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The persistently patent arterial duct in the premature infant

AA Karatza,[*] DV Azzopardi,[**] and HM Gardiner[***]

[*]*Research Fellow, Division of Paediatrics, Obstetrics and Gynaecology, Imperial College School of Medicine, London, UK*

[**]*Senior Lecturer/Consultant in Neonatology, Division of Paediatrics, Obstetrics and Gynaecology, Imperial College School of Medicine, London, UK*

[***]*Senior Lecturer/Consultant in Perinatal Cardiology, Division of Paediatrics, Obstetrics and Gynaecology, Imperial College School of Medicine, London, UK*

Contact information: Dr Helena Maria Gardiner, Senior Lecturer and Consultant in Perinatal Cardiology, Imperial College School of Medicine, Ducane Road - W12 ONN - UK Tel: +44-20-7351-8179 Fax: +44-20-7351-8179 ; Email: gelena.gardiner@ic.ac.uk

Abstract

The presence of a persistently patent arterial duct is common in premature neonates and may be associated with high morbidity. Early accurate diagnosis, assessment of the significance of the left to right shunt and prompt treatment are required to improve the outcome in this infant population.

MeSH: Ductus Arteriosus, Patent, Infant, Premature, Echocardiography, transthoracic, Prostaglandins, Prostaglandin antagonists, Indomethacin

The arterial duct is a vascular structure found in all normal fetuses. It is a continuation of the pulmonary trunk to the descending aorta with variable insertion, but most commonly opposite to the origin of the left subclavian artery. Right ventricular output preferentially flows along this low impedance circulation rather than through the higher impedance pulmonary circulation toward the descending aorta and back to the placenta.

The patency of the arterial duct is ensured by the low oxygen content of fetal blood and the vasodilating action of the prostaglandins but is less sensitive (mainly prostaglandin E2), to those that are produced locally in the wall of the duct.[1] After birth the lungs expand, the oxygen content of the blood raises and the lung prostaglandin catabolism is enhanced. Both contribute to normal ductal constriction and closure. The arterial duct closes functionally within the first 96 hours after birth in healthy term and preterm infants,[2] whilst its anatomical closure takes place over a few weeks.

The duct of the premature infant is more sensitive to the vasodilating action of the prostaglandins, but is less sensitive to the normal rise of partial pressure of oxygen that takes place after birth. This phenomenon depends on the gestational age of the

infant. The more immature the infant is the higher the partial pressure of oxygen that is required to initiate ductal constriction.[3] In preterm baboons ductal muscular constriction produces less local tissue hypoxia, therefore permanent sealing of the lumen is delayed.[4]

It is normal for preterm infants to have a patent arterial duct, but it is the degree of shunting through it that contributes to the morbidity (necrotising enterocolitis, hypotension) that is seen. However after birth, because the pulmonary vascular resistance remains relatively high, there is no significant left to right flow through the duct. Subsequently, as the pulmonary resistance falls, shunting may occur from left to right, from aorta to pulmonary artery.

During the last years more premature infants survive. The additional use of surfactant in these infants improves lung compliance and leads to a rapid fall in pulmonary resistance. This favours earlier left to right shunting through the anatomically open duct.[5] The incidence of patent arterial duct in sick premature neonates is inversely related to birth weight and varies according to the population studied and the diagnostic criteria used. In singleton infants born at 24-34 weeks and were exposed antenatally to a single or multiple doses of gluccocorticosteroids the incidence of medically treated patent arterial duct is 20% and 13% respectively.[6]

Pathophysiology

Blood flows from the descending aorta to the pulmonary trunk through the patent arterial duct. This leads to high pulmonary blood flow, high venous return to the left atrium and finally volume loading of the left heart. This causes dilation of the left atrium and ventricle and can lead to congestive heart failure due to the reduced myocardial reserves of the premature infant. As left atrial pressure increases, left to right shunting occurs at the atrial level through the patent oval foramen, which may reduce left heart volume loading.

Clinical picture

The following clinical signs of hyperdynamic circulation accompany the presence of a haemodynamically significant arterial duct:

- The pathognomonic continuous machinery-like murmur of the patent arterial duct described in older infants and children is often not present. Most frequently a high parasternal systolic murmur is found on examination. No murmur may be heard on auscultation, in very immature neonates, especially when the duct is very large - the so-called “silent duct”.[7] The murmur may be intermittent for several days depending on the oxygenation status of the infant.
- Hyperdynamic precordium, because of volume loading of the left heart.
- Bounding pulses in the peripheral arteries.

