Isolated Ductus Arteriosus Aneurysm in the Fetus and Infant: A Multi-Institutional Experience

Umesh Dyamenahalli, MBBS, FRCPC,* Jeffrey F. Smallhorn, MBBS, FRCPC,* Tal Geva, MD,§ Jean-Claude Fouron, MD, FRCPC,¶ Patricia Cairns, MD, FRCPC,† Luc Jutras, MD, FRCPC,‡ Victoria Hughes,‡ Marlene Rabinovitch, MD, FRCPC,§ Catherine A. E. Mason,† Lisa K. Hornberger, MD, FACC†

Toronto and Montreal, Canada and Boston, Massachusetts

OBJECTIVES
The purpose of this study was to describe the clinical characteristics and outcome and to elucidate the pathogenesis of ductus arteriosus aneurysm (DAA).

BACKGROUND
Ductus arteriosus aneurysm is a rare lesion that can be associated with severe complications including thromboembolism, rupture and death.

METHOD
We reviewed the clinical records, diagnostic imaging studies and available histology of 24 cases of DAA, diagnosed postnatally (PD) in 15 and antenatally (AD) in 9 encountered in five institutions.

RESULTS
Of PD cases, 13 presented at <2 months, and all AD cases were detected incidentally after 33 weeks of gestation during a late trimester fetal ultrasound study. Of the 24, only 4 had DAA-related symptoms and 6 had associated syndromes: Marfan, Smith-Lemli-Opitz, trisomies 21 and 13 and one possible Ehlers-Danlos. Three had complications related to the DAA: thrombus extension into the pulmonary artery, spontaneous rupture, and asymptomatic cerebral infarction. Six underwent uncomplicated DAA resection for ductal patency, DAA size or extension of thrombus. In the four examined, there was histologic evidence of reduced intimal cushions in two and abnormal elastin expression in two. Five of the 24 died, with only one death due to DAA. Of 19 survivors, all but one remain clinically asymptomatic at a median follow-up of 35 months; however, two have developed other cardiac lesions that suggest Marfan syndrome. A review of 200 consecutive third trimester fetal ultrasounds suggests an incidence of DAA of 1.5%.

CONCLUSIONS
Ductus arteriosus aneurysm likely develops in the third trimester perhaps due to abnormal intimal cushion formation or elastin expression. Although it can be associated with syndromes and severe complications, many affected infants have a benign course. Given the potential for development of other cardiac lesions associated with connective tissue disease, follow-up is warranted. (J Am Coll Cardiol 2000;36:262–9) © 2000 by the American College of Cardiology

Ductus arteriosus aneurysm (DAA) is characterized by a localized saccular or tubular dilation of the ductus arteriosus. Although congenital DAA may be identified in infants, children and adults, published case reports suggest the most common age of diagnosis is less than two months (1–24). Ductus arteriosus aneurysm may be observed in patients with connective tissue abnormalities such as Marfan, Ehlers-Danlos and Larsen syndromes (2,20,21). Previous reports suggest that congenital DAA encountered postnatally may be associated with a high rate of serious complications (2,7–9,15). This probably represents presentation bias of only symptomatic patients with congenital DAA. Spontaneous rupture, erosion, thromboembolism, infection and compression of adjacent structures are some of the reported complications.

Recently, congenital DAA has been recognized in the fetus by echocardiography (18,23,24). These case reports suggest that congenital DAA may be more common than observed postnatally, with the majority of affected fetuses being asymptomatic at birth. The purpose of our study was to define the clinical presentation and outcome and to elucidate the pathogenesis of isolated congenital DAA based on our experience. We further attempted to determine the antenatal incidence by review of pregnancies undergoing third trimester fetal ultrasounds.

