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The preoperative management of severe neonatal left ventricular outflow obstruction

Newborn infants with severe left heart obstruction are extremely difficult to manage prior to mechanical correction of the lesion. This article describes the pathophysiology of the condition, its presentation, how to confirm the diagnosis and management of both the moribund, critically ill baby and the stable, relatively well infant. Also included are short sections on the problems associated with the use of prostaglandin E, inhaled oxygen and on the chronic management of low birthweight babies with hypoplastic left heart syndrome.

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Key points

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1. Infants often present as extremely unwell as a result of arterial duct constriction or closure.
2. Successful resuscitation of the moribund infant depends on rapid intubation and ventilation, intravenous access, IV prostaglandin E and IV vasoconstricting inotropes.
3. Stable infants should be commenced on low dose prostaglandin E and oxygen should be avoided.
4. Elective ventilation should only be undertaken if absolutely necessary and by the most experienced person available.
5. Longer term management relies on carefully balancing the pulmonary and systemic circulations using systemic vasodilators and avoiding added oxygen.

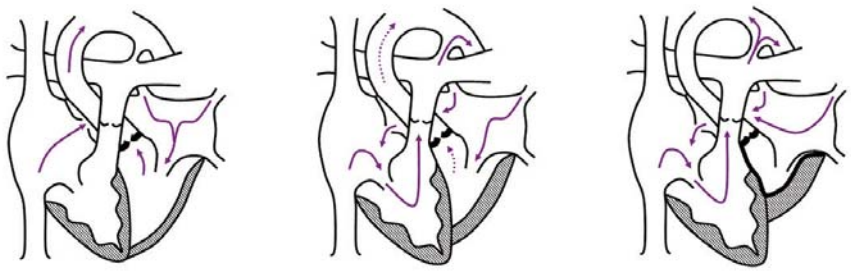
Pathophysiology

Changes *in utero*

In the neonate left heart outflow obstruction almost always occurs at the level of the aortic valve. Coarctation and interruption of the aorta will not be discussed here as the physiology and management differ significantly. Aortic valve obstruction forms a spectrum of disease ranging from minor stenosis to complete atresia.

In utero aortic valve obstruction causes a rise in the diastolic pressure within the left ventricle. In a subset of children where significant obstruction occurs early in development, the high left ventricular pressures cause blood in the left atrium to flow away from the mitral valve through the atrial septum to the right atrium and on to the pulmonary artery. In this situation the systemic circulation, including the aortic root and coronary arteries, must be supplied by flow through the arterial duct. *In utero* the left ventricle has little or no flow through it and so fails to develop resulting in the pathological complex of hypoplastic left heart syndrome (HLHS) (**FIGURE 1**). It has been postulated that relief of the obstruction early in fetal life may prevent progression to HLHS and work is ongoing to examine this hypothesis[1].

Where obstruction occurs at a later gestational age or is of only moderate severity, flow continues through the left ventricle albeit with raised diastolic intraventicular pressures. This high diastolic pressure can impair coronary artery flow to the myocardium resulting in high myocardial wall stress, particularly in the endocardial region. Subsequent damage to the endocardium results in a



Aortic stenosis at 12 weeks' gestation – pressure in left ventricle is starting to rise but pattern of fetal circulation remains normal.

Progression of aortic stenosis – high left ventricular diastolic pressures impair filling. Flow through patent foramen ovale (PFO) becomes left to right increasing right ventricular flow. Duct flow becomes increasingly important for systemic circulation.

Progression to HLHS – cessation of flow through left ventricle. High left ventricular pressures cause damage to endocardium (endocardial fibroelastosis). Entire systemic circulation is supplied through duct with retrograde aortic arch flow.

FIGURE 1 Aortic stenosis – fetal progression to hypoplastic left heart syndrome (HLHS).

fibrotic change known as endocardial fibroelastosis (EFE) that severely impairs the function of the left heart in the infant period[2].

Changes in newborn period

Severe left heart obstruction is a 'duct-dependent' lesion. That is to say ongoing survival of the child is absolutely dependent on patency of the arterial duct. In the case of left heart obstruction it is the systemic circulation that relies on blood flow through the duct (**FIGURE 2**). Affected infants are often well at delivery with modest cyanosis and tachypnoea. However when the duct starts to constrict, systemic blood flow will be reduced resulting in a cool, grey child with a rapidly developing metabolic acidosis. Renal failure, hepatic failure and gut ischaemia will subsequently develop as organ perfusion becomes impaired. Simultaneously, blood will be forced to recirculate around the lungs causing pulmonary oedema and the right ventricle will fail, dilate and become more ischaemic[3]. In effect, what starts as mild mottling and tachypnoea can rapidly become a life threatening emergency.