Non-specific signs of left to right shunt and heart failure include

- The rumbling diastolic murmur of increased mitral flow
- Rhales on the auscultation of the lungs
- Liver enlargement in the presence of heart failure

- Reduction of both systolic and diastolic blood pressure. High pulse pressure difference due to lowering of the peripheral resistance and diastolic blood pressure is more common in older infants and children.[8]

Indirect clinical signs include

- Failure to show improvement in respiratory status at a certain postnatal age
- Respiratory instability and swinging in ventilatory requirements
- Increase in oxygen requirement and carbon dioxide retention
- Tachycardia and tachypnea
- Bradycardias and apnoeas
- Extreme sensitivity in small increases in fluid and sodium supplementation

Diagnosis

The electrocardiogram is not helpful. With sustained left to right shunting it may show signs of left ventricular hypertrophy and left atrial enlargement. The chest X-Ray may show enlarged cardiac silhouette and lung congestion. Echocardiography is the milestone of diagnosis, as it is more precise and accurate than clinical signs alone.[9] It is also useful to evaluate myocardial function and exclude coexistent congenital heart disease. Cardiac catheterization is nowadays never done, considering the accuracy of diagnosis provided by echocardiography.

Echocardiographic diagnosis

The duct can be directly visualized using the “duct shot”, which is a modified high left parasternal short axis view of the heart on cross-sectional echocardiography.
The flow through the duct into the pulmonary trunk and from the aortic insertion can be identified using color flow mapping. The minimal diameter of the color flow jet has been used as a surrogate for the assessment of ductal shunting.[10]
In cases when the flow through the arterial duct cannot be directly recorded, the presence of disturbance of flow in the pulmonary artery on color or pulsed wave Doppler may be identified more easily.
The following echocardiographic findings accompany the presence of a significant left to right shunt through a patent arterial duct:[11]

1. **Left atrial and ventricular dilation**
2. **Bowing of the oval foramen flap to the right and additional left to right shunt at the atrial level**
3. **Left atrium (in systole)/aorta (in diastole) ratio greater than 1.5:1, signifying a significant left to right shunt with left heart volume loading.**
4. **Reversal of flow in the descending aorta on Pulsed Doppler with the sample volume positioned distally to the origin of the duct**
5. **Minimal diameter of ductal color flow jet more than 1.5mm**

The direction of flow through the patent arterial duct depends upon the pressure gradient between pulmonary trunk and aorta. When pulmonary and systemic pressures are approximately equal, the flow becomes bi-directional. It occurs from right to left in systole and from left to right in diastole. When pulmonary pressure is suprasystemic shunting occurs from pulmonary artery to aorta throughout the cardiac

cycle. This is rare in the acute phase of hyaline membrane disease,[13] while it is a common echocardiographic finding in severe neonatal Pulmonary Hypertension caused by meconium aspiration, congenital diaphragmatic hernia or septicemia.[14]

Conditions to be considered

1. Duct dependent lesions
Right sided

- Severe pulmonary stenosis
- Pulmonary atresia/ventricular septal defect
- Absent right connection (tricuspid atresia)

Left sided

- Aortic stenosis or atresia
- Mitral stenosis or atresia

2. Left to right shunts

- Vein of Gallen aneurysm with large left to right shunt and right heart volume overloading
- Coronary arteriovenous fistula with pulmonary atresia/ventricular septal defect
- Aortopulmonary window (rarely)

3. Aggravation of chronic lung disease

Complications

The presence of a significant left to right shunt through a patent arterial duct may interfere with systemic organ perfusion[15] because of a reduction or absence of end-diastolic flow. The consequences are inadequate blood flow to the central nervous system,[16] the kidneys and the gastrointestinal tract[15] and therefore increased risk for intraventricular haemorrhage, renal dysfunction, aggravation of heart failure and necrotising enterocolitis. In contrast, the lungs are overperfused, which is associated with a higher incidence of pulmonary haemorrhage[17] and is considered a risk factor for bronchopulmonary dysplasia.[18]

Treatment

This includes:

1. Moderate fluid restriction
2. Adequate tissue oxygenation using the appropriate ventilatory support
3. Maintenance of a satisfactory haemoglobin level
4. Cautious use of diuretics
5. Provision of adequate nutrient supplementation
6. Careful enteral feeding preferably using maternal breast milk

Specific pharmacologic treatment

The drug that is used almost exclusively is indomethacin, which is a potent inhibitor of prostaglandin synthesis. Indomethacin has been used prophylactically in the first hours after birth.[19] The usual approach is the administration of Indomethacin either after the infant develops any clinical sign consistent with a patent arterial duct, usually a murmur (early symptomatic) or when the infant starts to show signs of cardiovascular compromise (late symptomatic).[20] In extremely premature infants clinical deterioration often precedes the presence of a murmur. The development of a murmur may indicate a small closing duct and is not an indication for treatment.

