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The Diagnosis of Patent Ductus Arteriosus in Infancy*

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In older children and young adults, the presence of a persistently patent ductus arteriosus presents a clinical picture so regular in appearance that the diagnosis may be made on clinical grounds in an estimated 80-95 per cent of the patients.1,3 Furthermore, the patients are usually asymptomatic or so mildly symptomatic, that the timing of surgery is largely a matter of reconciling the conveniences of the parents and the opinions of the surgeon. Special diagnostic procedures, such as cardiac catheterization, need rarely be done, except for suspected pulmonary hypertension.

The picture in infants is in sharp contrast.4,6 Generally, these infants are referred for initial care because of pneumonia, symptoms of congestive heart failure or failure to thrive. Death has all too often occurred prior to contemplated diagnostic or surgical procedures. The murmurs heard in this group vary both in timing and in location, frequently resembling those of ventricular septal defects. Since closure of a patent ductus is feasible at virtually any age while definitive intracardiac surgery is usually delayed to the age of three, the problem then is the proper selection of infants for special diagnostic procedures.

This publication deals with diagnostic problems involved in a group of patients with patent ductus arteriosus who had surgical closure of the ductus prior to the age of one year. The relative importance of clinical, electrocardiographic, and radiologic examinations will be described. In-

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Infants with Isolated Patent Ductus Arteriosus Age and Sex Distribution

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Figure 1: Distribution of infants with isolated patent ductus arteriosus according to sex and age at the time of surgery.
dications for early surgical intervention and the surgical results will be discussed in a later paper.

Methods and Materials

All hospital charts coded as patent ductus arteriosus at the University of Minnesota Hospitals during the years 1939-1960, were reviewed. Cases were retained for study only if the diagnosis of patent ductus arteriosus had been confirmed by surgery, prior to one year of age and where the patent ductus was the sole lesion or where the secondary lesions were judged to be of little hemodynamic significance, e.g. left superior vena cava. The age and sex distribution of these cases is shown in Fig. 1.

In addition to a review of the patients' hospital charts, the electrocardiograms and x-rays films, both the plain films and those where contrast media were utilized, were re-examined. Radiographic views of the heart, taken in the four standard positions, were available for review in 38 of the 39 patients. All three venous angiograms and 18 of the 19 retrograde aortograms were also reviewed by the authors.

Cardiac catheterizations were performed in nine patients prior to ligation of the ductus. In no case was general anesthesia used, and the majority of cases, especially in recent years, had no premedication other than penicillin.

Results

Antecedents: Among the 39 patients with isolated patent ductus arteriosus, there were seven definite cases (18 per cent) where the mother contracted rubella during her first trimester of pregnancy. In contrast, among 309 patients in whom the ductus was ligated between one and 16 years of age, there were only seven cases of definite maternal rubella (2.3 per cent).

Sixteen of the patients (41 per cent) were premature by birth weight (2500 gm. or less). Again, this is in contrast to only 33 premature births (11 per cent) in the group of 309 patients previously reported. Four of the patients were one of a pair of twins.

In a study of older patients with patent ductus', a second case of congenital heart disease occurring in a sibling or parent was present in 4 per cent. Among the infants of the current study, there was one premature sibling twin who died at 36 hours and was found to have a patent ductus at necropsy. This somewhat tenuous case was the only close family history elicited.

Symptoms

As would be expected, patients selected for surgery during the first year were nearly universally symptomatic (Table 1). Rapid respirations, feeding difficulty, fatigue, and slow motor development were common symptoms. In 15 (38 per cent) evi-

<table>
<thead>
<tr>
<th>Table 1—Symptoms</th>
<th>Under one year Per cent</th>
<th>Over one year Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>38</td>
<td>3</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>51</td>
<td>27</td>
</tr>
<tr>
<td>Growth failure (less than 3rd percentile)</td>
<td>89</td>
<td>22</td>
</tr>
<tr>
<td>History of rheumatic fever</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Subacute bacterial endocarditis</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

dence of congestive heart failure was sufficient to warrant digitalization.

