Evaluation of asymptomatic heart murmurs

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Summary Cardiac murmurs are a common finding in asymptomatic paediatric patients. The most common causes are innocent murmurs and minor structural heart disease. Beyond the age of 6 weeks patients are unlikely to have major underlying heart disease. Presentation of asymptomatic murmurs may be variable and assessment strategies depend on the age of the patient and should include clinical examination with measurement of blood pressure, evaluation for presence of cyanosis, electrocardiogram and echocardiography in selected patients.

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Practice points

- Sole clinical evaluation by non-specialists is inadequate in differentiating innocent from pathological murmurs
- Clinical examination is not sufficiently sensitive to identify cyanosis in children
- Simple clinical examination combined with pulse oximetry and an electrocardiogram (ECG) will allow effective prioritization of referrals between non-specialists and paediatric cardiologists
- The chest X-ray (CXR) is of no value in the routine evaluation of asymptomatic murmurs

- It is unlikely that a major or complex congenital cardiac lesion will present for the first time after 6 weeks of age

Introduction

Heart murmurs are a common finding in children, their incidence depending partly on the effort with which they are sought.\textsuperscript{1} The 'diagnosis' of a heart murmur induces a high degree of anxiety in parents, who usually associate a suggestion of possible heart disease with poor prognosis and terminal illness, as not infrequently witnessed in elderly relatives. They are unprepared for the possibility of heart disease in their child, and usually lack knowledge and understanding of basic paediatric cardiac entities such as 'innocent murmurs'.
However, there are some simple rules that enable practitioners to make an educated guess about the nature and significance of heart murmurs. In his 1960 review Fogel emphasizes that the cardiac cycle is not silent. The flow of blood around the heart and great vessels always produces some sound, although frequently at a threshold below that of the human ear aided by a stethoscope. It is therefore not unusual for a murmur to be audible in patients without heart disease, even though the incidence of murmurs in routine practice does not seem to reach the 50–60% quoted by some authors.

Innocent murmurs are most commonly of crescendo–decrescendo mid-systolic type, of lower intensity (grade I–II) being audible at the (lower) left sternal border, non-radiating, and increasing in intensity in supine position. They usually have associated normal, variable splitting of the second heart sound, but are not associated with clicks or snaps. In contrast to systolic murmurs it is axiomatic that diastolic murmurs, whilst unusual, are always pathological with the exception of venous hums that occasionally extend into diastole when the patient is sitting up. Functional murmurs are more readily audible in high-output cardiac states, for example, with fever or excitement. Apart from their specific character, innocent murmurs are defined through the normality of all other findings. However, the lack of identifiable abnormality does not necessarily guarantee cardiac normality. Significant lesions do not always have classical associated findings, and even if they do, the average clinician may find it difficult to identify subtleties such as fixed splitting of the second heart sound, clicks or opening snaps. Frequently these findings are only confirmed retrospectively after echocardiography has demonstrated a specific cardiac abnormality.

Age considerations

The neonate and young infant

A lower threshold for referring asymptomatic infants with ‘routine’ murmur for a more detailed cardiac evaluation, will result in a higher probability of identifying structural heart disease. Physiological changes that occur during the transition from in utero to ex utero life may mask even significant congenital cardiac lesions, which should be considered during the initial assessment. A good example is a large ventricular septal defect (VSD) in which a left-to-right shunt may be minimal soon after birth due to the high pulmonary vascular resistance, which only gradually declines over the first few weeks of life. Neonates with large VSDs are therefore commonly asymptomatic early in life, and the classical finding of an audible murmur is often not present during this period. Similarly, infants with duct-dependent lesions such as pulmonary atresia, may have only very subtle symptoms or signs early on, but are likely to become acutely unwell if a detailed evaluation is delayed and the duct constricts a few days after birth.

However, even though there is a relatively high incidence of structural heart disease in neonates presenting with, for the most part, asymptomatic cardiac murmurs (50–75%), it is clear that even in this population serious lesions generally present symptomatically, with a murmur being identified subsequently.

However, not all infants require immediate specialist assessment once a murmur has been identified and the key to an appropriate management strategy is thorough clinical assessment and prioritization.

The older child

In contrast to neonates and infants, an asymptomatic murmur identified in an older child is much more likely to be ‘innocent’ in nature, and it is frequently an incidental finding during an intercurrent illness. Cardiac abnormalities that can present with an asymptomatic murmur in the older child are either acquired cardiac lesions such as rheumatic heart disease, or more commonly congenital cardiac abnormalities that are either of minor severity or that have slowly progressed over time (Table 1). Acquired cardiac abnormalities are less likely to present with asymptomatic murmurs, and instead frequently present with symptoms of the primary pathological process before the development of an audible murmur.

In the absence of a characteristic history of a progressive cardiac lesion there is no immediate need to refer older children with asymptomatic murmurs for specialist cardiac assessment. In fact the re-evaluation of an incidental murmur noted during an acute illness, once the child has recovered, will allow the practitioner to reassure parents in those cases where the murmur has spontaneously disappeared.

Murmur variability: now you hear it now you don’t

There are several possible reasons for a murmur being audible on some occasions and not on others.
This is obviously a feature of an innocent murmur that may appear with high output states such as fever. This is particularly the case with pulmonary flow murmur.

However, this variability is not only limited to innocent murmurs. The physiological changes of the neonatal period, for example, characterized by a slow drop in pulmonary vascular resistance, explain why VSD and persistent arterial duct (PDA) murmurs may be inaudible in the first few days of life.

Murmurs secondary to congenital regurgitation of the atrio-ventricular (AV) valves (tricuspid or mitral) are likely to be apparent early in life, but they may become more audible if progressive ventricular dilatation leads to a higher degree of AV valve regurgitation.

In contrast, murmurs that result from congenital stenosis of a semi-lunar valve (aortic or pulmonary) are usually present from birth unless the stenosis is acquired or progressive. As in most cases flow across these valves is ‘obligatory’ there is little opportunity for change; though absolute intensity will vary with flow and gradient. It is important to emphasize that any progressive congenital or acquired cardiac lesion can be associated with change in appearance and intensity of associated cardiac murmurs.

### Cardiac lesions and asymptomatic murmurs

#### Minor lesions

Haemodynamically insignificant lesions such as mild pulmonary stenosis, mild aortic stenosis and small ventricular septal defects usually give characteristic cardiac murmurs of ejection systolic or pansystolic type. The intensity of these murmurs should be grade 1–3 and there is usually no associated thrill. Unless a murmur is very loud and ‘omnipresent’, it is localization and radiation is expected to match standard clinical descriptions.

Minor lesions are unlikely to be associated with findings other than the murmur itself. Heaves and thrills are extremely rare, although not impossible, especially in slim children with, for example, mild–moderate pulmonary valve stenosis.

Generally most minor lesions do not require any immediate intervention at presentation, and can be followed with a ‘watch-and-wait’ approach. Thus there is no need for immediate referral for definitive cardiac assessment in those patients in whom a minor lesion is suspected.

#### Significant ‘asymptomatic’ lesions

There is a small, but significant, group of patients with congenital heart disease, who do not follow the classical rules of clinical presentation. Remarkably severe lesions can balance themselves so as to minimize clinical symptoms. For example in our own institution we have seen patients with tetralogy of Fallot presenting as late as 50 years of age with clinical symptoms related to atrial arrhythmias, having lived a virtually normal life up to this stage.

Sometimes these conditions become evident when a secondary illness, such as a viral respiratory tract infection, disturbs the cardiovascular balance to a point where decompensation occurs. However, sometimes an apparently minor murmur in an otherwise asymptomatic patient may be the first

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This is obviously a feature of an innocent murmur that may appear with high output states such as fever. This is particularly the case with pulmonary flow murmur.
hint of a significant cardiac problem. In this context one should bear in mind that the intensity of a murmur is a product of both the flow and pressure gradient, and may not necessarily reflect the severity of the underlying cardiac disease.

Progressive pulmonary vascular disease as a result of a moderate or large VSD, for example, may lead to a reduced intensity of the associated cardiac murmur. A high pulmonary vascular resistance will also mask heart failure as it will lead to a reduced left-to-right shunt. In a few children, these changes can occur quite quickly, in others, the pulmonary vascular resistance may never fall significantly after birth. These children may consider themselves unlucky in that their unusual physiology has prevented them from developing symptoms related to the underlying disease, which would otherwise ring alarm bells.

Asymptomatic cyanosis—an oxymoron some might say—is not common but is physiologically quite easy to comprehend. The body does not require full saturation of haemoglobin per se as long as oxygen delivery to the tissue is adequate. As oxygen delivery is the product of cardiac output and oxygen carriage it follows that a mild degree of desaturation may well be compensated through a slight increase in cardiac output, without any noticeable symptoms. However, it is unlikely that careful assessment with our scheme would be normal in such a child. At the very least they will have abnormal saturations or electrocardiogram (ECG) patterns.

Evaluation of asymptomatic murmurs

The aim of any evaluation strategy of asymptomatic cardiac murmurs should be to limit unnecessary investigations and referrals as much as possible, whilst at the same time providing an appropriate safety net to diagnose severe underlying heart disease at an early stage before any adverse events occur. Any such strategy has to be adapted further to the needs and level of anxiety of the individual patient and family.

Around 80% of all congenital heart disease that will eventually present in the first year of life will have had neonatal screening check without symptoms. 

However, the mortality of undiagnosed congenital heart disease in older infants that have correctly or incorrectly passed the 6-weeks screening examination has been reported to be extremely low, if not close to 0%. These figures illustrate very well the importance of differentiating between infants and older children when applying an evaluation strategy for asymptomatic cardiac murmurs (Fig. 1).

Clinical examination

Any child with a heart murmur deserves a full examination of the cardiovascular system, at least incorporating an assessment of peripheral pulses, evaluation for possible cyanosis and documentation of a non-invasive blood pressure (BP) recording. As by definition this article deals with asymptomatic murmurs we would not expect to find any evidence of heart failure or respiratory compromise on clinical examination (and therefore will not discuss the clinical signs of decompensated cardiac disease).

Peripheral pulses

Both brachial (infant) or radial (older child) and both femoral pulses should be routinely examined and compared. Weak femoral pulses, especially if discrepant to the quality of brachial or radial pulses or associated with radio-femoral delay, are suggestive of aortic coarctation or aortic arch obstruction, and should, therefore, lead to further more detailed investigations. Weak pulses all round can be an incidental finding, but could also be the result of significant left ventricular outflow tract obstruction or aortic stenosis, as well as poor ventricular function, although the latter is unlikely in the absence of symptoms.

Cyanosis and transcutaneous oxygen saturations

Though the identification of cyanosis is considered a standard clinical skill there is remarkably little evidence regarding the sensitivity and specificity of clinical examination for varying degrees of cyanosis. Surprisingly cyanosed children can be missed by medical services at a number of levels. It is important to emphasize that a cyanosed child is not necessarily 'blue' but may instead present with a subtle degree of paleness, especially in the context of coexisting anaemia, such as physiological anaemia of the newborn. One should also remember to differentiate between central and peripheral cyanosis during clinical examination. Circumoral pallor is a particularly common finding in children and does not have a significant association with cardiac disease. In one study of emergency referrals of children with respiratory difficulties, in whom cyanosis might be more easily recognized because of a higher index of suspicion, a
clinical examination was found to be only 33% sensitive at a threshold of 92%. The value and feasibility of routine screening pulse oximetry in identifying congenital cardiovascular malformations is questionable when used non-selectively in neonates, but it may serve as a helpful technique when evaluating infants in whom congenital heart disease is suspected. When using pulse oximetry to screen for congenital cardiovascular malformations the sensitivity can be further increased through comparison of right arm and lower limb saturations. Even though it is probably not feasible to use these devices in primary care environments it seems foolhardy not to use such a technology in secondary and tertiary care.

**BP**

The standard oscillometric method of obtaining BP recordings in the neonate should be routinely applied in all infants upon first clinical encounter. However, the value of four limb BP measurements in the neonate is questionable with differences of as high as 20 mmHg having been identified to be 'more likely to be due to random variability in measurement than to coarctation of the aorta'. If the evaluation of the femoral pulses suggests possible coarctation in a neonate, then echocardiography is clearly indicated. Straightforward upper limb BP measurements may be more valuable in the older child where these measurements are less fraught and more reproducible. For coarctation in the older child absolute levels of upper limb BP are much more important, representing as they do the risk of end-organ damage.

**ECG and chest X-ray**

The value of chest X-ray in the diagnosis of congenital heart disease is limited. Several studies have shown that chest X-rays have an extremely low sensitivity and specificity for identifying cardiac lesions. Because chest X-rays also expose the child to ionizing radiation, their routine use cannot be considered appropriate in the asymptomatic child.

