The Pulmonary Vascular Bed in Patients with Complete Transposition of the Great Arteries

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SUMMARY Histological material obtained at autopsy from 35 patients over three months of age with complete transposition of the great arteries (TGA) was examined. Two of six patients less than a year of age with an intact ventricular septum and closed ductus arteriosus were found to have pulmonary vascular changes of at least grade 3 severity; in addition, two of seven patients with a large ventricular septal defect in this age group showed changes of similar severity. The reported low incidence of marked pulmonary vascular changes in patients with only an interatrial communication dying during the first year of life would appear to be due in part to the high proportion of cases less than three months old in whom there was not sufficient time for such changes to develop. Although the incidence is not as high as that found beyond a year of age, it is sufficiently high to influence the management of infants beyond three months of age.

THE EARLY DEVELOPMENT of markedly abnormal changes in the pulmonary vascular bed of patients with complete transposition of the great arteries (TGA) has been well documented.1 Most investigations have been based on autopsy data,2,4 but lung biopsies obtained at operation were studied by Wagenvoort et al., who found less striking changes.4 In a recent study, Newfeld et al.5 did not encounter pulmonary vascular disease (PVD) of greater than grade 2 severity in patients less than a year of age with an intact ventricular septum in the absence of a patent ductus arteriosus.

In the present study we have reviewed autopsy and hemodynamic data in an attempt to define further the spectrum of PVD in patients with TGA.

Materials and Methods

This study is concerned with patients in whom TGA was present as an isolated anomaly or associated with potentially correctable lesions who were seen at Green Lane Hospital between 1961 and 1971. Histological material was obtained from 35 of 43 patients who died during medical management or after palliative or corrective surgery. Specimens were obtained from each lung, formalin fixed, and stained with hematoxylin and eosin and elastic van Gieson stain. Pulmonary vascular disease was graded by one of us (JCW) according to the classification of Heath and Edwards2 without prior knowledge of the clinical status of the patients. Because of the difficulty in distinguishing normal from abnormal in the first few months of life, this investigation was limited to children over three months of age who died.

In another group of patients hemodynamic data were available in 34 of 49 hospital survivors 14-67 (average 28) months after atrial baffle repair. Significant residual intracardiac shunts were not encountered. Pulmonary arteriolar resistance (mean pulmonary artery pressure minus mean pulmonary venous atrial or pulmonary arterial wedge pressure/cardiac output in litres/min/M2g) was estimated at rest. Cardiac output was calculated from indicator dilution curves using a modified Stewart Hamilton technique6 in all but one patient. The latter had a small ventricular septal defect which was not closed surgically and the Fick method was used. Eleven patients also had estimations made after infusion of isoproterenol at a dose sufficient to increase the heart rate by about 50% of the control value once a steady state had been achieved.

Pathological Studies

Intact Ventricular Septum

Data were available in 16 of 21 patients with an intact (14) or essentially intact (2) ventricular septum and a closed ductus arteriosus (fig. 1). Two had a naturally occurring atrial septal defect; in the remainder an interatrial communication had been created, usually during the first two weeks of life.

Four patients had normal pulmonary vasculature (fig. 1); five showed grade 2 changes and in the remaining seven patients more extensive abnormalities were present. The most striking changes were seen in an infant 11 months of age where there were widespread grade 4 changes (fig. 2) and occasional necrotizing arteritis. Two patients in this group, aged 6 and 15 months, who died from pulmonary venous obstruction 3 and 11 months after a Mustard atrial baffle repair, showed grade 2 and 3 changes respectively.

Ventricular Septal Defect (VSD)

Histological material was available in 12 of 15 patients with an important VSD (fig. 1). The defect was greater than 5 mm in diameter in all but one patient in whom it appeared more significant early in life.
months; grade 3 in two aged 3½ and 10 months, and grade 4 in one aged 39 months.

Two patients underwent atrial septectomy and banding of the main pulmonary artery, one at 11 days, the other at four months. The former died at 11 months with a mesenteric thrombosis. Cardiac catheterization shortly before death showed a distal pulmonary artery pressure of 17/12 mmHg and a pulmonary arteriolar resistance (Rpa) of 2.9 units M² and at autopsy the pulmonary vasculature was normal. The other died at 43 months, with grade 3 changes at autopsy.

In two patients early septostomy was followed by atrial baffle repair and closure of the VSD at one and four months. Both had normal pulmonary vasculature at 10 and 12 months of age.