METHODS
We retrospectively reviewed the experience of five institutions with postnatally and antenatally diagnosed DAA. Patients were identified from the cardiac data bases of the Hospital for Sick Children, Toronto, Children’s Hospital, Boston, Sainte-Justine Hospital, Montreal Children’s Hospital, Montreal and IWK-Grace Health Center, Halifax. All cases of isolated congenital DAA without other major associated cardiac anomalies were included. Medical records, echocardiograms, chest X-rays (Fig. 1), angiograms, computerized tomography (CT) scan reports,
magnetic resonance imaging (MRI) and autopsy reports were reviewed. All available echocardiograms were reviewed by two authors (U.D., L.K.H.) to assess DAA morphology and to identify the presence or absence of thrombus associated with the DAA. The DAA size was considered the largest measurable diameter.

To determine the incidence of congenital DAA, 302 consecutive obstetrical ultrasounds, performed at >30 weeks of gestation in one of the larger antenatal imaging practices in the metropolitan Toronto area, were reviewed (P.C., V.H.). All ultrasound scans were performed for obstetrical reasons and included fetal anatomical imaging. The criteria for an antenatal diagnosis of DAA was the presence of a tortuous ductus arteriosus with a fusiform or saccular dilation that protruded leftward of the aortic arch. The diameter of the dilated portion of the ductus arteriosus had to be more than the 95th percentile of the normal cross-sectional diameter for gestational age as published by Tan et al. (25).

**Histology.** Ductal tissue was available from four patients, including three with surgical resection of DAA and one who died as a result of diaphragmatic hernia. The findings were compared with the histology of the normal ductus arteriosus from a term newborn who died of sepsis. They were examined by light microscopy after Movatpentachrome and fibronectin immunostaining. The distribution of elastin and the formation of intimal cushions were assessed qualitatively, and the intensity of immunostaining for fibronectin was judged semiquantitatively (by C.M., M.R., U.D.).

**RESULTS**

Twenty-four cases of isolated congenital DAA were identified. Fifteen were diagnosed postnatally and nine antenatally. Table 1 summarizes the clinical features, echocardiographic findings and outcome of all cases.

**Postnatal diagnosis and clinical features.** Of those postnatally diagnosed, all but one was born at full term. Ductus arteriosus aneurysm was detected in infancy by echocardiography alone in 10, echocardiography and MRI in 1, echocardiography and angiography in 1, CT and MRI in 1 and at autopsy in 2. Reasons for initial cardiac assessment included: respiratory distress, dysmorphic features, stridor, heart murmur, clinical signs of a large patent ductus arteriosus (PDA), severe perinatal hypoxia and diaphragmatic hernia.

Only four of the 15 infants had symptoms, directly or indirectly associated with the DAA. One presented at eight months (Case 8) with symptoms of a large PDA. Echocardiography demonstrated the PDA with DAA and evidence of pulmonary hypertension. Another infant (Case 10) had features suspicious of Marfan syndrome and the clinical diagnosis of a large PDA at two months. Echocardiography revealed a dilated ascending aorta, but the images were insufficient to demonstrate the DAA. After sudden demise at four months of age, autopsy revealed a ruptured DAA at the aortic end. The third patient (Case 12) had mild cyanosis and a right ventricular outflow tract systolic murmur. Echocardiography revealed a DAA with thrombus extension into the branch pulmonary arteries resulting in significant pulmonary outflow tract obstruction (Fig. 4). The last infant presented in the first week of life with stridor, a systolic murmur and a “ductal bump” on chest X-ray and had a family history of type IV Ehlers-Danlos syndrome. Echocardiography showed PDA with DAA. The infant is currently being evaluated for surgical resection of DAA and for Ehlers-Danlos.

Of the 10 available chest X-rays, six demonstrated a “ductal bump” and in one (Case 11) there was a calcified ring in the ductal area (Fig. 1).

