, and in two others
the defect had clearly become much smaller.

The earliest documented closure occurred between 2 days and 8 months and the latest between 4 and 9 years of age. As a predictor of VSD narrowing, or closure, the level of left ventricular pressure was not particularly helpful since it was low (less than 75% of systemic pressure) at the first study in only two of the patients with diminution of VSD. Ventricular angiography was more useful in that the defect appeared small on the films in six patients at the first study. The systemic arterial oxygen saturation was perhaps the best indicator that a VSD may eventually close since in eight of the nine patients the initial saturation was 65% or less, only slightly higher than the initial oxygen saturation of patients with an intact ventricular septum.

One may summarize, then, in saying that a little over 20% of VSDs close, or get significantly smaller, and that angiographic demonstration of a small defect or a low initial systemic arterial saturation, in a patient with or without significant PS, is the best predictor of small or closing VSDs.

**Atrial Septal Defects**

Six patients had an adequate natural ASD at the first catheterization, and all appeared to have about the same size defect at the repeat study, an average of 8 years later. Four of these, with an intact ventricular septum, were alive at 11, 15, 15, and 18 years of age; all had PVO and arterial saturations of 53, 53, 72, and 79%, respectively. The other two patients had VSD and PS. One may say, then, that a natural ASD that is adequate at the time of the first study will probably persist at least through the teens, that PVO may develop eventually, even with an intact ventricular septum, and that the arterial saturation in those without an associated VSD will become quite low in time.

In 46 patients an ASD was created at or after the first catheterization (table 2) because of low arterial saturation (less than 70%) or an appreciable mean pressure gradient (3

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**Figure 1**

General trends in natural history of transposition of the great arteries. See text. ○ = pulmonic stenosis (PS) developing; □ = closing ventricular septal defect (VSD); Δ = PS disappearing; ···· = banding of pulmonary artery (band); Δ = change; no Δ = no change.
Table 3
Arterial Oxygen Saturation and Atrial Blood Pressure on Initial and Final Study

<table>
<thead>
<tr>
<th></th>
<th>Age ( \text{av} ) (yr)</th>
<th>Systemic arterial ( O_2 ) saturation (%)</th>
<th>( \text{Qp/Qs av} )</th>
<th>( \text{P}_{\text{PLA}} ) (mm Hg) ( \text{av} )</th>
<th>( \text{P}_{\text{PLA-PRA}} ) ( \Delta ) (mm Hg) ( \text{av} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Surgical ASD creation in 19 patients with TGA and intact ventricular septum</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preop. study</td>
<td>17 days</td>
<td>44</td>
<td>–</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>(17/19 &lt; 60 days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Final study</td>
<td>30 mo</td>
<td>67</td>
<td>–</td>
<td>5</td>
<td>(5/19 &gt; 2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(17/19 = 0)</td>
</tr>
<tr>
<td>B. Surgical ASD creation in 18 patients with TGA and VSD without PS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preop. study</td>
<td>39 days</td>
<td>54</td>
<td>–</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>(12/18 &lt; 60 days)</td>
<td></td>
<td></td>
<td></td>
<td>(10/14 &gt; 2, 4 NK)</td>
</tr>
<tr>
<td>Final study</td>
<td>40 mo</td>
<td>69</td>
<td>–</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(15/17 = 0, 1 NK)</td>
</tr>
<tr>
<td>C. Surgical ASD creation and PA banding in 6 patients with TGA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preop. study</td>
<td>66 days</td>
<td>83</td>
<td>–</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Final study</td>
<td>39 mo</td>
<td>70</td>
<td>2.0</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>D. No surgical or natural ASD in 13 patients with TGA and VSD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial study</td>
<td>25 mo</td>
<td>75</td>
<td>–</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Final study</td>
<td>8 4/12 yr</td>
<td>74</td>
<td>–</td>
<td>7</td>
<td>3</td>
</tr>
</tbody>
</table>

Abbreviations: ASD = atrial septal defect; TGA = transposition of the great arteries; VSD = ventricular septal defect; \( \text{Qp/Qs} \) = pulmonary-to-systemic pressure ratio; \( P \) = mean pressure; \( \text{LA} \) = left atrium; \( \text{RA} \) = right atrium; \( \Delta \) = gradient; \( \text{ave} \) = average; NK = not known.

mm Hg or greater) between the atria, or for both conditions. Nine of these patients underwent balloon atrial septostomy, and eight had a satisfactory immediate rise in arterial saturation. In only three, however, did this gratifying result last to final catheterization at ages 7, 9, and 13 months. The other six patients subsequently had to have an ASD created surgically. A total of 43 patients, then, including the six with previous balloon septostomy, required surgical ASD creation based on the indications mentioned above. Thirty-seven of these had solitary atrial septostomy (19 with intact ventricular septum and 18 with VSD), and in six ASD creation was associated with pulmonary artery banding (table 2).

