Functional Diagnosis of Patent Ductus Arteriosus
Studied by Cineangiocardiography in Fifty-three Cases

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The hemodynamic alterations revealed by cineangiocardiography in 53 cases of patent ductus arteriosus made possible the correct angiocardiographic diagnosis in 90 per cent of the cases. The most constant functional sign is "blanching of the pulmonary artery," which is seen during diastole and consists of a decrease in density of the pulmonary artery and its branches. This phenomenon has been analyzed by projecting the cineangiograms frame by frame and measuring angiographic density and diameter at the same points of the pulmonary artery. The curves obtained were correlated with each other and plotted against time. The findings were correlated with clinical, surgical, and pathologic information. The hemodynamics of the shunt in patent ductus arteriosus are discussed and a theoretical explanation is offered.

Patent ductus arteriosus is one of the most frequent congenital cardiac anomalies. This condition occurred in 24.2 per cent of the cases in the Abbott report on 1,000 autopsies of congenital heart diseases,1 and Heim de Balsac2 found this same incidence. The ductus was patent in 18 per cent of the congenital heart cases studied in our department. According to Benn3 and Lynnxwiler and Wells,4 this anomaly occurs more frequently in females (66 per cent), whereas in our statistics the distribution is the same for both sexes. Patent ductus arteriosus was complicated by other congenital anomalies in 66 per cent of Abbott's cases, in 61 per cent of Castellanos,2 and in 36 per cent of our cases.

The "isolated" form of patent ductus arteriosus does not present diagnostic difficulties. However, the clinical diagnosis of the "complicated" forms may offer a problem, especially when catheterization, gas analysis, and other procedures are inconclusive.2 5-8

Because of the evolution of the disease itself, the anatomic alterations may be quite variable9 and in many cases the heart has a normal configuration. Departures from the norm, that are sometimes referred to as "typical," are actually not specific and are common to other anomalies. Conventional angiocardiography has been reported to be unreliable in the diagnosis of patent ductus arteriosus.10-14 Because of the low exposure frequencies (2 to 4 films per second) this technic has failed to represent all phases of the cardiac cycle15 and thus the altered hemodynamics, which are the reliable indicators of the underlying changes, often were undetected.

It is our opinion that the diagnosis of patency of the ductus arteriosus can be based on functional alterations due to the aortic-pulmonary artery shunt. These phenomena can be demonstrated by high-speed angiography giving at least 6 exposures per cardiac cycle, and can be studied in some detail when the exposure frequency reaches a minimum of 10 per cardiac cycle. The cineangiocardiographic method, with its high exposure fre-
TABLE 1.—Changes in Optical Transmission in the Pulmonary Artery of Normal Hearts and Cases with Patent Ductus Arteriosus

<table>
<thead>
<tr>
<th>Cardiac cycle</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trunk</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>9.25*</td>
<td>5.25</td>
<td>3.50</td>
<td>2.75</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Ductus</td>
<td>14.92</td>
<td>10.00</td>
<td>10.80</td>
<td>9.08</td>
<td>6.80</td>
<td>4.24</td>
</tr>
<tr>
<td>Bifurcation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>16.50</td>
<td>9.00</td>
<td>5.00</td>
<td>4.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Ductus</td>
<td>17.00</td>
<td>20.00</td>
<td>18.75</td>
<td>16.41</td>
<td>11.00</td>
<td>7.37</td>
</tr>
<tr>
<td>Left branch</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>15.00</td>
<td>8.50</td>
<td>7.50</td>
<td>4.50</td>
<td>3.50</td>
<td>0.00</td>
</tr>
<tr>
<td>Ductus</td>
<td>15.70</td>
<td>16.00</td>
<td>14.43</td>
<td>13.43</td>
<td>7.31</td>
<td>7.25</td>
</tr>
</tbody>
</table>

*The averages of the differences between the maximum diastolic, optical transmission and the minimum systolic optical transmission measured in 6 consecutive cardiac cycles of the right cineangio cardiogram on the trunk, on the bifurcation and on the left branch of the pulmonary artery in 15 normal hearts and in 30 cases of patent ductus arteriosus. This table shows that in patent ductus arteriosus the angiographic density of the pulmonary artery decreases far more than in normal cases, especially after the second cardiac cycle. This phenomenon is caused by the dilution of contrast material in the pulmonary artery by the blood coming from the aorta via the ductus.