**Antenatal diagnosis.** In nine cases, the diagnosis was made antenatally between 34 and 41 weeks (mean age 38 ± 2 [SD] weeks). Initial fetal echocardiograms were performed given the suspicion of arch anomalies in six, other intracardiac pathology in one (excluded at the time of fetal echocardiography), family history of congenital heart disease in one and maternal diabetes in one. Two had earlier fetal anatomical scans at <27 weeks, with no obvious cardiac abnormalities. All nine were born at term with no clinical evidence of significant cardiovascular abnormalities. Postnatal echocardiography was performed in all within the first week of life given the prenatal findings.

On review of 302 consecutive obstetrical ultrasound scans performed at >30 weeks of gestation, 200 had adequate images of the fetal cardiac structures. Of these, three cases fulfilled our criteria for the diagnosis of isolated DAA.

**Morphology of DAA.** By echocardiography, CT, MRI and angiography, DAA was seen as a tortuous and dilated vascular structure that protruded leftward of the aortic arch (Fig. 2 and 3). The maximum diameter of the DAA was towards the aortic end in all but the infant with pulmonary hypertension, and its diameter ranged from 8 mm to 24 mm. By color Doppler, there was swirling of blood within the aneurysm. The ductus arteriosus was patent at the time of the initial echocardiogram in 20 cases and at autopsy in 2 cases. Of the 20 with echocardiographic evidence of ductal patency, 15 had spontaneous ductus arteriosus closure at less than 20 days of age.

Thrombus formation was associated with the DAA in nine, and in seven there was no echocardiographic evidence of thrombus extension beyond the duct. In one infant, there was thrombus extension into the main and left pulmonary arteries (Fig. 4). In another, echocardiography suggested thrombus extension into the descending aorta, but this was

<table>
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<th>Abbreviations and Acronyms</th>
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<tr>
<td>CT = computerized tomography</td>
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<td>DAA = ductus arteriosus aneurysm</td>
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<td>MRI = magnetic resonance imaging</td>
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<td>PDA = patent ductus arteriosus</td>
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excluded by MRI (Fig. 5). One neonate with a normal neurological examination and thrombus in the DAA had a head CT scan to look for evidence of thromboembolism. This study revealed an area of cerebral infarction.

Management and outcome. Seven of the 24 cases of DAA underwent surgery. In one case, diagnostic exploratory surgery was performed without DAA resection due to uncertainty of the nature of the “pulsatile mass.” Further cardiac imaging after the exploratory surgery confirmed the diagnosis of a thrombosed and calcified DAA. Six patients underwent surgical resection of the DAA for large DAA size in three (≥10 mm), suspected thrombus in two and a hemodynamically significant PDA with pulmonary hypertension in one. In five cases the surgery was performed through a median sternotomy on cardiopulmonary bypass, and in one case the approach was through a lateral thoracotomy with no perioperative complications.

Among the 24 cases of DAA, there were five deaths, with only one related to the DAA (spontaneous rupture). Median follow-up of the 19 surviving patients was 35 months with a range of 14 weeks to 11 years and a mean of 44.6 months. Eighteen survivors are currently asymptomatic, including the six who underwent surgical resection. The patient who was diagnosed at eight months (Case 8) has

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Table 1. Summary of Postnatally and Antenatally Diagnosed DAA