There are several protocols of indomethacin administration. A more prolonged course of six doses does not produce more side effects and has lower relapse rate.[21] After completion of the dose schedule the duct may reopen[22] and then a second therapeutic trial of indomethacin may be attempted. Indomethacin is ineffective for the closure of the patent arterial duct in infants of advanced postnatal age.[23] The duct of the term neonate is not sensitive in prostaglandins and therefore Indomethacin is not given in term infants with patent arterial duct.

Ibuprofen is another potent inhibitor of Prostaglandin synthesis that has been used in premature infants. It is considered as efficacious as indomethacin and has been shown to have fewer renal side effects.[24] While indomethacin administration causes reduction of cerebral blood flow, cerebral blood volume and cerebral oxygen delivery as assessed by near infrared spectroscopy, ibuprofen has no adverse effects on cerebral haemodynamics and may play a protective role against the development of cerebral injury in preterm infants with patent arterial duct.[25] The side effects of Indomethacin include renal dysfunction[26] with sodium and fluid retention, impairment of platelet aggregation and neutrophil function and gastrointestinal haemorhage or perforation.[27]

Surgical treatment

In cases of indomethacin failure, contraindication or discontinuation because of severe adverse effects, surgical closure of a haemodynamically significant duct should be considered. In neonates the usual technique is duct ligation using a transthoracic or thoracoscopic approach.[28] The transdermal closure of a patent arterial duct via an occluding device is a popular procedure for older children and adults but is still rarely considered in neonates[29] due to its potential to harm the small femoral artery.[30] The surgical closure of a patent arterial duct can be accomplished with minimal mortality in the neonatal period.

Maintenance of ductal patency

The maintenance of the patency of the ductus arteriosus may be crucial when considering neonates with certain types of congenital heart disease, in which the flow through the duct is the only way to support systemic or pulmonary circulation.[31] After birth despite the deficient arterial oxygenation the arterial duct constricts and this causes rapid deterioration and severe cyanosis. Continuous infusion of Prostaglandin E1 or E2 maintains ductal patency until the infant is transported safely to a cardiothoracic unit for reparative or palliative surgery. Examples of such congenital heart disease are cyanotic lesions (transposition complexes, critical pulmonary stenosis or atresia, Tetralogy of Fallot, tricuspid atresia) or certain critical forms of left ventricular outflow obstruction (coarctation of the aorta, interruption of the aortic arch, hypoplastic left heart syndrome).

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Figure 1 The “ice-hockey stick” appearance of the ductal arch in a 20-week normal fetus

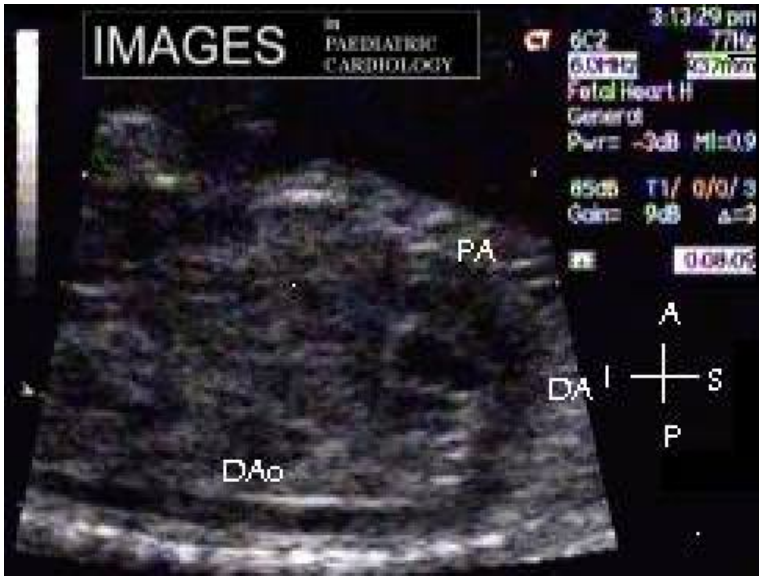


Figure 2 The “3 vessel view” in a 20-week fetus. The ascending aorta, the arterial duct and the superior caval vein are seen via a high mediastinal transverse cut

