Measurement of Bronchial Blood Flow in Tetralogy of Fallot

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SUMMARY

Bronchial blood flow was measured in nine patients with tetralogy of Fallot and in two of these cases after radical operation also. The study was made of simultaneous recording of dye-dilution curves from the left atrium and the ear following dye injection into the aortic root. A method of calculating the bronchial blood flow was devised by combining the dye-dilution method with the Fick principle. The bronchial blood flow was increased in all cases. The mean value was 0.46 ± 0.31 L/min, with a range from 0.14 to 1.27 L/min; this is equivalent to 15.3% of the pulmonary artery flow on the average. This study showed no definite relationships among pulmonary artery blood flow, pulmonary artery pressure, arterial oxygen saturation, severity of disease, and patient's age. The postoperative measurement revealed no significant change in bronchial blood flow though its ratios to the pulmonary artery or aortic blood flows were considerably decreased.

Additional Indexing Words:
Dye-dilution curves
Pulmonary artery flow
Techniques
Cardiac catheterization
Fick principle

Morphotological Studies1-7 have made it apparent that the bronchial arteries are developed remarkably in tetralogy of Fallot. The bronchial circulation may be extremely important because it might improve the symptoms of this malformation with an advantage of compensating a restricted blood supply to the lung. However, there had been no adequate method of measuring precisely the bronchial blood flow in the patients. In 1963, one (R.K.)* of the present authors reported preliminarily a method for estimating the flow in tetralogy of Fallot using the dye-dilution method. The purpose of this paper is to present detailed data of bronchial blood flow in nine patients including two postoperative measurements.

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Methods

Nine patients with tetralogy of Fallot were included in the study. Clinical and laboratory findings are listed in Table 1. Two of these patients underwent postoperative measurement, at 1 month in case 8 and at 2 months in case 9, after radical operation. The operation was completely successful in case 8, but was not successful in case 9 because of persistence of a large left-to-right shunt and appearance of right-heart failure. Diagnosis was made by the right-heart catheterization in all cases and confirmed by autopsy in case 1 and by surgical operation in the other eight cases. The ductus arteriosus was not patent in all patients. One patient had an atrial septal defect and two had a patent foramen ovale. Patient 1 had suffered from severe pulmonary tuberculosis, and he died 1 year after the study. Patient 2 had had systemic hypertension of unknown etiology. The age of the patients ranged from 9 to 36 years.

Principle for Calculating Bronchial Blood Flow

When the bronchial artery is developed and the communication between the bronchial and pulmonary circulations is produced, the blood entering the bronchial artery should return to the left atrium through such an aortopulmonary communication without circulating the right side of
the heart. In this condition, if a dye-dilution curve is inscribed in the left atrium following injection of dye into the aortic root, an early appearance of the dye which recirculates normally in the systemic circulation. Bronchial blood flow can be calculated by comparing this early appearing dye curve (LA curve) with the dye-dilution curve (SA curve) recorded simultaneously in the peripheral systemic artery. This design was previously used to measure the bronchial blood flow in pulmonary disease by Cudkowicz and associates. In patients with tetralogy of Fallot, however, the following treatment is required to calculate the flow because of intracardiac shunt.

The next two equations hold on the SA curve:

$$Q_{Ao} = \frac{I_t}{S_{sa}} \quad (1)$$

$$Q_{BA} = \frac{I_{ba}}{S_{sa}} \quad (2)$$

where $Q_{Ao}$ (L/min) is aortic blood flow, $I_t$ (mg) is the total amount of the dye injected, $S_{sa}$ (mg/L/min) is the dye-concentration area under the SA curve, $Q_{BA}$ (L/min) is bronchial blood flow, and $I_{ba}$ (mg) is the amount of the dye entering the bronchial arteries.