Optical density can be measured as ‘‘absorption’’ or as ‘‘transmission.’’ Transmission expresses the quantity of light emerging from the film and projected on the screen. The quantity of emerging light measured on the pulmonary artery before the passage of the contrast material was made equal to 100 per cent transmission. The measurement obtained in this manner expresses the ratio between the actual density and the density measured before the passage of contrast material. These measurements are comparable to each other in the same film and to those in other films because they are not affected by the variation of density (due to the factor of exposure, the processing, and the printing and finally the technic of projection).

Materials and Methods

Fifty-three cases of patent ductus arteriosus, representing 18 per cent of the congenital heart cases observed in our department, have been studied by cineangiography.

The clinical study of each patient included physical examination, electrocardiogram, and phonocardiogram. Successful cardiac catheterization studies were obtained in 16 patients, surgical findings were available in 30, and autopsy findings in 3.

Cineangioangiography was performed on unanesthetized patients seated in an oblique position, usually left anterior oblique or right posterior oblique. The cineangiograms were recorded on either 35- or 70-mm. film at camera speeds of 15, 30, or 60 frames per second.16, 17 A special analytic projector developed in this department19 was used to view the 16-mm. reduction prints.

The contrast media used were 70 per cent Diodrast and 70 per cent Urokon. The dose injected was 1 to 1.5 ml./Kg. of body weight. The contrast medium was injected by an ordinary syringe or semiautomatic injector, into the veins of the arm through a polyethylene tube or into the superior vena cava through a Cournand or a Lehman catheter.

The movements of the heart structures and great vessels have been represented graphically by the new method of cineangiometry.19 The borders of the heart chambers and great vessels were traced from single frame projections18 of the cineangiographic films. By utilizing specific anatomic reference points, diameters and area were measured on the drawings and their percentage deviations from their arithmetic average were plotted against time. Specific curves were obtained from these measurements showing the variations of chosen diameters and areas. These curves are similar to electrokymographic tracings and can be correlated with angiographic density curves recorded at the same time. These density changes of the chosen areas of the heart
FUNCTIONAL DIAGNOSIS OF PATENT DUCTUS ARTERIOSUS

Fig. 1. Angiographic density (dotted lines) and vessel diameter (solid lines) measured on trunk (upper curves) and on the left branch (lower curves) of pulmonary artery of normal cineangiogram in left anterior oblique position at 30 frames/sec. Electrocardiographic tracing at bottom of figure recorded synchronously. The angiographic density of the pulmonary artery reaches a plateau with the second cardiac cycle of the right angiogram. Slight variations of density due to change in diameter of vessel (pulsation).

and great vessels have been recorded by projecting the films, frame by frame, on a specially adapted screen and measuring the optical density with a densitometer.

RESULTS

The angiographic density of the pulmonary artery has been measured in the first 6 consecutive cardiac cycles of right cineangiograms in normal subjects and in those with patent ductus arteriosus.

In the normal subject, the angiographic density of the pulmonary artery usually reaches the maximum during the second cardiac cycle of the right angiogram following peripheral injection of medium. See figure 1. The degree of opacification of the vessel depends upon concentration, quantity, and flow rate of the contrast medium injected and upon the heart rate. Other factors being equal, the greater the heart rate, the less is the concentration of contrast medium per stroke volume.

The angiographic density of the pulmonary artery is greater in the trunk than in the branches. This density is proportional to the cross-sectional area of the vessels except for density changes produced by overlapping structures.