**VSD and Pulmonary Stenosis**

Histological data were available in all seven patients with VSD and important pulmonary stenosis (fig. 1). Grade 4 changes were encountered in one patient aged seven years who had not had palliative surgery. Three patients had a systemic-pulmonary artery anastomosis aged 2-21 months; the lung vasculature appeared normal in two at 48 and 75 months and showed grade 2 changes in the other at 34 months. Lung vasculature was normal in the remaining three patients.

In summary, 12 of 35 patients had grade 3 or more marked changes which were not confined to those with a large VSD. The most marked changes were seen in an 11-month-old infant with an essentially intact ventricular septum. Lesions resembling those seen in pulmonary thromboembolism were also found in five patients (fig. 1).

**Hemodynamic Studies**

Rpa was measured in 34 patients (fig. 3). All but one of the 16 patients who underwent atrial baffle repair prior to

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**Figure 1.** Pulmonary vascular changes in patients dying with complete transposition of the great arteries. Open circles refer to late postoperative deaths following atrial baffle repair. B = main pulmonary artery banded; PVOD = pulmonary vascular disease; T = additional thromboembolic lesions.

Eight patients either received no palliation or had an atrial septal defect created. Grade 1 changes were found in one patient aged 3½ months; grade 2 in four aged 3-14 months; grade 3 in two aged 3½ and 10 months, and grade 4 in one aged 39 months.

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**Figure 2.** Left) Dilatation lesions with intimal fibrosis in parent artery (EVG) in 11-month-old infant with transposition of the great arteries and essentially intact ventricular septum (VSD 2mm × 2½mm and partially obstructed). Right) Same patient. Gross intimal fibro-elastosis extends from parent vessel showing medial elastosis into thin walled “blow out” lesion (arrows). (EVG)
two years of age had a Rpa less than 3 units M² at the time of review. This included one who had a large VSD and two with a large PDA undergoing repair prior to two months of age. Although repair at an older age did not preclude a low Rpa on follow-up, in 11 of the 18 patients who were two to five years of age at the time of repair it was greater than 3 units M² and in five of these it was over 6 units M². None of these patients had a large VSD or PDA. Nor was there evidence that pulmonary venous obstruction had contributed to the development of PVD.

In 11 patients Rpa was also measured after infusion of isoproterenol (table 1). Two of the five patients with significant elevation of Rpa at rest showed a fall to a more modest level with isoproterenol.

Preoperative and postoperative studies in two patients with only an interatrial communication in whom the Rpa was known to be high before operation are detailed in table 2. Case 1 was previously reported prior to late postoperative assessment.a

Discussion

The early development of PVD in patients with TGA has been emphasized,1 but in patients less than one year of age in whom the only significant associated lesion was an interatrial communication, changes of grade 3 or greater severity are considered uncommon. In the autopsy studies of Ferencz et al., Viles et al.,4 and Newfeld et al.,6 such changes were found in only five of 128 patients during the first year of life (table 3). These series, however, contained a high proportion of infants less than three months of age in whom advanced PVD was rare. In the 3-11 months age group, four of 29 patients showed grade 3 or greater changes. In our series two of six patients aged 3-11 months showed such appearances, the most striking being found in an 11-month-old infant. While the types of patients studied by the various authors are not necessarily identical, they would appear sufficiently similar to allow some comparison between patients of different age groups (table 3). It would seem that approximately 15-20% of infants with TGA, an essentially intact ventricular septum, and closed ductus arteriosus coming to autopsy at 3-11 months of age showed advanced PVD. This incidence is sufficiently high to provide an indication for early atrial baffle repair.

In the present series, postoperative hemodynamic studies showed that only one of the surviving 13 patients without an important VSD or PDA in whom atrial baffle repair was performed before two years of age had a Rpa greater than 3 units M². When repair was performed at an older age 10 of 17 patients were found to have Rpa over 3 units M².

Comparison of autopsy and postoperative hemodynamic data in patients with an essentially intact ventricular septum and closed ductus arteriosus supports the conclusion that advanced PVD is associated with early death, as previously suggested by Wagenvoort et al.7 The role of increased Rpa in this situation is uncertain, but it may be related to limitation of effective pulmonary blood flow. It appears a

<table>
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<tr>
<th>Case</th>
<th>BSA (m²)</th>
<th>CI (L/min/m²)</th>
<th>Rpa (µM²)</th>
<th>Rpa/Rs</th>
<th>Isop (µg/kg/min)</th>
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<td>2.9</td>
<td>4.2</td>
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<td>0.12</td>
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Abbreviations: BSA = body surface area; CI = cardiac index; I = with infusion of isoproterenol; R = rest; Rpa = pulmonary arterial resistance; Rs = systemic resistance; uM² = units M²; µg = micrograms; Isop = isoproterenol.