On the LA curve, the following equation holds:

$$Q_{BA} + Q_{PA} = \frac{I_{ba}}{S_{la}} \quad (3)$$

where $Q_{PA}$ (L/min) is pulmonary artery blood flow, and $S_{la}$ (L/min) is the dye-concentration area under the early appearing dye curve of the LA curve. The equation 3 can be written as,

$$I_{BA} = S_{la} \times Q_{BA} + S_{la} \times Q_{PA}. \quad (4)$$

Combining the equation 4 with the equation 2,

$$\frac{Q_{BA}}{Q_{PA}} = \frac{S_{la}}{S_{sa} - S_{la}}. \quad (5)$$

According to the Fick principle, $Q_{PA}$ and $Q_{BA}$ are calculated as follows:

$$Q_{PA} = \frac{V_{OpPA}}{C_{PVO_2} - C_{PAO_2}}. \quad (6)$$

Table 1

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr), sex</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>Hematocrit (%)</th>
<th>Red blood cell (million 1 mm³)</th>
<th>Systemic pressure (mm Hg)</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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<td>174.0</td>
<td>39.0</td>
<td>64</td>
<td>5.90</td>
<td>112/64</td>
<td>Pulmonary tuberculosis, patent foramen ovale</td>
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<tr>
<td>2</td>
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<td>170.2</td>
<td>55.0</td>
<td>67</td>
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<td>175/120</td>
<td>Systemic hypertension, etiology unknown</td>
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<td>40.3</td>
<td>59</td>
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<td>130/80</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>F 14</td>
<td>151.7</td>
<td>47.0</td>
<td>74</td>
<td>6.05</td>
<td>110/80</td>
<td>Patent foramen ovale</td>
</tr>
<tr>
<td>5</td>
<td>F 13</td>
<td>147.5</td>
<td>38.5</td>
<td>41</td>
<td>5.91</td>
<td>105/70</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>M 14</td>
<td>155.0</td>
<td>46.0</td>
<td>50</td>
<td>4.96</td>
<td>100/60</td>
<td>Atrial septal defect</td>
</tr>
<tr>
<td>7</td>
<td>M 36</td>
<td>154.8</td>
<td>51.0</td>
<td>43</td>
<td>5.20</td>
<td>140/88</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>M 11</td>
<td>140.1</td>
<td>30.0</td>
<td>47</td>
<td>5.60</td>
<td>115/80</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>M 9</td>
<td>128.6</td>
<td>28.0</td>
<td>55</td>
<td>6.35</td>
<td>96/68</td>
<td>Patent foramen ovale</td>
</tr>
<tr>
<td>8</td>
<td>M 11</td>
<td>140.3</td>
<td>31.2</td>
<td>35</td>
<td>4.12</td>
<td>125/80</td>
<td>1 mo after radical operation</td>
</tr>
<tr>
<td>9</td>
<td>M 9</td>
<td>128.7</td>
<td>29.0</td>
<td>36</td>
<td>4.30</td>
<td>100/70</td>
<td>2 mo after radical operation, evidences of right-heart failure</td>
</tr>
</tbody>
</table>

Abbreviations: S = systolic pressure; D = diastolic pressure.

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\[ Q_{RA} = \frac{V_{O_2,PA}}{C_{PV,O_2} - C_{PA,O_2}} \]  

where \( V_{O_2,PA} \) (ml/min) is the amount of oxygen taken up by the pulmonary artery blood flow, \( V_{O_2,BA} \) (ml/min) is amount of oxygen taken up by the bronchial blood flow, \( C_{PV,O_2} \) (ml/L) is oxygen content of the pulmonary venous blood, \( C_{PA,O_2} \) (ml/L) is oxygen content in the pulmonary artery blood, and \( C_{BA,O_2} \) (ml/L) is oxygen content in the systemic artery blood.

By using equations 6 and 7, equation 5 can be written as,

\[ \dot{Q}_{RA} = \frac{S_{sa} \cdot V_{O_2}}{S_{sa} \cdot (C_{PV,O_2} - C_{PA,O_2}) - S_{ba} \cdot (C_{BA,O_2} - C_{PA,O_2})} \]

where \( V_{O_2} \) (ml/min) is oxygen consumption, which is a sum of \( V_{O_2,PA} \) and \( V_{O_2,BA} \).

