Real-time Cross-sectional Echocardiographic Imaging and Measurement of the Patent Ductus Arteriosus in Infants and Children

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SUMMARY While echocardiography has been used to noninvasively document indirect effects on the heart of left-to-right shunting through a patent ductus arteriosus, no noninvasive technique has been developed to image the duct itself. In this study, 35 sequential studies were performed on 28 patients with a mechanical sector scanner to image the distal pulmonary artery and its bifurcation by scanning along the axis of the right ventricular outflow tract. Cross-sectional imaging, just superior to the take-off of the right ventricle, provided visualization of the patent ductus as a distal continuation of the pulmonary artery connecting to the descending aorta. Ductal visualization by cross-sectional echo was validated by saline echo contrast observations of right-to-left and left-to-right shunting through the duct in 14 patients, by surgical observations in 11, angiographic observations in 13 and autopsy observations in three. Angiographic size of the ductus arteriosus, whether constricted or widely patent, tortuous or straight, was predicted correctly and echo/angiographic correlations for smallest inner ductal dimension were excellent (r = 0.97). This study provides a method for and validates the direct imaging of the ductus arteriosus and suggests that cross-sectional echocardiography can accurately predict ductal contour and quantitative ductal cross-sectional size noninvasively.

PATENT DUCTUS ARTERIOSUS, a common condition in pediatric patients, has recently assumed major importance as a life-threatening disease of small premature infants, who now survive due to advances in neonatology. While in an older child, the classical physical findings of ductus arteriosus and the minimal risk of surgery have at times obviated the need for compulsory catheterization before ductal ligation, atypical physical findings and the presence of concomitant respiratory disease in premature infants have often created problems of ductal identification, as well as problems in determining which infants might benefit by ductal closure.

Echocardiography has achieved importance in assessing the hemodynamics of ductal shunting by demonstrating quantitative left atrial enlargement and/or left ventricular enlargement in premature infants, and has been most important when serially applied to the same infant throughout his course. Nonetheless, many of the M-mode echocardiographic features can be mimicked by sepsis, hypoglycemia, hypervolemia or severe anemia in premature infants, and are nonspecific for ductal shunting. Recently, concern has been expressed over the failure to identify infants who have ductal shunting without an audibly detectable murmur. In order to aid in the detection and serial followup of these infants, our laboratory recently developed an arterial saline echo contrast technique for identification of left-to-right shunting patent ductus arteriosus. Unfortunately, this latter technique requires the presence of an umbilical arterial catheter above the level of the diaphragm,
identifies only left-to-right shunting patent ductus arteriosus and cannot demonstrate a balanced or right-to-left shunt through an equally large ductus. None of the available noninvasive techniques directly demonstrate the anatomy of the area of concern — the ductus itself. Rapid identification of the infant who can benefit from a ductal closure is becoming increasingly important, in view of the potential of using prostaglandin inhibitors to noninvasively induce ductal constriction. Additionally, while echocardiographic indices of left atrial size have been of assistance in following medical manipulation of the patent ductus, these measures are affected by other hemodynamic changes and are nonspecific and indirect indicators of ductal patency. As such, the need has not been met for a specific technique to follow noninvasively the effects of these drugs on the ductus. Accordingly, we have applied a high frequency portable real-time cross-sectional echocardiographic system to the identification and direct measurement of the ductus arteriosus and the visualization of right-to-left and left-to-right shunting through the ductus using saline contrast echocardiographic techniques.

Methods

Patient Population

Thirty-five serial cross-sectional echocardiographic studies were performed on 28 patients, five of whom underwent postoperative cross-sectional echocardiographic examinations as well. Patients could be subdivided into four groups:

Group A

Group A consisted of three infants with hypoplastic left heart syndrome proven by autopsy as well as confirmed premortem by cardiac catheterization in one. The infants had a mean age of 5 days (range 1 to 6 days) and a mean weight of 3,010 g (range 2,910–3,245 g). They were all initially evaluated by single crystal echo within the first week of life, the oldest surviving five and one-half weeks. Cross-sectional echocardiograms were performed in the week before death on all infants and the inner ductus diameter was compared to postmortem measurements.