The 19 patients with intact ventricular septum in whom an ASD was created surgically were for the most part very young and had very low systemic arterial oxygen saturations initially (table 3). At restudy mixing through the ASD was sufficient to maintain an acceptable arterial oxygen saturation in all but four. In two of these, at reoperation at ages 5 and 7 months, the ASD was found to be satisfactory in size and they did not survive the thoracotomy. Autopsy indicated severe pulmonary vascular changes and absence of PS. Of the remaining two patients with low saturations at restudy, one had moderate PAH and the other had developed moderate PS.

In 18 patients with VSD an isolated ASD was created surgically. Table 3 indicates that the results of surgery were similar to those in patients with an intact ventricular septum. Of the five patients with relatively low arterial saturation at the final study, one was proved to have PVO; another was suspected of having this complication; in one the VSD had closed and there was moderate PS, and in the remaining two the surgically created ASD had closed. We have no explanation of why these two atrial defects closed since ASDs were established by use of the same technic. An individual predisposition may play some role since in one of the two patients in whom re-
operation was performed, an ASD was re-created and it closed a second time. An additional point contributing to the low arterial saturation in this patient was that he was one of the nine in whom the VSD diminished markedly in size, the defect being barely probe patent at postmortem examination.

The six patients in whom an ASD was created and the pulmonary artery banding will be discussed in detail later. A summary of the studies in these patients is presented in table 3.

There were 13 patients without a detectable ASD at the initial study, in whom no surgery was attempted (table 3). Eight of these were studied initially before aggressive palliative treatment of TGA became a policy of this institution (1963), and they all had a large VSD with an average initial arterial saturation of 75%. In addition six patients had relatively severe PS, limiting pulmonary flow and keeping them out of congestive heart failure. Two patients with severe congestive failure underwent pulmonary artery banding as an isolated procedure and two infants with severe PS underwent systemic arterial-to-pulmonary artery shunts. The remaining nine patients were all doing reasonably well with varying degrees of PS or PAH. At the time of the last catheterization (averaging 6 years after the first study) their arterial saturations were essentially unchanged as were the left atrial mean pressures and left atrial-right atrial mean pressure gradients. The state of the pulmonary vasculature will be discussed later.

In summary, then, it seems that naturally occurring large ASDs persist throughout childhood. Balloon septostomy in our experience gives an excellent immediate increase in oxygen saturation which, however, is not likely to persist. Surgically created ASDs, with very few exceptions, persist and result in maintenance of a relatively satisfactory systemic arterial oxygen saturation in the absence of PS or PVO. The presence of an ASD is mandatory for survival in all but the patients with a large VSD.

**Pulmonary Stenosis**

We were not able to demonstrate PS in any of our 22 patients with an intact ventricular septum at the time of the initial study (fig. 1). This may have been due, at least in part, to the difficulty in entering the pulmonary artery at a time when the flow-guided technic was not available. At the time of the final study, PS was present in six of these 22 patients. PS also appeared to have developed in two of the seven patients in whom a VSD had closed spontaneously (fig. 1). There were, then, eight examples of PS among 29 patients in whom the ventricular septum was intact at final study. The left ventricular outflow gradient in this group averaged 40 mm Hg (range, 21 to 64) at a mean age of 4½ years (range, 15 months to 17½ years). One of the patients had PVO despite a 62-mm Hg gradient and died at age 18 years with hypoxia and congestive heart failure. The other patients have normal pulmonary artery pressures and resistances and are doing reasonably well clinically. The pulmonary-to-systemic blood flow ratio ($Q_l/Q_s$) was greater than 2.0 in six and 1.7 and 1.4 in the other two. Only in these latter two patients did the PS seem to reduce pulmonary blood flow significantly, and arterial saturations of less than 60% were present in both. Although we cannot be absolutely certain, it seems, on the basis of catheterization and angiographic data, that most of the gradients are subvalvular in nature.

Twenty-eight of the 43 patients with VSD were felt to be free of significant PS at the first study (fig. 1). Seven of these had PS at the time of the second study, two with closed VSDs and five with persisting VSDs.