<table>
<thead>
<tr>
<th>Case</th>
<th>Gender</th>
<th>Age at Diagnosis</th>
<th>Clinical Features and CXR Findings</th>
<th>DAA Size (mm)</th>
<th>Initial Echo Findings in Addition to DAA</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>2 days</td>
<td>Trisomy 13, respiratory distress</td>
<td>12.5</td>
<td>PDA, mildly dysplastic MV/TV, no thrombus</td>
<td>Pericardial effusion with severe bronchiolitis at 5 yrs. Died of RV perforation during pericardiocentesis</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>1 day</td>
<td>Respiratory distress, meconium aspiration, CXR “ductus bump”</td>
<td>10.3</td>
<td>PDA</td>
<td>Spontaneous PDA closure at 5 days, surgical DAA resection at 14 days, no thrombus at surgery, asymptomatic at 25 months</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>1 day</td>
<td>Trisomy 21, respiratory distress</td>
<td>10.4</td>
<td>PDA with thrombus</td>
<td>Spontaneous PDA closure at 1 week, asymptomatic at 6 yrs</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>1 day</td>
<td>Respiratory distress, CXR- “ductus bump”</td>
<td>12.2</td>
<td>PDA</td>
<td>Spontaneous PDA closure at 20 days, asymptomatic at 3 yrs</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>12 days</td>
<td>Born at 33 weeks, Smith-Lemli-Opitz syndrome, murmur and respiratory distress</td>
<td>9</td>
<td>Closed PDA with thrombus</td>
<td>Died of multiple respiratory and gastrointestinal problems at 2 yrs</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>2 days</td>
<td>Murmur</td>
<td>15</td>
<td>PDA</td>
<td>Surgical resection at 4 days, asymptomatic at 11.5 yrs</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>1 day</td>
<td>Marfan and complex 1 deficiency, respiratory distress, CXR-“ductus bump”</td>
<td>11</td>
<td>PDA mild MV/TV prolapse</td>
<td>Spontaneous PDA closure at 4 days, echo at 7 yrs showed features of HCM and aortic root dilation to 4.43 cm</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>8 months</td>
<td>Failure to thrive, respiratory distress and pulmonary hypertension, CXR-“ductus bump”</td>
<td>20</td>
<td>PDA, maximum diameter at PA end, large ASD</td>
<td>DAA resection at 8 months, ASD closed at 2 yrs, echo at 10.5 yrs showed MV prolapse and aortic root dilation: Marfan variant</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>3 days</td>
<td>Severe birth asphyxia with demise</td>
<td>13</td>
<td>No echocardiogram performed</td>
<td>Autopsy revealed congenital DAA, no thrombus</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>2 months</td>
<td>Dysmorphic, PDA murmur, CXR-“ductus bump”</td>
<td>8</td>
<td>Dilated aortic root, PDA missed</td>
<td>Marfan syndrome, sudden cardiac arrest at 4 months, autopsy showed rupture of DAA at aortic end, and MV, TV prolapse</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>2 weeks</td>
<td>Respiratory distress, CXR- “Calcified mass”</td>
<td>N/A</td>
<td>“Normal”</td>
<td>“Pulsatile” mass on surgical exploration at 4 days, CT and MRI confirmed thrombosed DAA with calcified ductal wall; head CT revealed area of infarction, asymptomatic at 6.5 yrs</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>11 days</td>
<td>Cyanosis, RV outflow tract murmur</td>
<td>10</td>
<td>PDA, large thrombus with extension into MPA and LPA</td>
<td>Surgical resection of DAA and thrombus at 12 days, asymptomatic at 2 months</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>1 day</td>
<td>Severe perinatal hypoxia, pulmonary hypertension CXR-“ductus bump”</td>
<td>13</td>
<td>PDA with no thrombus</td>
<td>At 7 days thrombus in PDA; at 14 days PDA closed with thrombus confined to DAA</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>3 days</td>
<td>Stridor, murmur, F/H type 4 Ehler-Danlos syndrome, CXR: “ductus bump”</td>
<td>15</td>
<td>PDA</td>
<td>At 14 weeks, PDA, thrombus within DAA. Undergoing further assessment for DAA resection</td>
</tr>
<tr>
<td>15</td>
<td>M</td>
<td>2 days</td>
<td>Left diaphragmatic hernia, dysmorphic</td>
<td>15</td>
<td>PDA</td>
<td>Died of severe lung hypoplasia</td>
</tr>
</tbody>
</table>

(continued on next page)
developed dilation of the ascending aorta and mitral valve prolapse nearly 11 years after the initial diagnosis. Genetic assessment has suggested the possibility of Marfan syndrome. The only symptomatic patient is one with Marfan syndrome and complex one deficiency (Case 7). This child has developed echocardiographic evidence of hypertrophic cardiomyopathy and dilation of the ascending aorta seven years after the initial diagnosis of DAA.