Clinical presentation

The speed of deterioration will depend on the severity of stenosis. Severe stenosis or complete atresia of the aortic valve will usually have a relatively short history of deterioration, whilst the symptoms of moderate stenosis may take a while to evolve. At presentation a child with severe obstruction will look sick with tachypnoea, tachycardia, cool peripheries and sweating. All pulses will be poor or impalpable, the liver will be enlarged, there will be a marked sub-xyphoid and parasternal heave and there may be a systolic murmur accompanied by an ejection click at the upper left sternal edge radiating to the neck.

The principle differential diagnoses will be congenital infection or a metabolic disorder, both of which can cause an abrupt deterioration and acute circulatory collapse in a previously well child. Clues to a cardiac aetiology would include significant hypoxia and cyanosis (poorly responsive to inhaled oxygen), normal inflammatory markers such as C-reactive protein and erythrocyte sedimentation rate and low venous saturation (but beware an unexpectedly high venous oxygen saturation which is a consequence of extremely poor tissue perfusion).

Children with only moderate obstruction usually present either as an asymptomatic murmur, or if more severe with failure to thrive, poor feeding and tachypnoea.

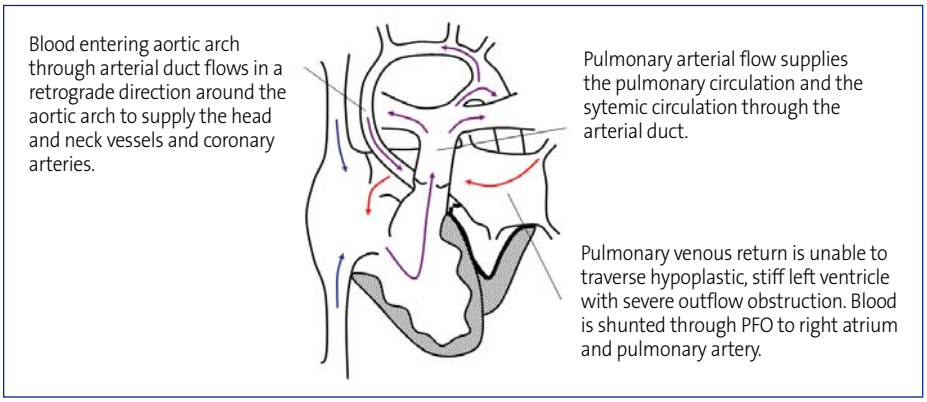


FIGURE 2 Physiology of circulation in HLHS.

Investigation

Investigation should not delay treatment. If the infant has circulatory collapse with hypoxia and poor pulses, treatment should be initiated without delay whilst investigations take place simultaneously.

Worthwhile investigations would include a full blood count and C-reactive protein in case of sepsis, urea, electrolytes, calcium, liver function tests and glucose, in case of a primary metabolic disorder or evolving renal or hepatic failure. An arterial blood gas will help assessment of acidosis and hypoxia. Unless an arrhythmia is suspected an electrocardiogram is unlikely to help acutely, but should be obtained at a later date. A chest X-ray will show hazy lung fields and possibly frank pulmonary oedema, however the heart size can vary enormously depending on the degree of right heart failure and size of the right ventricle.

The diagnosis can be confirmed by an echocardiogram (**FIGURE 3**). This may be performed and assessed by an experienced neonatologist or alternatively the images can be transferred over a telemedicine link for remote diagnosis. Where the left ventricle is hypoplastic the diagnosis is straightforward, the left ventricle appearing as a thick knot of muscle with a very small cavity lined by bright endocardium. The aortic and mitral valves will be small, thick and may have very restricted opening or be atretic. Where the left ventricle is not hypoplastic the lining of the left ventricle may be very bright because of EFE with reduced contraction and the aortic valve may appear thickened and tethered. Colour flow Doppler will show acceleration or 'aliasing' at the level of the valve and may also demonstrate retrograde flow around the aortic arch if the duct is patent. This retrograde aortic arch flow suggests that little blood is passing through the aortic valve and flow to the head and neck vessels is derived from the arterial duct. Echo measurement of the 'gradient' across the aortic valve can be misleading. A low measured gradient may well reflect how poor the left ventricular function is rather than how narrow the valve is.

