

The fetal circulation

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The fetal circulation (Fig. 1) is markedly different from the adult circulation. In the fetus, gas exchange does not occur in the lungs but in the placenta. The placenta must therefore receive deoxygenated blood from the fetal systemic organs and return its oxygen rich venous drainage to the fetal systemic arterial circulation. In addition, the fetal cardiovascular system is designed in such a way that the most highly oxygenated blood is delivered to the myocardium and brain. These circulatory adaptations are achieved in the fetus by both the preferential streaming of oxygenated blood and the presence of intracardiac and extracardiac shunts. Thus, the fetal circulation can be defined as a 'shunt-dependent' circulation.

In the fetus, deoxygenated blood arrives at the placenta via the umbilical arteries and is returned to the fetus in the umbilical vein. The partial pressure of oxygen (P_{O_2}) in the umbilical vein is around 4.7 kPa and fetal blood is 80–90% saturated. Between 50–60% of this placental venous flow bypasses the hepatic circulation via the ductus venosus (DV) to enter the inferior vena cava (IVC). In the IVC, the better oxygenated blood flow from the DV tends to stream separately from the extremely desaturated systemic venous blood, which is returning from the lower portions of the body with an $S\bar{v}O_2$ of around 25–40%. At the junction of the IVC and the right atrium (RA) is a tissue flap known as the Eustachian valve. This flap tends to direct the more highly oxygenated blood, streaming along the dorsal aspect of the IVC, across the foramen ovale (FO) and into the left atrium (LA). In the LA, the oxygen saturation of fetal blood is 65%.¹ This better oxygenated blood enters the left ventricle (LV) and is ejected into the ascending aorta. The majority of the LV blood is delivered to the brain and coronary circulation thus ensuring that blood with the highest possible oxygen concentration is delivered to these vital structures.

Desaturated blood ($S\bar{v}O_2$ 25–40%), from the superior vena cava (SVC) and the coronary sinus, in addition to the IVC's anteriorly streamed flow (comprised mainly of venous

return from lower body and hepatic circulation), is directed across the tricuspid valve and into the right ventricle (RV). This blood is then ejected into the pulmonary artery (PA). Because of the high pulmonary vascular resistance (PVR) only about 12% of the RV output enters the pulmonary circulation, the remaining 88% crossing the ductus arteriosus (DA) into the descending aorta. The lower half of the body is thus supplied with relatively desaturated blood ($P_{O_2} \sim 2.7$ kPa).

Combined ventricular output (CVO)

In the adult circulation, where the circulatory system is in series and there are no shunts, the stroke volume of the RV should equal that of the LV and cardiac output can be defined in terms of the volume of blood ejected by one ventricle in 1 min. In the fetus, as a result of intracardiac and extracardiac shunting, the stroke volume of the fetal LV is not equal to the stroke volume of the RV. The RV receives about 65% of the venous return and the LV about 35%. Thus, in the shunt dependent circulation of the fetus, the situation is much more complex and cardiac output must be defined in different terms.

The cardiac output of the fetus can only be spoken of in terms of the total output of both ventricles—the combined ventricular output (CVO).² About 45% of the CVO is directed to the placental circulation with only 8% of CVO entering the pulmonary circulation.

Control of the fetal circulation

Control of the fetal circulation is extremely complex and poorly understood. It is set against a background of multiple control processes, which mature and develop with gestational age. Circulating catecholamines, other circulating hormones and locally released vasoactive substances all play a part.³ Circulating catecholamines exert their effect through activation of α - and β -adrenergic receptors.

Key points

In the fetus, gas exchange occurs in the placenta.

The fetal circulation is 'shunt-dependent'.

Cardiac output in the fetus is defined in terms of combined ventricular output (CVO).

The presence of fetal haemoglobin and a high CVO help maintain oxygen delivery in the fetus despite low oxygen partial pressures.

The transition from fetal to neonatal life involves closure of circulatory shunts and acute changes in pulmonary and systemic vascular resistance.