Growth failure, especially with respect to weight gain, was a common symptom. Thirty-five (89 per cent) of the infants had a preoperative weight less than the third percentile for age, and two additional patients equaled the third percentile.

All but one of the patients presented with one or more of the above complaints. This girl was first seen at the age of six weeks for evaluation of a systolic heart murmur. By the age of eight months, the murmur had become classic for a patent ductus and she was operated on at nine months of age in an attempt to improve a worsening growth curve, although her preoperative weight was still at the tenth percentile for age. Among the infants in the present series, ten were noted to have a classic, machinery-like murmur, although
in a few instances this was maximal in intensity at the third or fourth interspaces near the left sternal border. Twelve additional infants were described as having a harsh, loud systolic murmur with a short early diastolic murmur, but in three of these, the diastolic component was considered equivocal. In four cases, the murmur was described as systolic in timing and maximal over the pulmonary area and in 13 cases as systolic in timing and maximal in other areas. Figure 2 illustrates the type of murmur heard, showing little correlation with the age of the patient.

Nearly two-thirds of the infants were noted to have thrills. Unfortunately, for diagnostic purposes, these were usually most readily palpable in the fourth left interspace. Of the 14 with a description of timing, only two were present in both systole and diastole. There was only one instance recorded of a thrill palpated in the suprasternal notch.

Auscultatory blood pressures were determined in 21 of the patients. None of the auscultatory pulse pressures was less than 40 mm. Hg while four were greater than 90 mm. Hg. This widened pulse pressure was present as early as one month of age.

Electrocardiograms: A total of 40 pre-operative electrocardiograms from 37 patients with isolated patent ductus were available for analysis. Table 2 offers a comparison of electrocardiographic findings in infants and older children while Table 3 compares the infants with isolated patent ductus arteriosus with 21 infants with proved isolated ventricular septal defects. Thirteen of these electrocardiograms exhibited a prolonged PR interval when judged by rate and age, but only four of these were abnormally prolonged in relation to age alone. There were eight instances where the P waves suggested left atrial enlargement.

In two electrocardiograms, the QRS interval was at the upper limits of normal. One of these patients had, in addition, the pre-excitation (Wolff - Parkinson - White).

### Table 2—Electrocardiographic Findings in Isolated Patent Ductus Arteriosus

<table>
<thead>
<tr>
<th></th>
<th>Under one year</th>
<th>Over one year</th>
</tr>
</thead>
<tbody>
<tr>
<td>QRS axis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>normal</td>
<td>85%</td>
<td>96%</td>
</tr>
<tr>
<td>LAD</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>RAD</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Minimal RAD (0-5°)</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Ventricular Hypertrophy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>22%</td>
<td>62%</td>
</tr>
<tr>
<td>LVH</td>
<td>17</td>
<td>28</td>
</tr>
<tr>
<td>RVH</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>CVH</td>
<td>54</td>
<td>8</td>
</tr>
<tr>
<td>WPW</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Concave RS-T segment</td>
<td>33%</td>
<td>63%</td>
</tr>
<tr>
<td>Deep Q in V6</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>Large isodiphasic precordial QRS</td>
<td>54</td>
<td>6</td>
</tr>
<tr>
<td>Inc. RBBB</td>
<td>10</td>
<td>4</td>
</tr>
</tbody>
</table>

### Table 3—Comparison of Electrocardiographic Findings in Infants with Isolated Patent Ductus Arteriosus and Isolated Ventricular Septal Defect