The ECG also has a low sensitivity in identifying congenital cardiac lesions in asymptomatic children with cardiac murmurs. As most of these murmurs

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**Figure. 1 Flowchart suggesting a strategy for evaluation of asymptomatic cardiac murmurs by the general paediatrician or practitioner.**
will either be innocent or the underlying cardiac abnormalities will have no physiological effect, ECG changes are not seen. In addition, the value of the ECG to the general paediatrician is also limited by confidence in its interpretation, not least related to the wide variation of normal during infancy and childhood. However, being able to identify the QRS and p-wave axis, bundle branch block patterns and the presence of ventricular hypertrophy goes a long way in making best use of this diagnostic modality in paediatric patients. Identifying ECG abnormalities may on occasions suggest a more specific cardiac abnormality, such as left superior axis being associated with atrioventricular septal defect, but more importantly it will provide a useful indicator for the need for further echocardiographic evaluation. The low prevalence of significant pathology in asymptomatic patients with cardiac murmurs makes the negative predictive value high despite low sensitivity. However, the ECG is non-invasive and easily transmitted for expert review, and should, therefore, be considered as part of the routine initial assessment.

Echocardiography

Echocardiography remains the gold standard for diagnosing congenital cardiac lesions. However, this method is not always readily available to the general paediatrician, and is used mostly as an assessment tool for the paediatric cardiologist.

The role of echocardiography in the evaluation of asymptomatic murmurs has changed significantly over the last 10 years. Though sensitivity and specificity of clinical assessment by a paediatric cardiologist are quite well validated\(^1\)\(^5\)–\(^8\) the ease and lack of contra-indication to echocardiography make it a difficult investigation to refuse, not least on the background of increasing medical litigation, as well as patient and parent expectation.

Even though it is quite unlikely that a significant pathology would be missed in older children when innocent murmurs are diagnosed solely on clinical examination, minor lesions may masquerade under the impression of innocence. Danford and colleagues identified 16 patients with cardiac abnormalities on echocardiography, out of 187 who were clinically thought to have innocent murmurs, four of whom required invasive interventions.\(^1\)\(^9\)

One of the major concerns using the strategy of echocardiographic evaluation in all patients with cardiac murmurs is the fact that it is associated with a significant pick-up of otherwise trivial conditions, such as silent and small arterial ducts, patent foramen ovale and small atrial septal defects, which may cause unnecessary anxiety in patients and relatives.

Whether or not general paediatricians and practitioners should diagnose innocent murmurs is a debate best summed up by Pelech\(^2\)\(^0\) who uses the term 'comfort factor' to refer to the degree of uncertainty which an individual clinician is willing to tolerate. Studies of the sensitivity and specificity of non-specialist assessment are mixed, but would not generally support an adequate degree of diagnostic precision\(^1\)\(^5\),\(^1\)\(^8\). On the background of increasing medical litigation it is probably wise for the non-specialist to have a low threshold for referring patients with asymptomatic murmurs that have been noted on multiple clinical encounters for further specialist assessment.

Conclusion

Asymptomatic murmurs are a common finding in infants and older children, with innocent murmurs, as well as minor structural heart disease, accounting for the majority of these cases. Assessment strategies employed by the general paediatrician and practitioner need to be customized to the age of the patient. If referral for specialist review by a paediatric cardiologist is considered the following information should be supplied, which will allow the cardiologist to appropriately prioritize the patient:

- Age and clinical status of the child including family history and associated extra-cardiac anomalies
- Description of the murmur (volume, character, position, radiation)
- Peripheral pulse assessment, as well as BP recording
- If possible, differential upper and lower limb saturations
- ECG evaluation

If all the above findings are normal the parents may be reassured that, even in the possible presence of structural heart disease, the possibility of a clinically significant lesion is low.

References

A neonate can be regarded as an infant of less than 44 weeks post conceptual age or a full term that is < 1 month old. For the purposes of this lecture slightly older infants will be included. Although neonates seldom present for surgery those who do usually have a multitude of problems. Cognisance must be taken of their unique physiology and different anatomy.

The conditions which may require surgery include:
- Necrotizing enterocolitis (NEC)
- Congential diaphragmatic hernia (CDH)
- Gastroscisis or omphalocoele
- Pyloric stenosis
- Bowel atresia
- Colostomy for anorectal malformation or rectal duplication or Hirshsprung’s disease
- Malrotation or volvulus of bowel
- Tracheo-oesophageal fistula
- Inguinal hernia – elective or incarcerated/strangulated
- Congenital lobar emphysema or cystic adenomatous malformation
- Direct laryngoscopy
- Choanal atresia
- Pierre Robin for glossoptexy
- Meningomyeloceles and VP shunts

Each of these conditions has specific problems as well as problems related to the neonatal period as a whole.

**NECROTIZING ENTEROCOLITIS**

This condition is found mainly in sick premature infants. It is the commonest surgical emergency in neonates. Mortality is 10–30%. A variety of reasons cause reduced mesenteric blood flow leading to bowel necrosis. There are a number of associated factors such as birth asphyxia, apnoea, systemic infections, early feeding with high osmolar feeds, respiratory distress syndrome and umbilical vessel cannulation. Breast fed infants have a lower incidence of NEC due possibly to the transfer of immunoglobulins which coat and protect the gut mucosa and the transfer of beneficial bacteria from the mother. Low birth weight (<1500g) is the commonest cause of NEC. Management is conservative (NPO, TPN, NGT, antibiotics, abdominal decompression with a drain, fluid resuscitation) but up to 50% will require surgery.
Indications for surgery are:
- Intestinal perforation as evidenced by pneumoperitoneum
- Haemodynamic instability despite adequate medical resuscitation
- Severe sepsis
- Abdominal mass with persistent signs of obstruction
- Intestinal stricture
- Increasing abdominal distension with abdominal wall discolouration

Infants who present for surgery are very ill and are usually already intubated and ventilated. They maybe anaemic, thrombocytopenic (if severe this is a poor prognostic sign), septic, hypotensive, hypovolaemic, hypoxic and have renal dysfunction.

Special Anaesthetic Points:
- Blood – Check adult size unit not paediatric unit is in theatre
- Platelets if needed, platelet set
- Good IV line, if in doubt insert central line
- Massive volume requirements in excess of circulating volume
- Avoid N₂O
- Regional not an option
- Very sensitive to volatile agents, may need narcotic muscle relaxant technique
- Will require post-op ventilation
- These infants often become severely hyperglycaemic especially in the postoperative period. This is associated with a poorer outcome.

**CONGENITAL DIAPHRAGMATIC HERNIA**

CDH is a very common anomaly (1:2500). It can syndromic (isolated) or nonsyndromic (nonisolated). Diaphragmatic fusion is completed during the 8th to 9th week of gestation. The majority of CDHs occur through the foramen of Bochdalek (80%) at the posterolateral aspect of the diaphragm. Herniation can occur through the foramen of Morgagni (substernal). Bilateral hernias are usually fatal (1%). The primary pathology is not due to compression of the lungs by herniated viscera. This is a secondary phenomenon and is preceded by impairment of lung growth. In animals there is a lack of FGF 10 which is lung fibroblast growth factor that causes branching of the airway and development of airway smooth muscle. A now banned herbicide, nitrofen, increases the incidence of CDH. Nitrofen affects the retinoic pathway and a diet deficient in vitamin A, at least in rats, will induce a CDH. The “dual hit” hypothesis proposes that there are 2 pathologies that result in the morbidity and mortality ie underdevelopment of the lungs as well as the diaphragmatic defect.

Survival depends on the degree of lung hypoplasia and pulmonary vascular abnormality. Severe persistent PHT accounts for 75% of all deaths. One third of all CDHs will have some other congenital abnormality. Another factor affecting survival is the presence and severity of congenital heart disease or some other major anomaly. One fifth of infants will have a cardiac defect, most commonly a patent ductus arteriosus. A small
percentage will have Cantrell’s Pentalogy viz: 1) cardiac defect usually tetralogy of Fallot; 2) absent pericardium; 3) CDH; 4) sternal cleft; 5) omphalocoele. Infants with CDH and a cardiac defect have a mortality rate of 73% vs 27% in those without. Fifty percent of babies with CDH are stillborn or die very soon after birth. The mortality remains high despite recent advances (40%).

Prenatal diagnosis and imaging studies can give an indication of outcome. This is very dependent on the competence of the ultrasonographer. Factors that are associated prenatally with a poor outcome are:
1. diagnosis before 24 weeks
2. liver herniation into the thorax (48% mortality vs 93% survival if not herniated)
3. LHR (lung to head ratio) <0.8 at 24-26/52 gestation = 100% mortality. LHR >1.4 has no mortality. Measure X-sectional area of contralateral lung to head circumference.

Other predictors that are not or not yet as reliable are foetal MRI and echo to measure lung volumes, LV mass and PA diameters.

CDH is no longer a surgical emergency. Early surgery makes no impact on survival. Infants are given a “trial of life”. They are stabilized and attempts are made to reduce pulmonary hypertension by:
1. Oxygenation,
2. “Gentle” ventilation (Pi <25mmHg to try to prevent barotrauma and improve venous return).
3. Permissive hypercapnia (<60-65mmHg) even allowing infants to breathe spontaneously in between pressure limited ventilator breaths*
4. HFOV or HFPPV can be tried if “gentle” ventilation fails ie pH <7.25; pCO₂ >60mmHg; O₂ saturation <80% and severe respiratory distress*
5. Sedation and analgesia to reduce catecholamine levels
6. Maintenance of temperature
7. Extracorporeal membrane oxygenation (ECMO) if above failed. These patients however did not do well long term (respiratory, feeding and neurodevelopmental problems).
8. iNO, pharmacotherapy eg steroids, surfactant have been disappointing
* Boloker’s criteria

Those with severe the pulmonary hypoplasia with congenital heart disease and persistent pulmonary hypertension have a low survival rate. These infants are not candidates for surgery.

Postnatal predictors of poor survival include:
1. Severe respiratory distress within 6 hours after birth requiring intubation and ventilation
2. <1kg
3. <33/52 gestation
4. Ventilation index >1000 preop and postop (within 2 hrs).
   VI = RR x Mean airway pressure (Bohn)
5. Hypercarbia (>40mm Hg), pre-op and within 2 hours of surgery requiring
   aggressive ventilation (ventilatory pressures of >20 H2O and frequencies in excess
   of 60b/min) (Bohn).
6. Post surgical pre-ductal P(A-a) DO2 >300mm Hg (90% mortality) (Bohn)

Favourable Bohn’s criteria are associated with 86% survival. Neonates who have poor
predictors are not presented for surgery.

“The Honeymoon Period”: This refers to the immediate postoperative period where the
infant seems to improve or stabilize. This is followed by severe pulmonary
hypertension which is unresponsive to treatment.

Special Anaesthetic Points:
- Avoid vigorous mask bag ventilation – gastric distension and further compression of
  lungs
- Seldom need blood in theatre if hernia is small but must have an adult unit on
  standby
- Avoid lower extremity IV access as IVC can be compressed with return of viscera to
  and closure of abdomen
- Abdominal approach, seldom need to open chest
- “Gentle ventilation”: this prevents barotrauma. If this does not work HFOV may have
  a role but these infants usually have a poor prognosis.
  Ventilator settings: PIP <25 cm H2O; RR <65/min; inspiratory time 0.35s; PEEP <2 cm
  H2O; pH >7.25
- Permissive hypercapnia up to 60mm Hg to avoid barotrauma
- Keep warm
- Avoid light anaesthesia
- Avoid N2O
- Sudden postoperative deterioration may be due to pneumothorax on contralateral
  side
- Ventilate postop unless very small hernia in a baby who is otherwise coping well
- Keep MABP >45 mmHg (despite age being < MAP)
- Inotropic support if required

Long term sequelae:
Most survivors have reasonable pulmonary function despite reduced lung function
parameters. They are often growth retarded and suffer other sequelae: neurodevelopmental delay; GERD; deafness (ototoxicity of drugs); cardiac complications – PHT; chronic lung disease.

FETO (foetal endoluminal tracheal occlusion): This has largely been abandoned except
for a few centres where their results are good. The foetal trachea is obstructed with a
balloon to encourage lung growth. It was found that infants with pharyngeal or laryngeal
stenosis and CDH had better outcomes as their lungs were less hypoplastic. The balloon
must be puncture at 34/52 as prolonged occlusion reduces type II alveolar cells and reduces the production of surfactant.