Group B

Group B consisted of 13 premature infants whose mean age at study was 2.2 days (range 22 hours–14 days). Mean weight in Group B infants was 1,557 g (range 625–1,870 g). In each, the cross-sectional echocardiogram was performed at the initial suspicion of a ductus identified by the neonatologist, either by increasing pulses, precordial activity or the presence of a murmur compatible with a ductus arteriosus. Nine of these infants with indwelling umbilical arterial catheters had ductus presence and shunting confirmed by visualization of shunting on the M-mode suprasternal contrast echo. This was also confirmed on the cross-sectional echocardiogram in real-time by saline contrast passing through the duct from the aortic end to the pulmonary artery end after descending aortic contrast injection. Two of the patients had right-to-left ductal shunting, visualized after peripheral venous contrast injections with echo contrast material passing from the duct, right-to-left, into the descending aorta. Six infants subsequently underwent operative ductal ligation because of unremitting congestive heart failure and had their ductus confirmed at surgery. Three of these infants underwent cross-sectional echocardiography in the postoperative period. As such, only one infant of the 13 did not have ductal patency verified by contrast or by surgical observation. This infant had a continuous murmur and bounding pulses at the time of his echo.

Group C

Eight older patients, with an uncomplicated ductus arteriosus (mean age 3.2 years, range 4 months–7 years) (mean weight 14.7 kg, range 3.8–23.2 kg), underwent ductal imaging by cross-sectional echocardiography on the day before cardiac catheterization to provide angiographic/echocardiographic correlations. Five of these subsequently underwent elective ductal ligations. Two patients had echo saline contrast studies performed in the catheterization laboratory for verification of ductal identification and one had a postoperative cross-sectional echo study.

Group D

Four additional infants with catheterization-proven coarctation of the aorta undergoing aortography before coarctectomy were selected for study to provide visualization of the juxtaductal area. They had a mean weight of 2.3 kg, range 1.8–3.1 kg, and were studied between 3 weeks–4½ months of age, mean age 42 days. All had spontaneously closed ductus, both by echo and by angiography, and therefore provided verification of the spontaneously closed duct.

Control Group

Cross-sectional echocardiograms were then reviewed retrospectively from 125 children (age 1 day–16 years) who had been proven angiographically not to have a ductus arteriosus. Their two-dimensional echoes had been performed before the development of our ductus examination technique and were reviewed in an attempt to identify false positives. In only 45 of these patients had the scanning procedure included visualization of the juxtaductal area, and so the comprehensively evaluated control group actually consisted of 45 patients.

Methods

Unsedated patients were studied in the supine position with a real-time cross-sectional echocardiographic system, a 30° mechanical sector scanner (the Smith Kline Ekosector 1), using a 3½ MHz or a 5 MHz transducer, both focused at 4 cm to provide maximal lateral resolution in the area of greatest in-
CROSS-SECTIONAL ECHO IN PDA/Sahn and Allen

**Figure 1.** Schematic drawing of the anatomy of the right ventricular outflow tract plane. The great arteries (aorta and pulmonary artery) are cut along the plane of the right ventricular outflow tract and viewed as if one were standing at the patient’s feet and looking at the heart from below. The orientation of the image and of all the echoes in this paper are as shown in the compass. R = right; L = left; Ant = anterior; Post = posterior; Sup = superior; Art = artery; Desc = descending.

