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Diagnosis of Patent Ductus Arteriosus in Preterm Infants

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Objectives  After completing this article, readers should be able to:

1. Delineate the clinical signs that can lead to late diagnosis of patent ductus arteriosus (PDA).
2. List the imaging study that allows accurate and timely diagnosis of PDA.
3. Describe how to determine the hemodynamic significance of PDA.
4. List the finding that predicts persisting patency.

Introduction
Patent ductus arteriosus (PDA) remains a common problem for the very preterm infant. Despite being a focus of neonatal research for many years, controversy still surrounds the role of PDA in adverse outcomes and the best method and appropriate timing of treatment. Some of the uncertainty over the importance of PDA to the preterm infant relates to common misconceptions about the natural history of preterm ductal shunting and about the best method for diagnosing PDA; that is, how PDA is recorded as an outcome. Echocardiography has provided a window on the preterm transitional circulation that raises questions about the relevance of much traditional thinking in this area of modern neonatal medicine.

This article focuses on the clinical and echocardiographic diagnosis of PDA and how prospective echocardiography has changed our understanding of the impact of ductal shunting in the very preterm infant. By describing echocardiographic assessment of the preterm ductus arteriosus in some detail, the authors hope to encourage more neonatologists to develop these very useful skills.

Clinical Diagnosis
Physical signs and symptoms of a PDA typically appear 3 to 4 days after delivery and are characterized by failure to wean ventilator pressures, a long systolic murmur at the left upper sternal edge radiating to the back, increased precordial impulses, and prominent peripheral pulses. The appearance of signs at this time and subsequent diagnostic echocardiographic evaluation led to the common belief that early ductal shunting is not hemodynamically significant. In fact, when ductal hemodynamic significance is evaluated prospectively from birth with echocardiography (using criteria described in this article), it becomes apparent that clinical signs and symptoms are a late feature of the significant preterm patent ductus.

Skelton and associates (1) examined a cohort of preterm infants daily over the first week after birth with independent and blinded clinical and echocardiographic examinations. On day 1, clinically silent ducts were universal in infants who had significant shunts. In the subsequent 3 to 4 days, each of the signs of bounding pulses, active precordium, and systolic murmur were of reasonable specificity but very low sensitivity for diagnosis of an echocardiographically defined significant PDA. The presence of signs often correlated with the presence of a PDA, but most significant PDAs did not produce clinical signs. This study demonstrated that relying on clinical signs led to a mean diagnostic delay of 2 days, with a range of 1 to 4 days. These observations were consistent with those of Davis and colleagues, (2) who performed a cross-sectional study on preterm babies between postnatal days 3 and 7. They also found that clinical signs of a PDA were specific but insensitive.

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Widened pulse pressure is believed commonly to indicate PDA, but the accuracy of this clinical sign also does not withstand critical evaluation, particularly during the first postnatal week. Evans and Moorcraft (3) found no difference in pulse pressure between babies who did and did not have significant PDAs. Instead, they demonstrated a global effect on blood pressure, with reduced systolic and diastolic pressures noted, particularly among infants whose birthweights were less than 1,000 g. These findings were consistent with those of Ratner and colleagues, (4) who conducted a prospective study of a cohort of babies and found PDA associated with reduced systolic and diastolic pressure. In summary, reliance on clinical signs results in a delayed diagnosis of PDA.

Echocardiographic Diagnosis
Accurate and timely diagnosis requires ready access to echocardiography. In many clinical neonatal intensive care units, echocardiography is a consultative diagnostic tool that requires a clinician from another department in the hospital (usually cardiology or radiology) or, probably more commonly, from another hospital. The consequence is accurate but rarely timely diagnosis because the consultation must be fitted into busy schedules. Echocardiography is a rich source of immediate hemodynamic information in the sick neonate that can be used to guide management more accurately than other, more common monitoring parameters, but timely use requires neonatologists to develop the skills to perform the imaging. Two primary questions can be answered by neonatal echocardiography: 1) What are the hemodynamics in this sick baby? and 2) Does this baby have a structurally normal heart? An appropriately trained intensivist can and should be able to answer the first question, but the second must be answered by a pediatric cardiologist. In Europe and Australasia, increasing numbers of neonatologists are developing echocardiographic skills. (5) The trend appears to be less common among North American neonatologists, not because of a lack of interest, but because of a lack of opportunity. For this reason, this article develops in some detail the methodology for diagnosing the PDA. Fundamental to applying this methodology is an understanding of the anatomy of the great vessels.

