Patent Ductus Arteriosus in Association with Pulmonic Stenosis

A Report of Six Cases with Additional Noncardiac Congenital Anomalies

By Douglas C. Heiner, M.D., and Alexander S. Nadas, M.D.

A review was made of patients recently seen at the Children's Medical Center, Boston, who qualified for the diagnosis of patent ductus arteriosus associated with pulmonic stenosis. Six such patients were observed. The cardiac findings were distinctive, allowing for presumptive diagnosis without catheterization in the majority of instances. Noncardiac congenital anomalies of a particular type were found to be a part of the clinical profile. This finding plus certain epidemiologic evidence suggests the possibility of a common etiologic factor.

PATENT ductus arteriosus and pulmonic stenosis as individual lesions are among the commonest of congenital defects of the heart, each constituting 10 to 15 per cent of congenital cardiac anomalies. A combination of the 2 has been thought to be relatively uncommon. Eckstrom found that of 255 patients carefully evaluated following operative repair of a patent ductus arteriosus, 17, or 6 per cent of the total, were found to have a murmur with a cause demonstrable by right heart catheterization. Twelve (4.7 per cent) had a significant gradient between the right ventricle and the pulmonary artery, indicating the presence of pulmonic stenosis. Gross performed simultaneous pulmonary valvotomy on 3 of 525 patients operated upon for a patent ductus arteriosus. He likewise observed that about 6 per cent of his patients had a persistent organic murmur following surgery for patent ductus arteriosus.

The purpose of this paper is to report our findings in patients with patent ductus arteriosus and pulmonic stenosis, to point out how these findings differ from those in patients with either lesion alone, and to discuss the possible significance of certain associated noncardiac anomalies that have been observed.

MATERIAL AND METHODS

A review of recent experience (1945-1956) in this hospital revealed 6 patients with good evidence of a patent ductus arteriosus and associated pulmonic stenosis. All 6 have been operated upon for repair of the patent ductus and have had findings during operation and in the postoperative period indicating the presence of pulmonic stenosis. Four of these children were also subjected to cardiac catheterization preoperatively.

Careful histories, physical examinations, routine laboratory studies, chest x-rays, fluoroscopy, and electrocardiograms were done on all patients. The methods and instruments used at cardiac catheterization were described in previous reports from this department.

CASE HISTORIES

Case 1. R. V. This boy was born following an apparently normal full-term pregnancy with no known evidence of maternal trauma, rubella, or other infections. He was thought to be normal at birth but has always been underweight for his age. Speech and hearing difficulties were present from early life, and he has consistently been slow in school work.

A murmur was discovered at the age of 3 years when he was taken to a physician because of "fainting spells." The fainting spells have not recurred.

On hospitalization at the age of 9, physical examination revealed his height and weight each to be under the third percentile on our developmental charts. Head circumference was 18.3 inches. The second heart sound was diminished in the pulmonic area and was narrowly split. A grade IV continuous murmur was heard in the second left and right interspaces and a separate, rough stenotic grade V systolic murmur was heard along the left sternal border, transmitting well to the neck and upper back. Additional findings are outlined in tables 1-3 and a preoperative electrocardiogram is shown in figure 1.

A diagnosis of patent ductus arteriosus with pulmonic stenosis was made. At operation, the
PATENT DUCTUS ARTERIOSUS AND PULMONIC STENOSIS

Table 1.—Catheterization Data

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Pressure measurement (mm Hg)</th>
<th>Oxygen content (vol. %)</th>
<th>Cardiac index (L/min./M.2)</th>
<th>Resistance (dyne-sec.-cm.-2)</th>
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<tbody>
<tr>
<td></td>
<td>Pulmonary artery (pre-op)</td>
<td>Pulmonary artery (post-op)</td>
<td>Right ventricle (mean)</td>
<td>Right atrium (mean)</td>
</tr>
<tr>
<td>6</td>
<td>37/20</td>
<td>27</td>
<td>58/0</td>
<td>3 100/47</td>
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<tr>
<td>2</td>
<td>21/13</td>
<td>17</td>
<td>72/6</td>
<td>0 125/55</td>
</tr>
<tr>
<td>1</td>
<td>16/9</td>
<td>13</td>
<td>97/0</td>
<td>4 105/60</td>
</tr>
<tr>
<td>4</td>
<td>90/55</td>
<td>65</td>
<td>100/12</td>
<td>11 122/55</td>
</tr>
<tr>
<td>(pre-op)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>26/7</td>
<td>17</td>
<td>42/3</td>
<td>9 115/64</td>
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</table>

* NSR = No sample recorded.
† Patent ductus arteriosus divided.