A generous amount of airless contact gel was placed on the chest. Next, the transducer was placed lightly on the left precordium in the third intercostal space and directed along the line of the left ventricular outflow tract to scan the long axis of the aorta. The plane of scanning was gradually rotated toward the left shoulder and the transducer was tilted somewhat superiorly to scan a more superiorly directed plane along the line of the right ventricular outflow tract to image the pulmonary artery wrapping around the aorta, the distal main pulmonary artery and the bifurcation of the pulmonary artery into its right and left branches\(^1,^2\) (figs. 1 and 2). As the transducer was

**Figure 2.** Echo still frame shows imaging of the distal main pulmonary artery (MPA) and the origin of the left pulmonary artery (LPA) in a normal patient. The back wall of the pulmonary artery at the point of bifurcation is well seen. R = right; L = left; Ant = anterior; Post = posterior; PV = pulmonary valve; AO = aorta.
rotated superiorly from this position, the ductus arteriosus was most often visualized as a distal continuation of the pulmonary artery space continuing posteriorly to the echo image of the descending aorta. The duct usually continued in the curvature of the main pulmonary artery posteriorly with a gradual angle superiorly and toward the right (fig. 3). When ductal visualization was achieved, fine reject and damping controls and overall gain of the instrument were adjusted to provide minimal background noise while imaging what was felt to be the ductal endothelium and the smallest inner ductal dimension. The studies were recorded in real-time and were evaluated by two observers in real-time, in slow motion and using frame-by-frame analysis on the analog videotape recorder as well as on Super 8 mm motion picture film and Polaroid stills. Measurements of ductal size (smallest inner echo dimension) were performed using the calibration standard on the two-dimensional echo image. Little variation of ductal size with the phase of the cardiac cycle was apparent on our images. Nevertheless, all measurements were made during mid-diastole.

With regard to the mechanical sector scanner examination of premature infants, we initially approached this examination with great trepidation, since on the only previous occasion when we were forced to use this technique (a 600 g premature infant with tricuspid atresia) the mechanical sector scanner produced reddening of the infant's chest and minor abrasions on the precordium. This experience suggested that we should accomplish this examination with essentially little or no transducer contact to the infants' chest, while the weight of a light mechanical transducer was supported by the examiner's hand. As a result, no significant mechanical abrasion or vibration was transmitted to the infants during the performance of this study, with the exception of minimal reddening of the examined area after the sector scan was performed. No complications occurred.

Contrast Echocardiographic Techniques

In nine Group B premature infants, as well as two older children in the catheterization laboratory, saline contrast verification of ductal shunting was obtained by injection of saline into the descending aorta, an arterial saline contrast technique as previously described.10,16 In the premature infants, during the sector scan echocardiogram, three consecutive 1 cc boluses of sterile D5 in ¼ normal saline were hand injected rapidly into the umbilical-aortic catheter using a 5 cc syringe while the ductus was imaged at high reject, low gain and images recorded on the videotape recorder. Contrast injections were identified verbally by the word "inject" recorded on the audio channel. These sequences were then reviewed in slow motion at the bedside. After performance of the arterial saline contrast study, the catheter was pulled down into the descending aorta well below the level of the renal arteries.

In the two older patients, cardiac catheters which had been passed through the ductus into the aorta were flushed with 5 cc of sterile heparinized saline and a contrast echo similarly recorded.

Four premature infants with severe respiratory distress syndrome and cross-sectionally identified patent ductuses underwent venous saline contrast injections as well.16 In three of these patients, the venous injection was adequate (contrast eventually was visualized within the pulmonary artery).
Angiographic Techniques

Standard biplane cineangiograms were performed in the eight patients undergoing cardiac catheterization with a clinical diagnosis of patent ductus arteriosus. Seventy-six percent Renografin was injected into the juxtaductal aorta through catheters which had been passed antegradely through the ductus from the pulmonary artery and cineangiograms recorded in AP and lateral or left and right anterior oblique views. The catheter size was recorded and the catheter image through the ductus was then used for calibration to allow quantitative ductal measurements from the angiograms. Since the catheter was passing through the duct, it was subject to the same magnification as the duct itself. For measurement, ductal contours were then traced from the angiographic frames along with the catheter dimensions. The smallest inner ductal diameter was measured at the narrowest point along the ductal silhouette on either the PA, lateral or left anterior oblique angiogram, whichever showed the ductus most clearly. In the infants with coarctation (Group D), all had actually closed the ductus at the time of catheterization, as confirmed by angiography.