Histology. Histologic features are shown in Table 2 and Figure 6. In one case there was complete absence of the intimal cushions, but the elastic laminae were normal. In the second, the intimal cushions were deficient, and, while the internal elastic lamina was intact, there was abnormal accumulation of glycosaminoglycans in the inner media. In the third case there were normal intimal cushions; however, the elastic laminae were fragmented and highly disorganized. Similarly, in the fourth case there were normal intimal cushions, but there was minimal elastin, which was highly disorganized. By immunostaining, fibronectin expression was decreased or absent in three cases and normal in one case of DAA compared with the control ductus arteriosus.

DISCUSSION

This report characterizes the morphology of congenital DAA and the clinical outcome of 24 affected patients who were diagnosed either before or after birth. Although DAA may be associated with symptoms secondary to ductal patency, compression of adjacent structures, erosion into airways and thrombus extension (2,4,6–20), in our series only 16% had symptoms related to the DAA at presentation. In most patients, the DAA was an incidental finding at the time of cardiac assessment. Interestingly, 6 of the 24 cases (25%) had chromosomal anomalies or syndromes. The association of trisomy 21, 13 or Smith–Lemli–Opitz syndrome with DAA has not been previously described. Three

Table 1. Continued

<table>
<thead>
<tr>
<th>Case</th>
<th>Gender</th>
<th>Fetal Diagnosis (Weeks)</th>
<th>DAA Size (mm)</th>
<th>Postnatal Echo</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>M</td>
<td>38</td>
<td>20</td>
<td>PDA with DAA at 1 day</td>
<td>Surgical resection at 3 days, asymptomatic at 25 months</td>
</tr>
<tr>
<td>17</td>
<td>M</td>
<td>40</td>
<td>14</td>
<td>PDA with DAA at 1 day</td>
<td>At 14 days revealed large thrombus in closed PDA, asymptomatic at 19 months</td>
</tr>
<tr>
<td>18</td>
<td>M</td>
<td>38</td>
<td>11</td>
<td>Closed DAA with thrombus at 8 days</td>
<td>Asymptomatic at 3 yrs</td>
</tr>
<tr>
<td>19</td>
<td>M</td>
<td>37</td>
<td>9.2</td>
<td>PDA with DAA at 1 day</td>
<td>At 1 month showed no PDA with thrombus in DAA, asymptomatic at 3.9 yrs</td>
</tr>
<tr>
<td>20</td>
<td>M</td>
<td>34</td>
<td>9.6</td>
<td>PDA, no thrombus at 1 day</td>
<td>Normal fetal ultrasound at 26 weeks; spontaneous closure of PDA by 7 days, asymptomatic at 3 yrs</td>
</tr>
<tr>
<td>21</td>
<td>F</td>
<td>40</td>
<td>9.6</td>
<td>PDA, no thrombus at 2 days</td>
<td>Spontaneous closure of PDA without thrombus by 21 days, asymptomatic at 25 months</td>
</tr>
<tr>
<td>22</td>
<td>M</td>
<td>41</td>
<td>24</td>
<td>Thrombus in DAA at 1, 3, 5 and 23 days</td>
<td>Surgical resection of DAA at 10 weeks for suspected thrombus extension into descending aorta, asymptomatic at 12 months</td>
</tr>
<tr>
<td>23</td>
<td>M</td>
<td>36</td>
<td>8.2</td>
<td>Closed DAA at 2 days</td>
<td>Asymptomatic at 3 months</td>
</tr>
<tr>
<td>24</td>
<td>M</td>
<td>41</td>
<td>10</td>
<td>Closed DAA at 9 days</td>
<td>Normal fetal ultrasound at 18 weeks; asymptomatic at 4 months</td>
</tr>
</tbody>
</table>

ASD = atrial septal defect; CT = computerized tomography; CXR = chest X-ray; DAA = ductus arteriosus aneurysm; F = female; F/H = family history; HCM = hypertrophic cardiomyopathy; LPA = left pulmonary artery; M = male; MPA = main pulmonary artery; mm = millimeter; MRI = magnetic resonant imaging; MV = mitral valve; N/A = not available; PA = pulmonary artery; PDA = patent ductus arteriosus; RV = right ventricle; TV = tricuspid valve.

