Aortic and Mitral Atresia -
Hypoplastic Left Heart Syndrome (HLHS)

Dynamic Factors Possibly Causing HLHS

Restricted flow in LV in the Fetus
Experimental reduction of inflow into the LV by closing the FO or occluding the LA results in LV hypoplasia.
Experimental LV outflow obstruction in fetal lambs induces progressive decrease in LV size.

Progressive reduction in LV size has been noted in human fetuses with aortic stenosis.

Primary LV dysfunction
LV function with myocardial changes are invariably noted early in fetuses that develop HLHS. Possibly this is the initial disturbance (e.g., fetal myocarditis).
The abnormal aortic valve may be the result of inability of the LV to provide forward flow; the valve is closed by the pressure in the aorta provided from the pulmonary artery through the ductus arteriosus.

Aortic Atresia in the Fetus – Blood Flows

Umbilical and systemic venous blood all returns to the right atrium. Pulmonary venous blood passes to the RA via the foramen ovale. Thus all blood ejected has the same \(O_2\) sat — my estimate is 55% in the human fetus.
Total output is ejected by the RV. Apart from pulmonary blood flow all blood ejected traverses the DA (includes all systemic and umbilical flow).
\(O_2\) sat of blood entering the pulmonary circulation and the descending aorta is higher than normal, whereas that delivered to the brain and heart is lower than normal.
Blood flow to the upper body, including the heart and brain, is provided from the ductus arteriosus by retrograde flow through the aortic isthmus, arch and ascending aorta.
There is a high incidence of aortic coarctation (about 80%) in aortic atresia, at the junction of the isthmus with the descending aorta. This raises the question of adequacy of flow to the upper body organs.
Cerebral Development in Aortic Atresia

Several studies have demonstrated developmental delay in children with HLHS. This had been attributed to postnatal problems e.g. surgery. Recently, decreased head circumference has been noted in neonates and fetuses with HLHS, as well as white matter injury in the brain, indicating that the cerebral insult may occur in utero. Doppler examination of cerebral arteries has frequently revealed decreased pulsatility indices. This has been interpreted as a reduced vascular resistance induced by the lowered O$_2$ sat of arterial blood; the cerebral insult has been attributed to cerebral hypoxia.

Donofrio MT et al. Pediatr Cardiol 2003:24;436

However, the reduction of arterial O$_2$ sat is modest and in studies in fetal lambs, the brain is able to tolerate large reductions in arterial O$_2$. I propose that the decreased pulsatility index is caused by the aortic coarctation and that the blood flow to the brain is reduced, with limitation of both oxygen and substrate supply.

Other Vascular Disturbances in Aortic Atresia

Foramen ovale
Little or no blood passes from R – L through the FO. Pulmonary venous return to the LA tends to close it. A restricted FO increases LA pressure. The pattern of pulmonary venous flow on Doppler examination is a useful indicator of the FO size. Continuous forward flow with minimal reversal during atrial systole denotes the FO is of reasonable size. Brief forward and reverse flow is consistent with FO closure. Identification of a closed or small FO in the fetus predicts a high mortality in the neonate. This has prompted attempts to open the FO in the fetus.

Pulmonary Circulation
The higher than normal O$_2$ sat of blood perfusing the lung will reduce PVR and possibly decrease vascular smooth muscle development. However, a restricted FO will elevate LA pressure and increase PVR and vascular smooth muscle. Thus afterload on the RV will be increased. In AA, the RV ejects a large volume (total CVO); addition of an increased afterload may elevate RA and venous pressure and induce fetal hydrops.

Coronary Circulation
In AA, blood supply to the ascending aorta and coronary arteries is derived by retrograde flow. Coarctation of the aorta could limit this flow; this could induce myocardial damage and affect function.

Postnatal Circulation in Aortic Atresia
Several factors influence the circulatory changes and clinical manifestations after birth. These include – Ductus arteriosus (DA) Foramen ovale (FO) Pulmonary and systemic vascular resistances Coarctation

Aortic atresia is a complete mixing lesion. All systemic and pulmonary venous blood mixes in the right atrium. The O$_2$ sat of all blood delivered to the pulmonary and systemic circulation is the same and is determined by the ratio of pulmonary to systemic blood flow (Qp:Qs). The higher the ratio, the higher is the O$_2$ sat.
Ductus Arteriosus in Infant with Aortic Atresia

