Hemodynamic Events during the Development of Cyanosis and Heart Failure in a Patient with Large Ventricular Septal Defect

By Harry A. Bliss, M.D., and Jean E. Moffat, M.B., B.S.

The late occurrence of cyanosis or congestive heart failure is not unusual in patients with a large ventricular septal defect and high pulmonary vascular resistance.\(^1\)\(^2\) The physiological changes producing these events remain somewhat unclear, however, although recent evidence\(^3\)\(^6\) indicates that pulmonary vascular resistance, if high early in life, may increase over a period of years. In two patients reported by Arcilla and co-workers,\(^3\) vascular resistance in the lungs rose sufficiently to cause right-to-left intracardiac shunting and cyanosis. Hemodynamic alterations during the appearance of heart failure have not been reported in these or other studies, however.\(^7\)\(^8\)

The present report describes serial hemodynamic findings in a patient with this syndrome during a period when cyanosis increased and cardiac failure occurred. Unlike the patients mentioned above, our patient showed a decrease in arterial oxygen saturation that did not result from a disproportionate rise in pulmonary compared to systemic vascular resistance. Rather, a progressive fall in the amount of blood pumped from both sides of the heart explained the intensification of cyanosis and the manifestations of heart failure.

Case Report

A Negro man (no. 493722), born in Alabama in 1936, was discovered to have a heart murmur shortly after birth. Historical details are lacking for the first few years of life, but exertional dyspnea severe enough to prevent him from running or playing with other boys was present as early as age 5. When he was 12, his physician observed cardiac enlargement and a loud murmur, rales in the right lung, and a palpable liver. Blood pressure was 130/70. An x-ray (fig. 1) showed cardiac enlargement and increased pulmonary vascular markings. He was placed on digitalis at that time. Improvement was gradual until in the late 1950's he could climb six flights of stairs or play basketball strenuously for an hour or two without more dyspnea than his cohorts. Digitalis was stopped during that period.

He first visited this hospital in 1959 for evaluation of cardiac murmur. No complaints were present at that time. He was a well-developed slim man showing slight cyanosis of fingers and toes, but no clubbing. The neck vessels were not remarkable. A mild thoracic scoliosis was apparent. A rather diffuse, though forceful apex impulse was visible in the fifth interspace 10 cm. to the left of the sternum. A slight precordial bulge was present. Rhythm was regular. The first sound

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Figure 1

May 26, 1950. Cardiotoracic ratio 0.57.

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From the Department of Medicine, Research and Educational Hospitals, University of Illinois, College of Medicine, Chicago, Illinois.


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was normal; the second sound was closely split and did not vary with respiration. An apical third sound was followed by a rumbling murmur. An ejection click, varying with respiration, was heard at the second left interspace. A grade-IV/VI pansystolic murmur was maximally heard in the fourth left interspace at the sternal edge. Otherwise the physical examination was not remarkable. Electrocardiogram showed normal P waves and P-R interval; QRS was 0.10 sec. and showed an indeterminate axis. An RsR' complex was present in V₃; R in V₅ measured 60 mm. and Q in V₆ was 5 mm. deep. The tracing was believed to afford evidence for left and right ventricular hypertrophy. Chest x-ray (fig. 2) revealed moderate right ventricular enlargement and considerable increase in pulmonary artery size. Since 10 years previously, cardiac transverse diameter and pulmonary vascular markings had returned somewhat toward normal. The diagnosis was made of large ventricular septal defect with considerable left-to-right shunt and pulmonary hypertension.

At a visit in 1960, he reported mild exertional dyspnea. Otherwise, except for the absence of a third heart sound, no change had taken place. In 1961 dyspnea, gradually increasing, troubled him after two flights of stairs. Cyanosis remained minimal; some qualified observers believed it to be absent.

In early 1963, orthopnea and paroxysmal nocturnal dyspnea appeared and he was placed on digitalis. Cyanosis, though mild, was definite. Despite therapy, shortness of breath increased.

Unable to walk more than a few steps without severe dyspnea, he was admitted to the hospital in August 1963. Obvious cyanosis was present. “a” and “v” waves of nearly equal magnitude reached a level about 11 cm. above heart level in jugular veins. The cardiac apex extended almost to the anterior axillary line in the sixth left interspace. A very loud third sound was heard over the entire precordium. The diastolic rumble had disappeared. The liver was felt 6 cm. below the costal margin. Otherwise physical findings were unchanged. X-ray (fig. 3) showed the heart to have enlarged since 1960. An electrocardiogram revealed that the QRS vector had shifted somewhat headward. S was greater than R in V₁, R in V₅ was 35 mm. tall and Q in V₆ was 2 mm. deep.

Treatment consisted of rest, diuretics, and phlebotomy, which reduced the hemocrit level from 63 to 50. He left the hospital somewhat improved but still dyspneic on walking at a moderate pace. The third heart sound persisted.

**Hemodynamic Findings**

Three cardiac catheterizations were performed. Methods and calculations were the
same as those outlined in a previous publication from this laboratory. This patient was no. 8 in that report, which showed that in 1961 he developed severe arterial oxygen unsaturation on exertion. All catheterizations were done in the supine position. He received 50 mg. of secobarbital before the second procedure, but otherwise local anesthesia was the only medication. An increase in oxygen content appeared at the right ventricular level in each instance.

Oxygen saturation values in the right ventricle and pulmonary artery differed little at each procedure. Of 25 blood samples taken from these two areas during the three catheterizations, all but one were at least 10 per cent less saturated than systemic arterial blood drawn during the same procedure. The following oxygen saturation percentage values, taken in a 14-minute period during the last catheterization, are typical: right ventricle tricuspid area 60.4, mid-right ventricle 62.0, outflow tract 68.0, 65.4, main pulmonary artery 66.1, 67.2, right pulmonary artery 65.3, 66.9. The consistency of these data was considered to provide definitive evidence for ventricular septal defect and effectively to rule out other entities such as single ventricle. Selective angiocardiography in the right ventricle was attempted, but useful results were not obtained, since the catheter slipped out of the ventricle at the onset of injection. Indocyanine-green dye injected at several locations showed a right-to-left shunt at the ventricular level.