Surgical Observations

Because our primary interest was measuring ductal luminal diameter and because the narrowest point was often difficult to identify externally, surgical observations consisted only of verification of patency of the ductus. No other surgical grading was attempted.

Autopsy Observations

The three infants with hypoplastic left heart (Group A) and one of the infants with postoperative ligation of a ductus arteriosus who had a postoperative cross-sectional echocardiogram were examined post-mortem. The position of the ductal ligature was the only gross observation made in the premature infant after ligation. In the other three infants with hypoplastic left heart syndrome, the ductus was opened longitudinally and the length of ductal circumference was measured with a millimeter ruler at the smallest circumference. This was then divided by \( \pi \) to provide an estimate of the smallest inner ductal diameter during life.

Results

Group A: Ductal Imaging in Group A — Hypoplastic Left Heart Syndrome

It is pertinent to review the appearance of the ductus arteriosus in hypoplastic left heart syndrome, since the duct is almost always large and should be easily imaged as a distal continuation of the pulmonary artery. Figure 4 shows the echocardiographic appearance of the ductus arteriosus in one of these infants. Historically, this female baby was quite important with regard to our study of ductal imaging. After an initial evaluation where she demonstrated findings compatible with complete mitral and aortic atresia and extremely hypoplastic left ventricle by M-mode echo, she survived for three weeks. It was apparent that she was ductus-dependent for her systemic blood flow and, by definition, must have had a large patent ductus arteriosus. The identification of her ductus represented our first successful ductal imaging and suggested to us that the ductus could be visualized as a direct distal continuation of the main pulmonary artery. Ductus were imaged in all three of the infants in Group A who had hypoplastic left heart syndrome. Ductal dimensions in this group were 5 mm in two and 6 mm in the third. At autopsy, ductus dimension estimated in the three infants was 4.5 mm in one, 5 mm in the second and 6 mm in the third. No infant later requiring a ductus ligation had a ductal dimension less than 3 mm.

Group B: Ductal Imaging in Group B — Premature Infants

Of the 13 infants studied to detect ductus arteriosus, the duct could be visualized in all, with images similar to that shown in figure 3, panel B (representing large unconstricted ducts) or in figure 5, a constricted patent ductus arteriosus. Ductal diameter ranged between 1.5 mm and 4.7 mm in the premature infant group. The infants could be subcategorized, since only eight had clinically large ductus at the time of echo, based on pulmonary edema on x-rays, requirements for prolonged ventilatory support, increased left atrial diameter on M-mode echos and the requirement for digitalis and fluid restriction. Left atrial/aortic ratio for the large ducts was 1.33 ± 0.05 (SEM) compared to 1.03 ± 0.04 (SEM) in the small ducts (\( P < 0.01 \)). Mean
Constricted PDA

Ligated PDA
2 days post-op

**Figure 5.** A constricted patent ductus arteriosus (PDA) is imaged in a premature infant. The dotted line shows the area of measurement of smallest inner ductal dimension. AO = aorta; MPA = main pulmonary artery; DESC AO = descending aorta.

**Figure 6.** Inner dimension of the patent ductus arteriosus (PDA) in millimeters (abscissa) is related to left atrial/aortic ratio (LA/AO ratio) on the ordinate, both as measured on the initial echo in each of the 13 premature infants in group B. SEE = the standard error of the estimate for the regression relationship shown by the equation.