Table 2. Studies Before and After Atrial Baffle Repair

<table>
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<tr>
<th>Case</th>
<th>Age (yr)</th>
<th>Rpa</th>
<th>Rpa/Rs</th>
<th>Hot</th>
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<td>10.1</td>
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<td>69%</td>
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<tr>
<td>Op</td>
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<td>0.95</td>
<td>38%</td>
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<tr>
<td>Postop</td>
<td>7-6/12</td>
<td>4.2</td>
<td>0.16</td>
<td>38%</td>
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<tr>
<td></td>
<td>3.3</td>
<td>0.17</td>
<td></td>
<td></td>
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<tr>
<td>Preop</td>
<td>11/12</td>
<td>10.8</td>
<td>0.88</td>
<td>65%</td>
</tr>
<tr>
<td>Op</td>
<td>1</td>
<td>5.9</td>
<td>0.88</td>
<td></td>
</tr>
<tr>
<td>Postop</td>
<td>3-3/12</td>
<td>3.6</td>
<td>0.13</td>
<td>38%</td>
</tr>
</tbody>
</table>

Abbreviations: R = rest; I = isoproterenol; Hot = hematocrit. For others see table 1.

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**Figure 3.** Pulmonary arteriolar resistance following atrial baffle repair. 1 = small ventricular septal defect (VSD); 2 = large VSD; 3 = VSD with pulmonary stenosis; 4 = small patent ductus arteriosus (PDA); 5 = large PDA.
relatively high pulmonary blood flow is an essential pre-requisite for satisfactory intracardiac mixing,\textsuperscript{19} perhaps simply because turbulent conditions within the atria necessary for adequate mixing are achieved only when flow is high. Most of the nonsurgical deaths in this series were associated with a relatively minor respiratory infection. When pulmonary flow is restricted, patients with TGA are unable to compensate for the associated increase in metabolic demands and impaired gaseous exchange, and it would seem likely that those patients with a high Rpa would be more vulnerable in this situation. Autopsy data were available in six of ten patients dying in this manner. All showed PVD. Grade 2 changes were present in four patients and more advanced changes were found in the others.

Advanced PVD at an early age has been found in patients with TGA and a large VSD. In the three series mentioned previously (table 3), Grade 3 or greater changes were found at autopsy in six of 32 patients less than three months of age, and in nine of 37 patients 3-11 months of age. Early definitive operation in patients with a large VSD or PDA should prevent the progression of PVD but to date there is little information about this. Viles\textsuperscript{4} encountered one patient who had a Senning operation\textsuperscript{11} and closure of a VSD at three months of age with minimal medial thickening at 11 months. In the present series two patients who underwent baffle repair and closure of a VSD at one and four months and died at 10 and 12 months respectively had normal pulmonary vasculature. Three surviving patients who had an atrial baffle repair and surgical closure of a large PDA or VSD prior to three months of age had an estimated Rpa of 1.5-2.5 units M\textsuperscript{2} postoperatively.

Bandaging of the pulmonary artery has been advocated in patients with a large VSD,\textsuperscript{12} and although this appears to prevent the development of severe PVD in some patients, it is not always successful, even when the procedure has been undertaken prior to six months of age.\textsuperscript{4} In one patient in our series grade 3 changes were present at 43 months, despite banding at four months of age. The presence of important pulmonary stenosis does not always prevent the development of severe pulmonary vascular changes, as illustrated by one patient in this series and noted by others.\textsuperscript{4}

Preoperative assessment of Rpa in patients with TGA has not been without problems.\textsuperscript{13} Failure to enter the pulmonary artery at a time when most of the present series of patients were assessed before operation precluded a meaningful estimate of resistance. This problem has been largely overcome with the introduction of the Swan-Ganz catheter,\textsuperscript{14} and the principal remaining difficulties relate to obtaining a reliable estimate of pulmonary venous oxygen content. Rpa should be measured as an absolute value or based on body surface area, rather than only related to systemic vascular resistance, to give a resistance ratio.\textsuperscript{15} The over-all hemodynamic state of the patient when this measurement is made should not be ignored. Preliminary data in patients with a variety of congenital heart lesions suggest that estimates of Rpa at rest and following infusion of isoproterenol are of good predictive value (Neute JM: unpublished observation, 1975). In general it would seem that "corrective" operative treatment is inadvisable unless the Rpa can be lowered substantially below 10 units M\textsuperscript{2} with isoproterenol or other agents. In patients with TGA, however, the viscosity of blood of high hematocrit may be an important determinant of elevated Rpa.\textsuperscript{9, 15}