**GASTROSCHISIS AND OMPHALOCELE**

These conditions result in a defect of the abdominal wall. The differences between the two conditions are tabulated below.

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<tr>
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<th>Omphalocoele</th>
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<tr>
<td>Caused by occlusion of omphalomesenteric artery</td>
<td>Caused by failure of gut migration from yolk sac into abdomen</td>
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<tr>
<td>Abdominal wall defect lateral to base of umbilical cord, cord remains intact</td>
<td>Herniation of abdominal contents into base of umbilical cord</td>
</tr>
<tr>
<td>Bowel is functionally abnormal</td>
<td>Bowel is usually normal</td>
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<tr>
<td>No membrane over viscera</td>
<td>Viscera within umbilical cord</td>
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<tr>
<td>1:30 000 live births</td>
<td>1:8 000 live births</td>
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<tr>
<td>60% premature</td>
<td>30% premature or LBW</td>
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<tr>
<td>Few associated anomalies or syndromes</td>
<td>2/3 have anomalies (NB CVS) or associated syndromes eg Beckworth-Weidemann, trisomy13 or 15, Pentalogy of Cantrell</td>
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Successful management of these infants starts immediately after birth. They must be kept warm, npo, fluid loss is replaced and the abdominal contents protected from damage (physical, infective or dehydration). The physiological disturbance can range from minimal to massive fluid and electrolyte derangements. Preop the abdomen is wrapped in plastic and the abdominal contents kept moist and warm.

Special Anaesthetic Points:
- Except for the smallest of defects, blood is needed in theatre
- Do not site IV line in lower extremities
- Decompress stomach with ngt if none present
- Avoid N₂O
- Fluid requirements can be enormous especially with gastrochisis
- Large defects are not closed as the increased intra-abdominal pressure may decrease organ perfusion (liver, kidneys, bowel) and affect ventilation. Venous return can also be compromised. The viscera are placed in a pouch and gradually reduced over a few days after which the abdomen is closed.
- Staged closure should be considered if reduction of the viscera causes any of the following: a CVP rise of more than 4mmHg, intragastric or intravesical pressure rise
by more 20mmHg, difficulty with ventilation, mottling of the legs or cessation of urine output.

- Monitor glucose if baby has Beckwith-Weidemann syndrome, may need up to 10mg/kg/min.

**PYLORIC STENOSIS**

Pyloric stenosis is a medical but not a surgical emergency it presents at about 40-49 weeks post-conceptual age, males > females. The post-anaesthetic complication rate (mainly apnoea) is largely determined by the adequacy of the pre-operative resuscitation.

Pathophysiology: Muscular hypertrophy of the gastric outlet causes projectile vomiting. These infants can present with:

- **severe dehydration**
- **chloride- (saline-) responsive hypochloraemic metabolic alkalosis**
- **hyponatraemia (usually mild)**
- **hypokalaemia (hypovolaemia → aldosterone release)**
- **malnutrition**

When the stomach produces acid an equivalent amount of HCO₃⁻ is produced by the pancreas. As there is a gastric outlet obstruction with pyloric stenosis, the bicarb is not lost with the acid (HCl) that is vomited. In an attempt to maintain pH, the urine is initially alkaline. As dehydration worsens the intravascular depletion leads to aldosterone secretion. Potassium is exchanged for sodium (and along with it water is absorbed), chloride is absorbed with the sodium to maintain electrical neutrality. The kidneys exchange even more potassium for hydrogen in an attempt to maintain pH. Continued chloride loss from the vomiting will cause the kidneys to maximally conserve chloride. The urinary chloride is low (<20meq/l) as chloride is also exchanged for bicarb. As dehydration continues, the kidney increases its ability to absorb bicarb proximally and loses hydrogen distally (under aldosterone control). Additionally the PaCO₂ rises in response to the metabolic alkalosis and enhances renal tubule acid secretion. All this results in a paradoxically acid urine.

Correction of the metabolic derangement consists of rehydration with normal saline (NS). If the deficit is mild to moderate (5-15% ie 50-150ml/kg), half the deficit is given over 6-8 hours. More severe dehydration (>15% ie >150ml/kg) is treated with a bolus of 20ml/kg and then half the deficit over 6-8 hours. Adequate rehydration can take a few days in severe cases. The pH, potassium and chloride usually begin to correct with NS rehydration. Occasionally a large potassium deficit will require replacement before the alkalosis will respond to NS. Potassium is only administered once urine output is established. A maximum of 3 meq/l/day is replaced. Hypoglycaemia is a danger as the hepatic glycogen stores are depleted. Once the infant is rehydrated, maintenance fluid with potassium supplementation is started.
Special Anaesthetic Points:
- If barium swallow performed (seldom done as sonar is preferred), the stomach must be emptied preop with a large bore orogastric tube and the baby turned from side to side to ensure adequate removal of barium.
- Once the urine chloride is >20meq/l, resuscitation is adequate and surgery can be booked.
- An infant that presents with a metabolic acidosis is in imminent danger of collapse.
- Post-anaesthetic apnoea will occur if the alkalosis is not improved pre-operatively.
- Chloride should be >95meq/l (alkalosis will only reverse when chloride is 105meq/l).
- pH<7.5
- Base excess <6mmol/l
- Serum bicarb <30mmol/l
- Rapid sequence induction or awake intubation
- Perfalgan and infiltrate wound with LA for analgesia
- Monitor for postop apnoea

**OBSTRUCTIVE LESIONS**

The condition of infants with bowel obstructions will depend on the underlying pathology and associated anomalies. Except for a well infant for a loop colostomy all these infants should have blood in theatre or at the very least on standby. The anaesthetic management will depend on the pathology.

**HERNIA REPAIR**

Premature infants have a 30% chance of incarceration of an inguinal hernia. The debate is when to operate. Surgeons would like to operate as soon as possible because of the risk of incarceration and anaesthesiologists would prefer to delay surgery because of the risk of post operative apnoea. The timing of surgery should be discussed by both parties taking into account the infant's co-morbid state.

Special Anaesthetic Points:
- Prematurity
- Postop apnoea
- GA vs regional
- Awake regional vs asleep
- Caudal vs spinal

**TRACHEOESOPHAGEAL FISTULA**

1:4 000 live births of whom 25% have CVS anomaly and 25% are prem.
Associated with VACTERL syndrome. They present with excessive salivation, cyanosis and a ng tube does not enter the stomach. Feeds are stopped and the oesophageal pouch suctioned. Antibiotics are started if aspiration has occurred.

Classification of TOF (Gross):

<table>
<thead>
<tr>
<th>Type</th>
<th>Percentage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>8%</td>
<td>pure oesophageal atresia no involvement of trachea</td>
</tr>
<tr>
<td>B</td>
<td>&lt;1%</td>
<td>oesophageal atresia with fistula connecting proximal pouch to trachea</td>
</tr>
<tr>
<td>C</td>
<td>80%</td>
<td>oesophageal atresia with fistula connecting distal pouch to trachea</td>
</tr>
<tr>
<td>D</td>
<td>2%</td>
<td>two fistula connecting proximally and distally to trachea</td>
</tr>
<tr>
<td>E</td>
<td>4%</td>
<td>H-type, no atresia, fistula to trachea</td>
</tr>
</tbody>
</table>

Prognostic criteria (Spitz):

<table>
<thead>
<tr>
<th>Group</th>
<th>Weight (kg)</th>
<th>Cardiac Anomaly</th>
<th>Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>&gt;1.5kg</td>
<td>no cardiac anomaly</td>
<td>99%</td>
</tr>
<tr>
<td>II</td>
<td>&lt;1.5kg</td>
<td>no cardiac anomaly</td>
<td>82%</td>
</tr>
<tr>
<td>III</td>
<td>&lt;1.5kg</td>
<td>with cardiac anomaly</td>
<td>50%</td>
</tr>
</tbody>
</table>

Investigation:

Bloods, CXR, cardiac echo

Anaesthetic Management:

This is one of the few indications for an awake intubation. However an asleep nasal intubation is usually performed. Often the exact position of the fistula is not known. The patient is kept breathing until tube placement is correct. PPV can distend the stomach through the fistula and make ventilation very difficult. If the fistula is very low the infant is kept breathing spontaneously for as long as possible. If hypoxia is a problem then IPPV is started. The stomach may require decompression via a gastrostomy or on occasion when there is no gastrostomy via the ETT. A gastrostomy can make ventilation difficult as volume is lost into it. The gastrostomy is then intermittently clamped. Fortunately few require gastrostomies. The bevel of the ETT can be turned so that it faces anteriorly and the post wall of the ETT seals off the fistula. Occasionally a fogarty is needed to seal off the fistula.

Once the ETT is well secured the patient is turned onto the L side with the right arm over the head. The ECG electrodes and diathermy pad must be positioned out of the surgical field. A small rolled up swab is placed under the chest to open up the chest. Air entry must be checked as a R lung intubation will result in no ventilation once the R lung is collapsed intra-op. A precordial steth is taped to the L axilla to check for tube placement intra-op. A R thoracotomy is performed and the approach is retropleural. It may be necessary to intermittently inflate the R lung - always warn the surgeon first. Tidal volume should be kept small. The anastomosis is done over a large bore ngt (Replogle type). It may be necessary to manipulate the ngt during surgery to locate a very high fistula. Thorascopic repair can be done. In such cases arterial line placement is desirable to monitor BP and for sampling of CO₂ as ET CO₂ is falsely low. CO₂ retention is often a problem. Hypoxia can occur with OLV.
Inability to ventilate or poor oxygen saturation may be cause by:
- Kinking of the trachea or ETT by retractor
- Compression of the R lung
- Blood or secretions in ETT
- Contra lateral pneumothorax
- ETT displaced down R bronchus – no ventilation as R lung collapsed down

Temperature and fluid loss is large with an open procedure. Once the repair is done the R lung is re-inflated under vision. The neck is kept flexed (esp while moving) so as not to stress the anastomosis. The patient is ventilated postop as there has been a period of OLV and there may also be pneumonia. Other reasons for ventilation include apnoea, requirement for the patient to remain motionless.

Very rarely is a primary anastomosis not possible because the infant is too small or the oesophagus too short. One of two approaches can be used. 1) A proximal draining pouch and a gastrostomy is made and the baby returned for repair at 1 yr of age or 9 kg wt. 2) The oesophagus is brought out posteriorly through the chest wall! A stitch is placed through the proximal end and the oesophagus placed on traction until it is long enough to anastomose (few days).

There is a high incidence of oesophageal stricture and dysmotility. Chronic aspiration is also a problem. Restrictive and obstructive lung disease is also common.

**CONGENITAL LOBAR EMPHYSEMA**

Hyperinflation and air trapping occurs in the affected lobe which does not take part in gas exchange. Compression of the adjacent lung and the mediastinal shift can result in haemodynamic compromise.

Sites: LUL >> RML>RUL
DDx: pneumothorax or CDH or congenital cystic adenomatous malformation (CCAM)
Age: <6 mo
Management: lobectomy

Anaesthetic Management
Will depend on the degree of compromise. Induction is the critical phase as a crying struggling infant will increase air trapping. Spontaneous ventilation is maintained and gentle PPV (low pressure and long expiratory time) applied only if absolutely necessary. N\textsubscript{2}O is absolutely C/I. Once the chest is opened IPPV can be started. The surgeon must be present at induction in the event that the lobe suddenly expands and requires urgent decompression. Decompression under ketamine and LA can be undertaken in very compromised infants. Anaesthesia is then induced and lobectomy performed. There is no place for palliation with repeated decompression (needle or ICD).
DIRECT LARYNGOSCOPY

Neonates who require DL usually have stridor or marked respiratory distress due to some form of obstruction. A neonate with stridor may have bilateral choanal atresia or stenosis. Laryngomalacia is the commonest cause of stridor in the neonatal period. The loudness of the stridor is also not always an indication of the severity of the obstruction. Quietening stridor and laboured breathing makes the situation more urgent.

The timing of the stridor in the respiratory cycle may indicate the level of the obstruction. Inspiratory stridor usually indicates supraglottic obstruction. This is caused by the collapse of nonrigid soft tissues above the glottis by the negative pressure generated during inspiration. Expiratory stridor may indicate an obstruction at the trachea or distal airways. Biphasic stridor indicates a glottic or subglottic (at or above the cricoid ring) obstruction. Improvement in the prone position may indicate laryngomalacia or a vascular ring.

Atropine is given to dry secretions, counteract the vagal response to airway instrumentation and also to help maintain cardiac output should there be a bradycardia from deep halothane anaesthesia.

Where appropriate good topicalization of the airway with lignocaine will help smooth the examination.