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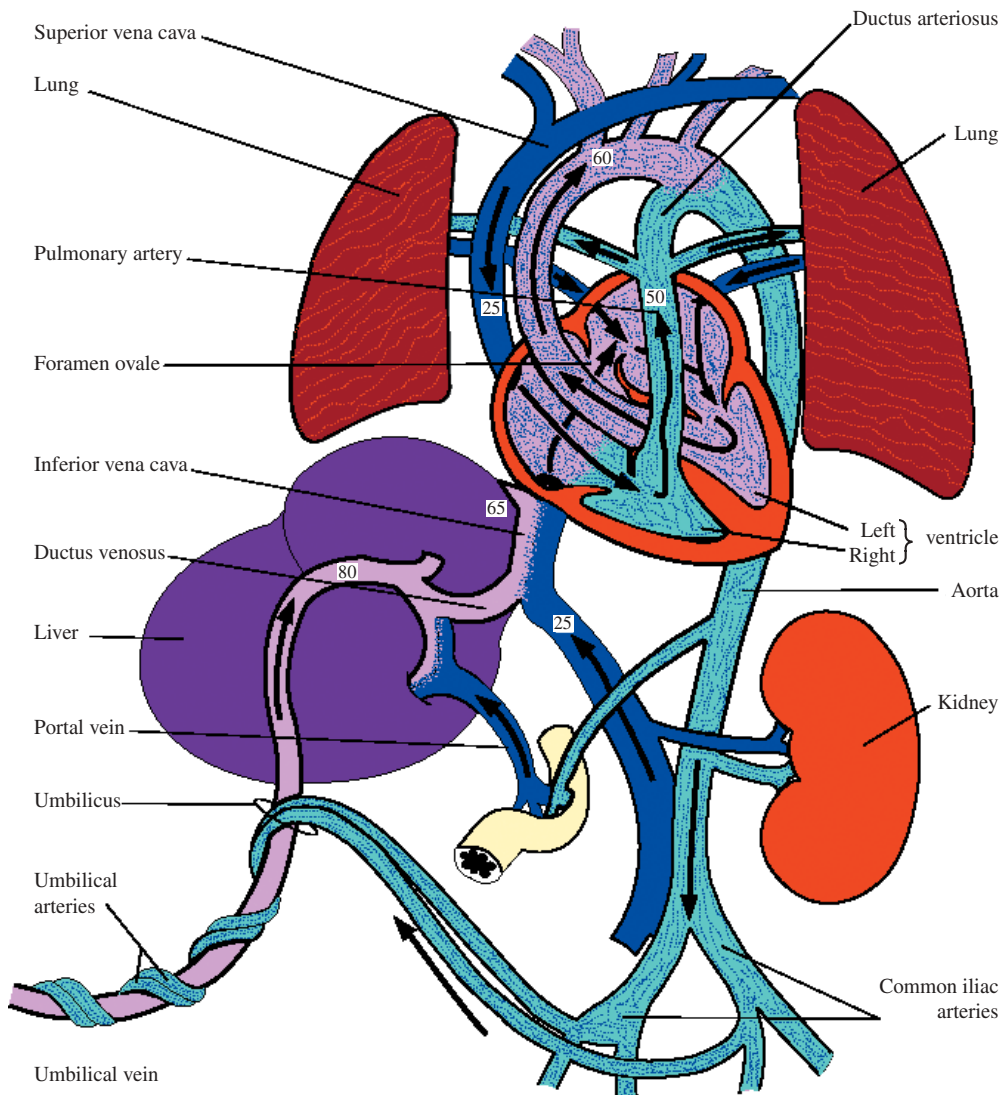


Fig. 1 The fetal circulation.

These receptors mature during early gestation independently of the autonomic innervation process, which occurs much later and is probably only completed during the neonatal period. The peripheral circulation of the fetus appears to be under a tonic adrenergic influence (predominantly vasoconstriction), probably mediated by circulating catecholamines and in particular by norepinephrine. Other factors such as arginine vasopressin (AVP) and the renin–angiotensin system may also have a role.

The high PVR of the fetus is multifactorial in origin. The fetal pulmonary arterioles have a high muscle mass and resting tone. The fetal lungs are collapsed and there is a low resting oxygen tension. The DA also contains muscle that is sensitive to oxygen tension and vasoactive substances. DA patency *in utero* is maintained by the low oxygen tension and the vasodilating effect of prostaglandin E₂ (PGE₂).