**Figure 7.** Imaging of the area of the patent ductus arteriosus (PDA) after ligation shows a decrease in ductal dimension as well as the position of the ligature. R = right; L = left; Ant = anterior; Post = posterior.
patent ductus arteriosus size was 3.9 ± 0.02 mm in the group with large ducts compared to 2.4 ± 0.02 mm in the group with small ducts (P < 0.01). However, left atrial/aortic ratio correlated poorly with patent ductus arteriosus size (r = 0.64) (fig. 6). The linear relationship in figure 6 shows much scatter and little predictive ability. Nonetheless, the extrapolation to 0 mm ductal lumen occurred at a left atrial/aortic ratio of 0.74. Six of the infants subsequently required ligation and postoperative echoes were obtained in three of these infants (fig. 7). The position of the ligature could be imaged echocardiographically in all three infants, with minimal ductal lumens proximal and distal to the point of ductal obliteration.

**Group B: Contrast Studies**

Nine of the infants had indwelling arterial catheters placed above the diaphragm at the level of T6 at the time of study. In all nine, the ductal visualizations could be verified by seeing contrast material passing from the descending aorta directly through the duct into the pulmonary artery. Four of the infants had peripheral IVs in place and had venous contrast studies performed. Contrast material initially appeared in the pulmonary artery successfully in three; and, in two, a right-to-left shunt was seen with contrast passing through the duct into the descending aorta. Both of the infants who had right-to-left shunts detected had clinically small ductus and significant hyaline membrane disease with inspirator dependency at the time of the study. Figure 8 was derived from one of the infants who had a bidirectional shunt through a small patent ductus arteriosus proven by both arterial and venous contrast studies. In figure 8, the ductus is seen in panel A followed by left-to-right filling of the ductus after an arterial contrast study (panel B). In panel C, the same image is shown after peripheral venous contrast injection filling the pulmonary artery and the ductus. In later frames, contrast appeared in the descending aorta. These two positive peripheral venous injections represent the first successful echocardiographic technique for identifying right-to-left ductal shunts. No temporal artery-descending aortic blood gas comparisons were available in the infants to document or assess the magnitude of the right-to-left shunting.

**Group C**

Ductal visualizations were achieved successfully in all eight of the older children studied before cardiac catheterization. The inner dimension of the ductus could be measured in all. Figure 9 shows the angio/echo comparison of a patient with a large un-constricted ductus arteriosus which measured ap-

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**Figure 8.** Imaging of a small ductus is visualized in panel A, left. Contrast opacification coming through the ductus and into the pulmonary artery (PA) is seen in the still frame panel B, after saline injection into the descending aorta (DESC AO). In panel C, contrast is visualized in the main pulmonary artery and in the patent ductus after peripheral venous saline contrast injection. All were derived from the same infant. R = right; L = left; Ant = anterior; Post = posterior; AO = aorta; PV = pulmonary valve; PDA = patent ductus arteriosus; LA = left atrium.
proximately 7 mm inner dimension. Figure 10 shows similar images in a patient with a constricted small patent ductus arteriosus (2.5 mm) which was minimally larger than the diameter of a 7 French catheter shown passing through it. Figure 11 shows the regression analysis of echo vs angiographic dimension and verifies that echo can quantitatively predict the smallest inner ductal dimension quite reliably \((r = 0.97)\) with minimal overestimation of the smaller ducts, as shown, suggested by the regression analysis and its intercept. We believe this minimal overestimation represents some lack of endocardial visualization because of echo dropout. Previous work from our lab suggested a similar overestimation by echo of the lumen size in supravalvar aortic stenosis.\textsuperscript{15} This potential dropout may be substantiated by the approximate 1 mm residual lumen apparent on the post-ligation echoes in Group B. Nonetheless, the experience verifies the quantitative accuracy of ductal imaging.

The two saline contrast injections during cardiac catheterization in Group C patients visualized left-to-right shunting through the ductal structure on echo.