There were 15 patients with a VSD in whom PS was known to be present at the initial study (fig. 1), nine with measured pulmonary artery-ventricular gradients and six with PS proven by ventricular angiogram. In two of the 15 patients, initial gradients of 36 and 44 mm Hg seemed to have disappeared by the time of the final study in a setting of increased pulmonary artery pressure and PVO. Whether these gradients, demonstrated during the first study by catheter withdrawal from the pulmonary artery to the left ventricle...
and finally right ventricle through the VSD, were real, in view of subsequent events, cannot be stated with certainty. It is possible that the catheter returned to the right ventricle through the large VSD directly from the pulmonary artery without, in effect, registering the true left ventricular pressure.

Of the 13 patients with persisting PS, one had a diminished gradient (much as in the two patients cited above) paralleling the development of PAH and PVO. Four patients had progressive outflow obstruction and, finally, eight seemed to have a more or less stable degree of PS through the years. In two patients, stenosis was severe enough to warrant an arterial shunt immediately after the initial catheterization, and in two others, progressive decreases in arterial saturation warranted it later on. The nature of the obstruction in these patients, like that in the intact ventricular septum group, was subvalvular.

Of the 15 patients with PS and a VSD at initial examination, four had PAH and PVO at the final study. These patients are doing reasonably well symptomatically, but for them the risk of total repair would be extremely high by present-day criteria.

In summary, a little over one quarter of the patients who had an intact ventricular septum had PS at restudy. The gradients were mild, and the development of PVO in this group was not evident within early childhood. One half of the patients with a VSD had PS at final study. In only a few was the obstruction severe enough initially to warrant an arterial shunt. In some it increased significantly in severity while in most it remained stable. In a very few the gradient seemed to diminish and even disappear. The presence of PS did not invariably protect the pulmonary vasculature.

**Pulmonary Artery Banding**

Eight of 43 patients with TGA and VSD underwent banding of the pulmonary artery. In two banding was the only procedure, while in six banding and surgical ASD creation were performed as a combined procedure (table 2). All eight patients had severe PAH and congestive failure preoperatively.

Banding of the pulmonary artery controlled congestive failure very well in seven while in one, only 5 months after banding, failure, requiring digitalis and diuretics, persisted. At recatheterization, at an average age of 3 9/12 years (range, 5/12 to 5 years), the pulmonary artery pressure distal to the band was normal in six, and only slightly elevated in two. The pulmonary vascular resistance was normal in all patients. By the time of restudy a rather low $Q_p/Q_s$ ratio (below 1.8) was present in six of the eight, and this was reflected by an arterial oxygen saturation of 70% or less in five patients. Four of these patients have undergone arterial shunting procedures since their last study with considerable improvement in each instance.

Banding unquestionably has protected the pulmonary vasculature of these patients, but it is not clear in this small group whether or not the ASD creation by lowering left atrial pressure has contributed an additional protective effect. Nevertheless, persisting left atrial hypertension (12 mm Hg) in one of the two patients with pulmonary artery banding alone, and very low systemic arterial oxygen saturation in the other (41%) at least suggest that ASD creation might have been beneficial at the time of the original banding.

**Pulmonary Arterial Hypertension and Pulmonary Vascular Obstruction**

**Intact Ventricular Septum**

In none of the 22 patients with an intact ventricular septum did we enter the pulmonary artery at the initial study and hence no measurements of pulmonary artery pressure and pulmonary vascular resistance were available. We assumed, however, on the basis of the criteria outlined in the section on "Methods" that at least moderate PAH was present in 15 patients and that pulmonary artery pressure was normal in four. In three patients the left ventricular pressure was not known.

At restudy, at an average of 4 years (range, 5/12 to 17 years), PAH was documented in six patients and inferred from left ventricular pressure in three others, giving a total of nine patients (41%) with PAH at the time of the
final study among the 22 with intact ventricular septum at the outset. Two of these nine started out with low left ventricular pressures (less than 50% of systemic pressure), and five had elevated left ventricular pressures.

Among the 13 patients without PAH at the last study in this group of 22, all of whom had left ventricular hypertension initially, six had PS.

No data are available on the status of the pulmonary arterioles at the initial study because of our inability to enter the pulmonary artery, but there were five examples of PVO (23%), as defined earlier, at the final study at an average age of 9 years (range, 2½ to 17 years). PVO could be shown to have developed as early as 2½ years of age in one patient and as late as 15 years of age in another. One of the five patients had PVO despite a left ventricular outflow gradient of 62 mm Hg and only slight elevation of pulmonary artery pressure.