Oxygen delivery in the fetus

Oxygen delivery is related to CVO and the oxygen content of blood. Oxygen content of blood is determined mainly by the quantity of haemoglobin and its oxygen saturation. The fetus has a high haemoglobin concentration (~16 g dl⁻¹ at term), with a high percentage of haemoglobin F (HbF), which has a lower content of 2,3-diphosphoglycerate, thus shifting the oxygen dissociation curve to the left (Fig. 2). This favours oxygen uptake in the placenta, where, if *P*_{O₂} values are similar in *uterine* and umbilical venous blood, the oxygen saturation in umbilical venous blood greatly exceeds that in *uterine* venous blood. High CVO, high haemoglobin concentrations and the presence of HbF help to maintain oxygen delivery in the fetus despite the relatively low partial pressures of oxygen. However, after birth, the presence of HbF becomes a disadvantage. This is because the *P*₅₀ value of fetal

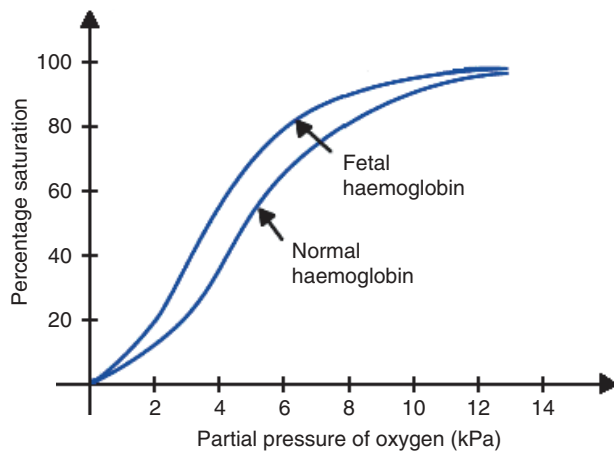


Fig. 2 Oxygen dissociation curves for fetal and adult blood. The P_{50} value is 3.6 kPa for fetal blood and 4.8 kPa for adult blood.

blood is ~ 3.6 kPa compared with 4.8 kPa in adult blood. Thus, when the P_{O_2} is ~ 5.3 kPa, which approximates to the normal neonatal venous value, the oxygen content of fetal blood is much higher than that of adult blood. Thus, in the neonate, the presence of HbF has the effect of impairing oxygen extraction at the tissue level.

The fetal circulation in transition

As the fetus begins its transition to post-natal life, several cardiopulmonary adaptations must be made. Gas exchange must be transferred from the placenta to the lungs, the fetal circulatory shunts must close and the left ventricular output must increase. At birth, several factors are involved in the cessation of the placental circulation.⁴ The umbilical vessels are reactive and constrict in response to longitudinal stretch and the increase in blood P_{O_2} . Obviously external clamping of the cord will augment this process.

With the placental circulation removed there is a dramatic fall in the flow through the ductus venosus and a significant fall in the venous return through the IVC. The ductus venosus closes passively 3–10 days after birth. During late gestation there is a gradual reduction in PVR. At birth, after expansion of the lungs, there is a dramatic fall in PVR and an 8–10-fold increase in pulmonary blood flow. In fetal lambs it has been shown that mechanical expansion of the lungs with non-oxygenated gas results in a massive fall in PVR. This fall in PVR may relate simply to lung expansion opening up pulmonary vessels. However, it is thought to be mediated, in part, by stimulation of pulmonary stretch receptors resulting in reflex vasodilatation. Better oxygenation of neonatal blood also reverses the pulmonary vasoconstriction caused by hypoxia, further reducing PVR.

The increase in pulmonary blood flow leads to a massive rise in pulmonary venous return to the LA. The decrease in IVC flow, described above, results in a fall in venous return to the RA. These two factors allow the pressures in the LA and RA to equalize.

At this point the flap of the foramen ovale is pushed against the atrial septum and the atrial shunt is effectively closed. This initial closure of the foramen ovale occurs within minutes to hours of birth. Anatomical closure occurs later via tissue proliferation.

Concomitant with the drop in PVR, the shunt at the level of the DA becomes bi-directional. The exact mechanism of ductal closure is not known but the increased P_{O_2} in neonatal blood produces direct constriction of smooth muscle within the duct. In addition, concentrations of PGE_2 , produced in the placenta, fall rapidly after birth,⁵ adding to ductal constriction. The ductal tissue itself may become less sensitive to the dilating influences of the prostaglandins.⁶ The actual closure of the ductus takes place in two stages. In healthy full term newborns, functional ductal closure occurs by 96 h. This functional closure is followed later by anatomical closure via endothelial and fibrous tissue proliferation. The neonatal circulation, with the redundant closed shunts identified, is shown in Figure 3.