In normal subjects, the angiographic density of the vessels decreases during diastole and may be seen by gross inspection during the first 2 cardiac cycles of the right angiogram. This is due to the mixing of the contrast medium with the blood present in the vessel during the first and second cycles. In the other cycles, if the injection, which is too slow, is discounted, the density depends on the systolic-diastolic variation of the cross-sectional area of the vessel (pulsation).

Differences between systolic and diastolic angiographic density have been measured at 3 different points on the pulmonary artery (trunk, bifurcation, and left branch) in each of the first 6 consecutive cardiac cycles of the right angiogram. In table 1 are reported the averages of these differences measured in 15 normal cases and in 30 cases with patent ductus arteriosus. The density is expressed as optical transmission (table 1, footnote). Thus, 9.25 (table 1, cycle 1, trunk, normal) means that the transmission of the light of the projector at the same point on the trunk of the pulmonary artery is 9.25 per cent greater in diastole than in systole, i.e. the opacity of the vessel at that point is diminished. The data of table 1 demonstrate clearly that a diastolic loss of density occurs during the first 2 cardiac cycles of the right angiogram in both normal and patent ductus arteriosus cases; and that in subsequent cardiac cycles, diastolic loss of density in patent ductus arteriosus is 2 or 3 times more than in normal subjects, particularly at the bifurcation of the pulmonary artery (fig. 2).

According to our experience, this diastolic loss of density in the pulmonary artery is visible by gross observation during the projection of the films when the diastolic trans-
mission increases above 5 or 6 per cent. For this reason (table 1) the phenomenon, "blanching sign of the pulmonary artery," is always visible in cases of patent ductus arteriosus.

We attempted to determine the onset of the "blanching" in 20 cases by plotting against time the variation of angiographic density and pulsation of the pulmonary artery (table 2). The beginning of the blanching was measured from the start of the ventricular ejection, which is always recognizable on the films projected in single frame and on the density tracings. The time in each case was expressed as a percentage of the duration of the cardiac cycle.

We found (table 2) that the "blanching of the pulmonary artery" began after a lapse of about 39/100 of the cardiac cycle. This is in diastole because, according to the electrokymographic findings of Heyer et al.,22 diastole begins 20 to 29/100 after the onset of ejection.

In only 2 cases presenting a very wide and short duc tus was the "blanching" demonstrable at the end of systole.

This cineangiocardio graphic sign (blanching of pulmonary artery) was noted by mem-
amount of the shunt measured by gas analysis. However, if we consider the size of the ducti found at surgery and reported in table 3, there is some doubt about the catheterization and gas analysis methods in measuring the amount of blood shunted from the aorta into the pulmonary artery via the ductus.

The reopacification of the pulmonary artery occurring during the left angiocardiogram is another well-known angiographic sign of patent ductus arteriosus. It may be difficult to differentiate it from a persistent opacification of an enlarged pulmonary artery and from any other left-to-right shunt.

For technical reasons, we could study this angiographic sign by densitometry and cine-electrokymography in only 5 cases. Densitometric tracings show that the density of the pulmonary artery begins to increase during diastole (reopacification).

This demonstrated that the "blanching sign" and reopacification of the pulmonary artery are a reciprocal aspect of the same phenomenon seen in different phases of the angiocardiogram, namely the diastolic component of the shunt coming from the aorta into the pulmonary artery via the ductus.

Differential Diagnosis and Discussion

Are the "blanching sign" and the "reopacification" of the pulmonary artery specific for isolated patent ductus arteriosus? Consider some other congenital communications between the aorta and the pulmonary artery. These have been classified as low or juxtaortical communications and high communications at the level of the trunk or branches of the pulmonary artery.

We have not had the opportunity to study any of these anomalies by cineangiography, but we believe that it should be possible, theoretically, to differentiate the low communications from isolated patent ductus arteriosus. The anatomic position of such a communication should produce a low defect of opacification of the trunk of the pulmonary artery or of the ascending aorta. The direction or vector of the blanching in this case should be mainly forward, toward the bifurcation and not retrograde as in patent ductus arteriosus, and lastly, the pulmonary artery enlargement, according to the descriptions of the few reported cases, should be greater in the low communications than in ductus.