Spatial Anatomy of the Great Vessels
Ultrasonography is a process of converting a three-dimensional structure into a series of two-dimensional images. The primary mistake made in learning ultrasonography is trying to understand the two-dimensional images before grasping the three-dimensional anatomy. Understanding ultrasonography requires first learning the anatomy; the two-dimensional images subsequently become self-explanatory to the clinician wielding the transducer.

Click here to view a rotating digital three-dimensional model of the heart (Video #1). The aorta leaves the left ventricle, heading toward the right shoulder before turning superiorly, posteriorly, and then to the left as it arches around behind the heart. The right ventricular outflow tract crosses from right to left, in front of (anterior to) the aortic root, before turning posteriorly into the main pulmonary artery (MPA), which runs posteriorly (and slightly superiorly) toward the spine to the left of the ascending aorta. The MPA bifurcates, with the right pulmonary artery (RPA) turning sharply to the right behind the ascending aorta (look at model from the right) and the left pulmonary artery (LPA) running less sharply to the left. The descending aorta runs directly behind the junction of the MPA and LPA. It is at this point that the ductus arteriosus joins the two great vessels, describing an arch running in continuity from the anterior wall of the MPA into the descending aorta (look at model from the left).

Echocardiographic Assessment of the Ductus Arteriosus
The ductus arteriosus is evaluated echocardiographically to determine whether it is patent and, if so, whether the PDA is hemodynamically significant. A further issue is the predictive properties of early echocardiographic assessment of the duct.

Is the Ductus Arteriosus Patent?
TURBULENCE IN THE MPA
When there is a left-to-right shunt through the ductus arteriosus, blood jets back into the MPA from the descending aorta. The result is a turbulent flow pattern in the MPA, which can be detected easily and accurately with pulsed Doppler echocardiography.

The MPA is imaged from the low parasternal window, with the transducer and beam in a true sagittal plane to the body (Video #2). The MPA is identified as the large vessel running posteriorly away from the transducer. The Doppler range gate is placed beyond the pulmonary valve and the flow recorded (Video #3). Normal pulmonary artery flow is characterized by systolic forward flow with minimal turbulence in diastole (Fig. 1). In the presence of a left-to-right ductal shunt, turbulence can be seen in diastole and sometimes through systole (Fig. 2).

This method of echocardiography diagnoses ductal patency simply and accurately, but it will not detect a
Figure 1. Echocardiographic tracing with pulsed Doppler of normal pulmonary artery flow, showing systolic forward flow and minimal turbulence in diastole.

Figure 2. Echocardiographic tracing with pulsed Doppler of left-to-right ductal shunt, showing turbulence in diastole and sometimes systole.
PDA with a right-to-left shunt (because there is no MPA turbulence), and it provides no information about the significance of the shunt.

DIRECT IMAGING OF THE DUCTUS ARTERIOSUS

The best method of assessing the ductus is to image it directly. Although this requires more practice than indirect methods, such as determination of MPA turbulence, the additional information acquired is well worth the effort.

The best window for imaging the ductus is in the high parasternal position slightly to the left of the sternum, with the transducer (and beam) in a true sagittal plane. We recommend starting with the beam angled slightly to the right and locating the ascending aorta running horizontally across the screen with the right pulmonary artery in cross-section beneath it (Video #4) (Video #5). If the beam is angled slowly back to the left, the next vessel imaged is the body of the MPA running posteriorly (Video #2) (Video #6). A slight further angulation to the left reveals the root of the LPA, appearing as a branch posteriorly, with the appearance of a diverticulum. The ductus arteriosus runs superiorly to the root of the LPA in an arch that is in continuity with the anterior wall of the MPA (Video #7) (Video #8).