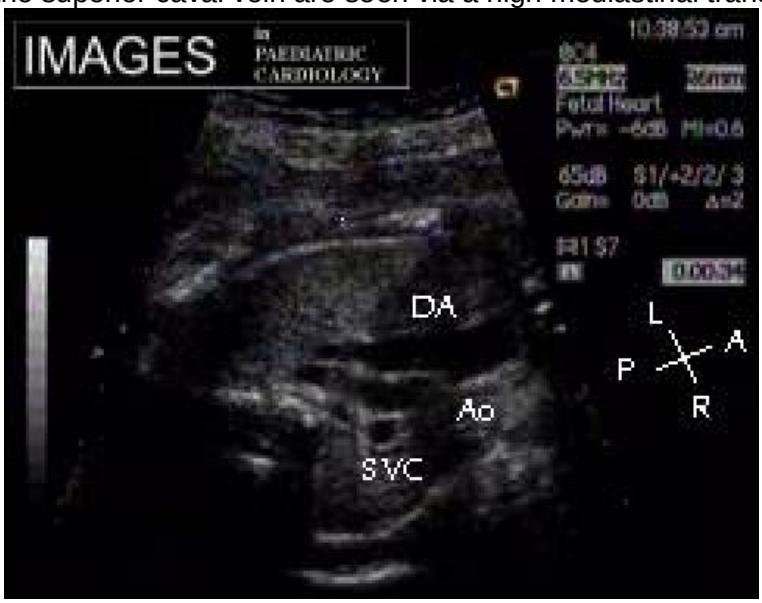


Figure 3 Magnetic resonance imaging of the thorax showing a very large patent arterial duct in the same infant. The image is equivalent to the “3 vessel view” seen on fetal echocardiography (figure 2 above)

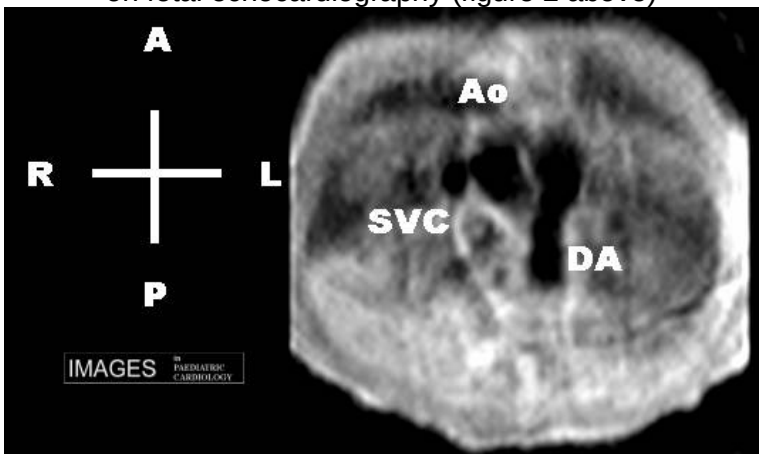


Figure 4 Pulsed wave Doppler of the arterial duct in a normal 20-week fetus

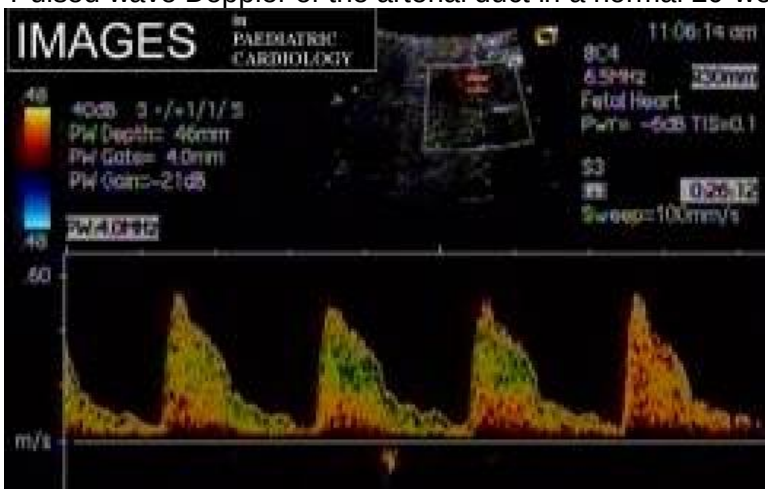


Figure 7 When the arterial duct is widely patent and unrestrictive the whole ductal arch, as present in fetal life, may be seen on subcostal short axis view