It could be difficult to differentiate ductus
Table 3.—Correlation of Magnitudes of Blanching Sign and Shunt

<table>
<thead>
<tr>
<th>No</th>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Surface Position</th>
<th>Complications</th>
<th>Pulm. art. pressure (mm Hg)</th>
<th>Shunt (% SBF)</th>
<th>Length (mm)</th>
<th>Ext. diam.</th>
<th>Bifurcation</th>
<th>Left branch</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1080</td>
<td>6</td>
<td>M</td>
<td>LAO</td>
<td>Coarct. Aorta</td>
<td>68-39</td>
<td>93%</td>
<td>large</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1290</td>
<td>6</td>
<td>F</td>
<td>LAO</td>
<td></td>
<td>17-8</td>
<td>59%</td>
<td>long</td>
<td>mm. 3</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>1060</td>
<td>27</td>
<td>M</td>
<td>LAO</td>
<td></td>
<td>24-8</td>
<td>57%</td>
<td>small</td>
<td>mm. 5</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1070</td>
<td>10</td>
<td>F</td>
<td>LAO</td>
<td></td>
<td>21-9.5</td>
<td>45%</td>
<td>very small</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1176</td>
<td>21</td>
<td>F</td>
<td>LAO</td>
<td></td>
<td>21-10</td>
<td>36%</td>
<td>?</td>
<td>?</td>
<td>11.33</td>
<td>11.5</td>
</tr>
<tr>
<td>6</td>
<td>1112</td>
<td>5</td>
<td>F</td>
<td>LAO</td>
<td>Coarct. aorta</td>
<td>30-18</td>
<td>36%</td>
<td>short</td>
<td>mm. 5</td>
<td>7.43</td>
<td>5.4</td>
</tr>
<tr>
<td>7</td>
<td>1172</td>
<td>5</td>
<td>M</td>
<td>LAO</td>
<td></td>
<td>26-14</td>
<td>31%</td>
<td>?</td>
<td>?</td>
<td>29.33</td>
<td>19.5</td>
</tr>
<tr>
<td>8</td>
<td>877</td>
<td>6</td>
<td>M</td>
<td>RPO</td>
<td>Pulmonic stenosis</td>
<td>17-7</td>
<td>30%</td>
<td>found during</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*SBF = Systemic blood flow

†Averages of diastolic loss of density (transmission) in 6 consecutive cardiac cycles of right cineangiographic films at the bifurcation and on left branch of the pulmonary artery.

This table shows that the blanching sign measured in cineangiographic films recorded in only one oblique projection is not proportional to the amount of the aorta-pulmonary artery shunt measured by catheterization and gas analysis.

from high aortic-pulmonary communications. We noted in 2 cases of patent ductus arteriosus of the "window type" that the diastolic blanching was associated with a systolic defect of opacification of the left branch and bifurcation of pulmonary artery. No such systolic defect was detectable in the other types of ductus, the "cylindrical" and "funnel." For this reason we believe that it would be impossible to differentiate between the "window-type" ductus and the high aortic-pulmonary communication, which functionally behaves in the same manner. However, the latter condition is extremely rare. Only about 30 cases were described between 1860 and 1949.

In our cases of ductus complicated by other defects, we observed that the "blanching sign" and reopacification of the pulmonary artery were present in all 7 cases complicated by coarctation of the aorta. The "blanching" was also present in 7 cases complicated by pulmonary stenosis. In these cases the pulmonary artery was greatly enlarged, especially at the bifurcation, and it pulsed vigorously. The reopacification of the pulmonary artery was confused by the persistence of the contrast material in the enlarged vessel.

In 2 cases complicated by pulmonary stenosis and interatrial septal defects, the findings were identical with the cases complicated by pure pulmonary stenosis. The blanching and reopacification were not demonstrable in 2 of the 3 cases complicated by multiple defects; one of these was in a patient with tricuspid atresia and aortic stenosis and the other in a patient with atrioventricular communis.