Table 2.—Factors Possibly Related to Etiology

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<tr>
<th>Patient number</th>
<th>History of maternal rubella in early pregnancy</th>
<th>Birth date</th>
<th>Birth place</th>
<th>Mental retardation</th>
<th>Motor retardation</th>
<th>Microcephaly</th>
<th>Eye abnormalities</th>
<th>Hearing deficit</th>
<th>Birth weight (percentile)</th>
<th>Height preop. (percentile)</th>
<th>Weight preop. (percentile)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
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<td>History of maternal rubella in early pregnancy</td>
<td>Birth date</td>
<td>Birth place</td>
<td>Mental retardation</td>
<td>Motor retardation</td>
<td>Microcephaly</td>
<td>Eye abnormalities</td>
<td>Hearing deficit</td>
<td>Birth weight (percentile)</td>
<td>Height preop. (percentile)</td>
<td>Weight preop. (percentile)</td>
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<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
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<tr>
<td></td>
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<td>Dec. '51</td>
<td>Vt.</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>5'</td>
<td>&lt;3</td>
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<td></td>
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<tr>
<td></td>
<td>Oct. '42</td>
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<td>Mass.</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>5'</td>
<td>&lt;3</td>
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<tr>
<td></td>
<td>Jan. '44</td>
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<td>Me.</td>
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<td>X</td>
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<td>5'</td>
<td>&lt;3</td>
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<td></td>
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</table>

patent ductus arteriosus was divided and a pulmonar
valvotomy was performed. Evaluation in the
immediate postoperative period revealed absence
of the continuous murmur, a persistence of the
rough stenotic murmur, and no significant change
in the electrocardiogram.

Case 2. R. C. Maternal pregnancy and delivery
were thought to be normal. The patient was seen
at Children's Medical Center at 19 months of age
for evaluation of hearing difficulty. Audiometric
tests revealed an 85 to 100 decibel loss bilaterally.
Since then he has been followed in the congenital
heart clinic where he has been noted to have fre-
quent respiratory infections but to be active and
without other cardiac symptoms.

At 2 years of age his arm blood pressure was
125/55. His pulmonic second sound was well split
and of normal intensity. There was a grade V rough
stenotic systolic murmur heard best in the supra-
ternal notch and a grade IV continuous murmur in
the second left interspace. Further findings are out-
lined in tables 1–3. A preoperative electrocardiogram
is shown in figure 1.

The diagnosis of patent ductus arteriosus with
pulmonic stenosis was made. At surgery, a patent
ductus arteriosus was divided and pulmonary
valvotomy was performed. Preoperative and post-
operative chest roentgenograms are shown in figures
2 and 3.

At age 3½ years the patient was asymptomatic
except for hearing and speech difficulties. Blood
pressure was 110/70. A thrill was palpable in the
second left interspace and a grade III to IV rough
systolic murmur was heard in this area, transmitting
to the neck and upper back. Chest x-ray revealed a
reduction in the previous cardiac enlargement and
electrocardiogram showed a significant decrease in both right and left ventricular potentials. Preoperative and postoperative phonocardiograms are shown in figure 4.

Case 3. L. W. This girl’s mother had rubella during the third month of pregnancy. Gestation was otherwise uncomplicated and led to a normal delivery at full term. No immediate neonatal difficulties were noted. However, the patient gained weight slowly and had frequent respiratory infections associated with dyspnea. A single “fainting spell” occurred at 1 year of age. Strabismus has always been present. An ophthalmologic consultant described a form of tapeto-retinal degeneration. Psychologic evaluation revealed mild mental retardation. At 5 years of age a patent ductus was suspected because of a systolic murmur extending into diastole at the base of the heart, and a wide pulse pressure (115/0). There was also a marked suprasternal thrill and rough systolic murmur, transmitting well to the neck and back (tables 1–3).