The patient with an obstructed airway should breathe spontaneously and muscle relaxants used only once ventilation is possible after the airway has been secured. There is the question of which volatile agent should be used, halothane vs sevoflurane. The case for sevoflurane is that it allows for a more rapid less irritant induction and it is more cardiac stable. Proponents for halothane prefer its greater potency which allows for a deeper level of anaesthesia and also as it more fat soluble its offset is slower which allows for a longer time to instrument the airway. Halothane also causes less upper airway obstruction in paediatric patients than sevoflurane. The downside is its cardiac depressant effects and potential dysrhythmogenic properties in the presence of hypercapnia. N₂O should be avoided. A deep level of anaesthesia may take a long time to establish because of the obstruction.

All anaesthetic agents decrease upper airway muscle activity. This results in varying degrees of upper airway collapse. Some agents affect muscle tone even at small doses eg isoflurane whereas other drugs do so in a dose dependent manner eg propofol. Propofol decreases both central respiratory output to upper airway dilator muscles as well as decreasing upper airway reflexes. In infants upper airway patency is very dependent on central neural control. Propofol depresses this mechanism more than it does in older children. Thus infants are very susceptible to upper airway obstruction if propofol is administered.

Once anaesthesia is induced obstruction may worsen as a result of loss of muscle tone. Application of CPAP may help to splint the airway open eg laryngomalacia. Pharyngeal
obstruction will not be relieved by an LMA if there is an anatomical problem / mass in the pharynx. Anaesthesia must be deep before laryngoscopy is performed.

**CHOANAL ATRESIA**

These infants are pink when they cry and dusky when quiet. A suction catheter will not pass through the nostrils. An oral airway is strapped in place and an orogastric tube is placed for feeding. These babies cannot suck without becoming hypoxic ( obligate nose breathers). This is not a surgical emergency. Care should be taken to ensure that the pharynx is kept well suctioned and that feeding tubes are correctly placed. These neonates may be syndromic eg CHARGE association (coloboma, heart anomaly, choanal atresia, mental and growth retardation, genital anomalies, ear anomalies). Post op ventilation will be required. The neonate is intubated with an oral RAE ETT. No throat pack is inserted. ETT’s are placed in the nostrils after the passage is opened up. The ends of the ETT are pulled out orally, stitched together and pulled up into the posterior nasal space. The ETTs are cut off at the nose and stay sutures secured to the cheek with plaster. The infant will return either for decannulation or redilatation.

**PIERRE ROBIN SYNDROME**

These neonates can present an extreme airway challenges. They have mandibular hypoplasia, micrognathia and glossoptosis. Most do not require surgery however a tiny minority will require airway management in the form of either glosopexy, tracheostomy or mandibular distraction. The prone position may be the only position where the airway is patent. They may of course also require intubation for some other neonatal emergency.

Special Anaesthetic Points:
- Vagal hyperreflexia
- At risk for aspiration because of reflux or swallowing difficulties
- Cardiac anomalies
- Apnoea (central or obstructive)
- Facemask seal difficult
- Insertion of oral airway difficult
- Laryngoscopy very difficult
- Subglottic stenosis
- Airway control may need
  - Nasopharyngeal airway
  - LMA
  - Intubation with Miller blade using right paraglossal approach and a bougie – needs practise
  - Intubation with FOB – most places do not have a 2.2mm FOB
- Needs ICU or high care postop to monitor airway
MENINGOMYEOLOCOELE REPAIR

Although this is not a true emergency it is a semi-elective emergency as closure is required to minimize the risk of infection. The procedure is done within the first few days of life. A VP shunt may be done at the time or a few days after the initial surgery if ICP rises (more often than not).

Special anaesthetic points:
- Have blood in theatre unless it is a tiny defect. Large skin flaps are undermined to allow for closure and this bleeds profusely.
- The body may need to be raised or the head turned sideways to allow for intubation.
- Good venous access with extension sets
- Procedure is done in the prone position. Pad or free up pressure points, check ETT is secured and not kinked, check ventilation.
- Hypothermia is a problem

ISSUES TO CONSIDER IN NEONATAL ANAESTHESIA

POST–OPERATIVE APNOEA

Former preterm infants who present for surgery are at risk for post-op apnoea (POA). The postconceptual age (PCA) as well as the postgestational age is important. Exprems of 48/52 PCA have a 5% chance of POA. This decreases to <1% at 55/52 PCA. Infants at higher risk are the exprems who are very young, those with Hb<10g/dl, those with a history of apnoea or respiratory problems. All exprems younger than 48/52 should be monitored for at least 12 hours after surgery or after any apnoeic episode. An infant who was very premature and had a stormy postgestational course should probably be considered at risk until 60/52 PCA.

Intra-operative factors that increase the risk of POA include:
- GA. Although POA has been described in infants undergoing regional anaesthesia
- Hypothermia, hypoxia, hypoglycaemia, hypocalcaemia, acidosis and hypercarbia
- High ventilatory pressures
- Sedative agents

These at risk infants are not candidates for day stay anaesthesia or for admission to hospitals that do not have neonatal ICU facilities. Although the use of aminophylline or caffeine to prevent POA is widely practised it is not universally accepted. The use of these agents do not abolish POA completely and monitoring for 12 hours is still required. A full term infant who has any respiratory episode after surgery should be regarded as at risk and also monitored for 12 hours.
RETINOPATHY OF PREMATURITY

Retinopathy of prematurity (ROP) is not related entirely to hyperoxia as infants who have never been exposed to supplemental oxygen have developed ROP. The at risk group is the sick LBW baby who has been exposed to oxygen for an extended period of time. ROP is rare in infants born after 30/52 PCA. There are many causes for ROP including candida sepsis, blood transfusions and hypoxia. The retina only matures at 42 to 44 weeks postconception. It has been suggested that elective surgery be delayed until after 44/52 PCA or if surgery cannot be delayed then to maintain oxygen saturations between 93 and 95% to prevent hyperoxia. Despite these concerns oxygen must not be withheld if the child is at risk for hypoxia.

HYPOTHERMIA

Neonates are at significant risk for hypothermia not only during surgery but pre-operatively as well. The neonate who is difficult to drip often becomes very cold (34°C!) if active measures are not taken to keep the child warm. These include warming the theatre, only exposing the area being worked on, wrapping the other areas and actively warming the baby. During surgery a wet baby will become hypothermic. We try to “waterproof” the non operated on area by sealing it off with plastic and waterproof plaster. The surface area of an infant’s head is 20% of BSA so keeping the head wrapped (eg stockinette hat) will help to reduce heat loss.

Hypothermia can worsen pulmonary hypertension by increasing oxygen consumption and worsening hypoxia. Other problems associated with hypothermia include prolongation of action of drugs, apnoea, decreased surfactant production and raised SVR.

Critical Temperature: ambient temperature below which an unclothed, unanaesthetized patient cannot maintain temperature.
Neutral temperature: temperature at which O₂ consumption is minimal

<table>
<thead>
<tr>
<th>Temperature</th>
<th>Premature</th>
<th>Term</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical temp (°C)</td>
<td>28</td>
<td>23</td>
<td>1</td>
</tr>
<tr>
<td>Neutral temp (°C)</td>
<td>34</td>
<td>32</td>
<td>28</td>
</tr>
</tbody>
</table>

INTRAVENTRICULAR HAEMORRHAGE

Premature infants are at risk for intraventricular haemorrhages. It is unknown whether anaesthetic practices can contribute towards these bleeds. As the outcome of infants
with large bleeds is poor, it is prudent to avoid factors which may cause these bleeds. Risk factors include:
- Awake intubation. It has been argued that the rise in anterior fontanelle pressure during crying is comparable to that during awake intubation.
- Any sudden severe hypertension eg awake neonatal circumcision; no analgesia in a premature infant who also has a coagulation defect.
- Large increases in osmolarity eg rapid bolus of hypertonic sodium bicarbonate or dextrose water with concentrations >10%.
- Large fluctuations in oxygen tension

**POTENTIAL CARDIAC SHUNTS**

All neonates who present for surgery are at risk for paradoxical air emboli as the foramen ovale maybe functionally but not anatomically closed. Half of all 5 year olds will have a probe patent foramen ovale. Infants with congenital intracardiac shunts are at particularly high risk. Care must be taken when connecting IV lines, flushing and injecting of drugs to avoid injection of air bubbles. A bubble trap should be used with high risk patients especially if a fluid warmer is used.

**ANALGESIA**

All babies feel pain even the premature ones. The expression of and assessment of pain maybe difficult in this age group. This is however no excuse not to give analgesia. Local anaesthetic infiltration and regional techniques are very useful. Paracetamol:. The PO or PR dose is reduced to a maximum of 60 mg/kg/day for 5 days or less; loading dose of 20mg/kg and maintenance dose of 15mg/kg six to eight hourly. Intravenous paracetamol has been shown to be safe and effective in neonates. Clear dosing guidelines are not available but preliminary data suggest the following to be safe (Stockholm protocol):

<table>
<thead>
<tr>
<th>PCA (weeks)</th>
<th>Dose</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>28-32</td>
<td>7.5mg/kg</td>
<td>8 hourly</td>
</tr>
<tr>
<td>33-36</td>
<td>7.5mg/kg</td>
<td>6 hourly</td>
</tr>
<tr>
<td>≥ 37</td>
<td>10-15mg/kg</td>
<td>6 hourly</td>
</tr>
</tbody>
</table>

Opiates can be used but respiratory depression is a real risk. Adequate postop monitoring and resuscitation facilities are needed if neonates are given opiates.
OXYGEN TOXICITY

Hyperoxia has been shown to be dangerous in neonates. Oxygen causes tissue damage by the formation of reactive oxygen intermediates that cause lipid peroxidation, DNA damage and protein sulfhydryl oxidation. Excess oxygen can cause neuronal death; pulmonary oedema and atelectasis; bronchopulmonary dysplasia; apnoea in neonates; ROP; survival was poorer after resuscitation with 100% oxygen versus room air. Oxygen saturation in neonates should be kept between 85 and 95%. Having said all this oxygen should not be withheld in a hypoxic patient.
Infantile pyloric stenosis is the most frequently encountered infant gastrointestinal obstruction in most general hospitals. Although the primary therapy for pyloric stenosis is surgical, it is essential to realize that pyloric stenosis is a medical and not a surgical emergency. Preoperative preparation is the primary factor contributing to the low perioperative complication rates and the necessity to recognize fluid and electrolyte imbalance is the key to successful anaesthetic management. Careful preoperative therapy to correct severe deficits may require several days to ensure safe anaesthesia and surgery. The anaesthetic records of 100 infants with pyloric stenosis were reviewed. Eighty-five per cent of the infants were male (i.e., 5.7:1 male to female ratio) 12% were prematures. Surgical correction was undertaken at an average age of 5.6 wk, and the average weight of the infants at the time of surgery was 4 kg. A clinical diagnosis of pyloric stenosis by history and physical examination alone was made in 73% of the infants presenting to The Hospital for Sick Children. All the infants received general anaesthesia for the surgical procedure and there were no perioperative deaths.

La sténose pylorique demeure la principale cause d'obstruction intestinale survenant chez les bébés. Même si son traitement ultime doit être chirurgical, elle représente d'abord une urgence médicale. Une réanimation préopératoire adéquate est nécessaire afin de prévenir les complications périopératoires et la reconnaissance par l'anesthésiste des perturbations hydro électrolytiques en est la clef. Il faut souvent passer plusieurs jours à corriger les déficits les plus importants afin d'assurer le succès de l'intervention. Nous avons revu 100 dossiers anesthésiques de pyloromyotomie. On y retrouvait 85% de garçons et 12% de prématurés. L'intervention survenait vers l'âge de 5,6 semaines alors que l'enfant pesait en moyenne 4 kg. Dans 73% des cas, on avait posé le diagnostic sur la base de l'anamnèse et de l'examen physique seulement. On a employé une anesthésie générale dans tous les cas et nous n'avons eu à déplorer aucun décès périopératoire.

Infantile hypertrophic pyloric stenosis is one of the most common gastrointestinal abnormalities occurring in the first six months of life. Usually its presentation is quite characteristic:

A four-week-old term infant is admitted to hospital with a five-day history of projectile vomiting. The baby is lethargic and dehydrated. His eyes are sunken and his skin feels cool and rather doughy, and when it is pinched it takes several seconds to return to its former position. The capillary refill time is more than eight seconds. He has worn the same diaper all day because his mother says that he did not produce stool or urine. He is 15% below his birth weight. During examination an olive-sized mass can be felt 3 cm below the right costal margin and gastric peristalsis is observed. He is admitted as a medical emergency due to dehydration and subsequently undergoes pyloromyotomy.