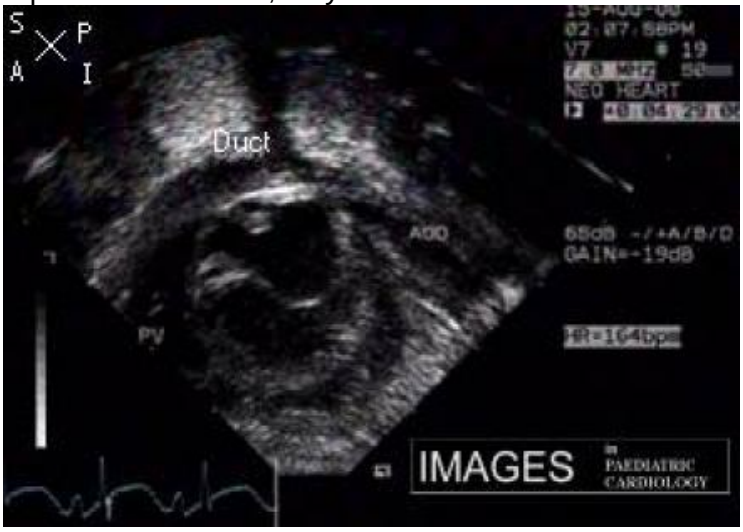


Figure 9 The “3-legged stool” view illustrates the right and left pulmonary branch arteries and the arterial duct seen from a high left parasternal short axis view (the “ductal cut”)

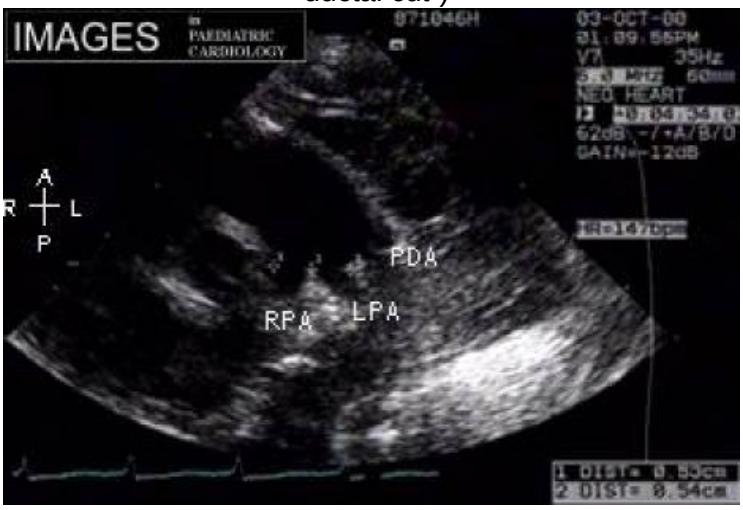


Figure 11 Normal pulsed wave Doppler of pulmonary artery at the valvular level. The flow is laminar and less than 1 m/s

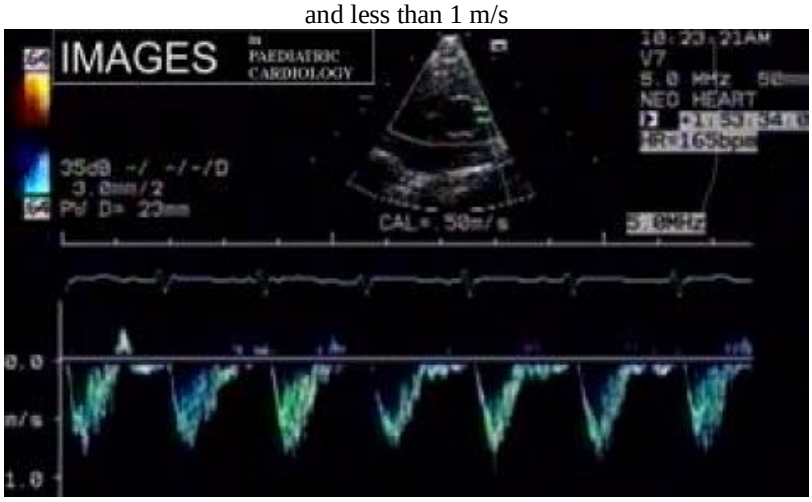


Figure 12 Pulsed wave Doppler of the pulmonary trunk showing a chaotic pattern. The disturbance of flow in diastole is due to the haemodynamically significant duct shunting from left to right