At 6 ½ years the patent ductus was divided. At operation a residual thrill of moderate intensity was felt over the pulmonary artery but not over the aorta. Valvotomy was not performed.

Postoperatively there has been no excessive respiratory infections or dyspnea. Her height and weight curves show that she has progressed from far below the third percentile preoperatively in height and weight, to the fifth percentile for height and the fifteenth percentile for weight. Blood pressure is 115/65. Physical findings are those of a patient with mild to moderately severe pulmonic stenosis. Electrocardiographic changes are shown in

<table>
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<tr>
<th>Patient number</th>
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<td>History</td>
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<td></td>
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<td>Age murmur discovered</td>
<td>3 yr</td>
<td>7 wk</td>
<td>18 mo</td>
<td>Birth</td>
<td>2 wk</td>
<td>3 mo</td>
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<td>Frequent respiratory infections</td>
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<td></td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
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<td>Physical examination</td>
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<td>Impulse</td>
<td>R + L</td>
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<td>P₂ widely split</td>
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<tr>
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<td>Main pulmonary artery prominent</td>
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<td>Left atrium prominent</td>
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<td>Right ventricular hypertrophy preop.</td>
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<td>x</td>
<td>x</td>
<td>ND§</td>
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<td>x</td>
<td>x</td>
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<tr>
<td>Left ventricular hypertrophy preop.</td>
<td></td>
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<td></td>
<td>ND</td>
<td>x</td>
<td>ND</td>
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<tr>
<td>postop.</td>
<td>x</td>
<td></td>
<td>x</td>
<td>x</td>
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<tr>
<td>Incomplete right bundle-branch block preop.</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
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<td>postop.</td>
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<td></td>
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<tr>
<td>Axis, preop.</td>
<td>100°</td>
<td>115°</td>
<td>95°</td>
<td>0°</td>
<td>100°</td>
<td>IN</td>
</tr>
</tbody>
</table>

* Not recorded.
† 2nd left intercostal space.
‡ Suprasternal notch.
§ Not determined.
|| Indeterminate.
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Figure 1. Preoperative electrocardiograms showing right axis deviation and right ventricular hypertrophy in patients who had 81 and 51 mm Hg peak systolic pressure gradients, respectively, across the pulmonic valve.

Figure 2. Preoperative roentgenograms of patient no. 2 with patent ductus arteriosus and pulmonic stenosis. There is slight cardiomegaly but pulmonary vascularity appears within normal limits. Left, right anterior oblique; middle, posteroanterior; right, left anterior oblique.

Figure 5, revealing a progression from left ventricular hypertrophy preoperatively to right ventricular hypertrophy postoperatively.

Case 4. F. K. The first trimester of gestation was complicated by frequent episodes of vomiting but there was no history of German measles or other infections. Delivery was at term, resulting in an infant with bilateral congenital cataracts. Weight gain was always slow even though her appetite was adequate. She first sat at 18 months, began walking at 3 years. She has had frequent respiratory infections, easy fatigability, and dyspnea on moderate exertion.

Physical examination at 7 years of age revealed a
wandering nystagmus and bilateral aphakia, the result of operative removal of cataracts. A grade IV rough systolic murmur was heard along the left sternal border and transmitted well to the neck and upper back. A grade III middiastolic rumble was heard at the apex. Some observers, in addition, heard a continuous murmur in the pulmonic area. Additional findings are noted in tables 1–3.

At age 71\(\frac{1}{2}\) the ductus arteriosus was divided. Studies several years later showed her to be in the twentieth percentile for weight and the twenty-fifth percentile for height (preoperatively she was below the third percentile for both height and weight). There was a grade II rough systolic murmur in the pulmonic area. The second sound was rather widely split but of normal intensity. Electrocardiograms have shown a disappearance of left ventricular hypertrophy but a persistence of incomplete right bundle-branch block. Postoperative catheterization data are included in table 1.

Case 5. L. R. This girl's mother was known to have had German measles approximately 1 month after conception. Pregnancy was otherwise uneventful as was delivery at full term. Developmental retardation was evidenced by poor weight gain and slow linear growth, inability to sit unassisted until after 18 months of age, markedly delayed onset of walking, and marked slowness in school.