**Group D**

Figure 12 demonstrates the visualization of the juxtaductal area of the descending aorta in an infant with coarctation showing the configuration of a proven spontaneously closed ductus and its orientation in comparison to the shelf of the coarctation coming off the back wall of the descending aorta. Images similar to this were obtained in the other three infants in this group and again verify that we are indeed imaging the spontaneously closed ductus and the juxtaductal area of the descending aorta.

**Control Group**

As stated in the Methods section, subsequent to the group specifically studied in this protocol, we reviewed cross-sectional echocardiograms, retrospectively,
from 125 children who had undergone echocardiography of the great arteries before cardiac catheterization, and who subsequently were shown on aortography or levophase angiography, if no other shunts existed, not to have a patent ductus arteriosus. In only 45 of these did the scan of the great arteries include the distal main pulmonary artery and views of the descending aorta which were suitable for assessing that the ductal area had been imaged. As such, of the 125 patients, only 45 were acceptable for this retrospective evaluation. In 10 of the 45, images suggesting a spontaneously closed ductus were obtained (all were infants under 7 months of age). In 34 of the 45 adequate examinations, no ductal structure was imaged at all. In the last of these adequate examinations, however, actual ductal patency was suggested and the examination would have been read as a blind false positive for a small patent ductus arteriosus if presented to us during the prospective study. The angiogram of the infant in question, who had a ventricular septal defect, showed a large ductus diverticulum. The aortogram of the same infant did not demonstrate a left-to-right patent ductus arteriosus; this represents the single known false positive for ductal imaging. The potential for echo dropout producing false positive examinations, and our inability to distinguish between a patent ductus arteriosus less than 1.5 mm vs a closed patent ductus arteriosus, are both problems further discussed in the next section.

Discussion

The ability to image a ductus at all rests with the lateral resolution of the instrument at the depth in question. An examination of the individual echo lines on our images suggests that in most patients, the ductal lumen continues the overall curvature of the pulmonary artery posteriorly and slightly to the right, passing around the aorta. Therefore, the ductus is oriented almost parallel to the incident sound beam. The smearing across of echoes from the bright back walls of the pulmonary artery after its bifurcation could completely obscure the ductal lumen and actually appears to do so when the gain is set too high or the reject too low. Once, having imaged the area of the ductus, echoes of the structure must be obtained at varying gain and reject in an attempt to visualize not only its outer contour but also its endothelial surfaces.

Having achieved direct ductal visualization, the present study further established the quantitative accuracy of ductal imaging techniques and the ability of the method to image both right-to-left and left-to-right ductal shunts. In closely examining the results of the ductal imaging studies in older children, it became obvious that, once again, ductal images must be obtained at varying gains and rejects in an attempt to produce the fine echoes within the ductal lumen at the very time they appear. Overdamped echoes probably demonstrate only the outer contour of the ductus because of endothelial dropout and will overestimate the angiographic size of the ductus, while underdamped studies may obscure the ductus completely. The problem of endothelial dropout caused by overdamping probably accounts for overestimation of those smaller ducts which might have been completely missed at higher gain settings. Nonetheless, in view of
the lateral resolution characteristics of the instrument in question, using a transducer focused at 4 cm, we believe that ductus lying at a depth of between 3–7 mm from the chest wall can probably be imaged with our 3.5 MHz system if they are greater than 1.5 mm in diameter. Theoretically, our present technique cannot distinguish between a lumen size of less than 1.5 mm and a completely closed duct. Dynamic focusing and higher frequencies in future instrumentation may further alleviate this resolution limitation. While wide angle (70–90°) sector scan instruments have recently become available, high line density with good line resolution over the limited juxtaductal region is required for accurate ductal imaging.