PAH, present in a majority of patients with an intact ventricular septum in early infancy, seems to disappear, if the patient survives, in most though not in all patients. On the other hand, some of the patients without PAH initially may still develop PAH and PVO later on. The earliest documented PVO was at 2½ years of age in this group.

Ventricular Septal Defect without Pulmonary Stenosis

Twenty-five of this group of 28 had PAH (measured in nine and inferred from left ventricular pressure in 16) at the initial study. The pulmonary artery pressure could not be estimated initially in two patients, and in only one of the 28 was the initial pulmonary artery pressure known to be normal. Eight of the 28, all with PAH, underwent banding of the pulmonary artery and their course has been discussed earlier. In nine of the remaining 20 patients, PAH persisted or progressed. ASD creation had been performed in six of these, and spontaneous closure of the VSD occurred in three. Among the 11 patients without PAH at final study, four underwent spontaneous complete closure of a VSD with the appearance of mild-to-moderate PS in two. Six appeared to have a small VSD with either left ventricular pressure or mild-to-moderate PS. In the final patient moderate peripheral PS that had not been appreciated at the initial catheterization was documented at restudy. All of the 11 had undergone ASD creation.

There were eight examples of PVO, all in unbanded patients, at an average age of 5½ years (range, 3/12 to 11 years). In three of these PVO developed from initially normal pulmonary vascular resistance, although two of them had mild-to-moderate PAH at the time of the initial study.

In summary, then, approximately half of the patients with known or suspected PAH, who were not banded, had normal or near-normal pulmonary artery pressures at restudy. This was the result of PS, narrowing or closure of a VSD, or both. ASD creation, while improving the mixing, did not seem to prevent PAH. PAH and PVO could be shown to develop, rarely, even with a background of normal pulmonary artery pressure and pulmonary vascular resistance, and in the face of spontaneous VSD closure.

Ventricular Septal Defect with Pulmonary Stenosis

Among the 15 patients with PS at the initial study, three were known to have mild-to-moderate PAH at the outset, and in one more this was suspected. In five the pulmonary artery pressure was known to be normal; in six it was suspected to be low.

Of the three patients with known PAH at the start, one demonstrated progressive PS with a fall in pulmonary artery pressure to normal levels. The other two, as well as the one with suspected PAH initially, exhibited progressive PAH, developed PVO and, at the time of the final study, no longer had evidence of PS. Of the five patients with proven normal pulmonary artery pressure and with what appeared to be severe PS at the initial catheterization, one developed moderate PAH and PVO in the course of 3½ years, while the other four seemed relatively unchanged. No examples of PAH or PVO were found among the six patients estimated to have normal or near-normal pulmonary artery pressure at the initial study.
In summary, then, although the presence of PS appeared to protect the pulmonary vasculature in most instances, this was not invariably the case. At least two of the 15 patients developed PAH and PVO at a relatively early age in the face of PS that we would have considered protective. This contrasts somewhat with the results of adequate pulmonary artery banding which, at least in our experience, extending through the first few years of life, has invariably forestalled PVO disease.

Discussion

We have been impressed by the variety and the extent of hemodynamic changes that have taken place in our patients between the initial and follow-up catheterizations. Restudy was undertaken because of clinical deterioration in only about a third (24 of 65) of the patients while the remainder were restudied primarily to assess their suitability for the Mustard operation. Slightly more than half the patients had at least one significant, unexpected finding at recatheterization.

One reason that so many of the hemodynamic changes were not anticipated was the relative unreliability of the conventional clinical parameters (physical examinations, x-rays, and electrocardiograms) in evaluating the hemodynamic state. A second, interesting reason to explain the unexpected nature of the catheterization data was the small structural change involved. Narrowing of an already small VSD or ASD, closure of a moderate-sized patent ductus arteriosus, or the development of mild-to-moderate PS would be trivial alterations in the setting of normally related great vessels, but in TGA where systemic-to-pulmonary mixing is usually tenuous at best, where maintenance of a moderately elevated pulmonary resistance is essential, and where the tendency toward PVO seems so prominent, even small changes may have significant effect on the immediate and long-term course of the patient. The early detection of undesirable hemodynamic changes seems to require almost routine recatheterization sometime within the first year of life in these survivors.