Preoperative physical examination revealed a grade III to IV murmur with systolic crescendo and diastolic decrescendo heard best in the pulmonic area, having a rough systolic element transmitting well to the upper back. Separate systolic and diastolic murmurs were heard at the apex (tables 1–3). Only standard limit leads were taken in preoperative electrocardiograms.

At 19 months of age the patent ductus arteriosus was divided and at operation it was noted that a systolic thrill persisted over the pulmonary artery. A valvotomy was not performed. Cardiac catheterization has not been obtained. Numerous postoperative examinations over a 10-year period have shown the existence of a rough systolic murmur in the pulmonic area well transmitted to the neck and back. Electrocardiogram 5 years postoperatively showed an axis of +115\(^\circ\) with definite right ventricular hypertrophy.

Case 6. V. T. This girl's mother had a febrile illness without rash when 2 months pregnant, at a time when a son in the family and others in the community had typical German measles. The prenatal course and delivery were otherwise normal. Congenital cataracts were noted at birth and were surgically removed at 18 months. The patient did not walk until 2 years of age. There have been frequent respiratory infections all her life including pneumonia 3 times during her second year. Exercise tolerance has been normal.

Physical examination showed her to be underdeveloped and undernourished. There was bilateral aphakia and lateral nystagmus. A grade IV rough systolic murmur was heard maximally in the pulmonary area and suprasternal notch and was well transmitted to the neck and upper back. A grade III continuous high frequency murmur was present under the left clavicle and a grade III middiastolic rumble was heard at the apex (tables 1–3).
C**L**INICAL **F**EATURES

A history of rubella in early pregnancy was present in 2 of the 6 mothers and possibly in a third. Each patient was born in New England, the birth dates lying between October 29 and March 21. Four of the 6 patients weighed 5½ lb. or less at birth, and the largest was 68 1/8 lb., although none was considered premature by expected date of confinement calculations. All continued to be below average in growth, 5 being under the third percentile for both height and weight at the time of operation. A growth spurt was noted in 2 postoperatively (patients 3 and 4). A heart murmur was heard within the first 3 months of life in 4 patients. Two had some dyspnea on exertion preoperatively, but 4 had no limitation of activity at any time. Four had frequent respiratory infections and 2 had a history of syncope in early life. None had a history of cyanosis or congestive failure. Associated congenital anomalies were present in each patient and are included in table 2.

Pulse pressures were in excess of 40 mm. Hg in all patients. The cardiac impulse, recorded preoperatively in 5 patients, was described to be maximal near the xiphoid in 1 patient and prominent at both the xiphoid and the apex in the other 4. The first heart sound was not recorded as being abnormal in any patient. The second sound had variable characteristics, in some instances being diminished in intensity in the pulmonic area without audible splitting. A continuous machinery-like murmur was heard in all patients but in some instances was rather difficult to make out because of the superimposed murmur of pulmonic stenosis. This latter rough, stenotic murmur was recognized in the second left interspace and had good transmission to the suprasternal notch, neck, and upper back in 5 patients preoperatively, and in all patients postoperatively. A suprasternal thrill was palpable more frequently than is our experience in patients with isolated patent ductus arteriosus. A diastolic murmur was not heard postoperatively in any patient. Typical preoperative and postoperative phonocardiograms are presented in figure 4.

Preoperative electrocardiograms included chest leads in 5 of the patients and revealed evidence of isolated right ventricular hypertrophy in 2 (fig. 1), combined right and left hypertrophy in 2, and left ventricular hypertrophy associated with incomplete right bundle-branch block in a fifth patient (fig. 5).
Postoperative electrocardiograms in 5 patients showed right axis deviation and isolated right ventricular hypertrophy in 4; the fifth patient showed incomplete right bundle-branch block with disappearance of the left ventricular hypertrophy, which was present in the preoperative tracing (fig. 5).

**Cardiac Catheterization**

Catheterization revealed definite evidence of pulmonic stenosis on withdrawal from the pulmonary artery in each of the 4 patients so examined (table 1). Peak systolic pressure gradients between the right ventricle and the pulmonary artery varied from 10 to 81 mm. Hg. A jump of more than 1.0 volume per cent in O₂ content at the pulmonary artery level compared with the right ventricle was found in each instance.