<table>
<thead>
<tr>
<th></th>
<th>PDA</th>
<th>VSD*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged PR (for age and rate)</td>
<td>33%</td>
<td>57%</td>
</tr>
<tr>
<td>Ventricular hypertrophy none</td>
<td>23</td>
<td>14</td>
</tr>
<tr>
<td>LVH</td>
<td>18</td>
<td>10</td>
</tr>
<tr>
<td>RVH</td>
<td>5</td>
<td>19</td>
</tr>
<tr>
<td>CVH</td>
<td>54</td>
<td>56</td>
</tr>
<tr>
<td>WPW</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Deep Q in V6</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Tall T in V6</td>
<td>5</td>
<td>29</td>
</tr>
<tr>
<td>Large isodiphasic precordial</td>
<td>51</td>
<td>57</td>
</tr>
<tr>
<td>Inc. RBBB</td>
<td>10</td>
<td>43</td>
</tr>
</tbody>
</table>

syndrome. The QRS intervals in the remaining electrocardiograms were within normal limits.

Ten of these infants had electrocardiograms that were probably normal. There were seven electrocardiograms compatible with a diagnosis of left ventricular hypertrophy and 21 with combined ventricular hypertrophy. Right ventricular hypertrophy was seen in only two infants, aged four weeks and ten weeks. Interestingly enough, a lung biopsy taken in the first case was within normal limits and the pulmonary artery pressure in the second case was only 42/25 with a mean of 30 mm. Hg. This may suggest that the usual criteria for diagnosis of right ventricular hypertrophy in adults and older children are not applicable to infants.

Correlation of the ratio of the length of the R wave to the combined length of the R and S waves in precordial leads V1 and V6 are shown against age in Figs. 3 and 4. Similar data for 20 infants with proved isolated ventricular septal defects are shown in the same figures. There is a tendency for those with patent ductus arteriosus to have a lower R/RS ratio in V1 (presumably due to less right ventricular hypertrophy) than the infants with isolated ventricular septal defects. Thus only two of the ventricular septal defects lie between the lower limit and mean normal lines, while 18 of the patent ductus arteriosus are in this range. There is, however, so much overlap for this ratio in both lead V1 and V6, that this is of no diagnostic value.

A concept of overloading patterns has been developed by Sodi-Pallares and associates. For purposes of comparison, we have used the criteria of a prior report from this institution on isolated ventricular septal defects.

Right ventricular diastolic overloading patterns were more common among patients with ventricular septal defects, being found in 43 per cent of the infants with ventricular septal defects and only 10 per cent of the infants with patent ductus arteriosus, but otherwise no consistent pattern is revealed. Contrary to the experience of Sodi-Pallares and associates, there was no correlation of pulmonary artery pressure and overloading patterns.

One of the features included in the descriptions of left ventricular diastolic overloading is the presence of a deep Q wave in lead V6. Four of the patients with patent ductus and two of those with ventricular septal defects had Q waves greater than the 95th percentile for age, or nearly identical percentages of each group. Diphasic high voltage precordial QRS complexes over 70 mv. (so-called Katz-Wachtel sign) were seen in 51 per cent of the infants with patent ductus arteriosus and 57 per cent of the infants with ventricular septal defect.
Thus, neither of these signs is of diagnostic value.

An upward concavity in the R-ST segment (Fig. 5) has been described previously as an additional sign of left ventricular diastolic overloading, particularly in association with patent ductus arteriosus. Among infants through six months of age, this was seen in 21 per cent of the electrocardiograms, in 47 per cent of the infants from seven months to a year, and in 63 per cent of the children over one year. A sampling of electrocardiographic tracings of other forms of congenital heart disease showed this sign in only 2 per cent of the cases.

Conventional Roentgenologic Findings: Infants with patent ductus arteriosus and significant left-to-right shunt share the findings seen with other left-to-right shunt lesions. (Figs. 6 and 7). The pulmonary arterial vasculature is increased. The pulmonary artery segment is visibly enlarged in almost all cases except those in which it is obscured by overlying thymus. In this series, all of the children had increased peripheral vessels. Of the 27 in whom the pulmonary artery segment area could be seen, 20 showed some enlargement of this vessel. (Table 4).