A ductus that is widely patent can be seen on two-dimensional imaging (Video #9), but it is difficult to differentiate a closed ductus from a constricting ductus; accurate definition of patency requires color Doppler. Color Doppler codes blood flow according to direction, conventionally red when flow is toward the transducer and blue when it is away from the transducer. When the color Doppler field is placed over the ductus shown on two-dimensional imaging in the previous video, the characteristic red jet of the ductal shunt appears to be streaming back up the anterior wall of the MPA (Video #10). The two blue streams of the LPA and the descending aorta are seen on either side of the ductal stream. For the occasional baby who has a predominantly right-to-left shunt, the ductal shunt appears in blue on color Doppler, which makes the shunt easy to confuse with the LPA and descending aortic flows (Video #11).

(The authors have developed an interactive multimedia program that can be downloaded from duct_drag1.htm [Video #12]. The program takes the user through the anatomy and primary ultrasonographic images and concludes with an interactive virtual echocardiography of the ductus. The program is 14 MB and requires downloading and installation of Macromedia Authorware Web Player (1.3 MB) and Quicktime 5.0 or later. A broadband connection is preferable for making this download.) © 2003 Nick Evans and Girvan Malcolm)

The combination of two-dimensional imaging and color Doppler allows accurate definition of whether the ductus is patent, but defining its significance demands further measures.

Is the Ductal Shunting Hemodynamically Significant?

DIRECTION OF DUCTAL SHUNTING

Although an impression of the dominant direction and velocity of ductal shunting can be derived from a color Doppler assessment, accurate determination requires pulsed Doppler. The method involves imaging the ductus as described previously, identifying the ductal shunt stream on color Doppler, and placing the pulsed Doppler range gate within the stream to assess the velocity pattern. Pulsed Doppler identifies the direction and velocity of blood flow at the site of the range gate. The tracing displays left-to-right flow as a positive trace (Fig. 3) and right-to-left flow as a negative trace, with velocity plotted against time.

The pattern of Doppler shunting is determined by the relative pressures at each end of the duct through the cardiac cycle. When the aortic pressure exceeds that in the MPA throughout the cardiac cycle, the shunt is pure left-to-right. When MPA pressure exceeds aortic pressure throughout the cardiac cycle (a rare occurrence), the shunt is pure right-to-left (Fig. 4). The complication in assessing ductal shunting in the range between the two “pure” shunts relates to the asynchronous nature of the pressure wave at each end of the duct. The pressure wave from the right heart arrives before that from the left. Accordingly, as right-sided pressures increase (but before they exceed systemic pressures), there is a period of right-to-left shunting in early systole but left-to-right shunting for the remainder of the cycle or bidirectional shunting (Fig. 5). Increasing right-sided pressure is reflected in increasing duration of right-to-left shunting within a bidirectional pattern (Fig. 6).

VOLUME OF DUCTAL SHUNTING

Several markers for the significance of a ductal shunt have been cited in the literature, including left atrial-to-aortic root ratio, left ventricular size, and left ventricular output. In cardiology, the significance of a left-to-right shunt is determined by the ratio of pulmonary to systemic blood flow (Qp:Qs). The larger the shunt, the higher the pulmonary blood flow relative to the systemic blood flow. Qp:Qs is determined by the relative ventricular outputs. Somewhat counterintuitively, the systemic
Figure 3. Echocardiographic tracing with pulsed Doppler of left-to-right flow, with velocity plotted against time.

Figure 4. Echocardiographic tracing with pulsed Doppler of right-to-left flow, with velocity plotted against time.
Figure 5. Echocardiographic tracing with pulsed Doppler of bidirectional shunting that can occur as right-sided pressures of the duct increase (before exceeding systemic pressures).

Figure 6. Echocardiographic tracing with pulsed Doppler of increasing duration of right-to-left shunting within a bidirectional pattern.
blood flow with a left-to-right ductal shunt is measured by right ventricular output, and the pulmonary blood flow is measured by left ventricular output. Unfortunately, the significance of a preterm ductus cannot be measured using relative ventricular output because many infants have coexisting left-to-right atrial shunts. (6) We measured Qp:Qs in a subset of infants who had ductal shunts in whom we knew there was minimal atrial shunting. Although the indirect measures cited previously correlated significantly with Qp:Qs, the closest correlation was with the direct measures of color Doppler ductal diameter and the direction of diastolic flow in the descending aorta. (6)