In this article reference is made to an experience in the anaesthetic management of 100 cases of infantile hypertrophic pyloric stenosis during 1986 and 1987. The demographic characteristics of this patient population are analyzed and compared with previous papers. Due to the frequent occurrence of this disease with its associated and potentially severe biochemical complications, it is appropriate to review current clinical practice and suggest improvements in management. A clinically useful relationship between the adequacy of fluid resuscitation and a urinary chloride concentration >20 mEq·L⁻¹ is proposed and the anaesthetic management of these infants is discussed.
Aetiolog\n
Hypertrophic pyloric stenosis is one of the most common gastrointestinal defects of infancy in the western hemisphere and surgical intervention is usually required to relieve the obstructed bowel. More recently an apparent increase in the frequency of pyloric stenosis has been noted. Frequencies of 1.4 per 1000 to 8.8 per 1000 live births have been reported. However, Katz et al. reported that the overall incidence may approach 1 in 300 live births with considerable regional variation.

While the condition is often labelled as being congenital, we know little of the true aetiology of this condition, and Spicer stated, "We are little nearer understanding the pathogenesis of infantile pyloric stenosis than we were 100 years ago." Many non-genetic factors have been implicated in the aetiology but scientific evidence for these claims has been difficult to confirm. Proposed causes have included infections (because a seasonal incidence exists), hypoganglionosis or immaturity of ganglion cells within the pyloric muscle, hypergastrinaemia with pylorospasm, and oedema with hypertrophy secondary to the increased work of emptying the stomach. Finally, it has been suggested that milk moving slowly through the pyloric sphincter could cause irritation, oedema, and progressive obstruction.

The condition appears to have some form of polygenic inheritance. First-born male patients are most commonly affected with a higher incidence occurring in the offspring of affected parents. An affected mother is calculated to have a 20% chance of producing an affected son whereas the risk to the son of an affected father is only five per cent. White infants are two and a half times more likely than black infants to develop pyloric stenosis and there is a male predominance of approximately 4:1. In the group under study there were 85 males and 15 females (male: female ratio of 5.7:1). This is a somewhat higher ratio than quoted values of 4:1 or 4.9:1, but comparable with that of MacDonald and FitzPatrick who found 84% of their study group of 350 patients to be male.

The clinical manifestations of pyloric stenosis usually present between the third and fifth week of life. It is rare for symptoms to occur before the second week or after five months of age. In this review there were some additional findings of interest. Twelve per cent of our cases were premature and a further four per cent were infants from multiple gestations (three unrelated twin infants and one triplet). This somewhat high proportion of premature and multiple gestation infants may be due to the bias caused by the referral of higher risk infants to a specialist hospital from peripheral community hospitals. The conceptual age at the time of surgery was 40 to 49 wk and appeared to be a more consistent finding than the time of birth to surgery. The three twins were delivered at 24 to 36 wk gestation, yet all underwent surgery at 42 to 45 wk post-conceptual age. The triplet infant was delivered at 33 wk gestation and underwent pyloromyotomy at 41 wk conceptual age. The term infants underwent surgical correction at 5.1 wk of age compared with ten weeks of age in the premature group, with an overall average age of 5.6 wk (45 ± 2 wk corrected gestational age) comparable to a previously reported age of 5.4 wk. The mean weight of the infant at the time of surgery was 4.0 ± 0.4 kg with a range from 2.2 to 5.5 kg.

Pathophysiology

The pathology is one of hypertrophy of the gastric outlet musculature. This initially produces regurgitation and eventually projectile vomiting. The aetiology is not precisely understood but the underlying pathological mechanism is known to be one of irritation with increasing oedema which evolves to muscular hypertrophy and subsequent obstruction.

Patients with pyloric stenosis may show a wide range of metabolic disturbances and can be characterized as being a chloride- (or saline)-responsive, hypochloraemic, hypokalaemic, hypovoltaemic, and in some degree, hyponnaemic metabolic alkalosis. It is so termed because the metabolic disturbance can be corrected by the administration of Cl− (NaCl or KCl). Initially, the urine is alkaline with a pH > 7.0 as a result of HCO3− losses, with little or no Cl− loss in the urine. Sodium losses are variable but are generally low in the face of extracellular fluid volume (ECFV) depletion while K+ losses may be considerable secondary to the effects of aldosterone. Later the urine may become more acidic as HCO3− reabsorption by the proximal renal tubule becomes more efficient, and as lactic acidosis and starvation ketosis become significant factors.

The wide spectrum of acid-base disturbances seen in pyloric stenosis has been previously reviewed by Touloukian et al. With each mEq of gastric acid secreted, 1 mEq of HCO3− is generated. Normally as the gastric acid passes into the duodenum, it is neutralized by the secretion of pancreatic HCO3−. However, with obstruction of the pylorus, gastric acid is lost in the vomitus and by gastric suction while the generated HCO3−, rather than being secreted by the pancreas, continues to rise in the plasma. As the increased HCO3− load is presented to the kidney, it overwhelms the resorptive capacity of the proximal tubule, resulting in increased amounts of NaHCO3 and water being delivered to the distal tubule and the collecting duct. As NaHCO3 cannot be reabsorbed in the distal tubule, the kidney attempts to conserve sodium (in the face of ECFV depletion) by stimulating aldosterone secretion, resulting in a significant kaliuresis. While some potassium is lost in the vomitus, its concentration is
concentration. The urine will not contain Cl~ when the present. Patients with ECFV contraction and Cl~ and K+ depletion respond to Na+ and K+ replacement. A status in infants awaiting a pyloromyotomy.

The urine Cl~ concentration is usually similar to that of Na+ in hypovolaemic states since Na+ and Cl~ are reabsorbed together. The finding of a low or absent urinary urine Na+ concentration is virtually pathognomonic of reduced tissue perfusion and is diagnostic of hypovolaemia. However, an exception occurs when Na+ is excreted with another anion. A patient who has vomited delivers more HCO3~ to the distal tubule and collecting duct than can be reabsorbed. As some Na+ (and K+) loss is obligatory with the HCO3~ delivered to the distal tubule and the collecting ducts, the urine contains Na+ and K+ which is not reabsorbed despite the contracted ECFV. Therefore, urinary Na+ cannot be relied on as an indirect measure of volume status. In contrast, since all Cl~ is reabsorbed in exchange for HCO3~, the urinary Cl~ concentration provides a much more accurate estimate of the volume status in pyloric stenosis. It should be measured when an apparently hypovolaemic patient has what appears to be an inappropriately high urinary Na+ concentration. The urine will not contain Cl~ when the ECFV is contracted and severe metabolic alkalosis is present.

Patients with ECFV contraction and Cl~ and K+ depletion respond to Na+, K+, and Cl~ replacement. A urine Cl~ concentration >20 mEq L~1 suggests volume status has been corrected. Urine Cl~ results are more relevant than serum electrolytes when assessing volume status in infants awaiting a pyloromyotomy.

Management

Diagnosis

It should be possible to diagnose pyloric stenosis by its clinical features alone in 90% of infants. The cardinal symptom is regurgitation and vomiting which usually starts between three and four weeks of age. Characteristically, the vomiting is forceful and projectile, emerging simultaneously from the mouth and nares. Jaundice is an interesting complication which occurs in about eight percent of cases and which seems to be associated with a deficiency of hepatic glucuronyl transferase and caloric deprivation. It resolves rapidly after successful treatment. Leahy et al. reported that 84% of infants with pyloric stenosis had an accurate diagnosis made on clinical examination alone. Visible gastric peristalsis may occur. The confirmatory physical finding is the presence of an olive-sized tumour which may be palpated at the lateral margin of the right rectus abdominus muscle or in the midline of the abdomen. Success in palpating the pyloric tumour varies from 40 to 100% but pride should not prevent the utilisation of an ultrasonographic scan or barium meal if the diagnosis is uncertain. False positive results are rare. However, false negative results may occur with ultrasonography in up to 19% of cases and with contrast studies in ten percent of cases.

The diagnosis of pyloric stenosis in this study was made by history and physical examination alone in 71% of cases (Table I). In two instances, the history, physical, and ultrasound examinations were not conclusive but required a barium meal to provide confirmation of pyloric stenosis. The time from diagnosis (as recorded in the infant’s chart) to the time of surgery was 23 ± 12 hr (range 2–72 hr). A majority of these patients had received some initial fluid resuscitation while differential diagnoses were being considered, consultations sought or investigations performed.

Preoperative medical preparation

Pyloric stenosis is a medical emergency. The surgical repair is considered a minor abdominal procedure but effective preoperative rehydration is imperative. The mortality in pyloric stenosis has been greatly reduced by aggressive therapy. The patient’s acid–base status, fluid deficit, and electrolyte disturbances must be corrected preoperatively. In this series, the electrolyte status was determined on admission and before fluid resuscitation had commenced. Severe imbalances were found in some cases with chloride concentrations in the range of 72–86 mEq L~1, urine chloride, ≈0 mEq L~1, and sodium and potassium concentrations as low as 123 mEq L~1 and 2.8 mEq L~1, respectively. Therefore, replenishment of intravascular volume and correction of electrolyte disturbances are mandatory and should always precede the surgical correction of the obstruction.

In recent years, with earlier diagnosis, we encounter fewer patients who are in a state of severe dehydration, alkalosis and malnutrition. All our infants had electrolyte concentrations within normal limits at the time of surgery. Two patients, however, had their operations delayed because of persistent electrolyte abnormalities.
The typical metabolic disturbance as described above is a hypochloremic metabolic alkalosis with elevated plasma bicarbonate associated with various degrees of dehydration. Blood gas determination and measurement of urine Cl\textsuperscript{−} is the most effective way to assess the severity of the alkalosis and contraction of the ECFV. A base excess >15 is not uncommon. Uncorrected alkalosis may delay recovery from anaesthetic agents and cause post-anaesthetic apnoea. For mild or moderate degrees of dehydration corresponding to 5–15% loss of body weight or a fluid deficit 50–100 ml\cdot kg\textsuperscript{−1} and moderate alkalaeosis (HCO\textsubscript{3}{−} 32–42 mEq\cdot L\textsuperscript{−1}) replacement is achieved preferably with normal saline with half the estimated deficit given over the first six to eight hours.

For severe degrees of dehydration corresponding to a loss in body weight of >15% or a fluid deficit >150 ml\cdot kg\textsuperscript{−1} with severe alkalaeosis (HCO\textsubscript{3}{−} >42 mEq\cdot L\textsuperscript{−1}), fluid resuscitation and correction of the acid–base disorder is achieved initially with 20 ml\cdot kg\textsuperscript{−1} of normal saline. The metabolic alkalosis responds to NaCl therapy even if the K\textsuperscript{+} deficit is not restored. Some patients with large K\textsuperscript{+} deficit (K\textsuperscript{+} < 2.0 mEq\cdot L\textsuperscript{−1}) will not respond to NaCl administration until the K\textsuperscript{+} deficit is replenished. Once urine output is established, K\textsuperscript{+} is added with a maximum replacement of 3 mEq\cdot L\textsuperscript{−1}\cdot day\textsuperscript{−1}.

Once the deficit is corrected, maintenance fluid (2/3, 1/3 or D5W-0.2N saline and potassium supplementation) is given at a rate of 4 ml\cdot kg\textsuperscript{−1}\cdot hr\textsuperscript{−1}. The plasma chloride concentration is used as a clinical guide in the assessment and correction of the biochemical disorder of these infants based on the rationale that when the hypochloremic alkalosis has been corrected, so too the alkalaeemia. The median adult Cl\textsuperscript{−} concentration of 100 mEq\cdot L\textsuperscript{−1} is accepted in clinical practice as a satisfactory concentration at which adequate resuscitation is achieved. In infants, a chloride concentration of 90 mEq\cdot L\textsuperscript{−1} is suggested as normal but it has been found in one series that 38% of infants with a Cl\textsuperscript{−} concentration of 90 mEq\cdot L\textsuperscript{−1} may remain alkalaeamic. It has been proposed recently that plasma chloride is a reliable variable for the assessment and correction of hypochloremic alkalaeemia during resuscitation in infants with pyloric stenosis and recommended that an appropriate target for plasma Cl\textsuperscript{−} concentration be at least 106 mEq\cdot L\textsuperscript{−1}. A plasma Cl\textsuperscript{−} concentration >105 mEq\cdot L\textsuperscript{−1} corresponds to a urine Cl\textsuperscript{−} concentration >20 mEq\cdot L\textsuperscript{−1} and the latter may be used to confirm that ECFV is restored. Once the infant has been properly prepared, surgery should be carried out expeditiously so that the infant may return as soon as possible to his normal environment.