The direct but noninvasive detection of ductal patency, as demonstrated in our study, can be applied to pediatric cardiology in several important circumstances, some of which parallel the patient groups that we studied. In the older child, the presence of the duct itself probably warrants a surgical ligation.\(^1\) Many of these children with classical findings for ductus arteriosus may undergo ductal ligation without cardiac catheterization. Catheterization is then reserved for two groups of patients, those with atypical physical findings where confusion may arise between this lesion and venous hums, aortopulmonary windows or coronary arteriovenous malformations, or those patients in whom pulmonary vascular resistance must be assessed. Since older children may represent a group in which ductal imaging is at times difficult to obtain because the structure is too small and far away, the inability to detect a ductus arteriosus on echo may not clarify the situation or avoid the need for cardiac catheterization. Nonetheless, a detectable ductus imaged adequately by this method may obviate the need for a catheterization in some of these patients.

In children who have a patent ductus coexisting with other forms of congenital heart disease, the assessment of ductal patency by this technique may also be quite important. In children with large ventricular septal defects, the murmur of the ventricular septal defect may mask the associated presence of a patent ductus arteriosus. Identification of concomitant large ductus arteriosus provides the opportunity to significantly improve cardiovascular status, without cardiopulmonary bypass, by performing ductal ligation early in some of these children. At cardiac catheterization, the demonstration of the ductal shunt itself in the presence of a ventricular septal defect requires an aortogram. Aortography can most often be achieved by entering the aorta through the ventricular septal defect from the right ventricle, but occasionally, ruling out a large concomitant ductus requires a retrograde left heart study, prolonging the cardiac catheterization and entailing an added risk.\(^1\)

Other infants with cyanotic forms of congenital heart disease secondary to right ventricular inflow or outflow tract obstruction may be ductus-dependent for their pulmonary blood flow. Emergency cardiac catheterization and possibly an infusion of prostaglandin E\(_1\), if there are signs of decreasing ductal patency, are indicated for these babies.\(^\text{20}\) In these forms of cyanotic heart disease, the duct is usually a smaller structure and more tortuous in direction. Nonetheless, we have recently encountered three infants (two with pulmonary atresia and one with tricuspid atresia) in whom ductal patency could be determined by our technique. In one of these infants, the duct was imaged quite well from the suprasternal notch.\(^\text{21}\)

While the surgical mortality of bedside ductal ligation performed in the nursery in premature infants appears to be quite low, and initial reports suggest the safety of producing noninvasive ductal constriction with inhibitors of prostaglandin E\(_1\) synthetase, the success of, for instance, indomethacin administration in various reports appears to vary with patient selection.\(^\text{22}\) A reliable indicator for the selection of infants who can benefit from medical therapy or ductal closure still remains to be delineated.\(^\text{23}\) We believe that the early diagnosis of ductal patency and images of ductal contour using our technique may hold prognostic significance. Figure 13 shows inner ductal dimensions in our 13 premature infants related to their subsequent course. Ductal dimensions were measured at the time of initial study when the suspicion of a ductus first arose. As shown, the infants who later required ductal ligation had a mean ductal dimension of 4.2 ± 0.2 mm. Those who subsequently had spontaneous closure had a mean ductal dimension of 2.6 ± 0.2 mm (\(P < 0.01\)). Further, as a corollary of the difference in size, those requiring ligation appeared to have unconstricted or uniform ducts, whereas those with smaller inner duct dimensions had a duct which appeared somewhat constricted in cross-sectional visualization. No infant later requiring ligation had a ductal dimension less than 3 mm on his initial echo, and all with ductal dimensions below this had spontaneous closure of their duct detected clinically within five days.

In the face of the increasingly widespread administration of prostaglandin inhibitors to premature infants, and in view of infants in all series who have on clinical grounds experienced partial or incomplete closure or only temporary closure\(^\text{24, 25}\) after indomethacin administration, it would be important to demonstrate the actual effect on the ductus of the drug administration in serial fashion. We believe that a comprehensive approach to the evaluation of the effects of prostaglandin inhibitors, which includes direct assessment of ductal contour or size, as has recently been achieved in animals,\(^\text{26}\) is an essential precursor of the wide clinical application of these compounds in humans.