**Operative Findings**

The patent ductus was divided in all 6 patients and a residual thrill was felt over the root of the pulmonary artery in each of 4 instances in which palpation of this area was recorded. Valvotomy was performed in 2 instances. No evidence of cardiovascular anomalies other than patent ductus arteriosus and pulmonic stenosis was found in any instance.

**Discussion**

**Etiology.** There is evidence²-⁹ that a number of maternal diseases or stresses during pregnancy may lead to congenital defects in the offspring. One of these, rubella or German measles, requires special discussion in view of the clinical features found in our patients.

Gregg¹⁰ first called attention to the importance of rubella during pregnancy when he reported in 1942 congenital cataracts in 78 children born to mothers who had rubella during early gestation. Forty-four of these children also were said to have had congenital heart disease. The cardiac lesion proved to be a patent ductus arteriosus in most instances where a definite diagnosis was made. Murphy¹¹ in 1947 collected 295 instances of rubella in pregnancy being followed by a defective offspring. Cataracts were found in 161 patients, congenital heart disease in 117, and deaf-mutism in 88. Campbell¹² in 1949 reported 259 patients with cyanotic congenital heart disease, stating that 3 resulted from pregnancies known to be complicated by maternal rubella; all 3 had pulmonic stenosis and a ventricular septal defect. One of the 3 had congenital cataracts. Rutstein et al.¹³ reported 27 patients with congenital heart disease whose mothers had rubella during pregnancy. A definite cardiac diagnosis was made in 18 of these patients, all of whom had a patent ductus arteriosus. (Subsequently it has been shown that at least 2 of these children had the combination of patent ductus arteriosus and pulmonic stenosis.) These authors emphasized the important point that in Massachusetts most rubella infections occur during the spring months and the majority of resultant defective children are born between October and March. This distribution of birthdays contrasts with that of patients with patent ductus arteriosus without a history of maternal rubella during pregnancy.¹³

Studies by a few authors¹⁴-¹⁷ have reported percentages of children who may be expected to be defective if born of mothers having known rubella in pregnancy. Ingalls¹⁸ has recently summarized these and other data and concluded that nearly 15 per cent of such infants will have congenital anomalies. Among these, patent ductus arteriosus is the most common cardiac lesion to be recognized.

Anderson¹⁹ found that noncardiac defects occurred in about half of his patients with patent ductus arteriosus and additional cardiac anomalies. Conversely, noncardiac congenital defects were found in only 14 per cent of patients with isolated patent ductus arteriosus. MacMahon and his co-workers²⁰ reported noncardiac defects in 10 per cent of all patients with patent ductus arteriosus.

Pulmonary stenosis is commonly associated with other cardiac anomalies, particularly ventricular septal defects. No references could be found in the literature citing the occurrence of noncardiac defects in patients with pulmonic stenosis. It is our impression, however, that noncardiac defects of the type reported in the present publication are quite rare in patients.
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with pulmonic stenosis, with or without associated cardiac lesions other than patent ductus arteriosus.

Thus, the fact that all 6 of the patients in whom we have proved the diagnosis of patent ductus arteriosus and pulmonic stenosis have had additional noncardiac defects of a particular type is interesting and suggests the possibility of a common etiologic factor in these patients. It should be emphasized that there is direct proof in only 2 instances (patients 3 and 5), and suggestive evidence in a third (patient 6), that the mothers of these patients had rubella during pregnancy. It is possible that other viral agents or noninfectious insults may have been etiologic factors in the remaining cases. Circumstantial evidence, however, may be in favor of rubella, particularly the fact that each patient's birthdate falls between October and March. Further support for such a hypothesis may come from the observation that a certain number of patients with congenital cataracts do not have a history of maternal rubella during pregnancy yet have birthdates clustered in the same period of time as similarly afflicted patients whose mothers did have rubella during pregnancy in an epidemiologic season.21 Krugman et al.22 and Anderson23 have made observations dealing with the probability of rubella infections without a rash.

It is of interest that embryologically the ductus arteriosus and the pulmonary artery are each derived from the artery of the sixth branchial arch. Thus, it is not difficult to imagine that an insult during the differentiation of these structures might result in both an abnormal persistence of the patent ductus arteriosus and an abnormal evolution of the root of the pulmonary artery.