Other aspects of the heart that should be assessed acutely by experienced echocardiographers include adequacy of the defect in the atrial septum and patency of the arterial duct. Survival of the infant requires reasonable flow through both of these structures.

Management

Moribund infants

Management of the collapsed, moribund infant with left heart obstruction needs to address three main problems simultaneously in order to restore adequate tissue

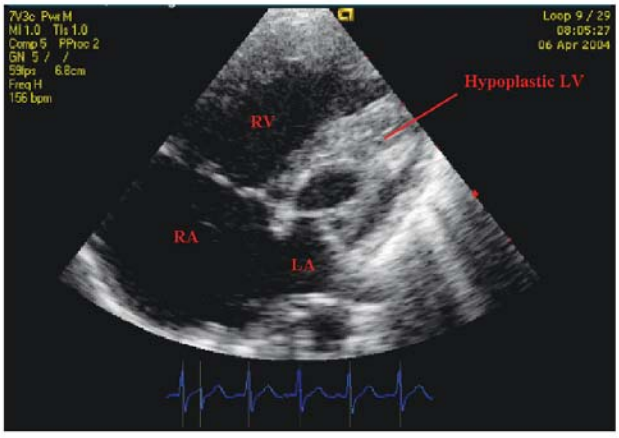


FIGURE 3 Echocardiogram of HLHS – apical 4 chamber view.

oxygen delivery – impending respiratory failure; arterial duct constriction or closure; and myocardial failure.

1. Impending respiratory failure

The combination of pulmonary recirculation, pulmonary oedema and weakening respiratory effort due to tiring and hypoxia will result in respiratory failure.

Intubation and ventilation should be undertaken immediately to achieve efficient gas exchange raising the oxygen content of the pulmonary circulation and improving the metabolic acidosis by removing carbon dioxide. Intubation in this setting usually requires very little sedation, but where required similar agents to those used for elective intubation should be employed (see below).

When ventilating infants with left heart obstruction, particularly those with HLHS the percentage of oxygen used has to be carefully controlled. As previously pointed out the entire systemic and pulmonary circulations arise from the right ventricle via the pulmonary artery. As a result, changes in the pulmonary vascular resistance can have a profound effect on the systemic circulation[4]. Oxygen is a potent pulmonary vasodilator, therefore if an infant is ventilated in oxygen the pulmonary vascular resistance will fall and pulmonary blood flow increase (pulmonary overcirculation) with a corresponding drop in systemic flow (**FIGURE 4**). This will cause hypotension and poor tissue perfusion although paradoxically there will usually be a rise in the child's arterial oxygen saturation. Since the left ventricular pressures are so high in left heart obstruction, any drop in systemic arterial pressure can precipitate myocardial ischaemia[6]. In addition oxygen can cause constriction of the arterial duct, further reducing systemic blood flow. Consequently infants should be ventilated using air or low fractional inspired oxygen concentrations and in general the child's saturations should not be allowed to rise above 80%. This saturation roughly corresponds to balanced pulmonary and systemic flow.

2. Arterial duct constriction or closure

Constriction of the arterial duct commonly precipitates collapse in these infants as the systemic circulation is dependent on duct flow. Re-establishing adequate duct patency using prostaglandin E (prostin) is therefore of paramount importance.

At the same time as the infant is being intubated, intravascular access should be obtained by any means possible (including interosseous needle) to allow prompt and reliable administration of prostin. Where possible at least two points of vascular access should be obtained to permit simultaneous administration of inotropes. Prostin can be administered peripherally or centrally but should not be mixed with other infusions. As it can cause apnoea and vasodilation, care should be taken to avoid boluses and all children receiving it require close observation, particularly if not intubated. As a result of this some centres have a policy of intubating and ventilating any child who is dependent on prostin and requires transfer to another centre.

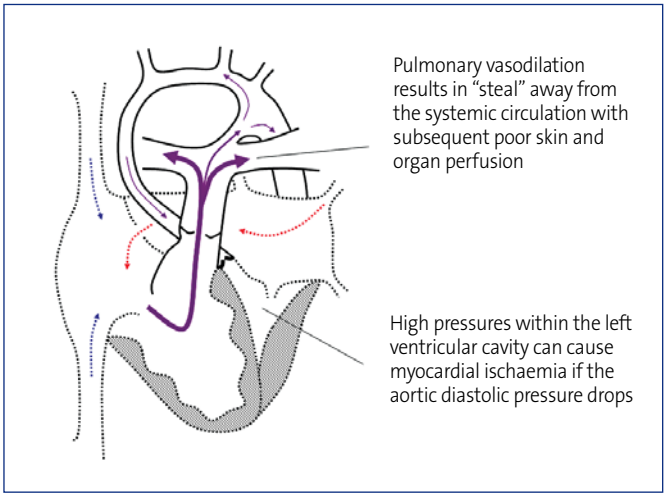


FIGURE 4 Haemodynamic consequences of pulmonary vasodilation (e.g. in response to oxygen).