**Color Doppler Ductal Diameter**

Color Doppler ductal diameter is a semiquantitative means of measuring what is readily apparent to the naked eye on the ultrasonography screen; that is, the degree of constriction varies widely in PDA. Because the walls of the ductus are difficult to define on two-dimensional imaging, color Doppler is used to determine the diameter of the ductus at the site of maximal constriction. The difference between two ducts can be obvious. Color Doppler imaging of a well-constricted duct reveals a thin stream of blood (Video #13) compared with a wide stream of blood in a duct that has only minimal constriction (Video #14). The diameter of the shunt on the well-constricted duct was approximately 1.1 mm compared with 3.1 mm for the less-constricted shunt (Fig. 7). Measurement of the color Doppler diameter requires close attention to image optimization, including ensuring that the Doppler gain is not too high, that the Doppler scale is set to the maximum that reflects the usual velocities of ductal shunts, and that the duct is imaged along its entire length. A video clip is stored and reviewed frame by frame to measure the minimum diameter (ie, site of maximum constriction). It is advisable to average three to five cardiac cycles. In our study, for babies who weighed less than 1,500 g during the first postnatal week, a ductal diameter of less than 1.5 mm usually indicated an insignificant shunt, and a diameter of more than 1.5 mm usually indicated a significant shunt. If the diameter was more than 2 mm, the Qp:Qs generally was more than 2:1 (ie, twice as much pulmonary blood flow as systemic). (6)

**Direction of Diastolic Flow in the Descending Aorta**

One common misconception about ductal shunting is that the primary drain on the systemic circulation is in diastole. In fact, more blood shunts through the ductus during systole, when the pressure difference between the
two circulations is greatest. However, the effect on the systemic flow pattern is most apparent during diastole, when the least flow occurs in the systemic circulation. This observation can be used to assess the direction of diastolic flow in the postductal descending aorta. The normal diastolic flow at this site is low-velocity forward flow (Fig. 8), as ductal shunting that increases the diastolic flow becomes progressively absent, and then retrograde (Fig. 9).

The descending aorta is imaged best from the same high left parasternal position as the ductus. It is critical that the Doppler range gate be placed beyond the aortic insertion of the ductus. A large ductal shunt results in increased forward diastolic flow in the preductal aorta (the ductus does not only drain blood from the lower body). Figure 10 shows forward diastolic flow in the preductal aorta and retrograde flow in the postductal aorta in the same infant. In the previously cited study, retrograde diastolic flow was associated with a mean Qp:Qs of 1.6 (i.e., pulmonary blood flow was 60% more than systemic flow). (6)

Other Measures of Significance
The same phenomenon that reduces diastolic flow in the postductal aorta increases diastolic flow in the branch pulmonary arteries. Increased diastolic velocities in the LPA have been described as a marker of significance. This measure has the advantage of being technically easier than Doppler in the postductal aorta, requiring only a small adjustment of the Doppler range gate from the ductus into the LPA (Fig. 11).

There is no described method of validating the volume of a right-to-left ductal shunt beyond empiric application of the laws of fluid mechanics such that the flow through a vessel is the product of the cross-sectional area and the velocity of the flow. Therefore, right-to-left shunting through a widely patent duct is more significant than that through a well-constricted duct.

In most circumstances, direct imaging is the preferred method of assessing the ductus. However, the presence of overinflated lungs or severe chronic lung disease can make it difficult to find an ultrasonography window. In these situations, indirect measures such as left atrial-to-aortic root ratio or reduced diastolic velocities in peripheral arteries such as the cerebral or renal vessels may have a role.

Natural History of Preterm Ductal Shunting
Using the previously described methodologies, it has been possible to observe the natural history of ductal shunting. (7)(8)(9)
Figure 9. As the ductal shunting that increases the diastolic flow becomes progressively absent, the diastolic flow becomes retrograde.

Figure 10. Forward diastolic flow in the preductal aorta and retrograde flow in the postductal aorta in an infant who has a PDA.
The Dominant Direction of Shunting is Left to Right
In the era of antenatal steroids and early use of surfactant, most babies are shunting left to right, even from the early postnatal hours. In one study of 124 babies born before 30 weeks' gestation and studied at a mean of 5 hours after birth, 52% had pure left-to-right shunts, 43% had bidirectional shunts but with a predominant left-to-right component, and 2% had pure right-to-left shunts. (7) Two of the babies had closed ducts.