### Anaesthesia

#### Considerations

While it is possible that medical therapy alone can be used to treat this condition in some cases, the most expedient, acceptable and definitive treatment remains the Ramstedt pyloromyotomy. The anaesthetic considerations for pyloromyotomy are:

1. Neonatal anaesthesia (physiological features of the newborn under general anaesthesia, e.g., respiratory and cardiovascular physiology, body temperature homeostasis, monitoring),
2. Restoration of fluid and electrolyte balance,
3. "Full stomach" due to high bowel obstruction (danger of regurgitation and pulmonary aspiration),
4. Adequate surgical muscle relaxation (danger of the duodenal mucosa tear during pyloromyotomy),
5. Postoperative analgesia and related complications.

#### Monitoring

A precordial stethoscope, blood pressure cuff, radial doppler, ECG, and pulse oximeter should be used routinely for induction. Further intraoperative monitoring should include an oxygen analyzer, airway pressure monitor with low pressure disconnect alarm, peripheral nerve stimulator, end-tidal CO\textsubscript{2} (ET\textsubscript{CO\textsubscript{2}}) monitor and temperature probe. The beneficial effect of warm room temperature before incision has been disputed. Studies at this institution have demonstrated that, in a warm or cold environment, there is an initial decrease in body temperature due to an internal redistribution of heat. It accounted for 0.6°C in the first hour of anaesthesia. We were unable to show differences with regard to complications or recovery from anaesthesia between a cold and warm group of patients undergoing abdominal surgical procedures lasting >90 min. There are no differences among tympanic membrane, oesophageal, rectal, and axillary temperatures. Since pyloromyotomy is a short surgical procedure, axillary temperature as monitor of core temperature is very convenient.

#### Pre-induction

It has been suggested that vomiting is usually not a problem in neonates and infants, as the stomach can be completely emptied by aspiration, whereas Unal et al. showed that even after gastric suction there is always a residual gastric volume of 30 to 100 ml. After atropine 20 µg\cdot kg\textsuperscript{−1} iv the gastric tube may be removed with continuous suction. With the infant placed on the right
side and after preoxygenation, a red rubber tube sized 8–12 french should be passed into the stomach to further insure reduction of gastric contents.

Either local or general anaesthesia techniques may be used for pyloromyotomy. However, complications have been reported during pyloromyotomy with local anaesthesia in 12.4% of patients compared with 7.5% with general anaesthesia. Thus, general anaesthesia is usually preferred.

**Induction and intubation**

While the method of tracheal intubation remains controversial (i.e., awake or asleep), the practice of inhalational induction of anaesthesia followed by intubation recommended by Steven et al. in 1973 appears to have been abandoned. The induction technique that will be chosen will depend upon whether an awake intubation or a rapid sequence induction of anaesthesia is planned. The Sellick manoeuvre is recommended. As these infants usually present for operative correction between their third and fifth weeks of life, some degree of mucosal damage may result from an awake intubation. Indeed, if the infant is not sufficiently vigorous, one should question whether fluid resuscitation has been adequate. A chart review of the 55 infants in this series who were intubated asleep failed to reveal any evidence of trauma on intubation, vomiting on induction, aspiration, or failed intubation.

While intubation following a rapid sequence intravenous induction may be accomplished more quickly and less traumatically, the anaesthetist must assess his experience and skills, as well as the infant’s airway, and decide which is the safer method. If the anaesthetist questions his ability to expose the larynx, he can attempt a quick direct laryngoscopy without anaesthesia. If adequate visualization of the larynx is achieved, he can proceed safely with an intravenous induction-intubation technique. If adequate visualization is not achieved, he should obtain more expert assistance or refer the patient to a specialist centre.

If a rapid sequence induction is chosen, with preoxygenation and cricoid pressure, thiopentone 3–5 mg · kg⁻¹ and succinylcholine 2 mg · kg⁻¹ should be given. It is by far the most popular technique (Table II). Ketamine dissociative anaesthesia has been suggested as an alternative to general tracheal anaesthesia. Chatterjee et al. suggested that intubation of neonates even in expert hands can be hazardous and ketamine could obviate this problem especially where expert help is not readily available. However, Bush states: "The only acceptable solution is that if general anaesthesia is deemed to be difficult in a particular circumstance, and where there is no emergency, an experienced anaesthetist should be available or the patient should be transferred to a paediatric facility. The safety of the patient is of paramount importance and it should never be compromised because of inexperience or inappropriate environment."

In the cases under review 44% were intubated awake compared with 32% in an earlier review. Awake intubation has continued to be popular in this institution because it is one of the few opportunities available to teach the technique.

**Maintenance**

The anaesthetic considerations during maintenance of anaesthesia are:

1. Anaesthetic agents,
2. Ventilation,
3. Muscular relaxation,
4. Fluid management,
5. Maintenance of body temperature.

Maintenance of anaesthesia in all but two of the patients in this review was by a mixture of N₂O in oxygen and a volatile agent. Halothane and isoflurane are suitable choices to maintain anaesthesia (Table III).

Intermittent positive pressure ventilation should be used in association with muscle relaxation. The use of muscle relaxation improves the surgical conditions and allows the dose of inhalational agents to be reduced. This not only makes the surgical task easier, but also minimizes the risks of perforation of the duodenal mucosa. The time taken from anaesthetic induction to arrival in the postanaesthetic recovery room was 70 ± 13 min with a range of 45 to 90 min. Atracurium in a dose of 0.3–0.4 mg · kg⁻¹ was used to provide satisfactory muscle relaxation in the majority of the cases. Other relaxants included d-tubocurarine, gallamine, and pancuronium.

Bleeding is not usually a problem. Perioperative iv fluid should consist of five per cent glucose in 0.2 N saline to

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**TABLE II Intubation**

<table>
<thead>
<tr>
<th>Method</th>
<th>Count</th>
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<tbody>
<tr>
<td>Thiopentone/atropine/succinylcholine*</td>
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</tr>
<tr>
<td>Atropine/succinylcholine</td>
<td>1</td>
</tr>
<tr>
<td>Halothane induction</td>
<td>1</td>
</tr>
<tr>
<td>ETT in situ</td>
<td>1</td>
</tr>
<tr>
<td>Awake intubation</td>
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</tr>
<tr>
<td>Total</td>
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</tr>
</tbody>
</table>

*Includes one patient after failed awake intubation.

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**TABLE III Anaesthetic agent used for maintenance**

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<th>Anaesthetic agent</th>
<th>Count</th>
</tr>
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<tbody>
<tr>
<td>Halothane</td>
<td>45</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>47</td>
</tr>
<tr>
<td>Halothane/isoflurane</td>
<td>6</td>
</tr>
<tr>
<td>Narcotic alone</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
</tr>
</tbody>
</table>

N₂O used in all but two cases.
avoid hypoglycaemia. (see postoperative management). If additional fluids are needed to replace lost extracellular fluid a multiple electrolyte solution such as Ringer's lactate is appropriate.

Maintenance of body temperature can be ensured by warming the inspired gases with a heat and moisture exchanger.  

Emergence
The anaesthetic considerations for emergence of anaesthesia are:
1 Elimination of anaesthetic agents,
2 Reversal of neuromuscular blockade,
3 Stomach contents.

At the end of the operation, time must be allowed for the elimination of anaesthetic agents. The tracheal should be extubated after muscle paralysis has been reversed with neostigmine and atropine (50 \( \mu g \cdot kg^{-1} \) and 20 \( \mu g \cdot kg^{-1} \) respectively). It is desirable that the trachea should not be extubated until the infant is fully awake, vigorous, and demonstrates purposeful movements, spontaneous respiration, and an active gag reflex.

Postoperative management
The anaesthetic considerations for the immediate postoperative period are:
1 Oxgenation and respiration,
2 Analgesia,
3 Intravenous fluid management,
4 Hypoglycaemia,
5 Vomiting.

All infants should receive supplemental oxygen and be placed on an apnoea monitor for at least two hours in the postanaesthetic recovery room.

The use of opiates in infants is controversial. Opiate analgesics are best avoided because infants <46 wk gestational age (full term plus 6 wk) exhibit an increased sensitivity to these drugs and there is a risk of postoperative apnoea. In our series, two infants received fentanyl 1 \( \mu g \cdot kg^{-1} \cdot iv \) post-induction. Despite this small dose in these full-term infants, both demonstrated abnormal respiratory patterns after surgery. As respiratory depression in the postoperative period has been described, the use of opiates in these infants is not recommended. Postoperative analgesia was most commonly provided by rectal acetaminophen (10 mg · kg\(^{-1}\)).

The technique of wound infiltration with bupivacaine is an effective alternative frequency forgotten. The only analgesic required by a large majority of infants is infiltration at the completion of surgery with 0.25% bupivacaine 0.25 to 0.50 mg · kg\(^{-1}\). Intravenous fluid administration should continue at the maintenance rate with five per cent glucose in 0.2 N saline until oral feeding is established. Previously, feeding was attempted 2–4 hr after surgery but this was often associated with vomiting due to depression of gastric motility for 12–18 hr postoperatively. Minor degrees of transient postoperative vomiting are common. More persistent vomiting is unusual and most often due to associated gastroesophageal reflux, which occurs in 10–13% of patients.

Potential fatalities can occur during recovery. Hypoglycaemia is always a serious hazard and is due to hepatic glycogen depletion. The first signs of hypoglycaemia are lethargy and irritability progressing to convulsions and cardiac arrest.

Morbidity and mortality
Although the morbidity of pyloric stenosis is likely to remain small but important, the mortality of this condition has been reduced considerably. The availability of skilled paediatric anaesthetists and the use of general anaesthesia has been of benefit to both surgeon and patient by enhancing the safety of the procedure. The operative mortality of ten per cent has declined steadily to <0.5%.

Recommendations
The essential concerns of the anaesthetist managing the infant with pyloric stenosis include:

1 Adequate fluid resuscitation before surgery. This should be confirmed by clinical examination with evidence of good urine output, and may be supported with the measurement of urinary chloride >20 mEq · L\(^{-1}\).

2 Correction of acid–base and electrolyte abnormalities. It is unsafe to operate with an uncorrected alkalosis because of delayed recovery from anaesthetic agents and the danger of post-anaesthetic apnoea occurring in alkalaeic infants.

3 Maintain normothermia intraoperatively.

4 Prevent gastric aspiration. Measures include maintaining the infant in a fasting state preoperatively with nasogastric suction, passing a red rubber catheter for gastric suction prior to induction, establishing general tracheal anaesthesia (either with an awake intubation or following a preoxygenation, rapid sequence intravenous intubation technique), and extubating the trachea with the infant awake on his side.

5 Inhibition of vagal reflexes. Atropine (20 \( \mu g \cdot kg^{-1} \)) is given prior to any airway or gastric manipulation.

6 Adequate muscle relaxation with intermittent positive pressure ventilation during the surgical division of the hypertrophied pylorus. The effects of the non-depolarizing muscle relaxants must be reversed before extubation.
7 Risks of parenteral narcotics. Rectal acetaminophen for postoperative analgesia or wound infiltration with 0.25% bupivacaine 0.25 to 0.50 ml·kg⁻¹ are recommended alternatives.

Acknowledgements
The authors would like to thank Drs. Bernard Braude, Lawrence Roy and John E.S. Relton for their advice in the preparation of the manuscript.

References


Self-assessment Questionnaire

EACH OF THE QUESTIONS BELOW IS FOLLOWED BY FIVE SUGGESTED ANSWERS OR COMPLETIONS. SELECT THE ONE THAT IS BEST IN EACH CASE.

1 In infants, hypokalaemic alkalosis may
A shift the oxygen dissociation curve to the right,
B occur in the presence of pyloric stenosis,
C is usually well compensated by respiratory acidos,
D occurs because the kidney excretes K⁺ in order to maintain normal Cl⁻ levels,
E always require therapy with dilute solutions of HCL.

2 The cardinal symptom of pyloric stenosis is
A the "olive-sized" tumour felt around the lateral margin of the right rectus abdominus,
B jaundice associated with failure to thrive,
C projectile vomiting which usually starts between six and eight wks of age,
D dehydration,
E none of the above.

3 Patients with pyloric stenosis usually have
A normal ECFV,
B normal urinary sodium,
C contracted ECFV with normal urinary Na⁺ concentration,
D urinary chloride >20 mEq·L⁻¹,
E normal serum K⁺ concentration.