Clinical Cardiac Findings. The combination of patent ductus arteriosus and pulmonic stenosis results in cardiac findings that should allow accurate preoperative diagnosis in the majority of instances. Some features of each anomaly are present, the most prominent findings depending on the relative severity of each lesion. The machinery murmur is attributable to the patent ductus arteriosus as is an accentuated pulmonic component of the second heart sound, pulmonary vasculature engorgement, evidence of left ventricular or left atrial hypertrophy, and frequent respiratory infections. Similarly, the presence of a rough stenotic systolic murmur and thrill in the second left interspace and suprasternal notched with maximal intensity during early or mid-systole reflects the presence of pulmonic stenosis, especially if combined with a pulmonary closure of diminished intensity, a xiphoid cardiac impulse, and radiologic or electrocardiographic evidence of right ventricular hypertrophy.

A few patients have been observed in our clinic who presented a history of maternal rubella during pregnancy, whose birthdates have fallen between October and March, and who have had noncardiac anomalies similar to those described herein yet have been shown to have patent ductus arteriosus in association with pulmonary vascular obstruction without pulmonic stenosis. One similar patient had a patent ductus arteriosus with a stenotic murmur in the second right interspace and no gradient across the pulmonic valve at catheterization. She was presumed to have aortic stenosis; operation was not performed. In some instances these patients may be clinical diagnostic problems requiring catheterization to enable differentiation from patent ductus arteriosus and pulmonic stenosis. Careful physical examinations, however, reveal that pulmonary hypertension may usually be recognized by a markedly accentuated pulmonic second sound. The continuous murmur is absent if pulmonary vascular obstruction is severe. The presence of a stenotic murmur heard best to the right of the sternal angle under the right clavicle leads to a suspicion of aortic stenosis.

Pathologic Physiology. For practical purposes the 2 anomalies discussed may be considered independent burdens on the 2 sides of the heart. The presence of a patent ductus arteriosus increases the volume work of the left ventricle and the left atrium without causing significant changes in intracardiac pressures. Pulmonary stenosis, on the other hand, increases systolic ejection pressure of the right ventricle without affecting the volume of blood passing through
unless there is severe stenosis and right ventricular failure.

Certainly the 2 lesions will not compensate for each other. In pulmonic stenosis without a right-to-left shunt, a patent ductus would merely recirculate fully oxygenated blood through the lungs and cause increased left ventricular work without alleviating right ventricular obstruction, improving cardiac output, or promoting peripheral oxygen transport. Therefore, in the patients described, there existed the usual indications for division of the patent ductus arteriosus plus the additional possibility of somewhat decreasing the work of the hypertensive right ventricle by decreasing pulmonary artery pressure.

Treatment. The need for surgical correction of each defect should be considered on the basis of the severity of the lesion and the operative risk.

Division of the patent ductus arteriosus—a safe surgical procedure—is recommended in all instances where a sizable left-to-right shunt is present.

If the existence of a significant degree of pulmonary stenosis is suggested by the clinical and electrocardiographic findings, cardiac catheterization should be performed preoperatively to determine more exactly the degree of obstruction caused by the stenotic lesion. If the gradient across the valve is great in relation to flow, or if right ventricular pressure exceeds 100 mm. Hg at rest, the patient should be considered a candidate for repair of both the patent ductus and the pulmonic stenosis. Frequently the risk of a combined operation on the 2 lesions may be less than that of 2 separate surgical interventions. Allowance should be made, however, for the possibility of lowering pulmonary arterial and even right ventricular pressures merely by ligating the ductus. It should be pointed out, also, that catheterization data do not provide the only basis for deciding upon valvotomy. Other factors are heart size (especially cardiomegaly not attributable to flow through the patent ductus), severity of right ventricular hypertrophy as indicated by the electrocardiogram, clinical evidences of right ventricular failure, and the presence of symptoms.

Summary

Six patients with the combination of patent ductus arteriosus and pulmonic stenosis are presented. All of these children have been found, in addition, to have several noncardiac anomalies, including mental retardation, microcephaly, congenital cataracts, nystagmus, retinal degeneration, strabismus, and deaf-mutism. The identity of these anomalies with those seen in offspring after pregnancies complicated by rubella is suggestive of a common etiologic factor. The gestation of at least 2 of these patients was complicated by known rubella.