**Procedures**

After the routine right-heart catheterization for diagnosis, transseptal left atrial puncture was performed by the Brockenbrough and Braunwald technique\(^\text{10}\) except in four cases in which there was an atrial septal defect or patent foramen ovale. The tip of the Brockenbrough catheter then lay in the left atrium. Odman-Ledin KIFA catheter was introduced into a femoral artery by the Seldinger percutaneous technique\(^\text{11}\) and it was advanced under fluoroscopic control until its tip lay just above the aortic valve. Sixty milligrams of Coomassie Blue (cases 1 to 4) or 10 mg of indocyanine green (Cardio-Green; cases 5 to 9) were rapidly injected into the aortic root through the latter catheter, and two dye-dilution curves, from the left atrium and from the ear, were simultaneously recorded by a Sanborn Twin-Viso Cardiobee using cuvette and ear densitometers, respectively. A cuvette was connected directly with the Brockenbrough catheter and blood was withdrawn at the speed of 0.9 ml/sec by an Erma Infusion-Withdrawal Pump* for recording of the dye-dilution curve. Capacity of a catheter-connector-cuvette system was 1.98 ml. For densitometers we employed the Erma Dye-Densitograph* which was devised in our laboratory.\(^\text{12}\) Its response was linear in the range of 0 to 130 mg of Coomassie Blue dye and 0 to 60 mg of indocyanine green per liter of whole blood. When a filter of comparable density was suddenly placed in the light path, the instrument responded to 90% of full scale in 0.24 second.

Figure 1 shows dye-dilution curves in case 4. The dye-dilution curve from the left atrium (lower panel) shows a two-peak contour of which an antecedent peak is considered to be the early appearing dye through the bronchial-pulmonary communication and a succeeding one corresponds to the recirculation dye curve through the systemic circulation. Calculation of dye-concentration area in the SA curve was made by the method of Hamilton and associates\(^\text{13}\) but for that of the early appearing curve in the LA curve the forward-triangle method of Hetzel and co-workers\(^\text{14}\) was applied:

\[ \text{Area} = \frac{1}{2} \times 2.70 \times t_{bp} \times C_{p} \]

where \( t_{bp} \) is buildup time and \( C_{p} \) is peak concentration. Calibration of dye-dilution curves was made by the following procedures. For Coomassie Blue dye, the blood sample was obtained from the left atrium about 2 minutes after injection of the dye, and plasma-dye concentration was measured by an electrometer using the wavelength of 610 m\(\mu\). A densitometer deflection from the base line of the dye curve at the time of blood sampling was used for one-point check of calibration both in the left atrial dye curve and the ear dye curve. For Cardio-Green dye, the cuvette densitometer was calibrated by the passage of known concentrations of the dye made up in the patient’s arterial blood immediately before inscription of the dye curve, and the earpiece dye curve was calibrated by comparing its deflection with the corresponding deflection of the left atrial dye curve.

Bronchial blood flow (\( Q_{BA} \)) was calculated by equation 8 and pulmonary artery blood flow (\( Q_{PA} \)) by equation 5. Aortic blood flow (\( Q_{AO} \)) was measured from the earpiece dye curve following injection of dye into the aortic root. Duplicate measurements were carried out at intervals of about 10 minutes in five cases. Pulmonary blood flow (\( Q_{P(FICK)} \)) and systemic blood flow (\( Q_{S(FICK)} \)) were calculated by the Fick method, in which for \( Q_{P(FICK)} \) oxygen consumption was divided by the oxygen content difference between

\*Erma Optical Work Company, 2-4, Kanda Kajimachi, Tokyo, Japan.
BRONCHIAL BLOOD FLOW

Figure 1
Simultaneously recorded dye-dilution curves following injection of 60 mg of Coomassie Blue dye (CB) into the aortic root in case 4. Upper panel shows dye curve recorded by an ear densitometer and lower panel shows that from the left atrium recorded by a cuvette. Time lag in the latter curve is 2.2 seconds.

Results

The results of the study are listed in tables 2, 3, and 4.

Catheterization Data

Pulmonary arterial pressure was lowered in all seven cases observed. Right ventricular systolic pressure was markedly elevated in all nine cases, ranging from 90 to 170 mm Hg. After operation it decreased to almost normal level in case 8, but in case 9 the decrease was insignificant. Right atrial pressure ranged from 2 to 7 mm Hg in the preoperative state, but it was high (10 mm Hg) postoperatively in case 9 in which there was clinical evidence of right-heart failure at that time.