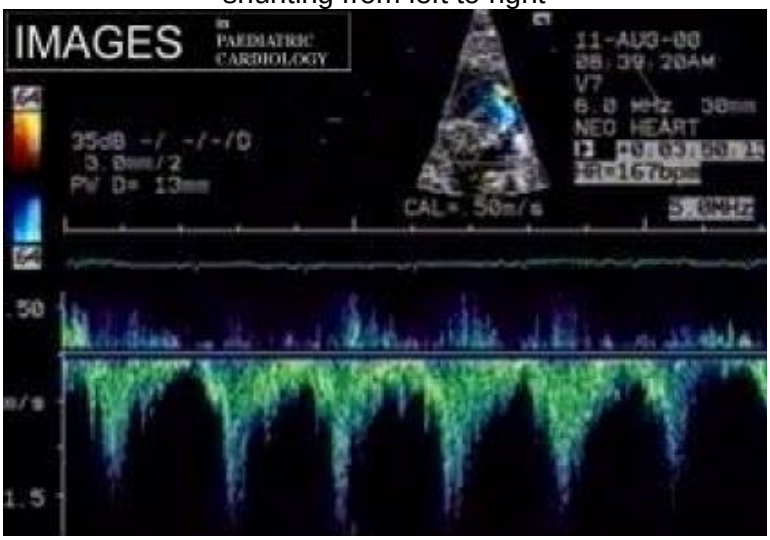


Figure 13 Pulsed wave Doppler of the arterial duct at a velocity of 2.65m/s in systole. Flow is from left to right throughout the cardiac cycle

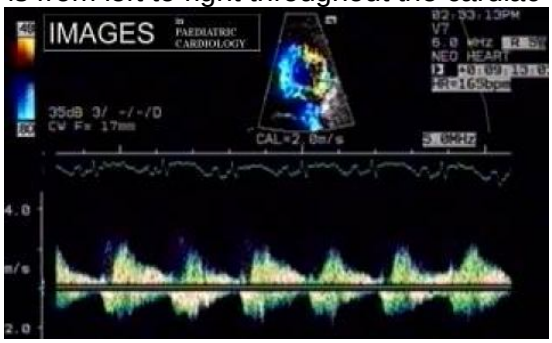


Figure 14 Apical 4-chamber view showing left heart dilatation and bowing of the oval foramen flap to the right

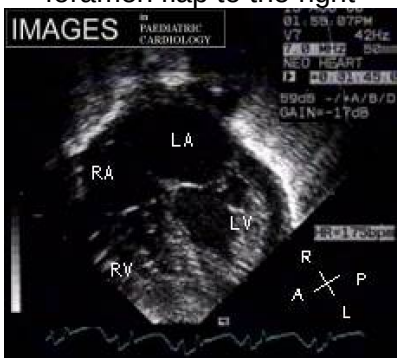


Figure 15 Parasternal long axis view of the heart in the same infant showing left atrial and ventricular dilation - the left atrial antero-posterior dimensions are greater than the aortic root dimensions

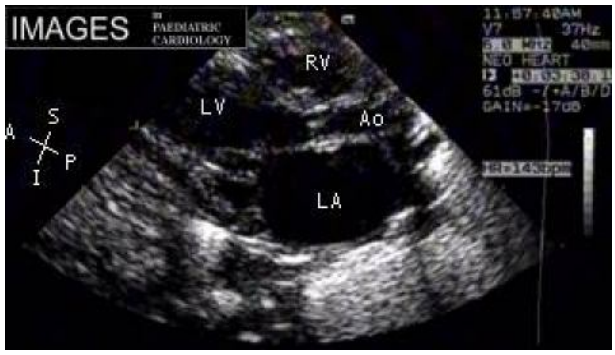


Figure 16 Magnetic resonance imaging of the thorax showing left heart volume loading in a premature infant with a significant shunt through the arterial duct

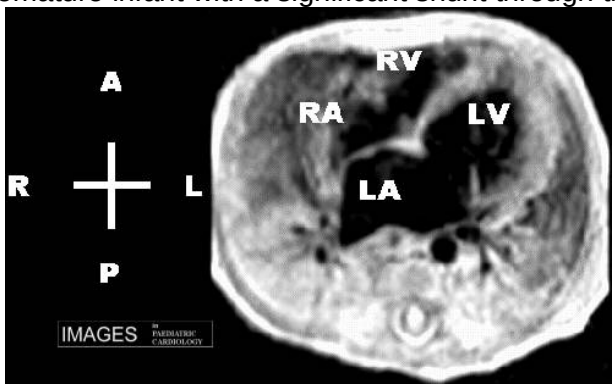


Figure 17 M-mode through left atrium and aortic valve on left parasternal long axis