4 Which of the following is not correct concerning anaesthesia for pyloric stenosis?
A spontaneous ventilation and light anaesthesia should not be used during pyloromyotomy,
B duodenal mucosa tear is the most common surgical complication,
C ketamine anaesthesia should be used when the anaesthetist considers that he would not be able to manage the infant's airway,
D when the infant FCFV has been completely replenished, an intravenous catheter is not necessary,
E when the infant has been corrected medically the surgery should be done in an expeditious manner to limit the separation time from the mother.

5 Which of the following statements regarding the jaundice associated with pyloric stenosis is true?
A it is caused by a high caloric intake but a deficiency in hepatic glucoronyl transferase,
B it is a contraindication to the use of halothane anaesthesia,
C it is observed in 30% of pyloric stenosis infants,
D it resolves spontaneously after successful surgical treatment,
E pyloromyotomy should be delayed until jaundice has been corrected medically.

6 Frequently associated with congenital hypertrophic pyloric stenosis
A vomiting starting usually in second or third week of life,
2 more common in female,
3 gastric peristaltic waves are visible,
4 hyperglycaemia is a common sign.

7 Potassium losses are increased in the presence of
1 nasogastric suction,
2 large renal excretion of $\text{HCO}_3^-$,
3 hyperventilation,
4 acidosis.

8 The adverse effects of metabolic alkalosis in infants are
1 increase in pH results in shifting of the oxygen
dissociation curve to the left, binding more $\text{O}_2$ to the
Hb and unloading less oxygen at the tissue level,
2 associated with high level of fetal Hb, the $P_{50}$ is
largely displaced to the right,
3 increased potential for postoperative delay in
recovery and respiratory depression with apnoea,
4 if uncorrected increase in blood potassium concen-
tration.

9 Which of the following features are to be considered
during post-anaesthesia recovery?
1 reinstitution as soon as possible of oral feeding,
2 incidence of vomiting remains elevated,
3 opiate agents should be used carefully to control
pain postoperatively,
4 hypoglycaemia could be fatal.
Physiology of the fetal circulation

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Summary Our understanding of fetal circulatory physiology is based on experimental animal data, and this continues to be an important source of new insight into developmental mechanisms. A growing number of human studies have investigated the human physiology, with results that are similar but not identical to those from animal studies. It is time to appreciate these differences and base more of our clinical approach on human physiology. Accordingly, the present review focuses on distributional patterns and adaptational mechanisms that were mainly discovered by human studies. These include cardiac output, pulmonary and placental circulation, fetal brain and liver, venous return to the heart, and the fetal shunts (ductus venosus, foramen ovale and ductus arteriosus). Placental compromise induces a set of adaptational and compensational mechanisms reflecting the plasticity of the developing circulation, with both short- and long-term implications. Some of these aspects have become part of the clinical physiology of today with consequences for surveillance and treatment.

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Introduction

Many of the mechanisms described in animal experiments also occur in the human fetus, but with differences. The reasons for variation are many, e.g. a sheep fetus has a different anatomy compared with a human fetus, with a longer intrathoracic inferior vena cava (IVC), a smaller brain, the fetal liver is positioned differently, two umbilical veins, a higher temperature, a lower Haemoglobin (Hgb), a higher growth rate and a shorter pregnancy. Ultrasound in obstetrics has been used increasingly to provide physiological data from human fetuses, and this is reflected in the present review.

Blood volume

The blood volume in the human fetus is estimated to be 10–12% of the body weight, compared with 7–8%
in adults. The main reason for this difference is the large pool of blood contained within the placenta; a volume that reduces as gestation progresses. The calculated blood volume of 90–105 ml/kg in fetuses undergoing blood transfusion during the second half of pregnancy is probably an underestimate. Other studies have indicated a volume of 110–115 ml/kg, which is more in line with experimental sheep studies. The estimated volume of 80 ml/kg contained within the fetal body is marginally more than that in adults. Compared with adults, the fetus is capable of much faster regulation and restoration of the blood volume due to high diffusion rates between fetal compartments.

Arterial and venous blood pressure

The mean arterial pressure in human fetuses was measured to be 15 mmHg during cordocentesis at gestational weeks 19–21. Intra-uterine recording of the intraventricular pressure in the human fetus suggests that the systemic systolic pressure increases from 15–20 mmHg at 16 weeks to 30–40 mmHg at 28 weeks. There was no obvious difference between the left and right ventricles. This increase was also seen for diastolic pressure, which was ≤5 mmHg at 16–18 weeks and 5–15 mmHg at 19–26 weeks.

Umbilical venous pressure, recorded during cordocentesis and corrected for amniotic pressure, increased from 4.5 mmHg at 18 weeks to 6 mmHg at term.

Cardiac output and distribution

The fetal systemic circulation is fed from the left and right ventricles in parallel. The left ventricle is predominantly dedicated to the coronary circulation and upper body, while the right ventricle is the main distributor to the lower part of the body, the placenta and the lungs. When using outer-inner diameter measurements of the vessels, the combined cardiac output (CCO) is reported to be 210 ml/min at mid-gestation and 1900 ml/min at 38 weeks (Table 1). When using inner diameters, these numbers are lower.

The two ventricles pump in parallel (Fig. 1) and the pressure difference between them is minimal compared with postnatal life. However, experimental studies show some variation in pressure and velocity waves between the two sides, ascribed to the difference in compliance of the great arteries and downstream impedance (upper body vs lower body and placenta). Some of the ‘stiffness’ of the fetal myocardium is attributed to the constraint of the pericardium, lungs and chest wall, all of which have low compliance before air is introduced. However, with the shunts in operation and a metabolism capable of extracting oxygen at low saturation levels, the fetal heart appears to be a very flexible, responsive and adaptive structure.

Cardiac performance

Structural details of the heart are organized during the embryonic period but are dependent on the physical environment, including blood flow, in order to develop normally. The myocardium grows by cell division until birth, and growth beyond birth is due to cell enlargement. The density of myofibrils increases particularly in early pregnancy and the contractility continues to improve during the second half of pregnancy. The two ventricles perform differently in pressure/volume curves and when tested with intact peripheral vasculature. The fetal heart has limited capacity to increase stroke volume by increasing diastolic filling pressure, the right ventricle even less than the left, as they are already operating at the top of their function curves. The Frank–Starling mechanism does operate in the fetal heart, which is apparent during arrhythmias. Adrenergic drive also shifts the function curve to increase stroke volume. However, increased heart rate may be the single most prominent means of increasing cardiac output in the fetus.

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and cerebral circuits. Conversely, a via dextra directs de-oxygenated blood from the caval veins through the tricuspid valve, pulmonary trunk and ductus arteriosus to reach the descending aorta, largely bypassing the pulmonary circuit.

Oxygen saturation gives a picture of distribution and blending of flows in the central fetal circulation (Fig. 1). The lowest saturation is found in the abdominal IVC, and the highest saturation is found in the umbilical vein. Interestingly, the difference between the left and right ventricles is only 10%, and this increases to 12% during hypoxaemia. The small difference between the left and right ventricles is due to the abundant volume of oxygenated blood presented to the foramen ovale. In addition to the ductus venosus blood flow, the umbilical blood passing through the liver has had a modest reduction in saturation and represents another sizeable volume of oxygenated blood flowing in much the same direction as the ductus

![Diagram of fetal heart pathways](image-url)
venosus towards the foramen ovale. In addition to some blending, the abundance of oxygenated blood will cause a spillover to the right side when reaching the foramen ovale with its crista dividens (limbus) (Fig. 2).

### Ductus venosus and liver circulation

In the human fetus, the ductus venosus is a slender trumpet-like shunt connecting the intra-abdominal umbilical vein to the IVC at its inlet to the heart. The inlet of the ductus venosus, the isthmus, is the restrictive area with a mean diameter of 0.5 mm at mid-gestation and hardly exceeds 2 mm for the rest of a normal pregnancy. The umbilical venous pressure ranges from 2 to 9 mmHg (the portocaval pressure gradient), and causes the blood to accelerate from a mean of 10-22 cm/s in the umbilical vein to 60-85 cm/s as it enters the ductus venosus and flows towards the IVC and foramen ovale. The blood flow with the highest oxygenation, coming from the ductus venosus, also has the highest kinetic energy in the IVC and predominantly presses open the foramen ovale valve to enter the left atrium, i.e. the 'preferential streaming' described in animal studies.

While 30% of the umbilical blood is shunted through the ductus venosus at mid-gestation, this fraction is reduced to 20% at 30 weeks and remains so for the rest of the pregnancy, but with wide variations (Fig. 3). These results are similar to those of another study but are at variance with experimental animal studies, admittedly using a different technique, which showed that approximately 50% was shunted through the ductus venosus. The redistributional mechanisms of increased shunting during hypoxaemia described in animal experiments also seem to operate in the human fetus.

<table>
<thead>
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<th>% of combined cardiac output at gestational age</th>
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<tbody>
<tr>
<td>20 weeks</td>
</tr>
<tr>
<td>Combined cardiac output</td>
</tr>
<tr>
<td>Left ventricle</td>
</tr>
<tr>
<td>Right ventricle</td>
</tr>
<tr>
<td>Foramen ovale</td>
</tr>
<tr>
<td>Lungs</td>
</tr>
<tr>
<td>Ductus arteriosus</td>
</tr>
</tbody>
</table>

**Table 1** Combined cardiac output and distribution in human fetuses during the second half of pregnancy according to Rasanen et al. The foramen ovale acts as a flow distributor of the inferior venous inlet. (a) Ultrasound scan shows the inferior vena cava (IVC) and left and right atria (LA, RA). The atrial septum (AS) with its crista dividens (postnatal: limbus) faces the inlet of the IVC to divide the ascending column of blood. The terminal portion of the IVC expands, more to the left side, to receive blood from the liver and ductus venosus (DV). The high velocity, its position to the left and steep direction makes the DV blood preferentially press open the foramen ovale valve (FOV) to enter the LA. IVC blood directed more anteriorly arrives predominantly in the RA. Increased pressure in LA or a premature apposition of FOV to the AS would divert more blood to the right. Reproduced with permission from ref. 36

The ductus venosus is under tonic adrenergic control, and distends under the influence of nitric oxide and prostaglandins. The most extensive dilatation is seen during hypoxaemia, leading to
a 60% increase of the diameter in fetal sheep. However, the changes in diameter are not restricted to the isthmus but also include the entire length of the vessel, which has a far greater impact on resistance. The shunt obliterates within 1–3 weeks of birth in term infants, although this takes longer in premature births and in cases with persistent pulmonary hypertension or cardiac malformation. In contrast to the ductus arteriosus where increased oxygen tension triggers the closure, no trigger has been found for the ductus venosus.

Equally important to the active regulatory mechanism is the passive regulation based on fluid dynamics, i.e. viscosity and pressure. Blood velocity in the ductus venosus is high and has Newtonian properties with low viscosity (similar to water). In contrast, liver tissue represents a huge capillary cross-section with a low blood velocity. At low velocities, the blood is non-Newtonian with an accordingly high viscosity (and resistance) and a closing pressure of 1–4 mmHg. It follows that an increase in haematocrit leads to increased viscous resistance in the low-velocity venous liver flow and has little effect on the high-velocity flow in the ductus venosus. Thus, the change in haematocrit alone leads to a shift of umbilical venous flow from the liver to the ductus venosus.

Along the same lines, variation in the umbilical venous pressure affects the two pathways differently. A reduction in venous pressure reduces liver perfusion more than ductus venosus flow, as a further reduction in an already low velocity in the large cross-section of the portal vasculature implies a considerable increase in viscous resistance. The result is a higher degree of shunting.

In addition to these fluid dynamic determinants, the neural and endocrine regulation of the hepatic vascular bed also play a role. The portal vasculature shows a more pronounced constricting response to adrenergic stimulation compared with the ductus venosus. It all combines to make a distribution system that is extremely sensitive to both active and passive regulation, which is in line with the substantial normal variation of shunting seen in human fetuses.

The physiological role of the ductus venosus is not well understood. The shunting seems more prominent in early pregnancy than after 30 weeks of gestation. The low degree of shunting through the ductus venosus during the last 8–10 weeks of pregnancy implies that approximately 80% of the umbilical blood perfuses the liver, signifying a very high developmental priority of the umbilical liver perfusion compared with the ductus venosus.

However, during hypoxic challenges, the priority seems to be different. Fetuses maintain a higher degree of ductus venosus shunting, probably as a redistributational adaptation to hypoxic pressure, ensuring oxygenation of the heart and brain. The cost for responding to such needs could be permanently altered liver development.

It should be borne in mind that oxygen extraction in the liver is rather modest (10–15% reduction in oxygen saturation), which means that blood coming from the median and left hepatic vein are important contributors of oxygenated blood. Actually, the position and direction of the left hepatic venous blood under the Eustachian valve (IVC valve) favour this blood to be delivered at the foramen ovale.