Right-to-left shunt ranged from 11 to 44%, and after operation it was completely corrected in both cases. Left-to-right shunt ranged from 2 to 31%, and after operation it was not detected in case 8 but remained high (28%) in case 9. Arterial oxygen saturation ranged from 78 to 90% in preoperative...
Bronchial Blood Flow

Bronchial blood flow ranged from 0.14 to 1.27 L/min, with a mean value of 0.46 ± 0.31 L/min (SD). The ratio of the bronchial blood flow to the pulmonary artery blood flow ranged from 7.4 to 30.3%, with a mean value of 15.3 ± 8.1%. The ratio of its flow to the aortic blood flow ranged from 4.4 to 14.2%, with a mean value of 7.9 ± 3.4%.

Table 2
Heart Catheterization Data on Nine Patients with Tetralogy of Fallot

<table>
<thead>
<tr>
<th>Case</th>
<th>Pulmonary arterial pressure, S/D mean (mm Hg)</th>
<th>Right ventricular pressure, S/D mean (mm Hg)</th>
<th>Right atrial pressure (mm Hg)</th>
<th>Right-to-left shunt (%)</th>
<th>Left-to-right shunt (%)</th>
<th>Arterial oxygen saturation (%)</th>
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<td>1</td>
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<td>90/3 35</td>
<td>3</td>
<td>21</td>
<td>31</td>
<td>88</td>
</tr>
<tr>
<td>2</td>
<td>17/4 7</td>
<td>170/7 52</td>
<td>7</td>
<td>43</td>
<td>5</td>
<td>79</td>
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<td>128/8 48</td>
<td>7</td>
<td>27</td>
<td>2</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>110/4 45</td>
<td>105/4 36</td>
<td>4</td>
<td>44</td>
<td>2</td>
<td>83</td>
</tr>
<tr>
<td>5</td>
<td>18/8 12</td>
<td>105/4 36</td>
<td>3</td>
<td>29*</td>
<td>29*</td>
<td>78</td>
</tr>
<tr>
<td>6</td>
<td>15/7 10</td>
<td>90/2 25</td>
<td>4</td>
<td>42*</td>
<td>18*</td>
<td>82</td>
</tr>
<tr>
<td>7</td>
<td>13/7 9</td>
<td>140/4 40</td>
<td>2</td>
<td>28</td>
<td>10</td>
<td>87</td>
</tr>
<tr>
<td>8</td>
<td>15/3 8</td>
<td>110/2 40</td>
<td>2</td>
<td>11*</td>
<td>7*</td>
<td>87</td>
</tr>
<tr>
<td>9</td>
<td>102/3 40</td>
<td>102/3 40</td>
<td>3</td>
<td>35</td>
<td>22</td>
<td>79</td>
</tr>
</tbody>
</table>

Postoperative study

| 8    | 39/2 21                                       | 2                              | 0                              | 0                       | 28*                       | 92                            |
| 9    | 85/10 30                                      | 10                             | 0                              | 28*                     | 93                        |                               |

Abbreviations: S = systolic pressure; D = diastolic pressure.
*Shunt was calculated by dye-dilution method.16

Table 3
Blood Flow Data on Nine Patients with Tetralogy of Fallot

<table>
<thead>
<tr>
<th>Case</th>
<th>QBA (L/min)</th>
<th>QPA (L/min)</th>
<th>QAO (L/min)</th>
<th>QP(FICK) (L/min)</th>
<th>Qs(FICK) (L/min)</th>
<th>QBA/QPA (%)</th>
<th>QBA/QAO (%)</th>
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</thead>
<tbody>
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<td>Preoperative study</td>
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<tr>
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<td>1.97</td>
<td>10.02</td>
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<td>22.1</td>
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<td>1.53</td>
<td>3.21</td>
<td>1.71</td>
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</tr>
<tr>
<td>Mean</td>
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<td>5.77</td>
<td>3.19</td>
<td>3.85</td>
<td>15.3</td>
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</tr>
<tr>
<td>Standard deviation</td>
<td>±0.31</td>
<td>±1.05</td>
<td>±2.44</td>
<td>±1.20</td>
<td>±0.97</td>
<td>±8.1</td>
<td>±3.4</td>
</tr>
</tbody>
</table>