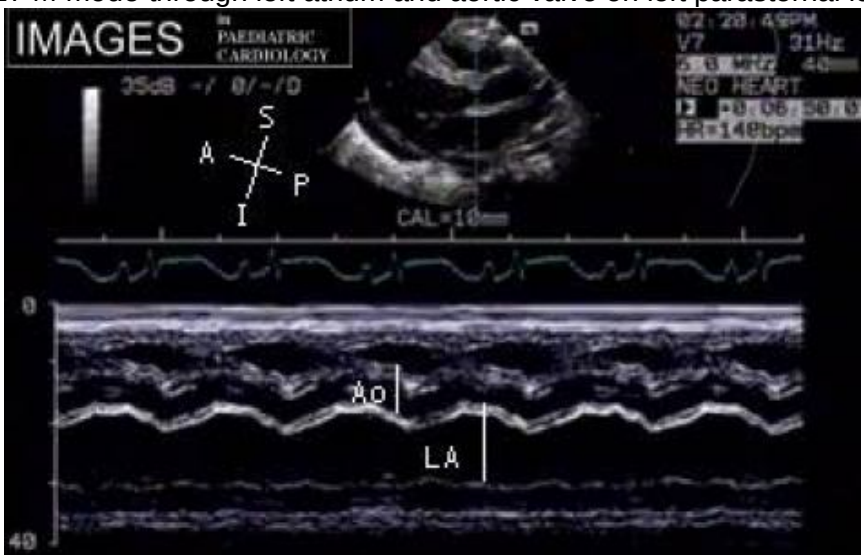


Figure 18 M-mode in the short axis in the same infant as in figure17 on right

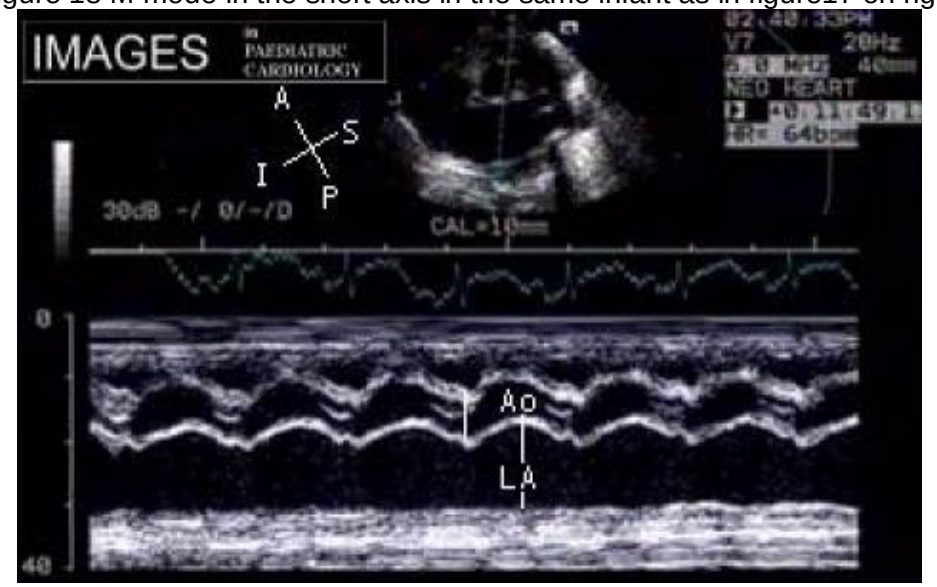


Figure 19 Pulsed wave Doppler of descending aorta. The diastolic flow is prograde when the sample volume is placed centrally and retrograde when the sample volume is placed distally to the aortic insertion of the arterial duct

Figure 21 Pure right to left flow through the arterial duct in a neonate with severe pulmonary hypertension and a congenital diaphragmatic hernia