Catheterization results are presented in table 1. The most arresting finding is the progressive fall in the "combined" cardiac output; i.e., the sum of the systemic and pulmonary blood flows. Summation of blood flows in this way is justified, since in patients with a large ventricular septal defect the two ventricles together eject blood which is apportioned between the systemic and pulmonary circulations in a ratio depending on the resistance in these circuits. In 1960 systemic blood flow and "combined" cardiac output were normal, but 40 months later both values had fallen to an extremely low level. The volume of the shunts across the defect in each direction fell slightly during this period.

Systemic and pulmonary arterial pressures remained quite steady. Therefore the calculated vascular resistance in each circuit rose inversely as the fall in blood flow. "Combined" vascular resistance climbed sharply to a level greater than twice normal. The ratio of systemic to pulmonary vascular resistance remained about the same, however.

Moderate arterial oxygen unsaturation was observed at the time of the first two catheterizations, but by the time of the third procedure it had become more intense. From data in table 1 one may calculate that, despite its smaller volume in 1963, the right-to-left shunt carried a larger quantity of reduced hemoglobin into the arterial circulation than in 1960 and 1961. This quantity mixed with a smaller amount of oxyhemoglobin returning from pulmonary veins than at the previous catheterizations, and as a result 21.8 per cent of the hemoglobin in arterial blood was reduced, a concentration larger than observed earlier. In making these calculations we have assumed 97 per cent oxygen saturation of pulmonary venous blood. Previous work from this laboratory supports the validity of this assumption even in the presence of severe pulmonary hypertension.

Inhalation of oxygen had only a moderate effect on arterial oxygen saturation; on the day after the third catheterization breathing 100 per cent oxygen raised it from 71 per cent to 81 per cent. The hematocrit value had increased considerably by the time of the last catheterization. Ventilation had also increased, but oxygen consumption was unchanged. Although pulmonary wedge pressure remained normal, right ventricular end-diastolic and right atrial pressures had risen to abnormal levels by the time of the third procedure.

Discussion

As a child this patient, like many with a large ventricular septal defect, experienced exertional dyspnea, and later enjoyed a remission of symptoms. During adolescence the improvement in exercise tolerance and reduction in heart size were probably related to falling pulmonary blood flow and rising pulmonary vascular resistance, a sequence of
Hemodynamic Observations

<table>
<thead>
<tr>
<th>Heart rate</th>
<th>Rt. atrium, mm. Hg</th>
<th>Pul. artery</th>
<th>PA “wedge”</th>
<th>Systemic artery</th>
<th>Flow, L/min./M.² BSA</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>S</td>
<td>D</td>
<td>Mean</td>
<td>S</td>
<td>D</td>
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<tr>
<td>April 27, 1960</td>
<td>73</td>
<td>2</td>
<td>115/67</td>
<td>78</td>
<td>124/77</td>
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<tr>
<td>April 25, 1961</td>
<td>80</td>
<td>5</td>
<td>112/69</td>
<td>85</td>
<td>6</td>
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<tr>
<td>August 27, 1963</td>
<td>100</td>
<td>8</td>
<td>92/69</td>
<td>78</td>
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* Indirect pressure recording, mean assumed.

S, systolic; D, diastolic; Q_s, systemic blood flow; Q_p, pulmonary blood flow; L-R, left-to-right shunt; R-L, right-to-left shunt; “Combined,” sum of pulmonary and systemic flows or resistances; S_a, arterial oxygen saturation; V_o₂, ml. oxygen consumed/min./M.² STPD; V_E, ventilation, liters/min./M.²; R_s/R_p, ratio of systemic to pulmonary vascular resistance.

In retrospect, surgical closure of the defect shortly after the first catheterization and before cardiac output had begun to decline might have been a wiser course, despite the presence at that time of high pulmonary vascular resistance.

Summary

A patient with large ventricular septal defect experienced cardiac failure in childhood but improved and participated vigorously in competitive athletics during adolescence. Subsequently exertional dyspnea gradually developed, followed by increasing cyanosis and cardiac failure.

Repeated cardiac catheterizations during the latter period showed that cardiac output into both the pulmonary and the systemic circuits gradually fell to very low levels while vascular resistance rose progressively. The ratios of flows, pressures, and resistances in the two circuits did not change. Left-to-right shunting always predominated. Right atrial pressure rose but pulmonary artery “wedge” pressure remained unaltered.

Progressive reduction in output from both sides of the heart explained the appearance of reduced arterial oxygen saturation, increased cyanosis, and the manifestations of cardiac failure.

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LARGE VENTRICULAR SEPTAL DEFECT

<table>
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<tr>
<th>Vascular resistance, dyne sec. cm.−2</th>
<th>O2 content, ml/100 ml blood</th>
<th>S(_{O_2}) per cent</th>
<th>V(_O_2)</th>
<th>V(_E)</th>
<th>BSA M(^2)</th>
<th>Hematocrit value</th>
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<td>1805</td>
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<td>9.82</td>
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</table>

**Acknowledgment**

The authors are grateful to A. F. Wilkerson, M.D., Marion, Alabama, for supplying details concerning the patient's illness in childhood.

**Addendum**

The patient experienced progressively severe dyspnea with increasing congestive failure and died suddenly on March 19, 1964. No autopsy was obtained.

**References**

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HARRY A. BLISS and JEAN E. MOFFAT

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