All except two of the infants had some degree of cardiomegaly, and half had marked cardiomegaly. It is interesting to note that the films were felt to show right ventricular enlargement in most cases and left ventricular enlargement only in one. This may reflect in part the results of the relative pulmonary hypertension known to exist in the smaller infants. However, this is probably largely a function of the difficulty of interpreting ventricular chamber enlargement in infants roentgenographically.

The left atrium was enlarged in 31 of the 32 patients in whom adequate films had been obtained. This is a striking finding of some significance in differential diagnosis (Fig. 8). Children with the foramen ovale type of atrial septal defect rarely show enlargement of this chamber. However, children with significant ventricular septal or atriocentricus communis defects also show left atrial enlargement.

Older children with patent ductus arteriosus often show a large, hyperpulsatile aorta. This finding, in association with the findings characteristic of left-to-right shunt, is considered diagnostic of an extra-cardiac shunt. In this series of infants, however, the aorta could not be visualized satisfactorily in 28 of 37 cases. This is due to the overlying thymic tissue which obscures the shadow of aorta. Of only nine patients in whom the aorta could be identified, five showed what was interpreted as slight en-
FIGURE 6: Posteroanterior, lateral, and right anterior oblique x-ray films of a 10-month-old female. Note especially the marked peripheral vascular engorgement and cardiomegaly. The predominant chambers involved in the cardiomegaly are the left atrium and right ventricle. These findings are emphasized when the x-ray films are compared to the followup film taken 11 months postoperative (d).

FIGURE 7: Posteroanterior and lateral x-ray views of a four week-old premature infant with congestive heart failure and pneumonia which persisted in spite of vigorous medical treatment. In spite of her early age and a weight of only 1760 gm. she was operated upon. Following a rather stormy postoperative course, she was discharged and appeared to have made an excellent recovery. At the age of seven months, she died at home following a brief febrile illness. Necropsy (done elsewhere) revealed bilateral pneumonia and a normal cardiovascular system. These x-rays films reveal a marked peripheral vascular engorgement, moderate cardiomegaly and slight left atrial enlargement.
Valuable information concerning the general type of lesions (left-to-right shunt) and the size and physiologic status of the heart may be obtained from conventional roentgenographic study. However, a definitive diagnosis cannot be made from the roentgenograms alone.

Retrograde Aortography: Thoracic aortography provides the most precise and definitive anatomic diagnostic method in patent ductus arteriosus. With a technically satisfactory examination, the ductus may be visualized and its length and caliber defined.

The diagnosis is simply and clearly definable on inspection of the films. Following opacification of the descending portion of the arch of the aorta, the ductus and pulmonary vessels are sequentially filled. (Fig. 9) Lesions important in the differential diagnosis, such as aortico-pulmonary window, truncus arteriosus, coronary artery fistula into the pulmonary artery, or sinus of Valsalva fistula, may be differentiated if the entire thoracic aorta is opacified.
In older children and adults, a selective injection through a catheter inserted into the ascending aorta is essential. Even in small infants, the counter-pressure method may result in failure to fill the entire thoracic aorta and consequent inability to exclude such lesions as aortico-pulmonary window. Consequently, injection through a catheter would appear to be desirable whenever feasible.

Examination is most revealing when performed in two planes (frontal and lateral) and films should be made at a rate of at least five per second. A rapid sequence is essential due to the fleeting appearance of the findings to be recorded. Although much more rapid film sequencing can be obtained utilizing cine apparatus, we have preferred a rapid film changer because of the larger area that can be covered by the latter and also because of the superior definition of the films.

**Discussion**

Ziegler has generally been credited with first emphasizing both the importance of patent ductus arteriosus and the feasibility of surgery in infancy. Several reports have since confirmed that surgical mortality and morbidity in this age group is no greater than for older age groupings, and that the response to surgery of even the sickest of these infants is generally dramatic.