The coexistence of patent ductus arteriosus and pulmonic stenosis is usually recognizable clinically without angiocardiograms or cardiac catheterization. This combination of defects should be considered in patients with the diagnosis of either patent ductus arteriosus or pulmonic stenosis resulting from a pregnancy complicated by rubella, or in the presence of noncardiac defects of the type described. The clinical profile also includes delivery at full term with less than usual birth weight, a murmur audible in early infancy, and slow weight gain and linear growth. Cardiac examination usually reveals a wide pulse pressure, a continuous murmur in the second left interspace, and a separate rough systolic murmur and thrill maximal in the pulmonic area and supra-sternal notch, with good transmission to the neck and back. Electrocardiograms show right ventricular hypertrophy or incomplete right bundle-branch block, sometimes in combination with left ventricular hypertrophy. Radiologic examination shows moderate cardiomegaly involving both ventricles and usually the left atrium, with engorged pulmonary vasculature.

Division of the patent ductus is recommended in each instance. Patients with evidence of a significantly increased right ventricular work load should have preoperative cardiac catheterization to determine the need for simultaneous valvotomy.

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**Summario in Interlingua**

Es presentate 6 patientes pediatric con le combination de patente ducto arterioso e stenosis pulmonic. In omnes esseva trovate in plus un o plur anormalitates noncardiac, incluse retardation mental, microcephalia, cataractas congenite, nystagmo, degeneration retinal, strabismo, e surdemutismo. Le identitate de iste anormalitates con le anormalitates vidite in prole post partus complicat per rubella suggere le presentia del mesmo factor etiologic in le duo situationes. Le gestation de al minus 2 del presente patientes esseva complicate cognoscentemente per un episodio de rubella.

Le coexistenza de patente ducto arterioso e stenosis pulmonic esseva usualmente recognozibile per medios clinico sin recurso a angiocardiogrammas o catheterisation cardica. Iste combination de defectos debe esser suscitate in patientes con le diagnose de o patente ducto arterioso o stenosis pulmonic como resultato de pregnanti complicate per rubella o in le presentia de defectos noncardiac del typo describite. Le profilio clinic include etiam partitturn to termino con peso natal infra le norma, un murmure audibile in le prime infanti, e lente augmentos de peso e de statura linear. Le examine cardica revela usualmente un large pression de pulso, un murmure continue in le secunde interspazio sinistre, e un separate e aspere murmure e fremito sytolic que atteige su maxim in le area pulmonic e del incisura suprasterernal con bon transmission verso le nucha e le dorso. Electrocardiogrammas revela hypertrophia dexteroven-tricular o incomplete bloco de branca dextere, a vices in combination con hypertrophia sinistro-ventricular. Le examine radiologic monstra moderate grados de cardiomegalia in ambe ventriculis e usualmente le atrio sinistre, con constipation del vasculatura pulmonar.

Le division del patente ducto arterioso es recommendate in omne tal casos. Patientes con manifestationes de un augmento significative del labor dexteroven-tricular debe esser subiecte a catheterisation cardica pro determinar le necessitate del simultanea execution de valvotomy.

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It is postulated that hypertension in both sexes is one of several factors involved in atherogenesis, atherosclerosis, and the causation of coronary occlusion and myocardial infarction. Other factors in these processes presumably are diabetes mellitus, certain disturbances in lipid metabolism, and the sex hormones. Until the menopause, women enjoy a fair degree of protection from atherosclerosis and from the accelerating effects of hypertension on atherogenesis. After menopause the number of coronary occlusions associated with, and presumably causally related to, hypertension approaches and eventually equals the number observed in men of similar age. Therefore, the hypertensive factor is presumed to be of equal absolute importance in both sexes. Because other factors operate additionally in the male to accelerate atherogenesis and to cause coronary occlusions, hypertension is of relatively less importance in the male. The positive correlation between hypertension and the incidence of coronary occlusion should be considered, among other factors, in deciding whether a patient with hypertension should receive hypotensive therapy.
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