In an infant with a constricting or closed arterial duct, high dose prostin (50-100 ng/kg/min) should be given initially to reopen the duct. Once the duct is fully open the dose can be reduced to 5-10 ng/kg/min to maintain patency. This dose is less likely to cause apnoea, pyrexia and vasodilation.

Problems with prostaglandin E:

- Inadvertent bolusing may occur when syringe pumps are raised suddenly. This can be avoided by using anti-syphon valves on syringe pump giving sets.
- The units of prostin are nanograms per kilo body weight per minute, which is unfamiliar to some doctors and nurses. This is a frequent source of confusion when setting up infusions and has caused problems with overdose in the past. The following formulae may help to avoid confusion:

  High Dose

  [Weight (kg) x 150] micrograms made up to 50mL with 5% dextrose

  1mL/hr = 50 nanogram/kg/min

  Low Dose

  [Weight (kg) x 30] micrograms made up to 50mL with 5% dextrose

  1mL/hr = 10 nanogram/kg/min
- If a hospital has an accident and emergency department but no neonatal unit, prostin may not be stocked. If asked to transfer any infant who may have duct-dependent congenital heart disease, prostin should be carried by the transport team.
- As prostaglandin E is only rarely used by non-cardiac neonatal units, confusion has arisen with prostaglandin I_2 (prostacyclin). It is often preferable to refer to prostaglandin E by its commercial name – prostin – to avoid confusion.

3. Myocardial failure

The combination of myocardial ischaemia due to high ventricular and low aortic pressures, and profound metabolic acidosis severely impairs myocardial function. As the right ventricle fails it dilates, further impairing its function. A vasoconstricting inotrope such as dopamine or adrenaline should be started early. Firstly this will improve coronary artery perfusion by raising the systemic arterial pressure, and secondly it will improve the force of contraction directly, helping the right ventricle return to a smaller, more efficient size (conversely, in the more stable neonate, a vasodilating inotrope may be needed to reduce pulmonary overcirculation and improve systemic blood flow).

Unfortunately when extreme acidosis is present the efficacy of inotropes is reduced. Although hyperventilation will help to compensate for the metabolic acidosis in the early stages of resuscitation it is useful to administer aliquots of bicarbonate to try and directly correct the extracellular pH and improve the effectiveness of endogenous and exogenous inotropes.

Stable infants

Where the arterial duct is widely patent and

the atrial gap unrestricted many infants tolerate even severe left heart obstruction reasonably well in the short term. Problems will start to arise as the pulmonary vascular resistance falls and pulmonary over-circulation develops, but this process may not happen for several weeks. It is important not to try and manipulate an infant's haemodynamics unnecessarily as the child is often far better at balancing their circulations than staff are[6].

Duct patency

As duct constriction can cause such rapid decline in this group of babies there is a strong case for giving low dose prostaglandin to all infants with severe left heart obstruction and patent arterial ducts. Where the aortic stenosis is moderate and the left ventricular function preserved, it is usually safe to withhold prostin and watch the effects of duct closure. In well infants the prostin dose should be kept low (5ng/kg/min) to minimise side effects. At this dose duct closure is very unlikely as is apnoea.

Elective ventilation

If an infant needs intubation either for a non-cardiac reason or as an elective event prior to transfer, the most experienced operator available should be involved. As mentioned these infants can decompensate suddenly when the pulmonary/systemic flow balance is altered. If possible, artificial ventilation should be avoided as it has been shown to worsen outcome in this group of patients[3].

The aim of sedation is to permit intubation without significantly altering the haemodynamic balance of the child. For that reason adrenaline and atropine should be drawn up in appropriate doses and be ready to use.

Pre-oxygenation should be tailored to the child's saturations, again trying to maintain arterial saturations no greater than 80% and thereby avoiding pulmonary vasodilation and overcirculation. Bag and mask air may well be sufficient.