Differentiation by clinical means of patent ductus arteriosus from other cardiac anomalies causing left-to-right shunts is especially difficult at this age. Murmurs generally considered characteristic, if not pathognomonic, of patent ductus in older patients were present in only ten of the 39 infants. Definite early diastolic murmurs in the pulmonary area were present in only an additional eight patients. In one-third of the cases, a systolic murmur of maximal intensity at the lower left sternal border and a thrill in the same area mimicked the findings of a ventricular septal defect.

In those infants where they could be obtained, auscultatory blood pressures were the next most valuable physical finding. Widened pulse pressures were noted in virtually all of the infants, including nine who did not have murmurs suggestive of patent ductus.

The conventional roentgenologic findings were generally non-specific suggesting the presence of a left-to-right shunt and cardiomegaly. Enlargement of the aortic shadow, of frequent help in eliminating intracardiac shunts in older children and adults, was generally obscured by thymic tissue at this age group. In only five instances was there sufficient enlargement of the aorta to suggest the presence of patent ductus.

The electrocardiogram was of little value except possibly for an upward concavity of the RS-T segment; this was virtually confined to patients with patent ductus arteriosus in our series and was found in 12 of the infants.

It is difficult to know how strongly to weigh a history of prematurity or maternal rubella during the first trimester, but our clinical leaning has often been toward a strong suspicion of patent ductus arteriosus in such cases.

The presence of patent ductus was suggested either by the classic murmur, a systolic and an early diastolic murmur, or a widened pulse pressure (over 50 mm. Hg), in 25 of these 39 infants. An enlarged aortic shadow on roentgenologic examination was found in an additional three infants and an upward concavity of the RS-T segment in the electrocardiograms of an additional five infants. In six of the infants, none of the above was present.

At this institution, we have come to favor the thoracic aortogram for diagnosis of the infant patent ductus arteriosus, while other centers favor cardiac catheterizations.

The diagnostic accuracy of these methods has been comparable, being 83 per cent for catheterization and 86 per cent for retrograde aortograms in this institution. In the presence of additional cardiac anomalies, particularly ventricular septal defect or atrioventricular communis, there have been occasions when the catheterization
data have been rather confusing. Another source of possible confusion is the combination of patent ductus arteriosus and pulmonary insufficiency, leading to arterIALIZATION at the ventricular level and generally a false localization of the level of the shunt. Pulmonary hypertension, either transient or sustained, may reduce the flow through the ductus and vitiate the usual jump in oxygen saturation as a diagnostic clue. The passage of a catheter through the ductus then offers the only means of detection. This was accomplished in four of the nine catheterizations in infants in our series. In another center, where catheterization is favored the catheter was passed through the ductus in 19 of 23 infants with patent ductus. It must be recognized that only cardiac catheterization can offer physiologic data that may be of interest, such as the pulmonary artery pressure and pulmonary flow.

Thoracic aortography offers the opportunity for a precise anatomic diagnosis and often the length and diameter of the ductus is defined. Since a systemic artery must be exposed, it is a simple procedure to examine a sample of blood for the presence of arterial desaturation and to measure the intraarterial blood pressure. We have found that aortography is less technologically demanding and less time consuming than cardiac catheterization. Perhaps in the final analysis, the method of choice depends more on the facilities available, and the interests and inclinations of the cardiologists rather than on objective criteria.

Summary

Thirty-nine infants with surgically proved patent ductus arteriosus were analyzed for clinical clues of diagnostic importance. The occurrence of rubella during pregnancy, a widened pulse pressure or a murmur heard during systole and diastole in the pulmonary area should alert the examiner to the possibility of patent ductus. In addition to those findings related to the presence of a left-to-right shunt, conventional x-rays films revealed left atrial enlargement in 31 and aortic knob enlargement in five instances. Comparison of the electrocardiograms with infants with VSD revealed no clues of differential diagnostic value, except possibly for presence of an upward concavity in the R-ST segment.