Changes in cardiac output

For the term fetus, CVO is high (~ 400 – 500 ml kg^{-1} min^{-1}). Equally in the neonatal period, the cardiac output is extremely high, ranging from 275 to 425 ml kg^{-1} min^{-1} (remember this is defined in terms of single ventricular output). Indeed the neonatal cardiac index has been measured at 4.0 litre min^{-1} m^{-2} at 1 h of age. The cardiac output of the neonate is tightly coupled with oxygen consumption. This increases after birth owing to the increased metabolic demands of thermogenesis, the increased work of breathing and the increased caloric utilization secondary to growth. The disparity between the LV and RV outputs disappears as the neonatal circulation is established.

The fetus, in late gestation appears to have a limited ability to augment its cardiac output when given added filling volume.⁷ The neonatal heart, on the other hand, can significantly increase its cardiac output with volume loading. The exact mechanism for this change is unknown but may be a maturational effect of the myocardium, allowing it to perform better.

The high resting cardiac output of the neonate, however, results in a somewhat limited reserve. The situation gradually improves as the cardiac output of the neonate decreases over the first few months of life. HbF is replaced by adult haemoglobin resulting in better oxygen delivery to the tissues. This change in oxygen delivery is thought to result in the gradual decrease in cardiac output.

Return to the fetal circulation

The changes outlined above, which occur in the transition to neonatal life, may not be permanent. Given the correct combination of circumstances, it is possible for a normal neonate to revert back to a fetal-type circulation, a pathophysiological state termed persistent fetal circulation (PFC).

In the neonate, pulmonary arterioles remain very reactive and will constrict in response to certain stimuli such as hypoxia, hypercarbia, acidosis and cold. This can lead to a rise in PVR that,