Prediction of the postoperative response of the pulmonary vascular bed is extremely difficult in patients with a high hematocrit. In case 1 (table 2) particularly, a marked drop in Rpa after operation would not have been anticipated had the preoperative hematocrit been normal. Early on in the period under review two patients were judged to be unsuitable for atrial baffle repair because of a high Rpa. There is no reliable way to assess the influence of a high hematocrit on resistance measurements and in rare cases it might be necessary to repeat the measurements after lowering the hematocrit by means of an exchange transfusion with plasma.

### References

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9. Drakeley MF: Case presentation: Transposition of the great arteries with
SUMMARY  To correlate anatomy with hemodynamics, the angio-
cardiographic findings were reviewed in 42 patients with common ven-
tricle (CV). Nine had normally related great arteries (NRGA), 12 d-
malposition, 21 l-malposition and 5 a common atrioventricular valve.
Selective outlet chamber (OLC) angiograms were available in 14 out of 29 patients with OLCs.

OLC position varied from anterior and to the right of the CV to
posterior and to the left of it; two categories (anterior and lateral
OLC) were delineated by a line 45° to the left of anterior in the
horizontal plane. The OLC was anterior in all patients with NRGA,
lateral in most l-malpositions, and almost equally divided between
anterior and lateral in d-malposition (P < 0.05).

Complete hemodynamic data were obtained in 29 patients.
Complete mixing of venous return occurred in four patients with
atresia of one valve. In the remainder complete mixing occurred in
36%, unfavorable streaming in 12% and favorable streaming in 52%.
Semilunar valve position and pulmonary stenosis did not affect
the nature of mixing. Systemic arterial (SA) minus pulmonary arterial
O₂ saturation was positive and significantly higher in patients with
malposition with lateral OLCs than anterior OLCs (P < 0.001).
However 79% of SA O₂ saturation variation could be predicted from
pulmonary and systemic blood flow alone.

COMMON OR SINGLE VENTRICLE presents to the in-
vestigating cardiologist perhaps the most challenging
diagnostic problem in congenital heart disease. This was so
even before there was any prospect of surgical correction of
the lesion. Now that reports of operative repair of this
anomaly are emerging,¹ ² and yet no clear criteria for selec-
tion of patients are established, it is evident that far more
detailed preoperative investigation is now needed. A
preliminary review of angiocardiograms of common ven-
cicle had demonstrated some significant differences from
other published reports. This prompted us to analyze cardiac
investigation data in greater detail and to see to what extent
the hemodynamic state could be explained by the angio-
cardiographic anatomy, and to what extent it was influenced
by other factors.

Definitions and Classification

The problems of matching angiographic with pathologic classifications of common ventricle have
previously been discussed.³ ⁴ Our classification is based
upon that of Hallermann et al.,⁵ modified in the light of

pathological studies by Quero,⁶ ⁷ and van Praagh et al.,⁸ and our
own radiological experience of selective angio-
cardiography of hypoplastic ventricles in mitral⁹ and tricuspid atresia.

Common or single ventricle is that condition in which
both atrioventricular valves, or a common atrioventricular
valves, are anatomically related to, and communicate ac-
tually or potentially with, a single ventricular chamber. If an
outlet chamber is present, neither atrioventricular valve an-
nulus is anatomically related to, or communicates actually or
potentially with, this chamber.

This definition therefore encompasses single (primitive)
ventricle,⁵ common ventricle,⁴ and those forms of mitral and
tricuspid atresia in which the atretic valve is anatomically
related to and therefore communicates potentially with the
same common ventricular chamber as the patent atrio-
ventricular valve.

Malposition of the great arteries exists when the semilun-
lar valves and great arterial trunks are abnormally in-
terrelated in space. In d- and l-malposition the midpoint
of the aortic valve lies respectively to the right and left of the
midpoint of the pulmonary valve.

It is recognized that when the aorta arises from the outlet
chamber and the pulmonary artery from the common ven-
tricle that transposition exists, if in fact the bulboventricular
septum, which lies between the common ventricle and outlet
chamber, is the true interventricular septum.⁷ However, un-
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