Postoperative study

| 8    | 0.21        | 5.73        | 6.57        | 4.97             | 4.97            | 3.6          | 3.2         |
| 9    | 0.16        | 4.22        | 5.28        | 5.12             |                 | 3.8          | 3.1         |

Abbreviations: Q_{BA} = bronchial blood flow; Q_{PA} = pulmonary artery blood flow (blood flow through pulmonic valve); Q_{AO} = aortic blood flow; Q_{P(FICK)} = pulmonary blood flow calculated by Fick principle; Q_{S(FICK)} = systemic blood flow calculated by Fick principle. *Mean values include data from five cases (cases 4, 5, 7 to 9) in which duplicate measurements were made.
Table 4

Duplicate Measurements of Bronchial Blood Flow on Five Patients with Tetralogy of Fallot

<table>
<thead>
<tr>
<th>Case</th>
<th>(Q_{BA}) (L/min)</th>
<th>(Q_{PA}) (L/min)</th>
<th>(Q_{AO}) (L/min)</th>
<th>(Q_{BA}/Q_{PA}) (%)</th>
<th>(Q_{BA}/Q_{AO}) (%)</th>
</tr>
</thead>
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<tr>
<td>4</td>
<td>0.45</td>
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<td>0.41</td>
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</tr>
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<td>0.28</td>
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<td>4.80</td>
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<td>5.8</td>
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<td>1.53</td>
<td>2.86</td>
<td>10.2</td>
<td>5.4</td>
</tr>
</tbody>
</table>

Abbreviations: symbols are similar to those in table 3.

Pulmonary artery blood flow ranged from 1.53 to 4.87 L/min, with a mean value of 3.02 ± 1.05 L/min. Aortic blood flow greatly exceeded the pulmonary artery blood flow in all except in one case; its mean value was 5.77 ± 2.44 L/min with a range from 2.41 to 10.02 L/min. Pulmonary blood flow calculated by the Fick method was slightly higher than the pulmonary artery blood flow mentioned earlier, ranging from 1.71 to 4.99 L/min with a mean value of 3.19 ± 1.20 L/min.

After radical operation, pulmonary artery blood flow, aortic blood flow, and pulmonary blood flow by the Fick method increased as compared with the preoperative values in both cases. Bronchial blood flow did not show any significant change in both cases. However, the ratio of the bronchial blood flow to the pulmonary artery blood flow was considerably decreased in both cases after operation on account of the marked increase in pulmonary flow.

Duplicate measurements revealed a good agreement with each other in the bronchial blood flow, the pulmonary artery blood flow, or the aortic blood flow as shown in table 4.

Discussion

The enlargement of bronchial blood flow has been confirmed physiologically by several investigators⁹, ¹⁸-²² in lung disease, while in heart diseases there have been only a few reports concerning the measurement of collateral blood flow in patients with atresia of the main pulmonary artery or unilateral absence of the pulmonary artery. Four patients with tetralogy of Fallot complicated by pulmonary arterial atresia were studied by Fishman and associates.¹⁸ Since blood flow to the lung was shown by Fishman and associates,¹⁸ pulmonary blood flow in patients with tetralogy of Fallot was derived entirely from the aorta, "effective" bronchopulmonary blood flow could be calculated by the Fick principle in their cases. The flow of the aorta was large, ranging from 1.35 to 5.00 L/min. Averill and co-workers²³ reported one case of congenital absence of the left pulmonary artery. Indocyanine dye was injected into the aortic root and simultaneous dye curves were recorded from the femoral artery and the left atrium. The total bronchopulmonary flow to the lung was about 25% of the total left ventricular output. Tabakin and co-workers²⁴ reported two cases in which the estimated flow (Fick principle) was 1.84 and 1.80 L/min, respectively. Oakley and associates²⁵ reported one case of congenital absence of the left pulmonary artery with the left ventricular output 35% larger than the right ventricular output.