It is our opinion that the blanching sign should be demonstrable in all cases of complicated patent ductus arteriosus when the hemodynamics pertinent to the complicating anomalies allow a sufficiently large shunt of relatively nonopaque aortic blood into a pulmonary artery well filled with contrast medium.

We have observed that in complicating intracardiac shunts the angiographic density of the pulmonary artery does not change during the cardiac cycle, since the blood is mixed upstream from the semilunar valves.

In considering the significance of the diastolic timing of the "blanching" and "reopacification of the pulmonary artery," certain hemodynamic and mechanical factors must be considered. Regardless of the timing
Fig. 3. Sequence from 15-frames/sec. cineangiogram in 7-year-old girl with patent ductus arteriosus. Cardiac cycle recorded by 7 frames (0.47 sec.). At surgery ductus measured 4 mm. outside diameter and 4 mm. in length. Typical machinery murmur and normal ECG found. Angiographic density of trunk and left branch of pulmonary artery less in diastole (1 and 6) than in systole (2 to 5). See third cardiac cycle in figure 2. This cyclic diastolic density change of pulmonary artery as observed on cineangiogram by continuous projection is "blanching sign of the pulmonary artery." Band of lesser density in distal portion of pulmonary artery trunk (arrows) is caused by left main bronchus.

of the shunt, be it truly continuous, or primarily systolic or diastolic, the velocity of pulmonary blood flow is so great in systole that we could not anticipate a "blanching" sign except during diastole when the blood column is stationary. We should expect, however, that a systolic defect of opacification could be seen at the site of the ostium of the
ductus or that angiographic density studies would show differences in the intensity of systolic opacification of the pulmonary artery along the direction of flow. Only 2 of the 53 patients studied showed an opacification defect during retarded ejection and both of these were of the very large ductus type. Density studies failed to reveal positive evidence of systolic dilution distal to the insertion of the ductus.

The classical concept of continuous shunting with systolic predominance has been questioned in the early phonocardiographic studies of Routier. Recently, Luisada stated, "when the ductus is small, the passage of blood takes place only during the last part of systole and slightly afterwards."

Direct visualization of the ductus during left heart opacification after peripheral angiography has been reported by Wegelius and Lind and Hilario, Lind, and Wegelius. The examinations were carried out at high-exposure frequencies, but it is interesting that the ductus was opacified sufficiently to be recognized only on the films made during ventricular diastole.

These findings led us to suspect that the shunt though very likely continuous, is predominantly diastolic. A plausible, and readily acceptable explanation of our concept is not available. However, we have postulated 2 factors that theoretically might influence blood flow through the ductus in such a manner as to produce a predominantly diastolic shunt.

The first is mechanical and is caused by the systolic forces acting on the pulmonary artery and aorta in different ballistic vectors. These forces could stretch or twist the ductus sufficiently to produce functional systolic narrowing. In support of this hypothesis are the observations of Janker and later of Terano, who observed an exaggerated lateral movement of the pulmonary artery in cases of patent ductus arteriosus studied by cinefluorography. We too have observed this movement. Kjellberg and associates intimated that the aortic movements can be transmitted to the pulmonary artery, necessarily, we comment, by the intermediary ductus.

The second factor is hemodynamic and is a result of the increased velocity of the aortic flow, which may influence the flow through the ductus by a Bernoulli-like effect during systole. A patient with large patent ductus and pulmonary hypertension was studied by catheterization approximately 1 hour before angiography. A mild pressure gradient between the aorta and pulmonary artery was demonstrated (103 to 97 mm. Hg), which should favor systolic flow from aorta to the pulmonary artery. At cineangiography the shunt could be seen very clearly as it entered the aorta during systole in spite of the pressure gradient.