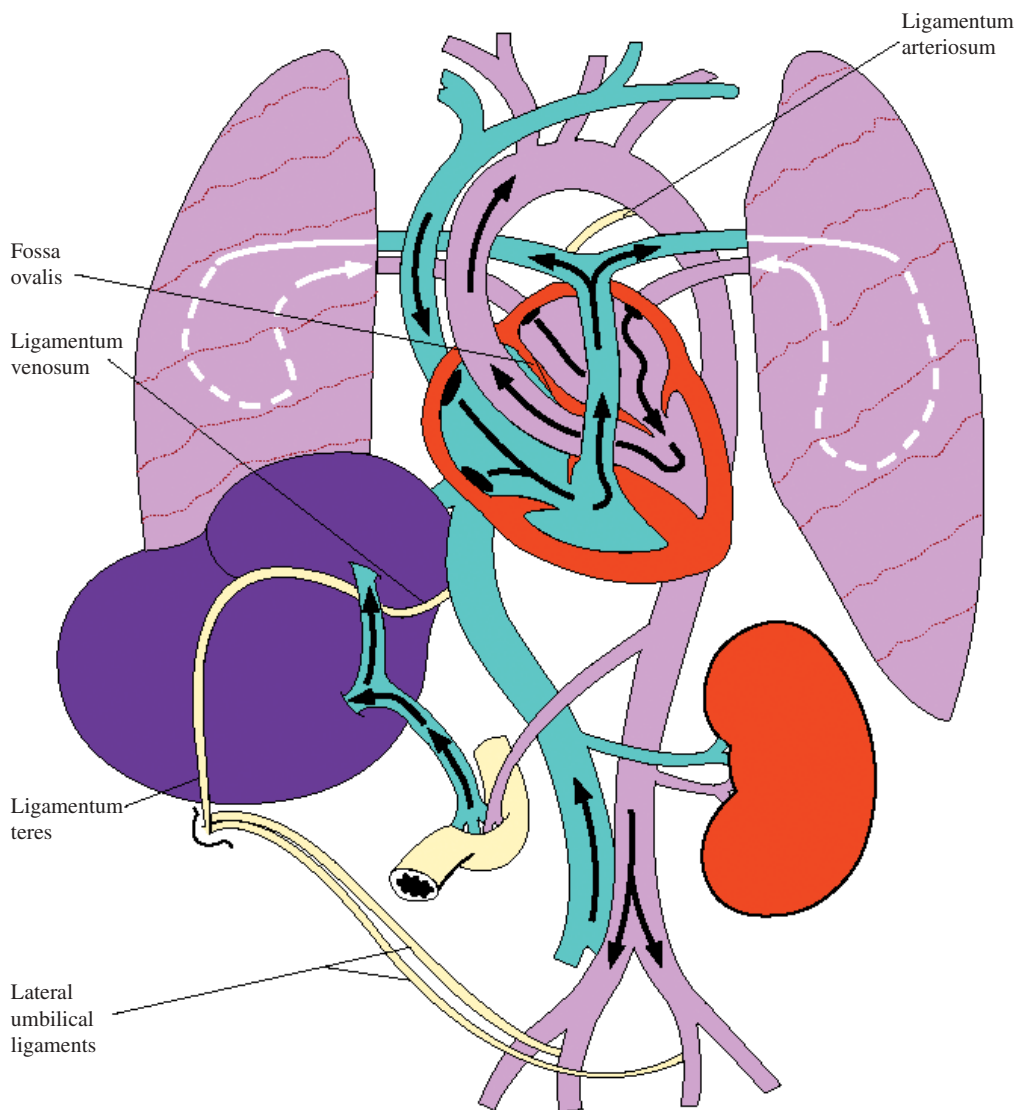


Fig. 3 The neonatal circulation.

in turn, favours right to left shunting through the FO and DA, which have not yet anatomically closed. This leads the neonate to revert to a fetal pattern of circulation with one major difference—there is no placenta to provide oxygenation. A vicious cycle of worsening hypoxia and acidosis is then set in motion (Fig. 4).

Abnormal circulations

In a review of this size it is impossible to cover all the possible abnormalities associated with congenital heart disease (CHD). However, included below is a brief discussion of a few types of CHD that helps illustrate how the change from fetal circulation to neonatal circulation can have significant effects.

The forms of CHD discussed below are well-tolerated *in utero*. Other forms of CHD can result in severe compromise of the fetal circulation and early fetal death.

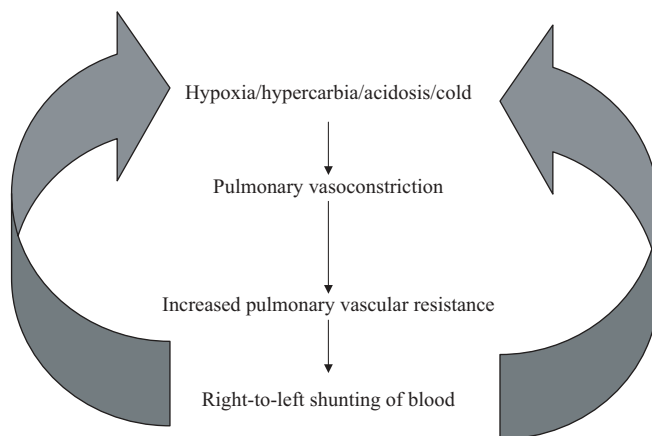


Fig. 4 The vicious cycle of PFC.

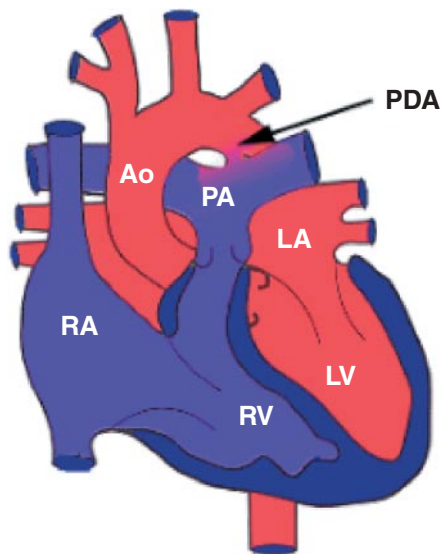


Fig. 5 Patent ductus arteriosus.

Patent ductus arteriosus (PDA)

The DA normally closes within the first 24 h of birth. Failure of the DA to close results in a left to right shunt (Fig. 5). This is because of the rise in SVR and fall in PVR that occurs after birth. In other words, the shunt is in the opposite direction to that in the fetus. The magnitude of the shunt increases as the PVR continues to fall. This results in an increased volume and workload with respect to the LA and LV and, eventually, left heart failure.