At least two points of intravascular access should be available; one for prostin and another for intravenous sedatives. Induction should avoid both systemic vasodilation which would drop coronary perfusion, and also tachycardia which will increase oxygen demand. A haemodynamically stable sedative such as ketamine should be given, often with low dose fentanyl to curtail any reactive tachycardia.

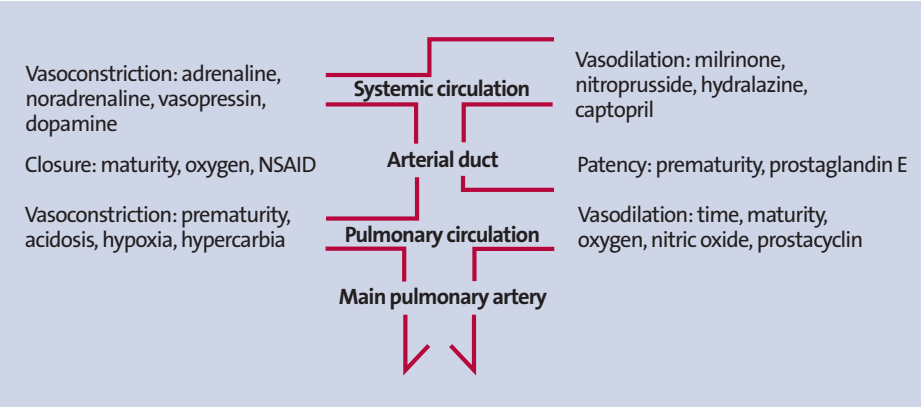


FIGURE 5 Summary of systemic and pulmonary vasodilators and vasoconstrictors.

Paralysis should be obtained with vecuronium, a haemodynamically neutral paralysing agent. Pancuronium can be used as an alternative in situations where an increase in heart rate is felt helpful, accepting that the myocardial oxygen demand will rise accordingly. Long term paralysis is not usually required and maintenance sedation usually requires little more than low dose parenteral opiate and oral sedatives.

Low birthweight infants and longer term management

The Norwood operation for hypoplastic left heart syndrome is now undertaken in children as small as 2kg, however many infants less than this weight require prolonged medical management to permit growth and maturation. Unfortunately most infants under 2kg are premature, with the associated problems of prematurity, notably chronic lung disease, which can complicate the haemodynamic management.

Before embarking on a course of prolonged intensive care leading up to the stage I Norwood operation (and further surgery that will be dependent on normal pulmonary artery pressures) the family need to be carefully counselled. The long term outlook is at best guarded and the care required will place great strain on the entire family. The opinion of a centre specialising in repair of HLHS should be sought soon after diagnosis to identify any negative prognostic features that might influence the decision to treat.

If after appropriate deliberation the decision is to pursue surgical palliation, the infant should be managed in a dedicated tertiary neonatal intensive care setting. A tunnelled intravenous line should be inserted to permit reliable long-term administration of low dose prostin.

The ventilatory management of these infants can be very difficult. The chronic lung changes associated with prematurity can necessitate relatively high ventilation requirements and oxygen therapy, whilst balancing the pulmonary and systemic circulations and maintaining ductal patency requires low oxygen concentrations. To further complicate the situation, the pulmonary vascular resistance will usually fall progressively and any septic event can dramatically alter the systemic vascular resistance. Infants can progress from an early stage of inadequate pulmonary blood flow to a later state of inadequate systemic flow.

The ultimate goal of the cardiovascular system is tissue oxygen delivery, a good indicator of which is the arterial/venous oxygen saturation difference[7]. Markers of tissue perfusion such as blood lactate concentration can also be used, however when perfusion is extremely poor lactate concentrations may be in the normal range. The arterial oxygen saturation can provide a rough but continuous guide to how balanced the two circulations are; high saturations (>80%) indicate excessive pulmonary flow and low saturations (<80%) inadequate pulmonary flow.

Usually optimal balance can be achieved by careful control of the inspired oxygen concentration and use of systemic vasodilators where appropriate. In the ventilated infant permissive hypercapnoea can been used to increase the pulmonary vascular resistance and reduce pulmonary blood flow[8]. Other ventilatory techniques aimed at raising the pulmonary vascular resistance, such as introducing carbon dioxide into the inspired gas mixture or dropping the inspired oxygen concentration to 18 or 19%, are no longer recommended. Generally speaking when the pulmonary vascular resistance has

fallen after birth, systemic vasodilation is preferred to pulmonary vasoconstriction as a means of increasing systemic blood flow[3] (**FIGURE 5**).

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