In terms of cardiac catheterization, a word should be said about the absolute necessity of entering the pulmonary artery to assess the flow, pressure, and resistance relationships in the pulmonary circuit. This was a relatively difficult feat to accomplish, particularly in a patient with an intact ventricular septum, prior to the introduction of the flow-guided catheter. With this technic, in our experience, the pulmonary artery may be entered in almost all instances.

The presence of a patent ductus arteriosus, in the patient material presented, did not seem to be a significant problem in terms of PAH or the development of PVO. We do know, however, from our own experience with critically ill infants, not presented here, as well as from the work of others that a large patent ductus arteriosus in TGA is often associated with severe congestive heart failure and PAH. In such a situation, it is mandatory that a large ASD be present, or be created, before the patent ductus arteriosus is divided. In infants without congestive failure, the ductus probably should not be divided. Frequent follow-up with serial determinations of oxygen saturation is extremely important in such patients to detect spontaneous narrowing of the duct, serving as an indication for ASD creation. It is also important for the optimal early management of the infant with TGA to establish by angiography at the initial catheterization whether a ductus is present and whether or not it is large.

VSD closure in patients with TGA seemed to occur with about the same or only slightly less frequency as in patients with normally related great vessels. A VSD that appeared small angiographically and a systemic arterial saturation below 65% were the two best guides for diagnosis of a small or closing VSD. Spontaneous closure of a VSD did not insure a normal pulmonary vascular bed since three of the seven with closure had at least moderate PAH at restudy and two had PVO.

Natural ASDs, if they were once large enough to permit adequate mixing and a reasonable systemic saturation, did not seem to narrow or close in our experience, but five
of the six patients developed PVO. An ASD was created in 46 of the 65 patients (70%) and in retrospect, probably would have benefited several more.

Balloon septostomy provided good immediate results in a relatively small number of patients, but the benefits were short-lived in the majority. Our experience differs from that of Rashkind and Miller8 and others9,10 in this respect. We do not have a good explanation for this, but our threshold for resorting to surgical ASD creation following balloon septostomy is low since our experience with the former technic is very good.2 Decreasing systemic oxygen saturation following balloon septostomy, in our experience, was invariably associated with a narrowing interatrial opening and, in two patients, concomitant closure of a VSD and PDA, respectively, were found.

Surgical ASD creation could be shown to provide adequate mixing, a lowering of left atrial pressure, and elimination of a gradient between the atria in almost all patients over a prolonged period of observation. A fall in systemic arterial saturation to low levels (<60%) was associated, most frequently, with the development of PS or PVO. Only two of 43 surgically created ASDs have closed spontaneously.

An ASD should be created, we believe, by balloon septostomy or surgery, in all patients with arterial oxygen saturation of 70% or less. Even in those in whom the low saturation is in part due to severe PS, creation of an ASD may facilitate accommodation to the increased pulmonary flow resulting from a shunt operation. In those with saturation greater than 70%, careful oximetric follow-up is indicated. It should be pointed out that in patients with a relatively high arterial saturation due to a VSD and accompanying PAH, banding of the pulmonary artery will commonly result in a significant enough drop in saturation to warrant ASD creation. Unfortunately, surgical ASD creation alone, like a natural ASD, does not prevent development of PVO.

We were surprised to find eight examples of PS, two of them progressive, among the 29 patients with an intact ventricular septum at the final study (28%). The gradients were moderate at most, and in only two did the PS seem to decrease Qp/Qs to below 2.0. PS was present in 50% of the patients with VSD at final study with gradients ranging from mild to severe. In the majority of such patients, the degree of PS seemed to remain about the same or to progress only slightly. In these patients, as in patients with an intact ventricular septum, the systemic arterial oxygen saturation was significantly diminished if the Qp/Qs was below 2.0. The patients who seemed to do best in both groups were those with adequate mixing, either at atrial or ventricular level or both, and in whom the Qp/Qs was between 2.0 and 3.0.

Pulmonary artery banding was effective in lowering pulmonary artery pressure in all, and controlled congestive heart failure in all but one of the eight patients. With time, the band became tight and subsequently half of the patients have required systemic-to-pulmonary arterial shunts. In terms of pulmonary vascular resistance all eight are still candidates for eventual repair. Obviously, only patients with at least a moderate-sized VSD should be subjected to pulmonary artery banding. Patients without severe congestive heart failure, but with pulmonary artery pressure persistently within the systemic range at repeat catheterization, should also have pulmonary banding within the first year of life to prevent irreversible pulmonary vascular changes. The need for simultaneous ASD creation has been discussed earlier. While advocating pulmonary artery banding for most, if not all, patients with a large VSD, we are fully cognizant of the technical problems this may cause if and when complete repair is attempted.