Ventricular septal defects

Ventricular septal defects (VSD) are one of the most common forms of CHD. They are well-tolerated in the fetus, as LV and RV pressures are equal. After birth the circulatory effects of a VSD are dependent on the size of the defect and the balance between PVR and SVR. In neonates with a large VSD, as SVR rises and PVR falls, a significant left to right shunt through the VSD becomes apparent. As PVR continues to fall during the first weeks of life, this shunt increases leading to congestive heart failure.

Tetralogy of Fallot

Tetralogy of Fallot (TOF) is one of the most common congenital heart malformations (Fig. 6). It is now recognized that the two most important features of TOF are: (i) RV outflow obstruction, nearly always infundibular and/or valvular in location, often associated with a hypoplastic pulmonary artery; and (ii) a large subaortic VSD associated with malalignment of the conal septum.

In the fetus, depending on the severity of the obstruction to pulmonary blood flow, the aorta will carry a larger percentage of CVO. If the obstruction to pulmonary blood flow is very severe, blood flow to the lungs will be supplied via the DA from the

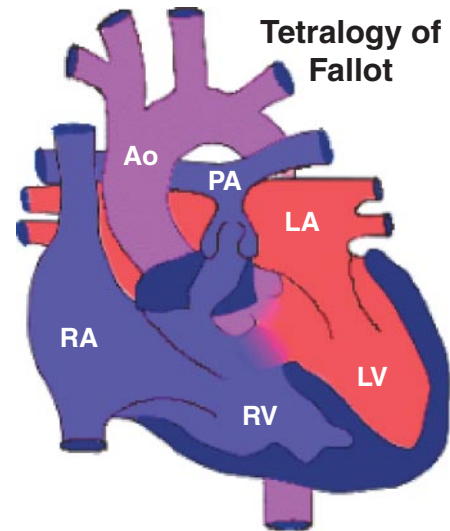


Fig. 6 Tetralogy of Fallot.

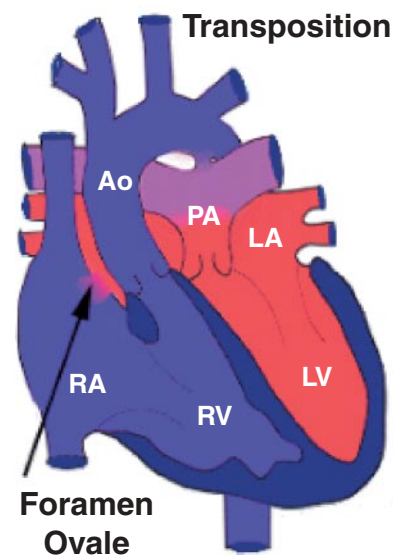


Fig. 7 Transposition of the great arteries.

descending aorta (i.e. the reverse of the normal situation). Even this significantly altered circulation results in no problems during intra-uterine life.

After birth, the effect of duct closure will depend on the severity of the pulmonary obstruction. If the pulmonary obstruction is severe, the neonatal circulation is said to be 'duct-dependent' and duct closure will lead to severe cyanosis. Re-establishment of the ductal flow by means of a prostaglandin infusion is an important intervention used to stabilize these neonates.

Transposition of the Great Arteries

Transposition of the great arteries (TGA) results from abnormal rotation and septation of the arterial truncus during embryogenesis (Fig. 7).⁸ The aorta arises from the RV and the

pulmonary artery from the LV. The FO and DA develop as normal and there are no major circulatory consequences of this lesion *in utero*. After birth, because the pulmonary and systemic circulations are arranged in parallel rather than in series, survival depends on the presence of one or more mixing points (ASD, VSD or PDA) between the two circulations in order to achieve an arterial oxygen saturation compatible with life. Thus, newborns with TGA and an intact ventricular septum (IVS) who have only a small patent FO (PFO) or ASD will be severely cyanosed after closure of the DA. Sometimes this severe cyanosis is associated with acidosis and cardiovascular collapse.

Immediate management of these neonates involves re-establishing ductal patency using a PGE₁ infusion and, if necessary, creating an ASD by means of a balloon atrial septostomy (BAS) to allow a larger degree of mixing at the atrial level. BAS is usually performed under echocardiographic guidance on the Paediatric Intensive Care Unit. Once the neonate has been stabilized, complete surgical repair of the lesion can be undertaken electively at a later date.

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See multiple choice questions 81–84.