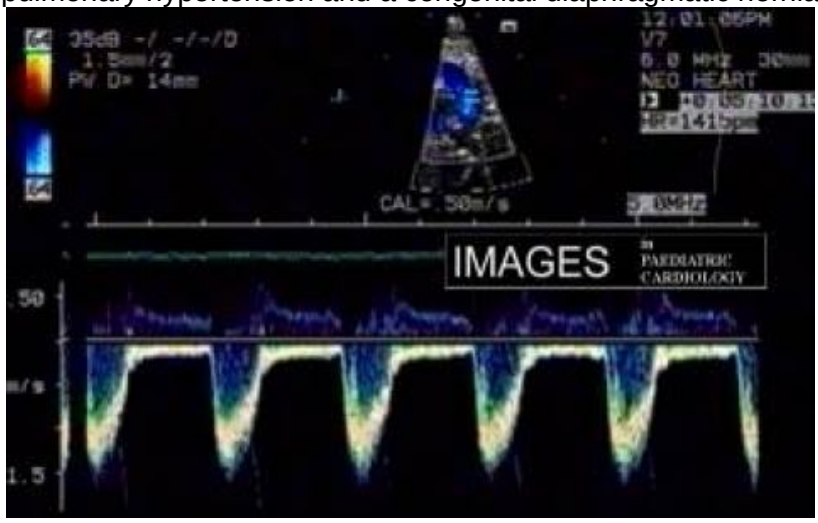


Figure 22 After transfer to a high frequency oscillatory ventilator and treatment with inhaled Nitric Oxide the ductal Doppler becomes bi-directional (right to left in systole and left to right in diastole) in this same infant

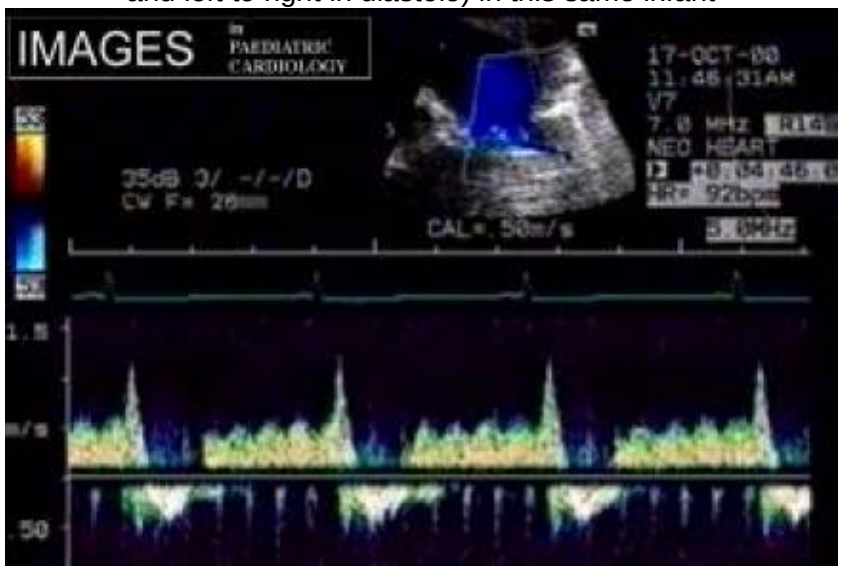
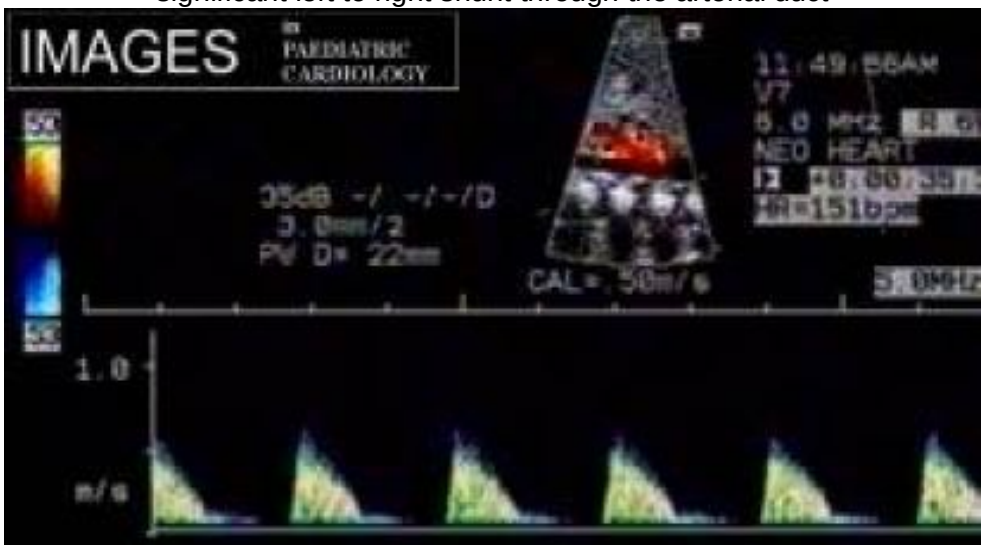


Figure 24 Absence of end diastolic flow in the celiac artery compatible with “ductal steal” in a premature infant with necrotising enterocolitis and renal failure due to a significant left to right shunt through the arterial duct



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