Because of the favorable surgical prognosis this diagnosis offers at any age a high index of suspicion and a willingness to perform special diagnostic procedure is warranted. In this institution we have come to favor the thoracic retrograde aortogram for diagnosis.

Resumen

Treinta y un niños con ductus arteriosus demostrado quirúrgicamente se estudiaron para buscar algunos indicios clínicos de valor diagnóstico. La ocurrencia de rubéola durante el embarazo, una presión amplia del pulso o un soplo cefálico durante la sístole y la diástole del área pulmonar, deben poner alerta al examinador sobre la posibilidad de persistencia del ductus arteriosus. Además de los hallazgos en relación con la presencia de un paso de izquierda a derecha, los rayos X comunes revelaron un crecimiento izquierdo de la aurícula en 31, y un ensanchamiento del botón aórtico en 5 casos. La comparación de electrocardiogramas en niños con VSD no reveló ninguna clave de valor diagnóstico diferencial, excepto posiblemente por la presencia de una concavidad hacia abajo en el segmento R-ST.

En vista del favorable pronóstico quirúrgico, este diagnóstico ofrece en cualquier edad un elevado índice de sospecha y se necesita buena voluntad para llevar a cabo procedimientos especiales de diagnóstico. En esta institución hemos llegado a favorecer el aortograma retrógrado torácico para el diagnóstico.

Zusammenfassung

Analyse von 39 Kindern mit chirurgisch bestätigtem offenen ductus arteriosus im Hinblick auf klinische Anhaltspunkte von diagnostischer Bedeutung. Das Auftreten von Röteln während der Schwangerschaft, eine erweiterte Blutdruckamplitude oder ein Herzgeräusch während Systole und Diastole im Bereich der pulmonalis sollte den Untersucher auf die Möglichkeit eines offenen ductus arteriosus aufmerksam machen. Zusätzlich zu diesem Befunden, die in Zusammenhang stehen zu dem Vorliegen eines Links-Rechts-Shunts, ergaben die üblichen röntgenologischen Untersuchungen eine Erweiterung des linken Vorhofes in 31 Fällen und eine solche des Aortenknopfes in

Wegen der günstigen chirurgischen Prognose bietet diese Diagnose in jedem Lebensalter einen hohen Grad von Verdacht und verbindet eine Genauigkeit zur Vornahme spezieller diagnostischer Maßnahmen. Auf unserer Abteilung sind wir dazu übergegangen, für die Diagnose in erster Linie das thorakale, retrograde Aortogramm heranzuziehen.

REFERENCES

CARDIOVASCULAR MANIFESTATIONS OF ACROMEGALY

Cardiovascular manifestations of acromegaly are worthy of attention. Their frequency excludes a mere coincidence and they are often very severe. The following points may be considered as acquired:

1. Cardiomegaly may not be connected to the simple splanchnomegaly described in the course of the disease. It is never noted alone, but coexists always with clinical manifestations (high blood pressure, heart failure) or electrocardiographic ones (coronary insufficiency, conduction disorders).

2. Branch block, particularly the left, is the more frequently met electrocardiographic anomaly.

3. Hypertrophism favors, without doubt, high blood pressure. The role it may play in arterial atheromatous involution is possible, but not proved.

4. Heart failure is one of the grave complications of acromegaly. It may be due to numerous factors: high blood pressure, coronary insufficiency, increase in cardiac output; on the other hand, the possible adverse effect of the hormonal disorder on myocardial fibers may not be eliminated.

In reference to treatment in some cases, the risk of surgery appears too high. In other cases cardiovascular manifestations may constitute additional argument for surgery, but it is chiefly in the prophyactic sphere that the risk of occurrence of cardiovascular complications becomes important. Such an occurrence favors early resection of eosinophilic pituitary adenomas.