In the fetus with AA, systemic and umbilical blood flows traverse the DA. After birth, with removal of umbilical blood flow, flow through the DA is reduced by about 40%, so that considerable constriction could occur without compromising systemic blood flow. More severe constriction will reduce aortic pressure and flow, and compromise tissue oxygen supply, resulting in hypoxia and acidemia. The distribution of blood from the pulmonary trunk to the pulmonary circulation or through the DA is determined by the PVR and combined resistance of the SVR and ductus arteriosus. If PVR is low, Qp will be large and Qp:Qs ratio will be high with a high mixed O\textsubscript{2} sat (as much as 90-94%). This may tend to induce DA constriction, further reducing Qs and enhancing the high Qp:Qs ratio. Despite the high O\textsubscript{2} sat, tissue hypoxia results from low blood flow. If PVR is high, as occurs with FO restriction, Qp is restricted, but flow through the DA is enhanced, so that aortic pressure and tissue flow are maintained. The Qp:Qs ratio is quite low, so mixed arterial O\textsubscript{2} sat may be quite reduced (80% or lower). The low O\textsubscript{2} sat may limit DA constriction. Although O\textsubscript{2} sat is reduced, tissue O\textsubscript{2} supply may be adequate because blood flow is maintained.

Administration of PGE\textsubscript{1} will dilate the ductus. Flow to the systemic circulation is increased and, with the fall in PA pressure, Qp may fall. This will relieve some of the volume load on the RV and could improve cardiac failure. However, because Qp:Qs will decrease, there will be some reduction of O\textsubscript{2} sat.

Administration of 100% O\textsubscript{2} could have an adverse effect on the infant with aortic atresia. The DA is crucial in providing flow to the systemic circulation. If Qp:Qs ratio is high, mixed arterial O\textsubscript{2} sat may be over 90% and Pa\textsubscript{O\textsubscript{2}} may be over 75 mm Hg. Administration of 100% O\textsubscript{2} may increase pulmonary venous Pa\textsubscript{O\textsubscript{2}} to levels above 400 mm Hg. This high Pa\textsubscript{O\textsubscript{2}} may further constrict the DA and reduce Qs. Arterial Pa\textsubscript{O\textsubscript{2}} may rise to levels above 200 mm Hg, but severe acidemia may develop because tissue flow is severely compromised.

Foramen Ovale in Infant with Aortic Atresia

A small or closed FO in the fetus with AA may result in elevated PVR, thus limiting the increase in Qp with ventilation. Also increased interstitial and alveolar fluid may interfere with establishing effective ventilation. Mortality is high in these infants. Although the FO size may be adequate in utero, a functional restriction may become manifest after birth in association with the marked increase in Qp occurring with ventilation. This will result in an increase in LA pressure and possibly cause pulmonary edema. The rise in LA and pulmonary venous pressure may increase PVR and Qp will be reduced. A balance between the increased Qp and the functional FO restriction has to be established. While Qp and Qp:Qs is high, mixed O\textsubscript{2} sat will be high, but with the reduction in Qp, O\textsubscript{2} sat will fall.
Pulmonary and Systemic Vascular Resistance in Infant with Aortic Atresia

With an unrestricted FO, PVR will fall and Qp will increase markedly with ventilation. The high Qp:Qs ratio will result in a high O₂ sat. This will tend to induce DA constriction and pulmonary vasodilation, enhancing Qp.

The RV is now presented with a very high volume load and DA constriction increases afterload. Cardiac failure is thus very likely. Because the low PVR appears to be the initiating factor, it has been proposed that inducing pulmonary vasoconstriction by inhalation of low O₂ gas mixtures could result in improvement. Considerable improvement has been reported in a few infants administered gases of 14-19% oxygen in nitrogen [Toiyama K et al. Circ J 2010:74;2125].

An increase in systemic vascular resistance will favor distribution of blood in the pulmonary trunk toward the pulmonary circulation and away from the aorta, thus limiting blood flow to the tissues. Both hypoxemia and hypotension induce sympathetic stimulation and catecholamine release. However, rather than improving perfusion by raising pressure, the vasoconstriction will increase SVR and flow across the DA will be decreased.

Coarctation of the Aorta in Infant with Aortic Atresia

Coarctation of the aorta between the DA and the aortic isthmus is present in about 80% of patients with aortic atresia. It is not known how it affects perfusion of the aortic arch and its branches and the coronary circulation.

I have proposed it may reduce cerebral blood supply and be responsible for cerebral insult in the fetus. It could also be responsible for myocardial damage due to inadequate coronary perfusion in the fetus. It is not known whether baroreceptor function is affected. Baroreflexes are functional in the normal neonate.

If pressures in the aorta and cantid arteries are reduced by the coarctation, baroreceptor stimulation could induce sympathetic stimulation and catecholamine release. This would increase SVR and interfere with tissue perfusion.