Our study has demonstrated for the first time that real-time cross-sectional echocardiography can be used to provide direct imaging of the ductus arteriosus in order to estimate its size and contour. From our study it appears that in premature infants, inner ductal dimension as well as contour on initial echo has prognostic significance which may be quite important in planning medical or surgical management. Ductus imaging alone or in combination with echo contrast techniques will be important not only for verification.
PDA IMAGING IN PREMATURE INFANTS

FIGURE 13. Individual patient values (open circles) and the group means (closed circles) ± one standard error (bars) are visualized for the six group B infants whose ducts required ligation compared to those who subsequently experienced spontaneous closure. Mean inner ductal dimensions in mm between the two groups were statistically different (P < 0.01) between the two groups. See text for discussion.

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Models of Congenital Heart Disease in Fetal Lambs

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SUMMARY Inotropic flow patterns were chronically altered by partially obstructing left ventricular (LV) inflow or outflow in midgestational fetal lambs. Physiological measurements of the fetal circulation were made serially through indwelling catheters and the use of radioactive microspheres. With LV inflow obstruction, mean LV output (LVO) decreased to 30% of control (P < 0.01). Within seven days, the LV/right ventricular (RV) weight ratio decreased to 70% of control (P < 0.01), and the mean LV/RV chamber volume decreased to less than one-half of control (P < 0.001), simulating an early form of the hypoplastic left heart syndrome. With LV outflow obstruction, mean LVO decreased to 64% of control (P < 0.05). Mean LV/RV wall thickness doubled (P < 0.0001) and mean LV/RV chamber volume decreased to less than one-half of control (P < 0.001). Within four to ten days after increasing LV afterload, a large increase in LV mass occurred, which was demonstrated by morphometric analysis to be due to hyperplasia of ventricular myocytes. LV chamber volume decreased somewhat, simulating moderately severe congenital aortic stenosis. Over the long term (30-36 days), the mean LV/RV weight ratio decreased and the LV chamber was nearly obliterated, simulating very severe congenital aortic stenosis.

The results suggest that by varying preload and afterload in both ventricles of the fetus, various forms of congenital heart disease may be simulated.

IT IS NOT KNOWN WHY the massive ventricular enlargement associated with severe congenital aortic or pulmonic stenosis cannot be duplicated experimentally in postnatal animals, nor why the structure of blood vessels is altered in fetuses with congenital heart disease. Improved understanding of early adaptation to a mechanical cardiovascular lesion should come from development of fetal animal models in which myocardial and vascular structure and function as well as circulatory reflexes can be measured. The possibility that non-genetic models of congenital heart disease could be induced in fetuses was suggested by the observations of pathologists and experimental embryologists. Lev et al. noted that the hypoplastic left heart syndrome in human fetuses is often associated with premature closure of the foramen ovale, and postulated that a decreased venous return was responsible for arrest of the left ventricle in those cases. Hahr et al. induced various forms of the hypoplastic left heart syndrome in chick embryos by obstructing flow through the left atrioventricular canal with a tiny nylon plug. Subsequently, Shapiro et al. showed that constriction of the pulmonary artery leads to marked thickening of the right ventricular (RV) wall in the fetal lamb.

We selected the fetal lamb as the experimental animal in which to attempt to induce models of congenital heart disease for several reasons. Fetal lambs and humans are similar in weight and have similar blood pressures, oxygen tensions, ventricular stroke volumes, and internal distribution of blood flows at corresponding stages of gestation. It is possible to operate on lamb fetuses without precipitating abortion, and physiological measurements of circulatory function can be made in utero for days or even weeks under normal physiological conditions through indwelling catheters.

A great deal of data has been accumulated from chronically catheterized fetal lambs concerningnor-
Real-time cross-sectional echocardiographic imaging and measurement of the patent ductus arteriosus in infants and children.
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