Figure 1. Left, Chest X-ray performed in a one-day-old newborn (Case 15), which reveals a rounded soft tissue shadow, the so-called “ductal bump” (arrow), in the upper left mediastinum. Right, A calcified mass can be seen in the ductal area (arrow) of another newborn with DAA (Case 11). DAA = ductus arteriosus aneurysm.
(13%) (and possibly a fourth) had an associated connective tissue disorder.

Echocardiography was the primary modality used to demonstrate DAA anatomy. However, at least in one case, echocardiography erroneously led us to suspect the presence of a thrombus extending from the DAA to the distal arch. As such, if extension of thrombus into adjacent vascular structures cannot be excluded, or if there is clinical evidence of compression of extravascular structures, alternative imaging in the form of MRI or CT scan should be considered.

Incidence. Several earlier reports have attempted to define the incidence of DAA. Thore (3) found DAA in eight cases out of 1,000 newborn autopsies. Heikkinen et al. (4) in their retrospective review of chest X-rays of newborns with respiratory distress, found a “ductal bump” in 1% of patients.

As most newborns with DAA have spontaneous closure of the ductus arteriosus early in life, the DAA may no longer be obvious by chest radiography, echocardiography or at autopsy. As such, the true incidence may be underestimated by reviewing a neonatal population only. Our pilot review of 200 fetal ultrasound studies performed at >30 weeks suggested an incidence of 1.5%. Based on this observation, we believe congenital DAA is more common than previously reported; however, most affected infants are asymptomatic, and, therefore, the DAA remains undetected.

Outcome and management. It is clear from the literature and from our series that DAA can be associated with lethal complications. To avoid such complications, a few of the patients in our series underwent successful resection with no perioperative complications. This is in contrast to a previous

Figure 2. Left, Postnatal two-dimensional echocardiogram in a newborn (case 13), which shows saccular dilation of the ductus arteriosus to the left of the main pulmonary artery. Right, Color Doppler shows left to right shunting through a constricted pulmonary end of the PDA. DAA = ductus arteriosus aneurysm; PA = main pulmonary artery; PDA = patent ductus arteriosus.

Figure 3. A, Echocardiogram obtained in a sagittal plane in a 38 week fetus, which demonstrates a large DAA with a tortuous course. B, Aortic arch view in the same fetus, which shows normal morphology of the distal aortic arch. DAA = ductus arteriosus aneurysm; dAo = descending aorta.
report that suggested an operative mortality as high as 25% (2). As this report represents a retrospective review, the indications for surgery, however, remain unclear. With respect to DAA size and the risk of spontaneous rupture, in fact, the DAA diameter in the infant with spontaneous rupture was only 8 mm. This would suggest that size, in and of itself, should not be the only guide for operation. The coexistence of a connective tissue disorder and DAA likely placed this infant at higher risk for spontaneous rupture. We elected to operate on patients with larger DAA diameter with the assumption that these infants were at higher risk for thromboembolism as well as rupture. In these patients, surgical intervention may have thwarted serious complications associated with DAA. Given our experience and perusal of literature, one might consider surgical resection if any of the following conditions existed: 1) a PDA and DAA beyond the newborn period, 2) an associated connective tissue disorder, 3) a thrombus within the DAA with extension to adjacent vessels, 4) evidence of thromboembolism, or 5) functional compromise of adjacent structures due to pressure effect. Surgical resection on cardiopulmonary bypass may permit adequate excision of the aneurysmal tissue. We believe simple surgical ligation of a PDA with DAA is contraindicated given the likelihood of inadequate discontinuation of the flow and the risk of sudden rupture both intraoperatively and long-term.