On the contrary, the measurement of bronchial blood flow in tetralogy of Fallot with pulmonic stenosis is not simple, because blood flow to the lung is supplied from both the pulmonary artery and the aorta through the bronchial artery and because intracardiac shunts are present. To our knowledge, Bing and associates,¹⁵, ²⁶ in 1947, have made the only report in which pulmonary capillary
blood flow was measured by indirect Fick principle using carbon dioxide. Pulmonary blood flow was calculated by the direct Fick method using carbon dioxide. The difference between the pulmonary capillary flow and the pulmonary flow represented bronchial blood flow (bronchopulmonary flow). In 30 of their 38 patients who underwent the measurement, ranging from 5 to 25 years in age, bronchial blood flow was increased with a mean value of 866 ml/min, ranging from 150 to 2,790 ml/min.

The present study revealed that bronchial blood flow was 0.46 L/min on the average, and corresponded to 15.3% of the pulmonary artery blood flow and to 7.9% of the aortic blood flow. These values are considerably lower than those in cases of atresia of the pulmonary artery reported by Fishman and associates. As blood supply to the lungs in the latter cases is entirely from the aorta, such an enlarged bronchial blood flow may be nothing to be wondered at. However, our results were much lower than the results in the cases of pulmonary stenosis studied by Bing and associates. This discrepancy may be referred to the analytical errors dependent upon the respective measurement methods. Duplicate measurements by the methods now in use gave fairly good agreement for the bronchial artery, pulmonary artery, and aortic blood flows (table 4). These results reveal good reproducibility of the procedures involved.

A technical problem involved in the present method may remain in the assumption that the early appearing dye curve in the left atrium after dye injection into the aortic root is solely due to the bronchial flow, because it has been reported that the renal and coronary circulations may serve as the fast pathway of the systemic circulation. In the present study, the appearance time of the early dye curve in the left atrium was 2.7 ± 1.4 seconds on the average in 11 cases including the two postoperative cases. This time coincided with 2.8 ± 1.0 seconds which is a mean of the appearance time in 10 cases with lung diseases indicating increased bronchial flow by the same principle as the present method. In nine cases in which bronchial flow could not be detected, the appearance time was 7.4 ± 1.5 seconds on the average. It was considered that the early systemic recirculation does not appear in the left atrium in less than 5 seconds after injection of dye into the aortic root in the usual condition of normal human subjects.

Selective bronchial arteriograms were taken in four patients according to the technique of Reuter and associates. The degree of enlargement of the bronchial arteries demonstrated on their arteriograms was consistent with the values of bronchial blood flow in those cases. Figure 2 shows the right bronchial artery in case 8 in which blood flow was 0.28 L/min and figure 3 shows the right bronchial artery in case 7 in which flow was 0.55 L/min.

Reduced pulmonary artery blood flow and lowered pulmonary arterial pressure would be cited as the most potential mechanism for an increase in bronchial circulation in tetralogy of Fallot. In this study, however, there were no definite relationships either between the bronchial and pulmonary artery blood flows or between the bronchial blood flow and pulmonary arterial pressure. Postoperative study

Figure 2
Selective right bronchial arteriogram in case 8 with tetralogy of Fallot. Bronchial blood flow measured was 0.28 L/min in this case.
revealed that the bronchial blood flow was not changed after radical operation in spite of a marked increase in pulmonary artery blood flow and a probable rise in pulmonary arterial pressure. There was no ground to affirm a simple mechanistic theory as the mechanism for the increased bronchial circulation.

The bronchial circulation in tetralogy of Fallot could play an important role in lessening oxygen desaturation in the arterial blood by compensating for reduced pulmonary capillary flow. The clinical course of the patients may be affected by the magnitude of its flow as a collateral circulation of the lung. In the present study, however, the increase in the flow was considerably smaller than that reported previously from anatomic and physiological studies, and then the values calculated did not necessarily correlate with arterial oxygen saturation, severity of disease, or patient's age. Thus, the advantage of increased bronchial circulation in tetralogy of Fallot is not so great as has been generally presumed.

**Figure 3**

Selective right bronchial arteriogram in case 7 with tetralogy of Fallot. Bronchial blood flow measured was 0.65 L/min in this case.

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