**Summary and Conclusions**

Fifty-three cases of patent ductus arteriosus were studied by classical methods and by cineangiography. The films obtained were studied by analytic projection. From them hemodynamic data were recorded by angiographic density measurement and the movements of the heart chambers and great vessels were represented graphically by cineangiometry and cine-electrokymography. The tracings obtained were timed and compared with each other.

The most significant and constant cineangiographic signs of the anomaly were the cyclic diastolic loss of density of the pulmonary artery (blanching sign) during the right angiogram and the reopacification of the pulmonary artery during the left angiogram.

Both were attributed to a shunt coming from the aorta into the pulmonary artery via the ductus during diastole.

The degree of "blanching" was not proportional to the amount of the shunt as calculated by the Fick method.

Angiographic density tracings of the pulmonary artery demonstrated that the blanching occurred at the time of the dicrotic wave and increased during diastole. The degree of dicrotism was roughly proportional to the degree of the "blanching" thus proving the relationship of these abnormal movements of the pulmonary artery to the diastolic component of the shunt.
This diastolic component is demonstrated by the blanching of the pulmonary artery, because in that phase the velocity of the pulmonary arterial flow approaches its minimum value, permitting the retrograde flow of non-opacified blood shunted from the aorta. However, since all our methods of investigation failed to demonstrate a systolic component of the shunt in the pulmonary artery, and since support was found in isolated observations reported by others, we advanced a hypothesis for future research that the shunt is represented mainly by a diastolic component, at least during cineangiographic procedure. Mechanical and hydrodynamic suppositions are offered as possible theoretic explanations.

The presence of other lesions complicating patent ductus arteriosus did not detract materially from the high degree of accuracy of these functional changes in establishing the cineangiographic diagnosis.

Acknowledgment

The authors wish to acknowledge the generous help of Dr. Lee B. Lusted in the preparation of the manuscript.

Summary in Interlingua

Cinquanta-tres casos de patent ducto arteriosoe esseva studiate per methodos classic e per cineangiografiographia. Le films obtenite esseva studiate per projection analytice. Ab istos, datos hemodynamic esseva registrate per mesuration angiographic de densitate, e le movimentos del cameras cardiac e del gran-de vasos esseva representate graphicamente per cinecardiometria e cine-electrokymografiographia. Le registrationes obtenite esseva chronometrate e comparate le unes con le alteres.

Le plus significative e le plus constante signos cineangiografiographic del anomalia esseva le cyclic perdita diastolic de densitate del arteria pulmonar (signo de blanchimento) in le curso del obtention del angio cardiogramma dextere, con re-opacification in le curso del obtention del angiocardiogramma sinistre.

Ambe ille signos esseva attribuite a un derivation ab le aorta a in le arteria pulmonar via le ducto in le diastole.

Le grado del “blanchimento” non esseva proportional al quantitate del derivation calculate secundo le metodo de Fick.

Registrationes de densitate angiographic in le arteria pulmonar demonstrava que le blanchimento occurreva al tempore del unda dicrotic e cresceva durante le diastole. Le grado del dicrotismio esseva plus o minus proportional al grado del “blanchimento.” Isto provava un relation del movimentos anormal del arteria pulmonar con le componenti diastolic del derivation.

Iste componenti diastolic es demonstrate per le blanchimento del arteria pulmonar, proque in ille phase le velocitate del fluxo in le arteria pulmonar approcha su valor minimal, lo que permite le fluxo retrograde del non-opacificate sanguine que es derive ab le aorta. Nonobstante, viste que omne nostre methodos de investigation non succedeva a demonstrun componento systolic del derivation in le arteria pulmonar e viste que isolate observationes in reportos per altere autores supportava un tal passo, nos formulava—pro un studio futur—le hypothese que le derivation es representate principalmente per un componento diastolic, al minus durante le manova angiocardiographic. Theses mechanic e hydrodynamic es presentate como possibile explications theorie.

Le presentia de altere lesions que complicava le patent ducto arterioso non disturbava de maniera notable le alte grado de accuratia con que iste alterationes functional establiva le diagnose cineangiocardiographic.

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