From this series, the majority of affected infants are asymptomatic at follow-up even without intervention. Given the relatively short duration of follow-up, at least some of the infants in our series may ultimately develop cardiovascular evidence of connective tissue disease. Follow-up as such may be warranted clinically and would provide further information about the natural history of the lesion.

Pathogenesis. Several theories concerning the pathogenesis of congenital DAA have been proposed. Delayed closure of the aortic end of the ductus arteriosus, which could result in exposure of the ductal wall to systemic pressure, is thought to be one reason for DAA formation (2); however, this does not explain the antenatal development of DAA. Congenital weakening of the ductal wall has been proposed as an etiology and supported by histologic changes such as

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**Figure 4.** Left, Two-dimensional echocardiogram, which demonstrates a large thrombus within the DAA with extension into main pulmonary artery (Case 12). Right, The parasternal short-axis view shows extension of the thrombus into the branch pulmonary arteries with near total occlusion of the LPA. Ao = aorta; DAA = ductus arteriosus aneurysm; LPA = left pulmonary artery; PA = main pulmonary artery; RPA = right pulmonary artery.

**Figure 5.** A, Spin echo MRI in the oblique sagittal plane, which shows the aortic arch and the neck of the aneurysm (An) at the aortic end of the duct (Case 19). B, An image in the same orientation, 1 cm leftward, shows the aneurysm superior and posterior to the left pulmonary artery (LPA). Ao = aorta; MRI = magnetic resonance imaging.
cytolytic necrotic and mucoid degeneration of the tissue; however, these changes may be observed in the normal closing ductus arteriosus (26,27). It has also been suggested that abnormal elastin fibers in connective tissue disorders could lead to weakening of the ductal wall (21).

In nearly a decade practice of fetal echocardiography, we found DAA to be present only in third trimester fetuses. Beginning in the third trimester, as observed in both the human fetus (26,27) and fetal lambs (28–30), intimal cushions form in the ductus arteriosus in preparation for postnatal closure. They form as a result of smooth muscle cell proliferation and migration into the subendothelium. Increased endothelial production of the glycosaminoglycans, hyaluronan, chondroitin sulphate and smooth muscle cell production of fibronectin, as well as impaired elastin fiber assembly, are critical for smooth muscle cell migration (28,30,31). We suspect that, in at least some cases, DAA may be the result of a reduced intimal cushion formation or abnormal deposition of elastin, which could result in weakening of the vessel wall. Concomitant exposure to an increased arterial pressure, which occurs in the third trimester (32), may also contribute. Infants with connective tissue disorders in whom there is either defective fibrillin (Marfan syndrome) or collagen (Ehlers-Danlos syndrome) would be predisposed to the development of DAA. Decreased fibronectin expression was associated with impaired intimal cushion formation in two of the four cases, which is consistent with the role of this glycoprotein in directing smooth muscle cell migration. In the third and fourth cases, where intimal cushions had formed, peptides from the disorganized and fragmented elastin may have provided chemotactic signals, facilitating smooth muscle cell migration in the absence of high levels of fibronectin.

Conclusions. Ductus arteriosus aneurysm likely develops in the third trimester and may be the result of abnormal intimal cushion formation or defective elastin in the ductus arteriosus. Although DAA can be associated with syndromes and severe complications, many affected infants have a benign early course. Given the potential for development of other cardiac lesions associated with connective tissue diseases, however, continued follow-up of affected infants may be warranted.

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Reprint requests and correspondence: Dr. Lisa K. Hornberger, Division of Cardiology, the Hospital for Sick Children, Toronto, Ontario, Canada, M5G 1X8. E-mail: hornberg@sickkids.on.ca.
REFERENCES