The Degree of Early Ductal Constriction Varies Substantially
Some preterm babies constrict the ductus to a similar degree as seen in term babies, but there is minimal constriction in others. This factor, combined with a predominantly left-to-right shunt, indicates that ductal shunts can be highly significant, even from the early postnatal period. In fact, our observations suggest that the hemodynamic impact of a ductal shunt may be most significant in the early hours after birth. (7)(8) The strongest association between ductal shunting and low systemic blood flow occurred in the first 6 hours after birth and preceded intraventricular hemorrhage.

Poor Early Postnatal Ductal Constriction Predicts Persisting Patency
The ductus that constricts poorly in the early postnatal period is not only likely to have a significant shunt at this time, but it is much more likely to remain patent and produce later clinical signs and symptoms. (8)(9) Figure 12 shows ductal diameters at 5 hours of age plotted against gestational age among 124 babies born before 30 weeks' gestation. The echocardiographic findings in this study were blinded to the attending clinicians, and PDA treatment was administered for clinical reasons. A ductal diameter of greater than 1.6 mm at a mean of 5 hours after birth predicted later clinically apparent PDA with 89% specificity and 55% sensitivity.

Conclusion
Accurate diagnosis of PDA requires ready access to ultrasonography equipment and echocardiographic skills. Early diagnosis of poor ductal constriction may allow early appropriately targeted treatment, although it remains to be proven that such an approach improves outcomes. Neonatologists can and should develop these skills to deliver timely appropriate therapy for PDA and other hemodynamic pathophysiology. Further guides toward developing these skills are available. (10)(11)
EDITOR’S NOTE  See also August and October 2003 issues of NeoReviews for more on PDA closure.

References

Figure 12. Ductal diameters at 5 hours of age among 124 babies born before 30 weeks’ gestation. The blue triangles mark the babies who eventually needed treatment for clinically and echocardiographically significant PDA, almost all of whom were above the median diameter of 1.6 mm.
### NeoReviews Quiz

1. The clinical signs of patent ductus arteriosus (PDA) include a systolic murmur at the left upper sternal edge, increased precordial impulses, and bounding peripheral pulses. Of the following, these clinical signs of PDA most typically manifest:
   - A. At birth.
   - B. 1 to 2 days after birth.
   - C. 3 to 4 days after birth.
   - D. 5 to 6 days after birth.
   - E. After 1 week of age.

2. A preterm neonate is suspected of having PDA based on blood pressure findings. Of the following, the most likely changes in blood pressure in this infant would be:
   - A. Decreased systolic and decreased diastolic pressures.
   - B. Decreased systolic and increased diastolic pressures.
   - C. Increased systolic and decreased diastolic pressures.
   - D. Increased systolic and increased diastolic pressures.
   - E. Normal systolic and normal diastolic pressures.

3. Direct imaging of the ductus arteriosus with color Doppler using the transducer in a true sagittal plane is the best method of determining ductal patency. Of the following, the best window for imaging the ductus arteriosus is in the:
   - A. High parasternal position slightly to the left of the sternum.
   - B. High parasternal position slightly to the right of the sternum.
   - C. Low parasternal position slightly to the left of the sternum.
   - D. Low parasternal position slightly to the right of the sternum.
   - E. Substernal position angled upward and to the left.

4. The hemodynamic significance of the ductus arteriosus can be determined by estimating the ductal diameter from color Doppler and by looking for abnormal diastolic flow in the left pulmonary artery (increased forward flow) or in the postductal descending aorta (absent or retrograde flow). Of the following, the ductal diameter most likely to result in a hemodynamically significant ductal shunt in a very low-birthweight (<1,500 g) neonate during the first week after birth is:
   - A. 0.4 mm.
   - B. 0.7 mm.
   - C. 1.0 mm.
   - D. 1.3 mm.
   - E. 1.6 mm.

5. The natural history of shunting through the ductus arteriosus can be assessed by serial echocardiography. Of the following, the most accurate statement regarding ductal patency and shunting in preterm neonates is that the:
   - A. Degree of early ductal constriction is consistent among infants.
   - B. Dominant direction of ductal shunting is left to right.
   - C. Ductal shunting in early hours after birth is hemodynamically insignificant.
   - D. Early diagnosis of poor ductal constriction and its targeted treatment improves clinical outcome.
   - E. Poor ductal constriction in the first few hours after birth has no bearing on its subsequent patency.
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