PAH or PVO, or both were present at follow-up in 10 of the 22 patients (45%) whose ventricular septum was intact originally and in 14 of the 43 patients (33%) with VSD. PAH and PVO seemed unavoidable in the presence of a large VSD unless the defect narrowed significantly, lowering left ventricular pressure and/or considerable PS developed or the pulmonary artery was banded surgically. Inter-

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estingly, pulmonary artery banding seemed more reliable in preventing PAH and PVO than naturally occurring PS was, probably because the banding becomes relentlessly more constrictive as the patient grows.

The findings of such a high incidence of PAH, PVO, or both, among patients in whom no VSD was present differs from the experience reported by other investigators.\textsuperscript{8, 9, 11, 12} It is not inconsistent, however, with the severe vascular disease described by Ferguson and associates\textsuperscript{13} and Ferencz\textsuperscript{14} on microscopic examination of the lungs in infants with TGA with or without VSD. Burchell\textsuperscript{15} has suggested that the disparity between the microscopic and hemodynamic findings may lie in deceptively high values calculated for pulmonary flow using the Fick method which does not take bronchial collateral flow into account. We can only say that the data reported here represent a reasonable cross section, we believe, of the survivors under our care.

We have documented severe PVO as early as 2½ years of age in patients with an intact ventricular septum and suspect that in certain patients within this group it may have occurred much earlier. The relatively high incidence of PAH and PVO among the survivors with an intact ventricular septum in this study is disturbing and suggests to us that the time interval between palliation and consideration for total surgical correction may be more limited than previously supposed (table 4). In patients with a VSD, the earliest documented PVO was at 3 months of age. (PA pressure/systemic, \(Q_p/Q_s = 1.2/1\); \(R_p/R_s = 0.3\)). It is possible that obstruction at this age may be reversible, but the implication is that, in patients with a large VSD and no PS, either pulmonary artery banding or total repair will have to be performed within the first year of life.

We thought it might be of interest to try to pinpoint the group of patients in our material who did not develop PAH or PVO. It may be seen in table 5 that patients with all types of physiologic variants may develop these complications with more or less frequency, except for those with naturally occurring small VSDs and those in whom the pulmonary artery has been surgically banded.

**Table 4**

PAH at Follow-up Cardiac Catheterization in 64* Patients with TGA

<table>
<thead>
<tr>
<th></th>
<th>Total patients</th>
<th>No. with PAH in each follow-up period</th>
<th>Total with PAH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt;2 yr</td>
<td>2-4 yr</td>
</tr>
<tr>
<td>No VSD</td>
<td>28*†</td>
<td>2/8†</td>
<td>5/15</td>
</tr>
<tr>
<td>VSD, no PS</td>
<td>10</td>
<td>2/2</td>
<td>2/3</td>
</tr>
<tr>
<td>VSD + PAB</td>
<td>8</td>
<td>0/1</td>
<td>0/4</td>
</tr>
<tr>
<td>VSD + PS</td>
<td>18</td>
<td>0/5</td>
<td>0/6</td>
</tr>
<tr>
<td>Total</td>
<td>64</td>
<td>4/16</td>
<td>7/28</td>
</tr>
</tbody>
</table>

*In one patient mild PAH could neither be proved nor disproved with certainty.
†Includes two patients whose PS disappeared by final catheterization.
‡Number with PAH among total followed for period.

**Table 5**

PAH, or PVO, or Both in 64* Patients with TGA

<table>
<thead>
<tr>
<th></th>
<th>VSD</th>
<th>No VSD</th>
<th>Closed</th>
<th>Small</th>
<th>Small + PS</th>
<th>Large</th>
<th>Large + PS</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAH or PVO or both</td>
<td></td>
<td>10</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>6</td>
<td>4</td>
<td>24</td>
</tr>
<tr>
<td>No PAH or PVO</td>
<td></td>
<td>12</td>
<td>5</td>
<td>1</td>
<td>3</td>
<td>9†</td>
<td>11</td>
<td>40</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>22</td>
<td>7</td>
<td>3</td>
<td>3</td>
<td>15</td>
<td>15</td>
<td>64</td>
</tr>
</tbody>
</table>

*In one patient mild PAH could neither be proved nor disproved with certainty.
†All with PA banding.
Abbreviations: Same as in previous tables.
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