Although agenesis of the ductus venosus has been linked to abnormalities and fetal demise, agenesis is also found in fetuses that have exhibited normal growth. Experimental obliteration of the vessel seems to have little haemodynamic effect, but causes an increase in insulin-like growth factor 2 and increases the growth of fetal organs. Recent studies have indicated that the fetal umbilical flow to the liver towards the end of pregnancy is influenced by the maternal nutritional state and diet. Umbilical venous flow constitutes 75% of the venous supply to the liver, with the remaining 25% coming from the main portal.
stem.\textsuperscript{41} In human fetuses, the arterial supply to the liver is not known but it seems to have a more prominent role during compromise.\textsuperscript{42}

Doppler examination of the ductus venosus is increasingly used to identify hypoxaemia, acidosis, cardiac decompensation and placental compromise, and is a promising tool for timing the delivery of critically ill fetuses.\textsuperscript{43,44} Increased pulsatility, mainly caused by the augmented atrial contraction wave, signifies increased atrial contraction due to adrenergic drive, or increased venous filling pressure, or both.

In early pregnancy, the augmented a-wave in the ductus venosus is associated with an increased risk of chromosomal aberration and has been suggested as a secondary screening test.\textsuperscript{45,46}

Foramen ovale

A defect in the atrial septum is commonly associated with left-right or right-left shunting in postnatal life. It is conceivable that this concept is carried over to describe the function of the foramen ovale in the fetus,\textsuperscript{47} but this is not a fair representation of the actual haemodynamics. Rather, the inferior venous inlet to the heart should be viewed as a column of blood that ascends between the two atria from below.\textsuperscript{36,48}

This column hits the interatrial ridge, the crista dividens, and is divided into a left and right arm (Fig. 2). The left arm fills the ‘windsock’, formed between the foramen ovale valve and the atrial septum, to enter the left atrium. The right arm is directed towards the tricuspid valve and joins the flow from the superior vena cava and coronary sinus to form the via dextra.

This is an equilibrium easily influenced by changes in pressure on the two sides. Increased resistance and pressure of the left side is instantaneously reflected in increased diversion of blood to the right side. In contrast to the hypertrophy of the left ventricle seen in aortic stenosis in adults, fetal stenosis commonly leads to a shift of blood volume from left to right at the level of the foramen ovale, with corresponding development of left-sided hypoplasia and compensatory growth of the right ventricle.

The developing ventricle responds to the demands of the afterload and is stimulated by the blood volume of the preload. However, for the left side of the heart, the foramen ovale is an important limiting factor, particularly in cases of a maldeveloped foramen or a premature closure.\textsuperscript{49}

Under physiological conditions, it is not the oval-shaped hole of the septum that constitutes the restricting area for the flow to the left atrium, but the horizontal area between the foramen ovale valve and the atrial septum above the foramen ovale.\textsuperscript{50} Interestingly, the growth of this area is somehow blunted after 28–30 weeks of gestation compared with the cross-section of the IVC. This effect coincides with changes in fetal lung perfusion\textsuperscript{12} and ductus venosus shunting,\textsuperscript{16} and may signify a transition into a more mature circulatory physiology.

Ductus arteriosus and pulmonary circulation

The ductus arteriosus constitutes a wide muscular vessel connecting the pulmonary arterial trunk to the descending aorta (Fig. 4).\textsuperscript{51} During the second trimester, the velocity in the ductus arteriosus increases more than that in the pulmonary trunk, reflecting the development of the wind-kessel function of the pulmonary trunk.\textsuperscript{52} During the

Figure 4  (a) The ductus arteriosus (arrow) is a sizeable connection between the pulmonary trunk (PA) and the aorta (AO) in fetal rats. (b) Indomethacin induces severe constriction. Reproduced with permission from ref.\textsuperscript{51}
second half of pregnancy, 40% or less of the CCO is directed through the ductus arteriosus.\textsuperscript{12,13} (Table 1). The lungs receive 13% of the CCO at mid-gestation and 20–25% after 30 weeks,\textsuperscript{12} which is more than that reported in fetal sheep experiments\textsuperscript{10} and a more recent human study.\textsuperscript{13} Normally, the shunt closes 2 days after birth,\textsuperscript{53} but a patent duct is a common clinical problem. An increase in oxygen tension is regarded as the main trigger for its closure.\textsuperscript{24} The vessel is under the general influence of circulating substances, particularly prostaglandin E\textsubscript{2}, which is crucial in maintaining patency.\textsuperscript{54} Sensitivity to prostaglandin antagonists is at its highest in the third trimester and is enhanced by glucocorticoids and fetal stress.\textsuperscript{55} Nitric oxide has a relaxing effect prior to the third trimester. The increased reactivity of the ductus arteriosus in the third trimester makes it vulnerable to prostaglandin synthase inhibitors, such as indomethacin, which may cause severe and longlasting constriction.\textsuperscript{55,56}

The ductus arteriosus bypasses the pulmonary circuit, but the distribution between these two pathways depends heavily on the impedance of the pulmonary vasculature, which is under the control of prostaglandin I\textsubscript{2} and modified by a series of substances.\textsuperscript{24} In an elegant study, Rasanen et al. showed how reactivity in the pulmonary vascular bed increased in the third trimester.\textsuperscript{14} While fetuses at gestational age 20–26 weeks showed no changes during maternal hyperoxegenation, fetuses at 31–36 weeks had lower impedance in the pulmonary arteries assessed by the pulsatility index, and increased pulmonary blood flow. Correspondingly, the blood flow in the ductus arteriosus was reduced.

### Brain circulation

Differences in circulation physiology between animal experiments and human fetuses are likely to be greatest when concerning the brain, as the human brain is relatively larger than in other species. In a study of human previable fetuses weighing 12–272 g (probably corresponding to 10–20 weeks of gestation), it was found that the brain received approximately 15% of the systemic venous return (equal to the CCO less the pulmonary circuit).\textsuperscript{33} The proportion directed to the brain increased with low arterial pH, increased pCO\textsubscript{2} and reduced placental perfusion. A study of the primate Macaca mulatta at an advanced stage of gestation found that 16% of the CCO was distributed to the brain, and this fraction increased to 31% during hypoxic challenge.\textsuperscript{21} Both of these studies reflect redistributional preferences to the brain during hypoxaemia and acidosis. Clinical obstetrics has taken advantage of such 'brain-sparing' mechanisms, and uses the increased diastolic blood velocity recorded in the middle cerebral artery as a marker of compensatory redistribution of blood to the brain.\textsuperscript{57}

### Fetoplacental circulation

In the fetal sheep, 45% of the CCO is directed to the umbilical arteries and placenta.\textsuperscript{58} This percentage is less in exteriorized human fetuses, but it increases from 17% at 10 weeks to 33% at 20 weeks of gestation.\textsuperscript{33} These results overestimate the placental fraction as the CCO calculation was based on systemic venous return, not including the pulmonary venous return. Secondly, the measurements were not performed under strict physiological conditions. Doppler studies of low-risk pregnancies have found similar results; one-third of the fetal CCO is directed to the placenta at 20–32 weeks of gestation,\textsuperscript{59,60} but this decreases to approximately one-fifth beyond 32 weeks of gestation.\textsuperscript{60}

The introduction of Doppler ultrasound made it possible to assess umbilical venous blood flow\textsuperscript{61} in the human fetus in utero. Recent longitudinal observations in low-risk pregnancies have found that the umbilical blood flow increases from a mean of 36 ml/min at 20 weeks to 265 ml/min at 40 weeks of gestation.\textsuperscript{62} Umbilical flow normalized for fetal weight is at its highest (117 ml/min/kg) at 25 weeks and at its lowest at 41 weeks (63 ml/min/kg) of gestation. These results are in accordance with earlier studies applying thermodilution at birth.\textsuperscript{63} The fact that human umbilical flow is considerably lower than that in the fetal sheep is not disconcerting as fetal sheep have a higher growth rate, a higher temperature and a lower Hgb.

Resistance to flow is mainly determined by the peripheral vascular bed of the placenta. This vasculature has no neural regulation and catecholamines have little effect on the vasculature. Endothelin and prostanoid have a constricting effect\textsuperscript{64} and nitric oxide has a vasodilatory effect,\textsuperscript{65} but the exact role of humoral regulation is not fully understood.\textsuperscript{66} Placental blood flow has been found to be fairly stable and chiefly determined by arterial blood pressure.\textsuperscript{10} The substantial increase in the vascular cross-section during late gestation accounts for a reduction in impedance and the corresponding fall in umbilical artery pulsatility seen in longitudinal studies.\textsuperscript{67} Placental vasculature is believed to account for 55% of the umbilical
Watershed areas and the compromised circulation

The watershed area in the brain circulation has long been used to explain certain lesions of neonates, and a concept of a watershed at the isthmus of the aorta, the left portal vein and the foramen ovale with its crista dividens has been proposed recently.

It has long been known that fetuses with critical aorta stenosis or hypoplastic left heart syndrome direct ductus arteriosus blood in a retrograde direction through the isthmus aortae to feed the aortic arch. Recent studies have highlighted the isthmus aortae as a watershed between the aortic arch and the ductus arteriosus in anatomically normal fetuses. Since this watershed also reflects the difference in impedance between the cerebral circuit and that of the placenta and lower fetal body, the blood velocity pattern across the isthmus with various degrees of reversed flow was suggested to be an indicator of placental compromise.

Similarly, the direction of flow in the left portal vein (Fig. 1) is suggested to reflect compromised venous return demanding a compensatory increase of blood from the main portal stem to maintain portal and umbilical pressure, with the result being a cessation of umbilical venous flow to the left portal branch, and, at a more advanced stage of compromise, reversed flow that permits splanchnic blood to enter the ductus venosus.

A third watershed, the foramen ovale (Fig. 2), differs from the two former watersheds. It distributes blood to the left and right atria by dividing the ascending venous blood into two arms at the crista dividens. The horizontal area between the foramen ovale valve and the atrial septum is thought to be the restricting area for flow to the left atrium. In cases with increased venous return (e.g. arteriovenous malformation), an increased volume of blood is diverted to the right side, leading to increased growth of the right ventricle. In cases of abnormally small foramen ovale, the left side of the heart develops less in size (one of the possible mechanisms leading to hypoplastic left heart syndrome).

These concepts are in need of detailed studies to make them clinically relevant.

Circulatory regulation

Circulatory responses to hypoxaemia and hypovolaemia have been particularly well studied in animals during the last trimester of pregnancy, but even during mid-gestation and earlier, there seem to be neural and endocrine responses in addition to the prominent direct effect on cardiac function caused by hypoxic insults. A hypoxic insult in late pregnancy activates a chemoreflex mediated by the carotid bodies (and, to a lesser extent, the aortic bodies), causing an immediate vagal effect with reduced heart rate and a sympathetic vasoconstriction. This is followed by endocrine responses (e.g. adrenaline and noradrenaline) maintaining vasoconstriction (α-adrenergic), increasing heart rate (β-adrenergic) and reducing blood volume with renin release and increased angiotensin II concentration. The responses involve angiotensin—vasopressin mechanisms, and increased concentrations of adrenocorticotropic hormone, cortisol, atrial natriuretic peptide, neuropeptide Y and adrenomedullin orchestrate a circulatory redistributional pattern that maintains placental circulation and gives priority to the adrenal glands, myocardium and brain (Fig. 5). In clinical medicine, this translates into a frequently visualized coronary circulation, a shift in left—right ventricular distribution, a cerebral circulation with high diastolic flow, and an increased impedance in the pulmonary circulation during circulatory compromise.

Sustained hypoxia forces an adaptational shift to less oxygen demand, reduced DNA synthesis...
and growth, with a gradual return towards normal concentrations of blood gases and endocrine status, although with a residual deviation that may have a longlasting effect on fetal and newborn life. There is an increasing awareness that even subtle differences in the development of autocrine, paracrine, endocrine and metabolic functions induced by nutritional or circulatory variations during pregnancy could have lasting effects with increased risks of cardiovascular and endocrine diseases in adult life.

Practice points

- Which of the two ventricles takes a larger volume load?
- From where comes the blood in the left atrium?
- How much of the umbilical venous return is shunted through the ductus venosus in the human fetus?
- In what sense is the aortic isthmus a watershed?

Research directions

- More information on human fetal circulation is expected to substitute animal experimental studies as the basis for clinical medicine.
- More detailed adaptational pattern is expected to give a better background for fetal surveillance.
- More detailed knowledge of human fetal responses and adaptation is expected to unveil the mechanisms involved in in utero conditioning of health risk in adult life.

References


